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(54) METHODS OF TREATING BRAIN INJURY

(71) Applicant: ASTELLAS INSTITUTE FOR
REGENERATIVE MEDICINE,
Westborough, MA (US)(72) Inventors: Erin KIMBREL, Westborough, MA
(US); Cesario BORLONGAN,
Westborough, MA (US); Daniel Paul
POZNIAK, Westborough, MA (US)

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(52) U.S. Cl.

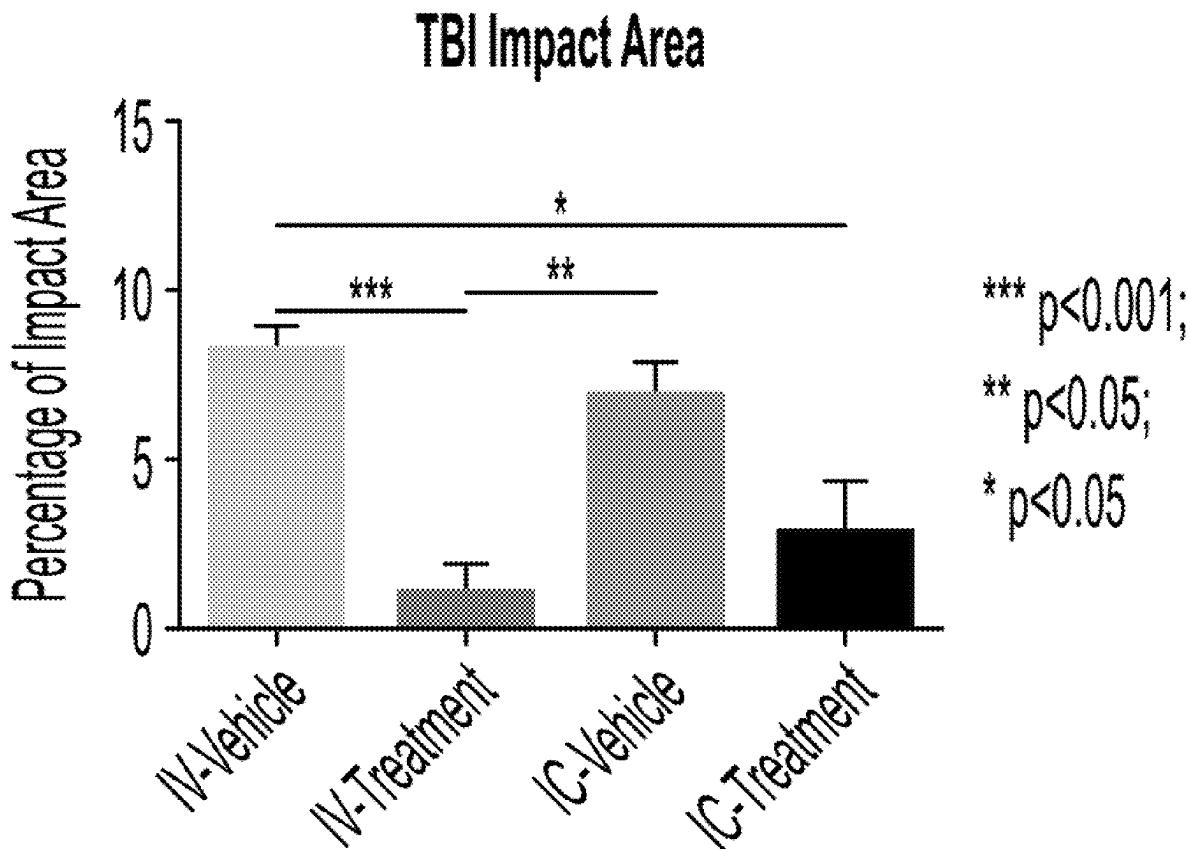
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(2013.01); *A61K 35/15* (2013.01); *A61P 25/00*
(2018.01); *C12N 5/0606* (2013.01); *G01N*
33/4833 (2013.01); *G01N 33/5005* (2013.01)

ABSTRACT

The present invention generally relates to compositions and methods useful for treating a brain injury such as stroke, optic neuropathy, traumatic brain injury, and cerebral palsy. The methods include administering HMCs obtained by in vitro differentiation of pluripotent stem cells and/or extracellular vesicles (EVs) derived from such HMCs (HMC-EVs) into a subject.

Related U.S. Application Data

(60) Provisional application No. 63/390,044, filed on Jul. 18, 2022.



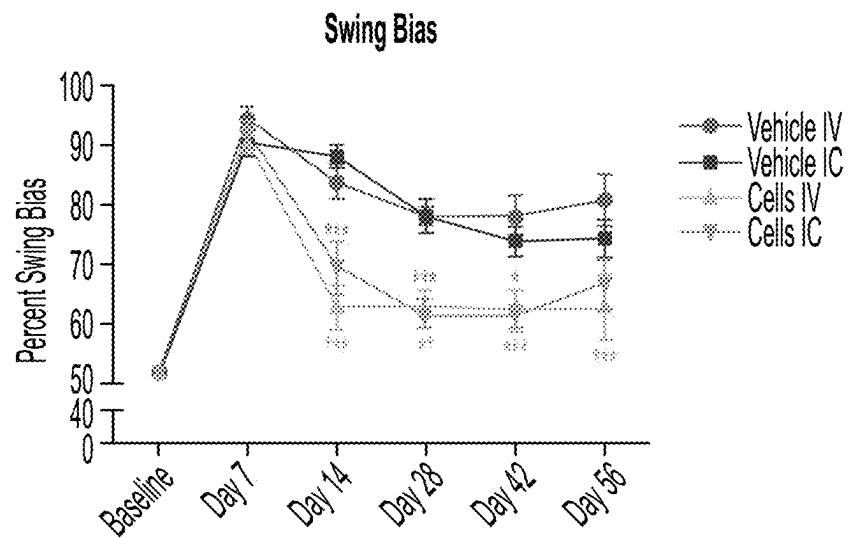


FIG. 1

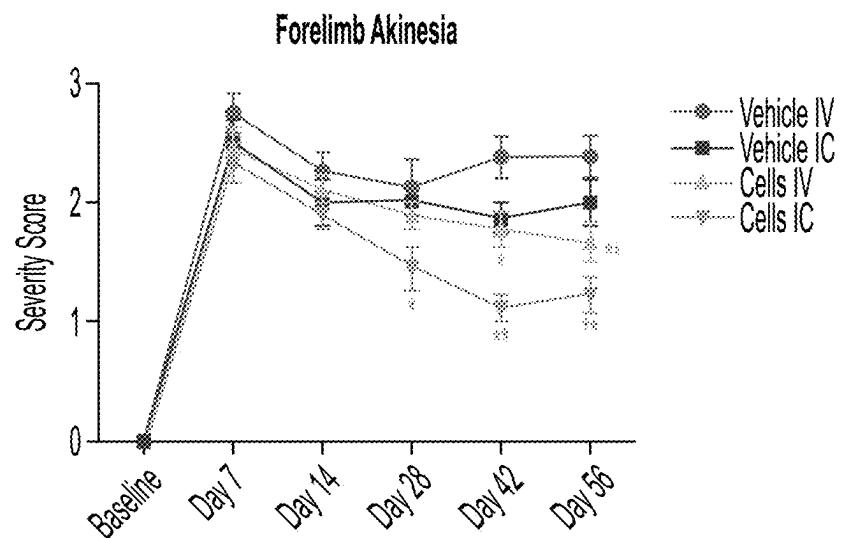


FIG. 2

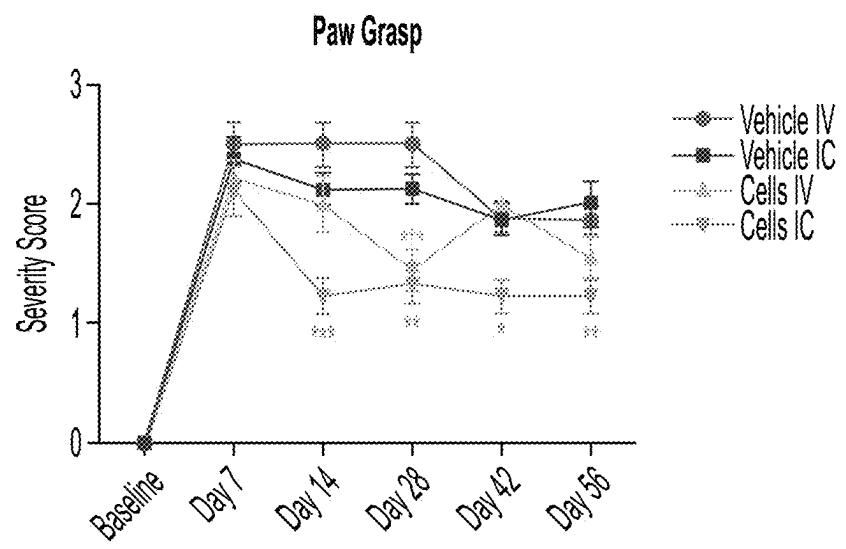


FIG. 3

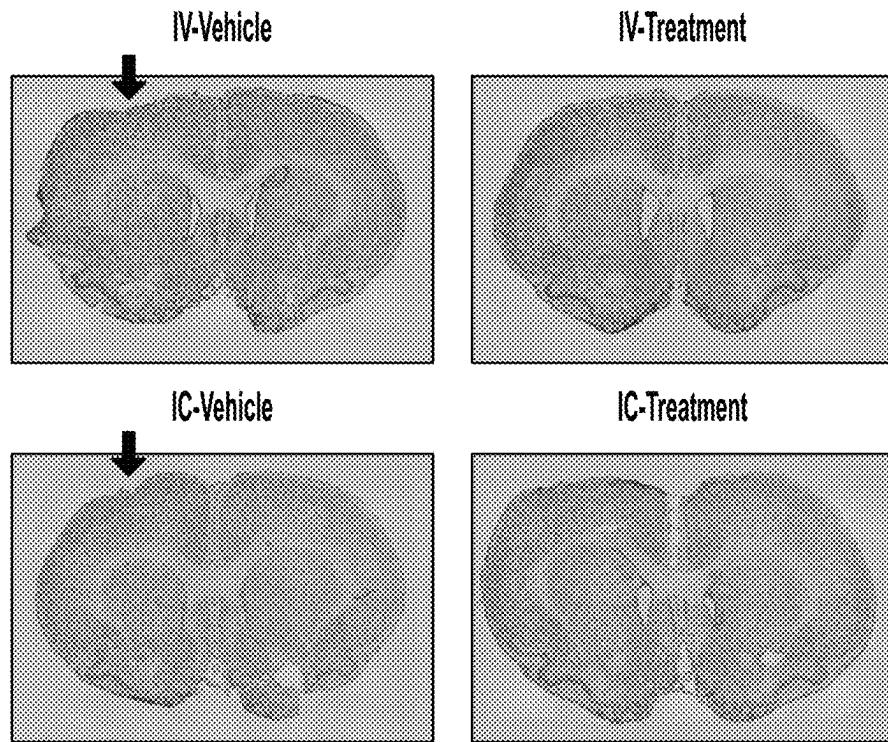


FIG. 4A

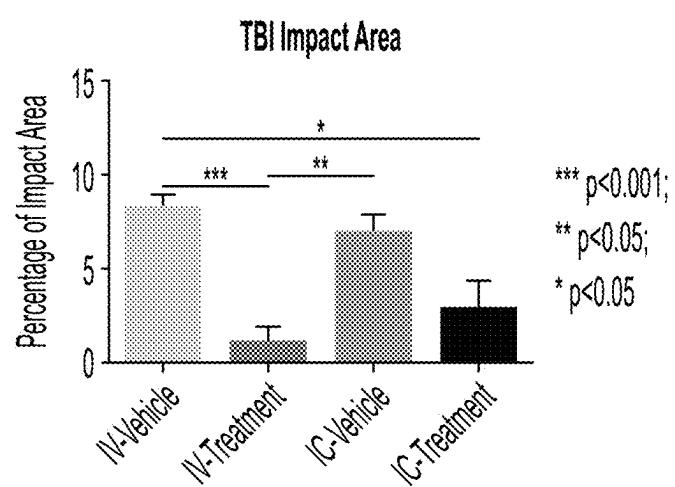


FIG. 4B

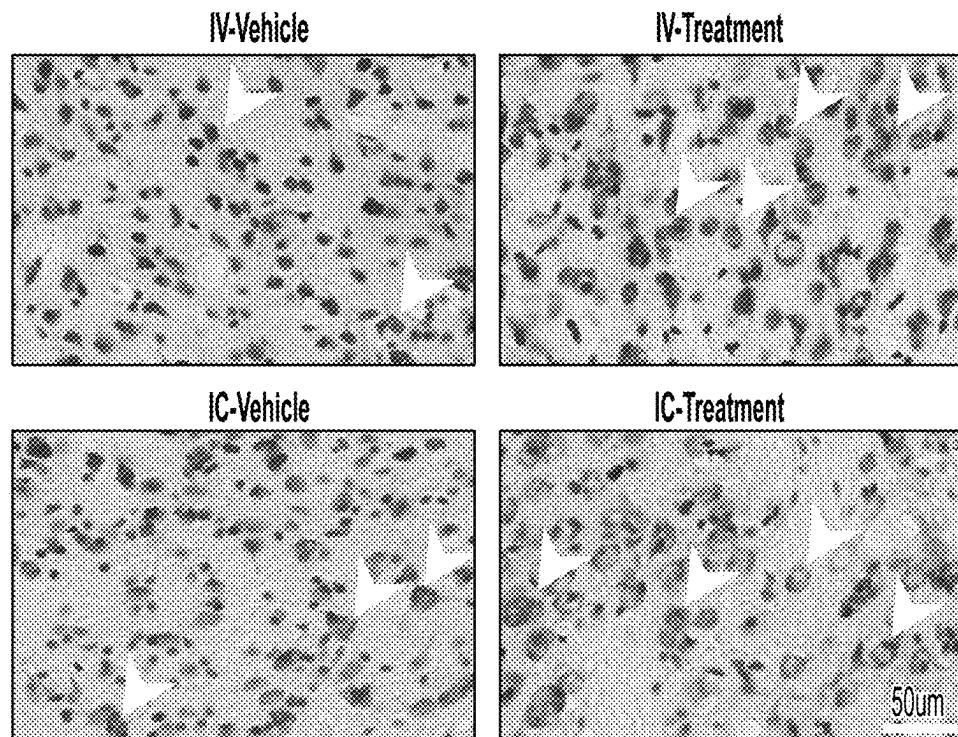


FIG. 5A

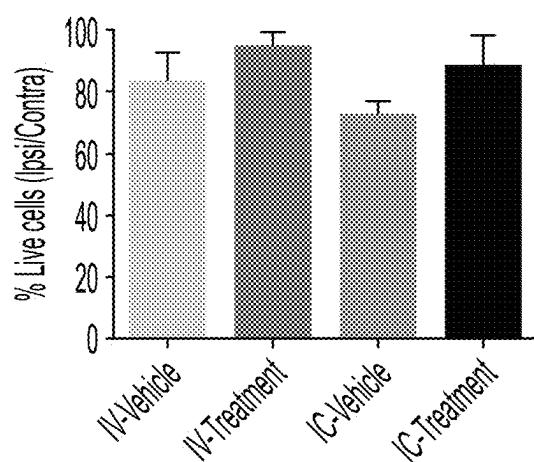


FIG. 5B

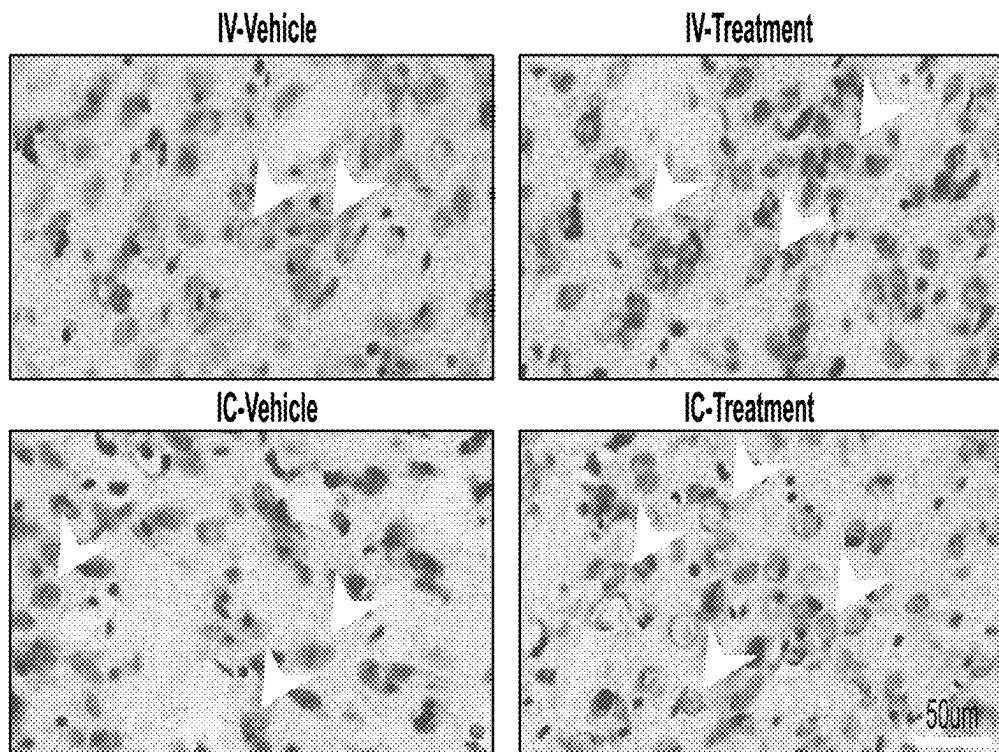


FIG. 5C

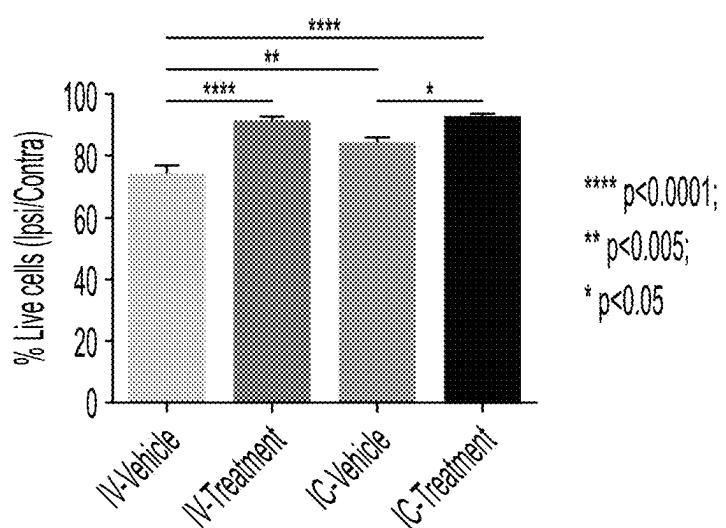


FIG. 5D

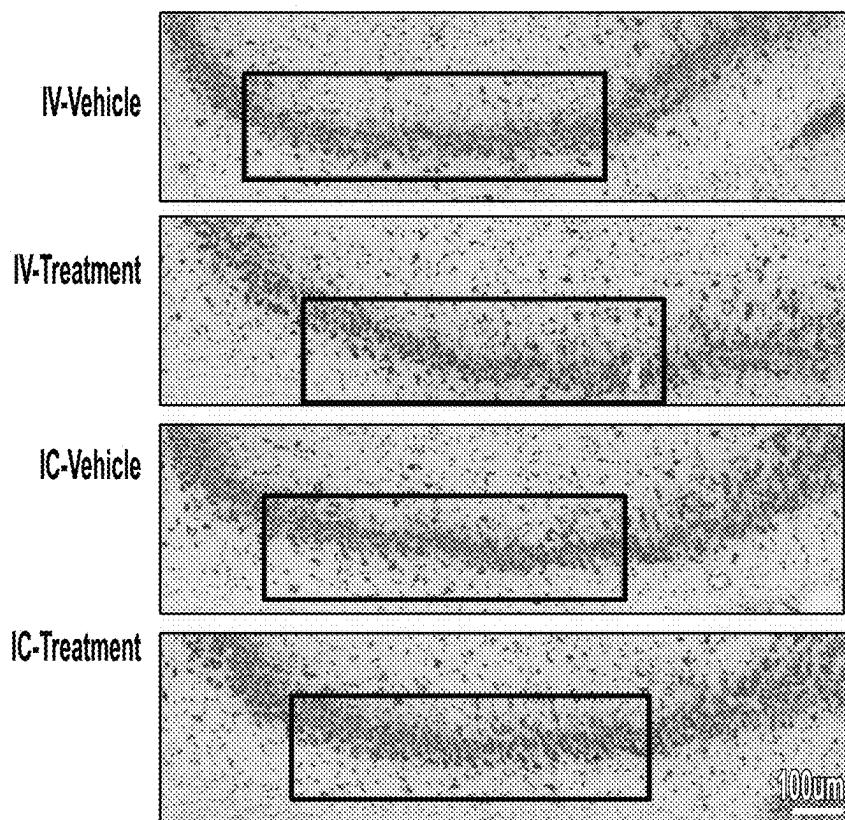


FIG. 5E

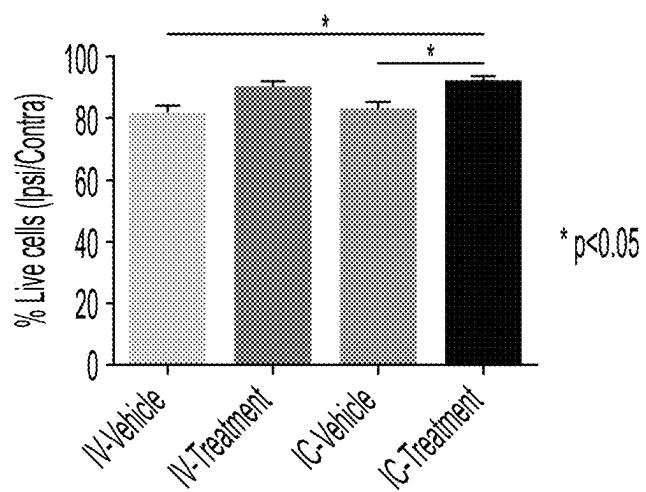


FIG. 5F

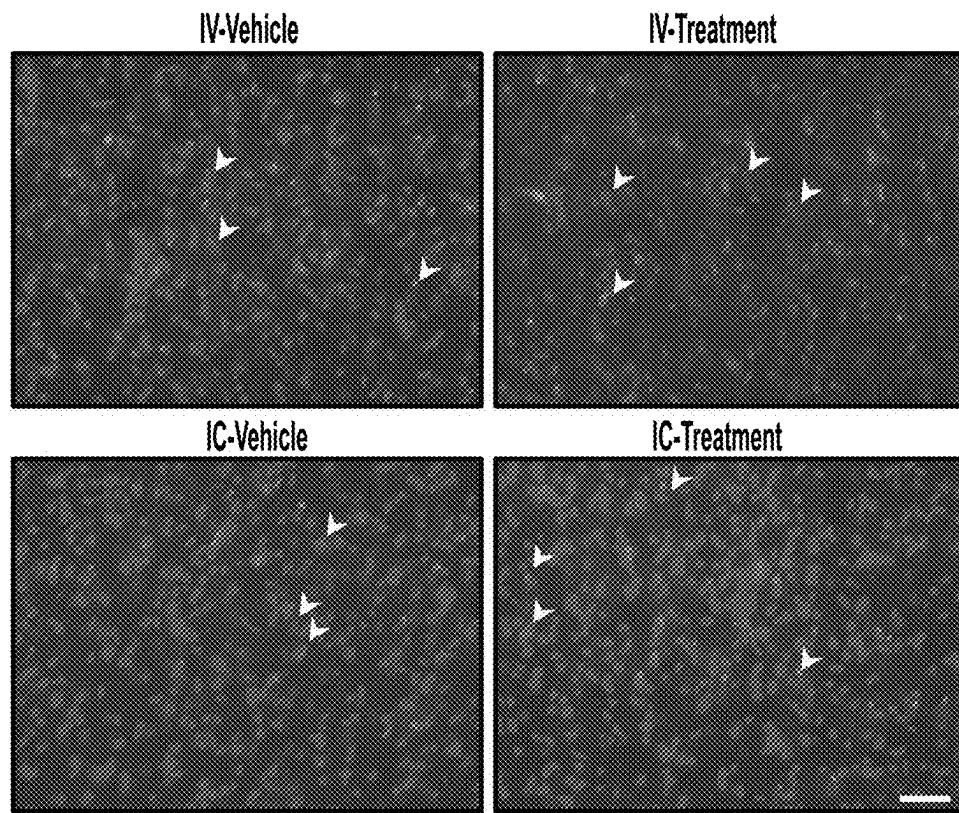


FIG. 6A

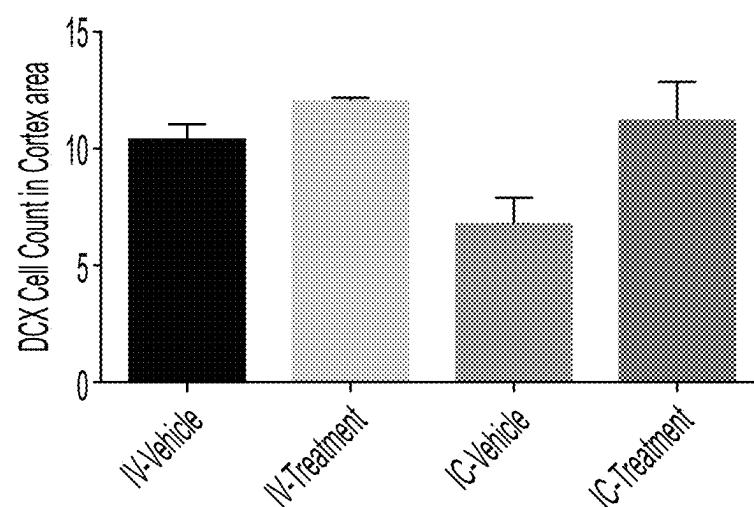


FIG. 6B

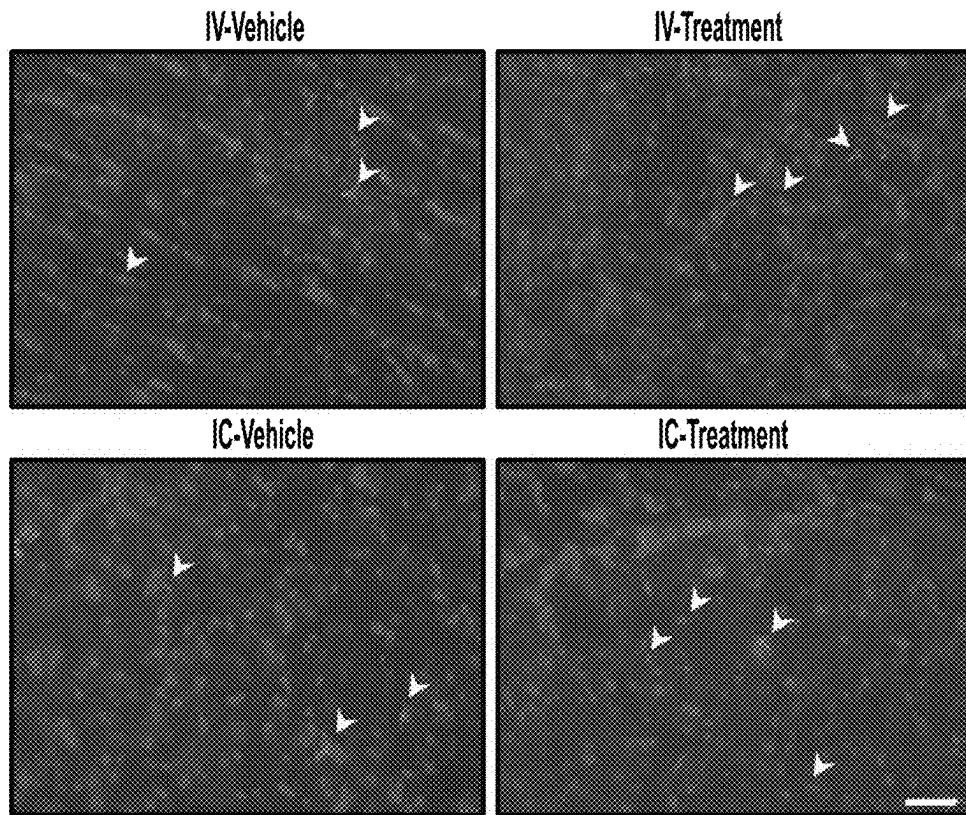


FIG. 6C

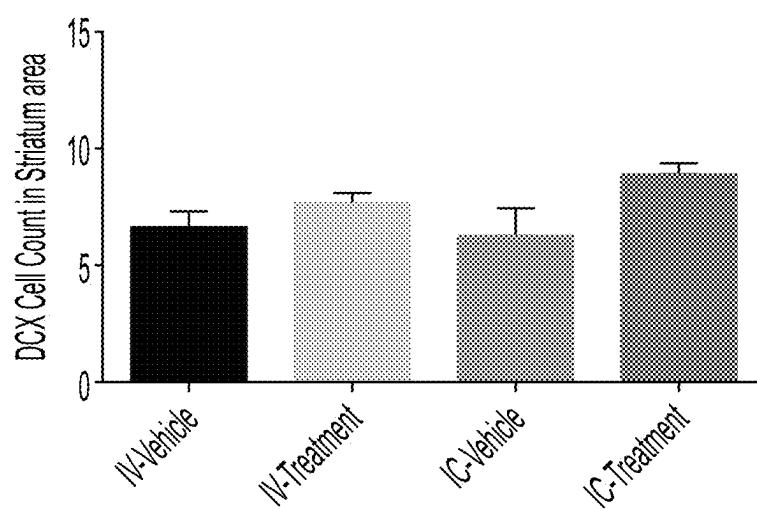


FIG. 6D

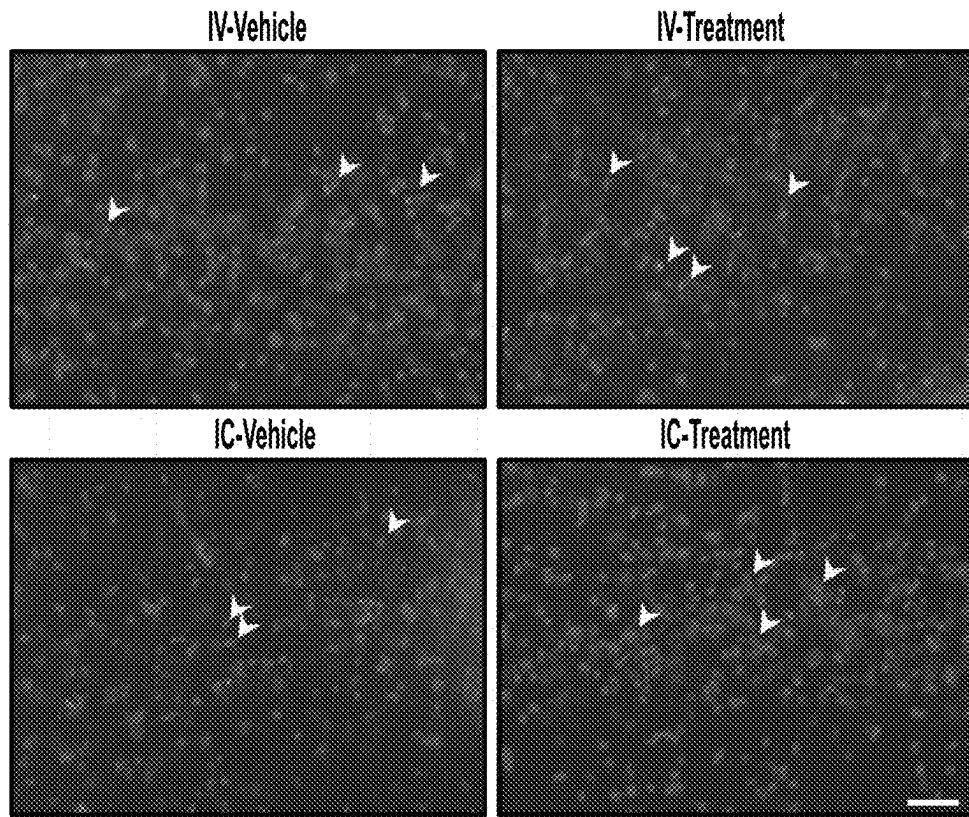


FIG. 6E

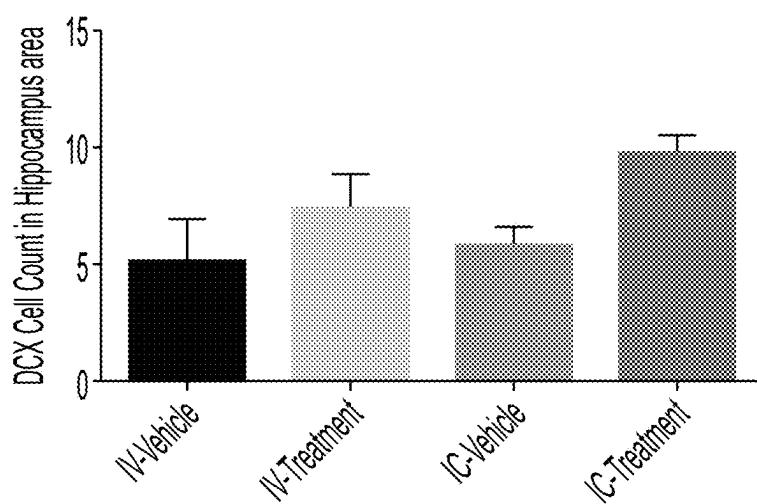


FIG. 6F

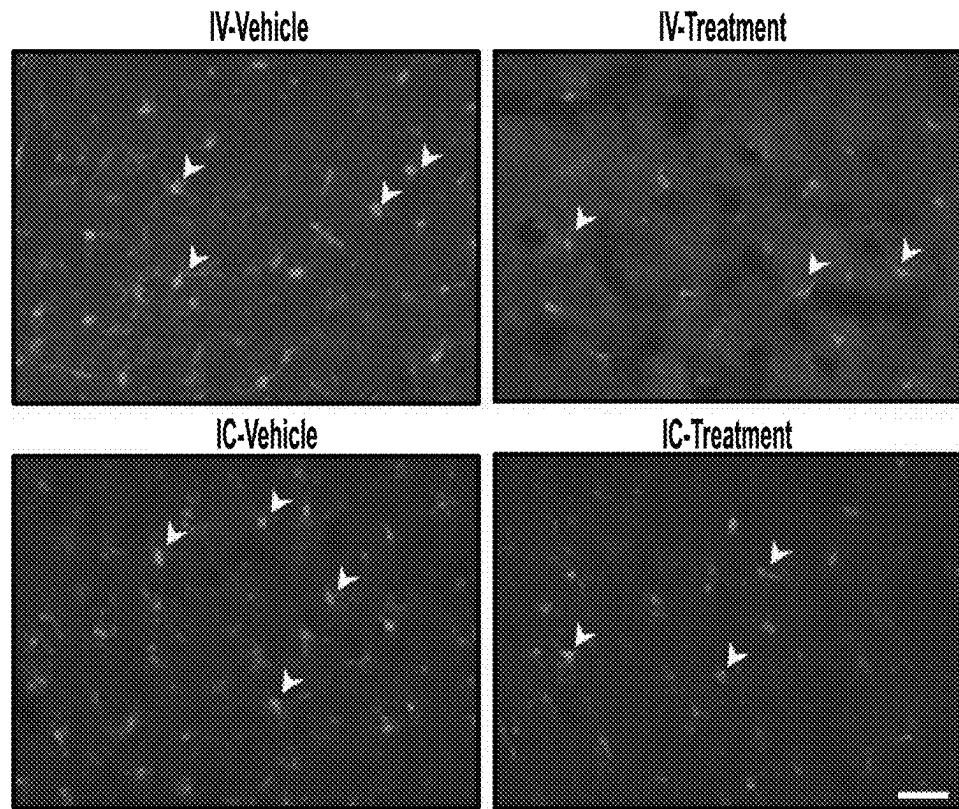


FIG. 7A

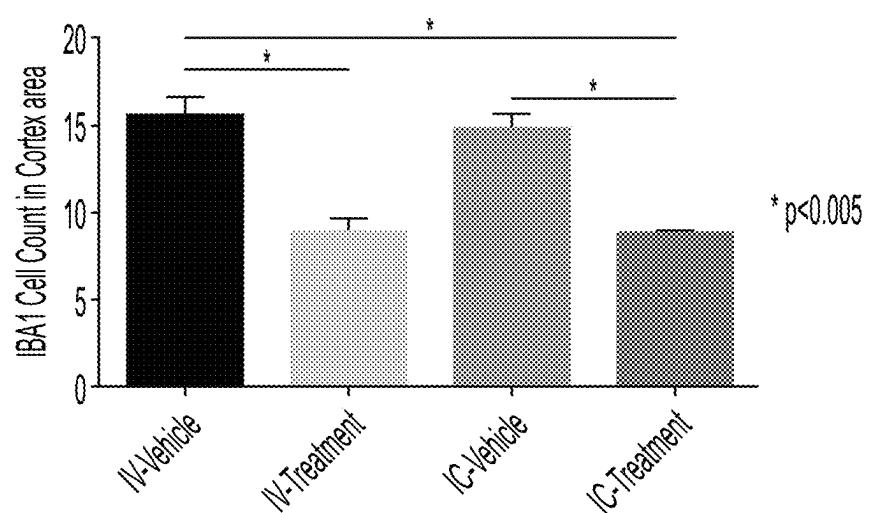


FIG. 7B

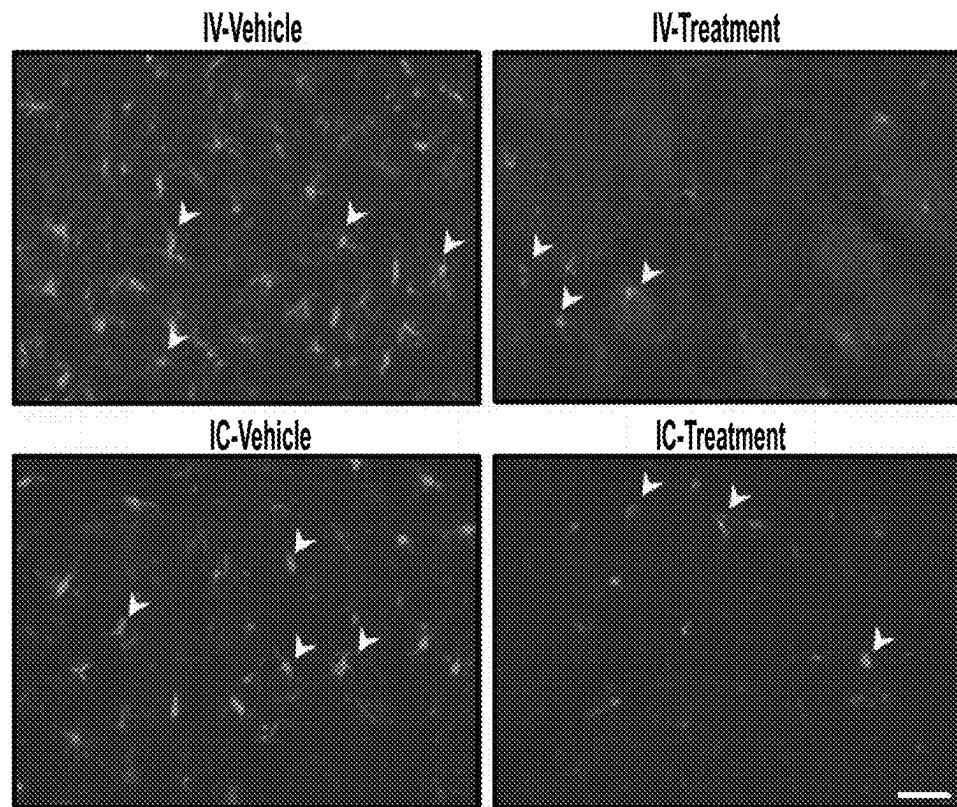


FIG. 7C

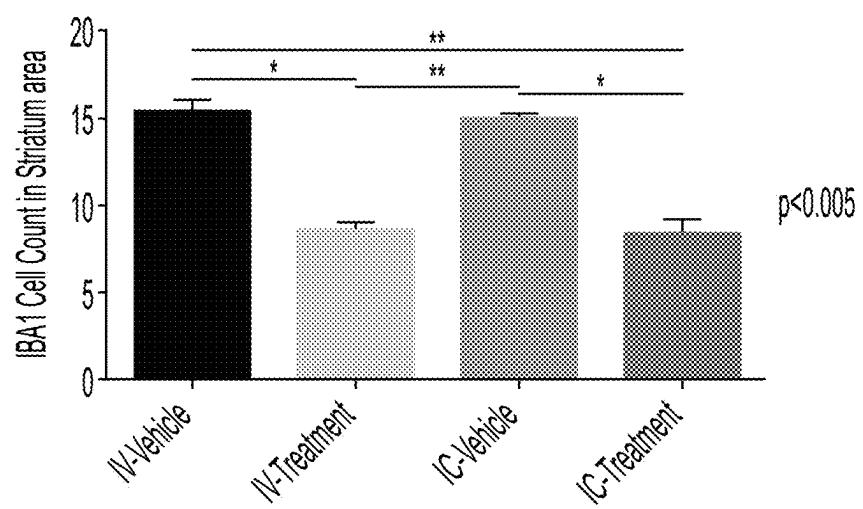


FIG. 7D

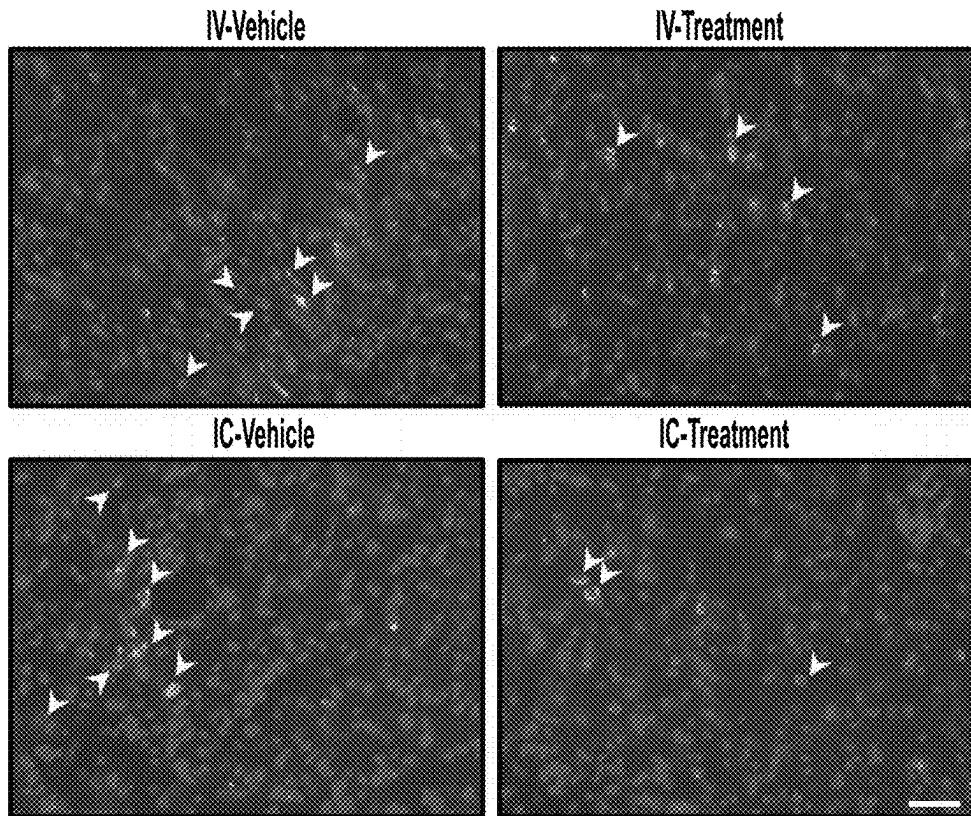


FIG. 8A

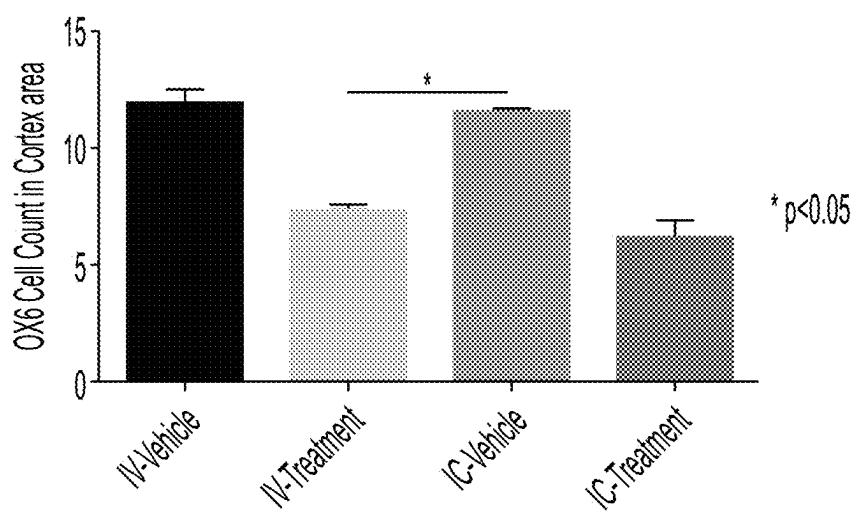


FIG. 8B

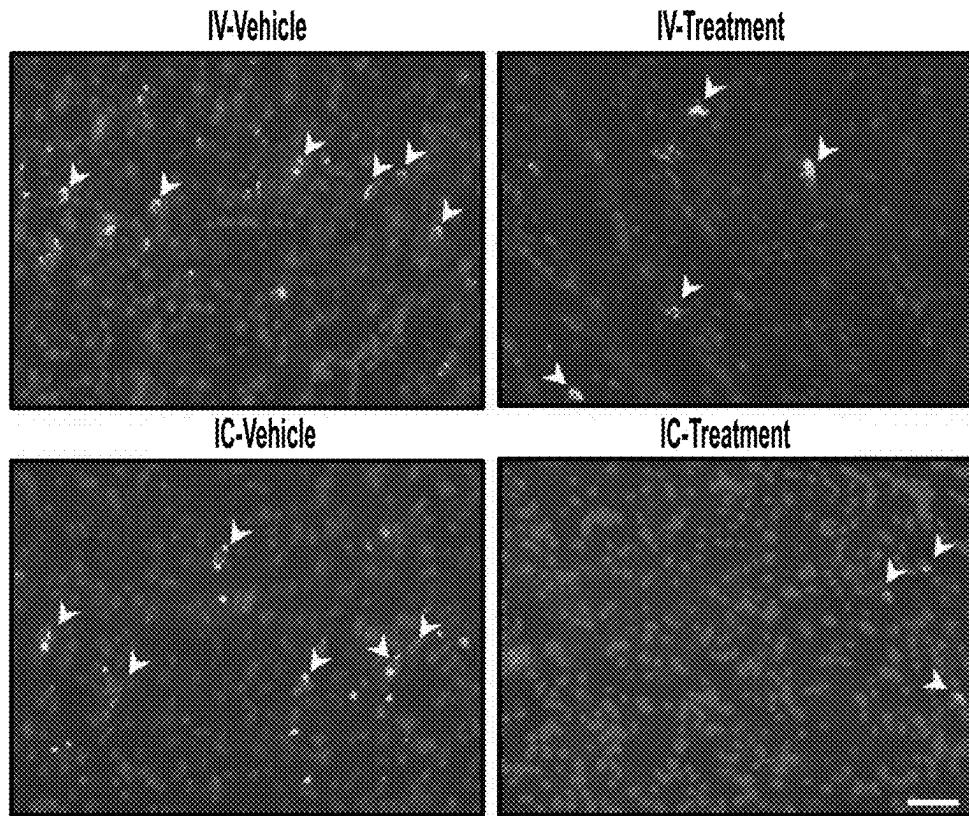


FIG. 8C

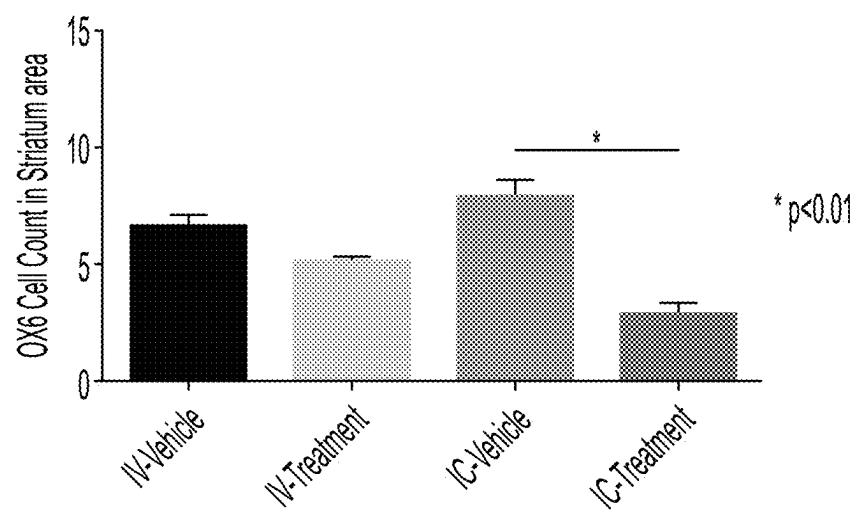


FIG. 8D

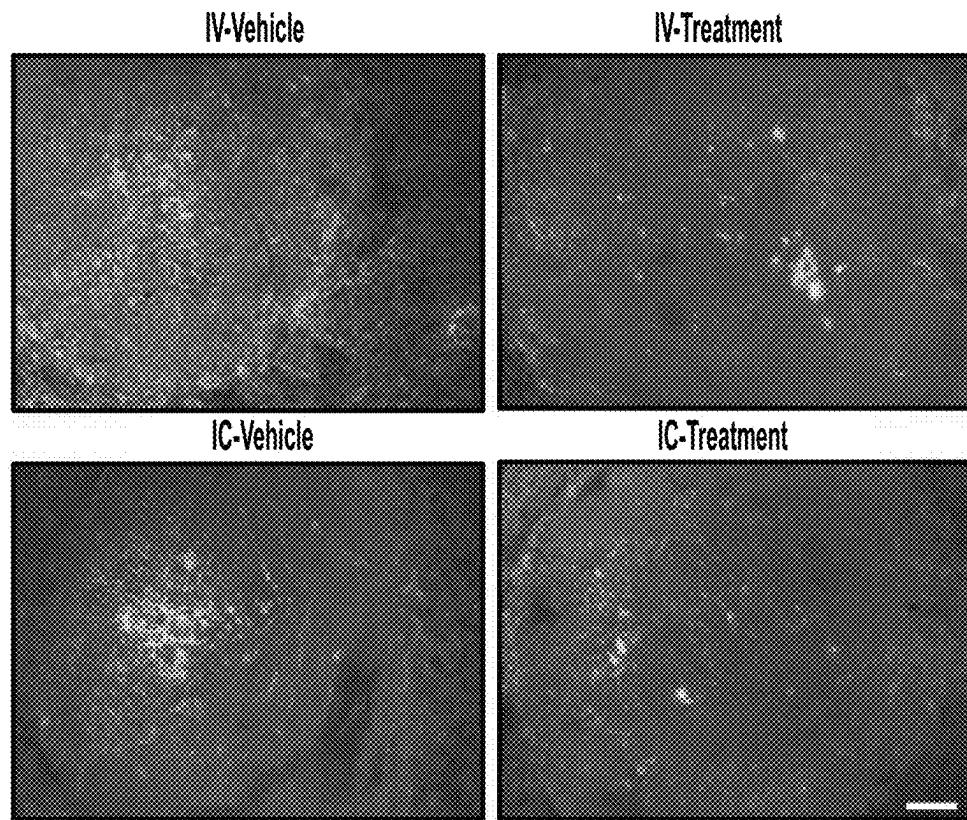


FIG. 9A

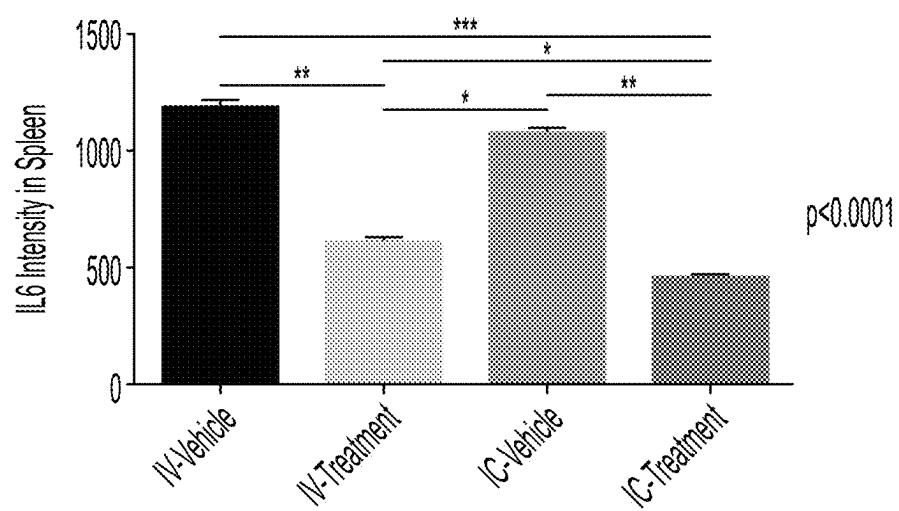


FIG. 9B

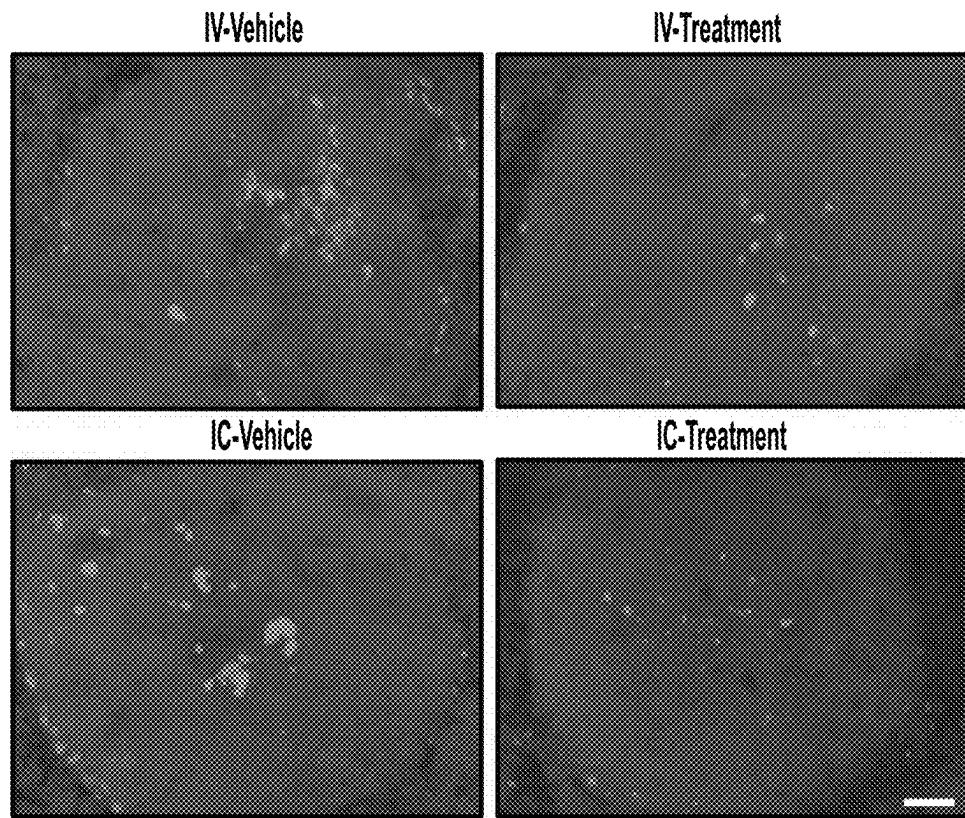


FIG. 10A

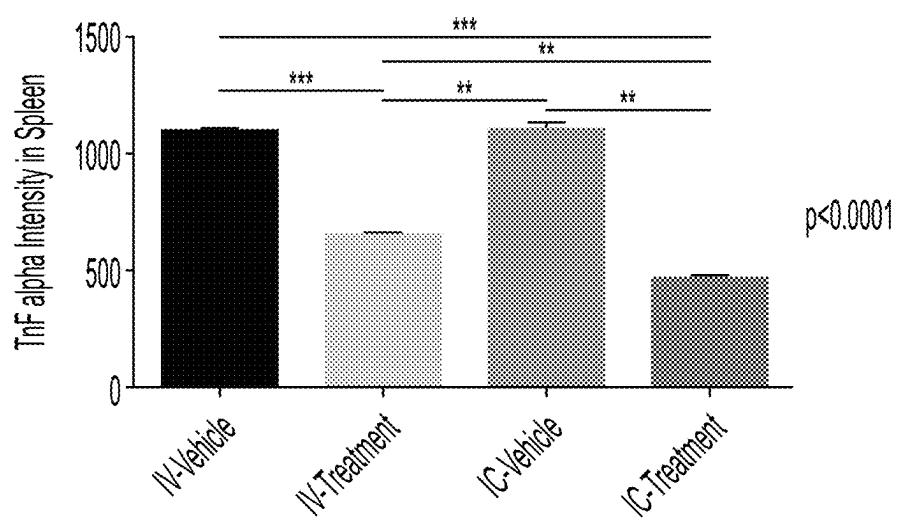


FIG. 10B

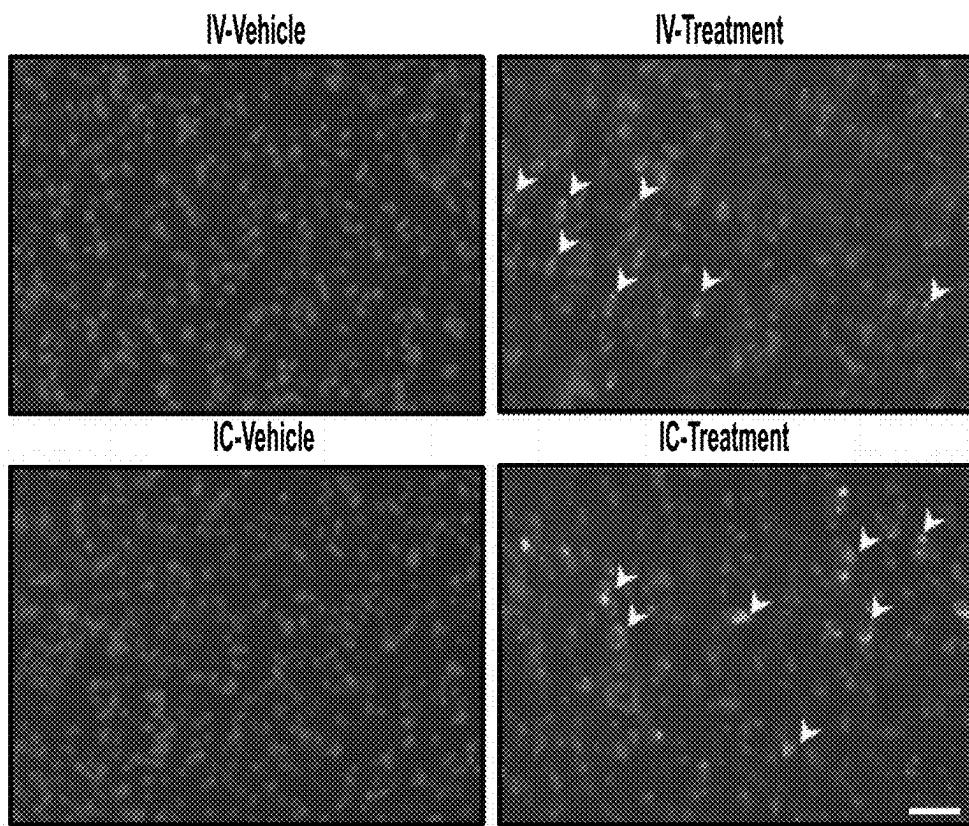


FIG. 11A

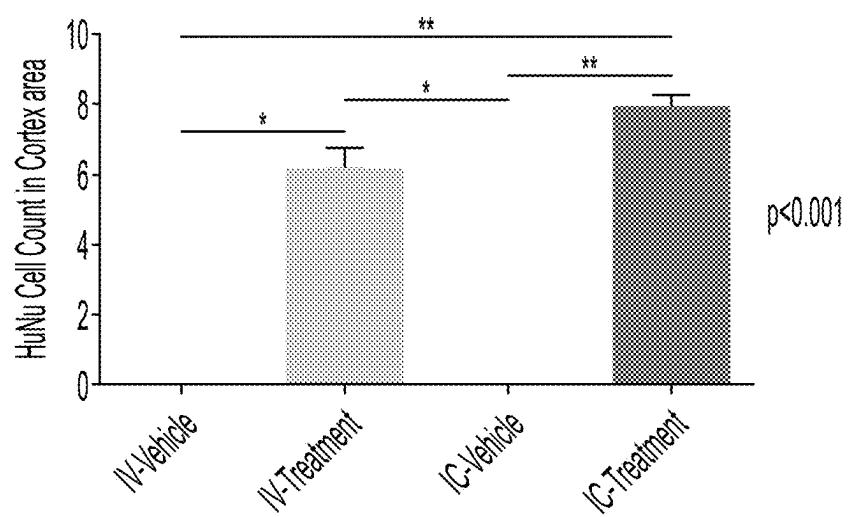


FIG. 11B

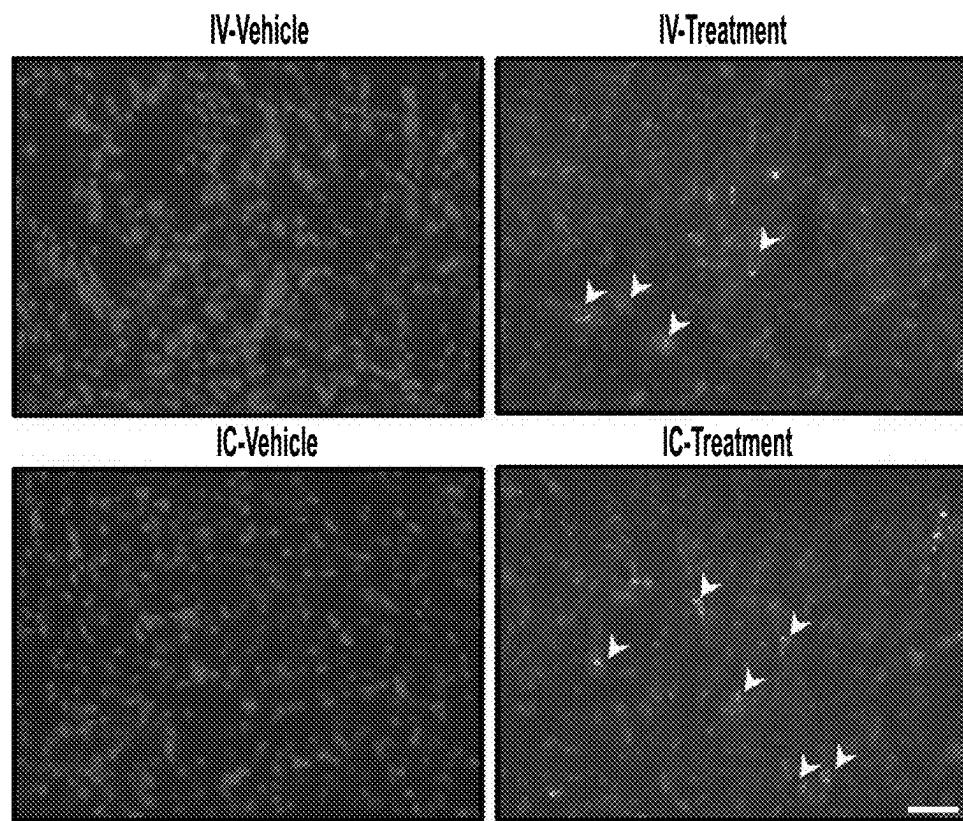


FIG. 11C

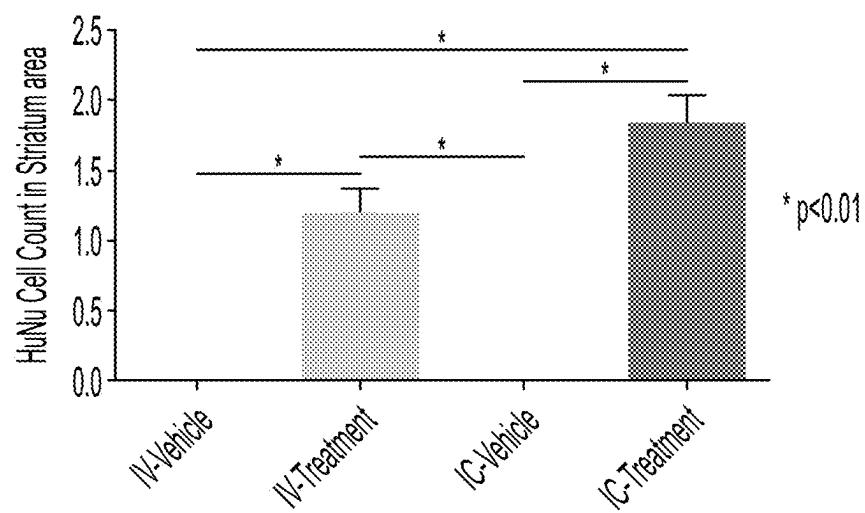


FIG. 11D

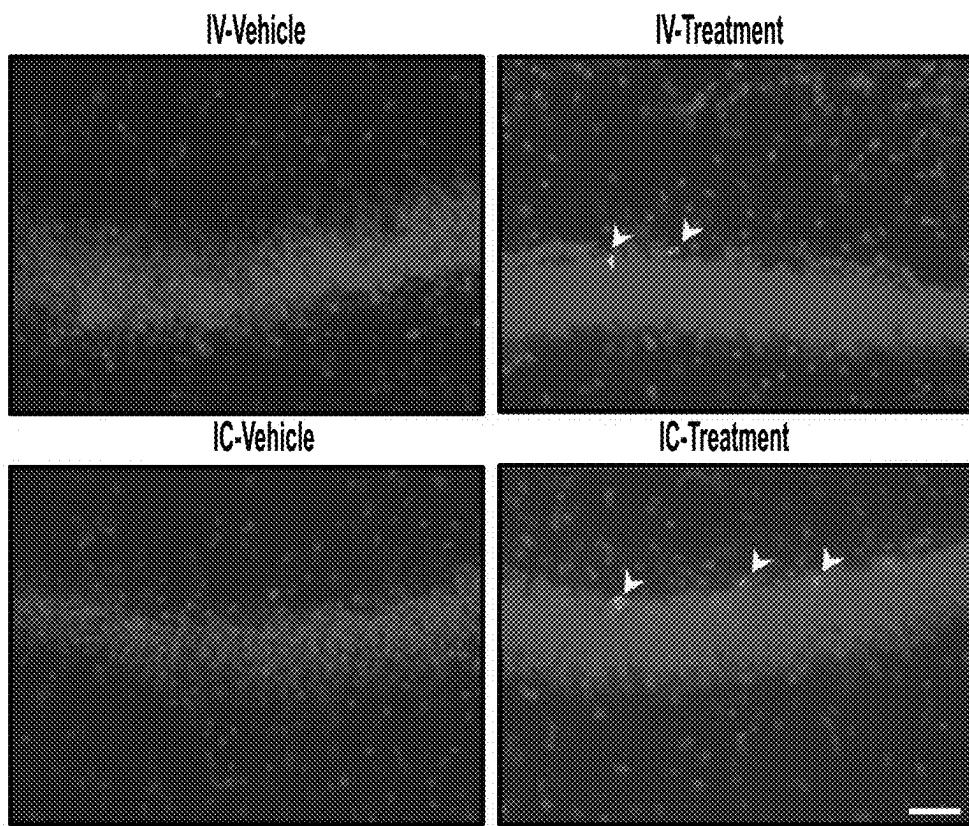


FIG. 11E

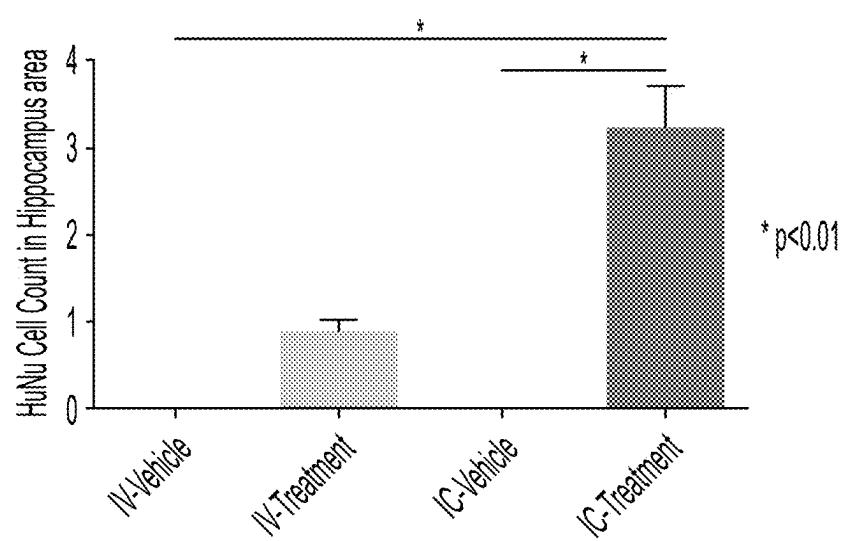
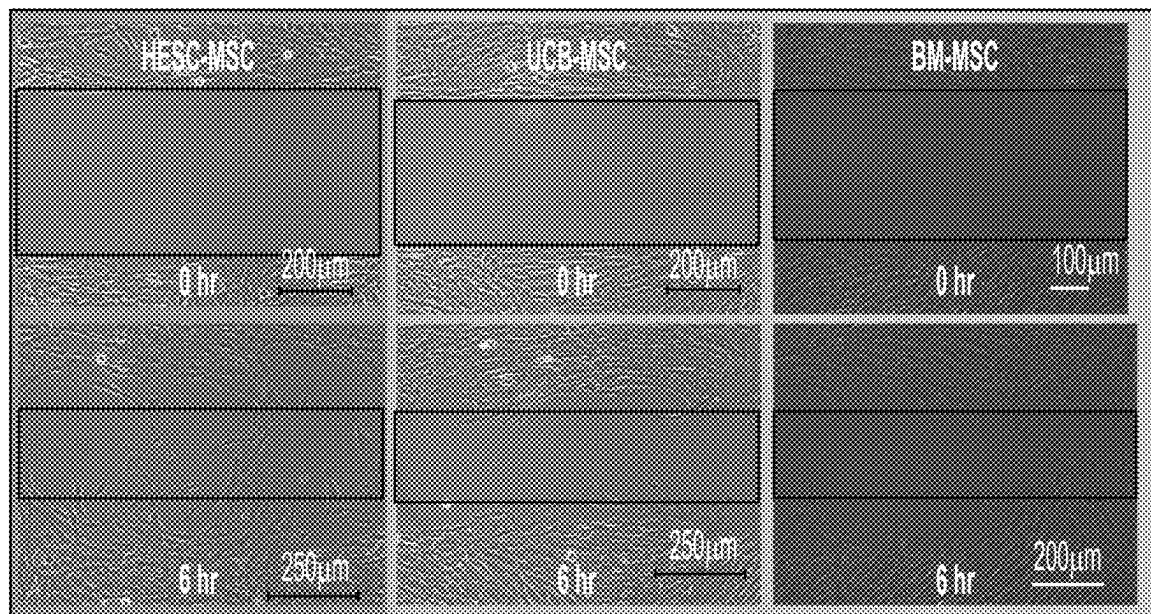


FIG. 11F



[^]Migration of MSCs into a gap ~500μm wide

FIG. 12A

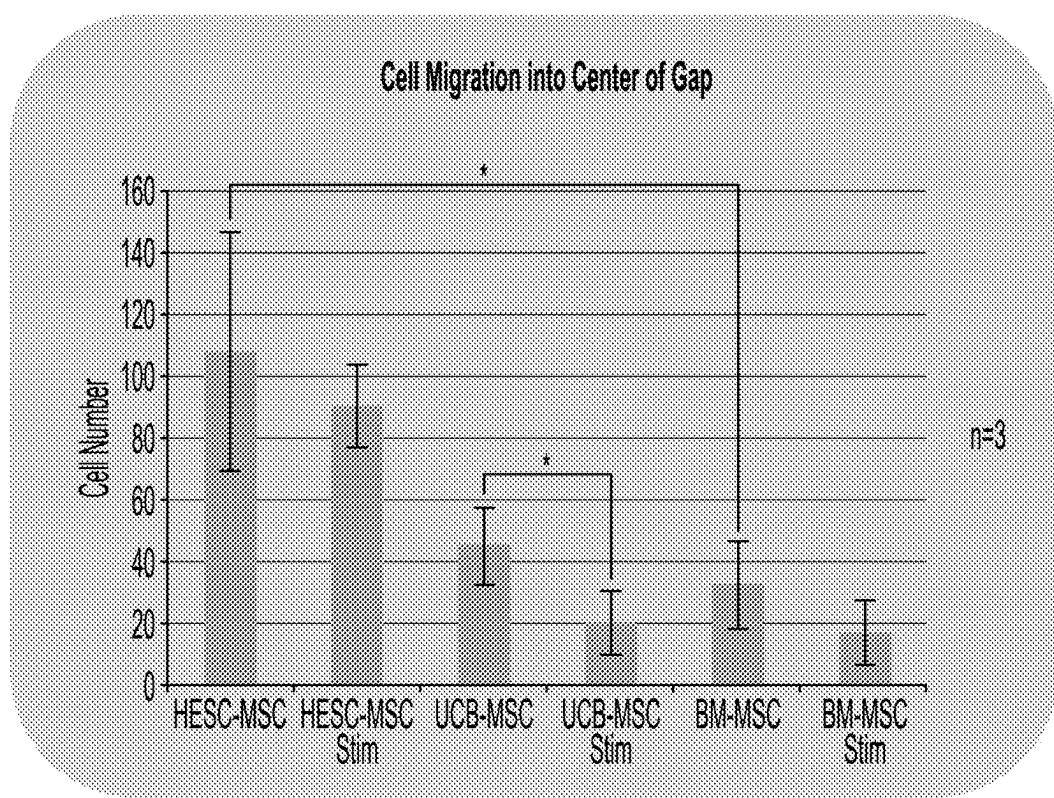


FIG. 12B

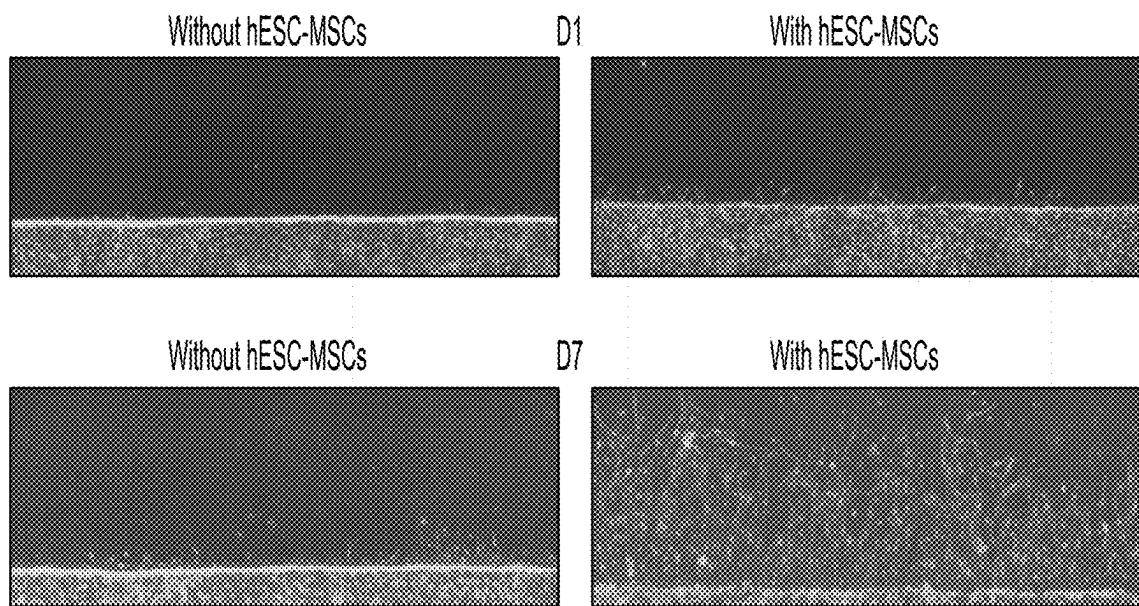


FIG. 13

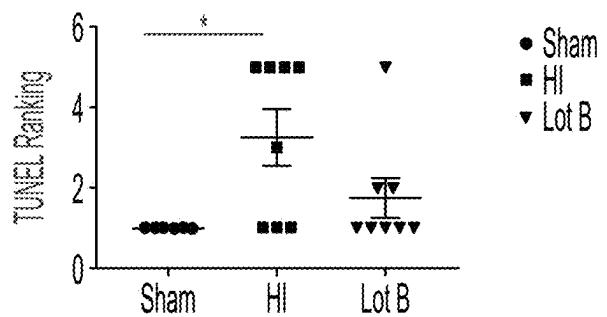


FIG. 14A

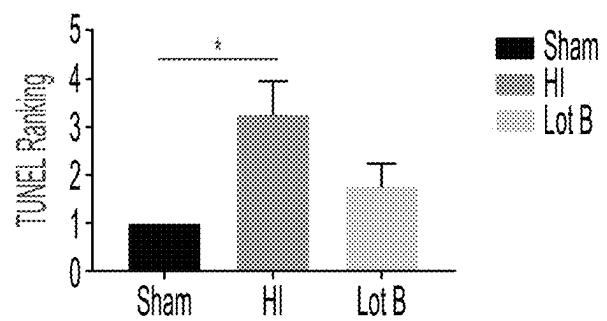


FIG. 14B

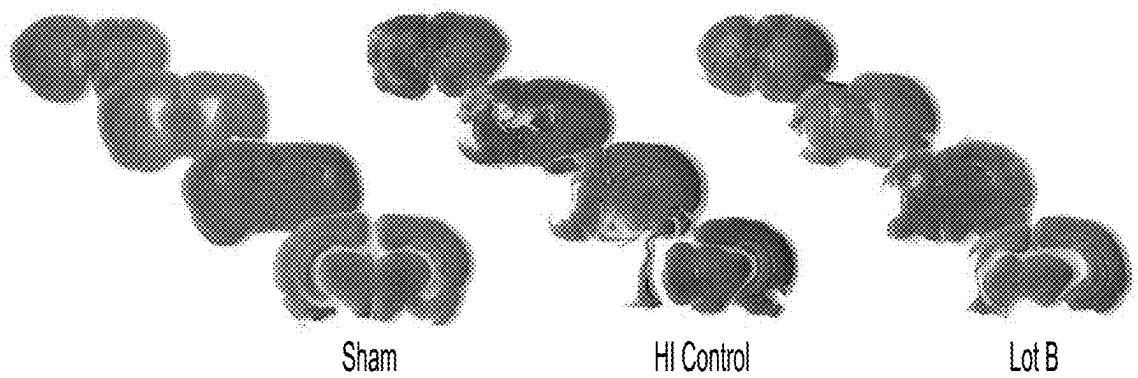


FIG. 15

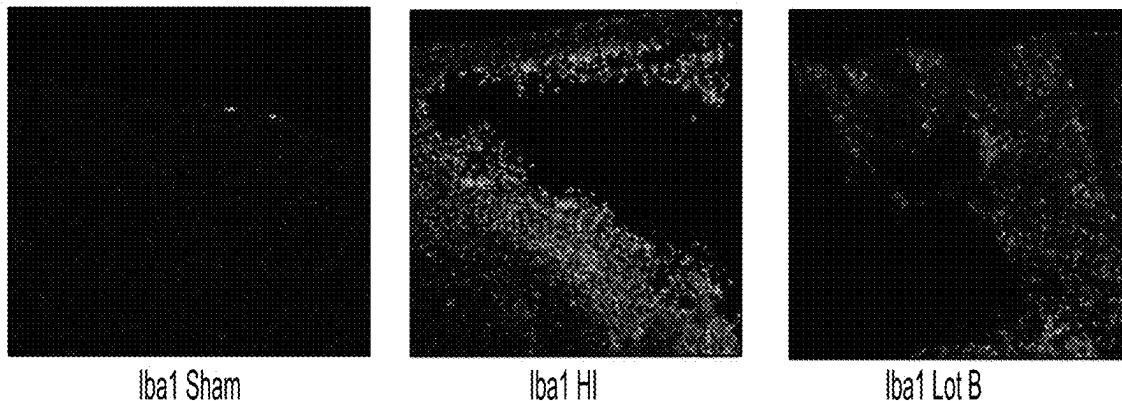


FIG. 16A

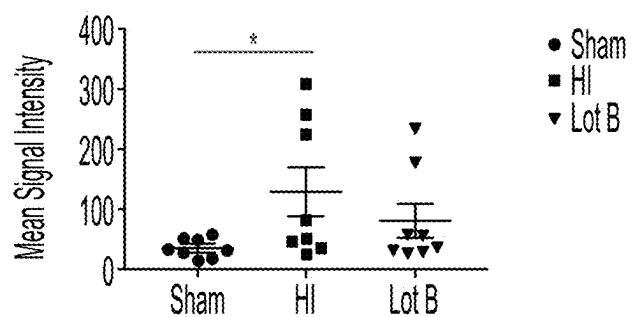


FIG. 16B

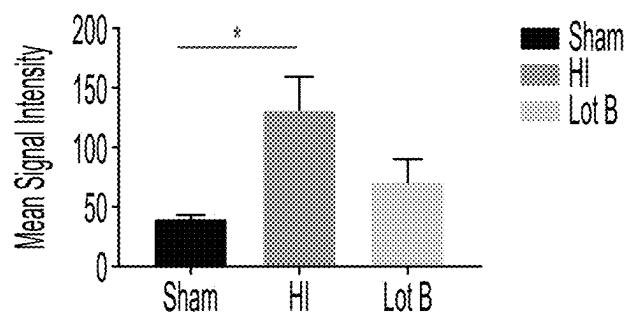


FIG. 16C

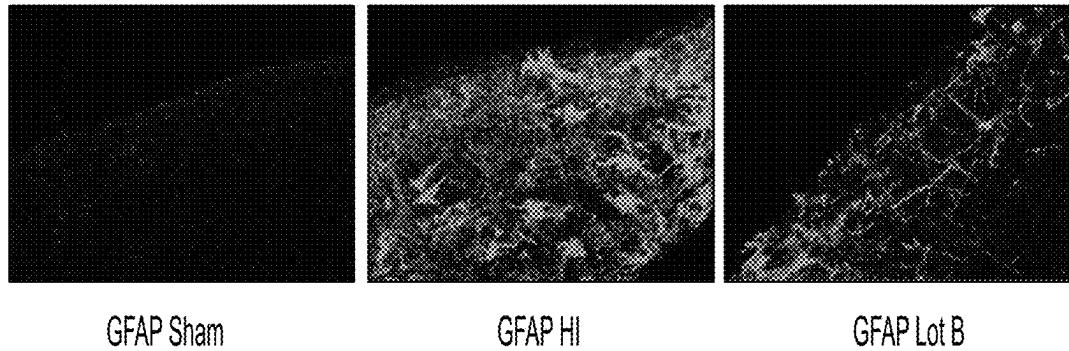


FIG. 17A

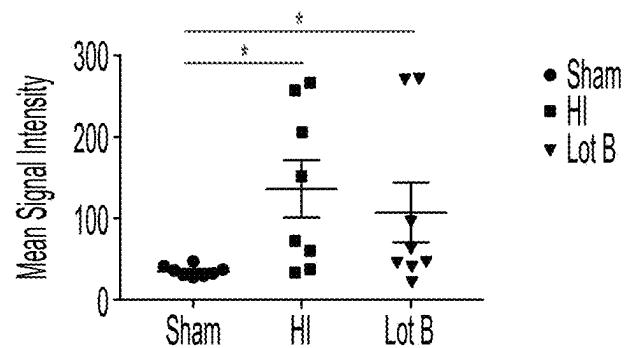


FIG. 17B

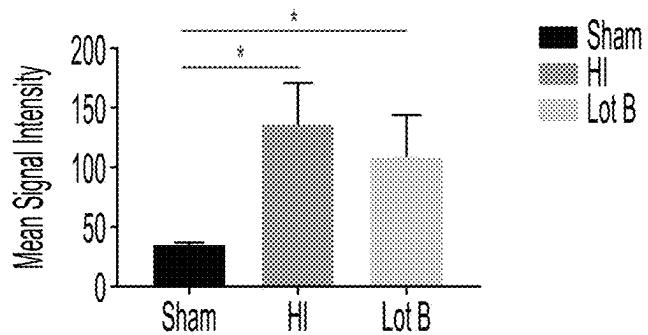


FIG. 17C

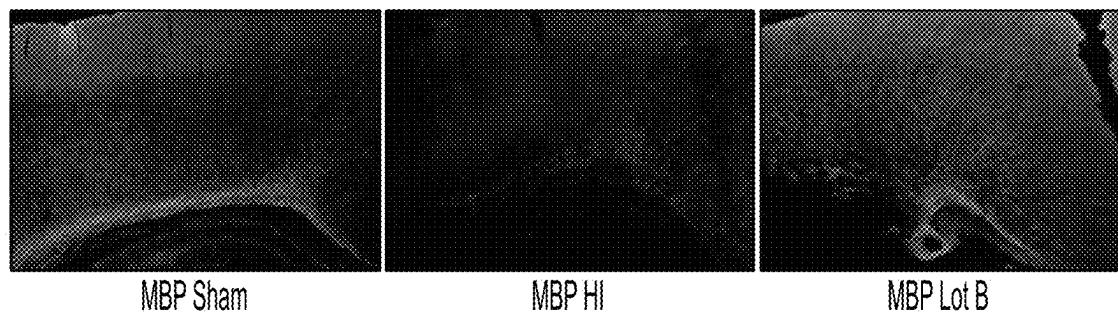


FIG. 18A

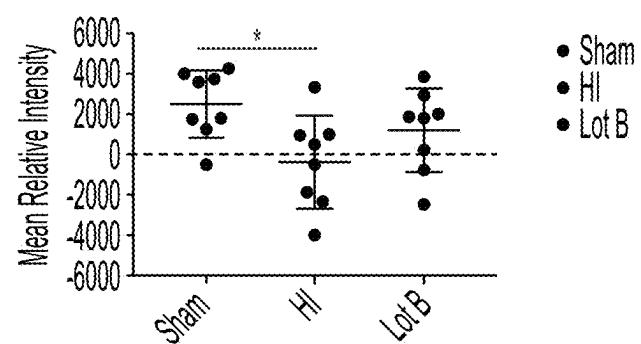


FIG. 18B

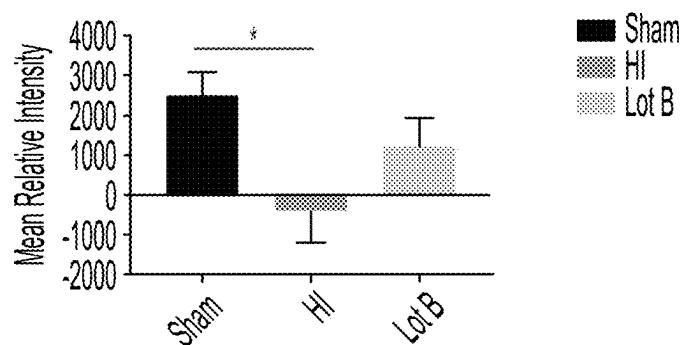


FIG. 18C

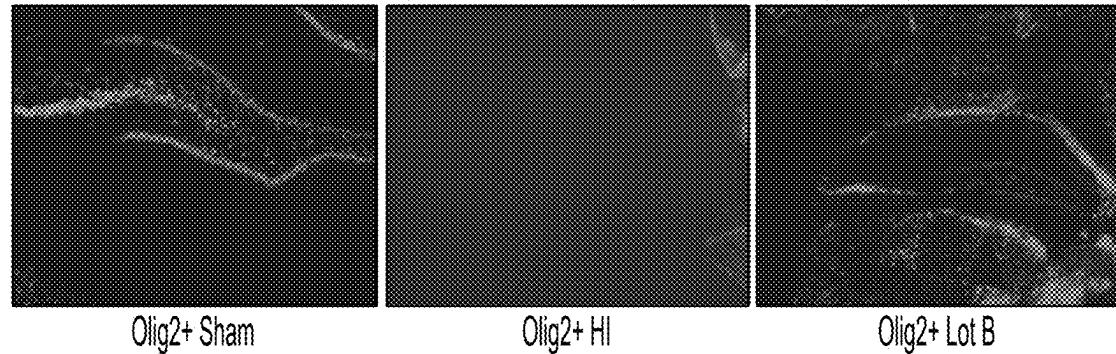


FIG. 19A

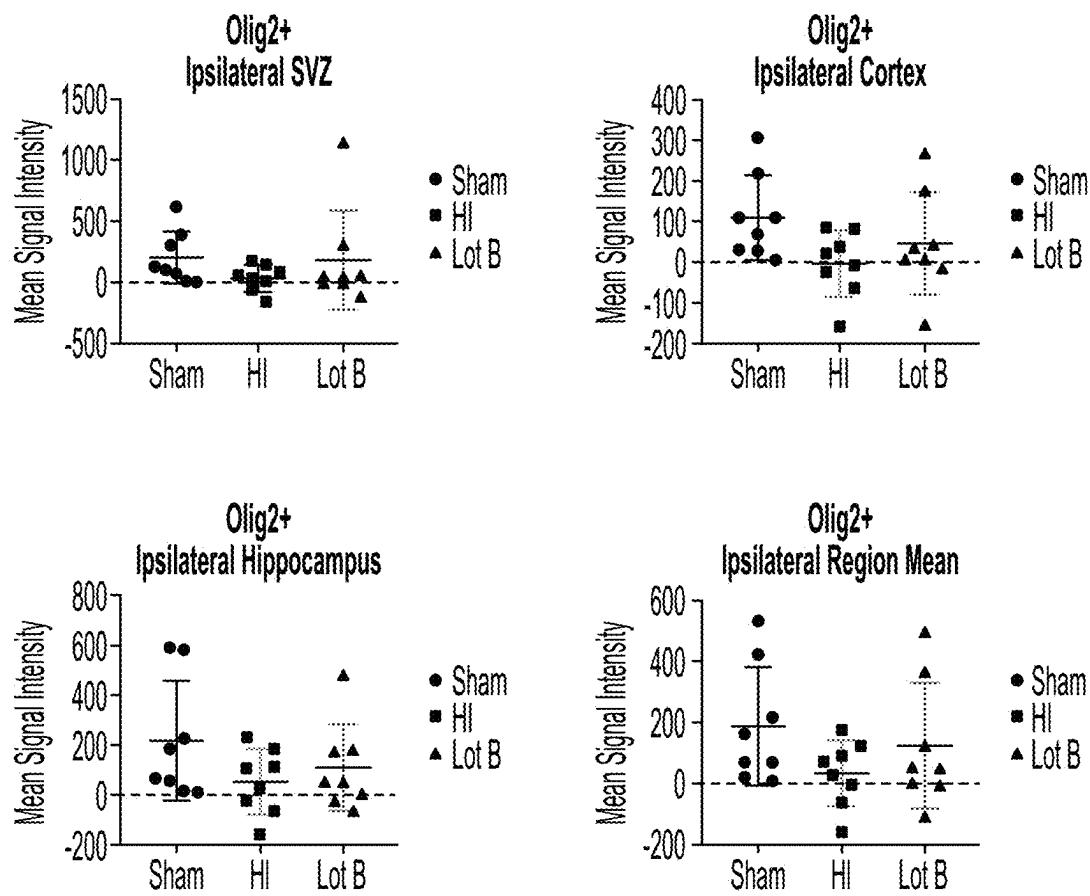


FIG. 19B

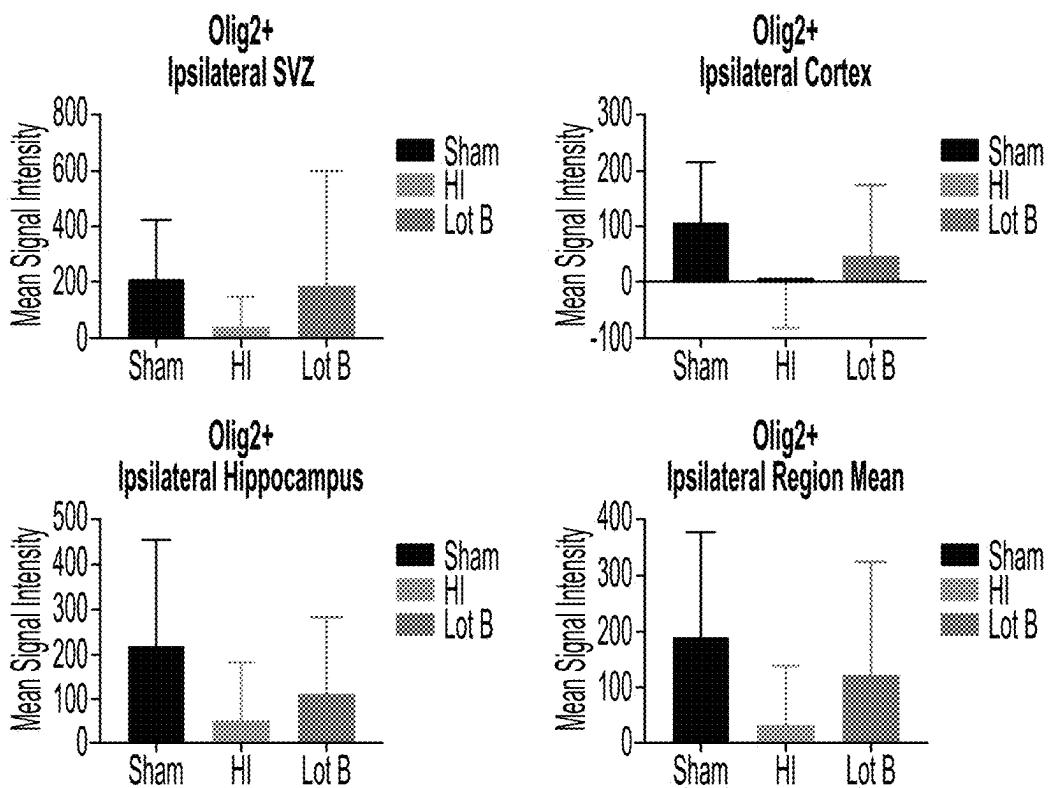


FIG. 19C

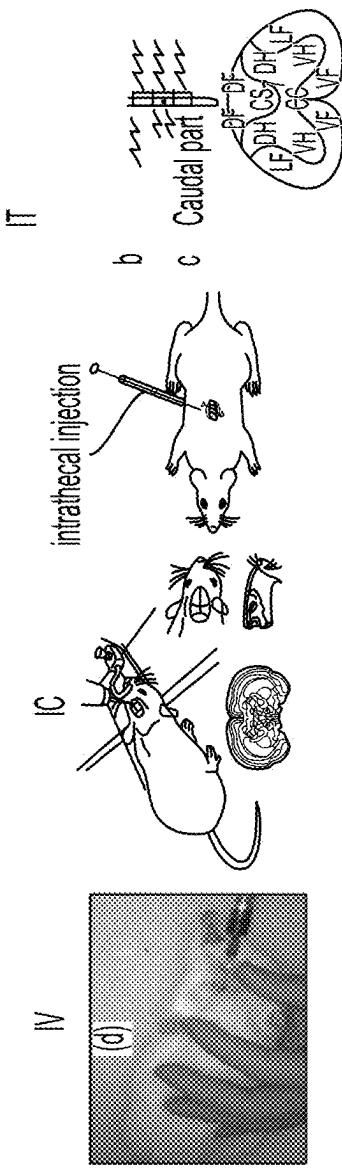
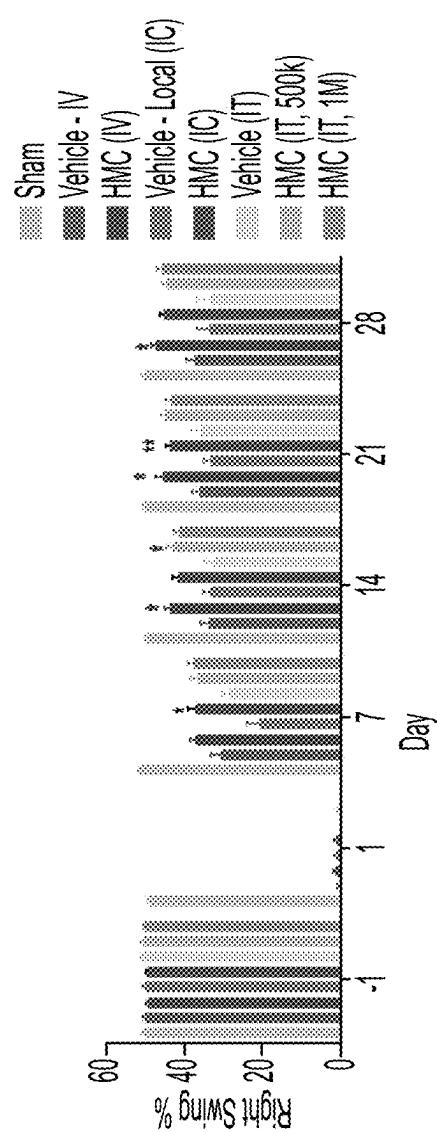


FIG. 20

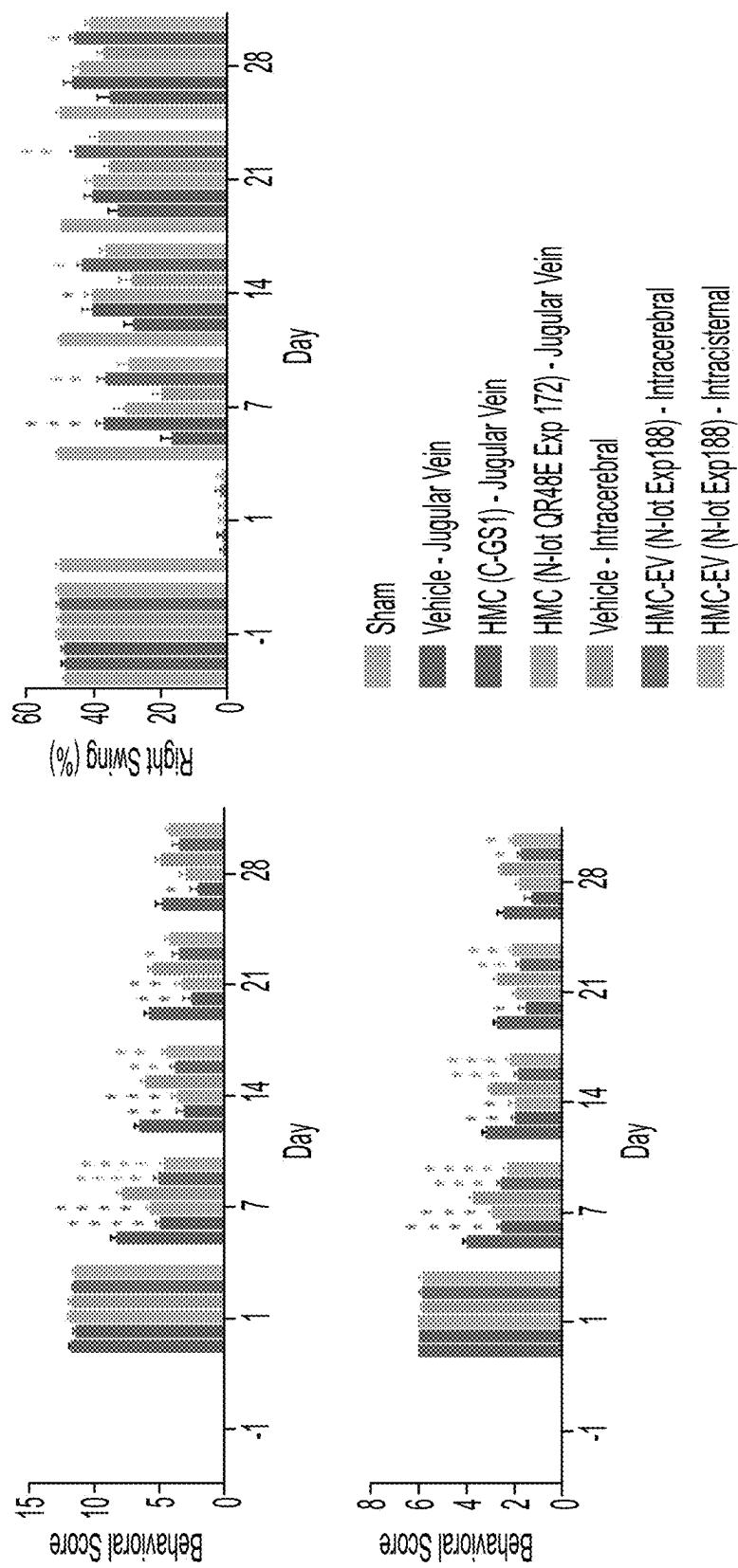


FIG. 21

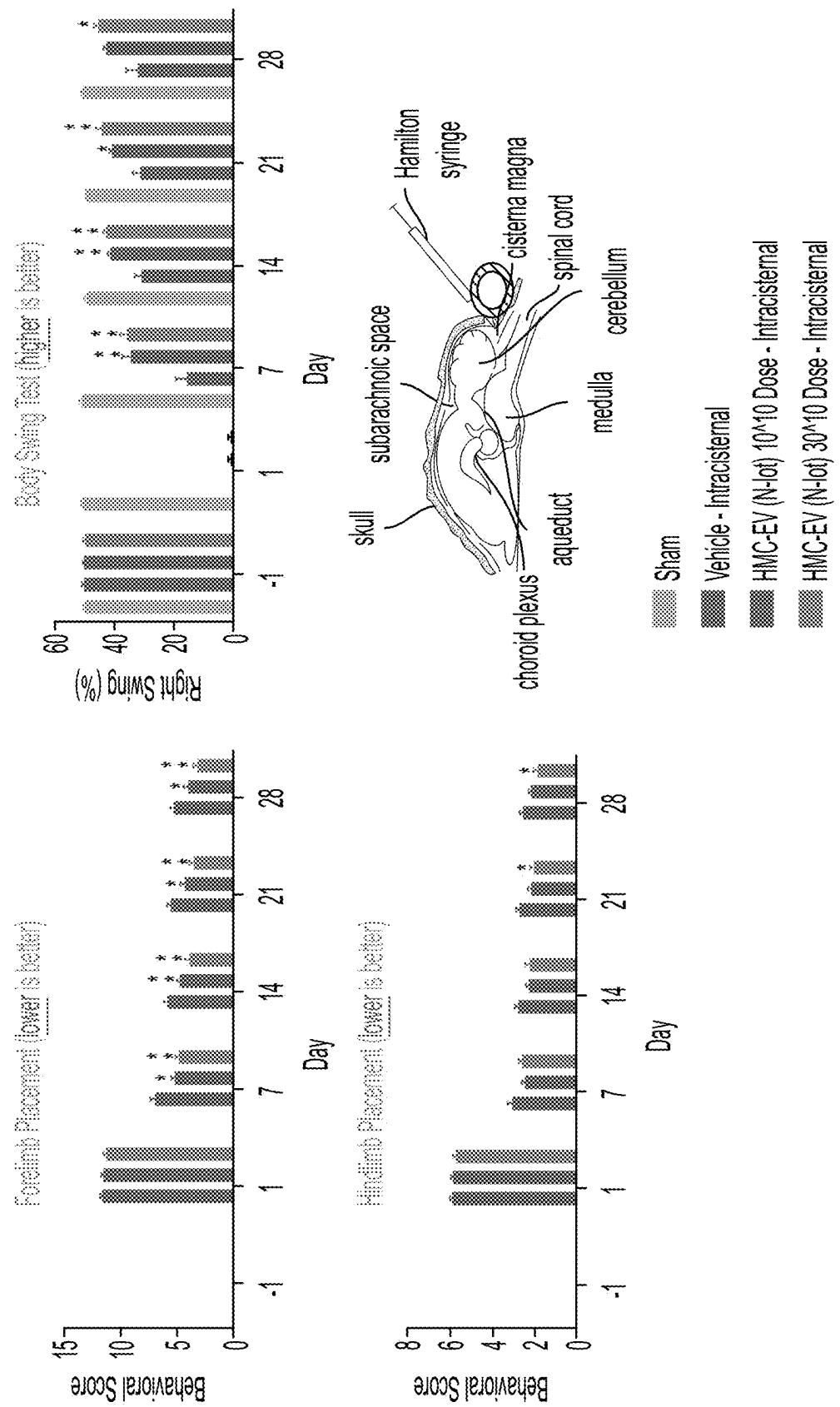


FIG. 22

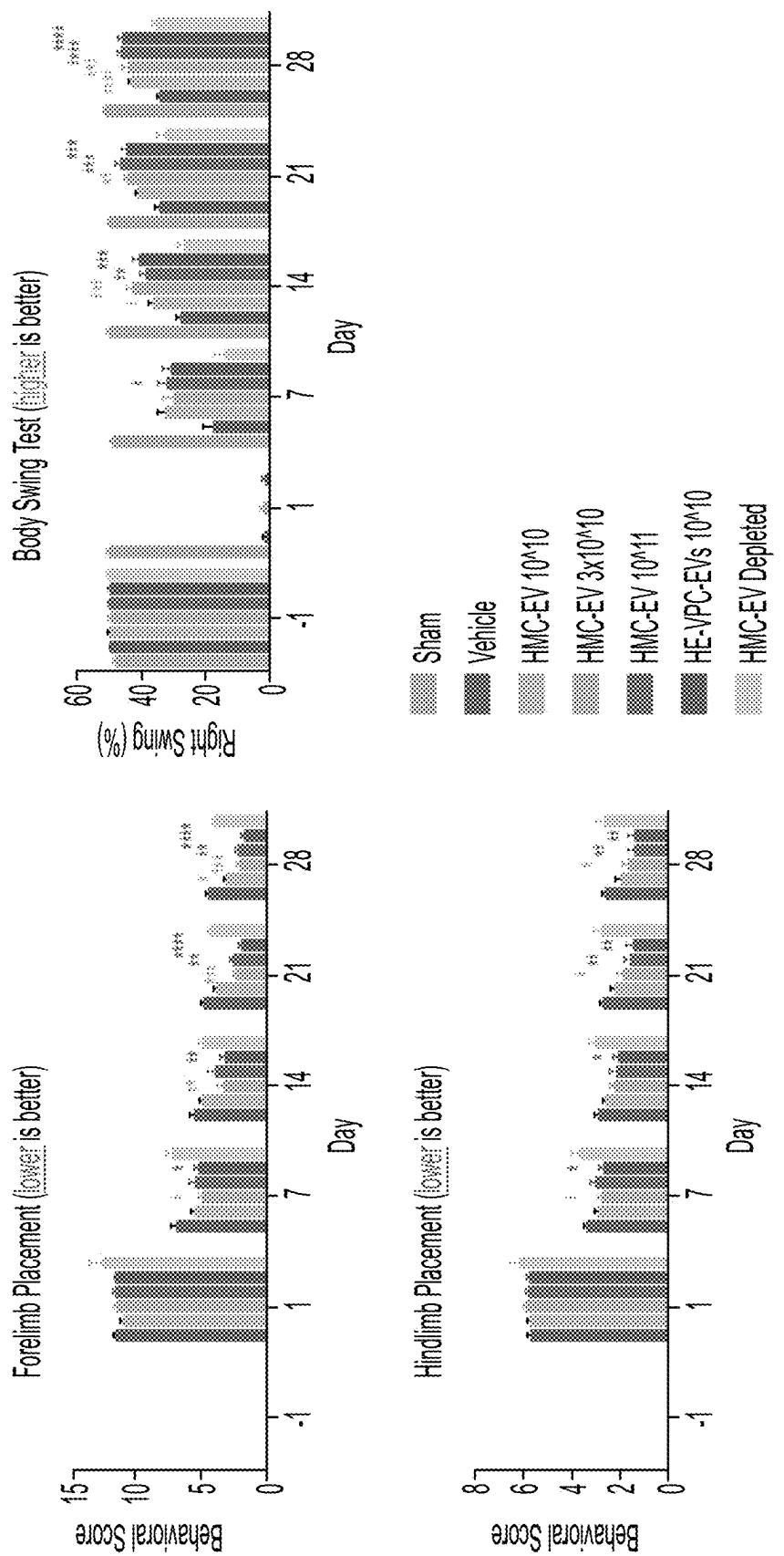


FIG. 23

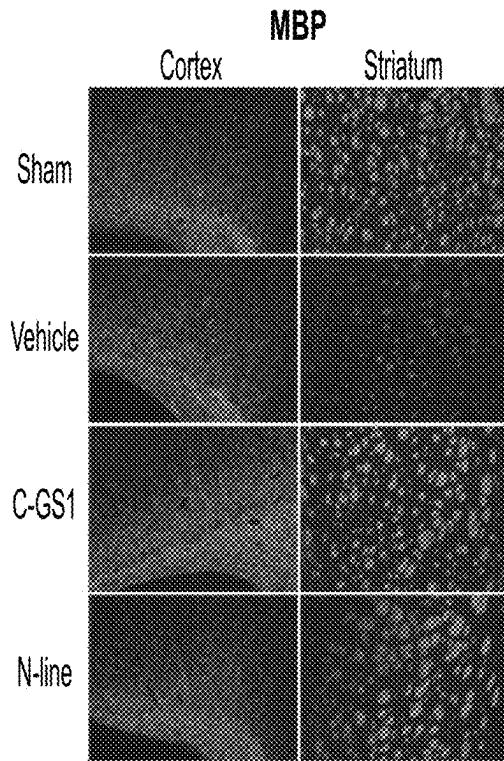


FIG. 24A

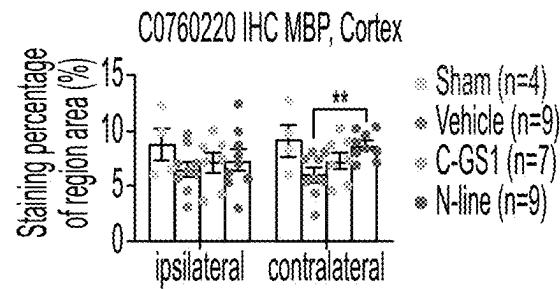


FIG. 24B

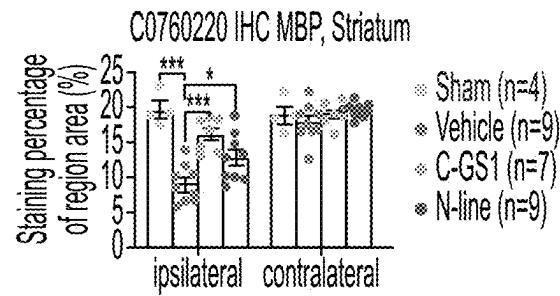


FIG. 24C

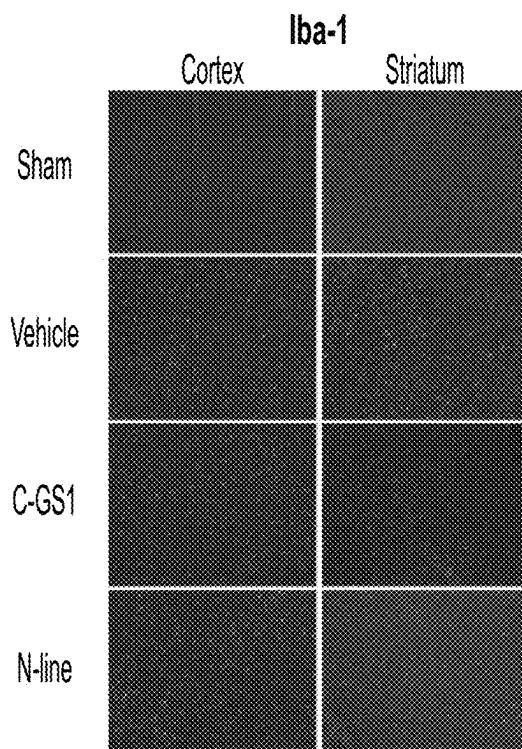


FIG. 25A

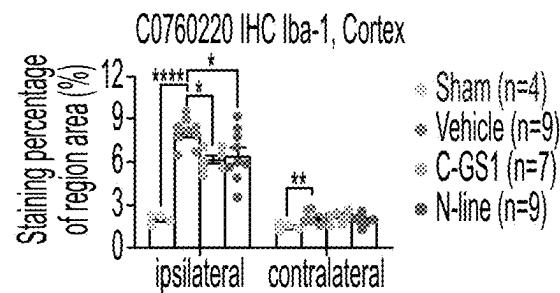


FIG. 25B

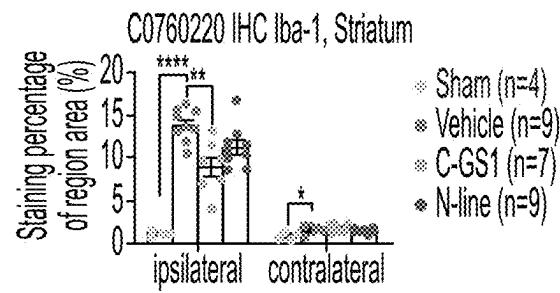


FIG. 25C

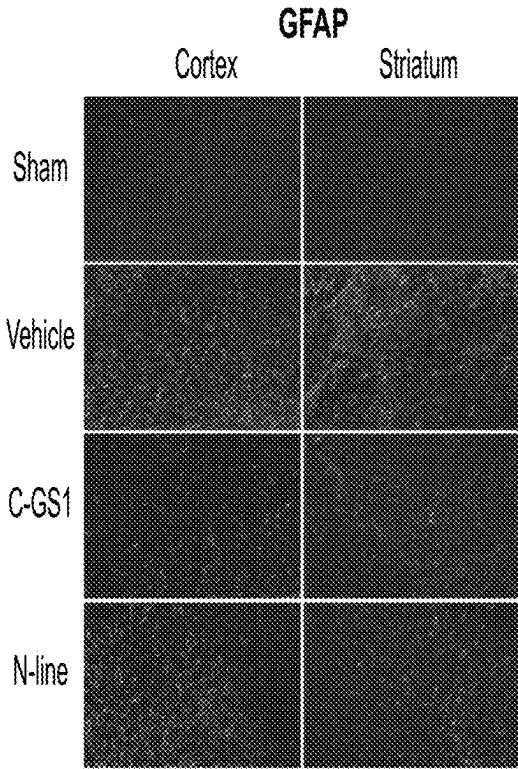


FIG. 26A

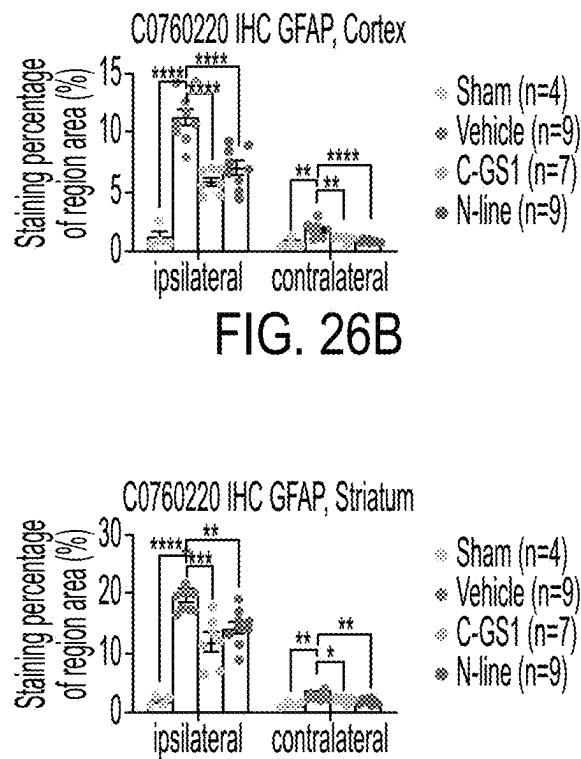


FIG. 26B

FIG. 26C

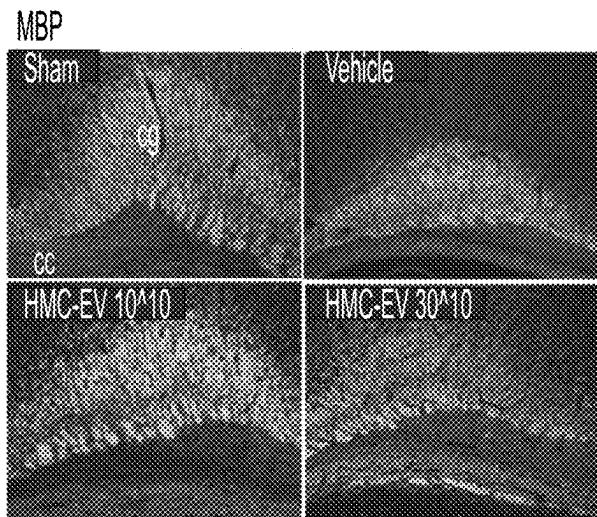


FIG. 27A

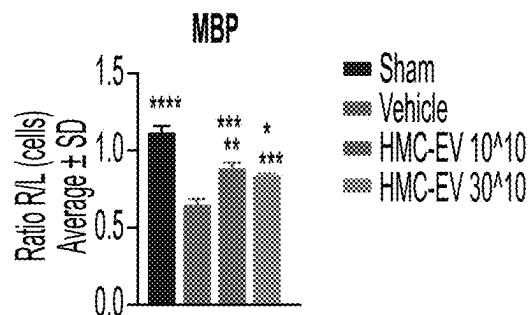


FIG. 27B

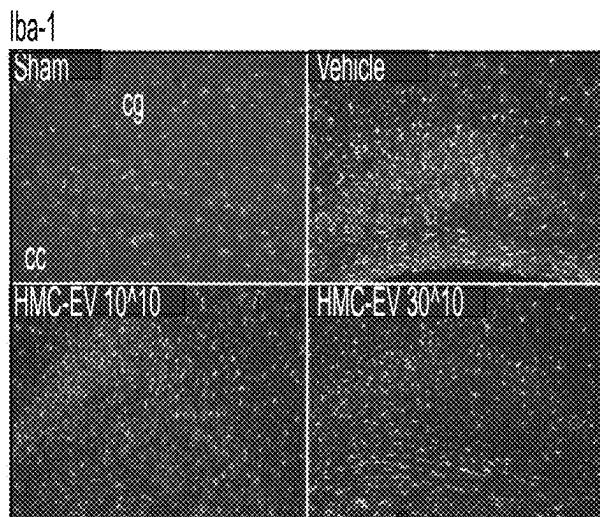


FIG. 28A

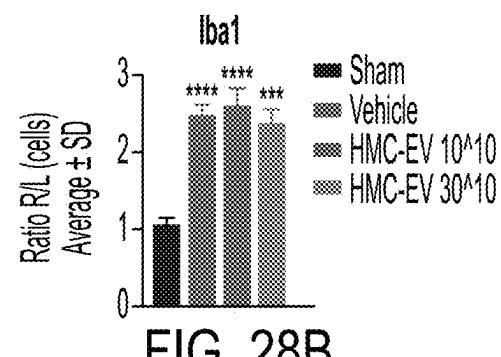


FIG. 28B

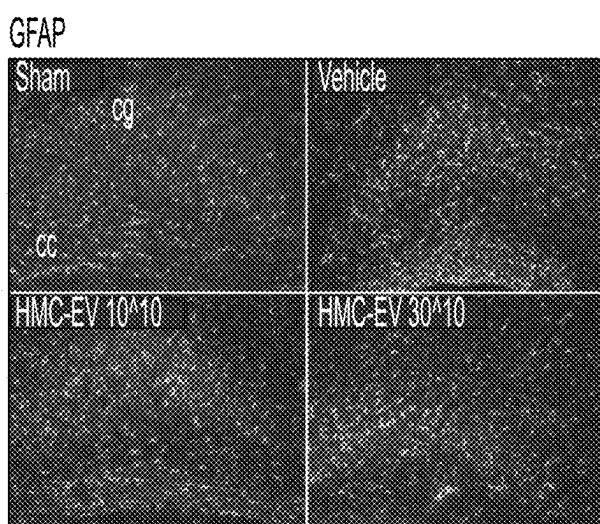


FIG. 29A

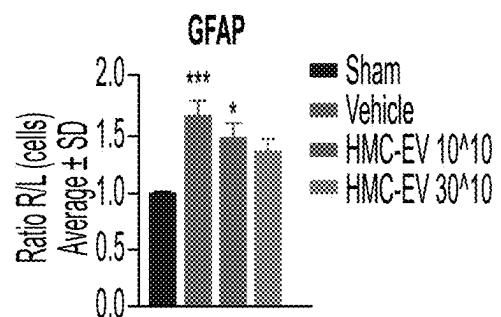


FIG. 29B

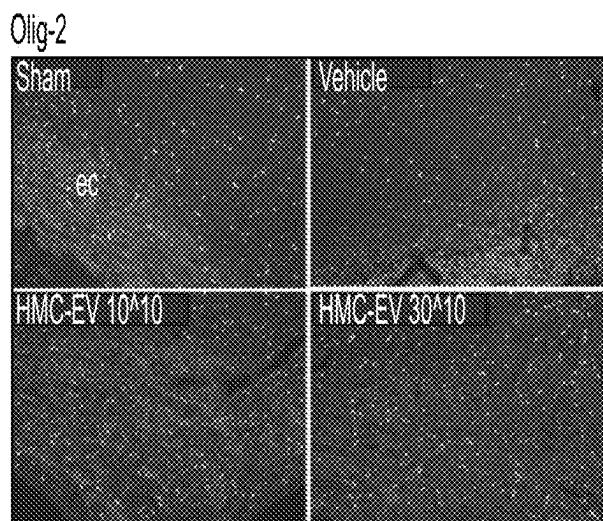


FIG. 30A

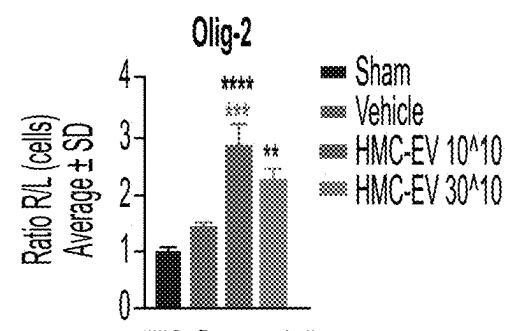


FIG. 30B

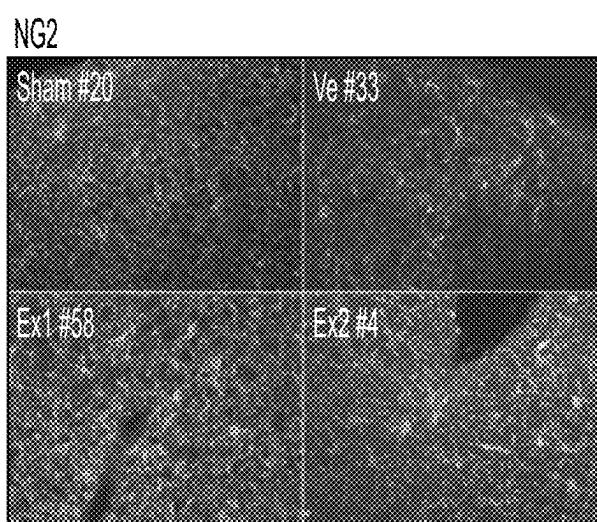


FIG. 31A

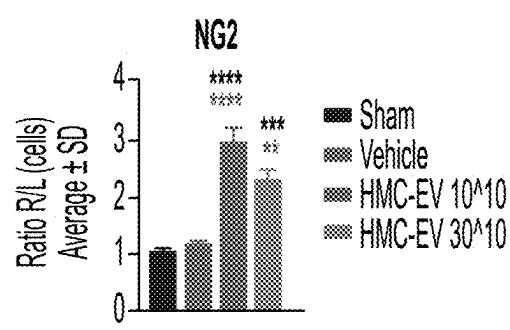


FIG. 31B

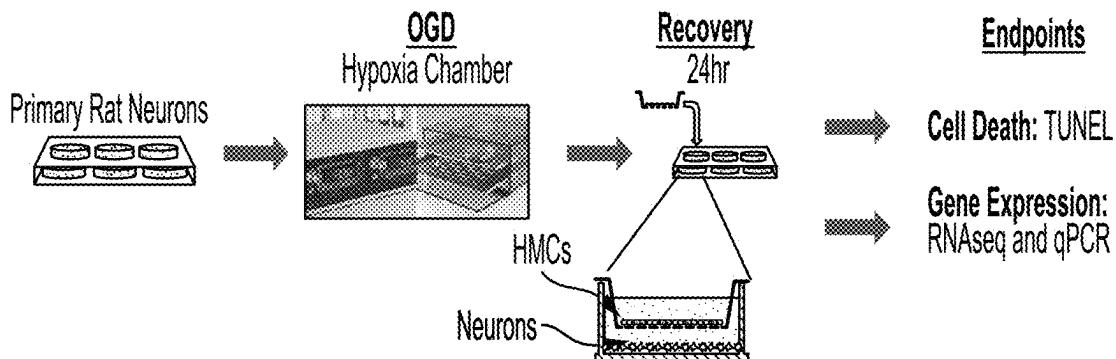


FIG. 32

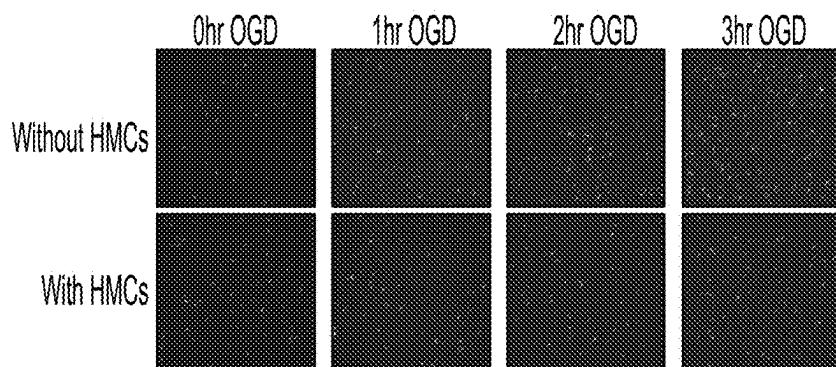


FIG. 33A

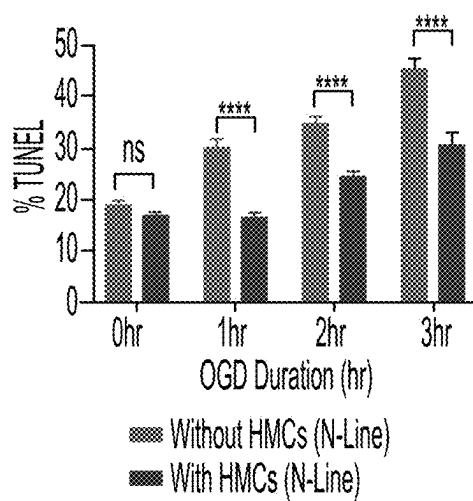


FIG. 33B

Top Canonical Pathways		p-value	Overlap
Name			
STAT3 Pathway	*	4.24E-11	19.7% 2612
Hepatic Fibrosis / Hepatic Stellate Cell Activation	*	5.14E-10	16.1% 2310
Cardiac Hypertrophy Signaling (Enhanced)	*	1.90E-08	9.8% 5161
CREB Signaling in Neurons	*	4.44E-08	9.4% 5359
LPS/IL-1 Mediated Inhibition of RXR Function	*	1.60E-07	12.6% 2223

FIG. 34A

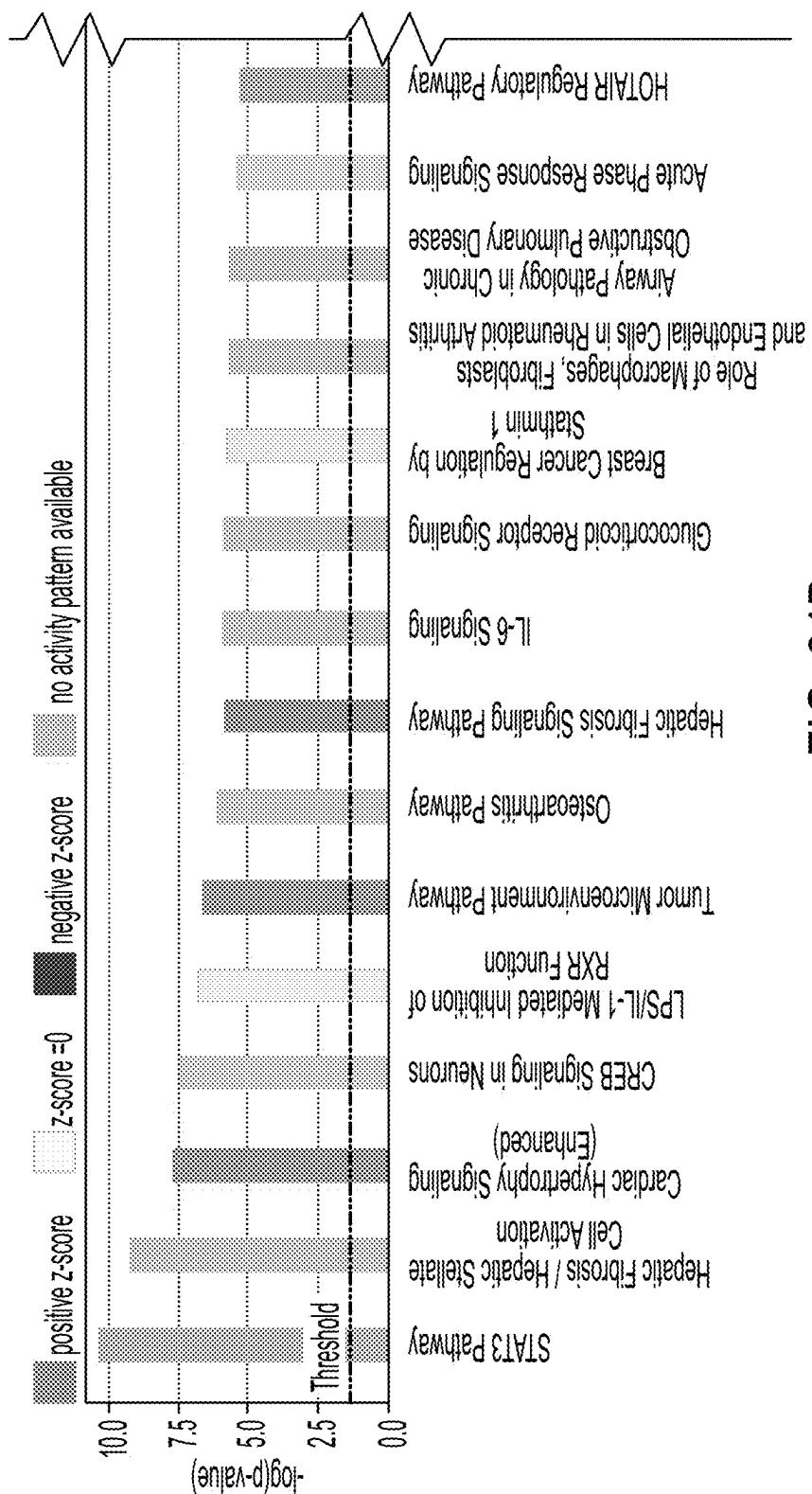


FIG. 34B

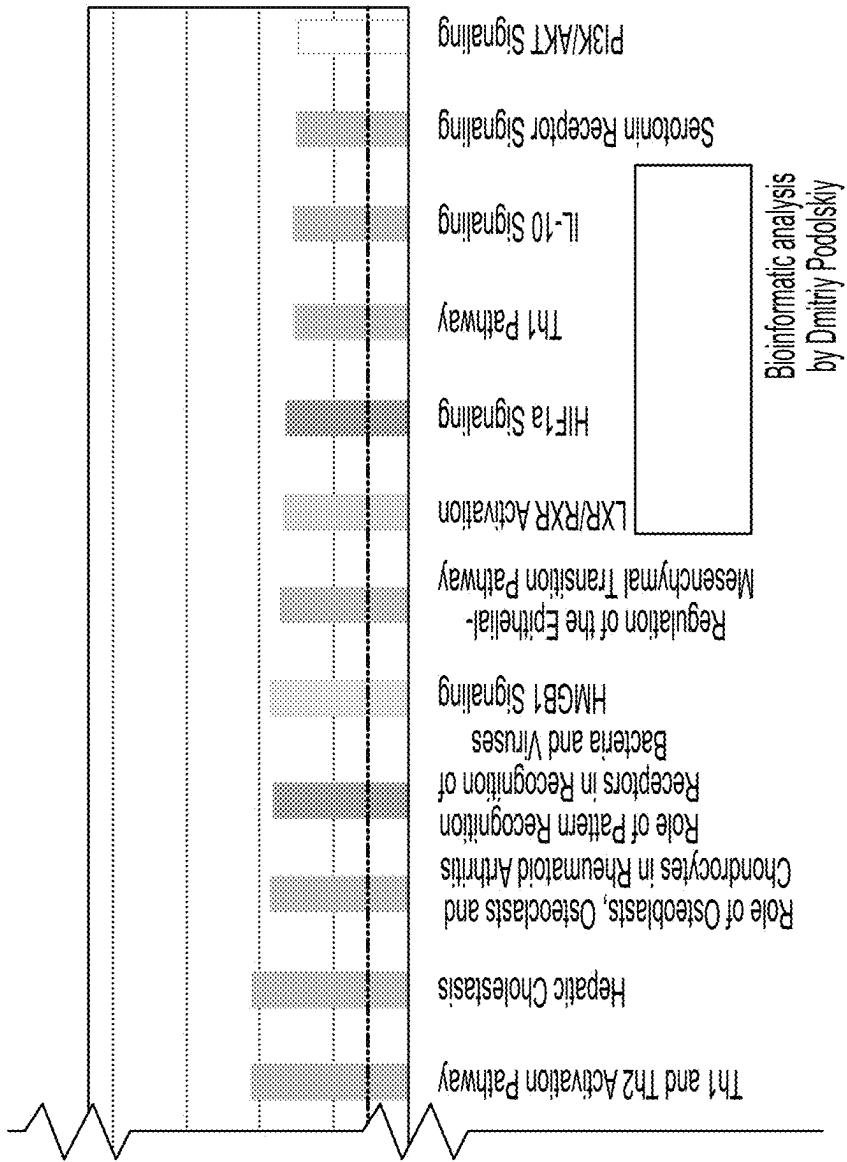


FIG. 34B
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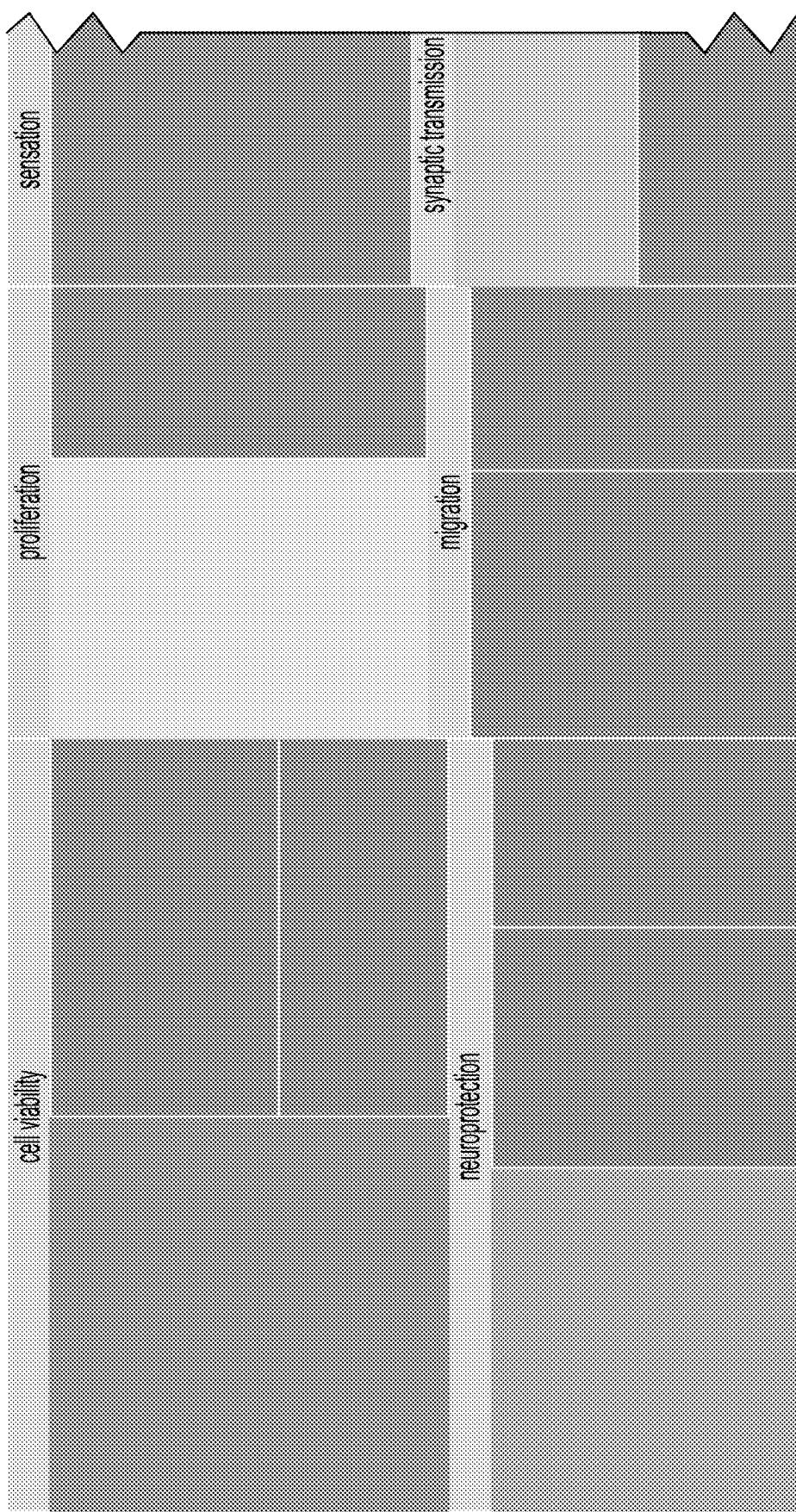


FIG. 34C

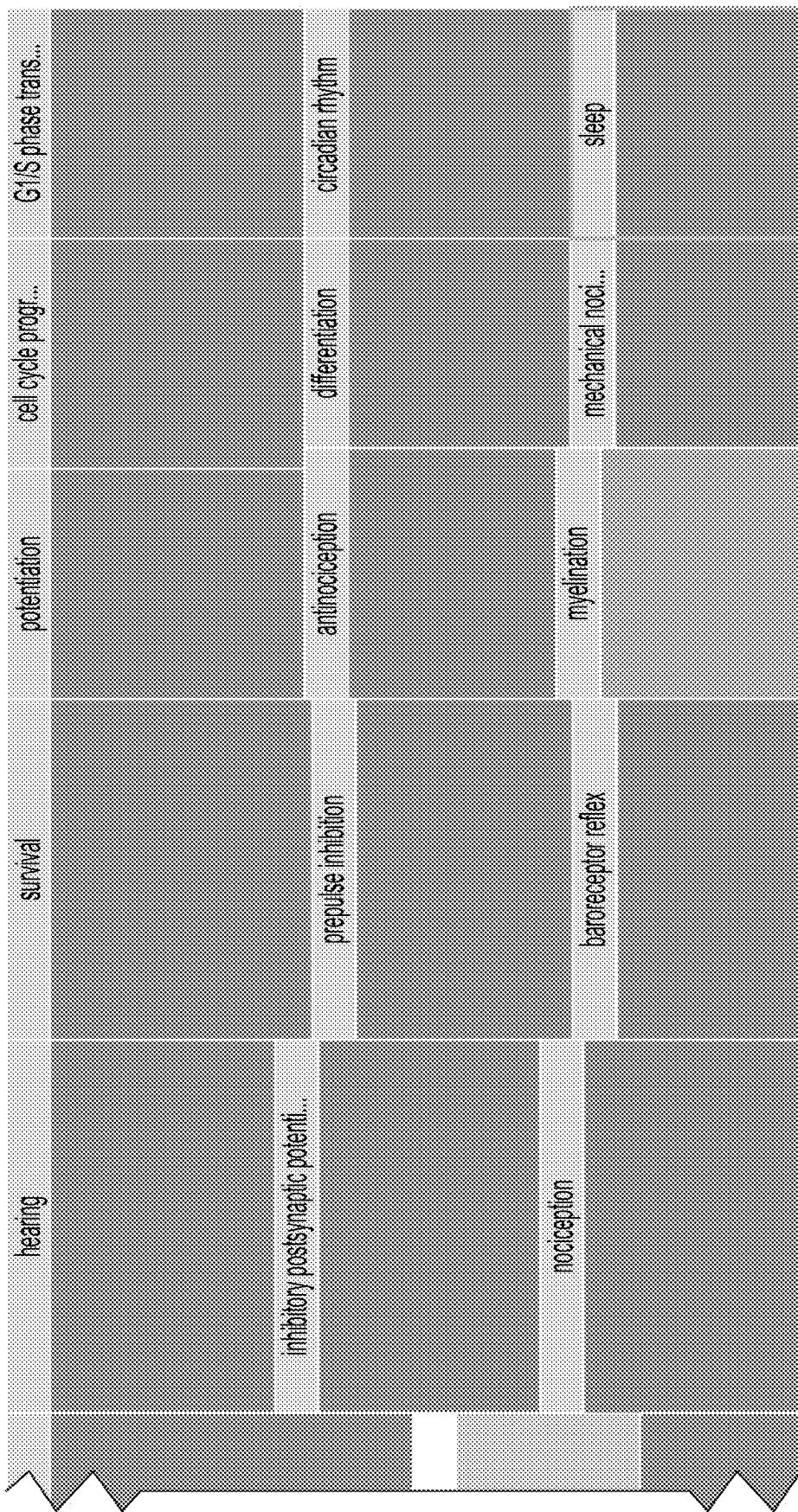


FIG. 34C
CONTINUED

ID	Genes in dataset	Prediction (based on meas...)	Expr Log Ratio	Findings
I27ra	ZTRK	Increased	1.976	Increases,
Adora2a	ADORA2A	Affected	1.886	Affects,
Fgf2	FGF2	Increased	1.325	Increases,
Stra3	STRA3	Decreased	1.153	Increases,
Nfatc4	NFKB1C	Increased	1.100	Increases,
Gm1	G1R	Decreased	-1.313	Increases,

FIG. 34D

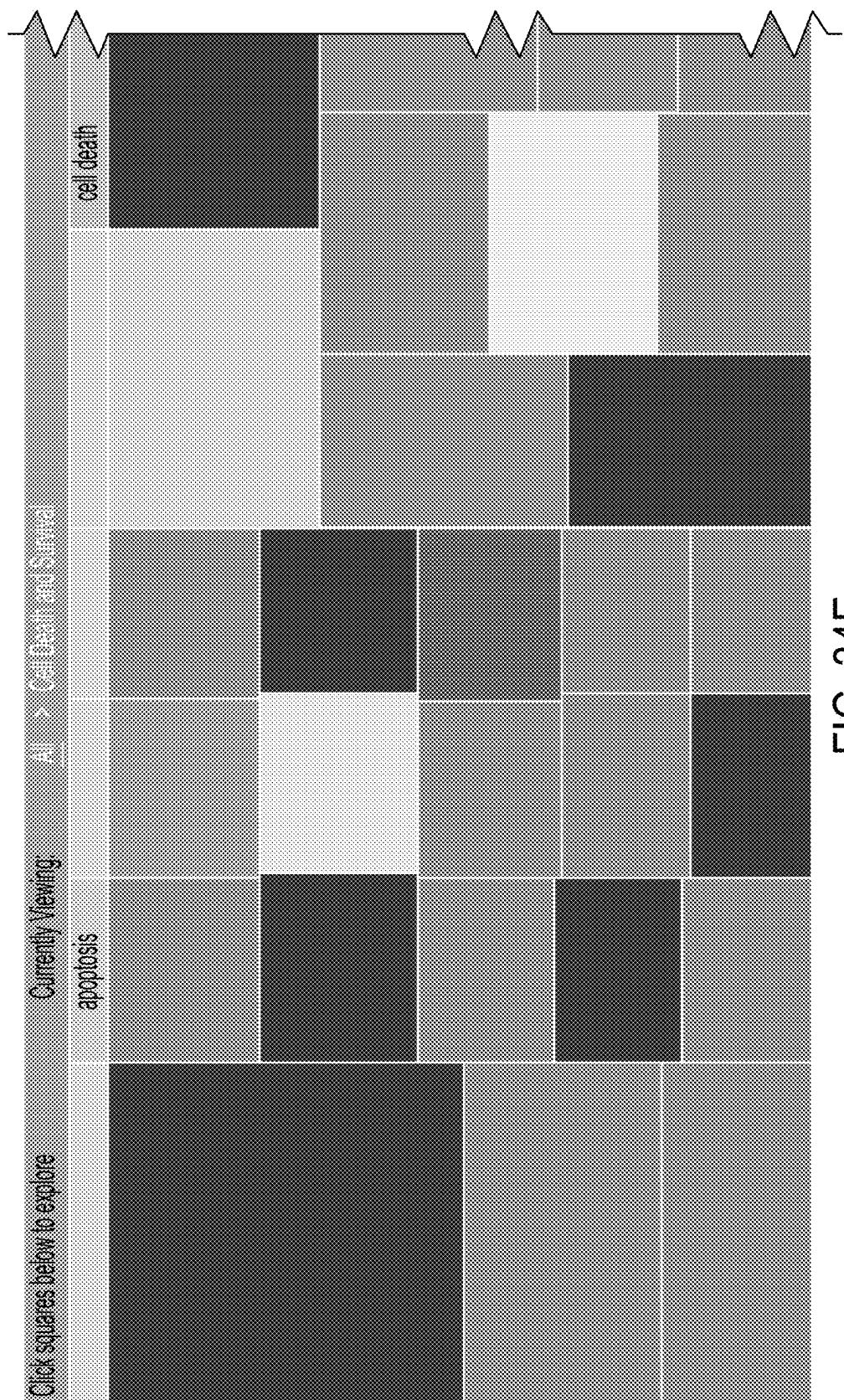


FIG. 34E

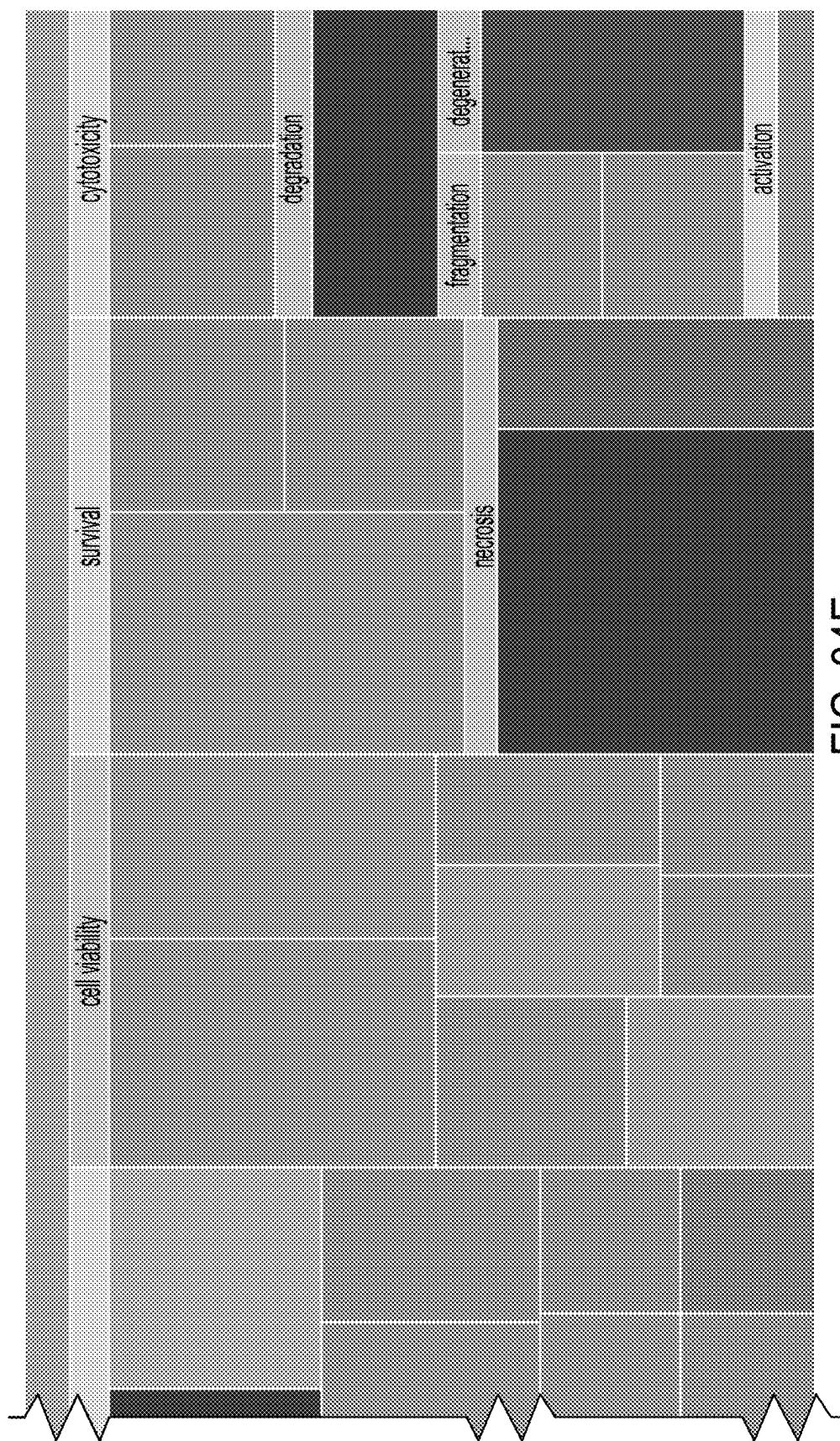


FIG. 34E
CONTINUED

ID	Genes in dataset	Prediction (based on meas...)	Expr Log Ratio	Findings
Igf2	GF2	Decreased	6.326	Decreases, (4)
Nos3	NOX	Decreased	3.222	Increases, (1)
Hspb1	HSF1	Decreased	2.980	Decreases, (6)
Cth	CTH	Decreased	2.860	Increases, (5)
Lcn2	LCN2	Increased	2.793	Increases, (3)
Aif3	AIF3	Decreased	2.499	Decreases, (7)
Spp1	SPP1	Decreased	2.484	Decreases, (6)
Osmr	OSMR	Decreased	2.474	Decreases, (6)
A2m	A2M	Increased	2.420	Increases, (0)
Ntk1	NTK1	Decreased	2.415	Decreases, (4)
Socs3	SOC3	Decreased	2.285	Decreases, (2)
Il18	IL18	Increased	2.208	Increases, (2)
Igfb3	IGFB3	Affected	2.054	Affects, (3)
Phf1h	PHF1H	Decreased	2.016	Decreases, (1)
Il1r1	IL1R1	Decreased	1.990	Decreases, (0)
Adm	ADM	Decreased	1.917	Decreases, (0)
Twist1	TWIST1	Decreased	1.858	Decreases, (0)
Thbs1	THBS1	Decreased	1.843	Decreases, (12)

FIG. 34F

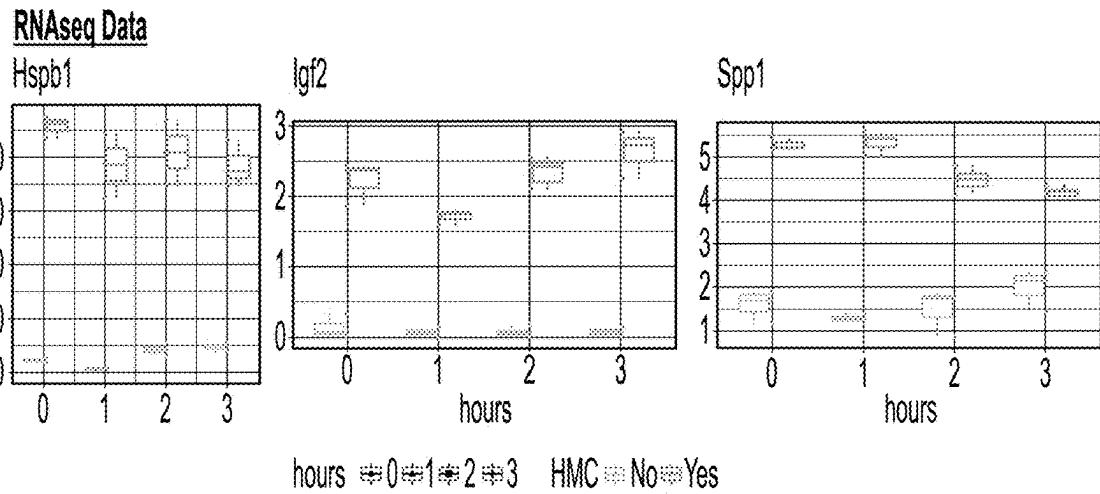


FIG. 35A

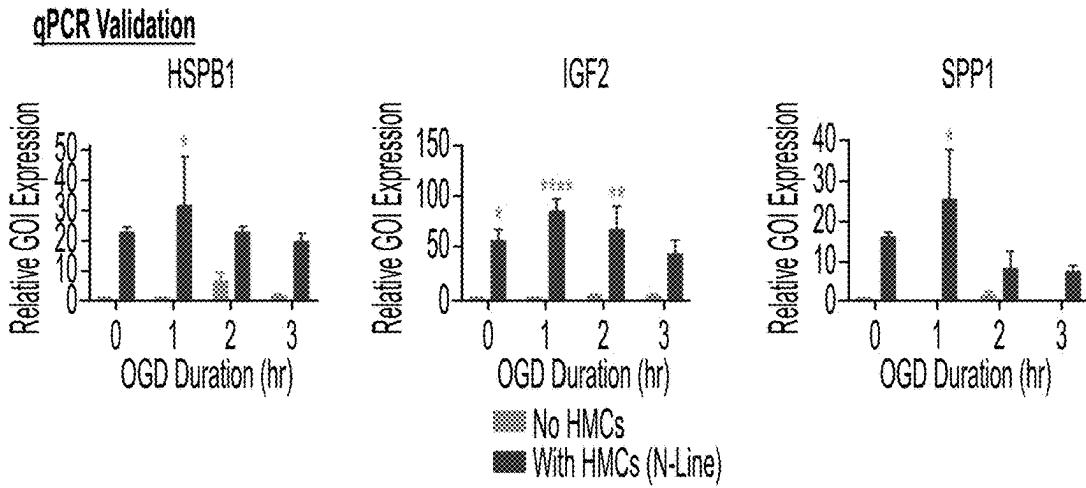


FIG. 35B

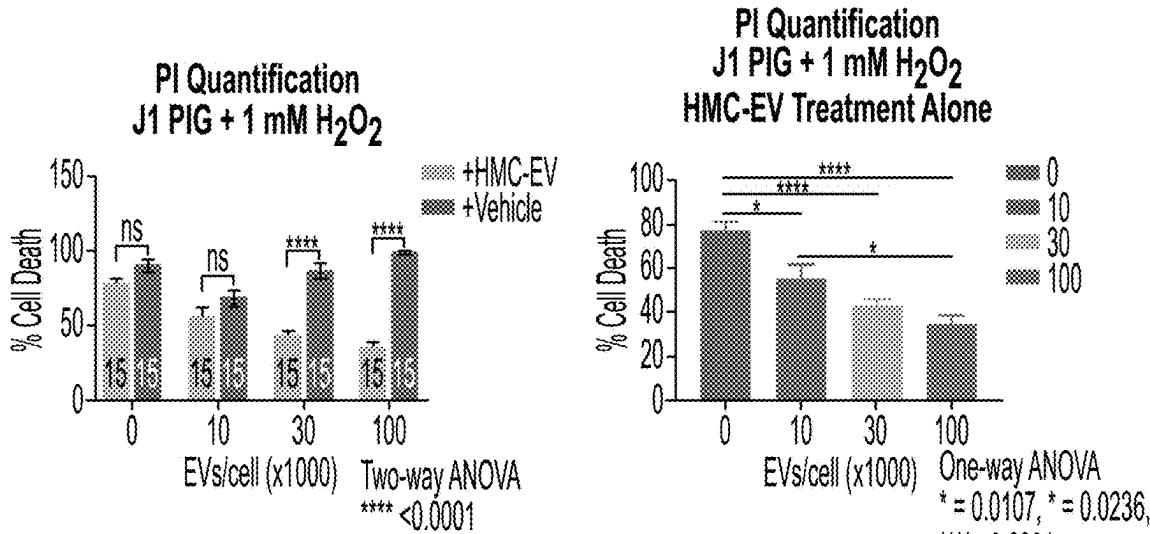


FIG. 36A

FIG. 36B

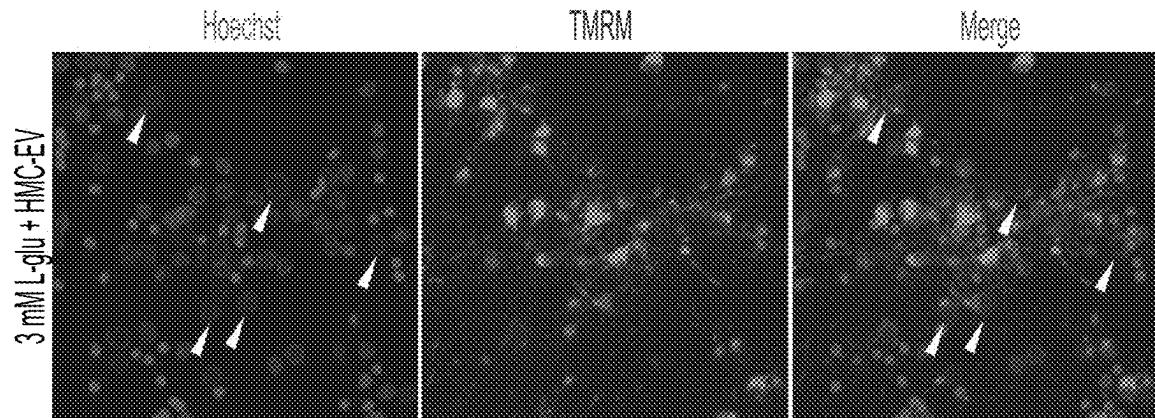


FIG. 37

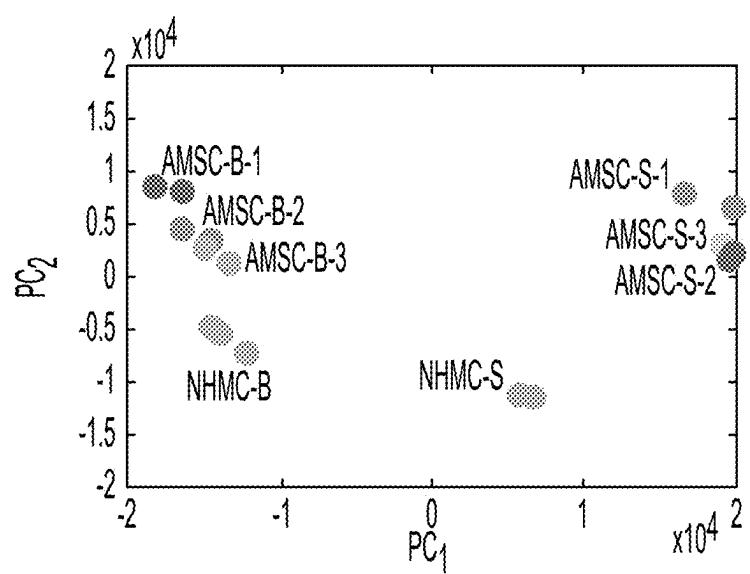


FIG. 38

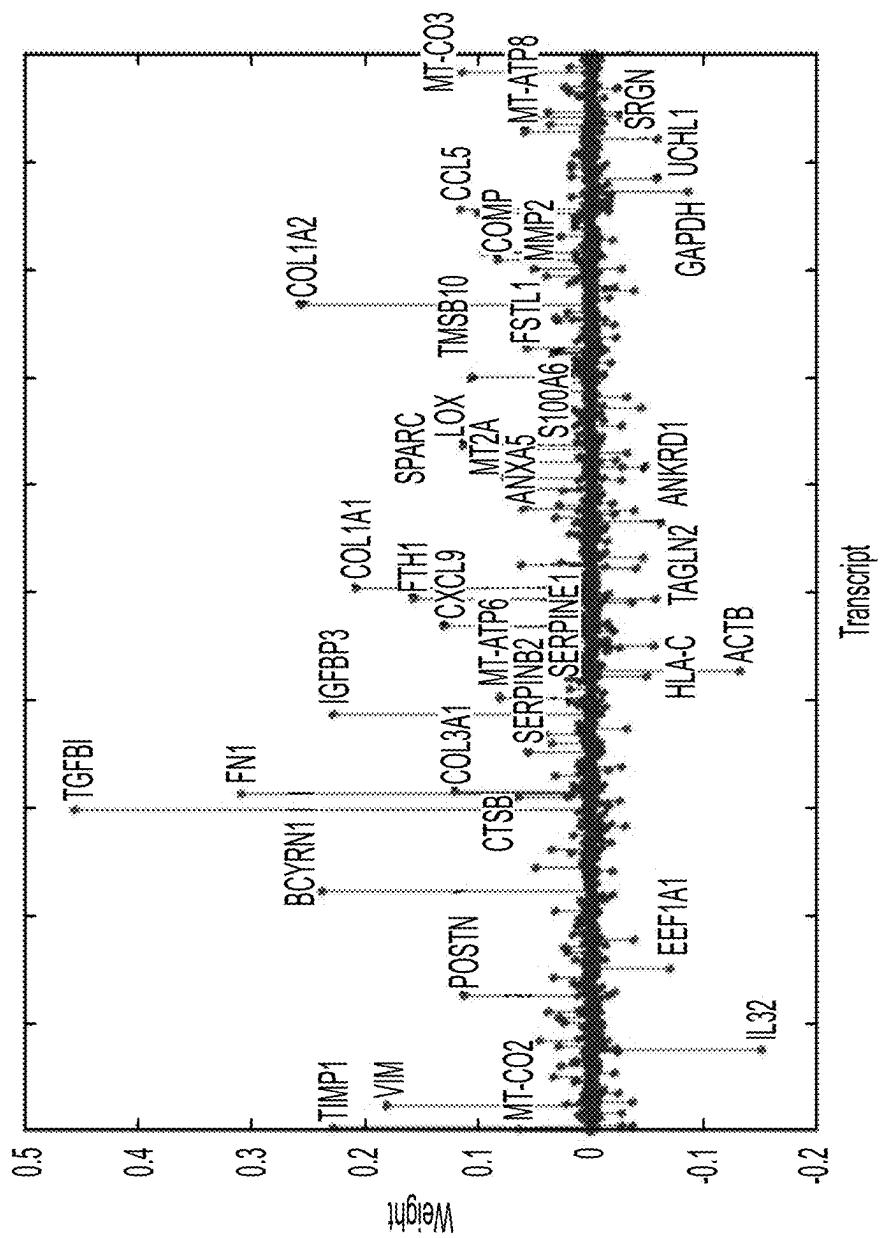


FIG. 39

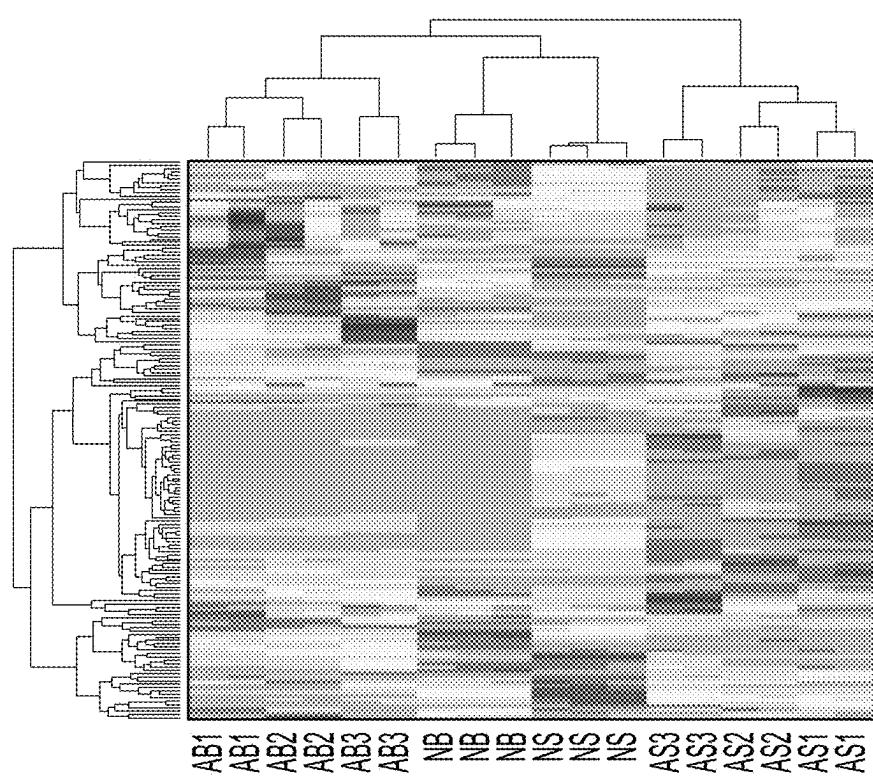


FIG. 40

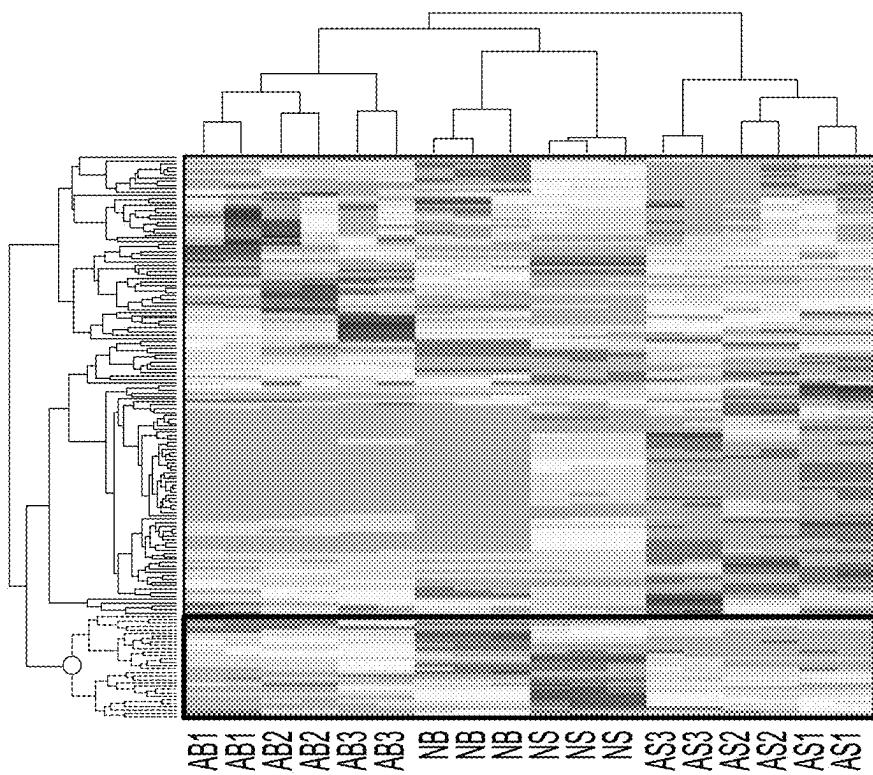


FIG. 41

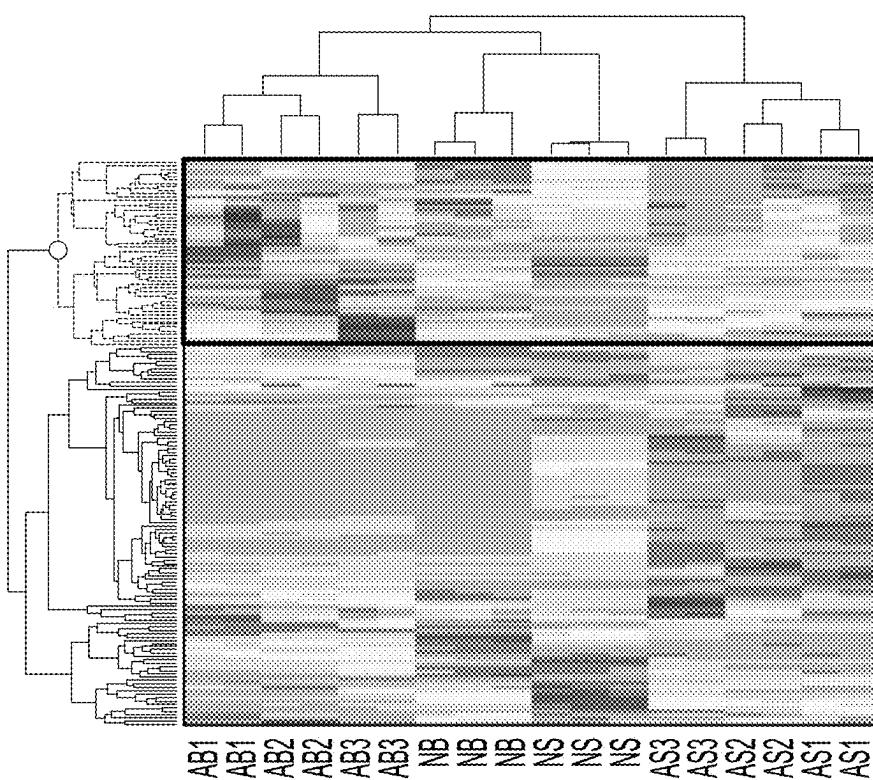


FIG. 42

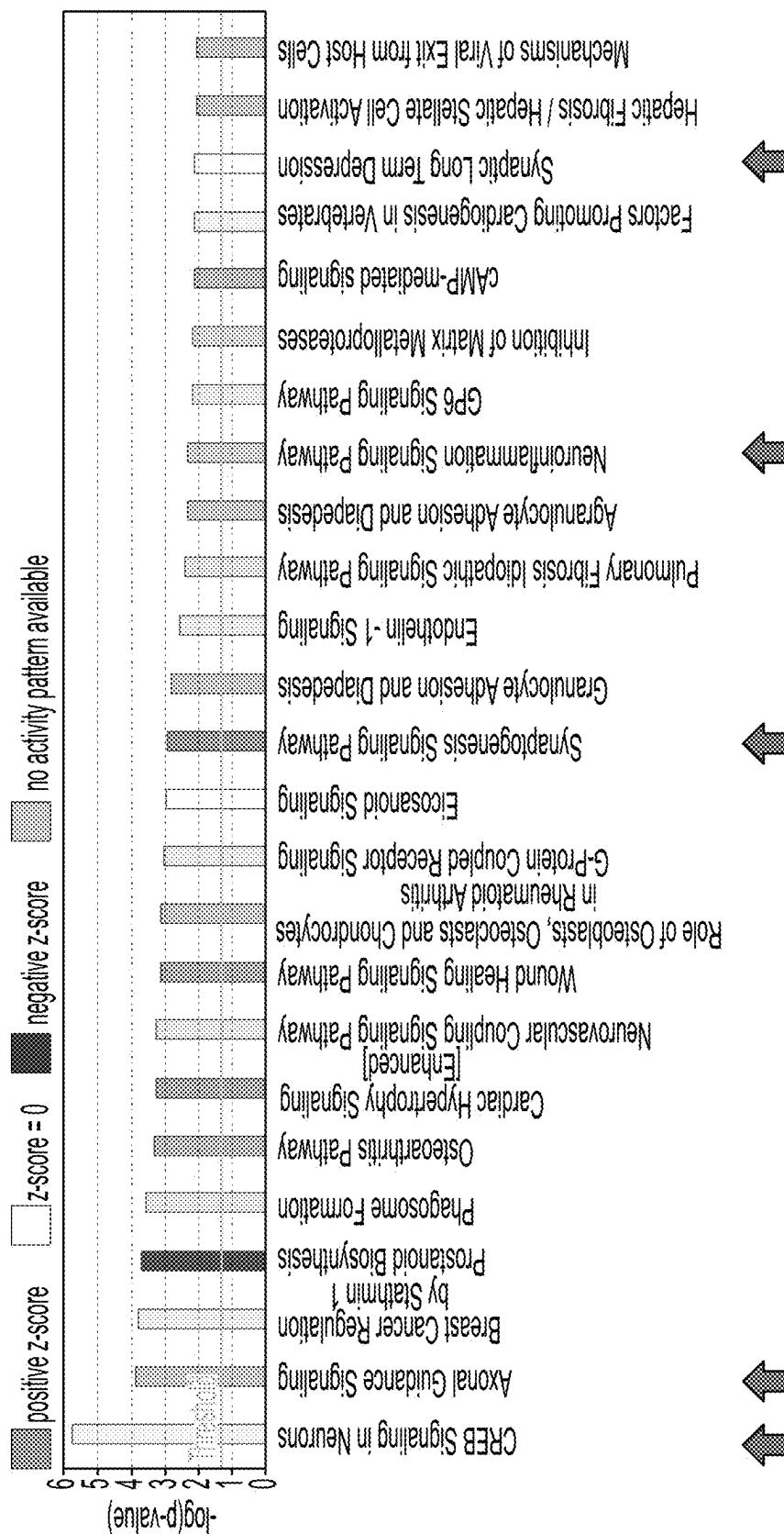


FIG. 43

Symbol	Entrez Gene Name	Measurement			Expected	Location
		Expr Log Ratio	+	X		
ADGRB3	adhesion G protein-coupled receptor B3	† 2.698	† Up	† Up	Plasma Membrane	
OPRD1	opioid receptor delta 1	† 2.358	† Up	† Up	Plasma Membrane	
CACNG4	calcium voltage-gated channel auxiliary subunit gamma 4	† 1.990	† Up	† Up	Plasma Membrane	
FZD_0	frizzled class receptor 10	† 1.903	† Up	† Up	Plasma Membrane	
TGFB2	transforming growth factor beta 2	† 1.852	† Up	† Up	Extracellular Space	
PLCH2	phospholipase C eta 2	† 1.790	† Up	† Up	Cytoplasm	
LPAR4	lysophosphatidic acid receptor 4	† 1.553	† Up	† Up	Plasma Membrane	
GPRC5D	G protein-coupled receptor class C group 5 member D	† 1.537	† Up	† Up	Plasma Membrane	
GLP2R	glucagon like peptide 2 receptor	† 1.531	† Up	† Up	Plasma Membrane	
GPRC5C	G protein-coupled receptor class C group 5 member C	† 1.440	† Up	† Up	Plasma Membrane	
CHRNL3	cholinergic receptor muscarinic 3	† 1.415	† Up	† Up	Plasma Membrane	
GNAZ	G protein subunit alpha Z	† 1.402			Plasma Membrane	
GRIA1	glutamate ionotropic receptor AMPA type subunit 1	† 1.274	† Up	† Up	Plasma Membrane	
PRKCQ	protein kinase C theta	† 1.222	† Up	† Up	Cytoplasm	
SHC2	SHC adaptor protein 2	† 1.211			Cytoplasm	

FIG. 44

Symbol	Entrez Gene Name	✖ Measurement	✚ Expected	✖
		▼ Expr Log Ratio	✖	
DCC	DCC netrin 1 receptor	◆ 2.123		
FZD10	frizzled class receptor 10	◆ 1.903		
PLCH2	phospholipase C eta 2	◆ 1.790		
L1CAM	L1 cell adhesion molecule	◆ 1.667		
EFNA1	ephrin A1	◆ 1.569		
MMP7	matrix metallopeptidase 7	◆ 1.547		
EPHB2	EPH receptor B2	◆ 1.509		
GNAZ	G protein subunit alpha z	◆ 1.402		
EFNB2	ephrin B2	◆ 1.388		
PAK3	p21 (RAC1) activated kinase 3	◆ 1.326		
TUBB2B	tubulin beta 2B class IIb	◆ 1.303		
GLIS1	GLIS family zinc finger 1	◆ 1.287		
PRKCQ	protein kinase C theta	◆ 1.222		
EFNA2	ephrin A2	◆ 1.158		
SEMA3D	semaphorin 3D	◆ 1.131		

FIG. 45

Symbol	Entrez Gene Name	Measurement	Expected	+	X
				Expr Log Ratio	X
SYT14	synaptotagmin 14	◆ 2.235	↑ Up		
CDH18	cadherin 18	◆ 2.003	↑ Up		
SYT13	synaptotagmin 13	◆ 1.993	↑ Up		
NLGN4Y	neuroligin 4Y-linked	◆ 1.735	↑ Up		
RASGRF1	Ras protein specific guanine nucleotide releasing factor 1	◆ 1.651	↑ Up		
EFNA1	ephrin A1	◆ 1.569	↑ Up		
EPHB2	EPH receptor B2	◆ 1.509	↑ Up		
CDH3	cadherin 3	◆ 1.491	↑ Up		
CADM1	cell adhesion molecule 1	◆ 1.399	↑ Up		
EFNB2	ephrin B2	◆ 1.388	↑ Up		
SHF	Src homology 2 domain containing F	◆ 1.301	↑ Up		
GRIA1	glutamate ionotropic receptor AMPA type subunit 1	◆ 1.274	↑ Up		
SNCA	synuclein alpha	◆ 1.218	↑ Up		
SHC2	SHC adaptor protein 2	◆ 1.211	↑ Up		
EFNA2	ephrin A2	◆ 1.158	↑ Up		

FIG. 46

Symbol	Entrez Gene Name	Measurement	+ Expected	X	Location	Expr Log Ratio	X
						▽	Expr Log Ratio
GABRB1	gamma-aminobutyric acid type A receptor subunit beta1	◆	1.896	◆ Up	Plasma Membrane		
TGFB2	transforming growth factor beta 2	◆	1.852	◆ Up	Extracellular Space		
GABRA3	gamma-aminobutyric acid type A receptor subunit alpha3	◆	1.492	◆ Up	Plasma Membrane		
GABRQ	gamma-aminobutyric acid type A receptor subunit theta	◆	1.477	◆ Up	Plasma Membrane		
GRIA1	glutamate-ionotropic receptor AMPA type subunit 1	◆	1.274	◆ Up	Plasma Membrane		
SNCA	synuclein alpha	◆	1.218	◆ Up	Cytoplasm		
BIRC7	baculoviral IAP repeat containing 7	◆	1.199	◆ Up	Cytoplasm		
S100B	S100 calcium binding protein B	◆	1.108	◆ Up	Cytoplasm		
NOX4	NADPH oxidase 4	◆	1.053	◆ Up	Cytoplasm		
PIK3R3	phosphoinositide-3-kinase regulatory subunit 3	◆	1.051	◆ Up	Cytoplasm		
MAPK15	mitogen-activated protein kinase 15	◆	1.050	◆ Up	Cytoplasm		
PLA2G5	phospholipase A2 group V	◆	-1.148	◆ Down	Extracellular Space		
NTF3	neurotrophin 3	◆	-1.207	◆ Down	Extracellular Space		
HMOX1	heme oxygenase 1	◆	-1.335	◆ Up	Cytoplasm		
RAK3	interleukin 1 receptor associated kinase 3	◆	-1.388	◆ Up	Cytoplasm		

FIG. 47

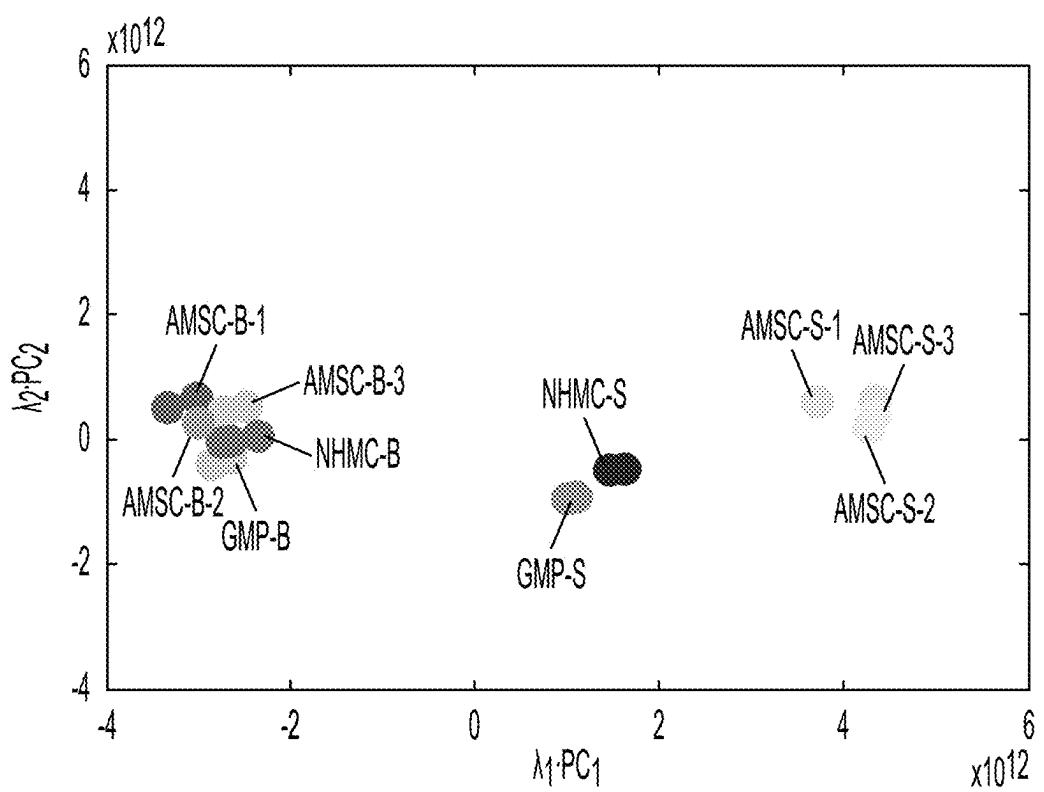


FIG. 48

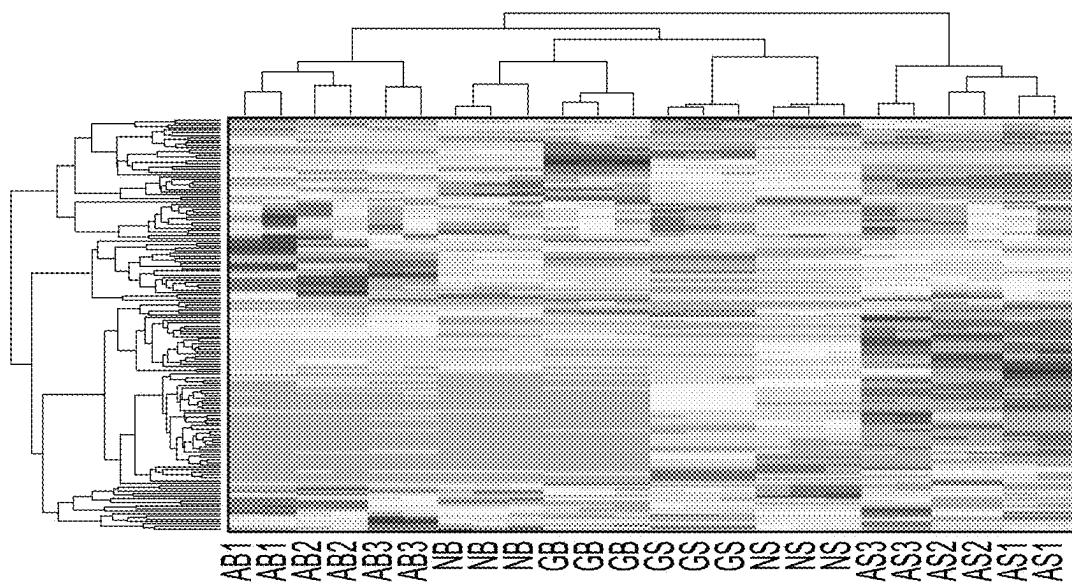


FIG. 49

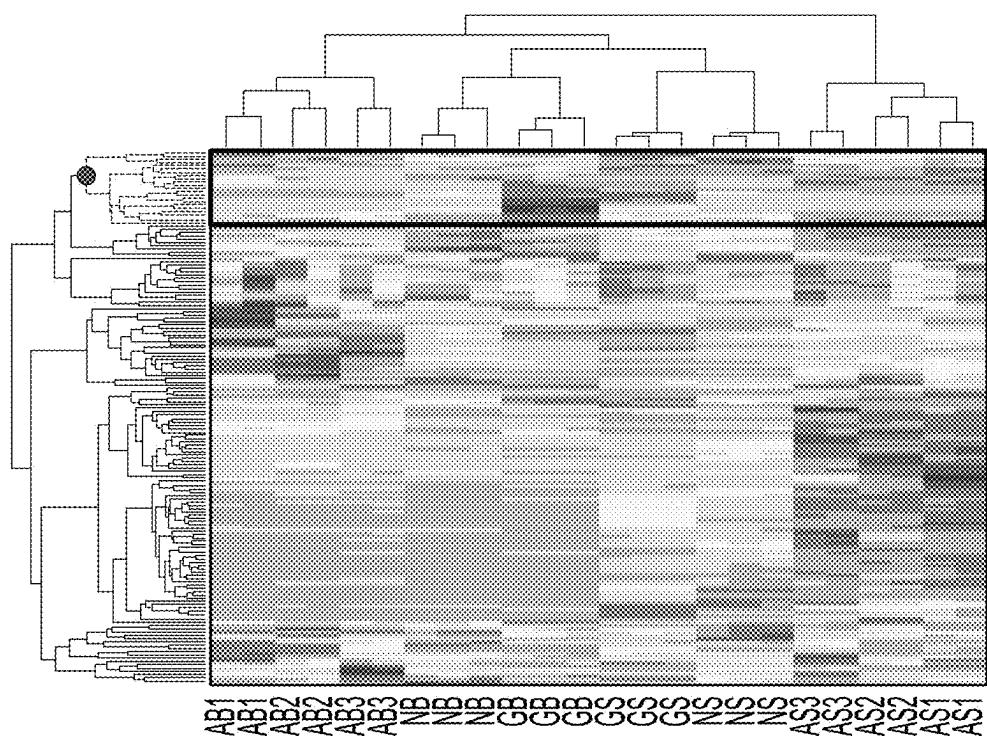


FIG. 50

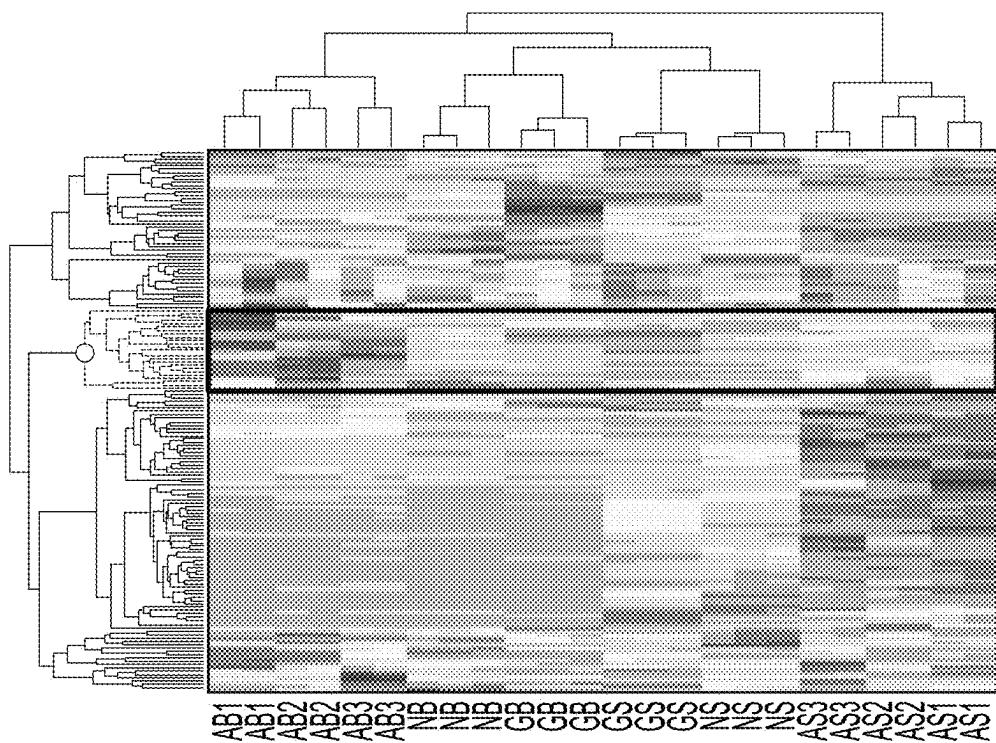


FIG. 51

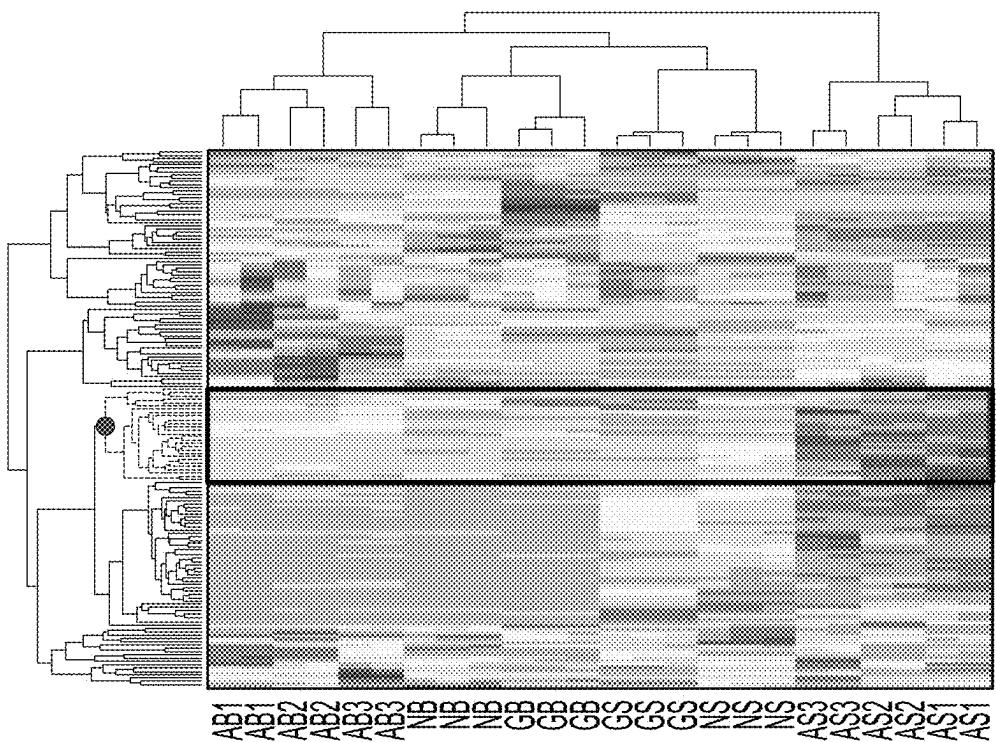


FIG. 52

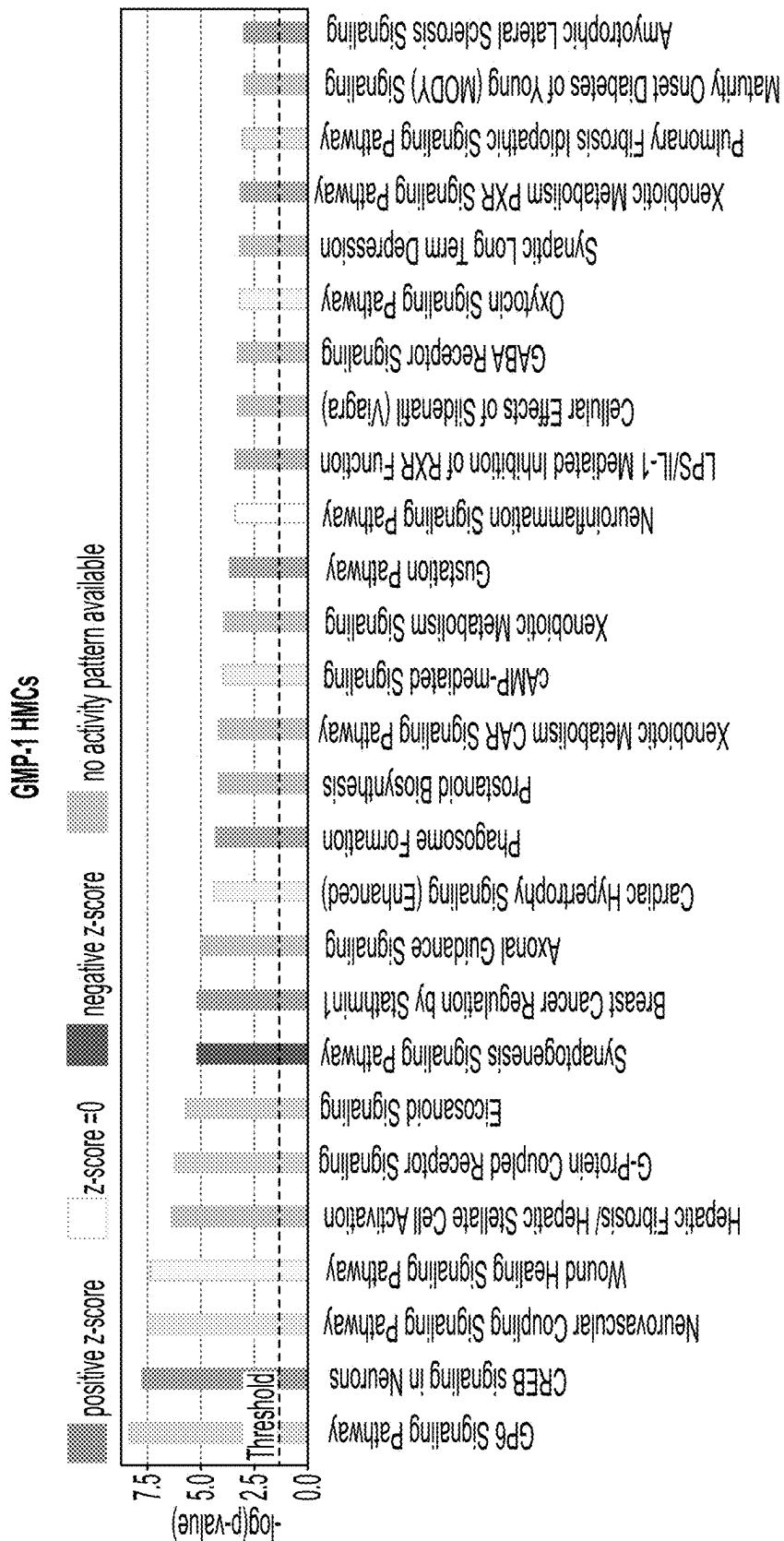


FIG. 53A

Top Canonical Pathways		Molecular and Cellular Functions		Physiological System Development and Function	
Name	p-value	Name	p-value range	Name	# Molecules
GPR Signaling Pathway	4.58E-09	Cellular Movement	9.19E-06 - 2.69E-09	Tissue Development	8.64E-05 - 2.23E-10
CREB Signaling in Neurons	1.83E-08	Cell-To-Cell Signaling and Interaction	2.61E-07 - 6.64E-09	Nervous System Development and Function	1.02E-05 - 6.64E-09
Neurovascular Coupling Signaling Pathway	3.59E-08	Molecular Transport	9.29E-05 - 6.39E-08	Cardiovascular System Development and Function	8.28E-05 - 8.25E-07
Wound Healing Signaling Pathway	4.35E-08	Carbohydrate Metabolism	4.84E-05 - 7.16E-06	Organ Morphology	2.99E-05 - 8.25E-07
Hepatic Fibrosis/Hepatic Stellate Cell Activation	4.39E-07	Small Molecule Biochemistry	9.29E-05 - 7.16E-06	Organismal Development	8.28E-05 - 8.25E-07

Overlap	
24/124	19.4 %
6/153	10.3 %
3/123	14.6 %
3/123	13.9 %
2/110	14.2 %

FIG. 53B

Upstream Regulator	Y	X	Expr Log Ratio	Y X	Molecule Type	Y	X	Predicted Activatio...
EWSPR1-FLJ11					fusion gene/product			Activated
GSTO1					enzyme			Activated
IL1B					cytokine			Activated
ZNF217					transcription regulator			Activated
PI3K(family)					group			Activated
IL1A					cytokine			Activated
CLOCK					transcription regulator			Activated
WNT5A					cytokine			Activated
Lh					complex			Activated
IL6			1.226		cytokine			Activated
CST5					other			Activated
FSH					complex			Activated
AURK					group			Activated
CCND1					transcription regulator			Activated
TWIST1					transcription regulator			Activated
ANLN					other			Activated
STAU1					transporter			Activated

FIG. 53C

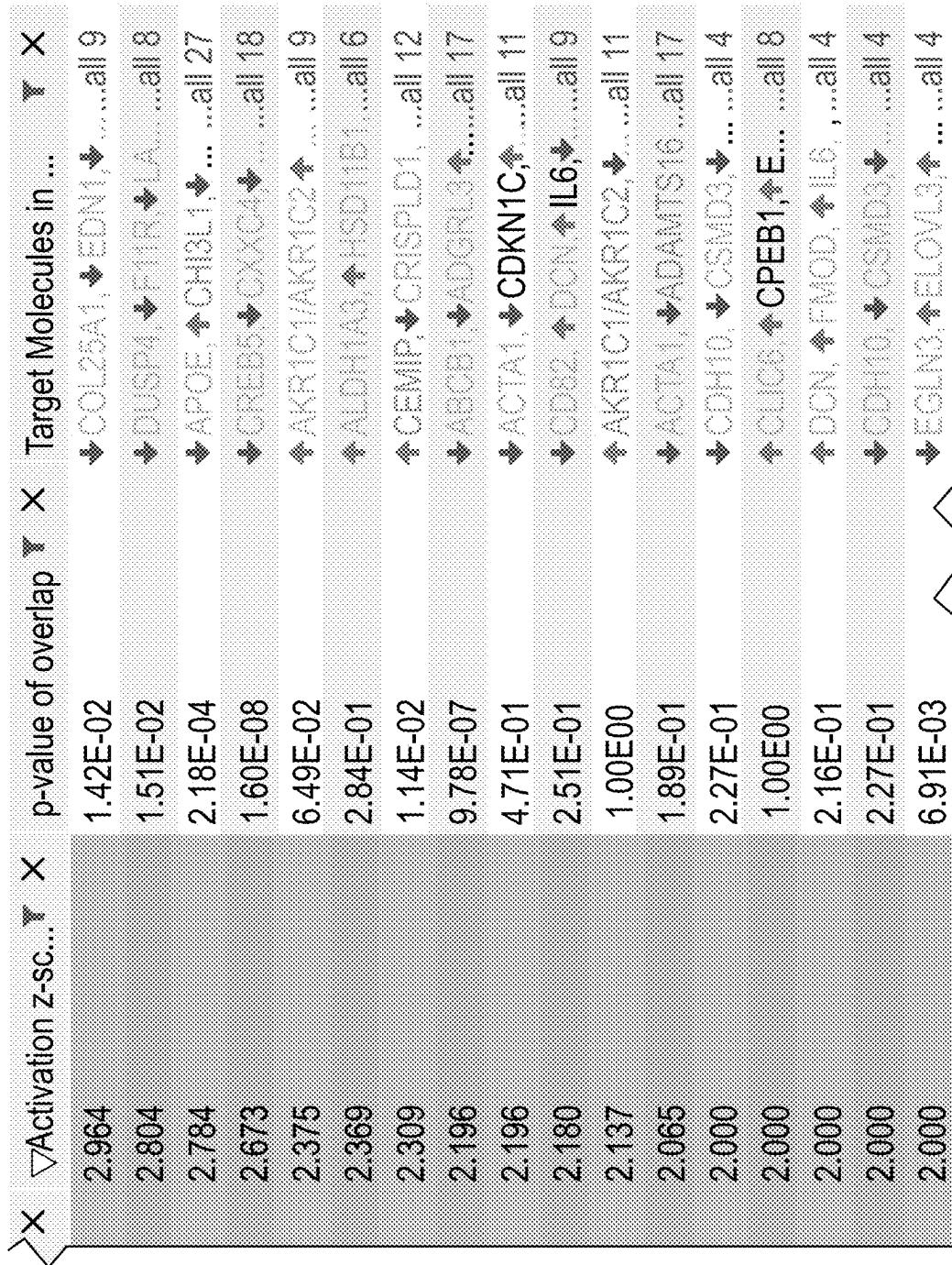


FIG. 53C
CONTINUED

IgG	Upstream Regulator	Expr Log Ratio	Molecule Type	Predicted Activatio...
ILF3			transcription regulator	Inhibited
MRTFB			transcription regulator	Inhibited
EOMES			transcription regulator	Inhibited
CCNS	♦ 1.594		growth factor	Inhibited
NR3C1			ligand-dependent nuclear r...	Inhibited
E2F3			transcription regulator	Inhibited
TP73			transcription regulator	Inhibited
PTEN			phosphatase	Inhibited
LINC00941			other	Inhibited
TEAD1			transcription regulator	Inhibited
TEAD4			transcription regulator	Inhibited
GPER1			G-protein coupled receptor	Inhibited
TEAD3			transcription regulator	Inhibited
PPP1R13L			transcription regulator	Inhibited
LMNA			other	Inhibited
TEAD2			transcription regulator	Inhibited

FIG. 53C
CONTINUED

\times	\triangle Activation Z-score	1.37E-02	p-value of overlap	\times	Target Molecules in ...
1.919	-2.789	6.83E-02		\downarrow CCND2, \downarrow EDN1, \downarrow ... all 14	
-2.555		3.87E-04		\downarrow C3AR1, \downarrow CH25H, \downarrow ... all 8	
-2.449		1.28E-02		\downarrow ANKRD1, \downarrow COL25A, ... all 11	
-2.433		1.21E-02		\downarrow ACTC1, \downarrow COL6A3, \downarrow ... all 7	
-2.398		2.85E-01		\downarrow CLDN, \downarrow FOXA1, \downarrow ... all 6	
-2.360		9.83E-02		\downarrow APOE, \downarrow CDKN1C, \downarrow ... all 23	
-2.261		9.79E-04		\downarrow ABCB1, \downarrow AKR1C1/AKR1C2, \downarrow ... all 9	
-2.183		2.51E-01		\downarrow CLDN, \downarrow FGF12, \downarrow IL6, ... all 5	
-2.000		1.28E-01		\downarrow FLG, \downarrow IGRBP5, \downarrow KR, ... all 4	
-2.000		2.49E-01		\downarrow EDN1, \downarrow GPR37, \downarrow IG, ... all 4	
-2.000		1.09E-01		\downarrow CGB3 (includes oth...), ... all 5	
-2.000		1.85E-01		\downarrow DJSP4, \downarrow EDN1, \downarrow E, ... all 4	
-2.000		1.75E-01		\downarrow EDN1, \downarrow GPR37, \downarrow IG, ... all 4	
-2.000		5.39E-03		\downarrow CCND2, \downarrow CLDN1, \downarrow ... all 4	
-2.000		3.37E-02		\downarrow CACNA1A, \downarrow KCNQ1, ... all 4	
-2.000		1.37E-01		\downarrow EDN1, \downarrow GPR37, \downarrow IG, ... all 4	

FIG. 53C
CONTINUED

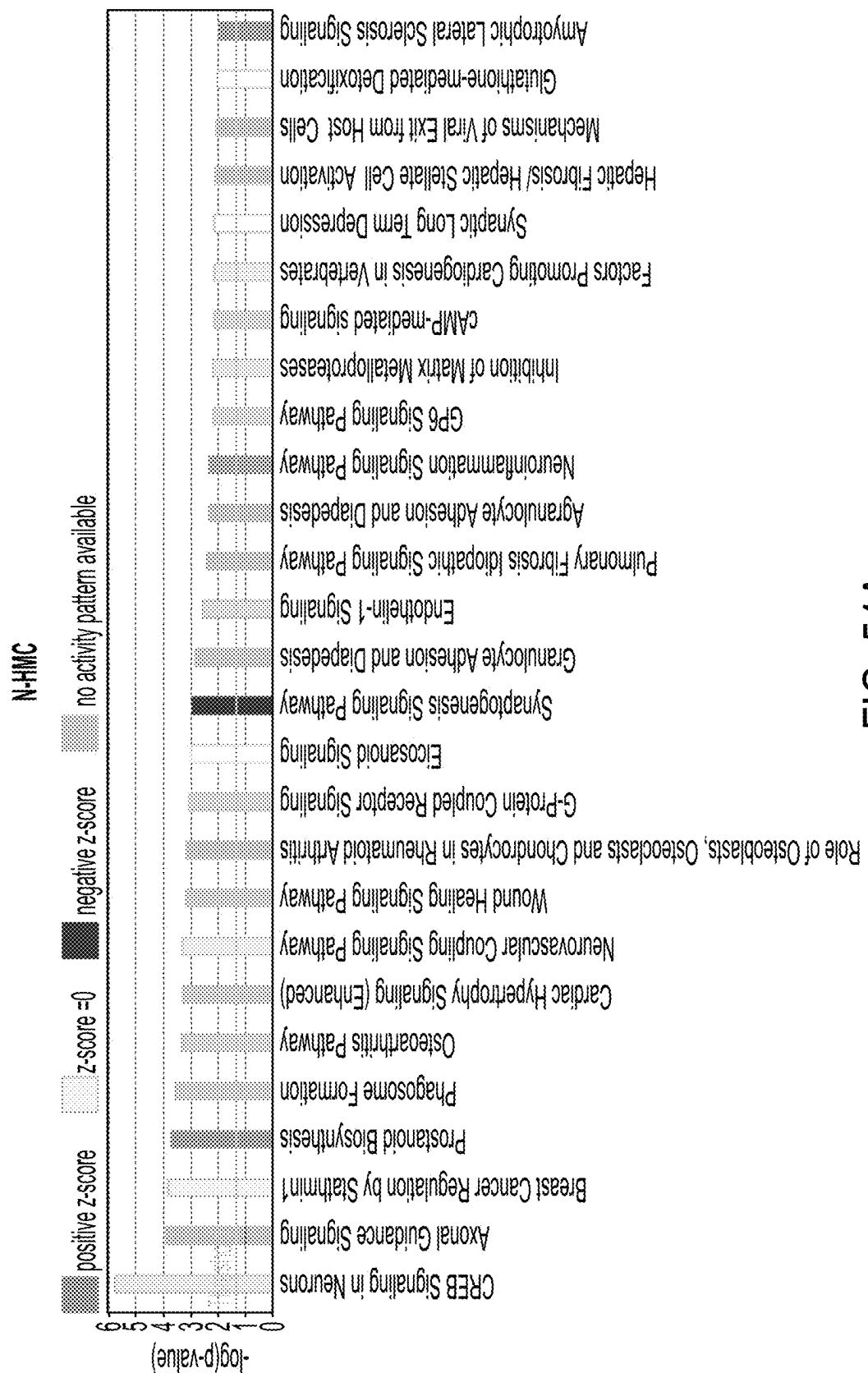
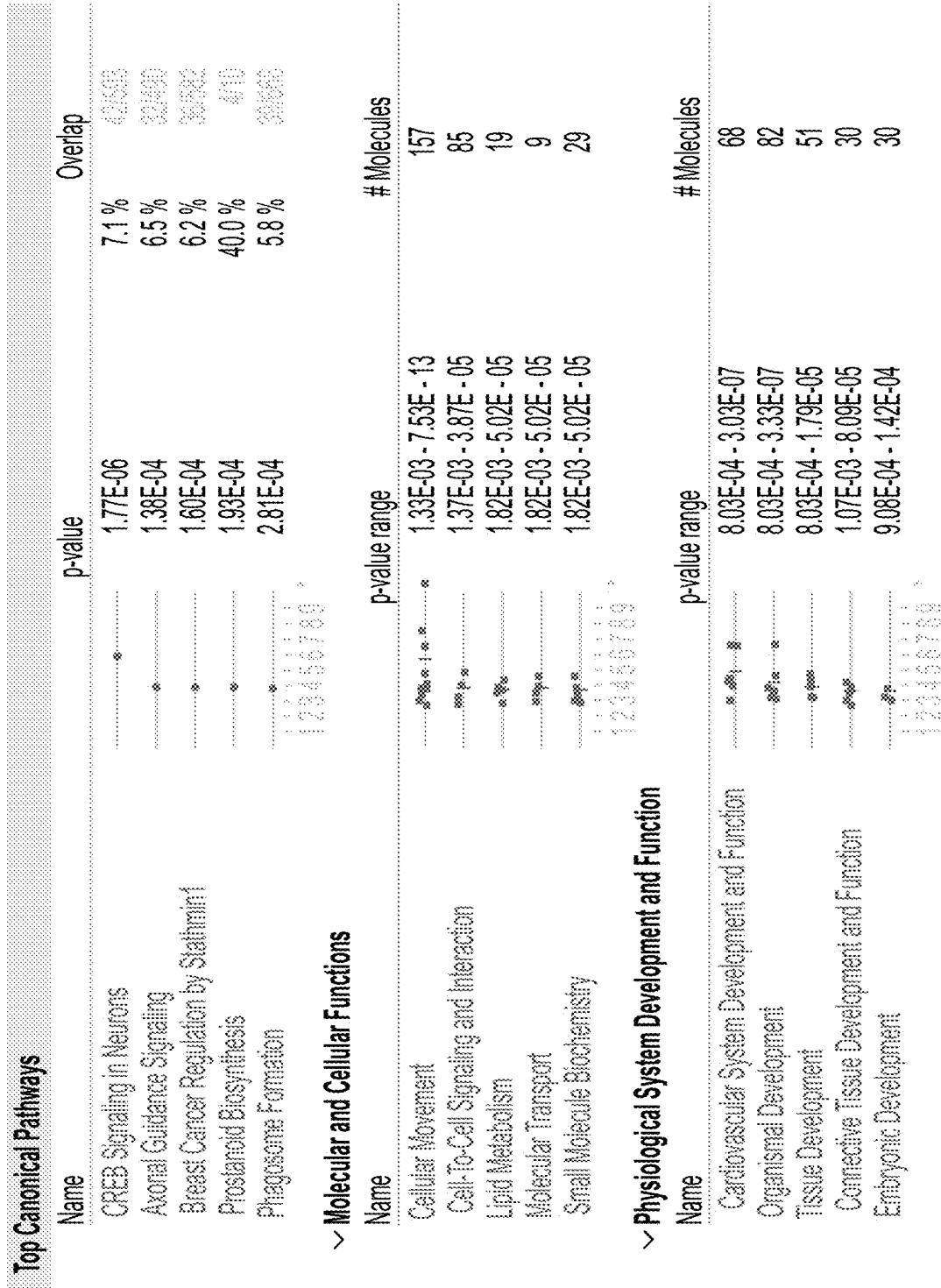


FIG. 54A


FIG. 54B

Upstream Regulator	Expr Log Ratio	Molecule Type	Predicted Activatio...
NUP98-DDX10		fusion gene/product	Activated
IL1B		cytokine	Activated
HOXB3	1.524	transcription regulator	Activated
IL1A		cytokine	Activated
STAT3		transcription regulator	Activated
IL13		cytokine	Activated
CLOCK		transcription regulator	Activated
ACSL5		enzyme	Activated
ERG	2.210	transcription regulator	Activated
CST5		other	
FSH		complex	
PI3K (Family)		group	
ZNF217		transcription regulator	
SPI1		transcription regulator	
TNF		cytokine	
IGF1	2.203	growth factor	

FIG. 54C

	∇	\times	Activation z-sc...	∇	\times	p-value of overlap	∇	\times	Target Molecules in ...	∇	\times
									Δ HOXA3, \blacklozenge HOXA5, \blacklozenge ... all 10		
3.162						1.42E-07			Δ A4GALT, \blacklozenge CHI3L1, \blacklozenge ... all 13		
2.693						1.10E-03			\blacklozenge HOXB4, \blacklozenge HOXB6, \blacklozenge ... all 5		
2.236						4.14E-08			\blacklozenge HSD11B1, \blacklozenge PTGES, \blacklozenge ... all 5		
2.216						1.78E-01			\blacklozenge CXCL5, \blacklozenge ... all 10		
2.168						2.00E-01			\blacklozenge ALDH1A2, \blacklozenge CCL26, \blacklozenge ... all 13		
2.040						9.58E-03			\blacklozenge CRISP1D1, \blacklozenge MCSF10, \blacklozenge ... all 4		
2.000						5.33E-01			\blacklozenge KCNUS, \blacklozenge MYRIP, \blacklozenge P, \blacklozenge ... all 4		
2.000						2.09E-03			\blacklozenge ARHGAP20, \blacklozenge ERG, \blacklozenge ... all 5		
2.000						1.00E00			\blacklozenge ANX43, \blacklozenge FBXO22, \blacklozenge ... all 4		
1.982						1.00E00			\blacklozenge ACTA1, \blacklozenge BCL11A, \blacklozenge ... all 13		
1.972						1.19E-01			\blacklozenge HMOX1, \blacklozenge MMP12, \blacklozenge ... all 4		
1.940						4.39E-01			\blacklozenge EPHX4, \blacklozenge HOXC6, \blacklozenge ... all 8		
1.890						3.26E-03			\blacklozenge ANK1, \blacklozenge C3S/CBSL1, \blacklozenge ... all 17		
1.868						1.50E-02			\blacklozenge A4GALT, \blacklozenge ADAMTS4, ... all 34		
1.783						8.35E-05			\blacklozenge EFNB2, \blacklozenge ELN, \blacklozenge IGF1, ... all 6		
1.591						1.61E-02					

FIG. 54C
CONTINUED

Upstream Regulator	Expr	Log Ratio	Molecule Type	Predicted Activatio...
INSR	Y	X	kinase	Inhibited
CCNS			growth factor	Inhibited
HAVCR1			Other	Inhibited
EOMES			transcription regulator	Inhibited
JUN			transcription regulator	Inhibited
CDK19			kinase	Inhibited
KDM1A			enzyme complex	Inhibited
IgG			transcription regulator	Inhibited
ILF3			transcription regulator	Inhibited
BCOR			transcription regulator	Inhibited
ARID1A				

FIG. 54C
CONTINUED

$\nabla \times \triangle$	Activation z-SC...	$\nabla \times$	p-value of overlap	$\nabla \times$	Target Molecules in ...
-2.742			1.38E-10		◆ CHRD, ◆ DPPA4, ◆ ... all 19
-2.219			9.29E-03		◆ CD2A, ◆ CLDN1, ◆ ... all 5
-2.216			1.15E-01		◆ ANPEP, ◆ CCNG3, ◆ C... ... all 6
-2.121			2.69E-04		◆ ACTC1, ◆ EGFLAM, ◆ ... all 8
-2.000			3.14E-02		◆ DIO2, ◆ DKK1, ◆ H... ... all 11
-1.982			3.41E-01		◆ HMOX1, ◆ KLF7, ◆ ... all 5
-1.964			1.35E-01		◆ DKK1, ◆ LGR5, ◆ MSX2 ... all 8
-1.951			5.36E-01		◆ LIPN, ◆ KRT3, ◆ ... all 5
-1.912			2.66E-02		◆ ALDH1A2, ◆ CD163L1, ... all 7
-1.744			1.50E-05		◆ CO18A1, ◆ COL18A1, ◆ ... all 9
-1.633			6.42E-03		◆ ALDH1A2, ◆ CD24, ◆ ... all 7

FIG. 54C
CONTINUED

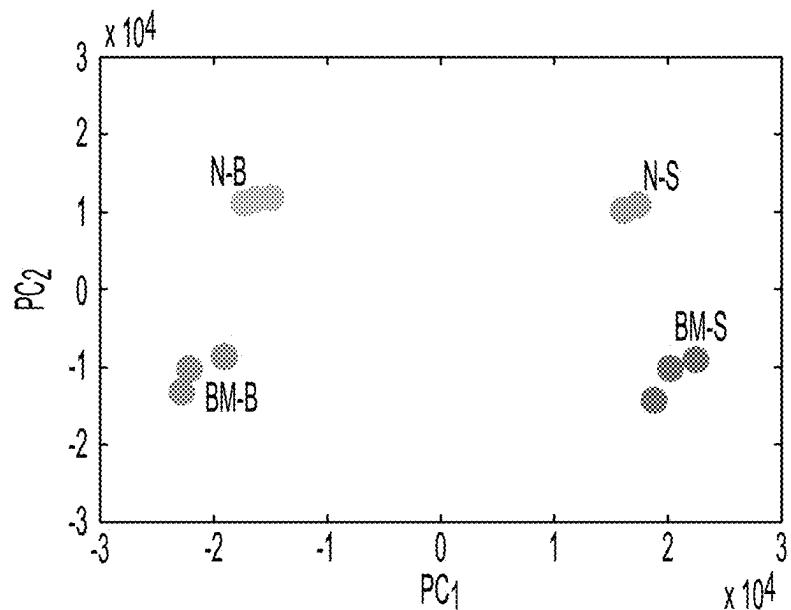


FIG. 55

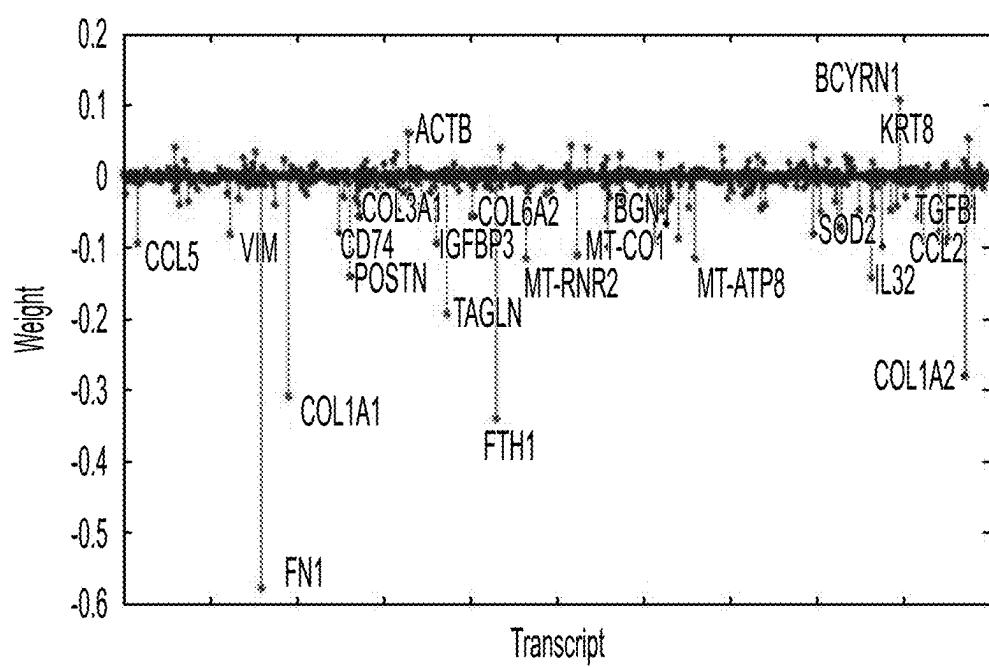


FIG. 56

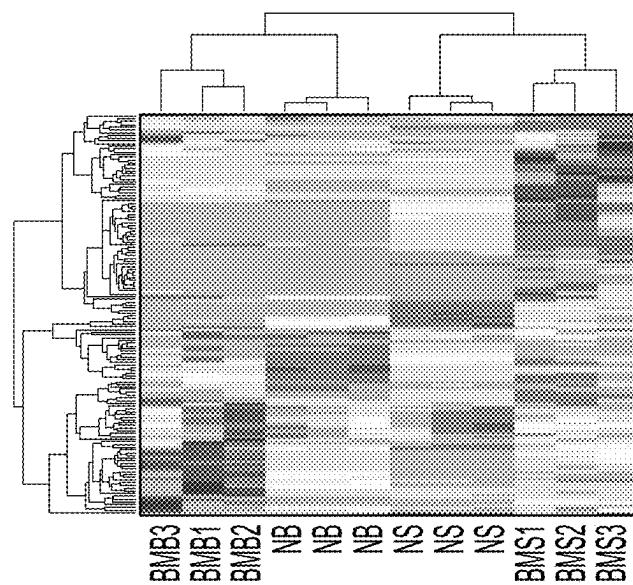


FIG. 57

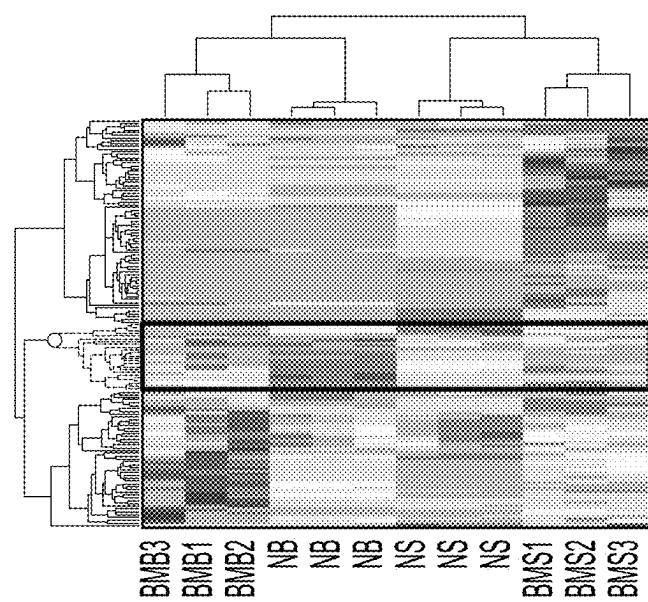


FIG. 58

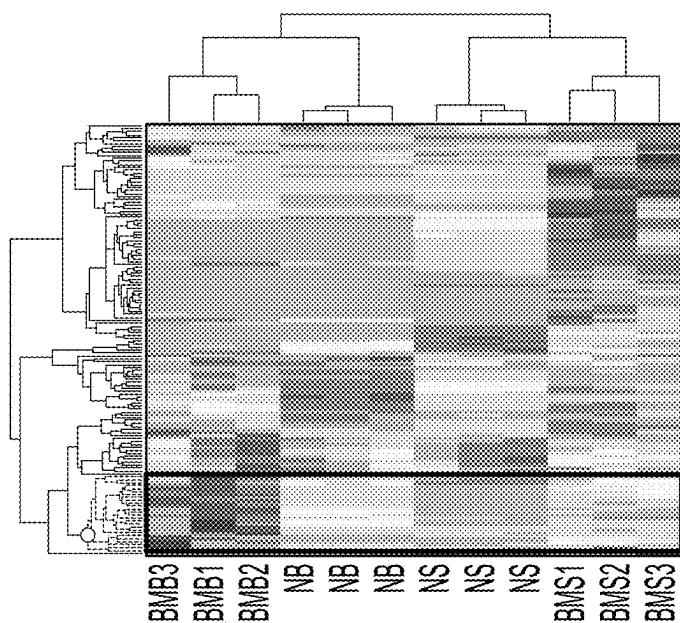


FIG. 59

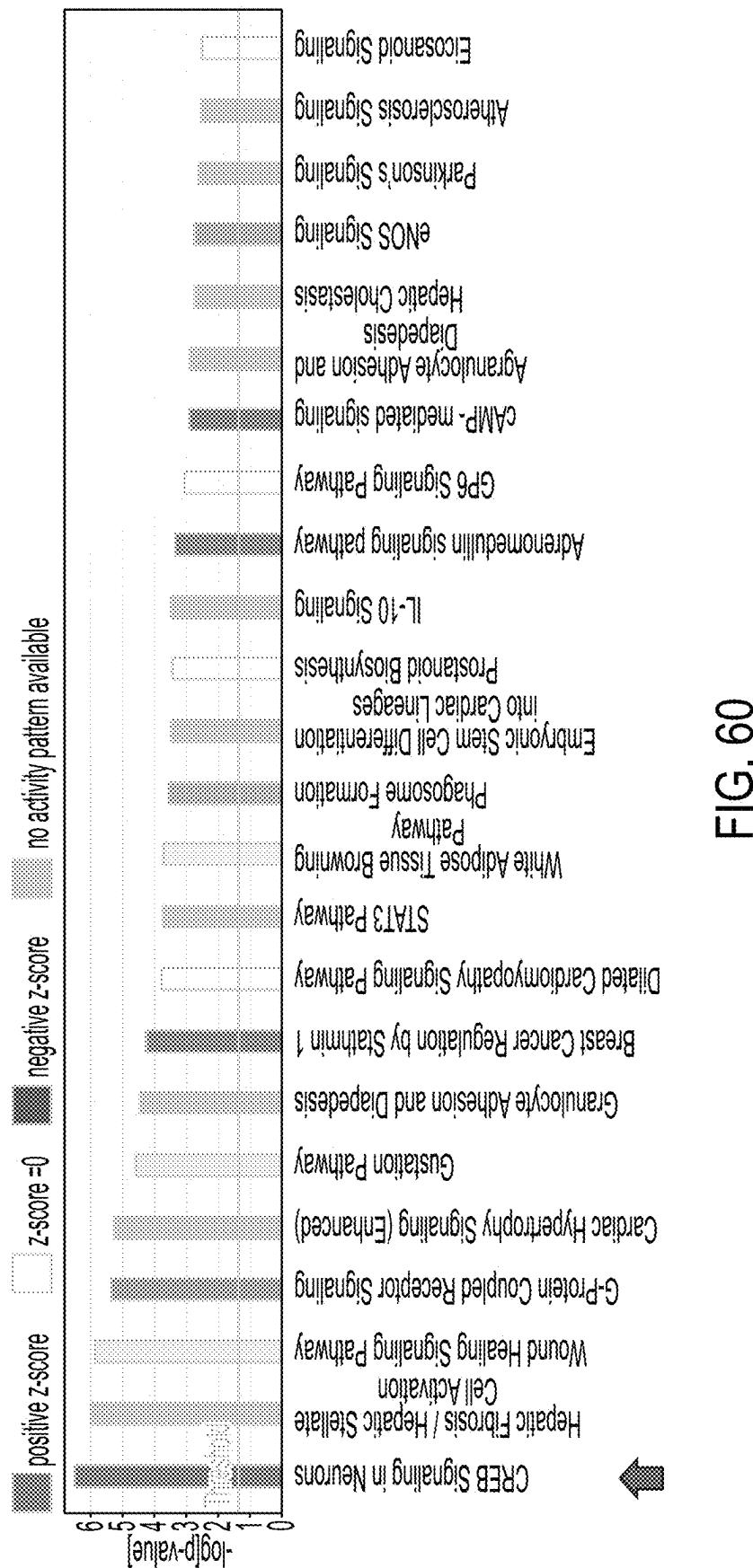


FIG. 60

Symbol	Entrez Gene Name	X	Identifier	+	Measurement	#	Expected	X	Location	X
			Gene Symbol - h...	X	▽ Expr Log Ratio	X				
GUCY1A3	guanylate cyclase 1 soluble subunit alpha 1	GUCY1A3		◆ 2.382					Cytoplasm	X
LPAR3	lysophosphatidic acid receptor 3	LPAR3		◆ 2.291		◆ Up			Plasma Membrane	
KDR	kinase insert domain receptor	KDR		◆ 2.111		◆ Up			Plasma Membrane	
ADGRB3	adhesion G protein-coupled receptor B3	ADGRB3		◆ 2.034		◆ Up			Plasma Membrane	
GPR143	G protein-coupled receptor 143	GPR143		◆ 1.916		◆ Up			Plasma Membrane	
SSTR1	somatostatin receptor 1	SSTR1		◆ 1.905		◆ Up			Plasma Membrane	
SUCNR1	succinate receptor 1	SUCNR1		◆ 1.794		◆ Up			Plasma Membrane	
FLT1	fms related receptor tyrosine kinase 1	FLT1		◆ 1.766		◆ Up			Plasma Membrane	
GPRC5B	G protein-coupled receptor class C group 5	GPRC5B		◆ 1.737		◆ Up			Plasma Membrane	
CHRM2	cholinergic receptor muscarinic 2	CHRM2		◆ 1.719		◆ Up			Plasma Membrane	
CHRM3	cholinergic receptor muscarinic 3	CHRM3		◆ 1.643		◆ Up			Plasma Membrane	
P2RY1	purinergic receptor P2Y1	P2RY1		◆ 1.602		◆ Up			Plasma Membrane	
GPR37	G protein-coupled receptor 37	GPR37		◆ 1.562		◆ Up			Plasma Membrane	

FIG. 61

Symbol	Entrez Gene Name	X	Measurement Expr Log Ratio	+	+	Expected X	X	Location
EPHA7	EPH receptor A7		◆ 2.634		◆ Up			Plasma Membrane
GUCY1A1	guanylate cyclase 1 soluble subunit alpha 1		◆ 2.382					Cytoplasm
SNCA	synuclein alpha		◆ 2.346		◆ Up			Cytoplasm
CDH10	cadherin 10		◆ 1.760		◆ Up			Plasma Membrane
SYT1	synaptotagmin 1		◆ 1.535		◆ Up			Cytoplasm
CADM1	cell adhesion molecule 1		◆ 1.533		◆ Up			Plasma Membrane
SYT9	synaptotagmin 9		◆ 1.230		◆ Up			Plasma Membrane
PRKAR2B	protein kinase cAMP-dependent type II regulatory		◆ 1.217		◆ Up			Cytoplasm
SHC3	SHC adaptor protein 3		◆ 1.122		◆ Up			Cytoplasm
CDH6	cadherin 6		◆ 1.110		◆ Up			Plasma Membrane
RELN	reelin		◆ 1.055		◆ Up			Extracellular Space
RASGRF1	Ras protein specific guanine nucleotide releasing		◆ 1.011		◆ Up			Cytoplasm
CAMK4	calcium/calmodulin dependent protein kinase V		◆ 1.006		◆ Up			Nucleus
EPHB3	EPH receptor B3		◆ -1.068		◆ Up			Plasma Membrane
ADCY5	adenylate cyclase 5		◆ -1.069		◆ Up			Plasma Membrane

FIG. 62

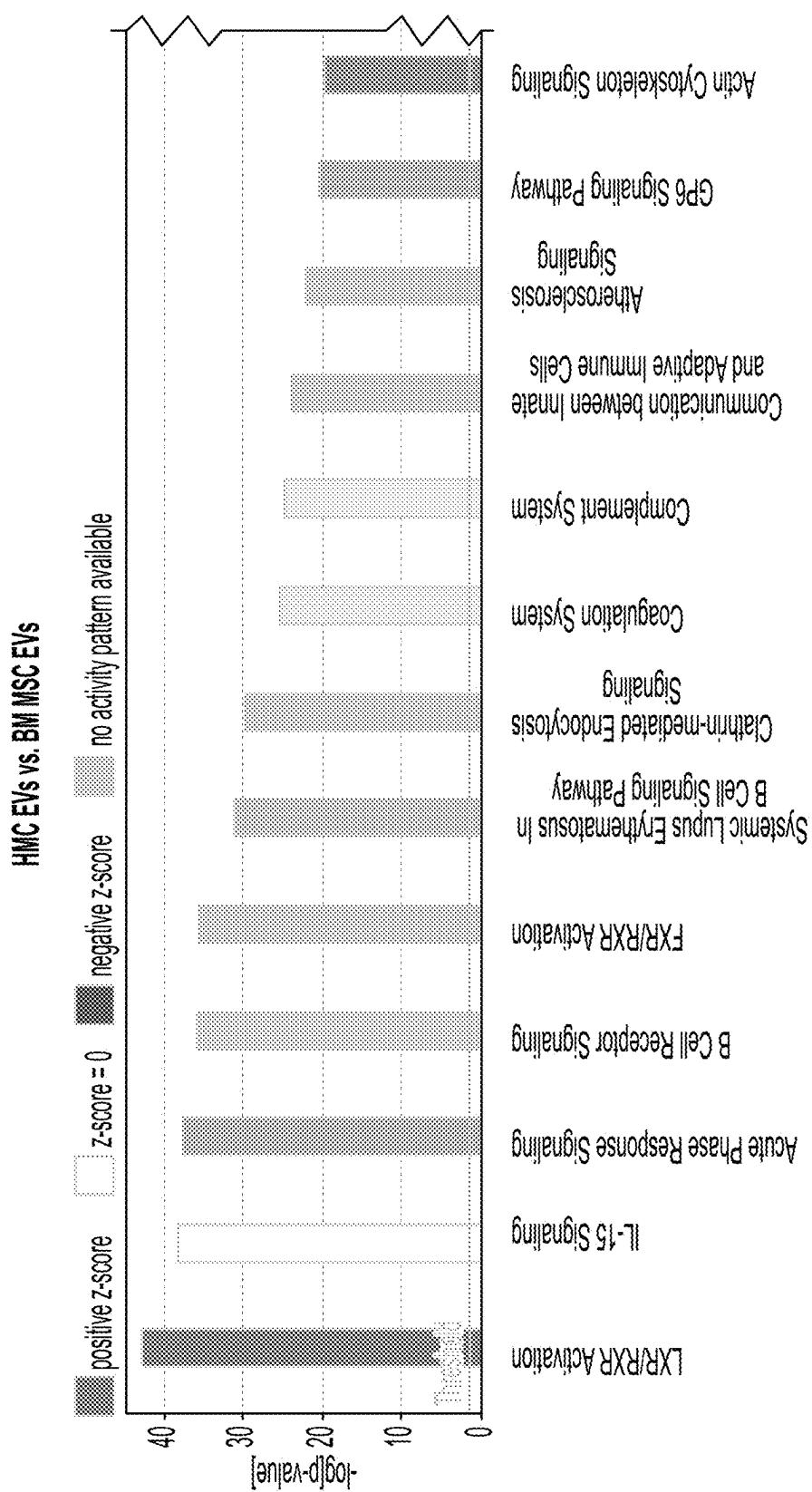


FIG. 63A

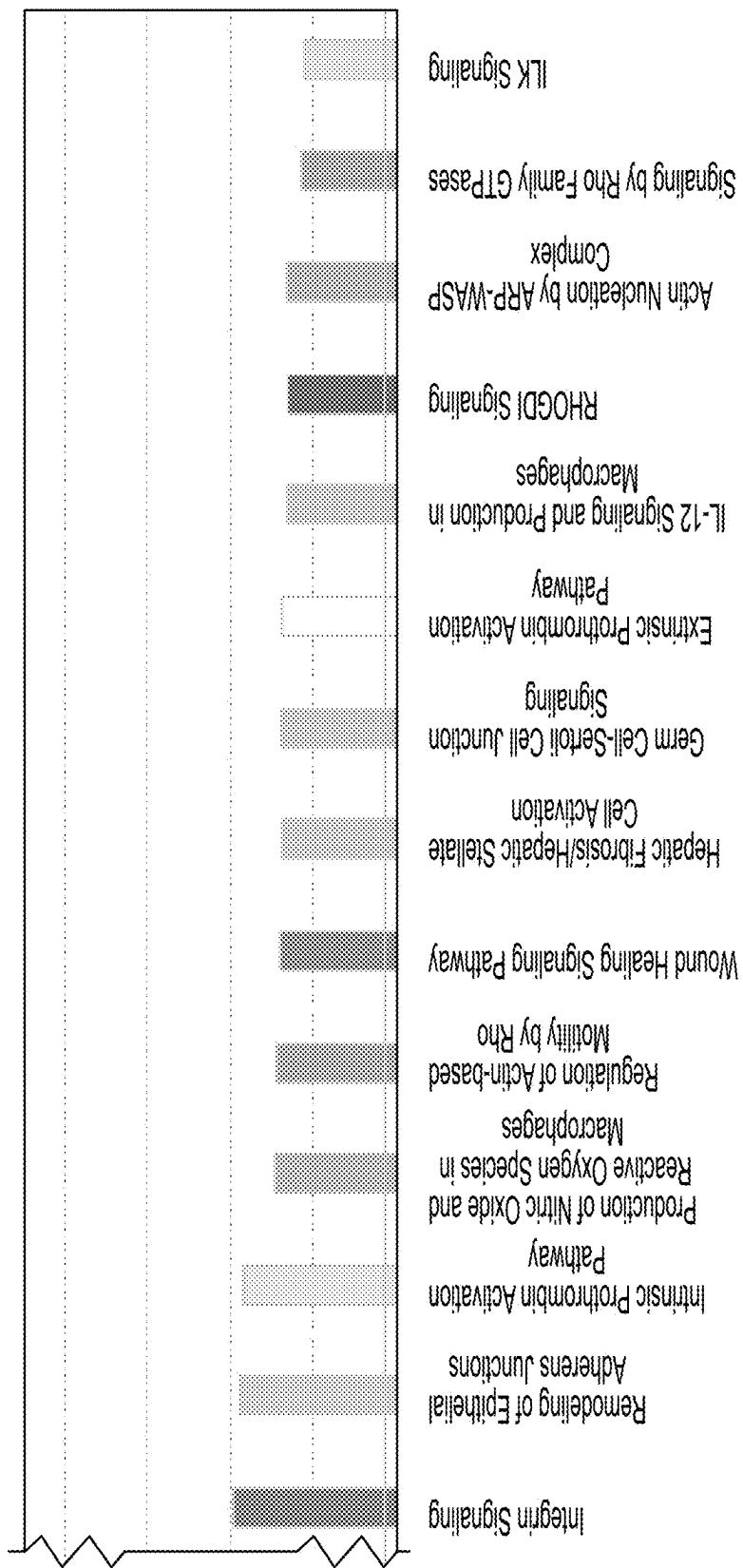


FIG. 63A
CONTINUED

HMC EVs vs. BM MSC EVs

Categories

Cell Death and Survival

Cell Death and Survival

Cellular Movement

Infectious Diseases, Organismal Injury and Abnormalities

Cell Morphology, Cellular Assembly and Organization, Cellular Function and ...

Cellular Movement

Cellular Assembly and Organization, Cellular Function and Maintenance

Cell-To-Cell Signaling and Interaction

Cardiovascular System Development and Function, Cell-To-Cell Signaling an...

Cell-To-Cell Signaling and Interaction

Cardiovascular System Development and Function, Cell-To-Cell Signaling an...

Cardiovascular System Development and Function, Cell-To-Cell Signaling an...

Cardiovascular System Development and Function, Cell-To-Cell Signaling an...

Organismal Injury and Abnormalities, Organismal Survival

Cellular Movement

Cardiovascular System Development and Function, Cell-To-Cell Signaling an...

Infectious Diseases, Organismal Injury and Abnormalities

Cellular Movement

Cell Morphology, Cellular Movement

Cell-To-Cell Signaling and Interaction, Hematological System Development ...

Cellular Function and Maintenance

Cellular Movement

Cell-To-Cell Signaling and Interaction, Hematological System Development ...

FIG. 63B

Diseases or Functions Annotation	T p-value	X	▽Activation z-score
Cell viability	3.25E-13	5.049	
Cell survival	7.24E-14	4.816	
Cell movement	2.01E-42	4.521	
Viral Infection	6.34E-36	4.496	
Formation of cellular protrusions	3.88E-11	4.275	
Migration of cells	6.36E-37	4.052	
Microtubule dynamics	3.79E-14	3.908	
Adhesion of blood cells	5.94E-35	3.855	
Binding of vascular endothelial cells	5.42E-21	3.818	
Binding of blood cells	3.47E-43	3.814	
Adhesion of endothelial cells	1.83E-16	3.779	
Interaction of endothelial cells	6.63E-29	3.766	
Adhesion of vascular endothelial cells	7.48E-11	3.734	
Organismal death	1.84E-17	3.729	
Cell movement of breast cancer cell lines	2.38E-12	3.691	
Binding of endothelial cells	3.63E-28	3.665	
Infection by RNA virus	6.75E-32	3.654	
Cell movement of tumor cell lines	7.30E-29	3.636	
Cell spreading	1.92E-24	3.560	
Binding of leukocytes	1.36E-26	3.470	
Engulfment of cells	2.18E-16	3.468	
Invasion of tumor cell lines	1.34E-14	3.392	
Interaction of mononuclear leukocytes	1.56E-11	3.373	

FIG. 63B
CONTINUED

X Molecules X

♦ACTN4, ♦ACTR2, ♦ADH5, ♦AHNAK, ♦AIFM1, ♦ALB*, ♦ALC... ...all 111
 ♦ACTN4, ♦ACTR2, ♦ADH5, ♦AHNAK, ♦AIFM1, ♦ALB*, ♦ALC... ...all 115
 ♦A2M, ♦ABCC4, ♦ACTA2, ♦ACTB, ♦ACTN1, ♦ACTN4, ♦ADA... ...all 201
 ♦ACE, ♦ACTA2, ♦ACTB, ♦ACTN1, ♦ACTR2, ♦ACTR3, ♦ADAM... ...all 195
 ♦ABCC4, ♦ACTN4, ♦ACTR2, ♦ACTR3, ♦AHNAK, ♦ALDOA, ♦A... ...all 46
 ♦A2M, ♦ABCC4, ♦ACTA2, ♦ACTN1, ♦ACTN4, ♦ADAM10, ♦A... ...all 180
 ♦ABCC4, ♦ACTN4, ♦ACTR2, ♦ACTR3, ♦AHNAK, ♦ALDOA, ♦A... ...all 65
 ♦A2M, ♦ADAM10, ♦ALCAM, ♦AOC3, ♦APCS, ♦APOA4, ♦APOE,...all 58
 ♦ADAM10, ♦ALCAM, ♦APP, ♦BGN, ♦CD36, ♦CD44, ♦CD47, ♦... ...all 33
 ♦A2M, ♦ADAM10, ♦ALCAM, ♦ANXA5, ♦AOC3, ♦APCS, ♦APO... ...all 70
 ♦ADAM10, ♦ALCAM, ♦CD36, ♦CD44, ♦CD63, ♦CDC42, ♦COL1... ...all 29
 ♦ADAM10, ♦ALCAM, ♦ANXA2, ♦APP, ♦BGN, ♦CD36, ♦CD44, ...all 46
 ♦ADAM10, ♦ALCAM, ♦CD36, ♦CD44, ♦CD63, ♦F2, ♦FERMT3, ...all 20
 ♦ABCC4, ♦ACE, ♦ACTR2, ♦ACTB, ♦ACTN4, ♦AGRN*, ♦AGT, ♦... ...all 86
 ♦ACTN1, ♦ACTN4, ♦ADAM10, ♦AGT, ♦AHNAK, ♦ANXA2, ♦A... ...all 49
 ♦ADAM10, ♦ALCAM, ♦ANXA2, ♦APP, ♦BGN, ♦CD36, ♦CD44, ...all 45
 ♦ACE, ♦ACTA2, ♦ACTB, ♦ACTR2, ♦ACTR3, ♦ADAM10, ♦AGT, ...all 143
 ♦A2M, ♦ABCC4, ♦ACTA2, ♦ACTN1, ♦ACTN4, ♦ADAM10, ♦A... ...all 141
 ♦ALB*, ♦ATRN, ♦C3, ♦C5, ♦CAP1, ♦CD36, ♦CD47, ♦CD81, ♦C... ...all 42
 ♦A2M, ♦ADAM10, ♦ALCAM, ♦AOC3, ♦APOA4, ♦APOE, ♦APO... ...all 49
 ♦ACTN1, ♦ACTN4, ♦ACTR2, ♦ACTR3, ♦AHSG, ♦APCS, ♦APM... ...all 48
 ♦ACTA2, ♦ACTN4, ♦ADAM10, ♦AHNAK, ♦ALCAM, ♦ALDOA, ♦... ...all 95
 ♦AOC3, ♦ATRN, ♦CD14, ♦CD44, ♦CD47, ♦CD81, ♦F2, ♦FERMT3, ...all 23

Cell-To-Cell Signaling and Interaction, Hematological System Development ...

Cellular Movement

Cell-To-Cell Signaling and Interaction

Cellular Assembly and Organization, Cellular Function and Maintenance

Cellular Movement

Molecular Transport

Cellular Movement

Cell-To-Cell Signaling and Interaction, Hematological System Development ...

Cellular Movement

Cellular Assembly and Organization, Cellular Function and Maintenance

Categories



Cellular Function and Maintenance

Cellular Movement

Cellular Movement

Cell-To-Cell Signaling and Interaction, Hematological System Development ...

Cellular Movement

Cellular Function and Maintenance

Cellular Movement

Cellular Movement, Renal and Urological System Development and Function

Cellular Function and Maintenance

Cellular Movement, Hematological System Development and Function, Immu...

Lipid Metabolism Small Molecule Biochemistry

Cell-To-Cell Signaling and Interaction, Hematological System Development ...

Adhesion of immune cells	4.25E-25	3.240
Invasion of cells	3.86E-16	3.208
Attachment of cells	4.18E-16	3.179
Organization of cytoplasm	6.31E-15	3.072
Migration of breast cancer cell lines	1.91E-10	3.039
Transport of molecule	1.46E-11	3.025
Homing of cells	1.48E-22	3.005
Binding of mononuclear leukocytes	3.45E-10	2.987
Cell movement of melanoma cell lines	1.91E-17	2.987
Organization of cytoskeleton	5.07E-17	2.972

HMC EVs vs. BM MSC EVs

Diseases or Functions Annotation	p-value	X	Activation z-score
Endocytosis	1.76E-18	2.963	
Chemotaxis	1.30E-21	2.931	
Cell movement of carcinoma cell lines	5.41E-12	2.915	
Interaction of lymphocytes	5.55E-12	2.908	
Migration of tumor cell lines	7.21E-23	2.889	
Endocytosis by eukaryotic cells	1.21E-13	2.881	
Migration of melanoma cell lines	6.11E-14	2.863	
Cell movement of kidney cell lines	1.15E-09	2.851	
Internalization of cells	9.02E-14	2.834	
Cell movement of phagocytes	4.21E-19	2.827	
Fatty acid metabolism	1.51E-11	2.825	
Binding of lymphocytes	2.24E-11	2.770	

FIG. 63B
CONTINUED

↑A2M, ↓ADAM10, ↑ALCAM, ↑AOC3, ↑APOA4, ↑APOE, ↑APO... ...all 45
↑ACTA2, ↑ACTN4, ↓ADAM10, ↑AHNAK, ↑ALCAM, ↓ALDOA, ...all 104
↑CD36, ↑CD44, ↓DCN, ↑FN1, ↑ILK, ↑ITGA2, ↑ITGA3, ↑ITGA5, ...all 22
↓ABCC4, ↑ACTN1, ↑ACTN4, ↑ACTR2, ↑ACTR3, ↑AHNAK, ↓AL... ...all 85
↑ACTN1, ↑ACTN4, ↑AGT, ↑AHNAK, ↑ANXA2, ↑ARHGDIB, ↓A... ...all 42
↑A2M, ↓ABCC4, ↑ACE, ↑AFM, ↑AGT, ↓ALB*, ↑ANO7, ↑ANX... ...all 84
↑ACTN1, ↓ADAM10, ↑AGT, ↑ANXA2, ↑APOA1, ↑APP, ↓ARRB1, ...all 61
↑AOC3, ↑CD44, ↑CD47, ↑CD81, ↑F2, ↑FERMT3, ↑FN1, ↑ITGA2, ...all 21
↑ACTN4, ↑AHNAK, ↑ALCAM, ↑CAPN1, ↑CD36, ↑CD44, ↑CD81, ...all 31
↓ABCC4, ↑ACTN1, ↑ACTN4, ↑ACTR2, ↑ACTR3, ↑AHNAK, ↓AL... ...all 82

Molecules

↑ACTN1, ↑ACTN4, ↑ACTR2, ↑ACTR3, ↑APCS, ↑APMAP, ↑AP... ...all 54
↑ACTN1, ↓ADAM10, ↑AGT, ↑ANXA2, ↑APOA1, ↑APP, ↓ARRB1 ...all 59
↑ACTA2, ↓ADAM10, ↑ALCAM, ↓ANGPTL4, ↑ANPEP, ↑APOC1, ...all 45
↑AOC3, ↑ATRN, ↑CD44, ↑CD47, ↑CD81, ↑F2, ↑FERMT3, ↑FN1, ...all 21
↑A2M, ↓ABCC4, ↑ACTA2, ↑ACTN1, ↑ACTN4, ↓ADAM10, ↑A... ...all 120
↑ACTN1, ↑ACTN4, ↑ACTR2, ↑ACTR3, ↑APCS, ↑APMAP, ↑APP, ...all 37
↑ACTN4, ↑AHNAK, ↑ALCAM, ↑CD36, ↑CD44, ↑CD81, ↓CDH1, ...all 25
↑AGT, ↑APOA1, ↑APP, ↑C3, ↑CDC42, ↑CHL1, ↑F10, ↑FGA, ↑F... ...all 21
↑ACTR2, ↑ACTR3, ↑APCS, ↑APMAP, ↑ARPC2, ↑ARPC3, ↓ARP... ...all 44
↓ABCC4, ↓ADAM10, ↑AGT, ↓ALB*, ↑APOA1, ↑APP, ↑ATRN, ↑... ...all 31
↓ABCC4, ↑ACOT7, ↑AGT, ↓ALB*, ↑APOA1, ↓APOA2, ↑APOA4, ...all 45
↑AOC3, ↑CD44, ↑CD47, ↑CD81, ↑F2, ↑FERMT3, ↑FN1, ↑ITGA2, ...all 20

HMC EVs vs. BM MSC EVs

Cellular Movement

Cell-To-Cell Signaling and Interaction,Hematological System Development ...

Cell-To-Cell Signaling and Interaction

Cell-To-Cell Signaling and Interaction

Cellular Movement

Cell-To-Cell Signaling and Interaction

Protein Synthesis

Cellular Movement,Hair and Skin Development and Function

Cell-To-Cell Signaling and Interaction

Cellular Movement

Cellular Movement,Hematological System Development and Function,Imm...
mu...

Cellular Movement

Cell-To-Cell Signaling and Interaction

Cell-To-Cell Signaling and Interaction

Cellular Function and Maintenance,Inflammatory Response

Cardiovascular System Development and Function,Cellular Movement

Cellular Movement,Hematological System Development and Function,Imm...
mu...

Cell-To-Cell Signaling and Interaction

Cellular Movement,Immune Cell Trafficking

Cell-To-Cell Signaling and Interaction

Cell-To-Cell Signaling and Interaction,Cellular Function and Maintenance,Inf...

FIG. 63B
CONTINUED

Cell movement of blood cells	7.04E-33	2.760
Adhesion of lymphocytes	7.95E-10	2.756
Interaction of lymphoma cell lines	1.86E-13	2.748
Binding of lymphoma cell lines	4.80E-13	2.748
Migration of carcinoma cell lines	3.87E-10	2.744
Binding of tumor cell lines	1.99E-31	2.714
Metabolism of protein	1.75E-11	2.709
Cell movement of epithelial cell lines	1.85E-14	2.709
Binding of lymphatic system cells	1.37E-12	2.695
Invasion of carcinoma cell lines	2.98E-11	2.692
Cell movement of leukocytes	1.23E-29	2.676
Migration of blood cells	2.09E-32	2.630
Interaction of gonadal cell lines	2.96E-11	2.630
Adhesion of tumor cell lines	2.60E-24	2.624
Phagocytosis	3.63E-15	2.604
Migration of endothelial cell lines	1.78E-10	2.578
Cell movement of mononuclear leukocytes	3.59E-24	2.549
Binding of leukemia cell lines	2.90E-18	2.539
Leukocyte migration	4.23E-31	2.525
Adhesion of leukemia cell lines	1.34E-11	2.514
Phagocytosis of cells	2.97E-15	2.509

FIG. 63B
CONTINUED

↓ABCC4, ↓ADAM10, ↑AGT, ↓ALB*, ↑AOC3, ↑APOA1, ↑APOD, ...all 74
↑AOC3, ↑CD44, ↑CD47, ↑CD81, ↑F2, ↑FERMT3, ↑FN1, ↑ITGA2, ...all 16
↑ALCAM, ↑AMXA2, ↑APOE, ↑APP, ↑CD44, ↓DCN, ↑DPP4, ↑F2, ...all 20
↑ALCAM, ↑ANXA2, ↑APOE, ↑APP, ↑CD44, ↓DCN, ↑DPP4, ↑F2, ...all 19
↑ACTA2, ↓ADAM10, ↑ALCAM, ↓ANGPTL4, ↑ANPEP, ↑APOC1, ...all 39
↑ACTN4, ↓ADAM10, ↑AGT, ↑ALCAM, ↓ANGPTL4, ↑ANXA2, ↑... all 77
↑ACE, ↓ADAM10, ↑AFM, ↑AGT, ↑APCS, ↑APOA1, ↓APOA2, ↓... all 66
↑AGT, ↑ALCAM, ↑APOA1, ↑APP, ↑C3, ↓CDC42, ↓CDH1, ↑CD... ...all 29
↑AOC3, ↑CD44, ↑CD47, ↑CD81, ↑F2, ↑FERMT3, ↑FN1, ↑ITGA2, ...all 22
↑ACTA2, ↓ADAM10, ↑ALCAM, ↓ANGPTL4, ↑APOC1, ↑APP, ↑... all 40
↓ABCC4, ↓ADAM10, ↑AGT, ↓ABL*, ↑AOC3, ↑APOA1, ↑APOD, ...all 67
↓ABCC4, ↓ADAM10, ↑AGT, ↓ALB*, ↑AOC3, ↑APOA1, ↑APOD, ...all 73
↑ANXA5, ↑APOE, ↑CD44, ↑CD47, ↑F2, ↑FGA, ↑FN1, ↑GP1BB, ...all 14
↑ACTN4, ↓ADAM10, ↑AGT, ↑ALCAM, ↑APOE, ↑APOH, ↑CD44, ...all 59
↑ACTR2, ↑ACTR3, ↑AHSG, ↑APCS, ↑APMAP, ↑APOA1, ↓APO... ...all 38
↑ALCAM, ↓ANGPTL4, ↑APOE, ↑CD44, ↑CD9, ↑CDH13, ↑COL1... ...all 18
↓ADAM10, ↑AGT, ↑AOC3, ↑APOA1, ↑APOD, ↑APP, ↑ATRN, ↑... all 50
↓ADAM10, ↑ALCAM, ↑ANXA2, ↑ANXA5, ↑APOH, ↑APP, ↑CD... ...all 33
↓ABCC4, ↓ADAM10, ↑AGT, ↓ALB*, ↑AOC3, ↑APOA1, ↑APOD, ...all 71
↓ADAM10, ↑APOH, ↑CD44, ↑CD47, ↓CDH1, ↑CPB2, ↑F10, ↑F2, ...all 21
↑ACTR2, ↑ACTR3, ↑AHSG, ↑APCS, ↑APMAP, ↑APOA1, ↓APO... ...all 36

FIG. 63B
CONTINUED

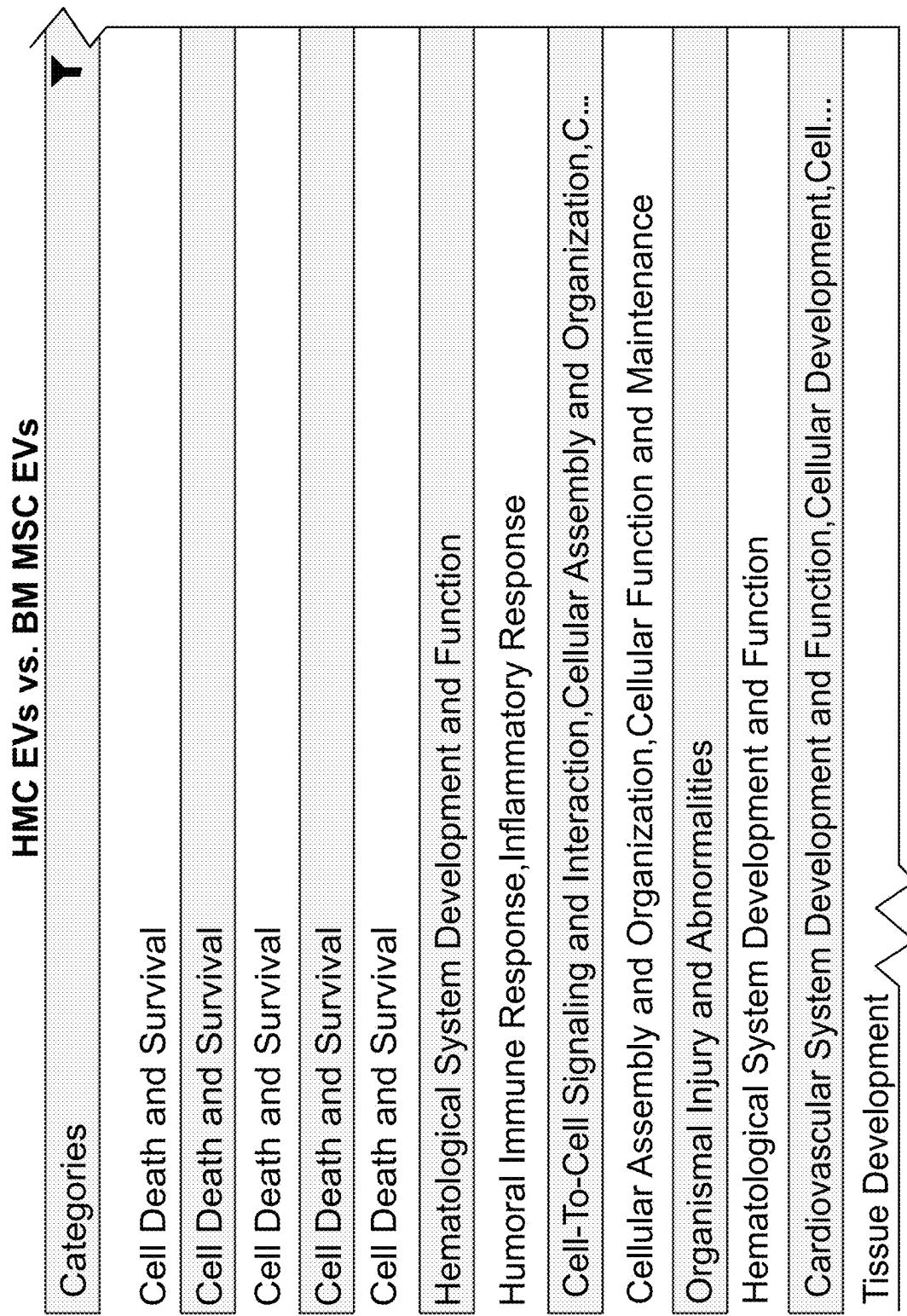


FIG. 63C

Diseases or Functions Annotation	p-value	Δ	Δ Activation z-score
Cell death of tumor cell lines	1.21E-14	-3.476	
Cell death of leukemia cell lines	1.07E-10	-2.727	
Apoptosis of tumor cell lines	9.77E-13	-2.519	
Necrosis	8.01E-20	-1.936	
Apoptosis	4.49E-18	-1.800	
Fibrinolysis	5.55E-17	-1.633	
Complement activation	1.54E-21	-1.246	
Formation of focal adhesions	1.99E-17	-0.466	
Organization of filaments	6.42E-13	-0.277	
Fibrosis	2.28E-12	-0.254	
Coagulation	1.68E-22	-0.200	
Proliferation of endothelial cells	1.78E-12	-0.078	
Growth of epithelial tissue	5.68E-12	-0.027	

FIG. 63C
CONTINUED



Molecules	Y	X
↓ ABCC4, ↓ ADAM10, ↑ ADAMTS12, ↑ ADH5, ↑ AHNAK, ↑ ALFM1, ...all 140		
↓ ADAM10, ♦ ALFM1, ↓ ARG1, ↓ B2M, ♦ C5, ↑ CBR1, ♦ CD44, ↑ CD... all 42		
♦ AHNAK, ♦ ALFM1, ↓ ALB*, ↑ ALCAM, ↑ ANGPTL4, ↑ ANXA2, ↑ ...all 115		
↓ ABCC4, ↑ ACTR2, ↓ ADAM10, ↑ ADAMTS12, ↑ ADH5, ↑ AGT, ↑ ...all 177		
↑ AGT, ♦ AHNAK, ♦ ALFM1, ↓ ALB*, ♦ ALCAM, ↓ ANGPTL4, ↑ A... ...all 160		
↑ APOH, ↓ F11, ↑ F12, ↑ F2, ↑ FGA, ↑ FGB, ↓ FGG, ↑ GP1BA, ↓ KLK... ...all 13		
↑ APOE, ↑ C1QA, ↑ C1QB, ↑ C1QC, ↑ C1R, ↑ C3, ↑ C4A/C4B*, ↑ C6, ...all 21		
↑ ACTA2, ↑ ACTN1, ♦ APOD, ↑ CD44, ↑ COL18A1, ↑ COR... ...all 27		
↑ ACTN1, ↓ ALDOA, ↑ BMP1, ↑ CDC42, ↑ CDH1, ↑ COL1A1, ↑ COL... ...all 22		
↓ ABCC4, ♦ ACE, ↓ ADAM10, ↑ AGT, ↓ ALB*, ↑ APOA1, ↓ APOA2, ...all 56		
♦ ANXA5, ♦ APOE, ↑ APOH, ↑ APP, ↑ C4BPB, ↑ CALU, ↑ CD36, ↑ ...all 32		
↑ APOE, ↑ APOH, ↑ C3, ↑ CD36, ↑ CD44, ↑ CDH13, ↑ COL18A1, ↑ C... ...all 35		
♦ ACTA2, ♦ APOE, ↑ APOH, ↓ B2M, ♦ C3, ↑ C5, ♦ CD36, ↑ CD44, ↑ ...all 44		

FIG. 63C
CONTINUED

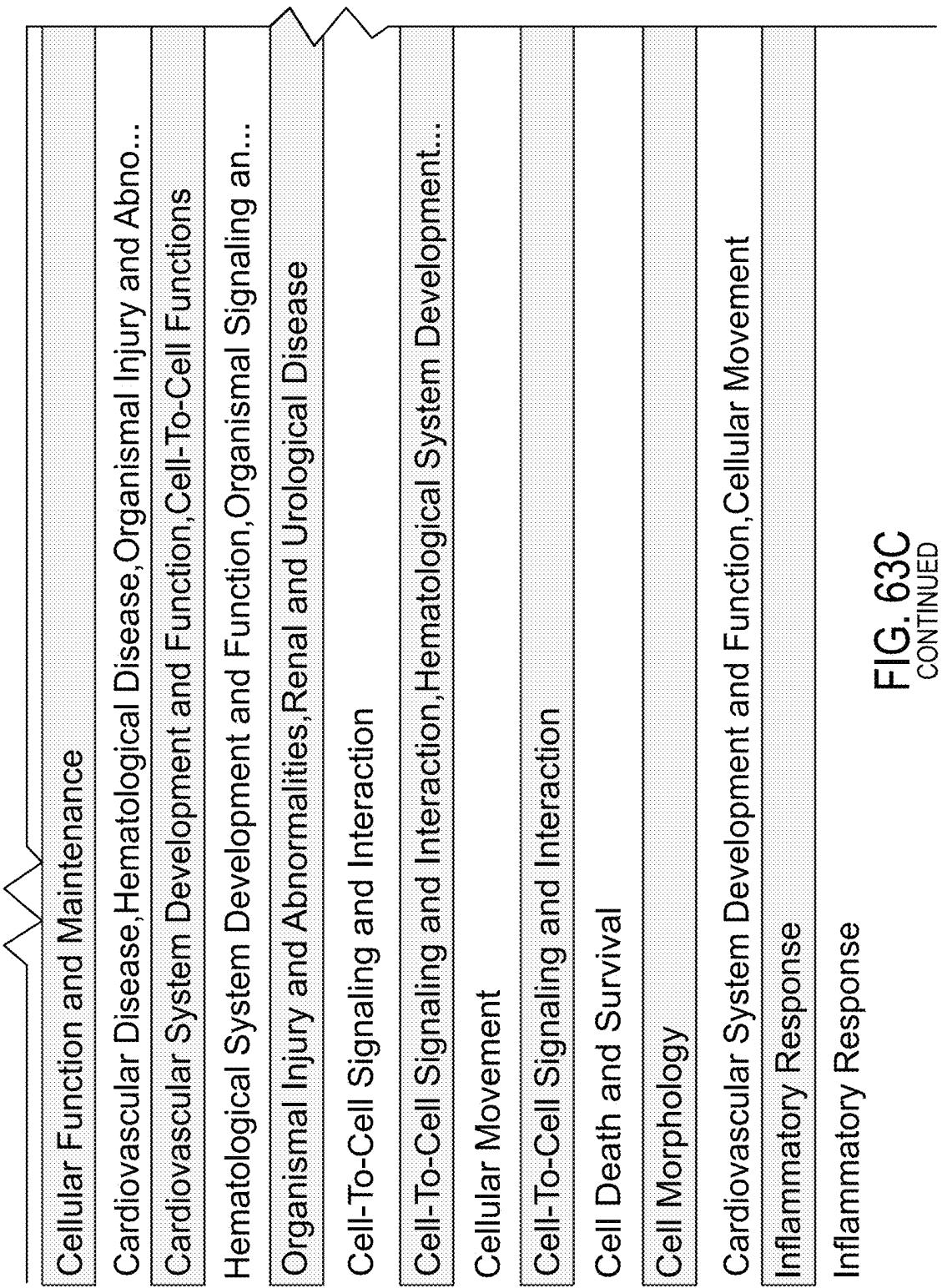


FIG. 63C
CONTINUED

Cellular homeostasis	3.94E-10	-0.016
Thrombus	2.16E-20	0.000
Binding of endothelial cell lines	3.19E-10	0.067
Coagulation of blood	9.50E-22	0.118
Renal impairment	7.61E-11	0.119
Adhesion of melanoma cell lines	4.39E-13	0.180
Aggregation of blood platelets	5.44E-19	0.227
Migration of myeloid cells	3.62E-10	0.233
Aggregation of cells	5.00E-27	0.299
Opsonization	8.50E-10	0.391
Orientation of cells	3.62E-10	0.409
Movement of vascular endothelial cells	3.02E-18	0.440
Inflammation of absolute anatomical region	4.37E-13	0.443
Inflammation of body cavity	5.41E-13	0.443

FIG. 63C
CONTINUED

↓ ADAM10,	↑ ADH5,	↑ AGT,	↑ AIFM1,	↓ ALDOA,	↑ ANXA7,	↑ AP...	...all 82
↑ ANXA5,	↑ APOH,	↑ C3,	↑ CFH,	↑ CFHR1,	↑ CFI,	↑ COL1A1,	...all 33
↑ AGT,	↓ ANGPTL4,	↑ AOC3,	↑ APOE,	↑ CD44,	↑ CDH13,	↑ F2,	↑ IT...
↑ ANXA5,	↑ APOE,	↑ APOH,	↑ APP,	↑ C4BPE,	↑ CALU,	↑ CD36,	↑all 31
↑ ACE,	↑ AGT,	↓ ALB*,	↑ AOC3,	↑ APOB,	↓ B2M,	↑ C3,	↑ C4A/C4B*, ...all 30
↑ ALCAM,	↑ CD44,	↓ CDH1,	↑ ITGA5,	↑ ITGA6,	↑ ITGB1,	↑ KNG1,	↑all 14
↓ ABCC4,	↓ ALB*,	↑ APP,	↑ CD9,	↑ CFH,	↑ F12,	↑ F2,	↑ FERMT3,
↓ ADAM10,	↓ ALB*,	↑ C5,	↑ CD47,	↑ CEH,	↑ CFHR1,	↑ FN1,	↑ ITGB3, ...all 18
↓ ABCC4,	↓ ALB*,	↑ ANO7,	↑ APCS,	↑ APP,	↑ ATRN,	↑ CD44,	↑ CD9, ...all 44
↑ APOH,	↑ C3,	↑ C4A/C4B*,	↑ C4BPA,	↑ C4BPB,	↑ FCN3,	↑ LBP,	↑all 9
↑ ACTN4,	↑ AHSG,	↑ ANPEP,	↑ CD47,	↑ CD81,	↑ CDC42,	↑ CITC,	↑all 18
↑ ALCAM,	↑ ANPERP,	↑ C3,	↑ C5,	↑ CD36,	↑ CD44,	↑ CD63,	↑ CD9, ...all 37
↑ ACE,	↑ ACTA2,	↑ ACTN4,	↑ AGT,	↑ AHNAK,	↓ ALB*,	↑ APOA1,	↓all 70
↑ ACE,	↑ ACTA2,	↑ ACTN4,	↑ AGT,	↑ AHNAK,	↓ ALB*,	↑ APOA1,	↓all 68

FIG. 63C
CONTINUED

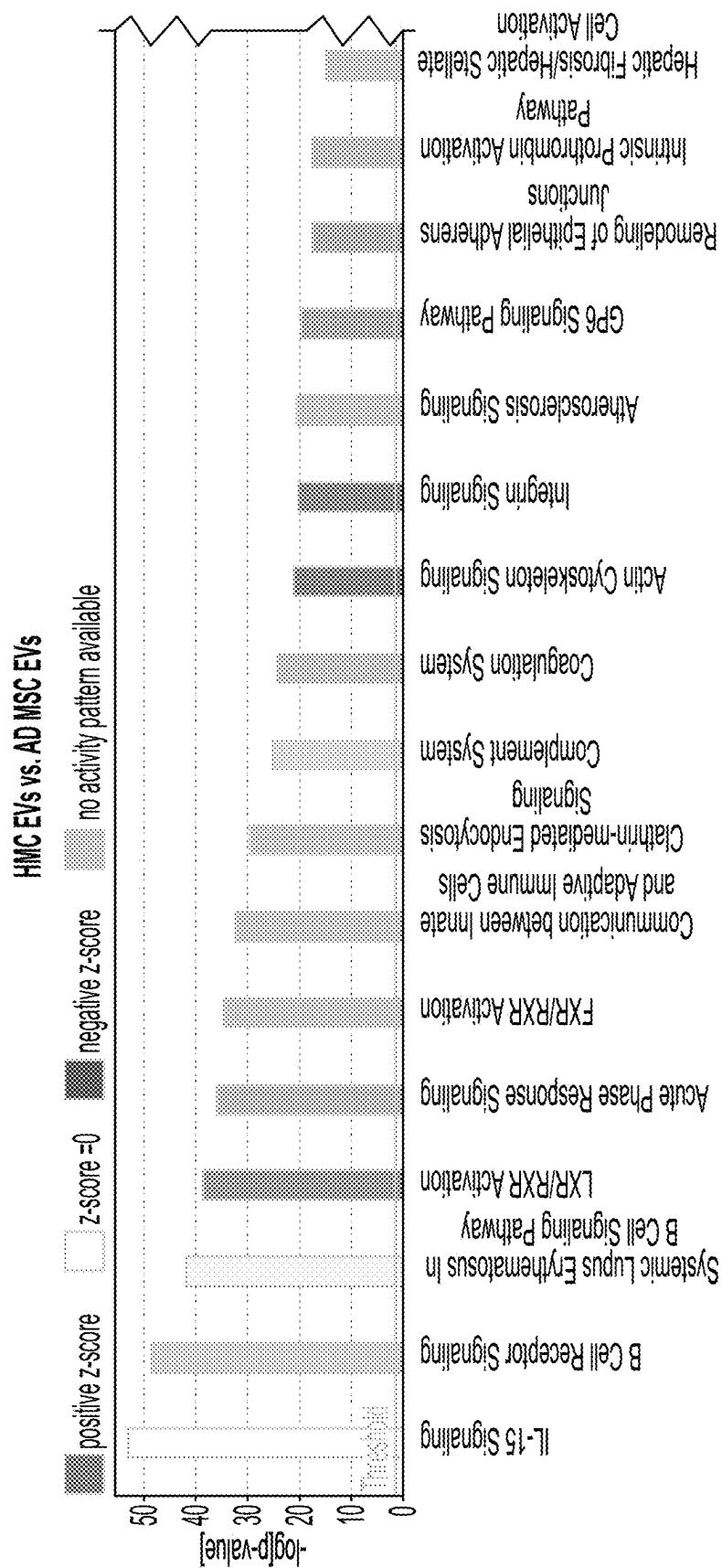


FIG. 64A

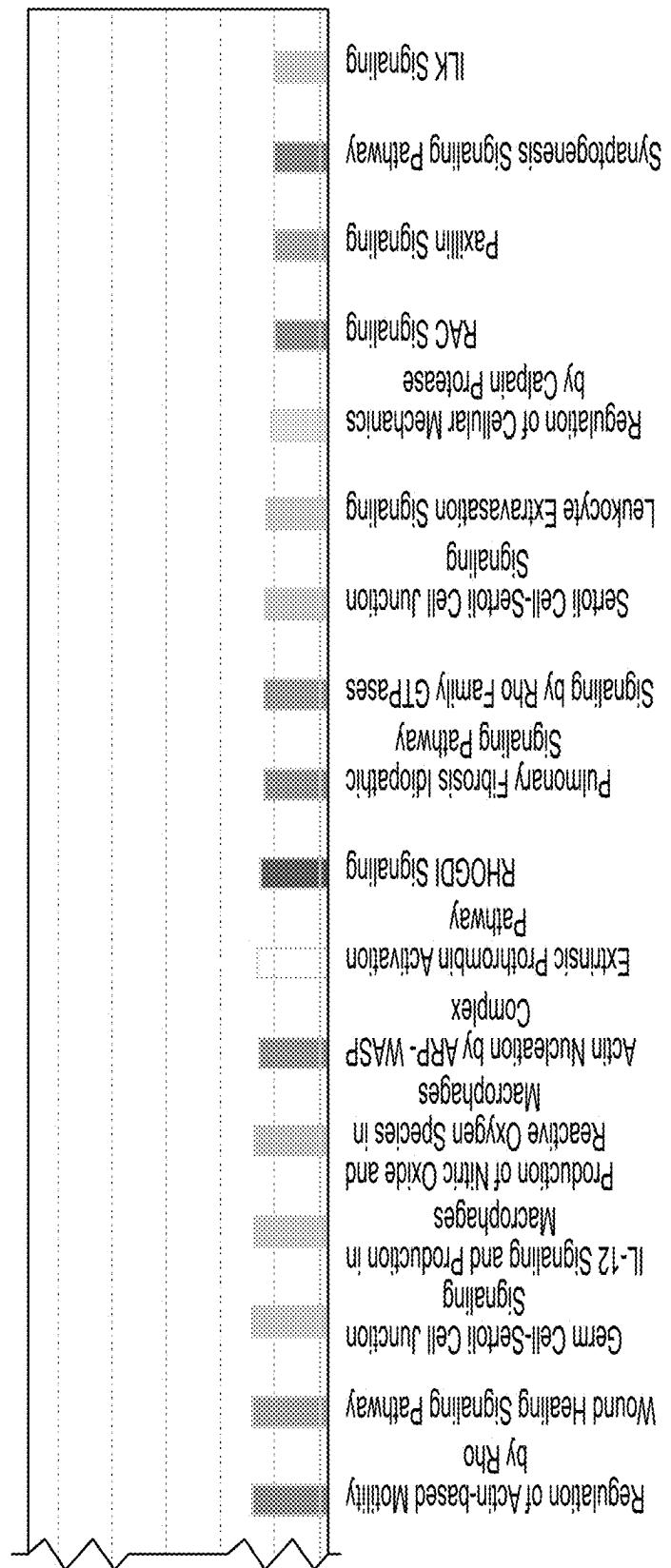


FIG. 64A
CONTINUED

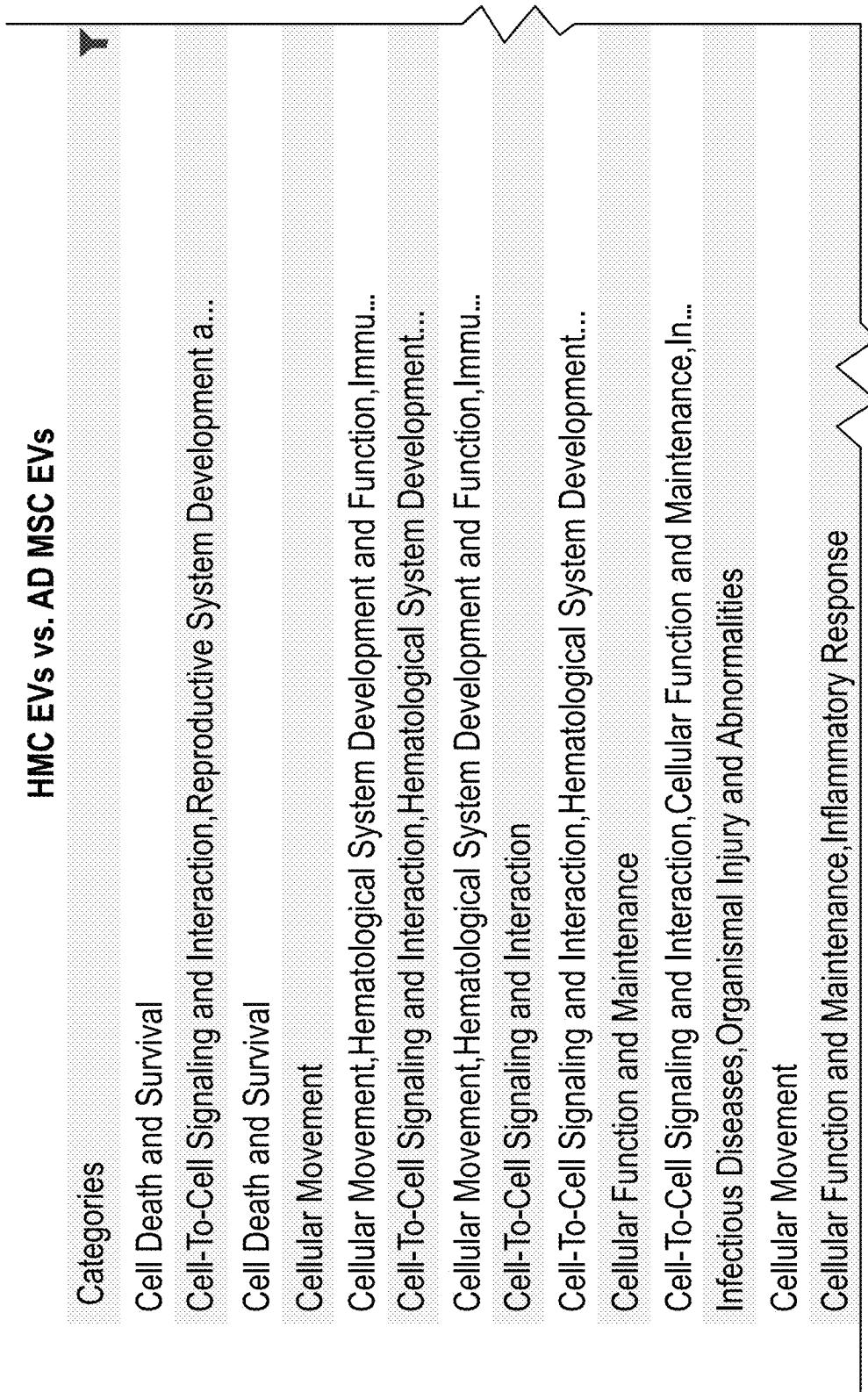


FIG. 64B

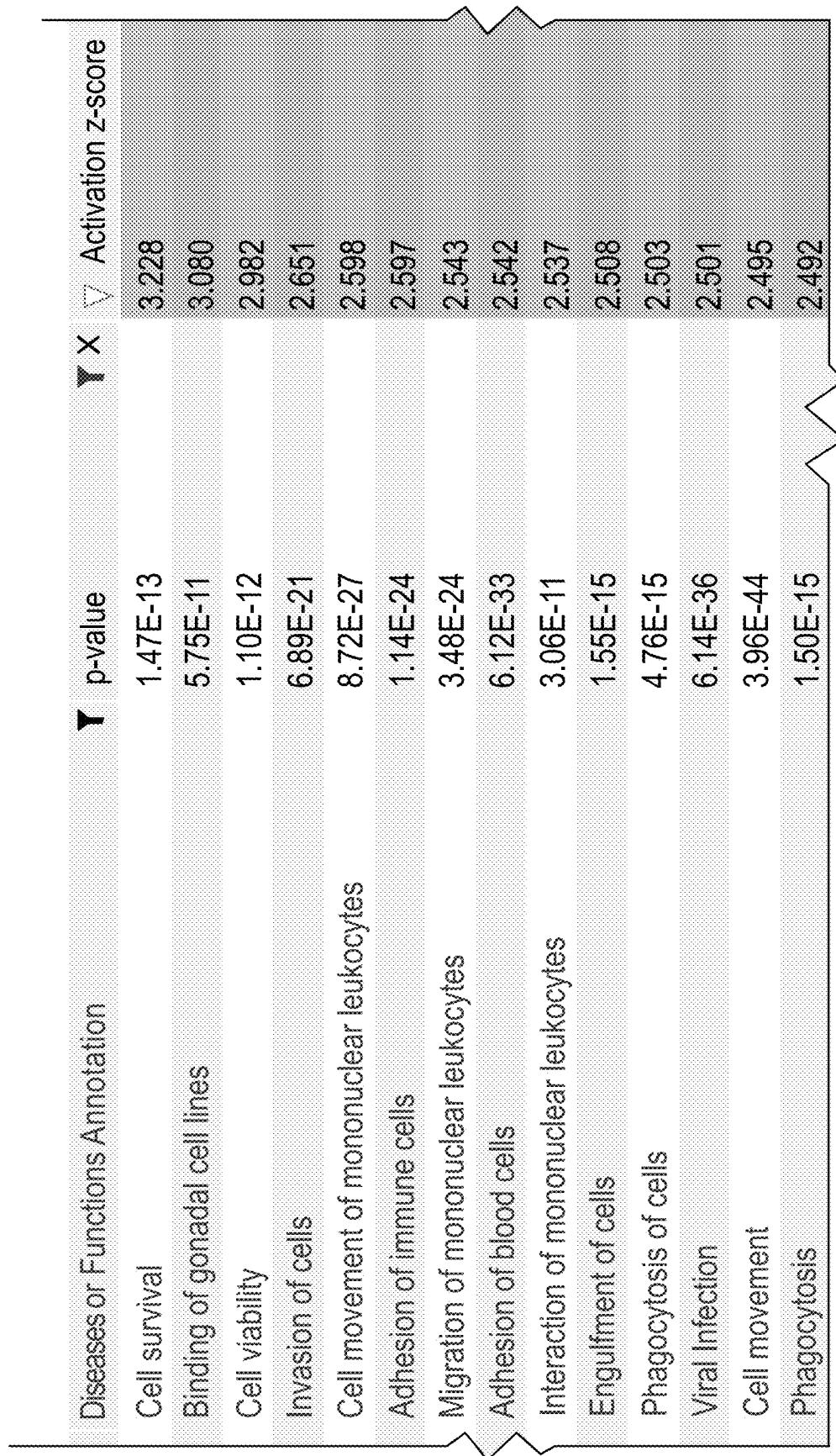


FIG. 64B
CONTINUED

Y X	Molecules
	↓ACTN4, ↑ACTR2, ↑ADH5, ↑AHNAK, ↓AIFM1, ↓ALB*, ↓ALCAM, ↑ALOX12, ↑ANXA2, ↑APOB ↑APOE, ↑CALR, ↑CD44, ↑F2, ↑FGA, ↑FN1, ↑GP1BB, ↑ITGA2, ↑ITGA5, ↑ITGB1
	↓ACTN4, ↑ACTR2, ↑ADH5, ↑AHNAK, ↓AIFM1, ↓ALB*, ↓ALCAM, ↑ALOX12, ↑ANXA2, ↑APOB ↑ACTA2, ↓ACTN4, ↑ADAM10, ↑AHNAK, ↓ALDOA, ↓ANGPTL4, ↑ANPEP, ↑ANXA1, ↑ANXA2 ↑ADAM10, ↑AGT, ↑ANXA1, ↑AOCA1, ↑APOD, ↑APP, ↑ATRN, ↓C5, ↓CAMP
	↓A2M, ↑ADAM10, ↓ALCAM, ↑ANXA1, ↑AOCA3, ↑APOA4, ↑APOE, ↑APOH, ↑ATRN, ↓C5 ↑ADAM10, ↑AGT, ↑AOCA3, ↑APOD, ↑APP, ↓C5, ↓CAMP, ↑CD44, ↑CLTC, ↑DEF1 (includes others)
	↓A2M, ↑ADAM10, ↓ALCAM, ↑ANXA1, ↑AOCA3, ↑APCS, ↑APOA4, ↑APOE, ↑APOH, ↑APP ↑AOC3, ↑ATRN, ↑CALR, ↑CD44, ↑F2, ↑FERMT3, ↑FGF2, ↑FN1, ↑ITGA2 ↓ACTN1, ↓ACTN4, ↑ACTR2, ↑ACTR3, ↑AHSG, ↑ANXA1, ↑APCS, ↑APMAP, ↓APOA1, ↑APOA2 ↑ACTR2, ↑ACTR3, ↑AHSG, ↑ANXA1, ↑APCS, ↑APMAP, ↓APOA1, ↑APOA2, ↑ARPC2, ↑ARPC3 ↑ACE, ↑ACTA2, ↑ACTB, ↓ACTN1, ↑ACTR2, ↑FACTR3, ↓ADA, ↑ADAM10, ↑AGT, ↑AHNAK ↓A2M, ↓ABCC4, ↑ACTA2, ↑ACTB, ↓ACTN1, ↓ACTN4, ↑ADAM10, ↑AGT, ↑AHNAK, ↓ALB*
	↑ACTR2, ↑ACTR3, ↑AHSG, ↑ANXA1, ↑APCS, ↑APMAP, ↓APOA1, ↑APOA2, ↑ARPC2, ↑ARPC3

FIG. 64B
CONTINUED

HMC EVs vs. AD MSC EVs

- Cellular Movement
- Cell Morphology, Cellular Assembly and Organization, Cellular Function and ...
- Cellular Movement, Hematological System Development and Function, Immu...
- Cellular Movement, Hair and Skin Development and Function
- Cell-To-Cell Signaling and Interaction, Hematological System Development ...
- Cardiovascular System Development and Function, Cell-To-Cell Signaling an...
- Cardiovascular System Development and Function, Cell-To-Cell Signaling an...
- Cellular Movement, Renal and Urological System Development and Function
- Cellular Movement
- Cell-To-Cell Signaling and Interaction, Hematological System Development...
- Cardiovascular System Development and Function, Cell-To-Cell Signaling an...
- Cellular Movement, Hematological System Development and Function, Immu...
- Cell-To-Cell Signaling and Interaction, Hematological System Development ...
- Cell-To-Cell Signaling and Interaction, Hematological System Development ...
- Cell-To-Cell Signaling and Interaction
- Cellular Function and Maintenance
- Cell-To-Cell Signaling and Interaction
- Cell-To-Cell Signaling and Interaction

FIG. 64B
CONTINUED

Invasion of tumor cell lines	7.93E-18	2.481
Formation of cellular protrusions	2.53E-10	2.439
Cell movement of lymphocytes	8.83E-20	2.436
Cell movement of epithelial cell lines	1.05E-14	2.399
Binding of leukocytes	8.97E-28	2.397
Binding of endothelial cells	7.38E-28	2.390
Interaction of endothelial cells	1.43E-29	2.389
Cell movement of kidney cell lines	3.39E-10	2.387
Migration of cells	5.49E-39	2.263
Binding of mononuclear leukocytes	5.63E-10	2.260
Adhesion of endothelial cells	7.61E-17	2.238
Lymphocyte migration	4.80E-20	2.224
Binding of professional phagocytic cells	5.14E-23	2.166
Binding of antigen presenting cells	2.96E-11	2.147
Adhesion of connective tissue cells	6.03E-10	2.140
Internalization of cells	2.48E-12	2.132
Binding of blood cells	1.56E-41	2.088
Adhesion of leukemia cell lines	1.94E-11	2.081

FIG. 64B
CONTINUED

† ACTA2, ‡ ACTN4, † ADAM10, † AHNAK, ‡ ALCAM, † ALDOA, ‡ ANGPTL4, † ANXA1, ‡ ANXA2, † APOC1
† ABCC4, ‡ ACTN4, † ACTR2, † ACTR3, † AHNAK, † ALDOA, † ANPEP, † APOE, † APP, † ARPC2
† ADAM10, † AOC3, † APOD, † APP, ‡ CAMP, † CD44, † CLTC, † DEFA1 (includes others), † DPP4, ‡ EGFR
† A2M, † ALCAM, ‡ APOA1, † APP, ‡ C3, ‡ CAMP, † CDH1, ‡ CDH13, ‡ CHL1
† A2M, † ADAM10, † ALCAM, † ANXA1, † AOC3, ‡ CAMP, † CDH13, ‡ CHL1
† A2M, † ADAM10, † ALCAM, † ANXA2, † APP, † APOA4, † APOE, † APOH, † ATRN, ‡ C5
† ADAM10, † ALCAM, † ANXA2, † APP, † BGN, † CD44, † CD63, † CDC42, † COL18A1, ‡ DCN
† ADAM10, † ALCAM, † ANXA2, † APP, † BGN, † CD44, † CD63, † CDC42, † CDH5, † COL18A1
† AGT, † APOA1, † APP, ‡ C3, ‡ CAMP, † CDH1, ‡ CHL1, † F10, † FGA, ‡ FLNA
† A2M, † ABCC4, † ACTA2, ‡ ACTN1, † ACTN4, † ADAM10, † AGT, † AHNAK, ‡ ALB*, ‡ ALCAM
† AOC3, † CALR, † CD44, † F2, † FERMT3, † FGF2, † FN1, † ITGA2, † ITGA5, † ITGB1
† ADAM10, † ALCAM, † CD44, † CD63, † CDC42, † COL18A1, † EGFR, † F10, † F2, † FERMT3
† ADAM10, † AOC3, † APOD, † APP, ‡ CAMP, † CD44, † CLTC, † DEFA1 (includes others), † DPP4, ‡ EGFR
† A2M, † ADAM10, † ALCAM, † APOE, † APOH, ‡ CAMP, † CD14, † CD44, ‡ CFH, † CFHR1
† A2M, † ALCAM, † APOE, † APOH, ‡ CAMP, † CD14, † ITGA6, † ITGB1, ‡ MSN
† CD44, † COL1A1, † COL7A1, † FBNI, † FN1, † ITGA5, † ITGAV, † ITGB1, † SDC4
† ACTR2, † ACTR3, † ANXA1, † APCS, † APMAP, † ARPC2, † ARPC3, † ARPC4, † C3, ‡ CAMP
† A2M, † ADAM10, † ALCAM, † ANXA1, † AOC3, † APCS, † APOA4, † APOE, † APOH, † APP
† ADAM10, † APOH, † CD44, † CD82, ‡ CDH1, † CPB2, † F10, † F2, † FERMT3, ‡ FLNA

FIG. 64B
CONTINUED

Categories	Y
Cell Death and Survival	
Cell Death and Survival	
Cellular Assembly and Organization, Cellular Function and Maintenance	
Hematological System Development and Function	
Cell Death and Survival	
Cell Death and Survival	
Cellular Movement, Hematological System Development and Function, Immu...	
Cell Morphology, Cellular Assembly and Organization, Cellular Function and...	
Tissue Development	
Cellular Compromise	
Cell Death and Survival, Connective Tissue Disorders, Hematological Disease...	
Cell Morphology, Cellular Function and Maintenance	
Gastrointestinal Disease, Hepatic System Disease, Organismal Injury and Ab...	
Cellular Assembly and Organization, Cellular Function and Maintenance	
Cell-To-Cell Signaling and Interaction, Cellular Assembly and Organization...	
Cancer, Organismal Injury and Abnormalities	
Cardiovascular Disease, Hematological Disease, Organismal Injury and Abno...	
Inflammatory Response	

FIG. 64C

HMC EVs vs. AD MSC EVs

Diseases or Functions Annotation	▼	p-value	▼ X	Δ	Activation z-score	▼ X
Apoptosis of tumor cell lines		2.42E-16			-2.785	
Cell death of tumor cell lines		1.63E-16			-2.693	
Organization of filaments		7.74E-12			-1.698	
Filimodysis		2.86E-16			-1.633	
Necrosis		2.88E-21			-1.563	
Apoptosis		2.12E-19			-1.444	
Cell movement of granulocytes		8.33E-16			-1.441	
Reorganization of cytoskeleton		1.76E-10			-1.405	
Growth of epithelial tissue		6.51E-13			-1.372	
Respiratory burst		1.13E-10			-1.333	
Hemolysis		6.09E-12			-1.329	
Permeability of cells		1.10E-09			-1.221	
Liver lesion		5.54E-15			-1.213	
Organization of actin cytoskeleton		2.40E-11			-1.111	
Formation of focal adhesions		4.60E-16			-1.092	
Embryonal tumor		3.68E-11			-1.067	
Thrombus		1.08E-19			-1.000	
Inflammation of body cavity		1.40E-13			-0.829	

FIG. 64C
CONTINUED

X	Molecules
	♦ AHNAK, ♦ ALPM1, ♦ ALB, ♦ ALCAM, ♦ ALOX12, ♦ ANGPTL4, ♦ ANXA2, ♦ APP, ♦ ARGP, ♦ ARG1, ♦ ATAD2
	♦ ABCC4, ♦ ADAM10, ♦ ADAMTS12, ♦ ADH5, ♦ AHNAK, ♦ ALM1, ♦ ALB*, ♦ ALCAM, ♦ ALOX12, ♦ ANGPTL4
	♦ ACTN1, ♦ ALDOA, ♦ CDC42, ♦ CDH1, ♦ COL1A1, ♦ COL1A2, ♦ COL3A1, ♦ COL5A1, ♦ COL6A2, ♦ DSP
	♦ APOM, ♦ F11, ♦ F12, ♦ F2, ♦ FGA, ♦ FGB, ♦ FGG, ♦ GP1BA, ♦ KLK81, ♦ PLG
	♦ ABCC4, ♦ ACTR2, ♦ ADAM10, ♦ ADAMTS12, ♦ ADH5, ♦ AGT, ♦ AHNAK, ♦ ALB*, ♦ ALB1, ♦ ALCAM
	♦ AGT, ♦ AHNAK, ♦ ALB*, ♦ ALB1, ♦ ALCAM, ♦ ALOX12, ♦ ANGPTL4, ♦ ANPEP, ♦ ANXA1, ♦ ANXA2
	♦ ADAM10, ♦ ALB*, ♦ ANXA1, ♦ APOA1, ♦ APP, ♦ C5, ♦ CAMP, ♦ CFH, ♦ CFHR1, ♦ DNMT1
	♦ ANXA1, ♦ APP, ♦ CDH1, ♦ EGFR, ♦ FLNA, ♦ FN1, ♦ ILK, ♦ ITGB3, ♦ JUP, ♦ KIT
	♦ ACTA2, ♦ APOE, ♦ APOH, ♦ C3, ♦ C5, ♦ CALR, ♦ CAMP, ♦ CAVIN2, ♦ CD44, ♦ CDH13
	♦ ANFEP, ♦ C3, ♦ C5, ♦ CD14, ♦ IGHM1, ♦ IGHM2, ♦ IGHG3, ♦ JCHAIN, ♦ PFA, ♦ PGAM1
	♦ ALB*, ♦ ALDOA, ♦ ANXA1, ♦ APOE, ♦ C1S, ♦ C3, ♦ C4NC4B*, ♦ C5, ♦ C8A, ♦ C8G
	♦ ADAM10, ♦ ANXA1, ♦ CAMP, ♦ CDH5, ♦ COL4A1, ♦ F2, ♦ ITGAS3, ♦ ITGB1, ♦ LAMA1, ♦ MCAM
	♦ A1BG, ♦ A2M, ♦ ABCG4, ♦ ABGBP, ♦ ACE, ♦ ACOT7, ♦ ACTA2, ♦ ACTB, ♦ ACTN1, ♦ ACTR2
	♦ ACTN1, ♦ ALDOA, ♦ ANXA1, ♦ CDCA2, ♦ CDH1, ♦ CFL1, ♦ CLU, ♦ CORO1A, ♦ EGFR, ♦ FLNA
	♦ ACTA2, ♦ ACTN1, ♦ APOD, ♦ CD44, ♦ COL18A1, ♦ CORO1C, ♦ FGF2, ♦ FMN, ♦ GNBI, ♦ HRG
	♦ ABCC4, ♦ ACTN1, ♦ ALCAM, ♦ ALDOA, ♦ APOB, ♦ APOC1, ♦ ARR81, ♦ C3, ♦ C4A/C4B*, ♦ C5
	♦ ADA, ♦ ALOX12, ♦ APOH, ♦ C3, ♦ C5, ♦ CAIR, ♦ CFH, ♦ CFHR1, ♦ CN1, ♦ COL1A1
	♦ ACE, ♦ ACTA2, ♦ ACTN4, ♦ AGT, ♦ AHNAK, ♦ ALB*, ♦ ALOX12, ♦ ANXA1, ♦ APOA1, ♦ APOA2

FIG. 64C
CONTINUED

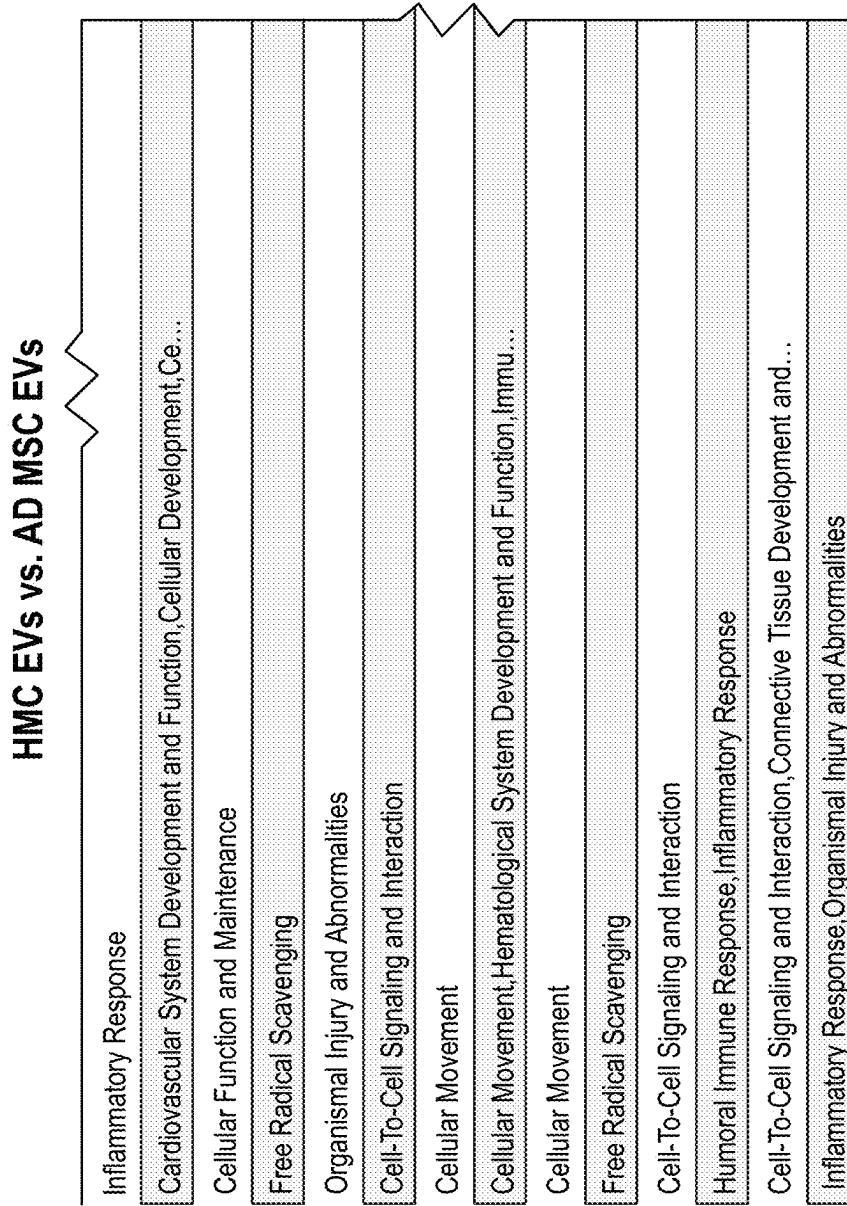


FIG. 64C
CONTINUED

HMC EVs vs. AD MSC EVs	
Inflammation of absolute anatomical region	1.42E-13 -0.829
Proliferation of endothelial cells	1.51E-13 -0.821
Cellular homeostasis	1.37E-10 -0.808
Synthesis of reactive oxygen species	2.32E-11 -0.801
Fibrosis	3.69E-11 -0.782
Response of myeloid cells	1.32E-09 -0.781
Chemotaxis of myeloid cells	1.04E-10 -0.778
Cell movement of neutrophils	1.11E-13 -0.772
Cell movement of colorectal cancer cell lines	1.06E-09 -0.754
Metabolism of reactive oxygen species	7.35E-14 -0.693
Binding of melanoma cell lines	1.50E-15 -0.665
Complement activation	6.80E-22 -0.603
Binding of fibroblasts	1.52E-09 -0.571
Inflammation of organ	2.76E-32 -0.566

FIG. 64C
CONTINUED

◆ ACE, ◆ ACTA2, ◆ ACTN4, ◆ ADA, ◆ AGT, ◆ AHNAK, ◆ ALB*, ◆ ALOX12, ◆ ANXA1, ◆ APOA1
◆ APCe, ◆ APOM, ◆ C3, ◆ CALR, ◆ CAMP, ◆ CAVIN2, ◆ CD44, ◆ CDH13, ◆ COL18A1, ◆ COL4A2
◆ ADAM10, ◆ ADCY5, ◆ ADH5, ◆ AGT, ◆ AIFM1, ◆ ALDOA, ◆ ANXA1, ◆ ANXA7, ◆ APOA1, ◆ APOL1
◆ AGT, ◆ AIFM1, ◆ ALB*, ◆ ANXA2, ◆ AOC3, ◆ APOE, ◆ APP, ◆ C5, ◆ CAMP, ◆ CAT
◆ ABCA4, ◆ ACE, ◆ ADAM10, ◆ AGT, ◆ ALB*, ◆ APOA1, ◆ APOA2, ◆ APOB, ◆ C3, ◆ C5
◆ ANFEP, ◆ ANXA1, ◆ APCS, ◆ C3, ◆ C5, ◆ CAMP, ◆ CD14, ◆ CFH, ◆ IGHAI1, ◆ IGHAI2
◆ ANXA1, ◆ APOA1, ◆ APP, ◆ C3, ◆ C5, ◆ CAMP, ◆ CSF1R, ◆ DEFAT1 (includes others), ◆ DNMTL, ◆ DPP4
◆ ADAM10, ◆ ALB*, ◆ ANXA1, ◆ APOA1, ◆ APP, ◆ C5, ◆ CAMP, ◆ CFH, ◆ CFHR1, ◆ DNMTL
◆ ARRB1, ◆ CAMP, ◆ CAPN1, ◆ CD44, ◆ CD82, ◆ CDH1, ◆ EFEMP1, ◆ EGFR, ◆ F2, ◆ FGF2
◆ AGT, ◆ AIFM1, ◆ ALB*, ◆ ANXA2, ◆ AOC3, ◆ APOA4, ◆ APOE, ◆ APP, ◆ C5, ◆ CAMP
◆ ALGAM, ◆ CD44, ◆ CDH1, ◆ EGFR, ◆ ITGA5, ◆ ITGA6, ◆ ITGAV, ◆ ITGB1, ◆ KNG1, ◆ MCAM
◆ APCe, ◆ C10A, ◆ C1QB, ◆ C1QC, ◆ C1R, ◆ C3, ◆ C4A/C4B*, ◆ C6, ◆ C7, ◆ C8A
◆ APCe, ◆ CD44, ◆ COL7A1, ◆ ITGAV, ◆ ITGB1, ◆ LGALS3BP, ◆ SDC1, ◆ SPARC, ◆ TGFBI*, ◆ THY1
◆ ACE, ◆ ACTA2, ◆ ACTN4, ◆ ADA, ◆ AGT, ◆ AHNAK, ◆ ALB*, ◆ ALOX12, ◆ ANXA1, ◆ APOA1

FIG. 64C
CONTINUED

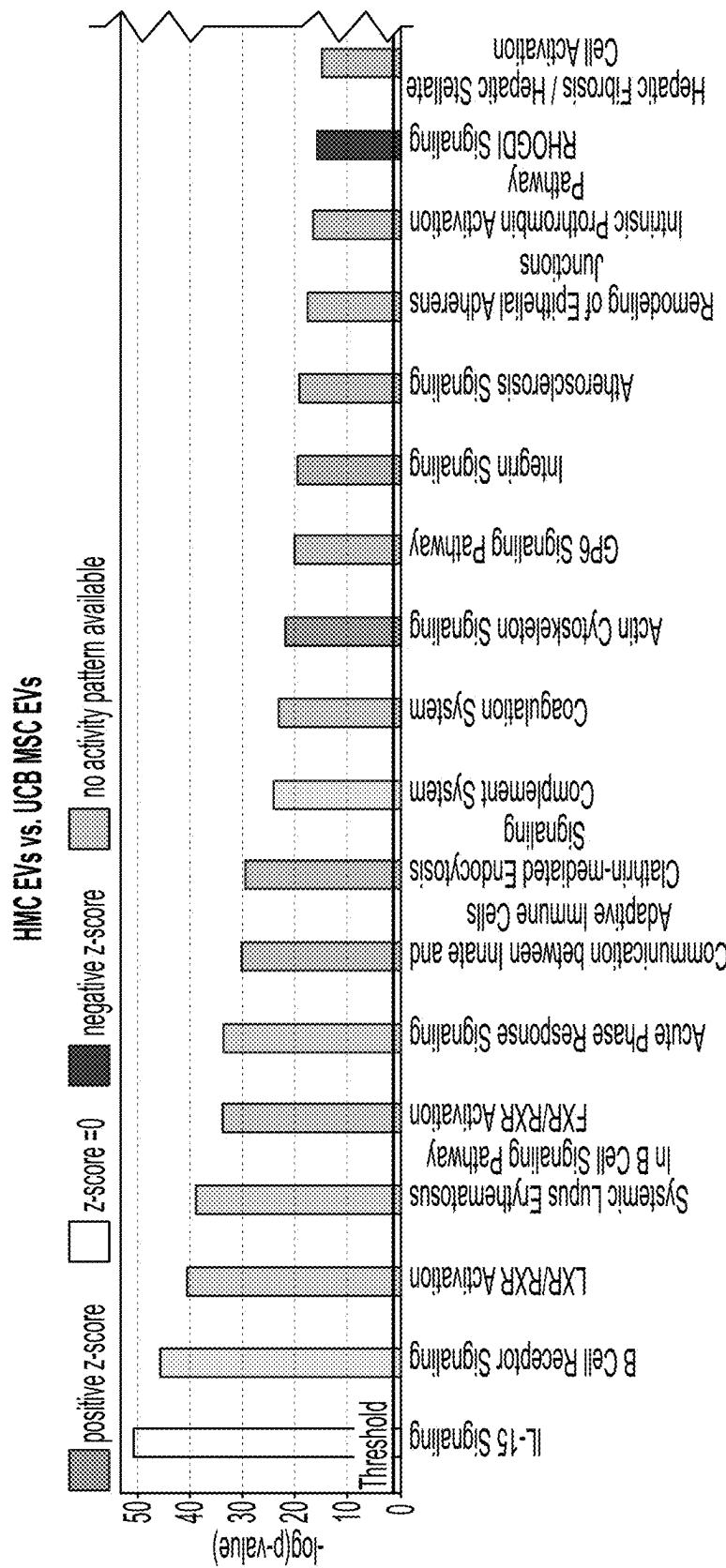


FIG. 65A

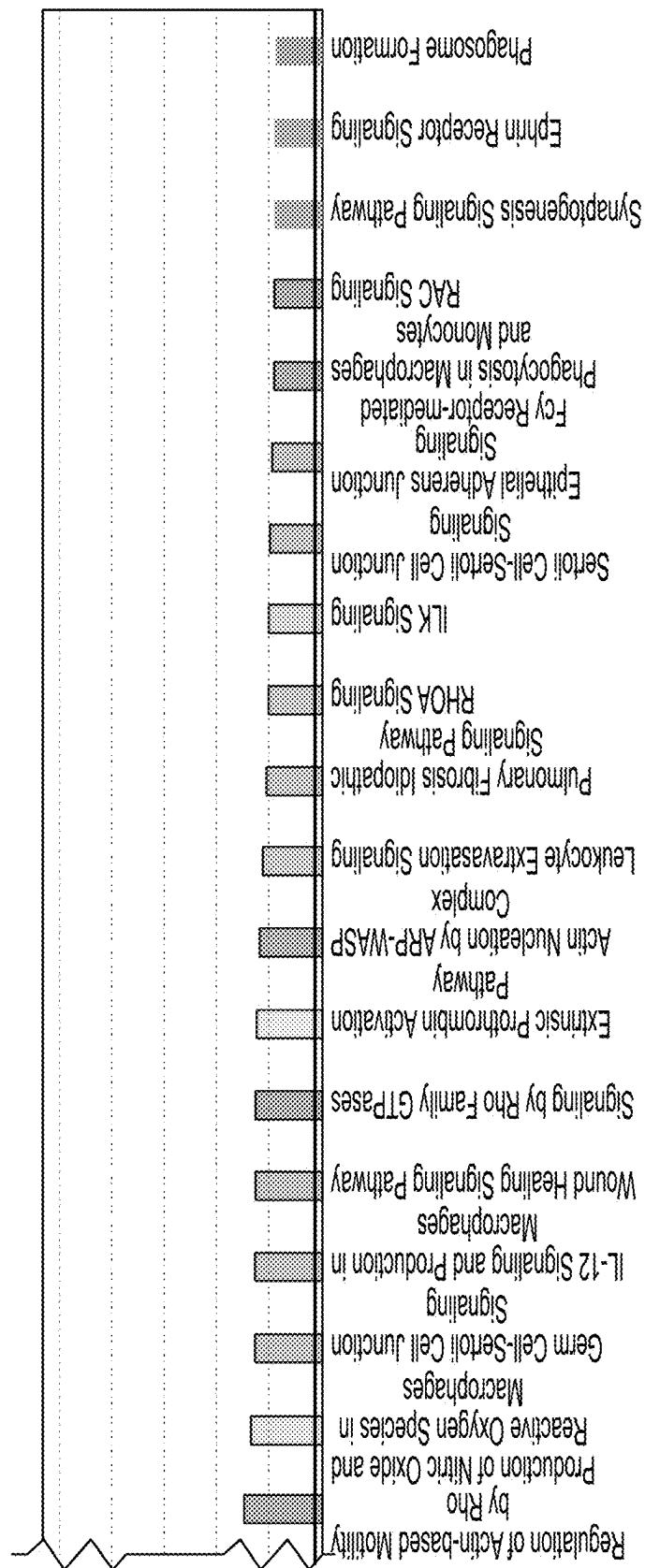
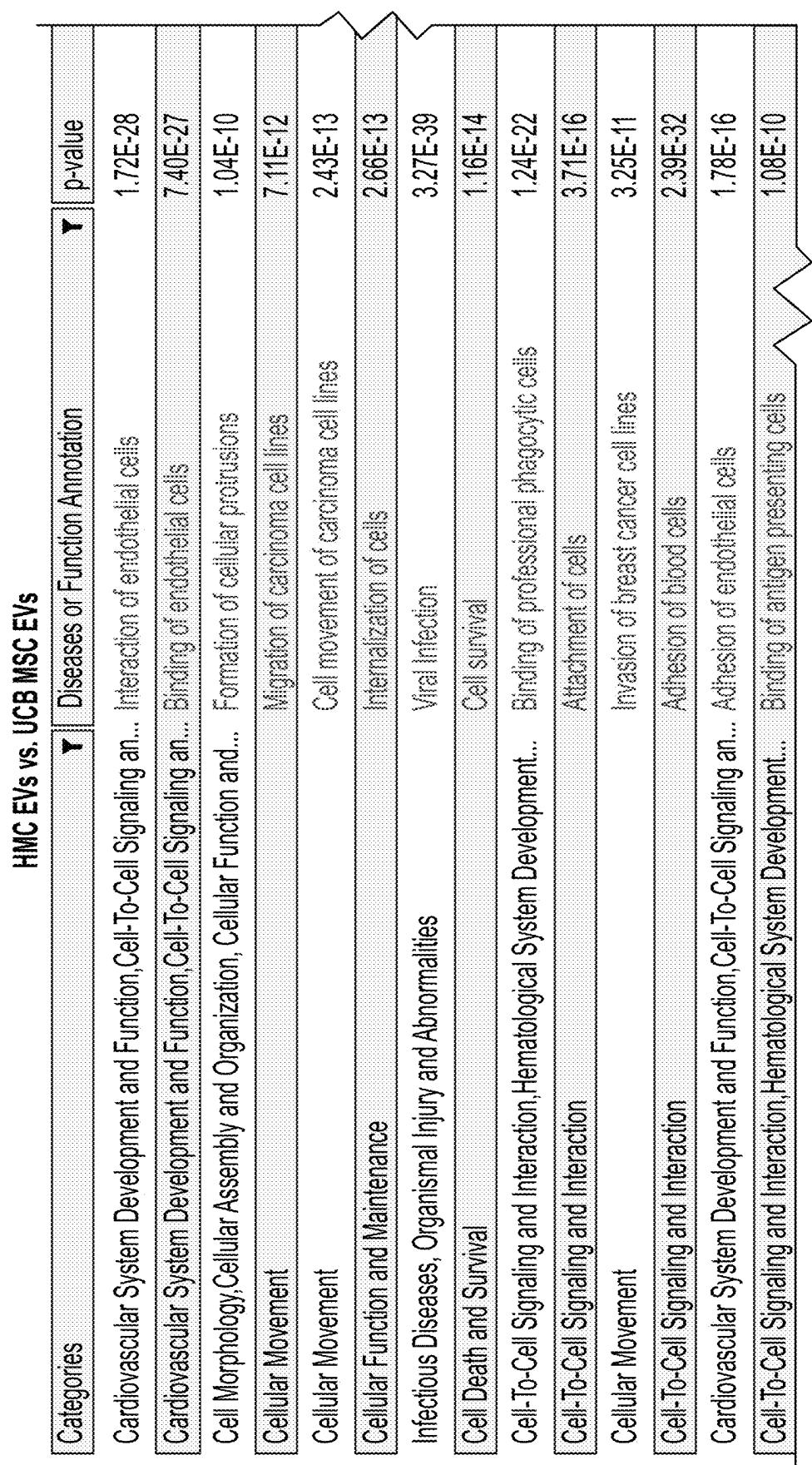


FIG. 65A
CONTINUED

**FIG. 65B**

HMC EVs vs. UCB MSC EVs		Molecules
YX	△ Activation z-score	▼ X
		↓ ADAM10, ↓ ALCAM, ↑ ANXA2, ↑ APP, ↑ BGN, ↑ CD36, ↑ CD44, ↑ CD63, ↑ CD42, ↑ CD15
		↓ ADAM10, ↓ ALCAM, ↑ ANXA2, ↑ APP, ↑ BGN, ↑ CD36, ↑ CD44, ↑ CD63, ↑ CD42, ↑ COL18A1
		↓ ABCC4, ↑ ACACA, ↓ ACTN4, ↑ ACTR2, ↑ ACTR3, ↑ AHNAK, ↑ ALDOA, ↑ ANPEP, ↑ APOE, ↑ APP
		↑ ACTA2, ↓ ADAM10, ↓ ALCAM, ↑ ANGPTL4, ↑ ANPEP, ↑ APOC1, ↑ BSG, ↑ CALR, ↓ CAMP, ↓ CAPNS1
		↑ ACTA2, ↓ ADAM10, ↓ ALCAM, ↑ ANGPTL4, ↑ ANPEP, ↑ APOC1, ↑ BSG, ↑ CALR, ↓ CAMP, ↓ CAPNS1
		↑ ACTR2, ↑ ACTR3, ↓ APCS, ↓ APMAP, ↑ ARPC2, ↑ ARPC3, ↑ ARPC4, ↓ C3, ↓ CAMP, ↓ CD14
		↑ ACE, ↑ ACTA2, ↑ ACTB, ↓ ACTN1, ↑ ACTR2, ↑ ACTR3, ↓ ADA, ↓ ADAM10, ↑ AGT, ↑ AHNAK
		↑ ACTA2, ↓ ADAM10, ↓ ALCAM, ↑ ADHS, ↑ AHNAK, ↓ AIFM1, ↓ ALB*, ↓ ALCAM, ↓ ALOX12, ↑ ANXA2
		↑ ACTACA, ↓ ACTN4, ↑ ACTR2, ↑ ADHS, ↑ AHNAK, ↓ AIFM1, ↓ ALB*, ↓ ALCAM, ↓ ALOX12, ↑ ANXA2
		↓ A2M, ↓ ADAM10, ↓ ALCAM, ↑ APOE, ↑ APOH, ↓ CAMP, ↑ CD14, ↑ CD44, ↓ CFH, ↑ CFHR1
		↓ CCN2, ↓ CD36, ↓ CD44, ↓ DCM, ↓ FN1, ↓ ILK, ↓ ITGA2, ↓ ITGA3, ↓ ITGA5, ↓ ITGA6
		↑ AHNAK, ↑ ANGPTL4, ↑ APP, ↑ BSG, ↑ CALR, ↓ CENZ, ↓ CD44, ↑ CD82, ↓ CD42, ↓ CDH1
		↓ A2M, ↓ ADAM10, ↓ ALCAM, ↑ AOC3, ↑ APCS, ↑ APOA4, ↑ APOE, ↑ APP, ↑ ATRN
		↓ ADAM10, ↓ ALCAM, ↑ CD36, ↑ CD44, ↑ CD63, ↑ CD42, ↑ COL18A1, ↑ EGFR, ↑ F10, ↑ F2
		↓ A2M, ↓ ALCAM, ↑ APOE, ↑ APOH, ↓ CAMP, ↑ CD44, ↑ CD63, ↑ ITGA6, ↑ ITGB1, ↑ MSN
2.781		

FIG. 65B
CONTINUED

HMC EVs vs. UCB MSC EVs

Cell-To-Cell Signaling and Interaction, Hematological System Development...	Binding of leukocytes	2.23E-27
Cell-To-Cell Signaling and Interaction, Hematological System Development...	Adhesion of immune cells	1.24E-23
Cellular Assembly and Organization, Cellular Function and Maintenance	Microtubule dynamics	4.10E-15
Cell Morphology, Cellular Movement	Cell spreading	2.12E-22
Cardiovascular System Development and Function, Cell-To-Cell Signaling an...	Binding of vascular endothelial cells	7.84E-21
Cellular Movement	Cell movement	2.16E-43
Cellular Movement, Hematological System Development and Function, Immu...	Cell movement of mononuclear leukocytes	1.56E-24
Cell-To-Cell Signaling and Interaction	Adhesion of leukemia cell lines	2.95E-12
Cell-To-Cell Signaling and Interaction	Binding of blood cells	2.18E-41
Cellular Assembly and Organization, Cellular Function and Maintenance	Organization of cytoskeleton	1.35E-17
Cell-To-Cell Signaling and Interaction, Hematological System Development...	Interaction of mononuclear leukocytes	7.08E-12
Cellular Movement	Invasion of tumor cell lines	1.44E-16
Cell Death and Survival	Cell viability	1.54E-13
Cellular Function and Maintenance	Endocytosis	3.42E-17
Cellular Movement	Migration of cells	4.85E-38
Cell-To-Cell Signaling and Interaction, Cellular Function and Maintenance, Inf...	Phagocytosis of cells	4.91E-15
Cellular Function and Maintenance, Inflammatory Response	Phagocytosis	2.12E-15

FIG. 65B
CONTINUED

2669	♦ A2M, ♦ ADAM10, ♦ ALCAM, ♦ AOC3, ♦ APOA4, ♦ APOE, ♦ APOH, ♦ ATRN, ♦ C5, ♦ CALR
2651	♦ A2M, ♦ ADAM10, ♦ ALCAM, ♦ AOC3, ♦ APOA4, ♦ APOE, ♦ C5, ♦ CALP
2630	♦ ABCC4, ♦ ACACA, ♦ ACTN4, ♦ ACTR2, ♦ ACTR3, ♦ AHNAK, ♦ ALDOA, ♦ ANPEP, ♦ APOE, ♦ APP
2627	♦ ALB*, ♦ ATRN, ♦ C3, ♦ C5, ♦ CAPI, ♦ CD36, ♦ CD9, ♦ CD42, ♦ CD44, ♦ CD63, ♦ DCN, ♦ EGFR, ♦ F10
2558	♦ ADAM10, ♦ ALCAM, ♦ APP, ♦ BGN, ♦ CD36, ♦ CD44, ♦ CD63, ♦ DCN, ♦ EGFR, ♦ F10
2557	♦ A2M, ♦ ABCC4, ♦ ACACA, ♦ ACTA2, ♦ ACTB, ♦ ACTN1, ♦ ACTN4, ♦ ADAM10, ♦ AGT, ♦ AHNAK
2541	♦ ADAM10, ♦ AGT, ♦ AOC3, ♦ APOA1, ♦ APOD, ♦ ATRN, ♦ C5, ♦ CAMP, ♦ CD44
2538	♦ ADAM10, ♦ APOH, ♦ CD44, ♦ CD82, ♦ CDH1, ♦ CPB2, ♦ ENG, ♦ F10, ♦ F2, ♦ FERM13
2521	♦ A2M, ♦ ADAM10, ♦ ALCAM, ♦ AOC3, ♦ APCS, ♦ APOA4, ♦ APOE, ♦ APOH, ♦ APP, ♦ ATRN
2476	♦ ABCC4, ♦ ACACA, ♦ ACTN1, ♦ ACTN4, ♦ ACTR2, ♦ ACTR3, ♦ AHNAK, ♦ ALDOA, ♦ ANPEP, ♦ APOE
2472	♦ AOC3, ♦ ATRN, ♦ CALR, ♦ CD14, ♦ CD44, ♦ ENG, ♦ F2, ♦ FERM13, ♦ FGF2, ♦ FN1
2460	♦ ACTA2, ♦ ACTN4, ♦ ADAM10, ♦ AHNAK, ♦ ALCAM, ♦ ANGPTL4, ♦ ANXA2, ♦ APOC1, ♦ APP
2446	♦ ACACA, ♦ ACTN4, ♦ ACTR2, ♦ ADH5, ♦ AHNAK, ♦ AIFM1, ♦ ALB*, ♦ ALCAM, ♦ ALOX12, ♦ ANXA2
2440	♦ ACTN1, ♦ ACTN4, ♦ ACTR2, ♦ ACTR3, ♦ APCS, ♦ APMAP, ♦ APOC1, ♦ APOC3, ♦ APOE, ♦ APP
2417	♦ A2M, ♦ ABCC4, ♦ ACACA, ♦ ACTA2, ♦ ACTN1, ♦ ACTN4, ♦ ADAM10, ♦ AGT, ♦ AHNAK, ♦ ALB*
2394	♦ ACTR2, ♦ ACTR3, ♦ AHSG, ♦ APGS, ♦ APGS, ♦ APOA1, ♦ APOA2, ♦ ARPC2, ♦ ARPC3, ♦ ARPC4
2387	♦ ACTR2, ♦ ACTR3, ♦ AHSG, ♦ APGS, ♦ APGS, ♦ APOA1, ♦ APOA2, ♦ ARPC2, ♦ ARPC3, ♦ ARPC4

FIG. 65B
CONTINUED

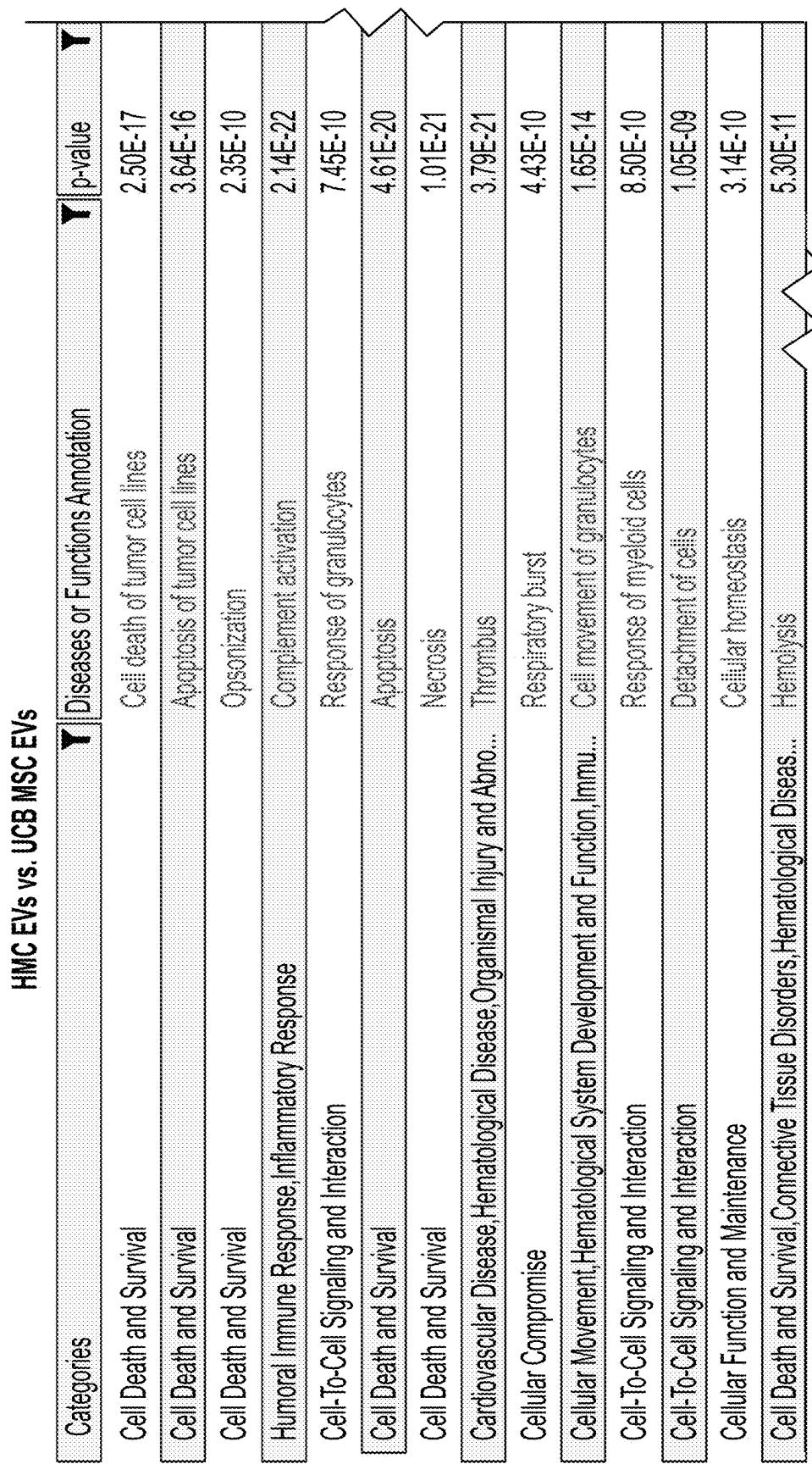


FIG. 65C

	∇	Activation z-score	\blacktriangledown	X	Molecules
	X	2.948			\downarrow ABCC4, \downarrow ACACA, \downarrow ADAM10, \downarrow ADAMTS12, \downarrow ADH5, \uparrow AHNAK, \downarrow AIFM1, \downarrow ALB*, \downarrow ALCAM, \downarrow ALOX12
		2.494			\downarrow ACACA, \uparrow AHNAK, \downarrow AIFM1, \downarrow ALB*, \downarrow ALCAM, \downarrow ALOX12, \downarrow ANGPTLA, \downarrow ANXA2, \downarrow APP, \downarrow ARGI
		2.425			\downarrow APOH, \downarrow C3, \downarrow C4AC4B*, \uparrow C4SPA, \downarrow C4SPB, \downarrow COLECT11, \downarrow FCN3, \downarrow LBP, \downarrow MBL2, \downarrow PLG
		2.195			\downarrow APCE, \uparrow C1QQA, \uparrow C1Q8, \uparrow C1QC, \uparrow C1R, \downarrow C3, \downarrow C4AC4B*, \downarrow C6, \downarrow C7, \downarrow C8
		2.110			\downarrow ANPEP, \uparrow APCS, \downarrow C3, \downarrow C5, \downarrow CAMP, \downarrow CD36, \downarrow CFH, \downarrow FCGR3AFCGR3B, \downarrow IGHA1, \downarrow IGHA2*
		2.068			\downarrow ACACA, \uparrow AGT, \uparrow AHNAK, \downarrow AIFM1, \downarrow ALB*, \downarrow ALCAM, \downarrow ALOX12, \downarrow ANGPTL4, \downarrow ANPEP, \downarrow ANXA2
		2.052			\downarrow ABCC4, \downarrow ACACA, \uparrow ACTR2, \downarrow ADAM10, \downarrow ADAMTS12, \downarrow ADH5, \downarrow AST, \downarrow AIFM1, \downarrow ALB*
		2.000			\downarrow ADA, \downarrow ALOX12, \downarrow APCH, \downarrow C3, \downarrow C5, \downarrow CALR, \downarrow CCNL2, \downarrow CFH, \downarrow CFHR1, \downarrow CFI
		-1.885			\downarrow ANPEP, \downarrow C3, \downarrow C5, \uparrow CD14, \downarrow IGHA1, \downarrow IGHA2*, \downarrow IGHC3, \downarrow JCHAIN, \uparrow PF4, \uparrow PGAM1
		-1.787			\downarrow ADAM10, \downarrow ALB*, \downarrow APOA1, \downarrow APP, \uparrow BSG, \downarrow C5, \downarrow CAMP, \downarrow CFH, \downarrow CFHR1, \downarrow DMNL
		-1.473			\downarrow ANPEP, \uparrow APCS, \downarrow C3, \downarrow C5, \downarrow CAMP, \downarrow CD14, \downarrow CD36, \downarrow CFH, \downarrow FCGR3A/FCGR3B, \downarrow IGHA1
		-1.435			\downarrow ADAM10, \downarrow CDH13, \downarrow ENG, \downarrow FERMT3, \downarrow FN1, \downarrow ITGB1, \downarrow LRP1, \downarrow MIP14, \downarrow PDCD6P, \downarrow PLG
		-1.352			\downarrow ADAM10, \uparrow ADCY5, \uparrow ADH5, \uparrow AST, \downarrow AIFM1, \downarrow ALDOA, \downarrow ANXA7, \downarrow APOA1, \downarrow APOL1, \downarrow APP
		-1.329			\downarrow ALB*, \uparrow ALDOA, \downarrow APOE, \uparrow C1S, \downarrow C3, \downarrow C4AC4B*, \downarrow C5, \downarrow CBA, \downarrow C8G, \downarrow CAMP

FIG. 65C
CONTINUED

Hematological Disease, Organismal Injury and Abnormalities	Hemorrhagic disease	1.01E-14
Cellular Movement, Hematological System Development and Function, Immuno... Hematological System Development and Function	Cell movement of neutrophils Coagulation	1.30E-12 1.68E-19
Cell Death and Survival	Cytolysis	1.18E-14
Cell Death and Survival	Cell death of leukemia cell lines	1.29E-09
Hematological System Development and Function, Organismal Functions	Coagulation of blood	7.59E-19
Hematological System Development and Function	Fibrinolysis	1.10E-15
Organismal Injury and Abnormalities	Fibrosis	7.56E-10
Hematological System Development and Function	Hemostasis	8.14E-30
Cellular Assembly and Organization	Development of cytoplasm	5.74E-10
Cellular Movement, Hematological System Development and Function, Immuno... Cellular Assembly and Organization	Migration of granulocytes Formation of cytoskeleton	3.63E-10 1.82E-09
Cell-To-Cell Signaling and Interaction, Renal and Urological System Develop... Cellular Movement	Binding of kidney cell lines Chemotaxis of myeloid cells	3.14E-11 1.10E-09

FIG. 65C
CONTINUED

-1.248	♦ APP, ♦ C3, ♦ C4A/C4B*, ♦ C5, ♦ CALR, ♦ CO4, ♦ CO42, ♦ DIAPH1, ♦ F10, ♦ F11
-1.219	♦ ADAM10, ♦ ALB*, ♦ APOA1, ♦ APP, ♦ BSG, ♦ C3, ♦ CAMP, ♦ CFH, ♦ CFHR1, ♦ DMDL
-1.190	♦ APOE, ♦ APOM, ♦ APP, ♦ C4BPB, ♦ CALU, ♦ CO36, ♦ CO59, ♦ F10, ♦ F11, ♦ F12
-1.030	♦ ALB, ♦ ALDOA, ♦ APOE, ♦ APP, ♦ C1S*, ♦ C3, ♦ C4AC4B, ♦ C5, ♦ C8A, ♦ C8G
-0.960	♦ ADAM10, ♦ ALFMI, ♦ ARCI, ♦ C5, ♦ CALR, ♦ CAMP, ♦ CAT, ♦ C4B1, ♦ CD44, ♦ CO39
-0.895	♦ APOE, ♦ APOM, ♦ APP, ♦ C4BPB, ♦ CALU, ♦ CO36, ♦ CO59, ♦ F10, ♦ F11, ♦ F12
-0.816	♦ APOM, ♦ F11, ♦ F12, ♦ F2, ♦ FGA, ♦ FGB, ♦ FGS, ♦ CP1BA, ♦ HKV81, ♦ PLG
-0.782	♦ ABCG4, ♦ ACE, ♦ ADAM10, ♦ AGT, ♦ ALB*, ♦ APOA1, ♦ APOA2, ♦ APOB, ♦ BSG, ♦ C3
-0.761	♦ APOA4, ♦ APOE, ♦ APOM, ♦ APP, ♦ C3, ♦ C4BPS, ♦ CALU, ♦ CO36, ♦ CO59, ♦ F10
-0.709	♦ ACTA2, ♦ APOA1, ♦ APOM, ♦ ARRBI1, ♦ CALD1, ♦ CAMP, ♦ CCN2, ♦ CO41, ♦ CO42, ♦ CO43
-0.603	♦ ADAM10, ♦ ALB*, ♦ C3, ♦ CAMP, ♦ CFH, ♦ CFHR1, ♦ FM1, ♦ ITGB3, ♦ LGALS1, ♦ MIF
-0.585	♦ ACTA2, ♦ APOA1, ♦ ARRBI1, ♦ CALM, ♦ CCON2, ♦ CO41, ♦ CO42, ♦ CO43, ♦ DIAPH1, ♦ F2
-0.524	♦ ANXA2, ♦ C3, ♦ CO4A, ♦ F10, ♦ FGA, ♦ FGB, ♦ FM1, ♦ ITGA3, ♦ ITGB1, ♦ ITGB3,
-0.509	♦ APOA1, ♦ APP, ♦ BSG, ♦ C3, ♦ CAMP, ♦ CSFR, ♦ DEAF1, ♦ includes others, ♦ DMDL, ♦ DPPI

FIG. 65C
CONTINUED

METHODS OF TREATING BRAIN INJURY**RELATED APPLICATION**

[0001] This application is a national phase filing under 35 C.F.R. § 371 of and claims priority to PCT Patent Application No. PCT/US2023/027882, filed on Jul. 17, 2023, which claims the benefit of priority to U.S. Provisional Application No. 63/390,044, filed on Jul. 18, 2022, the entire contents of which are incorporated herein by reference.

FIELD OF THE DISCLOSURE

[0002] The instant presently disclosed subject matter relates to methods of treating a brain injury using mesenchymal stem cells and/or extracellular vesicles secreted from the mesenchymal stem cells.

BACKGROUND OF THE DISCLOSURE

[0003] Brain injuries are complex and can have multiple severe clinical outcomes. An acquired brain injury is an injury to the brain that is not hereditary, congenital, degenerative, or induced by birth trauma. The injury results in a change to the brain's neuronal activity, which affects the physical integrity, metabolic activity, or functional ability of nerve cells in the brain. There are two main types of acquired brain injury: traumatic and non-traumatic.

[0004] Traumatic brain injury (TBI) is a major cause of death and disability in the United States. More than 1.7 million individuals suffer annually from TBI in US. A TBI is caused by an external force, such as a bump, blow, or jolt to the head that disrupts the normal function of the brain. The severity of a TBI may range from "mild" (i.e., a brief change in mental status or consciousness) to "severe" (i.e., an extended period of unconsciousness or memory loss after the injury). TBIs contribute to about 30% of all injury deaths. (Taylor et al. MMWR Surveill. Summ. 2017; 66(No. SS-9):1-16). Every day, about 153 people in the United States die from injuries that include TBI. Id. Those who survive a TBI can face effects that last a few days, or the rest of their lives. Effects of TBI can include impaired thinking or memory, movement, sensation (e.g., vision or hearing), or emotional functioning (e.g., personality changes, depression).

[0005] Approximately 20%-40% of people with TBI experience related vision disorders (Houston K E, et al., *Am J Phys. Med. Rehabil.* 2017, 96: e70-4). This can include blurred vision, visual field loss, and decreased visual acuity. These symptoms can occur acutely or chronically depending on injury type, location, and severity. TBI can affect diverse parts of the visual system ranging from the optic nerve and tract, lateral geniculate nucleus, and optic radiations, resulting in a variety of visual problems (Barnett B P, et al., *Curr Treat Options Neurol.*, 2015;17:329). One known site of afferent pathway damage is via the optic nerve and tract. Structurally, the optic nerve is vulnerable to compression, traction, crush, laceration, and avulsion injuries. Rapid acceleration, or deceleration, of the head may indirectly lead to optic nerve traction or axonal shearing, which can result in optic neuropathy.

[0006] Several treatment options to date for TBI include hyperbaric oxygen therapy, noninvasive brain stimulation, task-oriented functional electrical stimulation, and behavioral therapies (Dang et al. *Neural Plasticity* 2017; Volume

2017, Article ID 1582182, 6 pages). However, there is still a need for improved treatments for TBI.

[0007] Non-traumatic brain injury is usually caused by damage to the brain by internal factors, such as lack of oxygen, exposure to toxins, pressure from tumor, etc. Stroke is an example of non-traumatic brain injury. Stroke is the fifth leading cause of death in the United States, and nearly 800,000 people have a stroke each year. Stroke occurs when a blockage or bleed of the blood vessels either interrupts or reduces the supply of blood to the brain. When this happens, the brain does not receive enough oxygen or nutrients, and brain cells start to die. A person experiencing a stroke needs immediate emergency treatment, such as drugs that break down clots and prevent continued formation of clots. Although strokes can be treatable, some can lead to disability or death.

[0008] Cerebral palsy occurs as a result of a brain injury sustained during fetal development or birth. Cerebral palsy is caused by damage to the motor cortex of the brain, which affects muscle control and coordination, including an individual's ability to move, grasp objects, and talk. It is a leading cause of disability in young children and affects about 500,000 children and adults. There is currently no known cure for cerebral palsy.

[0009] Nerve and brain cells damaged in brain injuries are generally irreparable because brain tissue cannot regenerate. Stem cell therapies have shown some promise in neuroregenerative treatments. However, there is still a need for improved treatments for brain injuries.

SUMMARY OF THE DISCLOSURE

[0010] The presently disclosed subject matter provides mesenchymal stem cells (MSCs, or also referred to herein as "HMCs") obtained by in vitro differentiation of pluripotent stem cells, and extracellular vesicles ("EVs") secreted from the HMCs (HMC-EVs) of the presently disclosed subject matter, and their use in methods of treating brain injuries. Specifically, the inventors of the presently disclosed subject matter have discovered that the HMCs and HMC-EVs of the presently disclosed subject matter are distinct from MSCs and EVs derived from other sources, e.g., adipose tissue-derived MSCs, bone marrow-derived MSCs, and/or umbilical cord blood-derived MSCs. Specifically, the HMCs of the presently disclosed subject matter have a distinct expression profile when compared to other MSCs, e.g., adipose tissue-derived MSCs, bone marrow-derived MSCs, and/or umbilical cord blood-derived MSCs. Proteins/genes that are involved in neuroprotection and cell viability/survival pathways are upregulated in the HMCs of the presently disclosed subject matter, suggesting that the HMCs of the presently disclosed subject matter are able to confer neuroprotective effects, and provide neurotrophic factors, i.e., factors involved in supporting neuronal survival, growth, health and/or recovery. Likewise, the HMC-EVs of the presently disclosed subject matter share a similar profile as the HMCs from which they were secreted. Similar signaling pathways enriched in the HMCs are also enriched in the HMC-EVs when compared to other tissue-derived MSCs and EVs. This distinct profile renders the HMCs and the HMC-EVs to be particularly useful and effective in treating disease, such as brain injuries. Examples of brain injuries treatable with the HMCs and/or HMC-EVs of the presently disclosed subject matter include stroke, traumatic brain injury, acquired brain injury, anoxic brain injury, diffuse axonal brain injury, focal

brain injury, subdural hematoma, brain aneurysm, coma, optic neuropathy, and cerebral palsy.

[0011] Accordingly, in one aspect, the presently disclosed subject matter provides a method of treating a brain injury in a subject suffering from, or suspected of suffering from, a brain injury, the method comprising administering to the subject an effective amount of EVs secreted from HMCs (HMC-EVs) obtained by in vitro differentiation of pluripotent stem cells, thereby treating the brain injury in the subject.

[0012] In some embodiments, the brain injury is selected from the group consisting of stroke, traumatic brain injury, optic neuropathy, cerebral palsy, acquired brain injury, anoxic brain injury, diffuse axonal brain injury, focal brain injury, subdural hematoma, brain aneurysm, and coma. In some embodiments, the brain injury is stroke. In some embodiments, the brain injury is optic neuropathy.

[0013] In some embodiments, the method comprises increasing oligodendrocyte and precursor cells in the brain following administration of the HMC-EVs into the subject. In some embodiments, the method comprises preserving myelin in the brain following administration of the HMC-EVs into the subject. In some embodiments, the method comprises preventing oxidative damage in neurons following administration of the HMC-EVs into the subject. In some embodiments, the method comprises preventing neuronal death due to glutamate excitotoxicity injury following administration of the HMC-EVs into the subject. In some embodiments, the method comprises reducing tissue loss in the brain following administration of the EVs into the subject. In some embodiments, the method comprises reducing cell death in the brain following administration of the HMC-EVs into the subject. In some embodiments, the method comprises stimulating pathways involved in the development of neuronal lineage following administration of the HMC-EVs into the subject.

[0014] In some embodiments, the HMC-EVs are administered systemically. In some embodiments, the HMC-EVs are administered intracerebrally. In some embodiments, the HMC-EVs are administered intrathecally. In some embodiments, the HMC-EVs are administered intracisternally. In some embodiments, the HMC-EVs are administered intraperitoneally.

[0015] In some embodiments, the subject is a human.

[0016] In some embodiments, the HMCs are obtained by in vitro differentiation of human pluripotent stem cells. In some embodiments, the pluripotent stem cells are further differentiated into hemangioblasts. In some embodiments, the pluripotent stem cells are embryonic stem cells. In some embodiments, the pluripotent stem cells are induced pluripotent stem cells. In some embodiments, the induced pluripotent stem cells are produced by contacting a cell with one or more reprogramming factors.

[0017] In some embodiments, the HMC-EVs express at least one of the miRNA in Table 9 at a higher level compared to EVs secreted from umbilical cord blood-derived MSCs (UCB-MSC-EVs).

[0018] In some embodiments, the HMC-EVs express at least one of the miRNA in Table 10 at a lower level compared to UCB-MSC-EVs.

[0019] In some embodiments, the HMC-EVs express at least one of the miRNA in Table 11 at a higher level compared to EVs secreted from bone marrow-derived MSCs (BM-MSC-EVs).

[0020] In some embodiments, the HMC-EVs express at least one of the miRNA in Table 12 at a lower level compared to BM-MSC-EVs.

[0021] In some embodiments, the HMC-EVs express at least one of the miRNA in Table 13 at a higher level compared to EVs secreted from adipose tissue-derived MSCs (AD-MSC-EVs).

[0022] In some embodiments, the HMC-EVs express at least one of the miRNA in Table 14 at a lower level compared to AD-MSC-EVs.

[0023] In some embodiments, the HMC-EVs express at least one of the proteins in Table 15 at a higher level compared to UCB-MSC-EVs.

[0024] In some embodiments, the HMC-EVs express at least one of the proteins in Table 16 at a lower level compared to UCB-MSC-EVs.

[0025] In some embodiments, the HMC-EVs express at least one of the proteins in Table 17 at a higher level compared to BM-MSC-EVs.

[0026] In some embodiments, the HMC-EVs express at least one of the proteins in Table 18 at a lower level compared to BM-MSC-EVs.

[0027] In some embodiments, the HMC-EVs express at least one of the proteins in Table 19 at a higher level compared to AD-MSC-EVs.

[0028] In some embodiments, the HMC-EVs express at least one of the proteins in Table 20 at a lower level compared to AD-MSC-EVs.

[0029] In some embodiments, the HMC-EVs express at least one of the miRNAs selected from the group consisting of hsa-miR-125b-5p, hsa-miR-181a-5p, hsa-miR-199b-5p, hsa-miR-21-5p, hsa-miR-23a-3p, hsa-miR-125a-5p, hsa-miR-106a-5p+hsa-miR-17-5p and hsa-miR-221-3p at a higher level compared to BM-MSC-EVs, UCB-MSC-EVs, and/or AD-MSC-EVs.

[0030] In some embodiments, the HMC-EVs express at least one of the proteins selected from the group consisting of ALDOC, ANXA5, APBB2, BASP1, CAV1, CD81, CD99, CKM, EPB41L3, FDPS, GNAQ, GNG12, GP9, H2AC20, H2AC21, H3-3A, H3-7, H4-16, HLA-A, ITGA2, KPNA2, KRAS, KRT4, LRRC59, MAMDC2, MARCKSL1, MDGA1, MERTK, MFGE8, MMP14, MVP, PCDH1, PDGFRB, PDIA3, RPL13, RPS18, RPS3A, RPS4X, SDCBP, SLC2A1, SLC3A2, TAGLN2, TNC, TSPAN14, TSPAN31, TSPAN9, TTYH3, UCHL1, VAT1, YWHAB, and YWHAQ at a higher level compared to BM-MSC-EVs, UCB-MSC-EVs, and/or AD-MSC-EVs.

[0031] In some embodiments, the HMC-EVs express at least one of the proteins selected from the group consisting of ADGRG6, AGRN, ANXA6, APOC4, ARHGAP1, ARGHIDIA, ARL8A, ARPC5, B2M, BBS1, BLVRA, BST1, CA2, CCN2, CCNB3, CD34, CD36, CD47, CORO1A, DTD1, EEF1D, EEF1G, ENG, ESD, GNAI2, GNB1, H1-3, H2BC15, HIP1, KIF11, LAMP1, LAP3, LGALS1, LTBP3, MAPK3, MARCKS, MBTD1, MDH1, MOB1B, MYL12B, MYO1F, MYO3A, NIBAN2, PEBP1, PF4, PGAP1, PLOD1, PPP2R1A, PRSS23, PXDN, RALA, RAP2A, RPS13, RPS3, RPSA, S100A11, SLC44A1, SLC44A2, SLTM, SMG1, SPARC, SRSF8, STRADB, STX11, STXBP2, TGM2, TPP1, TPTE2, TRIM5, TRPM2, TUBA8, TUBB3, VCAN, YWHAE, and ZFN607 at a higher level compared to BM-MSC-EVs, UCB-MSC-EVs, and/or AD-MSC-EVs.

[0032] In some embodiments, the HMC-EVs express at least one of the proteins selected from the group consisting of ADIPOQ, CAT, CEP290, IGLV6-57, TAS2R33, and TMEM198 at a lower level compared to EVs secreted from BM-MSC-EVs, UCB-MSC-EVs, and/or AD-MSC-EVs.

[0033] In some embodiments, the HMC-EVs express at least one of the proteins selected from the group consisting of AKAP9, ALB, ALOX5, APLP2, CD109, CDSN, CHST9, ERC1, F11, ARMCX5, LAMB4, LRRTM2, LTF, MSH6, OAF, OLFML3, PAK6, RGS14, SEMA7A, SURF1, and TRIM4 at a lower level compared to BM-MSC-EVs, UCB-MSC-EVs, and/or AD-MSC-EVs.

[0034] In some embodiments, the HMC-EVs express at least one of the miRNA in Table 21 at a higher level compared to the HMCs.

[0035] In some embodiments, the HMC-EVs express at least one of the miRNA in Table 22 at a lower level compared to the HMCs.

[0036] In some embodiments, about 1×10^6 to about 1×10^{13} HMC-EVs are administered to the subject. In some embodiments, about 10×10^{10} or about 30×10^{10} HMC-EVs are administered to the subject.

[0037] In some embodiments, the HMC-EVs are administered in a pharmaceutical composition.

[0038] In some embodiments, the pharmaceutical composition comprises (a) a buffer, maintaining the solution at a physiological pH; (b) at least 2 mM or at least 0.05% (w/v) glucose; and (c) an osmotically active agent maintaining the solution at a physiological osmolarity.

[0039] In some embodiments, the glucose is D-glucose (Dextrose). In some embodiments, the osmotically active agent is a salt. In some embodiments, the osmotically active agent is a magnesium salt, phosphate salt, sulfate salt, chloride salt, poorly absorbed disaccharides, such as lactulose, sugar alcohols, such as mannitol and sorbitol, and polyethylene glycol, or a combination thereof. In some embodiments, the osmotically active agent is CaCl₂, KCl, NaCl, KH₂PO₄, Na₃HPO₄, MgCl₂, MgSO₄, HEPES, NaHCO₃, or a combination thereof. In some embodiments, the salt is sodium chloride.

[0040] In some embodiments, the method further comprises administering to the subject an effective amount of HMCs obtained by in vitro differentiation of pluripotent stem cells.

[0041] In one aspect, the presently disclosed subject matter provides a method of treating a brain injury in a subject suffering from, or suspected of suffering from, a brain injury, the method comprising administering to the subject an effective amount of HMCs obtained by in vitro differentiation of pluripotent stem cells, thereby treating the brain injury in the subject.

[0042] In some embodiments, the brain injury is selected from the group consisting of stroke, traumatic brain injury, cerebral palsy, acquired brain injury, anoxic brain injury, diffuse axonal brain injury, focal brain injury, subdural hematoma, brain aneurysm, optic neuropathy, and coma.

[0043] In some embodiments, the brain injury is stroke.

[0044] In some embodiments, the brain injury is optic neuropathy.

[0045] In some embodiments, the method comprises preserving myelin in the brain following administration of the HMCs into the subject. In some embodiments, the method comprises suppressing neuroinflammatory responses following administration of the HMCs into the subject. In some

embodiments, the method comprises reducing microglial and astrocyte activation in the brain following administration of the HMCs into the subject. In some embodiments, the method comprises stimulating pathways involved in cell survival following administration of the HMCs into the subject. In some embodiments, the method comprises stimulating expression of a neuroprotective gene in the brain following administration of the HMCs into the subject. In some embodiments, the neuroprotective gene is selected from the group consisting of heat shock protein family B member 1 (HSPB1), insulin-like growth factor 1 (IGF2), and secreted phosphoprotein 1 (SPP1). In some embodiments, the method comprises stimulating pathways involved in synaptic transmission in the brain following administration of the HMCs into the subject. In some embodiments, the method comprises stimulating pathways involved in the development of neuronal lineage following administration of the HMCs into the subject. In some embodiments, the method comprises reducing apoptosis following administration of the HMCs into the subject.

[0046] In some embodiments, the brain injury is traumatic brain injury.

[0047] In some embodiments, the method comprises reducing tissue loss in the brain following administration of the HMCs into the subject. In some embodiments, the method comprises reducing cell death in the brain following administration of the HMCs into the subject. In some embodiments, the method comprises increasing neurogenesis following the administration of the HMCs into the subject. In some embodiments, the method comprises reducing the presence of microglia and macrophages in the cortex and striatum following the administration of the HMCs into the subject. In some embodiments, the method comprises reducing inflammation of the spleen following the administration of the HMCs into the subject. In some embodiments, the method comprises migration of HMCs across the blood-brain barrier to the cortex, striatum, and/or hippocampus.

[0048] In some embodiments, the brain injury is cerebral palsy.

[0049] In some embodiments, the method comprises reducing apoptosis in the brain following administration of the HMCs into the subject. In some embodiments, the method comprises reducing lesion size in the brain following administration of the HMCs into the subject. In some embodiments, the method comprises reducing microglial and astrocyte activation in the brain following administration of the HMCs into the subject. In some embodiments, the method comprises preserving myelin of the corpus callosum following administration of the HMCs into the subject. In some embodiments, the method comprises at least a partial rescue of Olig2 in the brain following administration of the HMCs into the subject.

[0050] In some embodiments, the HMCs are administered systemically. In some embodiments, the HMCs are administered intracerebrally. In some embodiments, the HMCs are administered intrathecally. In some embodiments, the HMCs are administered intracisternally. In some embodiments, the HMCs are administered intraperitoneally. In some embodiments, the mesenchymal stem cells are human cells.

[0051] In some embodiments, the subject is a human.

[0052] In some embodiments, the pluripotent stem cells are further differentiated into hemangioblasts. In some

embodiments, the pluripotent stem cells are embryonic stem cells. In some embodiments, the pluripotent stem cells are induced pluripotent stem cells. In some embodiments, the pluripotent stem cells are human pluripotent stem cells.

[0053] In some embodiments, the HMCs have been passed no more than 5 times in vitro before administration into the subject.

[0054] In some embodiments, the HMCs express at least one of the genes in Table 3 at a higher level compared to bone marrow-derived MSCs (BM-MSCs).

[0055] In some embodiments, the HMCs express at least one of the genes in Table 4 at a lower level compared to BM-MSCs.

[0056] In some embodiments, the HMCs express at least one of the genes in Table 5 at a higher level compared to umbilical cord blood-derived MSCs (UCB-MSCs).

[0057] In some embodiments, the HMCs express at least one of the genes in Table 6 at a lower level compared to UCB-MSCs.

[0058] In some embodiments, the HMCs express at least one of the genes in Table 7 at a higher level compared to adipose tissue-derived MSCs (AD-MSCs).

[0059] In some embodiments, the HMCs express at least one of the genes in Table 8 at a lower level compared to AD-MSCs.

[0060] In some embodiments, the HMCs express, in a basal state, mRNA encoding interleukin-6 (IL-6) at a level less than ten percent of the IL-6 mRNA level expressed by BM-MSCs, in a basal state, and wherein the HMCs express, in a basal state, mRNA encoding CD24 at a level that is greater than the CD24 mRNA level expressed by BM-MSCs in a basal state.

[0061] In some embodiments, the HMCs express at least one of the genes selected from the group consisting of CALR, UBB, PKM, CXCL8, C15orf48, PSME2, TPM3, ANKRD1, PFN1, SRGN, ACTB, MDK, TAGLN2, CFL1, HSP90AA1, HSPA8, CXCL12, UCHL1, HMGA2, HMGA1, HN1, PTMA, SP90AB1, PRDX1, GSTP1, KRT18, IGFBP4, CALD1, COL4A1, COL4A2, and GAPDH at a higher level compared to adipose tissue-derived MSCs (AD-MSCs).

[0062] In some embodiments, the HMCs express at least one of the genes selected from the group consisting of TMSB4X, ACTG1, GSTP1, KRT18, IGFBP5, NPY, KRT8, PRDX6, MDK, DKK3, UCHL1, TUBB3, HN1, PTMA, HSP90AB1, HMGA1, HSPA8, TAGLN2, ANKRD1, PFN1, CYBA, and UBB at a higher level compared to AD-MSCs.

[0063] In some embodiments, the HMCs express at least one of the genes selected from the group consisting of SERPINE1, ACTA2, TPM2, CTGF, SERPINE2, CRYAB, ELN, MFGE8, ANXA2, POSTN, VIM, MFAP5, ISLR, THBS1, TIMP3, DKK1, COL6A3, COL6A1, TPT1, BCYRN1, COL1A1, SPARC, TPM1, BGN, COL1A2, COL3A1, TGFB1, CRLF1, COMP, NEAT1, MT-CO3, MT-CO2, MT-ATP8, MT-CYB, MT-CO1, MT-ATP6, MT-ND4, MT-ND4L, MT-ND5, MT-ND6, MT-ND3, MT-ND1, MT-ND2, GREM1, TMSB4X, ITGB1, LMNA, H2AFZ, FTL, EEF1G, NPM1, EEF1A1, RACK1, ACTG1, and TPM4 at a lower level compared to AD-MSCs.

[0064] In some embodiments, the HMCs express at least one of the genes selected from the group consisting of SERPINE1, S100A6, CD59, POSTN, VIM, MFAP5, ISLR, THBS1, COL6A3, TIMP3, ELN, ANXA2, COL1A1, BCYRN1, CCDC80, COL6A1, COL6A2, BGN, COL1A2,

COL3A1, TGFB1, CRLF1, COMP, and GREM1 at a lower level compared to AD-MSCs.

[0065] In some embodiments, the HMCs express at least one of the genes selected from the group consisting of MT1X, MT1G, TMSB10, CCL8, INHBA, CTSB, SERPINB2, ADM, APOL1, FTH1, CCL2, CCL5, CSF1, IL1B, IGFBP3, P4HB, DCN, FSTL1, ANXA5, LOX, CD63, CTSZ, FN1, LGALS1, LDHA, RCN3, MMP2, and TIMP1 at a lower level compared to AD-MSCs.

[0066] In some embodiments, the HMCs express at least one of the genes selected from the group consisting of PPIA, NPM1, HNRNPA1, IGFBP5, KRT19, KRT18, GSTP1, TUBB, TUBA1B, KRT8, HN1, PTMA, TUBA1C, HSPA8, HMGA1, CFL1, MYL6, ACTB, UCHL1, TAGLN2, MDK, GREM1, MMP1, and CTSC at a higher level compared to bone marrow-derived MSCs (BM-MSCs).

[0067] In some embodiments, the HMCs express at least one of the genes selected from the group consisting of ANXA2, TPT1, VIM, COL6A1, BGN, COL6A2, CTGF, TIMP3, ACTA2, COL3A1, SPARC, ITGB1, SERPINH1, TPMP2, TGFB1, COL1A1, TPM1, COL6A3, TPM4, SERPINE2, CALD1, COL1A2, TAGLN, MYL9, MT-RNR2, POSTN at a lower level compared to BM-MSCs.

[0068] In some embodiments, the HMCs express at least one of the miRNA in Table 21 at a lower level compared to the HMC-EVs secreted from the HMCs.

[0069] In some embodiments, the HMCs express at least one of the miRNA in Table 22 at a higher level compared to the HMC-EVs secreted from the HMCs.

[0070] In some embodiments, about 1×10^6 to about 1×10^{13} HMCs are administered to the subject.

[0071] In some embodiments, the HMCs are administered in a pharmaceutical composition.

[0072] In some embodiments, the pharmaceutical composition comprises (a) a buffer, maintaining the solution at a physiological pH; (b) at least 2 mM or at least 0.05% (w/v) glucose; and (c) an osmotically active agent maintaining the solution at a physiological osmolarity.

[0073] In some embodiments, the glucose is D-glucose (Dextrose). In some embodiments, the osmotically active agent is a salt. In some embodiments, the salt is sodium chloride.

[0074] In another aspect, the presently disclosed subject matter provides a method of treating a brain injury in a subject suffering from, or suspected of suffering from, a brain injury, the method comprising administering to the subject an effective amount of EVs secreted from HMCs obtained by in vitro differentiation of pluripotent stem cells, and an effective amount of HMCs obtained by in vitro differentiation of pluripotent stem cells, thereby treating the brain injury in the subject.

[0075] In one aspect, the presently disclosed subject matter provides a composition comprising HMCs obtained by in vitro differentiation of pluripotent stem cells, wherein the HMCs express at least one of the genes selected from the group consisting of CALR, UBB, PKM, CXCL8, C15orf48, PSME2, TPM3, ANKRD1, PFN1, SRGN, ACTB, MDK, TAGLN2, CFL1, HSP90AA1, HSPA8, CXCL12, UCHL1, HMGA2, HMGA1, HN1, PTMA, SP90AB1, PRDX1, GSTP1, KRT18, IGFBP4, CALD1, COL4A1, COL4A2, and GAPDH at a higher level compared to AD-MSCs.

[0076] In one aspect, the presently disclosed subject matter provides a composition comprising HMCs obtained by in vitro differentiation of pluripotent stem cells, wherein the

HMCs express at least one of the genes selected from the group consisting of TMSB4X, ACTG1, GSTP1, KRT18, IGFBP5, NPY, KRT8, PRDX6, MDK, DKK3, UCHL1, TUBB3, HN1, PTMA, HSP90AB1, HMGA1, HSPA8, TAGLN2, ANKRD1, PFN1, CYBA, and UBB at a higher level compared to AD-MSCs.

[0077] In one aspect, the presently disclosed subject matter provides a composition comprising HMCs obtained by in vitro differentiation of pluripotent stem cells, wherein the HMCs express at least one of the genes selected from the group consisting of PPIA, NPM1, HNRNPA1, IGFBP5, KRT19, KRT18, GSTP1, TUBB, TUBA1B, KRT8, HN1, PTMA, TUBA1C, HSPA8, HMGA1, CFL1, MYL6, ACTB, UCHL1, TAGLN2, MDK, GREM1, MMP1, and CTSC at a higher level compared to BM-MSCs.

[0078] In one aspect, the presently disclosed subject matter provides a composition comprising HMCs obtained by in vitro differentiation of pluripotent stem cells, wherein the HMCs express at least one of the genes selected from the group consisting of SERPINE1, ACTA2, TPM2, CTGF, SERPINE2, CRYAB, ELN, MFGE8, ANXA2, POSTN, VIM, MFAP5, ISLR, THBS1, TIMP3, DKK1, COL6A3, COL6A1, TPT1, BCYRN1, COL1A1, SPARC, TPM1, BGN, COL1A2, COL3A1, TGFB1, CRLF1, COMP, NEAT1, MT-CO3, MT-CO2, MT-ATP8, MT-CYB, MT-CO1, MT-ATP6, MT-ND4, MT-ND4L, MT-ND5, MT-ND6, MT-ND3, MT-ND1, MT-ND2, GREM1, TMSB4X, ITGB1, LMNA, H2AFZ, FTL, EEF1G, NPM1, EEF1A1, RACK1, ACTG1, and TPM4 at a lower level compared to AD-MSCs.

[0079] In one aspect, the presently disclosed subject matter provides a composition comprising HMCs obtained by in vitro differentiation of pluripotent stem cells, wherein the HMCs express at least one of the genes selected from the group consisting of SERPINE1, S100A6, CD59, POSTN, VIM, MFAP5, ISLR, THBS1, COL6A3, TIMP3, ELN, ANXA2, COL1A1, BCYRN1, CCDC80, COL6A1, COL6A2, BGN, COL1A2, COL3A1, TGFB1, CRLF1, COMP, and GREM1 at a lower level compared to AD-MSCs.

[0080] In one aspect, the presently disclosed subject matter provides a composition comprising HMCs obtained by in vitro differentiation of pluripotent stem cells, wherein the HMCs express at least one of the genes selected from the group consisting of MT1X, MT1G, TMSB10, CCL8, INHBA, CTSB, SERPINB2, ADM, APOL1, FTH1, CCL2, CCL5, CSF1, IL1B, IGFBP3, P4HB, DCN, FSTL1, ANXA5, LOX, CD63, CTSZ, FN1, LGALS1, LDHA, RCN3, MMP2, and TIMP1 at a lower level compared to AD-MSCs.

[0081] In one aspect, the presently disclosed subject matter provides a composition comprising HMCs obtained by in vitro differentiation of pluripotent stem cells, wherein the HMCs express at least one of the genes selected from the group consisting of ANXA2, TPT1, VIM, COL6A1, BGN, COL6A2, CTGF, TIMP3, ACTA2, COL3A1, SPARC, ITGB1, SERPINH1, TPM2, TGFB1, COL1A1, TPM1, COL6A3, TPM4, SERPINE2, CALD1, COL1A2, TAGLN, MYL9, MT-RNR2, POSTN at a lower level compared to BM-MSCs.

[0082] In some embodiments, the HMCs further express at least one of the genes in Table 3 at a higher level compared to BM-MSCs.

[0083] In some embodiments, the HMCs further express at least one of the genes in Table 4 at a lower level compared to BM-MSCs.

[0084] In some embodiments, the HMCs further express at least one of the genes in Table 5 at a higher level compared to UCB-MSCs.

[0085] In some embodiments, the HMCs further express at least one of the genes in Table 6 at a lower level compared to UCB-MSCs.

[0086] In some embodiments, the HMCs further express at least one of the genes in Table 7 at a higher level compared to AD-MSCs.

[0087] In some embodiments, the HMCs further express at least one of the genes in Table 8 at a lower level compared to AD-MSCs.

[0088] In one aspect, the presently disclosed subject matter provides a pharmaceutical composition comprising the HMCs of the presently disclosed subject matter, and a pharmaceutically acceptable carrier.

[0089] In one aspect, the presently disclosed subject matter provides a population of HMC-EVs of the presently disclosed subject matter.

[0090] In some embodiments, the HMC-EVs express at least one of the miRNA in Table 9 at a higher level compared to UCB-MSC-EVs.

[0091] In some embodiments, the HMC-EVs express at least one of the miRNA in Table 10 at a lower level compared to UCB-MSC-EVs.

[0092] In some embodiments, the HMC-EVs express at least one of the miRNA in Table 11 at a higher level compared to BM-MSC-EVs.

[0093] In some embodiments, the HMC-EVs express at least one of the miRNA in Table 12 at a lower level compared to BM-MSC-EVs.

[0094] In some embodiments, the HMC-EVs express at least one of the miRNA in Table 13 at a higher level compared to AD-MSC-EVs.

[0095] In some embodiments, the HMC-EVs express at least one of the miRNA in Table 14 at a lower level compared to AD-MSC-EVs.

[0096] In some embodiments, the HMC-EVs express at least one of the proteins in Table 15 at a higher level compared to UCB-MSC-EVs.

[0097] In some embodiments, the HMC-EVs express at least one of the proteins in Table 16 at a lower level compared to UCB-MSC-EVs.

[0098] In some embodiments, the HMC-EVs express at least one of the proteins in Table 17 at a higher level compared to BM-MSC-EVs.

[0099] In some embodiments, the HMC-EVs express at least one of the proteins in Table 18 at a lower level compared to BM-MSC-EVs.

[0100] In some embodiments, the HMC-EVs express at least one of the proteins in Table 19 at a higher level compared to AD-MSC-EVs.

[0101] In some embodiments, the HMC-EVs express at least one of the proteins in Table 20 at a lower level compared to AD-MSC-EVs.

[0102] In some embodiments, the HMC-EVs express at least one of the miRNA in Table 21 at a higher level compared to the HMCs.

[0103] In some embodiments, the HMC-EVs express at least one of the miRNA in Table 22 at a lower level compared to the HMCs.

[0104] In some embodiments, the HMC-EVs express at least one of the miRNAs selected from the group consisting of hsa-miR-125b-5p, hsa-miR-181a-5p, hsa-miR-199b-5p, hsa-miR-21-5p, hsa-miR-23a-3p, hsa-miR-125a-5p, hsa-miR-106a-5p+hsa-miR-17-5p and hsa-miR-221-3p at a higher level compared to EVs secreted from BM-MSC-EVs, UCB-MSC-EVs, and/or AD-MSC-EVs.

[0105] In some embodiments, the HMC-EVs express at least one of the proteins selected from the group consisting of ALDOC, ANXA5, APBB2, BASP1, CAV1, CD81, CD99, CKM, EPB41L3, FDPS, GNAQ, GNG12, GP9, H2AC20, H2AC21, H3-3A, H3-7, H4-16, HLA-A, ITGA2, KPNA2, KRAS, KRT4, LRRK59, MAMDC2, MARCKSL1, MDGA1, MERTK, MFGE8, MMP14, MVP, PCDH1, PDGFRB, PDI3, RPL13, RPS18, RPS3A, RPS4X, SDCBP, SLC2A1, SLC3A2, TAGLN2, TNC, TSPAN14, TSPAN33, TSPAN9, TTYH3, UCHL1, VAT1, YWHAB, and YWHAQ at a higher level compared to BM-MSC-EVs, UCB-MSC-EVs, and/or AD-MSC-EVs.

[0106] In some embodiments, the HMC-EVs express at least one of the proteins selected from the group consisting of ADGRG6, AGRN, ANXA6, APOC4, ARHGAP1, ARGHDIA, ARL8A, ARPC5, B2M, BBS1, BLVRA, BST1, CA2, CCN2, CCNB3, CD34, CD36, CD47, CORO1A, DTD1, EEF1D, EEF1G, ENG, ESD, GNAI2, GNB1, H1-3, H2BC15, HIP1, KIF11, LAMP1, LAP3, LGALS1, LTBP3, MAPK3, MARCKS, MBTD1, MDH1, MOB1B, MYL12B, MYO1F, MYO3A, NIBAN2, PEBP1, PF4, PGAP1, PLOD1, PPP2RIA, PRSS23, PXDN, RALA, RAP2A, RPS13, RPS3, RPSA, S100A11, SLC44A1, SLC44A2, SLTM, SMG1, SPARC, SRSF8, STRADB, STX11, STXBP2, TGM2, TPP1, TPTE2, TRIM5, TRPM2, TUBA8, TUBB3, VCAN, YWHAE, and ZFN607 at a higher level compared to BM-MSC-EVs, UCB-MSC-EVs, and/or AD-MSC-EVs.

[0107] In some embodiments, the HMC-EVs express at least one of the proteins selected from the group consisting of ADIPOQ, CAT, CEP290, IGLV6-57, TAS2R33, and TMEM198 at a lower level compared to BM-MSC-EVs, UCB-MSC-EVs, and/or AD-MSC-EVs.

[0108] In some embodiments, the HMC-EVs express at least one of the proteins selected from the group consisting of AKAP9, ALB, ALOX5, APLP2, CD109, CDSN, CHST9, ERC1, F11, ARMCX5, LAMB4, LRRTM2, LTF, MSH6, OAF, OLFML3, PAK6, RGS14, SEMA7A, SURF1, and TRIM4 at a lower level compared to BM-MSC-EVs, UCB-MSC-EVs, and/or AD-MSC-EVs.

[0109] In one aspect, the presently disclosed subject matter provides a pharmaceutical composition comprising the HMC-EVs of the presently disclosed subject matter, and a pharmaceutically acceptable carrier.

[0110] In one aspect, the presently disclosed subject matter provides a population of HMC-EVs secreted from HMCs obtained by in vitro differentiation of pluripotent stem cells, wherein the HMC-EVs express at least one of the miRNA in Table 9 at a higher level compared to UCB-MSC-EVs.

[0111] In one aspect, the presently disclosed subject matter provides a population of HMC-EVs secreted from HMCs obtained by in vitro differentiation of pluripotent stem cells, wherein the HMC-EVs express at least one of the miRNA in Table 10 at a lower level compared to UCB-MSC-EVs.

[0112] In one aspect, the presently disclosed subject matter provides a population of HMC-EVs secreted from HMCs obtained by in vitro differentiation of pluripotent stem cells,

wherein the HMC-EVs express at least one of the miRNA in Table 11 at a higher level compared to BM-MSC-EVs.

[0113] In one aspect, the presently disclosed subject matter provides a population of HMC-EVs secreted from HMCs obtained by in vitro differentiation of pluripotent stem cells, wherein the HMC-EVs express at least one of the miRNA in Table 12 at a lower level compared to BM-MSC-EVs.

[0114] In one aspect, the presently disclosed subject matter provides a population of HMC-EVs secreted from HMCs obtained by in vitro differentiation of pluripotent stem cells, wherein the HMC-EVs express at least one of the miRNA in Table 13 at a higher level compared to AD-MSC-EVs.

[0115] In one aspect, the presently disclosed subject matter provides a population of HMC-EVs secreted from HMCs obtained by in vitro differentiation of pluripotent stem cells, wherein the HMC-EVs express at least one of the miRNA in Table 14 at a lower level compared to EVs secreted from AD-MSC-EVs.

[0116] In one aspect, the presently disclosed subject matter provides a population of HMC-EVs secreted from HMCs obtained by in vitro differentiation of pluripotent stem cells, wherein the HMC-EVs express at least one of the proteins in Table 15 at a higher level compared to UCB-MSC-EVs.

[0117] In one aspect, the presently disclosed subject matter provides a population of HMC-EVs secreted from HMCs obtained by in vitro differentiation of pluripotent stem cells, wherein the HMC-EVs express at least one of the proteins in Table 16 at a lower level compared to UCB-MSC-EVs.

[0118] In one aspect, the presently disclosed subject matter provides a population of HMC-EVs secreted from HMCs obtained by in vitro differentiation of pluripotent stem cells, wherein the HMC-EVs express at least one of the proteins in Table 17 at a higher level compared to BM-MSC-EVs.

[0119] In one aspect, the presently disclosed subject matter provides a population of HMC-EVs secreted from HMCs obtained by in vitro differentiation of pluripotent stem cells, wherein the HMC-EVs express at least one of the proteins in Table 18 at a lower level compared to BM-MSC-EVs.

[0120] In one aspect, the presently disclosed subject matter provides a population of HMC-EVs secreted from HMCs obtained by in vitro differentiation of pluripotent stem cells, wherein the HMC-EVs express at least one of the proteins in Table 19 at a higher level compared to AD-MSC-EVs.

[0121] In one aspect, the presently disclosed subject matter provides a population of HMC-EVs secreted from HMCs obtained by in vitro differentiation of pluripotent stem cells, wherein the HMC-EVs express at least one of the proteins in Table 20 at a lower level compared to AD-MSC-EVs.

[0122] In one aspect, the presently disclosed subject matter provides a population of HMC-EVs secreted from HMCs obtained by in vitro differentiation of pluripotent stem cells, wherein the HMC-EVs express at least one of the miRNA in Table 21 at a higher level compared to the HMCs.

[0123] In one aspect, the presently disclosed subject matter provides a population of HMC-EVs secreted from HMCs obtained by in vitro differentiation of pluripotent stem cells, wherein the HMC-EVs express at least one of the miRNA in Table 22 at a lower level compared to the HMCs.

[0124] In one aspect, the presently disclosed subject matter provides a population of HMC-EVs secreted from HMCs obtained by in vitro differentiation of pluripotent stem cells, wherein the HMC-EVs express at least one of the miRNAs selected from the group consisting of hsa-miR-125b-5p, hsa-miR-181a-5p, hsa-miR-199b-5p, hsa-miR-21-5p, hsa-

miR-23a-3p, hsa-miR-125a-5p, hsa-miR-106a-5p+hsa-miR-17-5p and hsa-miR-221-3p at a higher level compared to BM-MSC-EVs, UCB-MSC-EVs, and/or AD-MSC-EVs.

[0125] In one aspect, the presently disclosed subject matter provides a population of HMC-EVs secreted from HMCs obtained by in vitro differentiation of pluripotent stem cells, wherein the HMC-EVs express at least one of the proteins selected from the group consisting of ALDOC, ANXA5, APBB2, BASP1, CAV1, CD81, CD99, CKM, EPB41L3, FDPS, GNAQ, GNG12, GP9, H2AC20, H2AC21, H3-3A, H3-7, H4-16, HLA-A, ITGA2, KPNA2, KRAS, KRT4, LRRK59, MAMDC2, MARCKSL1, MDGA1, MERTK, MFGE8, MMP14, MVP, PCDH1, PDGFRB, PDIA3, RPL13, RPS18, RPS3A, RPS4X, SDCBP, SLC2A1, SLC3A2, TAGLN2, TNC, TSPAN14, TSPAN33, TSPAN9, TTYH3, UCHL1, VAT1, YWHAZ, and YWHAQ at a higher level compared to BM-MSC-EVs, UCB-MSC-EVs, and/or AD-MSC-EVs.

[0126] In one aspect, the presently disclosed subject matter provides a population of HMC-EVs secreted from HMCs obtained by in vitro differentiation of pluripotent stem cells, wherein the HMC-EVs express at least one of the proteins selected from the group consisting of ADGRG6, AGRN, ANXA6, APOC4, ARHGAP1, ARGHDIA, ARL8A, ARPC5, B2M, BBS1, BLVRA, BST1, CA2, CCN2, CCNB3, CD34, CD36, CD47, CORO1A, DTD1, EEF1D, EEF1G, ENG, ESD, GNAI2, GNB1, H1-3, H2BC15, HIP1, KIF 11, LAMP1, LAP3, LGALS1, LTBP3, MAPK3, MARCKS, MBTD1, MDH1, MOB1B, MYL12B, MYO1F, MYO3A, NIBAN2, PEPB1, PF4, PGAP1, PLOD1, PPP2RIA, PRSS23, PXDN, RALA, RAP2A, RPS13, RPS3, RPSA, S100A11, SLC44A1, SLC44A2, SLTM, SMG1, SPARC, SRSF8, STRADB, STX11, STXBP2, TGM2, TPP1, TPTE2, TRIM5, TRPM2, TUBA8, TUBB3, VCAN, YWHAE, and ZFN607 at a higher level compared to BM-MSC-EVs, UCB-MSC-EVs, and/or AD-MSC-EVs.

[0127] In one aspect, the presently disclosed subject matter provides a population of HMC-EVs secreted from HMCs obtained by in vitro differentiation of pluripotent stem cells, wherein the HMC-EVs express at least one of the proteins selected from the group consisting of ADIPOQ, CAT, CEP290, IGLV6-57, TASR33, and TMEM198 at a lower level compared to BM-MSC-EVs, UCB-MSC-EVs, and/or AD-MSC-EVs.

[0128] In one aspect, the presently disclosed subject matter provides a population of HMC-EVs secreted from HMCs obtained by in vitro differentiation of pluripotent stem cells, wherein the HMC-EVs express at least one of the proteins selected from the group consisting of AKAP9, ALB, ALOX5, APLP2, CD109, CDSN, CHST9, ERC1, F11, ARMCX5, LAMB4, LRRTM2, LTF, MSH6, OAF, OLFML3, PAK6, RGS14, SEMA7A, SURF1, and TRIM4 at a lower level compared to BM-MSC-EVs, UCB-MSC-EVs, and/or AD-MSC-EVs.

[0129] In one aspect, the presently disclosed subject matter provides a pharmaceutical composition comprising the HMC-EVs of the presently disclosed subject matter, and a pharmaceutically acceptable carrier.

[0130] The presently disclosed subject matter also provides a method of determining neurite outgrowth of an HMC and/or HMC-EV population. The method comprises (a) preparing a mixed neuronal culture from an isolated cerebral cortex, (b) plating the HMC and/or HMC-EV population on a permeable membrane, (c) applying strain on the mixed

neuronal culture, (d) overlaying the strained mixed neuronal culture with the permeable membrane of step (b), and (e) measuring neurite outgrowth of the mixed neuronal culture. In an embodiment, step (d) is cultured in a media substantially lacking in serum. In another embodiment, the method further comprises determining gene expression of the mixed neuronal culture in the presence and absence of the HMC and/or HMC-EV population. In another embodiment, the strain is a physical scratch made in the mixed neuronal culture. In another embodiment, the strain is vacuum pressure and positive air pressure applied to the mixed neuronal culture. In another embodiment, the strain may be applied at 15% to 0% stretching oscillations.

[0131] The presently disclosed subject matter also provides a method of determining neurite outgrowth of an HMC and/or HMC-EV population. The method comprises preparing a mixed neuronal culture from an isolated cerebral cortex, (b) plating the HMC and/or HMC-EV population on a permeable membrane, (c) applying strain on the mixed neuronal culture, (d) overlaying the strained mixed neuronal culture with the permeable membrane of step (b), and (e) measuring neurite outgrowth of the mixed neuronal culture. In an embodiment, the method further comprises determining gene expression of the mixed neuronal culture in the presence and absence of the HMC and/or HMC-EV population. In another embodiment, the strain is a physical scratch made in the mixed neuronal culture. In another embodiment, the strain is vacuum pressure and positive air pressure applied to the mixed neuronal culture. In another embodiment, the strain is applied at 15% to 0% stretching oscillations.

BRIEF DESCRIPTION OF THE DRAWINGS

[0132] FIG. 1 shows results of the elevated body swing test (EBST) in rats induced with TBI by controlled cortical impact (CCI) and administered with HMCs or vehicle intracerebrally (IC) or intravenously (IV).

[0133] FIG. 2 shows forelimb akinesia in rats induced with TBI by controlled cortical impact (CCI) and administered with HMCs or vehicle intracerebrally (IC) or intravenously (IV).

[0134] FIG. 3 shows paw grasp in rats induced with TBI by controlled cortical impact (CCI) and administered with HMCs or vehicle intracerebrally (IC) or intravenously (IV).

[0135] FIG. 4A shows H&E staining of the brains of rats induced with TBI by controlled cortical impact (CCI) and administered with HMCs or vehicle intracerebrally (IC) or intravenously (IV). FIG. 4B shows a bar graph of the TBI impact area in the rats as measured by H&E staining.

[0136] FIG. 5A shows Nissl staining of the peri-impact cortex of rats induced with TBI by controlled cortical impact (CCI) and administered with HMCs or vehicle intracerebrally (IC) or intravenously (IV). FIG. 5B shows a bar graph of the percentage of live cells in the peri-impact cortex of the rats as determined by Nissl staining. FIG. 5C shows Nissl staining of the striatum in the rats induced with TBI by controlled cortical impact (CCI) and administered with HMCs or vehicle intracerebrally (IC) or intravenously (IV). FIG. 5D shows a bar graph of the percentage of live cells in the striatum of the rats as determined by Nissl staining. FIG. 5E shows Nissl staining of the hippocampus of rats induced with TBI by controlled cortical impact (CCI) and administered with HMCs or vehicle intracerebrally (IC) or intrave-

nously (IV). FIG. 5F shows a bar graph of the percentage of live cells in the hippocampus of the rats as determined by Nissl staining.

[0137] FIG. 6A shows doublecortin (DCX) staining of the cortex of rats induced with TBI by controlled cortical impact (CCI) and administered with HMCs or vehicle intracerebrally (IC) or intravenously (IV). FIG. 6B shows a bar graph of the DCX cell count in the cortex area of the rats. FIG. 6C shows DCX staining of the striatum of rats induced with TBI by controlled cortical impact (CCI) and administered with HMCs or vehicle intracerebrally (IC) or intravenously (IV). FIG. 6D shows a bar graph of the DCX cell count in the striatum area of the rats. FIG. 6E shows DCX staining of the hippocampus of rats induced with TBI by controlled cortical impact (CCI) and administered with HMCs or vehicle intracerebrally (IC) or intravenously (IV). FIG. 6F shows a bar graph of the DCX cell count in the hippocampus area of the rats.

[0138] FIG. 7A shows Iba1 staining in the cortex of rats induced with TBI by controlled cortical impact (CCI) and administered with HMCs or vehicle intracerebrally (IC) or intravenously (IV). FIG. 7B shows a bar graph of the Iba1 cell count in the cortex of the rats.

[0139] FIG. 7C shows Iba1 staining in the striatum rats induced with TBI by controlled cortical impact (CCI) and administered with HMCs or vehicle intracerebrally (IC) or intravenously (IV). FIG. 7D shows a bar graph of the Iba1 cell count in the striatum of the rats.

[0140] FIG. 8A shows OX6 staining of the cortex of rats induced with TBI by controlled cortical impact (CCI) and administered with HMCs or vehicle intracerebrally (IC) or intravenously (IV). FIG. 8B shows a bar graph of the OX6 cell count in the cortex of the rats.

[0141] FIG. 8C shows OX6 staining of the striatum of rats induced with TBI by controlled cortical impact (CCI) and administered with HMCs or vehicle intracerebrally (IC) or intravenously (IV). FIG. 8D shows a bar graph of the OX6 cell count in the striatum of the rats.

[0142] FIG. 9A shows 1L6 staining in the spleens of rats induced with TBI by controlled cortical impact (CCI) and administered with HMCs or vehicle intracerebrally (IC) or intravenously (IV). FIG. 9B shows a bar graph of the 1L6 staining intensity in the spleens of the rats.

[0143] FIG. 10A shows TNF-alpha staining in the spleens of rats induced with TBI by controlled cortical impact (CCI) and administered with HMCs or vehicle intracerebrally (IC) or intravenously (IV). FIG. 10B shows a bar graph of the TNF-alpha staining intensity in the spleens of the rats.

[0144] FIG. 11A shows HuNu staining in the cortex of rats induced with TBI by controlled cortical impact (CCI) and administered with HMCs or vehicle intracerebrally (IC) or intravenously (IV). FIG. 11B shows a bar graph of the HuNu cell count in the cortex of the rats. FIG. 11C shows HuNu staining in the striatum of rats induced with TBI by controlled cortical impact (CCI) and administered with HMCs or vehicle intracerebrally (IC) or intravenously (IV). FIG. 11D shows a bar graph of the HuNu cell count in the striatum of the rats. FIG. 11E shows HuNu staining in the hippocampus of rats induced with TBI by controlled cortical impact (CCI) and administered with HMCs or vehicle intracerebrally (IC) or intravenously (IV). FIG. 11F shows a bar graph of the HuNu cell count in the hippocampus of the rats.

[0145] FIG. 12A shows migration of unstimulated hESC-MSCs ("HMC"), BM-MSCs, and UCB-MSCs into a gap of

about 500 μm wide at 0 hrs and 6 hrs. FIG. 12B shows a bar graph of the number of unstimulated and stimulated cells that had migrated into the gap.

[0146] FIG. 13 shows images of neurite outgrowth staining at days 1 and 7 post-scratch and co-culture of hESC-MSCs ("HMC") with a mixed neuronal culture.

[0147] FIG. 14A shows TUNEL ranking of each rat tested in the in vivo neonatal hypoxia-ischemia model of cerebral palsy. FIG. 14B shows a bar graph of the average TUNEL ranking of each group of rats tested. TUNEL ranking was as follows: 1=no structural damage and No TUNEL; 2=structural damage and Low TUNEL; 3=structural damage and Medium TUNEL; 4=structural damage and High TUNEL; 5=extreme damage/tissue gone. A comparison of the rats in the Sham vs HI groups showed a t-test of 0.006284 and Mann-Whitney of 0.0256; Sham vs Lot B groups showed a t-test of 0.148904 and Mann-Whitney of 0.2; and HI vs Lot B groups showed a t-test of 0.101453 and Mann-Whitney of 0.1841.

[0148] FIG. 15 shows H&E staining of the brains of rats tested in the in vivo neonatal hypoxia-ischemia model of cerebral palsy.

[0149] FIG. 16A shows images of Iba-1 staining in peri-infarct tissue of rats tested in the in vivo neonatal hypoxia-ischemia model of cerebral palsy. FIG. 16B shows the mean signal intensity of Iba-1 staining in each rat tested in the in vivo neonatal hypoxia-ischemia model of cerebral palsy. FIG. 16C shows the average mean signal intensity of Iba-1 staining in each group of rats tested. A comparison of the rats in the Sham vs HI groups showed a t-test of 0.039335 and Mann-Whitney of 0.065; Sham vs Lot B groups showed a t-test of 0.129562 and Mann-Whitney of 0.1949; and HI vs Lot B groups showed a t-test of 0.353204 and Mann-Whitney of 0.4418.

[0150] FIG. 17A shows images of GFAP staining in peri-infarct tissue of rats tested in the in vivo neonatal hypoxia-ischemia model of cerebral palsy. FIG. 17B shows the mean signal intensity of GFAP staining in each rat tested in the in vivo neonatal hypoxia-ischemia model of cerebral palsy. FIG. 17C shows the average mean signal intensity of GFAP staining in each group of rats tested. A comparison of the rats in the Sham vs HI groups showed a t-test of 0.011749 and Mann-Whitney of 0.0047; Sham vs Lot B groups showed a t-test of 0.070012 and Mann-Whitney of 0.0207; and HI vs Lot B groups showed a t-test of 0.57941 and Mann-Whitney of 0.7984.

[0151] FIG. 18A shows images of MBP staining in the corpus callosum in rats tested in the in vivo neonatal hypoxia-ischemia model of cerebral palsy. FIG. 18B shows the mean signal intensity of MBP staining in each rat tested in the in vivo neonatal hypoxia-ischemia model of cerebral palsy. FIG. 18C shows the average mean signal intensity of MBP staining in each group of rats tested. A comparison of the rats in the Sham vs HI groups showed a t-test of 0.012963 and Mann-Whitney of 0.007; Sham vs Lot B groups showed a t-test of 0.189251 and Mann-Whitney of 0.3282; and HI vs Lot B groups showed a t-test of 0.172857 and Mann-Whitney of 0.2345.

[0152] FIG. 19A shows images of Olig2 staining in the hippocampus of the ipsilesional hemisphere of rats tested in the in vivo neonatal hypoxia-ischemia model of cerebral palsy.

[0153] FIG. 19B shows the mean signal intensity of Olig2 staining in the SVZ, cortex, hippocampus, and region mean

of each rat tested in the in vivo neonatal hypoxia-ischemia model of cerebral palsy. FIG. 19C shows the average mean signal intensity of Olig2 staining in the SVZ, cortex, hippocampus, and region mean of each group of rats tested. A comparison of the rats in Lot B vs HI for Olig2 staining in the SVZ showed a t-test of 0.3962; in the cortex a t-test of 0.4399; in the hippocampus a t-test of 0.5435; and the region mean showed a t-test of 0.3597.

[0154] FIG. 20 depicts the results of the body swing test in rats having middle cerebral artery occlusion (MCAO) stroke and receiving HMCs via three routes of administration: intravenous (IV), intracerebral (IC) and intrathecal (IT) administration. Two-way ANOVA with Tukey's MCT was used for statistical analysis, *p<0.05, **p<0.01, ***p<0.001, and ****p<0.0001.

[0155] FIG. 21 depicts the results of the forelimb placement, the hindlimb placement, and the body swing test in rats having middle cerebral artery occlusion (MCAO) stroke and receiving HMCs and HMC-EVs via intravenous, intracerebral and intracisternal administration. Two-way ANOVA Tukey's MCT was used for statistical analysis, *p<0.05, **p<0.01, ***p<0.001, and ****p<0.0001.

[0156] FIG. 22 depicts the results of the forelimb placement, the hindlimb placement, and the body swing test in rats having middle cerebral artery occlusion (MCAO) stroke and receiving HMC-EVs via intracisternal administration. Two-way ANOVA with Tukey's MCT was used for statistical analysis, *p<0.05, **p<0.01, ***p<0.001, and ****p<0.0001.

[0157] FIG. 23 depicts the results of the forelimb placement, the hindlimb placement, and the body swing test in rats having middle cerebral artery occlusion (MCAO) stroke and receiving HMC-EVs via intrathecal administration. Two-way ANOVA with Turkey's MCT was used for statistical analysis, *p<0.05, **p<0.01, ***p<0.001, and ****p<0.0001.

[0158] FIG. 24A shows images of MBP staining in the cortex and striatum in rats having MCAO stroke and receiving HMCs (obtained from C-GS1 and N-line cells) via IV administration. FIG. 24B shows the average signal intensity of MBP staining in the cortex of rats tested in the vivo MCAO stroke model. FIG. 24C shows the average signal intensity of MBP staining in the striatum of rats tested in the vivo MCAO stroke model. For sham vs Vehicle groups: Welch's test was used for statistical analysis, ***p<0.001. For vehicle vs treatment groups: one-way ANOVA with Dunnet's multiple comparisons test was used for statistical analysis, *p<0.05, **p<0.01, and ***P<0.001.

[0159] FIG. 25A shows images of Iba1 staining in the cortex and striatum in rats having MCAO stroke and receiving HMCs (obtained from C-GS1 and N-line cells) via IV administration. FIG. 25B shows the average signal intensity of Iba1 staining in the cortex of rats tested in the vivo MCAO stroke model. FIG. 25C shows the average signal intensity of Iba1 staining in the striatum of rats tested in the vivo MCAO stroke model. For sham vs Vehicle groups: Welch's test was used for statistical analysis, ***p<0.001. For vehicle vs treatment groups: one-way ANOVA with Dunnet's multiple comparisons test was used for statistical analysis, *p<0.05, **p<0.01, and ***P<0.001.

[0160] FIG. 26A shows images of GFAP staining in the cortex and striatum in rats having MCAO stroke and receiving HMCs (obtained from C-GS1 and N-line cells) via IV administration. FIG. 26B shows the average signal intensity

of GFAP staining in the cortex of rats tested in the vivo MCAO stroke model. FIG. 26C shows the average signal intensity of GFAP staining in the striatum of rats tested in the vivo MCAO stroke model. For sham vs Vehicle groups: Welch's test was used for statistical analysis, ***p<0.001. For vehicle vs treatment groups: one-way ANOVA with Dunnet's multiple comparisons test was used for statistical analysis, *p<0.05, **p<0.01, and ***P<0.001.

[0161] FIG. 27A shows images of MBP staining in rats having MCAO stroke and receiving HMC-EVs (obtained from N-line cells, treated with IFNgamma for 96 hours at 50 ng/mL) via intracisternal administration. FIG. 27B shows the average signal intensity of MBP staining in rats tested in the vivo MCAO stroke model. cc: corpor callosum; ec: external capsule; cg: cingulate gyrus. For vehicle vs treatment groups: Bonferroni comparisons was used for statistical analysis, **p<0.01.

[0162] FIG. 28A shows images of Iba1 staining in rats having MCAO stroke and receiving HMC-EVs (obtained from N-line cells, treated with gamma interferon for 96 hours at 50 ng/mL) via intracisternal administration. FIG. 28B shows the average signal intensity of Iba1 staining in rats tested in the vivo MCAO stroke model. cc: corpor callosum; ec: external capsule; cg: cingulate gyrus. For vehicle vs treatment groups: Bonferroni comparisons was used for statistical analysis, **p<0.01.

[0163] FIG. 29A shows images of GFAP staining in rats having MCAO stroke and receiving HMC-EVs (obtained from N-line cells, treated with gamma interferon for 96 hours at 50 ng/mL) via intracisternal administration. FIG. 29B shows the average signal intensity of GFAP staining in rats tested in the vivo MCAO stroke model. cc: corpor callosum; ec: external capsule; cg: cingulate gyrus. For vehicle vs treatment groups: Bonferroni comparisons was used for statistical analysis, **p<0.01.

[0164] FIG. 30A shows images of Olig2 staining in rats having MCAO stroke and receiving HMC-EVs (obtained from N-line cells, treated with gamma interferon for 96 hours at 50 ng/mL) via intracisternal administration. FIG. 30B shows the average signal intensity of Olig2 staining in rats tested in the vivo MCAO stroke model. cc: corpor callosum; ec: external capsule; cg: cingulate gyrus. For vehicle vs treatment groups: Bonferroni comparisons was used for statistical analysis, **p<0.01.

[0165] FIG. 31A shows images of NG2 staining in rats having MCAO stroke and receiving HMC-EVs (obtained from N-line cells, treated with gamma interferon for 96 hours at 50 ng/mL) via intracisternal administration. FIG. 31B shows the average signal intensity of NG2 staining in rats tested in the vivo MCAO stroke model. cc: corpor callosum; ec: external capsule; cg: cingulate gyrus. For vehicle vs treatment groups: Bonferroni comparisons was used for statistical analysis, **p<0.01.

[0166] FIG. 32 is a schematic of the study design for the in vitro oxygen glucose deprivation (OGD) assay for modeling stroke.

[0167] FIG. 33A shows TUNEL staining and imaging of primary rat neurons treated with or without HMCs following 0 hr, 1 hr, 2 hr and 3 hr oxygen glucose deprivation (OGD) injury.

[0168] FIG. 33B shows the average TUNEL quantification of primary rat neurons treated with or without MSCs following 0 hr, 1 hr, 2 hr and 3 hr OGD injury.

[0169] FIGS. 34A-F depict the pathway enrichment analysis of the differential expression between neurons subjected to 3 hours of oxygen glucose deprivation injury and grown on HMC-enriched and control media. FIGS. 34A-B depict the pathways enriched by the differential expression. FIGS. 34C-F depict the differential expression between OGD neurons grown on HMC-enriched and control media for Gene Oncology terms. FIG. 34C shows the upregulation of pathways involved in cell viability, neuroprotection, and synaptic transmission in OGD neurons grown on HMC-enriched culture. FIG. 34D shows upregulation of genes involved in neuroprotection in OGD neurons grown on HMC-enriched culture. FIG. 34E shows the downregulation of pathways involved in apoptosis in OGD neurons grown on HMC-enriched culture. FIG. 34F shows downregulation of genes involved in apoptosis or general response to cell death in OGD neurons grown on HMC-enriched culture.

[0170] FIG. 35A depicts the in vitro OGD assay RNAseq analysis of primary rat neurons treated with or without HMCs following 0 hr, 1 hr, 2 hr and 3 hr oxygen glucose deprivation (OGD) injury. FIG. 35B depicts the qPCR analysis of primary rat neurons treated with or without HMCs following 0 hr, 1 hr, 2 hr and 3 hr oxygen glucose deprivation (OGD) injury. Two-way ANOVA with Sidak multiple comparison test was used for statistical analysis: *p<0.05, **p<0.01, and ****p<0.0001.

[0171] FIG. 36A shows attenuation of cell death by HMC-EVs. Percentage of cell death was determined as the number of PI+ cells out of the total Hoechst+ cells. Two-way ANOVA was used for statistical significance analysis. ****p<0.0001. FIG. 36B shows dose-dependent attenuation of cell death by HMC-EV treatment. Percentage of cell death was determined as the number of PI+ cells out of the total Hoechst+ cells. One-way

[0172] FIG. 37 shows maintenance of the mitochondrial membrane potential in HMC-EV treated cells undergoing nuclear swelling. HMC-EV treatment sustained cells in the nuclear swelling stage after glutamate-induced injury.

[0173] FIG. 38 shows the principal component analysis of transcriptomes of HMCs (obtained from N-line cells), and adipose tissue-derived MSCs shows that HMCs are distinct from adipose tissue-derived MSCs in both basal and interferon-gamma stimulated state. AMSC-B-1,2,3: adipose tissue-derived MSCs collected from 3 different adult donors, 2 technical replicate samples for each biological replicates. AMSC-S-1,2,3: adipose tissue-derived MSCs, but stimulated with gamma interferon. NHMC-B: 3 technical replicates of MSCs derived from N-line cells, basal state. NHMC-S: MSCs derived from N-line cells, but stimulated with gamma interferon.

[0174] FIG. 39 depicts the weights of different genes contributing to the second principal component which determines the variance between HMCs (obtained from N-line cells) and adipose tissue-derived MSCs.

[0175] FIG. 40 depicts the hierarchical clustering map demonstrating that HMCs (obtained from N-line cells) are distinct from adipose tissue-derived MSCs in both basal and gamma interferon-stimulated states. AB1, AB2, AB3—adipose tissue-derived MSCs collected from 3 different adult donors, 2 technical replicates per donor; basal cell state. AS1, AS2, AS3—adipose tissue-derived MSCs, stimulated with gamma interferon. NB—MSCs derived from N-line cells, basal states, 3 technical replicates. NS—MSCs derived from N-line cells, stimulated with gamma interferon.

[0176] FIG. 41 depicts the basal HMC-specific cluster of genes.

[0177] FIG. 42 depicts the basal adipose tissue-derived MSC-specific cluster of genes.

[0178] FIG. 43 depicts the pathway enrichment of differential expression pattern between HMCs (obtained from N-line cells) and adipose tissue-derived MSCs showing noticeable HMC-specific up-regulation of several pathways (denoted by arrows) involved in the development of neuronal lineage including axon guidance, CREB signaling in neurons, and synaptogenesis signaling.

[0179] FIG. 44 depicts the top 15 most strongly differentially expressed genes contributing to activation of neuronal CREB signaling in HMCs (obtained from N-line cells).

[0180] FIG. 45 depicts the top 15 most strongly upregulated genes contributing to the enrichment of axon guidance pathway in HMCs (obtained from N-line cells).

[0181] FIG. 46 depicts the top 15 most strongly expressed genes contributing to activation of synaptogenesis signaling pathway in HMCs (obtained from N-line cells).

[0182] FIG. 47 depicts the top 15 most up-regulated genes contributing to activation of neuroinflammation signaling pathway in HMCs (obtained from N-line cells).

[0183] FIG. 48 shows the principal component analysis of transcriptomes of HMCs obtained from N-line cells, HMCs obtained from GMP1 cells, and adipose tissue-derived MSCs. AMSC-B-1,2,3—adipose tissue-derived MSCs collected from 3 different adult donors, basal state, 2 technical replicate samples for each biological replicate. AMSC-S-1, 2,3—adipose tissue-derived MSCs collected from 3 different adult donors, but stimulated with gamma interferon. NHMC-B—HMCs derived from N-line cells, basal state. NHMC-S—HMCs derived from N-line cells, but stimulated with gamma interferon. GMP-B—HMC derived from GMP1 cell line, basal state. GMP-S—HMC derived from GMP1 cell line, but stimulated with gamma interferon.

[0184] FIG. 49 depicts the hierarchical clustering map demonstrating that HMCs (obtained from N-line cells) and HMCs (obtained from GMP1 cells) are distinct from adipose tissue-derived MSCs in both basal and gamma interferon-stimulated cell states. AB1, AB2, AB3—adipose tissue-derived MSCs collected from 3 different adult donors, 2 technical replicates per donor; basal cell state. AS1, AS2, AS3—adipose tissue-derived MSCs collected from 3 different adult donors, stimulated with gamma interferon. NB—HMCs derived from N-line cells, basal state, 3 technical replicates. NS—HMCs derived from N-line cells, stimulated with gamma interferon. GB—HMC derived from GMP1 cell line, basal state, 3 technical replicates. GS—HMC derived from GMP1 cell line, stimulated with gamma interferon.

[0185] FIG. 50 depicts the HMC-specific cluster of genes.

[0186] FIG. 51 depicts the basal adipose tissue-derived MSC-specific cluster of genes.

[0187] FIG. 52 depicts the stimulated adipose tissue-derived MSC-specific cluster of genes.

[0188] FIG. 53A depicts the pathway enrichment of differential expression pattern between HMCs (obtained from GMP1 cells) and adipose tissue-derived MSCs showing noticeable HMC-specific up-regulation of several pathways involved in the development of neuronal lineage including axon guidance, CREB signaling in neurons, and synaptogenesis signaling.

[0189] FIG. 53B depicts the top canonical pathways that are differentially regulated in HMCs. FIG. 53C depicts exemplary regulators being activated and inhibited in HMCs.

[0190] FIG. 54A depicts the pathway enrichment of differential expression pattern between HMCs (obtained from N-line cells) and adipose tissue-derived MSCs showing noticeable HMC-specific up-regulation of several pathways involved in the development of neuronal lineage including axon guidance, CREB signaling in neurons, and synaptogenesis signaling.

[0191] FIG. 54B depicts the top canonical pathways that are differentially regulated in HMCs. FIG. 54C depicts exemplary regulators being activated and inhibited in HMCs.

[0192] FIG. 55 shows the principal component analysis of transcriptomes of HMCs (obtained from N-line cells) and bone marrow-derived MSCs shows that HMCs are distinct from bone marrow-derived MSCs in both basal and interferon-gamma stimulated states. BM-B—bone marrow-derived MSCs collected from 3 different adult donors, basal states, 2 technical replicate samples for each biological replicate. BM-S—bone marrow-derived MSCs, but stimulated with gamma interferon. N-B—3 technical replicates of HMCs derived from N-line cells, basal state. N-S—HMCs derived from N-line cells, but stimulated with gamma interferon.

[0193] FIG. 56 depicts the weights of different genes contributing to the second principal component which determines the variance between HMCs and bone marrow-derived MSCs.

[0194] FIG. 57 depicts the hierarchical clustering map demonstrating that HMCs (obtained from N-line cells) are distinct from bone marrow-derived MSCs in both basal and gamma interferon-stimulated cell states. BMB1, BMB2, BMB3—bone marrow-derived MSCs collected from 3 different adult donors, 2 technical replicates per donor; basal cell state. BMS1, BMS2, BMS3—bone marrow-derived MSCs, stimulated with gamma interferon. NB—HMCs derived from N-line cells, basal states, 3 technical replicates. NS—HMCs derived from N-line cells, stimulated with gamma interferon.

[0195] FIG. 58 depicts the basal HMC-specific cluster of genes.

[0196] FIG. 59 depicts the basal bone marrow-derived MSC-specific cluster of genes.

[0197] FIG. 60 depicts the pathway enrichment of differential expression pattern between HMCs (obtained from N-line cells) and bone marrow-derived MSCs showing noticeable HMC-specific up-regulation of several pathways (denoted by arrows) involved in the development of neuronal lineage such as CREB signaling in neurons.

[0198] FIG. 61 depicts the top 15 most strongly differentially expressed genes contributing to activation of neuronal CREB signaling in HMCs (obtained from N-line cells).

[0199] FIG. 62 depicts the top 15 most strongly upregulated genes contributing to activation of synaptogenesis signaling in HMCs (obtained from N-line cells).

[0200] FIG. 63A depicts the pathway enrichment of differential expression pattern between HMC-EVs and EVs secreted from bone marrow-derived MSCs (BM-MSC-EVs). Pathways that are upregulated in HMC-EVs have a positive z-score and are represented by orange bars. Pathways that are downregulated in HMC-EVs have a negative

z-score and are represented by blue bars. White/gray bars represent pathways that are enriched in HMC-EVs, i.e., proteins contributing to these pathways are enriched. FIG. 63B depicts the disease or functional annotation of proteins that have higher expression levels in HMC-EVs when compared to BM-MSC-EVs. FIG. 63C depicts the disease or functional annotation of proteins that have lower expression levels in HMC-EVs when compared to BM-MSC-EVs. An activation z-score above 2 or below -2 is considered as the threshold value.

[0201] FIG. 64A depicts the pathway enrichment of differential expression pattern between HMC-EVs and EVs secreted from adipose tissue-derived MSCs (AD-MSC-EVs). Pathways that are upregulated in HMC-EVs have a positive z-score and are represented by orange bars. Pathways that are downregulated in HMC-EVs have a negative z-score and are represented by blue bars. White/gray bars represent pathways that are enriched in HMC-EVs, i.e., proteins contributing to these pathways are enriched. FIG. 64B depicts the disease or function annotation of proteins that have higher expression levels in HMC-EVs when compared to AD-MSC-EVs. FIG. 64C depicts the disease or function annotation of proteins that have lower expression levels in HMC-EVs when compared to AD-MSC-EVs. An activation z-score above 2 or below -2 is considered as the threshold value.

[0202] FIG. 65A depicts the pathway enrichment of differential expression pattern between HMC-EVs and EVs secreted from umbilical cord blood-derived MSCs (UCB-MSC-EVs). Pathways that are upregulated in HMC-EVs have a positive z-score and are represented by orange bars. Pathways that are downregulated in HMC-EVs have a negative z-score and are represented by blue bars. White/gray bars represent pathways that are enriched in HMC-EVs, i.e., proteins contributing to these pathways are enriched. FIG. 65B depicts the disease or function annotation of proteins that have higher expression levels in HMC-EVs when compared to UCB-MSC-EVs. FIG. 65C depicts the disease or function annotation of proteins that have lower expression levels in HMC-EVs when compared to UCB-MSC-EVs. An activation z-score above 2 or below -2 is considered as the threshold value.

DETAILED DESCRIPTION

Definitions

[0203] “Pluripotent cells,” “pluripotent stem cells,” and “PSCs” as used herein, refer broadly to a cell capable of prolonged or virtually indefinite proliferation in vitro while retaining their undifferentiated state, exhibiting a stable (preferably normal) karyotype, and having the capacity to differentiate into all three germ layers (i.e., ectoderm, mesoderm and endoderm) under the appropriate conditions. Typically pluripotent cells (a) are capable of inducing teratomas when transplanted in immunodeficient (SCID) mice; (b) are capable of differentiating to cell types of all three germ layers (e.g., ectodermal, mesodermal, and endodermal cell types); and (c) express at least one hES cell marker (such as Oct-4, alkaline phosphatase, SSEA 3 surface antigen, SSEA 4 surface antigen, NANOG, TRA 1 60, TRA 1 81, SOX2, REX1). Exemplary pluripotent cells may express Oct-4, alkaline phosphatase, SSEA 3 surface antigen, SSEA 4 surface antigen, TRA 1 60, and/or TRA 1 81. Additional exemplary pluripotent cells include but are not limited to

embryonic stem cells, induced pluripotent cells (iPS) cells, embryo-derived cells, pluripotent cells produced from embryonic germ (EG) cells (e.g., by culturing in the presence of FGF-2, LIF and SCF), parthenogenetic ES cells, ES cells produced from cultured inner cell mass cells (ICM), ES cells produced from a blastomere, and ES cells produced by nuclear transfer (e.g., a somatic cell nucleus transferred into a recipient oocyte). Exemplary pluripotent cells may be produced without destruction of an embryo. For example, induced pluripotent cells may be produced from cells obtained without embryo destruction. As a further example, pluripotent cells may be produced from a biopsied blastomere (which can be accomplished without harm to the remaining embryo); optionally, the remaining embryo may be cryopreserved, cultured, and/or implanted into a suitable host. Pluripotent cells (from whatever source) may be genetically modified or otherwise modified to increase longevity, potency, homing, or to deliver a desired factor in cells that are differentiated from such pluripotent cells (for example, MSCs, and hemangioblasts). As non-limiting examples thereof, the pluripotent cells may be genetically modified to express Sirt1 (thereby increasing longevity), express one or more telomerase subunit genes optionally under the control of an inducible or repressible promoter, incorporate a fluorescent label, incorporate iron oxide particles or other such reagent (which could be used for cell tracking via *in vivo* imaging, MRI, etc., see Thu et al., Nat Med. 2012 Feb. 26; 18(3):463-7), express bFGF which may improve longevity (see Go et al., J. Biochem. 142, 741-748 (2007)), express CXCR4 for homing (see Shi et al., Haematologica. 2007 Jul; 92(7):897-904), express recombinant TRAIL to induce caspase-mediated apoptosis in cancer cells like Gliomas (see Sasportas et al., Proc Natl Acad Sci USA. 2009 Mar. 24; 106(12):4822-7), etc.

[0204] “Embryo” or “embryonic,” as used herein refers broadly to a developing cell mass that has not implanted into the uterine membrane of a maternal host. An “embryonic cell” is a cell isolated from or contained in an embryo. This also includes blastomeres, which may be obtained as early as the two-cell stage, and aggregated blastomeres.

[0205] “Embryonic stem cells” (ES cells or ESC) encompasses pluripotent cells produced from embryonic cells (such as from cultured inner cell mass cells or cultured blastomeres). Frequently such cells are or have been serially passaged as cell lines. Embryonic stem cells may be used as a pluripotent stem cell in the processes of producing hemangioblasts as described herein. For example, ES cells may be produced by methods known in the art including derivation from an embryo produced by any method (including by sexual or asexual means) such as fertilization of an egg cell with sperm or sperm DNA, nuclear transfer (including somatic cell nuclear transfer), or parthenogenesis. As a further example, embryonic stem cells also include cells produced by somatic cell nuclear transfer, even when non-embryonic cells are used in the process. For example, ES cells may be derived from the ICM of blastocyst stage embryos, as well as embryonic stem cells derived from one or more blastomeres. Such embryonic stem cells can be generated from embryonic material produced by fertilization or by asexual means, including somatic cell nuclear transfer (SCNT), parthenogenesis, and androgenesis. As further discussed above (see “pluripotent cells”), ES cells may be genetically modified or otherwise modified to increase longevity, potency, homing, or to deliver a desired factor in cells

that are differentiated from such pluripotent cells (for example, MSCs, and hemangioblasts).

[0206] ES cells may be generated with homozygosity or hemizygosity in one or more HLA genes, e.g., through genetic manipulation, screening for spontaneous loss of heterozygosity, etc. day ES cells may be genetically modified or otherwise modified to increase longevity, potency, homing, or to deliver a desired factor in cells that are differentiated from such pluripotent cells (for example, MSCs and hemangioblasts). Embryonic stem cells, regardless of their source or the particular method used to produce them, typically possess one or more of the following attributes: (i) the ability to differentiate into cells of all three germ layers, (ii) expression of at least Oct-4 and alkaline phosphatase, and (iii) the ability to produce teratomas when transplanted into immunocompromised animals. Embryonic stem cells that may be used in embodiments of the presently disclosed subject matter include, but are not limited to, human ES cells (“hESC” or “hES cells”) such as CT2, MA01, MA09, ACT-4, No. 3, H1, H7, H9, H14 and ACT30 embryonic stem cells. Additional exemplary cell lines include NED1, NED2, NED3, NED4, NED5, and NED7. See also NIH Human Embryonic Stem Cell Registry. An exemplary human embryonic stem cell line that may be used is MA09 cells. The isolation and preparation of MA09 cells was previously described in Klimanskaya, et al. (2006) “Human Embryonic Stem Cell Lines Derived from Single Blastomeres.” Nature 444: 481-485. The human ES cells used in accordance with exemplary embodiments of the presently disclosed subject matter may be derived and maintained in accordance with GMP standards.

[0207] Exemplary hES cell markers include, but are not limited to: alkaline phosphatase, Oct-4, Nanog, Stage-specific embryonic antigen-3 (SSEA-3), Stage-specific embryonic antigen-4 (SSEA-4), TRA-1-60, TRA-1-81, TRA-2-49/6E, Sox2, growth and differentiation factor 3 (GDF3), reduced expression 1 (REX1), fibroblast growth factor 4 (FGF4), embryonic cell-specific gene 1 (ESG1), developmental pluripotency-associated 2 (DPPA2), DPPA4, telomerase reverse transcriptase (hTERT), SALL4, E-CADHERIN, Cluster designation 30 (CD30), Cripto (TDGF-1), GCTM-2, Genesis, Germ cell nuclear factor, and Stem cell factor (SCF or c-Kit ligand). Additionally, embryonic stem cells may express Oct-4, alkaline phosphatase, SSEA 3 surface antigen, SSEA 4 surface antigen, TRA 1 60, and/or TRA 1 81.

[0208] The ESCs may be initially co-cultivated in any culture media known in the art that maintains the pluripotency of the ESCs, with or without feeder cells, such as murine embryonic feeder cells (MEF) cells or human feeder cells, such as human dermal fibroblasts (HDF). The MEF cells or human feeder cells may be mitotically inactivated, for example, by exposure to mitomycin C, gamma irradiation, or by any other known methods, prior to seeding ESCs in co-culture, and thus the MEFs do not propagate in culture. Additionally, ESC cell cultures may be examined microscopically and colonies containing non ESC cell morphology may be picked and discarded, e.g., using a stem cell cutting tool, by laser ablation, or other means. Typically, after the point of harvest of the ESCs for seeding for embryoid body formation no additional MEF cells or human feeder cells are used.

[0209] Alternatively, hES cells may be cultured under feeder-free conditions on a solid surface such as an extra-

cellular matrix e.g. by any method known in the art, e.g., Klimanskaya et al., Lancet 365:1636-1641 (2005). Accordingly, the hES cells used in the methods described herein may be cultured on feeder-free cultures.

[0210] “Embryo-derived cells” (EDC), as used herein, refers broadly to pluripotent morula-derived cells, blastocyst-derived cells including those of the inner cell mass, embryonic shield, or epiblast, or other pluripotent stem cells of the early embryo, including primitive endoderm, ectoderm, and mesoderm and their derivatives. “EDC” also includes blastomeres and cell masses from aggregated single blastomeres or embryos from varying stages of development, but excludes human embryonic stem cells that have been passaged as cell lines.

[0211] “Potency”, as used herein, refers broadly to the concentration, e.g., number of cells (such as hemangioblast-derived MSCs) that produces a defined effect. Potency may be defined in terms of effective concentration (EC50), which does not involve measurements of maximal effect but, instead, the effect at various locations along the concentration axis of dose response curves. Potency may also be determined from either graded (EC50) or quantal dose-response curves (ED50, TD50 and LD50); however, potency is preferably measured by EC50. The term “EC50” refers to the concentration of a drug, antibody or toxicant which induces a response halfway between the baseline and maximum effect after some specified exposure time. The EC50 of a graded dose response curve therefore represents the concentration of a compound where 50% of its maximal effect is observed. The EC50 of a quantal dose response curve represents the concentration of a compound where 50% of the population exhibit a response, after a specified exposure duration. The EC50 may be determined using animal studies in which a defined animal model demonstrates a measurable, physiological change in response to application of the drug; cell-based assays that use a specified cell system, which on addition of the drug, demonstrate a measurable biological response; and/or enzymatic reactions where the biological activity of the drug can be measured by the accumulation of product following the chemical reaction facilitated by the drug. Preferably, an immune regulatory assay is used to determine EC50. Non-limiting examples of such immune regulatory assays include intracellular cytokine, cytotoxicity, regulatory capacity, cell signaling capacity, proliferative capacity, apoptotic evaluations, and other assays.

[0212] “Mesenchymal stem cells” (MSCs) as used herein refers to multipotent stem cells with self-renewal capacity and the ability to differentiate into osteoblasts, chondrocytes, and adipocytes, among other mesenchymal cell lineages. Unless otherwise specifically noted, MSCs of the presently disclosed subject matter are MSCs generated from in vitro differentiation of pluripotent stem cells, and which may be referred to herein as HMCs. In an embodiment, the HMCs may be generated by in vitro differentiation of pluripotent stem cells followed by differentiation to hemangioblasts, which are then differentiated into HMCs. HMCs may be identified by the expression of one or more markers as further described herein. HMCs may also have any of the characteristics described in WO 2013/082543, U.S. Pat. Nos. 8,962,321, and 8,961,956, the entire contents of which are hereby incorporated herein by reference.

[0213] HMCs may be genetically modified or otherwise modified to increase longevity, potency, homing, or to deliver a desired factor in the HMCs or cells that are

differentiated from such HMCs. As non-limiting examples thereof, the HMCs may be genetically modified to express Sirt1 (thereby increasing longevity), express one or more telomerase subunit genes optionally under the control of an inducible or repressible promoter, incorporate a fluorescent label, incorporate iron oxide particles or other such reagent (which could be used for cell tracking via in vivo imaging, MRI, (see Thu et al., Nat Med. 2012 Feb. 26; 18(3):463-7), express bFGF which may improve longevity (see Go et al., J. Biochem. 142, 741-748 (2007)), express CXCR4 for homing (see Shi et al., Haematologica. 2007 July; 92(7): 897-904), express recombinant TRAIL to induce caspase-mediated apoptosis in cancer cells like Gliomas (see Sastropas et al., Proc Natl Acad Sci USA. 2009 Mar. 24; 106(12):4822-7).

[0214] As used herein, the term “extracellular vesicle” or “EV” refers to lipid bound vesicles secreted by cells into the extracellular space. The three main subtypes of EVs are microvesicles (MVs), exosomes, and apoptotic bodies, which are differentiated based upon their biogenesis, release pathways, size, content, and function (Zaborowski M. P., et al. *Bioscience*. 2015; 65:783-797). Generally extracellular vesicles range in diameter from 20 nm to 5000 nm, and can comprise various macromolecular payload either within the internal space (i.e., lumen), displayed on the external surface of the extracellular vesicle, and/or spanning the membrane. Said payload can comprise nucleic acids, e.g., microRNAs (miRNA), long non-coding RNAs (lncRNA), mRNAs, DNA fragments; proteins, carbohydrates, lipids, small molecules, and/or combinations thereof. By way of example and without limitation, extracellular vesicles include apoptotic bodies, fragments of cells, vesicles derived from cells by direct or indirect manipulation (e.g., by serial extrusion or treatment with alkaline solutions), vesiculated organelles, and vesicles produced by living cells (e.g., by direct plasma membrane budding or fusion of the late endosome with the plasma membrane). Extracellular vesicles can be derived/secreted from a living or dead organism, explanted tissues or organs, prokaryotic or eukaryotic cells, and/or cultured cells.

[0215] “Optic neuropathy”, as used herein, includes any disease, disorder or condition that involves damage to the optic nerve. Optic neuropathy includes hereditary (e.g., autosomal dominant optic atrophy (Kjer’s disease) and maternally inherited Leber’s hereditary optic neuropathy) and non-hereditary optic neuropathy (e.g., ischemic optic neuropathy). In one embodiment, optic neuropathy is glaucoma/glaucomatous optic neuropathy.

[0216] “Therapy,” “therapeutic,” “treating,” “treat” or “treatment”, as used herein, refers broadly to treating a disease, arresting or reducing the development of the disease or its clinical symptoms, and/or relieving the disease, causing regression of the disease or its clinical symptoms. “Therapy”, “therapeutic,” “treating,” “treat” or “treatment” encompasses prophylaxis, prevention, treatment, cure, remedy, reduction, alleviation, and/or providing relief from a disease, signs, and/or symptoms of a disease. “Therapy”, “therapeutic,” “treating,” “treat” or “treatment” encompasses an alleviation of signs and/or symptoms in patients with ongoing disease signs and/or symptoms. “Therapy”, “therapeutic,” “treating,” “treat” or “treatment” also encompasses “prophylaxis” and “prevention”. Prophylaxis includes preventing disease occurring subsequent to treatment of a disease in a patient or reducing the incidence or severity of the disease in a patient. The term “reduced”, for

purpose of therapy, "therapeutic," "treating," "treat" or "treatment" refers broadly to the clinical significant reduction in signs and/or symptoms. "Therapy", "therapeutic," "treating," "treat" or "treatment" includes treating relapses or recurrent signs and/or symptoms. "Therapy", "therapeutic," "treating," "treat" or "treatment" encompasses but is not limited to precluding the appearance of signs and/or symptoms anytime as well as reducing existing signs and/or symptoms and eliminating existing signs and/or symptoms. "Therapy", "therapeutic," "treating," "treat" or "treatment" includes treating chronic disease ("maintenance") and acute disease. For example, treatment includes treating or preventing relapses or the recurrence of signs and/or symptoms.

[0217] As used herein, the term "effective amount," is intended to include the amount of HMCs and/or HMC-EVs that, when administered to a subject having a brain injury, is sufficient to effect treatment of the disease (e.g., by diminishing, ameliorating, or maintaining the existing disease or one or more symptoms of disease). Ameliorating the disease includes slowing the course of the disease or reducing the severity of later-developing disease. The "effective amount" may vary depending on the nature of the HMC and/or HMC-EVs, how the HMC and/or HMC-EVs are administered, the disease and its severity and the history, age, weight, family history, genetic makeup, the types of preceding or concomitant treatments, if any, and other individual characteristics of the subject to be treated.

[0218] An "effective amount" also includes an amount of HMC and/or HMC-EVs that produces some desired effect at a reasonable benefit/risk ratio applicable to any treatment. The HMC and/or HMC-EVs employed in the methods of the presently disclosed subject matter may be administered in a sufficient amount to produce a reasonable benefit/risk ratio applicable to such treatment.

[0219] "Normalizing a pathology", as used herein, refers to reverting the abnormal structure and/or function resulting from a disease to a more normal state. Normalization suggests that by correcting the abnormalities in structure and/or function of a tissue, organ, cell type, etc. resulting from a disease, the progression of the pathology can be controlled and improved. For example, following treatment with the HMCs of the presently disclosed subject matter the abnormalities of the brain as a result of brain injury, e.g., traumatic brain injury, may be improved, corrected, and/or reversed.

[0220] "Induced pluripotent stem cells" or "iPSCs" or "iPS cells" as used herein refer to pluripotent stem cells generated by reprogramming a somatic cell. iPSCs may be generated by expressing or inducing expression of a combination of factors ("reprogramming factors"). iPSCs may be generated using fetal, postnatal, newborn, juvenile, or adult somatic cells. iPSCs may be obtained from a cell bank. Alternatively, iPSCs may be newly generated (by processes known in the art) prior to commencing differentiation to MSCs or another cell type. The making of iPSCs may be an initial step in the production of differentiated cells. iPSCs may be specifically generated using material from a particular patient or matched donor with the goal of generating tissue-matched MSC cells. iPSCs cells can be produced from cells that are not substantially immunogenic in an intended recipient, e.g., produced from autologous cells or from cells histocompatible to an intended recipient. As further discussed above (see "pluripotent cells"), pluripotent cells including iPSCs may be genetically modified or

otherwise modified to increase longevity, potency, homing, or to deliver a desired factor in cells that are differentiated from such pluripotent cells (for example, MSCs and hemangioblasts).

[0221] As a further example, induced pluripotent stem cells may be generated by reprogramming a somatic or other cell by contacting the cell with one or more reprogramming factors. For example, the reprogramming factor(s) may be expressed by the cell, e.g., from an exogenous nucleic acid added to the cell, or from an endogenous gene in response to a factor such as a small molecule, microRNA, or the like that promotes or induces expression of that gene (see Suh and Blelloch, Development 138, 1653-1661 (2011); Miyoshi et al., Cell Stem Cell (2011), doi:10.1016/j.stem.2011.05.001; Sancho-Martinez et al., Journal of Molecular Cell Biology (2011) 1-3; Anokye-Danso et al., Cell Stem Cell 8, 376-388, Apr. 8, 2011; Orkin and Hochedlinger, Cell 145, 835-850, Jun. 10, 2011, each of which is incorporated by reference herein in its entirety). Reprogramming factors may be provided from an exogenous source, e.g., by being added to the culture media, and may be introduced into cells by methods known in the art such as through coupling to cell entry peptides, protein or nucleic acid transfection agents, lipofection, electroporation, biolistic particle delivery system (gene gun), microinjection, and the like. In certain embodiments, factors that can be used to reprogram somatic cells to pluripotent stem cells include, for example, a combination of Oct4 (sometimes referred to as Oct 3/4), Sox2, c-Myc, and Klf4. In other embodiments, factors that can be used to reprogram somatic cells to pluripotent stem cells include, for example, a combination of Oct-4, Sox2, Nanog, and Lin28. In other embodiments, somatic cells are reprogrammed by expressing at least 2 reprogramming factors, at least three reprogramming factors, or four reprogramming factors. In another embodiment, somatic cells are reprogrammed by expressing Oct4, Sox2, MYC, Klf4, Nanog, and Lin28. In other embodiments, additional reprogramming factors are identified and used alone or in combination with one or more known reprogramming factors to reprogram a somatic cell to a pluripotent stem cell. iPS cells typically can be identified by expression of the same markers as embryonic stem cells, though a particular iPS cell line may vary in its expression profile.

[0222] The induced pluripotent stem cell may be produced by expressing or inducing the expression of one or more reprogramming factors in a somatic cell. In an embodiment, the somatic cell is a fibroblast, such as a dermal fibroblast, synovial fibroblast, or lung fibroblast, or a non-fibroblastic somatic cell. In an embodiment, the somatic cell is reprogrammed by expressing at least 1, 2, 3, 4, 5 reprogramming factors as described above. In another embodiment, expression of the reprogramming factors may be induced by contacting the somatic cells with at least one agent, such as a small organic molecule agent, that induces expression of reprogramming factors.

[0223] The somatic cell may also be reprogrammed using a combinatorial approach wherein the reprogramming factor is expressed (e.g., using a viral vector, plasmid, and the like) and the expression of the reprogramming factor is induced (e.g., using a small organic molecule.) For example, reprogramming factors may be expressed in the somatic cell by infection using a viral vector, such as a retroviral vector or a lentiviral vector. Also, reprogramming factors may be expressed in the somatic cell using a non-integrative vector,

such as an episomal plasmid or mRNA. See, e.g., Yu et al., Science. 2009 May 8; 324(5928):797-801, which is hereby incorporated by reference in its entirety. When reprogramming factors are expressed using non-integrative vectors, the factors may be expressed in the cells using electroporation, transfection, or transformation of the somatic cells with the vectors.

[0224] Once the reprogramming factors are expressed in the cells, the cells may be cultured by any method known in the art. Over time, cells with ES characteristics appear in the culture dish. The cells may be chosen and subcultured based on, for example, ES morphology, or based on expression of a selectable or detectable marker. The cells may be cultured to produce a culture of cells that resemble ES cells—these are putative iPS cells. iPS cells typically can be identified by expression of the same markers as other embryonic stem cells, though a particular iPS cell line may vary in its expression profile. Exemplary iPS cells may express Oct-4, alkaline phosphatase, SSEA3 surface antigen, SSEA4 surface antigen, TRA160, and/or TRA181.

[0225] To confirm the pluripotency of the iPS cells, the cells may be tested in one or more assays of pluripotency. For example, the cells may be tested for expression of ES cell markers; the cells may be evaluated for ability to produce teratomas when transplanted into SCID mice; the cells may be evaluated for ability to differentiate to produce cell types of all three germ layers. Once a pluripotent iPS cell is obtained it may be used to produce hemangioblast and MSC cells.

[0226] “Hemangioblasts” or “HBs” as used herein refer to multipotent cells and serve as the common precursor to both hematopoietic and endothelial cell lineages. During embryonic development, they are believed to arise as a transitional cell type that emerges during early mesoderm development and colonizes primitive blood islands (Choi et al. Development 125 (4): 725-732 (1998). Once there, hemangioblasts are capable of giving rise to both primitive and definitive hematopoietic cells, HSCs, and endothelial cells (Mikkola et al. J. Hematother. Stem Cell Res 11(1): 9-17 (2002).

[0227] Hemangioblasts may be derived *in vitro* from both mouse PSCs (Kennedy et al, Nature (386): 488-493 (1997); Perlingeiro et al, Stem Cells (21): 272-280 (2003)) and human PSCs (ref. 14, 15, Yu et al., Blood 2010 116: 4786-4794). Other studies claim to have isolated hemangioblasts from umbilical cord blood (Bordoni et al, Hepatology 45 (5) 1218-1228), circulating CD34- lin- CD45- CD133- cells from peripheral blood (Ciraci et al, Blood 118: 2105-2115), and from mouse uterus (Sun et al, Blood 116 (16): 2932-2941 (2010)). Both mouse and human PSC-derived hemangioblasts have been obtained through the culture and differentiation of clusters of cells grown in liquid culture followed by growth of the cells in semi-solid medium containing various cytokines and growth factors (Kennedy, Perlingeiro, ref 14, 15); see also, U.S. Pat. No. 8,017,393, which is hereby incorporated by reference in its entirety. In an embodiment, hemangioblasts may be generated *in vitro* from pluripotent stem cells according to the methods described in, for example, U.S. Pat. Nos. 9,938,500; 9,410,123; and WO 2013/082543, all of which are incorporated herein by reference in their entireties. The term hemangioblasts also includes the hemangio-colony forming cells described in U.S. Pat. No. 8,017,393 (incorporated herein by reference in its entirety), which in addition to being capable of differentiating into hematopoietic and endothelial cell

lineages, are capable of becoming smooth muscle cells and which are not positive for CD34, CD31, KDR, and CD133. In another embodiment, the hemangioblasts are positive for the blood markers CD43 and CD45 and express low levels or are negative for the pericyte markers CD146, PDGRb, and/or NG2.

[0228] Hemangioblasts useful in the methods described herein may be derived or obtained from any of these known methods or any method described herein. For example, embryoid bodies may be formed by culturing pluripotent cells under non-attached conditions, e.g., on a low-adherent substrate, in a “hanging drop”, or through the Able Biott spin bioreactor. In these cultures, PSCs can form clumps or clusters of cells denominated as embryoid bodies. See Itskovitz-Eldor et al., Mol Med. 2000 February; 6(2):88-95, which is hereby incorporated by reference in its entirety. Typically, embryoid bodies initially form as solid clumps or clusters of pluripotent cells, and over time some of the embryoid bodies come to include fluid filled cavities, the latter former being referred to in the literature as “simple” EBs and the latter as “cystic” embryoid bodies. Id. The cells in these EBs (both solid and cystic forms) can differentiate and over time produce increasing numbers of cells. Optionally EBs may then be cultured as adherent cultures and allowed to form outgrowths. Likewise, pluripotent cells that are allowed to overgrow and form a multilayer cell population can differentiate over time.

[0229] In one embodiment, hemangioblasts are generated by the steps comprising (a) culturing a PSC line for 2, 3, 4, 5, 6 or 7 days to form clusters of cells (embryoid bodies; EBs), and (b) inducing said clusters of cells or EBs to differentiate into hemangioblasts. In a further embodiment, the clusters of cells or EBs in step (b) of are cultured in a cytokine-rich serum-free methylcellulose based medium. In an embodiment, hemangioblasts are generated by inducing differentiation of any pluripotent cell as described herein.

[0230] In one embodiment, the clusters of cells or EBs are cultured for at least 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 days in culture in a serum free methylcellulose medium comprising one or more ingredients selected from the group comprising penicillin/streptomycin (pen/strp), EX-CYTE® growth supplement (a water-soluble concentrate comprising 9.0-11.0 g/L cholesterol and 13.0-18.0 g/L lipoproteins and fatty acids at pH 7-8.4), Flt3-ligand (FL), vascular endothelial growth factor (VEGF), thrombopoietin (TPO), basic fibroblast growth factor (bFGF), stem cell derived factor (SCF), granulocyte macrophage colony stimulating factor (GM-CSF), interleukin 3 (IL3), and interleukin 6 (IL6), and producing hemangioblasts. In a preferred embodiment of the instant presently disclosed subject matter, hemangioblasts are harvested between 6-14 days, of being cultured in, for example, serum-free methylcellulose plus one or more of the ingredients of the previous embodiment. In a preferred embodiment, the one or more ingredients may be present in said medium at the following concentrations: Flt3-ligand (FL) at 50 ng/ml, vascular endothelial growth factor (VEGF) at 50 ng/ml, thrombopoietin (TPO) at 50 ng/ml, and basic fibroblast growth factor (bFGF) at 20-30 ng/ml, 50 ng/ml stem cell derived factor (SCF), 20 ng/ml granulocyte macrophage colony stimulating factor (GM-CSF), 20 ng/ml interleukin 3 (IL3), and 20 ng/ml interleukin 6 (IL6).

In vitro Generation of Mesenchymal Stem Cells

[0231] An embodiment of the instant presently disclosed subject matter comprises methods of producing mesenchymal stem cells (hereinafter, "HMCs") by in vitro differentiation of hemangioblasts. The hemangioblasts may be obtained by any of the methods described herein. In an embodiment, the hemangioblasts are obtained by in vitro differentiation of pluripotent stem cells. Pluripotent stem cells can be cultured on feeders (e.g., human dermal fibroblasts, or mouse embryonic fibroblasts), or in feeder-free conditions. In some embodiments, hemangioblasts are cultured in feeder-free conditions then plated on an extracellular matrix. In another embodiment, said extracellular matrix is selected from the group consisting of laminin, fibronectin, vitronectin, proteoglycan, entactin, collagen, collagen I, collagen IV, heparan sulfate, a soluble preparation from Engelbreth-Holm-Swarm (EHS) mouse sarcoma cells, Matrigel, and a human basement membrane extract. In a still further embodiment, said extracellular matrix may be derived from any mammalian, including human, origin.

[0232] In another embodiment, hemangioblasts are re-plated and cultured for at least 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, or 36 days forming a preparation of HMCs. In an embodiment, initial plating of hemangioblasts onto substrate-coated tissue culture dishes may be done at a concentration of about 50,000 to about 100,000 cells/cm². During culturing of hemangioblasts, a portion of hemangioblasts adheres to the culture plate and begins to differentiate into HMCs. Adherent cells are passaged every 3-6 days or more than 6 days, e.g., about 6-10 days, or about 10-15 days, depending on their growth rate, plating density, and perceived degree of confluence. For passaging, harvest density may be about 5,000 to about 20,000 cells/cm², or about 20,000 to about 40,000 cells/cm². After the cells are harvested, cells are counted and may be replated at a density of between about 2500 to about 6000 cells/cm². In one embodiment, HMCs are generated by the steps comprising (a) culturing ESCs for 8-12 days and producing hemangioblasts, (b) harvesting hemangioblasts, (c) re-plating the hemangioblasts of step (b), and (d) culturing the hemangioblasts of step (c) for between 14-30 days.

[0233] In one embodiment, the hemangioblasts are harvested, re-plated and cultured in liquid medium under feeder-free conditions wherein no feeder layer of cells such as mouse embryonic fibroblasts, OP9 cells, or other cell types known to one of ordinary skill in the art are contained in the culture. In a preferred embodiment, hemangioblasts are cultured on an extracellular matrix. In a further preferred embodiment, hemangioblasts are cultured on an extracellular matrix, wherein said matrix comprises a soluble preparation from Engelbreth-Holm-Swarm (EHS) mouse sarcoma cells that gels at room temperature to form a reconstituted basement membrane (Matrigel). In a still further preferred embodiment, hemangioblasts are formed according to the steps comprising (a) culturing said hemangioblasts on an extracellular matrix for at least 7 days, (b) transferring the hemangioblasts of step (a) to non-coated tissue culture plate and further culturing said hemangioblasts of step (b) for between about 7 to 14 days. The hemangioblasts may be cultured in the presence of one or more of the factors selected from the group consisting of: transforming growth factor beta (TGF-beta), epidermal growth factor (EGF), insulin-like growth factor 1, bovine fibroblast growth factor

(bFGF), and/or platelet-derived growth factor (PDGF). In an embodiment, the extracellular matrix is selected from the group consisting of Human Basement Membrane Extract (BME) (e.g., Cultrex BME, Trevigen) or an EHS matrix, laminin, fibronectin, vitronectin, proteoglycan, entactin, collagen (e.g., collagen I, collagen IV), and heparan sulfate. Said extracellular matrix or matrix components may be of mammalian, or more specifically human, origin. In one embodiment, hemangioblasts are cultured in a liquid medium comprising serum on an extracellular matrix protein-coated plate, wherein the culture medium may comprise ingredients selected from αMEM (Sigma-Aldrich) supplemented with 10-20% fetal calf serum (αMEM+20% FCS), αMEM supplemented with 10-20% heat-inactivated human AB serum, and IMDM supplemented with 10-20% heat inactivated AB human serum.

[0234] In another embodiment, hemangioblasts are cultured in a medium comprising serum or a serum replacement, such as αMEM supplemented with 20% fetal calf serum. In another embodiment, hemangioblasts are cultured in a serum-free medium.

[0235] In a further embodiment, hemangioblasts are cultured on an extracellular matrix for about 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30 days. In a still further embodiment of the instant presently disclosed subject matter, HMCs are generated by the steps comprising (a) culturing hemangioblasts on an extracellular matrix for about 7 days, (b) transferring the hemangioblasts of step (a) to an uncoated tissue culture dish and culturing the hemangioblasts for an additional 9-100 days, about 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 35, 40, 50, 60, 70, 80, 90 or 100 days. In yet another embodiment, HMCs are generated by the steps comprising (a) culturing hemangioblasts on an extracellular matrix for about 7 days, (b) transferring the hemangioblasts of step (a) to a coated tissue culture dish and culturing the hemangioblasts for an additional 9-100 days, about 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 35, 40, 50, 60, 70, 80, 90 or 100 days.

[0236] In an embodiment of the instant presently disclosed subject matter, hemangioblasts are differentiated from PSCs by following the steps comprising: (a) culturing PSCs in the presence of vascular endothelial growth factor (VEGF) and/or bone morphogenic protein 4 (BMP-4) (by way of non-limiting examples) to form clusters of cells or EBs; (b) culturing said clusters of cells or EBs in the presence of at least one growth factor (e.g., basic fibroblast growth factor (bFGF), vascular endothelial growth factor (VEGF), bone morphogenic protein 4 (BMP-4), stem cell factor (SCF), Flt 3L (FL), thrombopoietin (TPO), and/or tPTD-HOXB4) in an amount sufficient to induce the differentiation of said clusters of cells or EBs into hemangioblasts; and (c) culturing said hemangioblasts in a medium comprising at least one additional growth factor (e.g., insulin, transferrin, granulocyte macrophage colony-stimulating factor (GM-CSF), interleukin-3 (IL-3), interleukin-6 (IL-6), granulocyte colony-stimulating factor (G-CSF), erythropoietin (EPO), stem cell factor (SCF), vascular endothelial growth factor (VEGF), bone morphogenic protein 4 (BMP-4), and/or tPTD-HOXB4), wherein said at least one additional growth factor is provided in an amount sufficient to expand said clusters of cells in said culture, and wherein copper is optionally added to any of the steps (a)-(c).

[0237] In an embodiment of the instant presently disclosed subject matter, HMCs are generated by culturing hemangioblasts, wherein said hemangioblasts are differentiated from PSCs by following the steps comprising: (a) culturing PSCs in the presence of vascular endothelial growth factor (VEGF) and bone morphogenic protein 4 (BMP-4) within 0-48 hours of initiation of said culture to form clusters of cells or EBs; (b) culturing said clusters of cells or EBs in the presence of at least one growth factor selected from the group comprising basic fibroblast growth factor (bFGF), vascular endothelial growth factor (VEGF), bone morphogenic protein 4 (BMP-4), stem cell factor (SCF), Flt 3L (FL), thrombopoietin (TPO), and tPTD-HOXB4 in an amount sufficient to induce the differentiation of said clusters of cells or EBs into hemangioblasts; and (c) culturing said hemangioblasts in a medium comprising at least one additional growth factor selected from the group consisting of insulin, transferrin, granulocyte macrophage colony-stimulating factor (GM-CSF), interleukin-3 (IL-3), interleukin-6 (IL-6), granulocyte colony-stimulating factor (G-CSF), erythropoietin (EPO), stem cell factor (SCF), vascular endothelial growth factor (VEGF), bone morphogenic protein 4 (BMP-4), and tPTD-HOXB4, wherein said at least one additional growth factor is provided in an amount sufficient to expand hemangioblasts in said culture.

[0238] In another embodiment, HMCs are generated by the steps comprising: (a) harvesting hemangioblasts after at least 6, 7, 8, 9, 10, 11, 12, 13, or 14 days of inducing PSCs to differentiate into said hemangioblasts, and (b) harvesting HMCs that are generated within about 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49 or 50 days of inducing said hemangioblasts from step (a) to differentiate into said mesenchymal cells.

[0239] In yet another embodiment, a preparation of at least 80, 85, 90, 95, 100, 125 or 125 million HMCs are generated from about 200,000 hemangioblasts within about 26, 27, 28, 29, 30, 31, 32, 33, 34, or 35 days of culturing the hemangioblasts, wherein said preparation of HMCs comprises less than about 10%, 9%, 8%, 7%, 6%, 5%, 4%, 3%, 2%, 1%, 0.9%, 0.8%, 0.7%, 0.6%, 0.5%, 0.4%, 0.3%, 0.2%, 0.1%, 0.09%, 0.08%, 0.07%, 0.06%, 0.05%, 0.04%, 0.03%, 0.02%, 0.01%, 0.009%, 0.008%, 0.007%, 0.006%, 0.005%, 0.004%, 0.003%, 0.002%, 0.001%, 0.0009%, 0.0008%, 0.0007%, 0.0006%, 0.0005%, 0.0004%, 0.0003%, 0.0002%, or 0.0001% human embryonic stem cells. In still another embodiment, at least 80, 85, 90, 100, 125 or 150 million HMCs are generated from about 200,000 hemangioblasts within about 26, 27, 28, 29, 30, 31, 32, 33, 34, or 35 days of culturing the hemangioblasts.

Extracellular Vesicles Secreted from Mesenchymal Stem Cells

[0240] The presently disclosed subject matter also provides extracellular vesicles isolated, derived, secreted, or released from a cell, e.g., the HMCs of the presently disclosed subject matter.

[0241] As used herein, the term "extracellular vesicle" or "EV" refers to lipid bound vesicles secreted by cells into the extracellular space. The three main subtypes of EVs are microvesicles (MVs), exosomes, and apoptotic bodies, which are differentiated based upon their biogenesis, release pathways, size, content, and function (Zaborowski M. P., et al. *Bioscience*. 2015; 65:783-797). Generally extracellular vesicles range in diameter from 20 nm to 5000 nm, and can comprise various macromolecular payload either within the

internal space (i.e., lumen), displayed on the external surface of the extracellular vesicle, and/or spanning the membrane. Said payload can comprise nucleic acids, e.g., microRNAs (miRNA), long non-coding RNAs (lncRNA), mRNAs, DNA fragments; proteins, carbohydrates, lipids, small molecules, and/or combinations thereof. By way of example and without limitation, extracellular vesicles include apoptotic bodies, fragments of cells, vesicles derived/secrated from cells by direct or indirect manipulation (e.g., by serial extrusion or treatment with alkaline solutions), vesiculated organelles, and vesicles produced by living cells (e.g., by direct plasma membrane budding or fusion of the late endosome with the plasma membrane). Extracellular vesicles can be derived/secrated from a living or dead organism, explanted tissues or organs, prokaryotic or eukaryotic cells, and/or cultured cells.

[0242] As used herein, the term "exosome" refers to a cell-derived small vesicle comprising a membrane that encloses an internal space (i.e., lumen), and which is formed from said cell by direct plasma membrane budding or by fusion of the late endosome with the plasma membrane (Yáñez-Mó M., et al. *J. Extracell. Vesicles*. 2015; 4:27066). Specifically, exosomes are involved in protein sorting, recycling, storage, transport, and release. Exosomes are generally between 20-300 nm in diameter. Exosomes are secreted by all cell types and have been found in plasma, urine, semen, saliva, bronchial fluid, cerebral spinal fluid (CSF), breast milk, serum, amniotic fluid, synovial fluid, tears, lymph, bile, and gastric acid.

[0243] Exosomes have been found to participate in cell-cell communication, cell maintenance, and tumor progression. In addition, exosomes have been found to stimulate immune responses by acting as antigen-presenting vesicles (Bobrie A., et al., *Traffic*. 2011; 12:1659-1668). In the nervous system, exosomes have been found to help promote myelin formation, neurite growth, and neuronal survival, thus playing a role in tissue repair and regeneration (Faure J., et al. *Mol. Cell. Neurosci.* 2006; 31:642-648). At the same time, exosomes in the central nervous system (CNS) have been found to contain pathogenic proteins, such as beta amyloid peptide, superoxide dismutase, and alpha synuclein that may aid in disease progression (Fevrier B., et al., *Proc. Natl. Acad. Sci. USA*. 2004; 101:9683-9688). Exosomes have also been shown as carriers for disease markers. The use of exosomes as carriers of biomarkers is ideal because these vesicles are found in bodily fluids, such as blood and urine, which allows for minimally to non-invasive "liquid biopsy" type methods to diagnose and even monitor a patient's response to treatment.

[0244] In addition to their natural role in cell-cell interactions, exosomes can be loaded with different cargos, e.g., drugs and exogenous nucleic acids or proteins, and deliver this cargo to different cells. The cargo can be conjugated to an extracellular vesicle, embedded within an extracellular vesicle, encapsulated within an extracellular vesicle, or otherwise carried by an extracellular vesicle, or any combination thereof. Thus, as used herein, a reference to a cargo being "present" in an extracellular vesicle or its lumen is understood to include any of the foregoing means of carrying the cargo.

[0245] A cargo can be an endogenous cargo, an exogenous cargo, or a combination thereof. Examples of cargos that can be conjugated, embedded, encapsulated within or otherwise carried by an extracellular vesicle described herein include,

without limitation, nucleic acid molecules (e.g., DNA, cDNA, antisense oligonucleotides, mRNA, inhibitory RNAs (e.g., antisense RNAs, miRNAs, small interfering RNAs (siRNAs), short hairpin RNAs (shRNAs), and agomirRNAs), antagomirRNAs, primary miRNAs (pri-miRNAs), long non-coding RNAs (lncRNAs), small nuclear RNA (snRNA), small nucleolar RNA (snoRNA), and microbial RNAs), polypeptides (e.g., enzymes, antibodies), lipids, hormones, vitamins, minerals, small molecules, and pharmaceuticals, or any combination thereof. Importantly, exosomes, are natural carriers for miRNAs and other non-coding RNAs, and the direct membrane fusion with the target cell allows contents to be delivered directly into the cytosol. This makes exosomes an excellent delivery system for small molecules (Lai R. C., et al. *Biotechnol. Adv.* 2013; 31:543-551).

[0246] Microvesicles are EVs that form by direct outward budding, or pinching, of the cell's plasma membrane. The size of microvesicles typically range from 100 nm up to 1000 nm in diameter. The route of microvesicles formation is not well understood, however, it is thought to require cytoskeleton components, such as actin and microtubules, along with molecular motors (kinesins and myosins), and fusion machinery (SNAREs and tethering factors) (Cai H., et al. *Dev. Cell.* 2007; 12:671-682). The number of microvesicles produced depends on the donor cell's physiological state and microenvironment (Zaborowski M. P., et al. *Bio-science.* 2015; 65:783-797). Likewise, it has been previously demonstrated that the number of microvesicles consumed depends on the physiological state and microenvironment of recipient cells. Like exosomes, microvesicles are involved in cell-cell communication between local and distant cells. The ability of these EVs to alter the recipient cell has been well demonstrated (Harding C. V., et al., *J. Cell Biol.* 2013; 200:367-371; White I. J., et al., *EMBO J.* 2006; 25:1-12). The uniqueness of EVs is that they have the ability to package active cargo (proteins, nucleic acids, and lipids) and deliver it to another cell, neighboring or distant, and alter the recipient cell's functions with its delivery.

[0247] Apoptotic bodies are released by dying cells into the extracellular space. They are reported to range in size from 50 nm up to 5000 nm in diameter, with the size of most apoptotic bodies tending to be on the larger side (Borges F., et al. *Braz. J. Med. Biol. Res.* 2013; 46:824-830). These bodies form by a separation of the cell's plasma membrane from the cytoskeleton as a result of increased hydrostatic pressure after the cell contracts (Wickman G., et al. *Cell Death Differ.* 2012; 19:735-742). The composition of apoptotic bodies is in direct contrast with exosomes and microvesicles. Unlike exosomes and microvesicles, apoptotic bodies contain intact organelles, chromatin, and small amounts of glycosylated proteins (Borges F., et al., *Braz. J. Med. Biol. Res.* 2013; 46:824-830; Thery C., et al. *J. Immunol.* 2001; 166:7309-7318).

Methods for Isolating Extracellular Vesicles

[0248] The EVs of the presently disclosed subject matter can be isolated, secreted, derived, or separated, from a medium or other source material, e.g., the HMCs of the presently disclosed subject matter, using routine methods known in the art (see, for example the techniques described in Taylor et al., *Serum/Plasma Proteomics*, Chapter 15, "Extracellular vesicle Isolation for Proteomic Analyses and RNA Profiling," Springer Science, 2011; and Tauro et al., *Methods* 56 (2012) 293-304, and references cited therein)

and as described in the Examples section below. The most commonly used method involves multiple centrifugation and ultracentrifugation steps.

[0249] Physical properties of EVs (e.g., HMC-EVs) may be employed for EV isolation, purification or enrichment, including separation on the basis of electrical charge (e.g., electrophoretic separation), size (e.g., filtration, molecular sieving, etc), density (e.g., regular or gradient centrifugation), Svedberg constant (e.g., sedimentation with or without external force, etc). Alternatively, or additionally, isolation may be based on one or more biological properties, and include methods that may employ surface markers (e.g., for precipitation, reversible binding to solid phase, FACS separation, specific ligand binding, non-specific ligand binding, immuno-magnetic capture of EVs using magnetic beads coated with antibodies directed against proteins exposed on EV membranes, etc.).

[0250] Methods based on the use of volume-excluding polymers, such as PEG, have been recently described by a number of different groups (U.S. Pat. Appl. 20130273544, U.S. Pat. Appl. 20130337440). Two such products are ExoQuick (System Biosciences, Mountain View, USA) and Total Exosome Isolation Reagent (Life Technologies, Carlsbad, USA). These polymers work by tying up water molecules and forcing less-soluble components such as extracellular vesicles, as well as proteins out of solution, allowing them to be collected by a short, low-speed centrifugation.

[0251] In some embodiments, isolation, purification, and enrichment can be done in a general and non-selective manner (typically including serial centrifugation). Alternatively, isolation, purification, and enrichment can be done in a more specific and selective manner (e.g., using producer cell-specific surface markers). For example, specific surface markers may be used in immunoprecipitation, FACS sorting, affinity purification, or bead-bound ligands for magnetic separation.

[0252] In some embodiments, tangential flow filtration may be used to isolate or purify the EVs (e.g., HMC-EVs).

[0253] In some embodiments, size exclusion chromatography can be utilized to isolate or purify the EVs (e.g., HMC-EVs). Size exclusion chromatography techniques are known in the art. In some embodiments, density gradient centrifugation can be utilized to isolate the EVs. In some embodiments, the isolation of EVs (e.g., HMC-EVs) may involve ion chromatography, such as anion exchange, cation exchange, or mixed mode chromatography. In some embodiments, the isolation of EVs (e.g., HMC-EVs) may involve desalting, dialysis, tangential flow filtration, ultrafiltration, or diafiltration, or any combination thereof. In some embodiments, the isolation of EVs (e.g., HMC-EVs) may involve combinations of methods that include, but are not limited to, differential centrifugation, size-based membrane filtration, concentration and/or rate zonal centrifugation. In some embodiments, the isolation of EVs (e.g., HMC-EVs) may involve one or more centrifugation steps. The centrifugation may be performed at about 50,000 to 150,000-g. The centrifugation may be performed at about 50,000×g, 75,000×g, 100,000×g, 125,000×g, or 150,000×g. In another embodiment, EVs (e.g., HMC-EVs) are separated from nonmembranous particles, using their relatively low buoyant density (Raposo et al., 1996; Escola et al., 1998; van Niel et al., 2003; Wubbolt et al., 2003). Kits for such isolation are commercially available, for example, from Qiagen, InVitrogen and SBI. Methods for loading EVs with a therapeutic

agent are known in the art and include lipofection, electroporation, as well as any standard transfection method.

[0254] In some embodiments, the presently disclosed subject matter provides methods for isolating HMC-EVs secreted from HMCs obtained by in vitro differentiation of pluripotent stem cells. The method comprises providing HMCs obtained by in vitro differentiation of pluripotent stem cells, and isolating extracellular vesicles. The HMC-EVs may be isolated by any method known in the art or as described herein. In some embodiments, the HMC-EVs are isolated by tangential flow filtration. In some embodiments, the HMC-EVs are isolated by ultracentrifugation. In some embodiments, the HMC-EVs are isolated by cation exchange chromatography. In some embodiments, the HMC-EVs are isolated by anion exchange chromatography. Characteristics and Compositions of HMCs and/HMC-EVs [0255] The presently disclosed subject matter further provides compositions comprising HMCs obtained by in vitro differentiation of pluripotent stem cells, and/or extracellular vesicles secreted from the HMCs (HMC-EVs) of the presently disclosed subject matter. In an embodiment, the HMCs are obtained by in vitro differentiation of hemangioblasts. Expression levels of certain phenotypic markers may be determined by any method known in the art, such as immunohistochemistry. Expression of certain genes may be determined by any method known in the art, such as RT-PCR and RNA-Seq.

[0256] In an embodiment, the HMCs of the presently disclosed subject matter express at least 2, at least 3, at least 4, at least 5, at least 6, at least 7 or at least 8 markers selected from the group comprising CD9, CD13, CD29, CD44, CD73, CD90, CD105, CD166, and HLA-ABC. A still further embodiment, the HMCs of the presently disclosed subject matter express at least 2, at least 3, at least 4, at least 5 or at least 6 markers selected from the group consisting of CD9, CD13, CD29, CD44, CD73, CD90 and CD105, and wherein said HMCs do not express CD2, CD3, CD4, CD5, CD7, CD8, CD14, CD15, CD16, CD19, CD20, CD22, CD33, CD36, CD38, CD61, CD62E and CD133. In another embodiment, the HMCs of the presently disclosed subject matter express at least 1, at least 2, at least 3, at least 4, at least 5 or at least 6 markers selected from the group consisting of AIRE-1, IL-11, CD10, CD24, ANG-1, and CXCL1.

[0257] In an embodiment, the composition comprises HMCs, wherein about 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, 98%, 99%, or 100% of the HMCs express CD9, CD13, CD29, CD44, CD73, CD90, CD105, CD166, and HLA-ABC after about 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, or 30 days in culture. In an embodiment of the instant presently disclosed subject matter at least 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, 98%, 99%, or 100% of the HMCs in a composition of the presently disclosed subject matter express at least 2, at least 3, at least 4, at least 5, at least 6, at least 7 or at least 8 markers selected from the group consisting of CD9, CD13, CD29, CD44, CD73, CD90, CD105, CD166, and HLA-ABC and lack expression of CD2, CD3, CD4, CD5, CD7, CD8, CD14, CD15, CD16, CD19, CD20, CD22, CD33, CD36, CD38, CD61, CD62E, CD133 and Stro-1 after about 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, or 30 days in culture. The HMCs in a composition of the presently disclosed subject matter may further express at least 1, at least 2, at least 3, at least 4, at least 5 or at least

6 markers selected from the group consisting of AIRE-1, IL-11, CD10, CD24, ANG-1, and CXCL1.

[0258] In an embodiment, the composition comprises HMCs, wherein at least 30% of the HMCs are positive for CD10. Additionally, at least 60% of the HMCs may be positive for markers CD73, CD90, CD105, CD13, CD29, CD44, and CD166 and HLA-ABC. In an exemplary embodiment, less than 30% of the HMCs may be positive for markers CD31, CD34, CD45, CD133, FGFR2, CD271, Stro-1, CXCR4 and TLR3.

[0259] In another embodiment, the composition comprises HMCs, wherein at least 50% of the HMCs are positive for CD105 or CD73 within about 7-20 (e.g., 15) days of culture. In a preferred embodiment of the instant presently disclosed subject matter, at least 50% of the HMCs are positive for CD105 or CD73 after about 7-15 days of culture. In a further embodiment of the instant presently disclosed subject matter, at least 80% of the HMCs are positive for CD105 and CD73 within about 20 days of culture. In still a further embodiment of the instant presently disclosed subject matter, at least 80% of a composition of HMCs are positive for CD105 and CD73 within about 20 days of culture.

[0260] In an embodiment, the composition comprises HMCs, wherein at least 20%, 30%, 40%, or 50% of said HMCs may be positive for (i) at least one of CD10, CD24, IL-11, AIRE-1, ANG-1, CXCL1, CD105, CD73 and CD90; (ii) at least one of CD10, CD24, IL-11, AIRE-1, ANG-1, CXCL1, CD105, CD73, CD90, CD105, CD13, CD29, CD44, CD166, CD274, and HLA-ABC; (iii) CD105, CD73 and/or CD90 or (iv) any combination thereof. At least 20%, 30%, 40%, or 50% of said HMCs may be positive for (i) at least two of CD105, CD73 and/or CD90 (ii) at least two of CD10, CD24, IL-11, AIRE-1, ANG-1, CXCL1, CD105, CD73 and CD90; or (iii) all of CD10, CD24, IL-11, AIRE-1, ANG-1, CXCL1, CD105, CD73, CD90, CD105, CD13, CD29, CD44, CD166, CD274, and HLA-ABC. At least 20%, 30%, 40%, or 50% of said HMCs (i) may be positive for CD105, CD73 and CD90; (ii) positive for CD10, CD24, IL-11, AIRE-1, ANG-1, CXCL1, CD105, CD73, CD90, CD105, CD13, CD29, CD 44, CD166, CD274, and HLA-ABC and/or (ii) may be negative for or less than 5% or less than 10% of the cells express CD31, 34, 45, 133, FGFR2, CD271, Stro-1, CXCR4, and/or TLR3. At least 20%, 30%, 40%, 50%, 60%, 70%, 80% or 90% of said HMCs may be positive for (i) one or more of CD105, CD73 and CD90 (ii) one or more of CD10, CD24, IL-11, AIRE-1, ANG-1, CXCL1, CD105, CD73 and CD90; or (iii) one or more of CD10, CD24, IL-11, AIRE-1, ANG-1, CXCL1, CD105, CD73, CD90, CD105, CD13, CD29, CD 44, CD166, CD274, and HLA-ABC.

[0261] In another embodiment, the composition comprises HMCs, wherein at least 20%, 30%, 40%, or 50% of said HMCs (i) may be positive for all of CD10, CD24, IL-11, AIRE-1, ANG-1, CXCL1, CD105, CD73, CD90, CD105, CD13, CD29, CD 44, CD166, CD274, and HLA-ABC and (ii) may be negative for or less than 5% or less than 10% of the cells express CD31, 34, 45, 133, FGFR2, CD271, Stro-1, CXCR4 and/or TLR3.

[0262] In a further embodiment, the composition comprises HMCs, wherein at least 20%, 30%, 40%, or 50% of said HMCs may be positive for (i) all of CD10, CD24, IL-11, AIRE-1, ANG-1, CXCL1, CD105, CD73 and CD90; or (ii) all of CD73, CD90, CD105, CD13, CD29, CD44, CD166, CD274, and HLA-ABC.

[0263] In yet another embodiment, the composition comprises HMCs, wherein at least 20%, 30%, 40%, 50%, 60%, 70%, 80% or 90% of said HMCs may be positive for (i) at least one of CD10, CD24, IL-11, AIRE-1, ANG-1, CXCL1, CD105, CD73 and CD90; or (ii) at least one of CD73, CD90, CD105, CD13, CD29, CD 44, CD166, CD274, and HLA-ABC.

[0264] In another embodiment, the HMCs may not express or less than 5% or less than 10% of the HMCs may express at least one of CD31, 34, 45, 133, FGFR2, CD271, Stro-1, CXCR4, or TLR3.

[0265] In addition to the characteristics described above, the HMCs of the presently disclosed subject matter may possess phenotypes of younger cells as compared to adult-derived MSCs. In one embodiment, the HMCs are capable of undergoing at least or about 5, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, or more population doublings in culture. In contrast, adult-derived MSCs typically undergo 2-3 doublings in culture. In another embodiment, the HMCs of the presently disclosed subject matter have longer telomere lengths, greater immunosuppressive effects, fewer vacuoles, divide faster, divide more readily in culture, higher CD90 expression, are less lineage committed, or combinations thereof, compared to adult-derived MSCs. In another embodiment, the HMCs of the presently disclosed subject matter have increased expression of transcripts promoting cell proliferation (i.e., have a higher proliferative capacity) and reduced expression of transcripts involved in terminal cell differentiation compared to adult-derived MSCs.

[0266] In an embodiment, the HMCs are “early passage” HMCs and may be passaged no more than 1, 2, 3, 4, 5, 6, 7, or 8 times. In an embodiment, early passage HMCs are passaged no more than 4 times. In another embodiment, the early passage HMCs are passaged no more than 5 times. In another embodiment, the early passage HMCs are passaged no more than 6 times. In addition to the HMCs characteristics described above, early passage HMCs may, in a resting or basal state, express mRNA encoding interleukin-6 (IL-6) at a level which may be less than ten percent of the IL-6 mRNA level expressed by BM-MSCs or AD-MSCs in a resting or basal state. VEGF mRNA levels may also be downregulated in early passage HMCs, in a resting or basal state, compared to BM-MSCs in a resting or basal state. In another embodiment, the HMCs may, in a resting or basal state, express mRNA encoding CD24 at a level that is greater than the CD24 mRNA level expressed by BM-MSC or AD-MSC preparations in a resting or basal state. Other mRNA levels that may be upregulated in early passage HMCs, in a resting or basal state, compared to BM-MSCs, in a resting or basal state, include AIRE, ANGPT1 (ANG-1), CXCL1, CD10, and IL-11. Additionally, the early passage HMCs, in a resting or basal state, may be negative for one or more of mRNAs encoding ANGPT2, CD31, CD34, CD45, HLA-G, IL2RA, IL3, IL12B.

[0267] In a further embodiment, the early passage HMCs express one or more markers selected from the group consisting of CD13, CD29, CD44, CD73, CD90, CD105, CD166, and HLA-ABC, as determined by immunohistochemistry. In another embodiment, the early passage HMCs are negative for one or more markers selected from the group consisting of CD31, CD34, CD45, CXCR4, HLA-DR, FGFR2, TLR3, CD106, CD133, and CD271, as determined by immunohistochemistry.

[0268] In an embodiment, expression levels of CD10 is upregulated in early passage HMCs compared with the expression levels of CD10 in BM-MSCs, as determined by immunohistochemistry. In another embodiment, expression levels of CD10 in early passage HMCs may be about the same the expression levels of CD10 in BM-MSCs. In another embodiment, expression levels of Stro-1 is down-regulated in early passage HMCs of the presently disclosed subject matter compared with the expression levels of Stro-1 in BM-MSCs, as determined by immunohistochemistry. In a specific embodiment, a composition comprises early passage HMCs, wherein about 5-10% of the early passage HMCs express Stro-1.

[0269] In a further embodiment, the HMCs of the presently disclosed subject matter express higher levels of certain genes compared to BM-MSCs, UCB-MSCs, or AD-MSCs. For example, the HMCs of the presently disclosed subject matter may express higher levels of any of the genes listed in Table 3 compared to BM-MSCs, and/or any of the genes listed in Table 5 compared to UCB-MSCs, and/or any of the genes listed in Table 7 compared to AD-MSCs. In another embodiment, the HMCs of the presently disclosed subject matter may express lower levels of any of the genes listed in Table 4 compared to BM-MSCs, and/or any of the genes listed in Table 6 compared to UCB-MSCs, and/or any of the genes listed in Table 8 compared to AD-MSCs.

[0270] In an embodiment, genes associated with increased migration and chemotaxis, such as MMP9 is expressed at a higher level in the HMCs of the presently disclosed subject matter compared to BM-MSCs or UCB-MSCs. In another embodiment, Lgr5, a marker of multipotent stem cells, is expressed at a higher level in the HMCs of the presently disclosed subject matter compared to BM-MSCs or UCB-MSCs. In a further embodiment, CD24 is expressed at a higher level in the HMCs of the presently disclosed subject matter compared to BM-MSCs and IL-6 is expressed at a lower level in the MSCs of the presently disclosed subject matter compared to BM-MSCs. In yet another embodiment, neuro-related genes, such as NGF, NTF-4, NTRK-2, NTRK-3, and DCC (Netrin-1), are expressed at a higher level in the HMCs of the presently disclosed subject matter compared to BM-MSCs or UCB-MSCs. MSCs of the presently disclosed subject matter may be selected or purified based on any of the genes that are differentially expressed.

[0271] In some embodiments, the HMCs of the presently disclosed subject matter may express lower levels of any of the miRNA listed in Table 21 compared to HMC-EVs. In some embodiments, the HMCs of the presently disclosed subject matter may express higher levels of any of the miRNA listed in Table 22 compared to HMC-EVs.

[0272] In a further embodiment, the HMC-EVs of the presently disclosed subject matter express higher levels of certain miRNA, genes, or proteins compared to BM-MSCs-EVs, UCB-MSCs-EVs, or AD-MSCs-EVs.

[0273] In some embodiments, the HMC-EVs of the presently disclosed subject matter may express higher levels of any of the miRNAs listed in Table 9 compared to UCB-MSCs-EVs, and/or any of the miRNAs listed in Table 11 compared to BM-MSC-EVs, and/or any of the miRNAs listed in Table 13 compared to AD-MSC-EVs. In another embodiment, the HMC-EVs of the presently disclosed subject matter may express lower levels of any of the miRNAs listed in Table 10 compared to UCB-MSCs-EVs, and/or any of the miRNAs listed in Table 12 compared to BM-MSC-

EVs, and/or any of the miRNAs listed in Table 13 compared to AD-MSC-EVs. In some embodiments, the HMC-EVs of the presently disclosed subject matter may express higher levels of any of the proteins listed in Table 15 compared to UCB-MSCs-EVs, and/or any of the proteins listed in Table 17 compared to BM-MSC-EVs, and/or any of the miRNA listed in Table 19 compared to AD-MSC-EVs. In another embodiment, the HMC-EVs of the presently disclosed subject matter may express lower levels of any of the proteins listed in Table 16 compared to UCB-MSCs-EVs, and/or any of the proteins listed in Table 18 compared to BM-MSC-EVs, and/or any of the proteins listed in Table 20 compared to AD-MSC-EVs.

[0274] In some embodiments, the HMC-EVs express at least one of the miRNAs selected from the group consisting of hsa-miR-125b-5p, hsa-miR-181a-5p, hsa-miR-199b-5p, hsa-miR-21-5p, hsa-miR-23a-3p, hsa-miR-125a-5p, hsa-miR-106a-5p+hsa-miR-17-5p and hsa-miR-221-3p at a higher level compared to BM-MSC-EVs, UCB-MSC-EVs, and/or AD-MSC-EVs.

[0275] In some embodiments, the HMC-EVs express at least one of the proteins selected from the group consisting of ALDOC, ANXA5, APBB2, BASP1, CAV1, CD81, CD99, CKM, EPB41L3, FDPS, GNAQ, GNG12, GP9, H2AC20, H2AC21, H3-3A, H3-7, H4-16, HLA-A, ITGA2, KPNA2, KRAS, KRT4, LRRC59, MAMDC2, MARCKSL1, MDGA1, MERTK, MFGE8, MMP14, MVP, PCDH1, PDGFRB, PDI A3, RPL13, RPS18, RPS3A, RPS4X, SDCBP, SLC2A1, SLC3A2, TAGLN2, TNC, TSPAN14, TSPAN33, TSPAN9, TTYH3, UCHL1, VAT1, YWHAQ, and YWHAQ at a higher level compared to BM-MSC-EVs, UCB-MSC-EVs, and/or AD-MSC-EVs.

[0276] In some embodiments, the HMC-EVs express at least one of the proteins selected from the group consisting of ADGRG6, AGRN, ANXA6, APOC4, ARHGAP1, ARGHDI A, ARL8A, ARPC5, B2M, BBS1, BLVRA, BST1, CA2, CCN2, CCNB3, CD34, CD36, CD47, CORO1A, DTD1, EEF1D, EEF1G, ENG, ESD, GNAI2, GNB1, H1-3, H2BC15, HIP1, KIF11, LAMP1, LAP3, LGALS1, LTBP3, MAPK3, MARCKS, MBTD1, MDH1, MOB1B, MYL12B, MYO1F, MYO3A, NIBAN2, PEBP1, PF4, PGAP1, PLOD1, PPP2RIA, PRSS23, PXDN, RALA, RAP2A, RPS13, RPS3, RPSA, S100A11, SLC44A1, SLC44A2, SLTM, SMG1, SPARC, SRSF8, STRADB, STX11, STXBP2, TGM2, TPP1, TPTE2, TRIM5, TRPM2, TUBA8, TUBB3, VCAN, YWHAE, and ZFN607 at a higher level compared to BM-MSC-EVs, UCB-MSC-EVs, and/or AD-MSC-EVs.

[0277] In some embodiments, the HMC-EVs express at least one of the proteins selected from the group consisting of ADIPOQ, CAT, CEP290, IGLV6-57, TAS2R33, and TMEM198 at a lower level compared to BM-MSC-EVs, UCB-MSC-EVs, and/or AD-MSC-EVs.

[0278] In some embodiments, the HMC-EVs express at least one of the proteins selected from the group consisting of AKAP9, ALB, ALOX5, APLP2, CD109, CDSN, CHST9, ERC1, F11, ARMCX5, LAMB4, LRRTM2, LTF, MSH6, OAF, OLFML3, PAK6, RGS14, SEMA7A, SURF1, and TRIM4 at a lower level compared to BM-MSC-EVs, UCB-MSC-EVs, and/or AD-MSC-EVs.

[0279] In some embodiments, the HMC-EVs of the presently disclosed subject matter may express higher levels of any of the miRNAs listed in Table 21 compared to the HMCs of the presently disclosed subject matter. In some embodi-

ments, the HMC-EVs of the presently disclosed subject matter may express lower levels of any of the miRNAs listed in Table 22 compared to the HMCs of the presently disclosed subject matter.

[0280] In an embodiment, genes associated with or involved in the development of neuronal lineage including axon guidance, CREB signaling in neurons, synaptogenesis signaling, or neuroinflammation signaling, are expressed at a higher level in the HMCs of the presently disclosed subject matter compared to AD-MSCs or BM-MSCs.

[0281] In another embodiment, the HMCs of the presently disclosed subject matter have a distinct expression profile when compared to mature MSCs, e.g., AD-MSCs or BM-MSCs or UCB-MSCs. Specifically, the HMCs of the presently disclosed subject matter are able to confer neuroprotective effects, and provide neurotrophic factors, i.e., factors involved in supporting neuronal survival, growth, health and recovery. Likewise, the HMC-EVs of the presently disclosed subject matter share a similar profile as the HMCs from which they were derived. Similar signaling pathways enriched in the HMCs are also enriched in the HMC-EVs when compared to other tissue-derived MSCs and EVs.

[0282] In an embodiment, the composition comprising HMCs of the presently disclosed subject matter is substantially purified with respect to pluripotent stem cells. In a further embodiment, a composition of HMCs of the presently disclosed subject matter is substantially purified with respect to pluripotent stem cells such that said composition comprises at least about 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% HMCs. The pluripotent stem cells may be any pluripotent stem cells described herein.

[0283] The composition may comprise less than about 50%, 45%, 40%, 35%, 30%, 25%, 20%, 15%, 10%, 9%, 8%, 7%, 6%, 5%, 4%, 3%, 2%, 1%, 0.9%, 0.8%, 0.7%, 0.6%, 0.5%, 0.4%, 0.3%, 0.2%, 0.1%, 0.09%, 0.08%, 0.07%, 0.06%, 0.05%, 0.04%, 0.03%, 0.02%, 0.01%, 0.009%, 0.008%, 0.007%, 0.006%, 0.005%, 0.004%, 0.003%, 0.002%, 0.001%, 0.0009%, 0.0008%, 0.0007%, 0.0006%, 0.0005%, 0.0004%, 0.0003%, 0.0002%, or 0.0001% pluripotent stem cells. The composition may be devoid of pluripotent stem cells.

[0284] In some embodiments, the composition comprising HMC-EVs of the presently disclosed subject matter is substantially purified with respect to the HMCs. In a further embodiment, a composition of HMC-EVs of the presently disclosed subject matter is substantially purified with respect to HMCs such that said composition comprises at least about 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% HMC-EVs.

[0285] The composition may comprise less than about 50%, 45%, 40%, 35%, 30%, 25%, 20%, 15%, 10%, 9%, 8%, 7%, 6%, 5%, 4%, 3%, 2%, 1%, 0.9%, 0.8%, 0.7%, 0.6%, 0.5%, 0.4%, 0.3%, 0.2%, 0.1%, 0.09%, 0.08%, 0.07%, 0.06%, 0.05%, 0.04%, 0.03%, 0.02%, 0.01%, 0.009%, 0.008%, 0.007%, 0.006%, 0.005%, 0.004%, 0.003%, 0.002%, 0.001%, 0.0009%, 0.0008%, 0.0007%, 0.0006%, 0.0005%, 0.0004%, 0.0003%, 0.0002%, or 0.0001% HMCs.

[0286] In another embodiment of the instant presently disclosed subject matter, a composition of HMCs and/or HMC-EVs generated by any one or more of the processes of the instant presently disclosed subject matter does not form a teratoma when introduced into a host.

[0287] In an exemplary aspect, the present disclosure provides a composition comprising at least 10^4 , 10^5 , 10^6 , 10^7 , 10^8 or 10^9 HMCs. In a specific embodiment, the composition comprises 10^6 HMCs and less than one percent of any other cell type, wherein the mesenchymal stem cells have replicative capacity to undergo at least 10 population doublings in cell culture with less than 25 percent of the cells undergoing cell death, senescing or differentiating into non-HMC cells by the tenth population doubling.

[0288] The HMCs may have replicative rates to undergo at least 10 population doublings in cell culture in less than 25 days. The HMCs may have a mean terminal restriction fragment length (TRF) that may be longer than 8 kb. The HMCs may have a statistically significant decreased content and/or enzymatic activity, relative to mesenchymal stem cell preparations derived from bone marrow that have undergone five population doublings, of proteins involved in one or more of (i) cell cycle regulation and cellular aging, (ii) cellular energy and/or lipid metabolism, and (iii) apoptosis. The HMCs may have a statistically significant increased content and/or enzymatic activity of proteins involved in cytoskeleton structure and cellular dynamics relating thereto, relative to mesenchymal stem cell preparations derived from bone marrow. The HMCs may not undergo more than a 75 percent increase in cells having a forward-scattered light value, measured by flow cytometry, greater than 5,000,000 over 10 population doublings in culture.

[0289] In an embodiment of the instant presently disclosed subject matter, a preparation of the subject HMCs (e.g., generated by culturing hemangioblasts) is provided, wherein said preparation comprises substantially similar levels of p53 and p21 protein, or wherein the levels of p53 as compared to p21 are 1.5, 2, 3, 4, 5, 6, 7, 8, 9, or 10 times greater. In an embodiment of the instant presently disclosed subject matter, a pharmaceutical preparation of the subject HMCs (e.g., generated by culturing hemangioblasts) is provided, wherein said pharmaceutical preparation comprises substantially similar levels of p53 and p21 protein, or wherein the levels of p53 as compared to p21 are 1.5, 2, 3, 4, 5, 6, 7, 8, 9, or 10 times greater.

[0290] In an embodiment, the presently disclosed subject matter provides a composition comprising HMCs, wherein the comprises a substantially similar percentage of HMCs positive for p53 and p21 protein, or wherein the percentage of HMCs positive for p53 as compared to p21 are 1.5, 2, 3, 4, 5, 6, 7, 8, 9, or 10 times greater.

[0291] In one embodiment, the present disclosure provides a composition comprising at least about 10^3 to about 10^{13} HMC-EVs. In another embodiment, the present disclosure provides a composition comprising at least 10^3 , 10^4 , 10^5 , 10^6 , 10^7 , 10^8 , 10^9 , 10^{10} , 10^{11} , 10^{12} , or 10^{13} HMC-EVs.

Methods of Determining Neurite Outgrowth of HMC and/or HMC-EV Populations.

[0292] The presently disclosed subject matter also provides a method of determining effects of the HMC and/or HMC-EVs on neurons, such as neurite outgrowth. In an aspect, the presently disclosed subject matter provides a method of determining neurite outgrowth of an HMC and/or HMC-EV population. In an embodiment, the method comprises (a) preparing a mixed neuronal culture from an isolated cerebral cortex, (b) plating the HMC and/or HMC-EV population on a permeable membrane, (c) applying strain on the mixed neuronal culture, (d) overlaying the

strained mixed neuronal culture with the permeable membrane of step (b), and (e) measuring neurite outgrowth of the mixed neuronal culture. In an embodiment, the method further comprises determining gene expression of the mixed neuronal culture in the presence and absence of the HMC and/or HMC-EV population. In another embodiment, the strain is a physical scratch made in the mixed neuronal culture. In another embodiment, the strain is vacuum pressure and positive air pressure applied to the mixed neuronal culture. In yet another embodiment, the strain may be applied at 15% to 0% stretching oscillations. In an embodiment, the stretching oscillations may be applied at 15%, 12.5%, 10%, 7.5%, 5%, 2.5%, or 0% cycles.

Pharmaceutical Preparations Comprising HMCs and HMC-EVs

[0293] Pharmaceutical preparations of the instant presently disclosed subject matter may comprise any of the HMCs or compositions of HMCs described herein, and/or HMC-EVs. Pharmaceutical preparations comprising HMCs and/or HMC-EVs of the presently disclosed subject matter may be formulated with a pharmaceutically acceptable carrier. For example, HMCs and/or HMC-EVs of the presently disclosed subject matter may be administered alone or as a component of a pharmaceutical formulation, wherein said HMCs and/or HMC-EVs may be formulated for administration in any convenient way for use in medicine. One embodiment provides a pharmaceutical preparation of HMCs and/or HMC-EVs comprising said HMCs and/or HMC-EVs in combination with one or more pharmaceutically acceptable sterile isotonic aqueous or non-aqueous solutions selected from the group consisting of: dispersions, suspensions, emulsions, sterile powders optionally reconstituted into sterile injectable solutions or dispersions just prior to use, antioxidants, buffers, bactericides, solutes or suspending and thickening agents.

[0294] Exemplary pharmaceutical preparations of the present disclosure may be any formulation suitable for use in treating a human patient, such as pyrogen-free or essentially pyrogen-free, and pathogen-free.

[0295] The preparation comprising HMCs and/or HMC-EVs used in the methods described herein may be transplanted in a suspension, gel, colloid, slurry, or mixture. Also, at the time of injection, cryopreserved HMCs and/or HMC-EVs may be resuspended with commercially available balanced salt solution to achieve the desired osmolality and concentration for administration by injection (i.e., bolus or intravenous).

[0296] One aspect of the presently disclosed subject matter relates to a pharmaceutical preparation suitable for use in a mammalian patient, comprising at least 10^4 , 10^5 , 10^6 , 10^7 , 10^8 , 10^9 , 10^{10} , 10^{11} , 10^{12} , or 10^{13} HMCs and/or HMC-EVs and a pharmaceutically acceptable carrier. Yet another aspect of the presently disclosed subject matter provides a cryogenic cell bank comprising at least 10^8 , 10^9 , 10^{10} , 10^{11} , 10^{12} or even 10^{13} HMCs and/or HMC-EVs. Still another aspect of the presently disclosed subject matter provides a pharmaceutical preparation free of or substantially free of non-human cells and/or non-human animal products, comprising at least 10^4 , 10^5 , 10^6 , 10^7 , 10^8 , 10^9 , 10^{10} , 10^{11} , 10^{12} , or 10^{13} HMCs and/or HMC-EVs and less than 1% of any other cell type, more preferably less than 0.1%, 0.01% or even 0.001% of any other cell type.

[0297] Concentrations for administration of pharmaceutical preparations of HMCs and/or HMC-EVs may be at any amount that is effective and, for example, substantially free of PSCs. For example, the pharmaceutical preparations may comprise the numbers and types of HMCs and/or HMC-EVs described herein. In a particular embodiment, the pharmaceutical preparations of HMCs and/or HMC-EVs comprise about 1×10^6 to about 1×10^7 , about 1×10^7 to about 1×10^8 , about 1×10^8 to about 1×10^9 , about 1×10^9 to about 1×10^{10} , about 1×10^{10} to about 1×10^{11} , about 1×10^{11} to about 1×10^{12} , or about 1×10^{12} to about 1×10^{13} of the HMCs and/or HMC-EVs for systemic administration to a host in need thereof or about 1×10^4 to about 1×10^3 , about 1×10^3 to about 1×10^6 , 1×10^6 to about 1×10^7 , about 1×10^7 to about 1×10^8 , about 1×10^8 to about 1×10^9 , about 1×10^9 to about 1×10^{10} , about 1×10^{10} to about 1×10^{11} , about 1×10^{11} to about 1×10^{12} , or about 1×10^{12} to about 1×10^{13} of said HMCs and/or HMC-EVs for local administration to a host in need thereof.

Methods of Treating Brain Injury

[0298] The HMCs and/or HMC-EVs and pharmaceutical preparations comprising HMCs and/or HMC-EVs described herein may be used for treating brain injury, e.g., stroke, or optic neuropathy. In particular, the instant presently disclosed subject matter provides methods for treating or preventing brain injuries described herein comprising administering an effective amount of HMCs and/or HMC-EVs, wherein the HMCs are obtained by in vitro differentiation of pluripotent stem cells. In another embodiment, the HMCs are obtained by in vitro differentiation of hemangioblasts.

[0299] In an embodiment, brain injury is selected from traumatic brain injury, acquired brain injury, anoxic brain injury, diffuse axonal brain injury, focal brain injury, subdural hematoma, brain aneurysm, coma, stroke, optic neuropathy, and cerebral palsy. In a particular embodiment, the brain injury is traumatic brain injury. In another embodiment, the brain injury is cerebral palsy. In yet another embodiment, the brain injury is stroke. In another embodiment, the brain injury is optic neuropathy.

[0300] The HMCs and/or HMC-EVs of the instant presently disclosed subject matter may be administered systemically or locally. The HMCs and/or HMC-EVs may be administered using modalities known in the art including, but not limited to, injection via intravenous, intracranial, intrathecal, intracerebral, intracisternal, intramuscular, intra-peritoneal, intravitreal, or other routes of administration, or local implantation, dependent on the particular pathology being treated.

[0301] The HMCs and/or HMC-EVs of the instant presently disclosed subject matter may be administered via local implantation, such as intracranial implantation, wherein a delivery device is utilized. Delivery devices of the instant presently disclosed subject matter are biocompatible and biodegradable. A delivery device of the instant presently disclosed subject matter can be manufactured using materials selected from the group comprising biocompatible fibers, biocompatible yarns, biocompatible foams, aliphatic polyesters, poly(amino acids), copoly(ether-esters), polyalkylenes oxalates, polyamides, tyrosine derived polycarbonates, poly(iminocarbonates), polyorthesters, polyoxaesters, polyamidoesters, polyoxaesters containing amine groups, poly(anhydrides), polyphosphazenes, biopolymers; homopolymers and copolymers of lactide, glycolide, epsilon-

caprolactone, para-dioxanone, trimethylene carbonate; homopolymers and copolymers of lactide, glycolide, epsilon-caprolactone, para-dioxanone, trimethylene carbonate, fibrillar collagen, non-fibrillar collagen, collagens not treated with pepsin, collagens combined with other polymers, growth factors, extracellular matrix proteins, biologically relevant peptide fragments, hepatocyte growth factor, platelet-derived growth factors, platelet rich plasma, insulin growth factor, growth differentiation factor, vascular endothelial cell-derived growth factor, nicotinamide, glucagon like peptides, tenascin-C, laminin, anti-rejection agents, analgesics, anti-oxidants, anti-apoptotic agents anti-inflammatory agents and cytostatic agents. In some embodiments, the HMCs and/or HMC-EVs are delivered through a slow release device, e.g., transdermal microneedle patch.

[0302] The particular treatment regimen, route of administration, and adjuvant therapy may be tailored based on the particular pathology, the severity of the pathology, and the patient's overall health. Administration of the HMCs and/or HMC-EVs may be effective to reduce the severity of the manifestations of a pathology or and/or to prevent further degeneration of the manifestation of a pathology.

[0303] In some embodiments, administration of the HMCs results in preservation of myelin. In some embodiments, administration of the HMCs results in suppression of neuroinflammatory response in a subject. In some embodiments, administration of the HMCs results in reduction of microglial and astrocyte activation in the brain. In some embodiments, administration of the HMCs results in stimulation and/or activation of pathways involved in cell survival. In some embodiments, administration of the HMCs results in stimulation of expression of a neuroprotective gene in the brain. In some embodiments, the neuroprotective gene is selected from the group consisting of heat shock protein family B member 1 (HSPB1), insulin-like growth factor 1 (IGF2), and secreted phosphoprotein 1 (SPP1). In some embodiments, administration of the HMCs results in stimulation and/or activation of pathways involved in synaptic transmission in the brain. In some embodiments, administration of the HMCs results in reduction of apoptosis. In some embodiments, administration of the HMCs results in stimulation and/or activation of pathways involved in development of neuronal lineage, e.g., axon guidance, BREB signaling in neurons, or synaptogenesis signaling.

[0304] In some embodiments, administration of HMC-EVs results in an increase in the oligodendrocyte and precursor cells in the brain. In some embodiments, administration of HMC-EVs results in preservation of myelin in the brain. In some embodiments, administration of HMC-EVs results in suppression of neuroinflammatory response in the subject. In some embodiments, administration of HMC-EVs results in reduction of microglial and astrocyte activation in the brain. In some embodiments, administration of HMC-EVs results in prevention or reduction of oxidative damage in neurons. In some embodiments, administration of extracellular HMC-EVs results in prevention or reduction of neuronal death due to glutamate excitotoxicity injury.

[0305] A treatment modality of the presently disclosed subject matter may comprise the administration of a single dose of HMCs and/or HMC-EVs. Alternatively, treatment modalities described herein may comprise a course of therapy where HMCs and/or HMC-EVs are administered multiple times over some period of time. Exemplary courses of treatment may comprise weekly, biweekly, monthly,

quarterly, biannually, or yearly treatments. Alternatively, treatment may proceed in phases whereby multiple doses are required initially (e.g., daily doses for the first week), and subsequently fewer and less frequent doses are needed.

[0306] The HMCs and/or HMC-EVs may be administered separately or in combination. In some embodiments, the methods comprise administering to the subject an effective amount of HMCs. In other embodiments, the methods comprise administering to the subject an effective amount of HMC-EVs. In another embodiment, the methods comprise administering to the subject an effective amount of HMCs and an effective amount of HMC-EVs.

[0307] The HMCs and HMC-EVs can be administered simultaneously or sequentially. In one embodiment, the HMCs and the HMC-EVs are mixed together before administering to the subject. In another embodiment, the subject receives an effective amount of HMCs, followed by an effective amount of HMC-EVs. Alternatively, the subject receives an effective amount of HMC-EVs, followed by an effective amount of HMCs.

[0308] In one embodiment, the HMCs and/or HMC-EVs are administered to a patient one or more times periodically throughout the life of a patient. In a further embodiment of the instant presently disclosed subject matter, the HMCs and/or HMC-EVs are administered once per year, once every 6-12 months, once every 3-6 months, once every 1-3 months, or once every 1-4 weeks. Alternatively, more frequent administration may be desirable for certain conditions or disorders. In an embodiment of the instant presently disclosed subject matter, the HMCs and/or HMC-EVs are administered via a device once, more than once, periodically throughout the lifetime of the patient, or as necessary for the particular patient and patient's pathology being treated. Similarly contemplated is a therapeutic regimen that changes over time. For example, more frequent treatment may be needed at the outset (e.g., daily or weekly treatment). Over time, as the patient's condition improves, less frequent treatment or even no further treatment may be needed.

[0309] In some embodiments, about 20 million, about 40 million, about 60 million, about 80 million, about 100 million, about 120 million, about 140 million, about 160 million, about 180 million, about 200 million, about 220 million, about 240 million, about 260 million, about 280 million, about 300 million, about 320 million, about 340 million, about 360 million, about 380 million, about 400 million, about 420 million, about 440 million, about 460 million, about 480 million, about 500 million, about 520 million, about 540 million, about 560 million, about 580 million, about 600 million, about 620 million, about 640 million, about 660 million, about 680 million, about 700 million, about 720 million, about 740 million, about 760 million, about 780 million, about 800 million, about 820 million, about 840 million, about 860 million, about 880 million, about 900 million, about 920 million, about 940 million, about 960 million, or about 980 million MSCs and/or MSC-EVs are administered into the subject. In some embodiments, about 1 billion, about 2 billion, about 3 billion, about 4 billion or about 5 billion HMCs and/or HMC-EVs or more are administered. In some embodiments, the number of HMCs and/or HMC-EVs ranges from between about 20 million to about 4 billion, between about 40 million to about 1 billion, between about 60 million to about 750 million, between about 80 million to about 400

million, between about 100 million to about 350 million, and between about 175 million to about 250 million.

[0310] The methods described herein may further comprise the step of monitoring the efficacy of treatment or prevention using methods known in the art.

EXAMPLES

[0311] The following examples are not intended to limit the presently disclosed subject matter in any way.

Example 1—Generating HMCs from Hemangioblasts

[0312] Hemangioblasts were generated from single-blastomere derived human ESC line, MA09 (Klimanskaya et al., Nature 444 (2006) 481-485). First, a 10 cm plate was coated with 0.1% gelatin and irradiated MEF was added at a concentration of about 25,000 cells/cm² in MEF media (high glucose DMEM+10% FCS) the day before adding ESCs to the plate. The MEF media was then aspirated, rinsed with PBS, and replaced with Reprocell Primate media (Reprocell) plus 10 ng/mL bFGF. A split of MA09 cells were added to the dish and fed with fresh media daily. The MA09s were cultured in Reprocell Primate Media plus 10 ng/mL bFGF until about 90% confluent. The MA09s were then harvested with 0.05% trypsin/EDTA or Reprocell dissociation buffer (Reprocell). After the cells detached, the cells were rinsed and collected. The cells were spun down at 300×g for 10 min. The supernatant was aspirated and the cell pellet was resuspended in Stemline II (Sigma) (plus pen/strep and L-glutamine) plus 50 ng/mL VEGF and 50 ng/mL BMP4. The MA09 ESCs were plated in 2×10 cm ultra low adherence plate (Corning) in 15 ml Stemline II medium (Sigma) supplemented with 50 ng/ml of VEGF and 50 ng/ml of BMP-4 (R & D or Peprotech) and incubated at 37° C. with 5% CO₂. After 40-48 hours, half of the medium (1.5 ml) was replaced with fresh Stemline II medium supplemented with 50 ng/ml of VEGF, 50 ng/ml of BMP-4, and 40-45 ng/ml bFGF so that the final concentration of bFGF ends up being 20-22.5 ng/ml bFGF, and continued incubation for an additional 40-48 hours (i.e., 3.5-4 days total).

[0313] Clusters of cells (embryoid bodies; EBs) were dissociated and plated as single cells in serum-free semisolid blast-colony growth medium (BGM). Specifically, clusters of cells were dissociated with trypsin for 2-5 min. or until clumps start to break up. The cell suspension was pipetted up and down and then DMEM+10% FCS was added to inactivate the trypsin. Cells were then passed through a 40 µm or 70 µm strainer to obtain a single cell suspension. Cells were then counted and resuspended in Stemline II medium at 1-1.5×10⁶ cells/ml.

[0314] The single cell suspension was mixed with hemangioblast (HB) Growth Medium (H4536 based medium recipe: base medium methylcellulose product H4536 (Stem-Cell Technologies) plus penicillin/streptomycin (pen/strp), Excyte growth supplement (Millipore), and the cytokines, Flt3-ligand (FL) at 50 ng/ml, vascular endothelial growth factor (VEGF) at 50 ng/ml, thrombopoietin (TPO) at 50 ng/ml, and basic fibroblast growth factor (bFGF) at 20-30 ng/ml) for a final concentration of about 1×10⁵ cells/ml with a brief vortex, and allowing the bubbles to settle. The cell mixture was then transferred to 4×10 cm ultra low adherence plates by using a syringe (30 ml) attached with an 18G needle, and incubated at 37° C. with 5% CO₂ for 8-12 days.

HBs will begin to appear within 3 or 4 days and continue to populate the plates and may be harvested between days 7-12 of culture. The HBs were harvested on day 9 of culture and frozen down.

[0315] The frozen HBs were thawed and replated onto Matrigel-coated tissue culture plates in MSC medium [α -MEM without nucleosides (Hyclone), 20% Defined FBS—Heat Inactivated (Hyclone), 1 \times Glutamax (Gibco), 1 \times MEM non-essential amino acids (Gibco), and 1 \times penicillin/streptomycin]. The cells were cultured for about 4-5 days and then passaged, and repeated for up to three passages (P3) to generate HMCs. The P3 HMCs (“MARP12” cells) were frozen down for further use.

Example 2—Traumatic Brain Injury (TBD In Vivo Study)

[0316] The HMCs obtained according to Example 1 were thawed and cultured in MSC medium described above for about 4 days in 37° C., 5% CO₂ in T225 culture flasks at about 4500 cells/cm². To harvest the cells for administration, the cells were washed with PBS, dissociated from the flasks with trypsin, and the trypsin was inactivated with addition of MSC medium. The cells were collected in 50 ml conical tubes and centrifuged at 300 \times g for 10 min. The supernatant was aspirated and 1 ml of GS2 buffer [for 552.2 mL of GS2: 0.9% Sodium Chloride Irrigation USP (408.6 mL); 5% Dextrose/0.9% Sodium Chloride, Injection USP (33.2 mL), and BSS Irrigation Solution (110.4 mL)], which is described in WO 2017/031312 and is incorporated herein by reference in its entirety, was added to each tube. The cells were strained through a 100 μ m cell strainer and centrifuged at 300 \times g for 5 min. The supernatant was aspirated and resuspended in GS2. The cells obtained are passage 4 (P4) HMCs.

[0317] Mild-to moderate experimental traumatic brain injury (TBI) was induced in 56 Sprague Dawley Rats by controlled cortical impact (CCI) (Lee et al., Theranostics 9:1029-1046 (2019)). Cells were injected locally by intracerebral (IC) transplantation or systemically (iv) into the rats and sacrificed at early or late time points according to Table 1.

TABLE 1

Groups	Animals	Time-points	End-points
EARLY			
IC Local Administration	7	Treatment with cells or vehicle 7 days post CCI.	Cortical and Hippocampal cell loss- H&E staining
Vehicle (3 ul-10 ul GS2)		Animals sacrificed 7 days post treatment (14 days post CCI).	CA3 neuron counting
IC Local Administration MSCs (400,000 cells in 3 ul-10 ul GS2)	7		Microgliosis- DCX, OX6, IBA-1 staining
I.V. (jugular vein) Admin Vehicle (500 ul GS2)	7		IHC for human cells
I.V. (jugular vein) Admin MSCs (4×10^6 cells in 500 ul GS2)	7		Swing Test Bederson Test
LATE			
IC Local Administration	7	Treatment with cells or vehicle 7 days post CCI.	All end points as early groups
Vehicle (3 ul-10 ul)			

TABLE 1-continued

Groups	Animals	Time-points	End-points
IC Local Administration	7	Behavioral testing every 7 days from Day 0 (CCI) to Day 56 plus baseline.	
MSCs (400,000 cells in 3 ul-10 ul)		Animals sacrificed at Day 56.	
I.V. (jugular vein) Admin Vehicle (500 ul GS2)	7		
I.V. (jugular vein) Admin MSCs (4×10^6 cells in 500 ul GS2)	7		

[0318] The rats were studied according to the following schedule:

Early

- [0319]** Day -1: Swing test and Bederson test for baseline
- [0320]** Day 0: Controlled Cortical Impact performed on all groups
- [0321]** Day 7: All groups treated with cells or vehicle, locally or intravenously; Swing test and Bederson test post treatment for all groups
- [0322]** Day 14: Swing and Bederson Tests for all groups; All groups sacrificed; H&E staining, CA3 neuron counting, DCX, OX6, IBA-1 staining, IHC for human cells on all groups

Late

- [0323]** Day -1: Swing Test and Bederson Test for baseline for all groups
- [0324]** Day 0: Controlled Cortical Impact performed on all groups
- [0325]** Day 7: All groups treated with cells or vehicle, locally or intravenously; Swing and Bederson tests post treatment for all groups
- [0326]** Day 14: Swing and Bederson tests for all groups
- [0327]** Day 28: Swing and Bederson tests for all groups
- [0328]** Day 35: Swing and Bederson tests for all groups
- [0329]** Day 42: Swing and Bederson tests for all groups
- [0330]** Day 49: Swing and Bederson tests for all groups
- [0331]** Day 56: Swing and Bederson tests for all groups; All groups sacrificed; H&E staining, CA3 neuron counting, DCX, OX6, IBA-1 staining, IHC for human cells on all groups.

Results from Behavioral Tests

[0332] The CCI in vivo TBI model causes significant behavioral deficits of the rats up to 56 days post-injury. Intracerebral (IC) transplantation of the HMCs significantly rescued against behavior deficits compared to their respective vehicles, including elevated body swing test (EBST) from day 14 to 42 after transplantation (FIG. 1), forelimb aknesia starting at day 28 up to day 56 after transplantation (FIG. 2), and paw grasp from day 14 to day 56 after transplantation (FIG. 3). Intravenous (IV) transplantation of the HMCs also significantly rescued against behavior deficits compared to their respective vehicles, including EBST from day 14 up to day 56 after transplantation (FIG. 1), forelimb aknesia starting at day 42 to day 56 after transplantation (FIG. 2), and paw grasp at day 28 after transplantation (FIG. 3). These findings support the use of HMCs for treatment of TBI.

Results from Histology

[0333] The CCI *in vivo* model causes significant histopathological effects in the rats post-injury. IV and IC transplantation of the HMCs demonstrated neuroprotective effects compared to their respective vehicles. For example, H&E staining showed a reduction in tissue loss compared to vehicle (FIGS. 4A-B), Nissl staining demonstrated a neuroprotective effect of HMC administration by reducing cell death (FIGS. 5A-F), and doublecortin (DCX) staining showed a slight increase in neurogenesis following the administration of HMCs post-injury (FIGS. 6A-F).

[0334] IV and IC transplantation of the HMCs also significantly reduced the activation of microglia and macrophages compared to their respective vehicles. Iba1 (FIGS. 7A-D) and OX6 (FIGS. 8A-D) staining demonstrated that the HMCs reduced the presence of microglia and macrophages, respectively, in the cortex and striatum post-injury.

[0335] Further, IV and IC transplantation of the HMCs significantly reduced inflammatory markers in the spleen compared to their respective vehicles. A reduction in I16 (FIGS. 9A-B) and TNF-alpha (FIGS. 10A-B) staining in the spleen demonstrates the HMCs reduced inflammation post-injury.

[0336] IV and IC transplantation of the HMCs also resulted in migration of HMCs across the blood brain barrier (BBB) to the cortex, striatum, and hippocampus as shown by HuNu staining (FIGS. 11A-F).

[0337] These finding support the use of HMCs for treatment of TBI.

Example 3—In Vitro Migration Assay of HMCs

[0338] HMCs were generated from the same bank of frozen hemangioblasts described in Example 1. Three separate lots of HMCs were generated, frozen at P4, thawed and cultured for 4 days, and the passage 5 (P5) cells were harvested according to the method described in Example 1. MSCs isolated from bone marrow (BM-MSCs) and umbilical cord blood (UCB-MSCs) were used as controls. Each of the HMCs, BM-MSCs, and UCB-MSCs were seeded into two wells of an ibidi insert with a defined gap in between and allowed to adhere overnight. Inserts were removed, leaving a 500 μ m gap. Cells were washed and MSC media (described in Example 1) was added to the chamber, with or without stimulation with 25 ng/mL TNF- α +50 ng/mL IFN- γ . Cells were incubated for 6 hours at 37° C. Pictures were then taken of the non-stimulated cells (FIG. 12A) and cells that had migrated into the center of the gap (middle ~250 μ m) were counted visually (FIG. 12B), using ImageJ, an open source image processing program (Schneider et al., *Nature Methods* 9:671-675 (2012)). As can be seen from FIGS. 12A-B, the HMCs (hESC-MSCs) had a greater capacity for cell migration than BM-MSCs or UCB-MSCs.

Example 4—In Vitro Neurite Outgrowth/Neuron Migration in the Presence of HMCs

[0339] Rat primary mixed neuronal cultures were prepared from whole brains of E18 Sprague Dawley rat pups obtained from BrainBits, LLC (Springfield, IL). The mid-brain, cerebellum, and hippocampus were removed to isolate the cerebral cortex. Cells were dissociated from the tissue and cultured for 14 days to allow for maturation. Although tissue is from an embryonic rat pup, the neurons have been shown to display mature receptor and electrophysiological

profiles after 14 days in culture. The mixed neuronal culture was used in an adapted migration assay to study neuroregeneration and as an *in vitro* TBI model (Darbinyan et al., *Methods Mol. Biol.* 1078:45-54 (2013); Ali et al., *High Content Screening with Primary Neurons*. 2013 Oct 15. In: Sittampalam GS, Coussens NP, Brimacombe K, et al., editors. *Assay Guidance Manual*. Bethesda (MD): Eli Lilly & Company and the National Center for Advancing Translational Sciences (2004)).

[0340] On day 0, the mixed neuronal culture was plated. On day 9, MARP12 cells that were frozen and thawed as described in Example 1 were plated in flasks for expansion. At Day 13, MARP12 cells were harvested and plated on transwell inserts for about a 10:1 ratio of neuron to MARP12 cells in MSC media. At day 14, two scratches were made per well in the mixed neuronal culture prepared as described above (Liang et al., *Nat. Protoc.* 2:329-333 (2007)). The MSC media in the transwell was changed to neuronal media (Neurobasal™ Plus (Thermo Fisher); 1x Gentamicin; 1x GlutaMAX™ (ThermoFisher); 1x B27™ Plus (Thermo Fisher)) to remove all traces of serum, and the transwell inserts containing MARP12 cells were added to wells containing the mixed neuronal cultures. As shown in FIG. 13, co-culture with MARP12 (hESC-MSCs or HMC) encouraged neurite outgrowth and increased migration.

[0341] RNA-seq data can also show that the presence of the co-cultured HMCs and/or HMC-EVs can affect gene expression in the neurons. Neurons are dissociated from the cortex of brains of E18 Sprague-Dawley rats and plated at a density of 1.2×10^6 cells per well on 6-well BioFlex culture plates (FlexCell Int.) that are coated with poly-D-lysine (Sigma). The neurons are supplemented with Neurobasal Plus/B27 Plus media (Gibco) and maintained for 14 days *in vitro* (DIV) at 37° C. in a humidified CO₂ incubator. Half media changes are performed every 3 days. For HMC treatment, HMCs are cultured for 4 days in α -MEM media (α -MEM (Hyclone) with 1x GlutaMAX (Gibco), 1xMEM-NEAA (Gibco), and Pen-strep (Gibco)) and then harvested and plated on transwell inserts (Corning) at a density of 1.2×10^5 cells per insert. After one day in culture, the α -MEM media is changed to Neurobasal Plus/B27 Plus media for 1 hour, and the inserts are then added to the 6-well plates containing the neurons at DIV14. For EV treatment, EVs were purified from HMCs (HMC-EVs) by tangential flow filtration. HMC-EVs are added to the plates containing the neurons. TNF- α is then added at a concentration of 100 ng/mL where appropriate and the plates are then placed on the FlexCell FX-6000. The culture is subjected to 15%-0/o stretching oscillations (15%, 12.5%, 10%, 7.5%, 5%, 2.5%, and 0% cycles) overnight. The neurons are then removed from the BioFlex plate, pelleted, washed with PBS, and subjected to RNA isolation via the RNeasy Mini Kit (QiaGen). RNA (300 ng) is then submitted to BGI Americas for RNAseq analysis, and data is analyzed by Rosalind software (<https://rosalind.onramp.bio/>). Cutadapt is used to trim the reads, and FastQC is used to assess quality scores. STAR is used to align the reads to the *Rattus norvegicus* genome build rn5. HTseq is used to quantify the individual sample reads, and they are normalized via Relative Log Expression (RLE) using DESeq2 R library.

Example 5—In Vivo Neonatal Hypoxia-Ischemia Model of Cerebral Palsy

[0342] The HMCs of the presently disclosed subject matter were tested in an *in vivo* neonatal hypoxia-ischemia (HI)

model of cerebral palsy. HMCs used were MARP12 cells described in Example 1 that were thawed and passaged as passage 5 (P5) cells for four days upon which time, the cells were harvested, rinsed and formulated for injection. To establish the in vivo model for cerebral palsy, the common carotid artery in post-natal day (PND) 7 Sprague Dawley male rat pups was ligated to induce ischemia. Following recovery, pups were subjected to a hypoxic episode, followed by normoxia for 25 additional minutes. Pups in the sham control group received an equivalent exposure, except that normoxia rather than hypoxia was presented. At 7 days following surgery and hypoxic exposure (i.e. PND14), pups were humanely euthanized, with blood, cerebrospinal fluid (CSF), and brain tissue harvested for further testing. The pups were treated according to Table 2.

TABLE 2

Treatment Groups			
Group	Treatment	Maximum # per Group	Purpose
Lot B	HI MARP12 1×10^6 cells 6 hours post-hypoxia via IP injection	8	Test article
HI	HI, Vehicle Control	8	Control
Sham	Sham Control	8	Control

End Points Assessed

[0343] CSF and blood used for ELISAs for inflammatory panel and others depending on amount of sample.

[0344] Brain tissue analyzed for:

- [0345] Cell death—TUNEL;
- [0346] Infarct volume—H&E;
- [0347] Iba-1—microglial activation in peri-infarct tissue;
- [0348] GFAP—Astrocyte activation in peri-infarct tissue;
- [0349] Olig2—Oligodendrocyte precursor cells in hippocampus

[0350] MBP—Myelin Basic Protein for mature oligodendrocytes in corpus callosum; and hippocampus.

Results

[0351] TUNEL staining as shown in FIGS. 14A-B suggests a neuroprotective effect by MARPS12 (Lot B) with reduced cell death. Further, H&E staining as shown in FIG. 15 suggests a neuroprotective effect by MARPS12 (Lot B) with reduced lesion size. A reduction in microglial activation via Iba-1 staining as shown in FIGS. 16A-C suggests an anti-inflammatory effect by MARPS12 (Lot B). A mild reduction in astrocyte activation via GFAP staining as shown in FIGS. 17A-C also suggests an anti-inflammatory effect by MARPS12 (Lot B). Preservation of myelin in the corpus callosum via MBP staining as shown in FIGS. 18A-C suggests a beneficial role of MARPS12 on oligodendrocytes. Moreover, FIGS. 19A-C suggest that Olig2 expression is partially rescued by administration of MARPS12.

[0352] These results support the use of HMCs in the treatment of cerebral palsy.

Example 6—RNAseq Analysis of HMC Vs BM-MSC Vs UCB-MSC

[0353] HMCs were generated from the same bank of frozen hemangioblasts described in Example 1. Three separate lots of HMC were generated and passaged up to five passages (P5) according to the method described in Example 1. RNA seq analysis was performed on the three lots of HMC under basal conditions. MSCs isolated from bone marrow (BM-MSCs) (9 lots) and umbilical cord blood (UCB-MSCs) (9 lots) under basal conditions were used as controls.

[0354] Table 3 shows genes that were more highly expressed in the HMCs compared with BM-MSCs. Table 4 shows genes that were more highly expressed in BM-MSCs compared with the HMCs. Table 5 shows genes that were more highly expressed in HMCs compared with UCB-MSCs. Table 6 shows genes that were more highly expressed in UCB-MSCs compared with the HMCs. HMCs of the presently disclosed subject matter may be selected or purified based on any of the genes that are differentially expressed.

TABLE 3

Genes more highly expressed in HMCs compared with BM-MSCs					
Gene Name	Description	Fold Change	Log Fold Change	p-Adj	
KCNN2	potassium channel_calcium activated intermediate/small conductance subfamily N alpha_member 2	3376.7	11.7214	9.68E-96	
GATA4	GATA binding protein 4	3374.36	11.7204	3.92E-74	
FAR2P1	fatty acyl CoA reductase 2 pseudogene 1	2722.47	11.4107	2.85E-33	
GATA3	GATA binding protein 3	2000.99	10.9665	9.13E-69	
NKX2-5	NK2 homeobox 5	1763.59	10.7843	1.21E-69	
VAT1L	vesicle amine transport 1-like	1436.96	10.4888	1.73E-168	
NRK	Nik related kinase	1233.89	10.269	1.08E-36	
NETO1	neuropilin (NRP) and tollloid (TLL)-like 1	1185.6	10.2114	9.67E-53	
BCHE	butyrylcholinesterase	1128.82	10.1406	1.24E-46	
OCA2	oculocutaneous albinism II	1052.28	10.0393	5.00E-52	
GABRA5	gamma-aminobutyric acid (GABA) A receptor_alpha 5	1034.77	10.0151	7.33E-112	
DPPA4	developmental pluripotency associated 4	1029.48	10.0077	6.22E-74	
KIF26A	kinesin family member 26A	990.004	9.95129	7.81E-55	
RELN	reelin	942.435	9.88025	1.16E-43	
LOC440416	NA	908.838	9.82788	1.42E-77	

TABLE 3-continued

Genes more highly expressed in HMCs compared with BM-MSCs				
Gene Name	Description	Fold Change	Log Fold Change	p-Adj
SNCA	synuclein_alpha (non A4 component of amyloid precursor)	880.69	9.78249	5.86E-40
GABRB1	gamma-aminobutyric acid (GABA) A receptor_beta 1	830.623	9.69805	1.47E-40
SNRPN	small nuclear ribonucleoprotein polypeptide N	778.66	9.60485	3.61E-42
CACNG4	calcium channel_voltage-dependent_gamma subunit 4	757.788	9.56565	2.68E-56
LRRTM1	leucine rich repeat transmembrane neuronal 1	717.547	9.48693	4.54E-44
LINGO2	leucine rich repeat and Ig domain containing 2	620.437	9.27714	4.01E-40
TNNT2	troponin T type 2 (cardiac)	594.602	9.21578	1.04E-36
ZNF804A	zinc finger protein 804A	586.802	9.19673	6.40E-56
ST6GAL2	ST6 beta-galactosamidase alpha-2_6-sialyltranferase 2	576.929	9.17225	7.18E-88
COL4A5	collagen_type IV_alpha 5	576.757	9.17182	2.11E-82
LIN28B	lin-28 homolog B (C. elegans)	563.605	9.13854	2.92E-39
MMP9	matrix metallopeptidase 9	554.502	9.11505	1.92E-42
SLC7A2	solute carrier family 7 (cationic amino acid transporter_y+ system)_member 2	520.325	9.02327	3.31E-149
COL4A6	collagen_type IV_alpha 6	497.261	8.95786	1.25E-97
FENDRR	FOXF1 adjacent non-coding developmental regulatory RNA	488.058	8.93091	1.86E-46
DSC2	desmocollin 2	478.415	8.90212	2.20E-39
KCTD8	potassium channel tetramerization domain containing 8	459.857	8.84504	3.51E-38
ARAP2	ArfGAP with RhoGAP domain_ankyrin repeat and PH domain 2	455.472	8.83122	4.05E-38
DIO2	deiodinase_iodothyronine_type II	450.443	8.8152	1.78E-98
CDH10	cadherin 10_type 2 (T2-cadherin)	448.881	8.81019	7.16E-25
SHC3	SHC (Src homology 2 domain containing) transforming protein 3	447.61	8.8061	3.60E-90
SULT1E1	sulfotransferase family 1E_estrogen-preferring_member 1	447.155	8.80463	2.93E-34
CPXM1	carboxypeptidase X (M14 family)_member 1	445.688	8.79989	1.94E-75
FGF20	fibroblast growth factor 20	428.96	8.7447	9.75E-34
LINC00890	long intergenic non-protein coding RNA 890	382.729	8.58018	1.14E-32
BAI3	adhesion G protein-coupled receptor B3	364.764	8.51082	8.84E-35
L1CAM	L1 cell adhesion molecule	361.67	8.49853	1.36E-94
CACNG8	calcium channel_voltage-dependent_gamma subunit 8	359.757	8.49088	1.88E-29
SULT1C4	sulfotransferase family_cytosolic_1C_member 4	324.225	8.34085	4.13E-29
TRIM55	tripartite motif containing 55	319.183	8.31824	9.79E-22
HOXB13	homeobox B13	313.091	8.29044	4.19E-32
DSG2	desmoglein 2	309.567	8.27411	3.18E-14
ELFN2	extracellular leucine-rich repeat and fibronectin type III domain containing 2	301.134	8.23426	1.62E-92
CTD-2297D10.2	uncharacterized LOC101929176	300.946	8.23336	5.57E-22
TRPC5	transient receptor potential cation channel_subfamily C_member 5	297.627	8.21736	6.17E-23
WT1	Wilms tumor 1	297.142	8.21501	4.53E-32
TMEM63C	transmembrane protein 63C	296.544	8.2121	1.88E-36
RERG	RAS-like_estrogen-regulated_growth inhibitor	292.372	8.19166	3.31E-32
CCND2	cyclin D2	288.586	8.17286	2.31E-48
NKX2-3	NK2 homeobox 3	287.642	8.16813	4.09E-28
SAMD5	sterile alpha motif domain containing 5	281.787	8.13846	2.29E-79
STMN2	stathmin 2	281.654	8.13778	7.49E-14
TMEM200C	transmembrane protein 200C	277.722	8.1175	9.71E-27
SOX17	SRY (sex determining region Y)-box 17	277.509	8.11639	2.49E-29
MGAT3	mannosyl (beta-1_4)-glycoprotein beta-1_4-N-acetylglucosaminyltransferase	269.263	8.07287	3.27E-96
FLT1	fms-related tyrosine kinase 1	266.319	8.05701	1.95E-173
NKAIN4	Na+/K+ transporting ATPase interacting 4	260.054	8.02267	3.36E-39
SYTL5	synaptotagmin-like 5	257.406	8.0079	8.81E-79
MDGA2	MAM domain containing glycosylphosphatidylinositol anchor 2	252.998	7.98298	4.70E-26
GATA3-AS1	GATA3 antisense RNA 1	249.784	7.96454	3.99E-22

TABLE 3-continued

Genes more highly expressed in HMCs compared with BM-MSCs				
Gene Name	Description	Fold Change	Log Fold Change	p-Adj
LGII1	leucine-rich_glioma inactivated 1	248.088	7.95471	5.19E-26
PKP2	plakophilin 2	247.539	7.95151	2.82E-15
KLHL4	kelch-like family member 4	238.045	7.89509	3.70E-63
GPR143	G protein-coupled receptor 143	235.692	7.88076	5.07E-44
ADAMTS18	ADAM metallopeptidase with thrombospondin type 1 motif_18	219.386	7.77733	5.32E-25
CHRM2	cholinergic receptor_muscarinic 2	218.008	7.76824	1.34E-14
TMEM40	transmembrane protein 40	216.144	7.75585	2.22E-25
NIPAL4	NIPA-like domain containing 4	213.309	7.7368	6.44E-119
SEMA3D	sema domain_immunoglobulin domain (Ig)_short basic domain_secreted_(semaphorin) 3D	212.776	7.73319	4.51E-37
PHOX2A	paired-like homeobox 2a	212.508	7.73137	1.17E-27
PRAC1	prostate cancer susceptibility candidate 1	200.695	7.64886	3.28E-20
CSMD3	CUB and Sushi multiple domains 3	191.196	7.57891	4.33E-23
B3GAT1	beta-1_3-glucuronyltransferase 1	189.606	7.56686	7.70E-26
TRIM58	tripartite motif containing 58	189.244	7.5641	4.32E-32
ANO4	anoctamin 4	186.743	7.54491	2.59E-41
GPR20	G protein-coupled receptor 20	186.668	7.54433	9.67E-22
EEF1A2	eukaryotic translation elongation factor 1 alpha 2	186.624	7.54399	9.79E-37
HOXD11	homeobox D11	184.825	7.53002	4.91E-37
LHX1	LIM homeobox 1	183.385	7.51873	6.08E-21
DCC	DCC netrin 1 receptor	177.536	7.47197	2.29E-36
SHC2	SHC (Src homology 2 domain containing) transforming protein 2	177.418	7.47101	3.45E-36
FIRRE	firre intergenic repeating RNA element	175.85	7.4582	2.53E-19
HAND2-AS1	HAND2 antisense RNA 1 (head to head)	173.707	7.44051	7.94E-44
MAB21L2	mab-21-like 2 (C. elegans)	171.99	7.42618	5.59E-25
TM6C	transmembrane channel-like 6	171.467	7.42179	1.23E-42
KDR	kinase insert domain receptor	171.259	7.42004	8.29E-26
C2CD4C	C2 calcium-dependent domain containing 4C	167.398	7.38714	1.53E-42
CXXC4	CXXC finger protein 4	164.691	7.36362	1.29E-19
LGR5	leucine-rich repeat containing G protein-coupled receptor 5	163.206	7.35055	4.04E-44
DSC3	desmocollin 3	162.352	7.34298	1.77E-10
IL1RAPL1	interleukin 1 receptor accessory protein-like 1	158.417	7.30758	2.79E-17
VANGL2	VANGL planar cell polarity protein 2	153.694	7.26392	2.36E-55
ABCB1	ATP-binding cassette_sub-family B (MDR/TAP)_member 1	147.802	7.20752	3.07E-26
AADAC	arylacetamide deacetylase	140.148	7.13081	7.12E-17
FSTL5	follistatin-like 5	139.259	7.12163	2.68E-15
MED15P9	mediator complex subunit 15 pseudogene 9	138.438	7.1131	5.39E-10
GCNT2	glucosaminyl (N-acetyl) transferase 2_I-branched enzyme (I blood group)	133.285	7.05837	1.16E-15
SULT1B1	sulfotransferase family_cytosolic_1B_member 1	132.429	7.04907	8.14E-21
GPR87	G protein-coupled receptor 87	132.396	7.04872	3.45E-10
LIN28A	lin-28 homolog A (C. elegans)	130.54	7.02835	7.46E-19
KRT8	keratin 8_type II	130.494	7.02784	2.19E-255
SLC35F3	solute carrier family 35_member F3	129.889	7.02114	4.02E-18
MYRF	myelin regulatory factor	127.908	6.99896	8.88E-97
TIE1	tyrosine kinase with immunoglobulin-like and EGF-like domains 1	125.933	6.97651	3.53E-48
FAT3	FAT atypical cadherin 3	125.595	6.97264	2.69E-61
C8orf49	chromosome 8 open reading frame 49	119.914	6.90586	2.72E-18
GABRA4	gamma-aminobutyric acid (GABA) A receptor_alpha 4	119.403	6.89969	1.79E-15
PCDH7	protocadherin 7	119.262	6.89799	3.97E-83
ST6GALNAC3	ST6 (alpha-N-acetyl-neuraminy1-2_3-beta-galactosyl1-1_3)-N-acetylgalactosaminide alpha-2_6-sialyltransferase 3	118.478	6.88848	2.53E-23
PPP2R2B	protein phosphatase 2_regulatory subunit B_beta	118.228	6.88543	3.56E-74
C6orf141	chromosome 6 open reading frame 141	117.977	6.88236	2.95E-18
SFBMT2	Scm-like with four mbt domains 2	116.043	6.85851	2.63E-33
SPINK5	serine peptidase inhibitor_Kazal type 5	115.386	6.85032	1.10E-08
SLC6A15	solute carrier family 6 (neutral amino acid transporter)_member 15	112.26	6.8107	6.07E-17

TABLE 3-continued

Genes more highly expressed in HMCs compared with BM-MSCs				
Gene Name	Description	Fold Change	Log Fold Change	p-Adj
FXYD6	FXYD domain containing ion transport regulator 6	108.606	6.76296	1.75E-17
DNAH11	dynein_axonemal_heavy chain 11	107.843	6.75279	8.79E-60
SCG2	secretogranin II	106.966	6.74101	4.54E-67
SEMA3E	sema domain_immunoglobulin domain (Ig)_short basic domain_secreted_(semaphorin) 3E	106.595	6.736	9.68E-18
GAL	galanin/GMAP prepropeptide	105.543	6.72169	4.15E-52
NPY	neuropeptide Y	104.525	6.70771	1.51E-15
KCNH2	potassium channel_voltage gated eag related subfamily H_member 2	102.046	6.67308	9.32E-33
SYTL1	synaptotagmin-like 1	99.8984	6.64239	1.73E-47
HOPX	HOP homeobox	98.9453	6.62856	1.74E-17
GPR37	G protein-coupled receptor 37 (endothelin receptor type B-like)	98.1407	6.61678	8.32E-36
CLSTN2	calsyntenin 2	97.1573	6.60225	6.01E-51
SLCO4A1	solute carrier organic anion transporter family_member 4A1	96.0211	6.58528	3.70E-20
LUZP2	leucine zipper protein 2	95.3037	6.57446	1.86E-13
ERP27	endoplasmic reticulum protein 27	87.6213	6.45321	5.22E-15
TAGLN3	transgelin 3	87.0661	6.44404	8.10E-50
CACNA1H	calcium channel_voltage-dependent_T type_alpha 1H subunit	86.7024	6.438	2.39E-85
NOVA1	neuro-oncological ventral antigen 1	85.9586	6.42557	1.21E-09
IGSF3	immunoglobulin superfamily_member 3	85.2324	6.41333	5.56E-38
P2RY14	purinergic receptor P2Y_G-protein coupled_14	84.4116	6.39937	7.54E-13
SLC5A4	solute carrier family 5 (glucose activated ion channel)_member 4	83.7995	6.38887	6.99E-15
NDST3	N-deacetylase/N-sulfotransferase (heparan glucosaminyl) 3	83.6463	6.38623	3.11E-20
HOXD10	homeobox D10	83.2622	6.37959	6.03E-24
FOXF1	forkhead box F1	82.2857	6.36257	9.91E-08
HAND1	heart and neural crest derivatives expressed 1	80.2556	6.32653	1.20E-12
CTTNBP2	cortactin binding protein 2	77.8222	6.28211	1.15E-09
ADAMTS16	ADAM metallopeptidase with thrombospondin type 1 motif_16	77.6573	6.27905	1.53E-57
ELOVL2	ELOVL fatty acid elongase 2	77.076	6.26821	6.48E-39
HOXB9	homeobox B9	76.7162	6.26146	2.85E-09
PLCXD3	phosphatidylinositol-specific phospholipase C_X domain containing 3	74.8868	6.22664	3.68E-13
SCN5A	sodium channel_voltage gated_type V alpha subunit	74.3881	6.217	3.97E-24
TRIL	TLR4 interactor with leucine-rich repeats	73.8563	6.20665	1.44E-14
HIST1H2BH	histone cluster 1_H2bh	73.8405	6.20634	2.65E-21
MYL7	myosin_light chain 7_regulatory	73.5177	6.20002	3.16E-17
TEPP	testis_prostate and placenta expressed	73.0296	6.19041	2.06E-15
HOXB8	homeobox B8	73.018	6.19018	6.99E-44
LIPG	lipase_endothelial	72.8496	6.18685	1.62E-38
SLCO6A1	solute carrier organic anion transporter family_member 6A1	72.6328	6.18255	3.74E-10
IGDCC3	immunoglobulin superfamily_DCC subclass_member 3	72.6258	6.18241	1.28E-22
GABRG3	gamma-aminobutyric acid (GABA) A receptor_gamma 3	72.1476	6.17288	4.13E-11
GRIA1	glutamate receptor_ionotropic_AMPA 1	71.9404	6.16873	1.08E-37
C8orf4	chromosome 8 open reading frame 4	71.2481	6.15478	9.53E-24
FABP4	fatty acid binding protein 4_adipocyte	70.9554	6.14884	1.96E-09
PLEKHG4B	pleckstrin homology domain containing_family G (with RhoGef domain) member 4B	70.7746	6.14516	8.93E-52
IP6K3	inositol hexakisphosphate kinase 3	69.7939	6.12503	1.34E-16
PDE9A	phosphodiesterase 9A	67.1097	6.06845	1.00E-15
KLHDC8A	kelch domain containing 8A	66.2124	6.04903	1.29E-09
FLJ16779	uncharacterized LOC100192386	65.8988	6.04218	5.66E-07
CCDC160	coiled-coil domain containing 160	64.6832	6.01532	1.22E-11
SPP1	secreted phosphoprotein 1	63.3767	5.98588	2.40E-37
PCDH17	protocadherin 17	63.0227	5.9778	1.49E-10
HOTTIP	HOXA distal transcript antisense RNA	62.4396	5.96439	3.67E-19
OXTR	oxytocin receptor	62.3043	5.96126	1.14E-36
SH2D3C	SH2 domain containing 3C	62.2667	5.96039	2.83E-68

TABLE 3-continued

Genes more highly expressed in HMCs compared with BM-MSCs				
Gene Name	Description	Fold Change	Log Fold Change	p-Adj
USP43	ubiquitin specific peptidase 43	61.9104	5.95211	1.62E-26
KC6	keratoconus gene 6	61.6005	5.94487	4.37E-07
CACNG7	calcium channel_voltage-dependent_gamma subunit 7	61.5198	5.94298	1.74E-114
SLC44A5	solute carrier family 44_member 5	60.9756	5.93016	4.59E-63
COL18A1	collagen_type XVIII_alpha 1	60.1278	5.90996	0.00E+00
LINC00491	long intergenic non-protein coding RNA 491	60.0324	5.90767	6.94E-12
TBX1	T-box 1	60.0149	5.90725	1.38E-30
GALNT14	polypeptide N-acetylgalactosaminyltransferase 14	59.4424	5.89342	9.44E-16
CLEC1A	C-type lectin domain family 1_member A	59.3592	5.89114	1.45E-09
CALY	calcyon neuron-specific vesicular protein	59.309	5.89018	1.54E-21
CD93	CD93 molecule	58.2498	5.86418	9.02E-15
HIF3A	hypoxia inducible factor 3_alpha subunit	58.2328	5.86376	2.36E-19
LPAR4	lysophosphatidic acid receptor 4	58.2304	5.8637	4.90E-18
TBX20	T-box 20	57.7408	5.85152	1.78E-06
TNRC6C-AS1	TNRC6C antisense RNA 1	57.652	5.8493	4.12E-13
CHMP4C	charged multivesicular body protein 4C	56.3561	5.8165	1.76E-18
CADM1	cell adhesion molecule 1	56.3186	5.81554	1.11E-89
SDK1	sidekick cell adhesion molecule 1	55.5517	5.79576	9.60E-52
MMP10	matrix metallopeptidase 10	55.3001	5.78921	4.28E-11
MERTK	MER proto-oncogene_tyrosine kinase	55.1428	5.7851	2.56E-26
DPY19L2P1	DPY19L2 pseudogene 1	55.0725	5.78326	1.10E-82
GPRC5B	G protein-coupled receptor_class C_group 5_member B	54.6061	5.77099	2.76E-17
VWDE	von Willebrand factor D and EGF domains	54.0424	5.75602	1.37E-13
CIDEA	cell death-inducing DFFA-like effector a	53.9432	5.75337	4.10E-11
RASGRF1	Ras protein-specific guanine nucleotide-releasing factor 1	53.6193	5.74468	1.80E-21
CACNG6	calcium channel_voltage-dependent_gamma subunit 6	53.5476	5.74275	8.41E-09
FAM189A1	family with sequence similarity 189_member A1	53.2323	5.73423	5.88E-18
IL2RB	interleukin 2 receptor_beta	52.6777	5.71912	9.40E-31
C1orf106	chromosome 1 open reading frame 106	52.1675	5.70508	8.35E-35
CRHBP	corticotropin releasing hormone binding protein	52.0357	5.70143	5.66E-12
HBD	hemoglobin_delta	51.5443	5.68774	4.43E-11
MGAT4C	MGAT4 family_member C	49.6272	5.63306	4.86E-10
RBM20	RNA binding motif protein 20	49.1418	5.61888	3.22E-14
KCNA1	potassium channel_voltage gated shaker related subfamily A_member 1	49.1238	5.61835	9.02E-12
SEMA3A	sema domain_immunoglobulin domain (Ig)_short basic domain_seceted_(semaphorin) 3A	48.3221	5.59461	4.17E-74
SORCS3	sortilin-related VPS10 domain containing receptor 3	48.1716	5.59011	3.21E-08
SLC22A31	solute carrier family 22_member 31	47.946	5.58334	8.45E-22
ZCCHC16	zinc finger_CCHC domain containing 16	47.7911	5.57867	2.49E-08
SHISA3	shisa family member 3	47.5212	5.5705	9.76E-18
VGF	VGF nerve growth factor inducible	47.2303	5.56164	2.03E-20
CPVL	carboxypeptidase_vitellogenin-like	47.0731	5.55683	3.13E-08
FAM213A	family with sequence similarity 213_member A	46.8767	5.5508	2.15E-17
HTR1D	5-hydroxytryptamine (serotonin) receptor 1D_G protein-coupled	46.5442	5.54053	1.25E-28
PCDHA12	protocadherin alpha 12	45.8017	5.51733	7.82E-06
NTSR1	neurotensin receptor 1 (high affinity)	44.7576	5.48406	6.68E-10
FAM69B	family with sequence similarity 69_member B	43.6101	5.44659	2.53E-96
LRRN4	leucine rich repeat neuronal 4	42.0904	5.39542	3.90E-26
LOC644919	uncharacterized LOC644919	40.994	5.35734	1.75E-09
COL9A3	collagen_type IX_alpha 3	40.5677	5.34226	3.87E-50
GIPC3	GIPC PDZ domain containing family_member 3	40.4621	5.3385	4.22E-140
CYT1	cytokine-like 1	40.3604	5.33487	2.91E-20
GBX2	gastrulation brain homeobox 2	39.8398	5.31614	1.15E-07
C2orf91	chromosome 2 open reading frame 91	38.997	5.28529	7.95E-09
TTL6	tubulin tyrosine ligase-like family member 6	38.9764	5.28453	1.48E-08
IFLT1	lamin tail domain containing 1	38.9187	5.28239	3.52E-12

TABLE 3-continued

Genes more highly expressed in HMCs compared with BM-MSCs				
Gene Name	Description	Fold Change	Log Fold Change	p-Adj
CECR2	cat eye syndrome chromosome region_candidate 2	38.553	5.26877	3.66E-08
PDGFB	platelet-derived growth factor beta polypeptide	38.5383	5.26822	6.45E-21
SSTR1	somatostatin receptor 1	37.612	5.23312	1.10E-06
RGS5	regulator of G-protein signaling 5	37.382	5.22427	1.21E-127
MMP23B	matrix metallopeptidase 23B	37.1557	5.21551	2.07E-27
ISL1	ISL LIM homeobox 1	36.8768	5.20464	1.70E-14
ABI3	ABI family_member 3	36.724	5.19865	2.86E-20
ZPLD1	zona pellucida-like domain containing 1	36.7237	5.19864	2.13E-11
PDE3B	phosphodiesterase 3B_cGMP-inhibited	36.6545	5.19592	7.16E-22
BEST3	bestrophin 3	36.5693	5.19256	3.02E-12
B4GALNT4	beta-1_4-N-acetyl-galactosaminyl transferase 4	36.2902	5.18151	1.97E-21
LRRC17	leucine rich repeat containing 17	36.1996	5.1779	9.35E-27
KCNA6	potassium channel_voltage gated shaker related subfamily A_member 6	36.0306	5.17115	1.91E-15
NRXN3	neurexin 3	36.0153	5.17054	4.93E-26
MGC2889	uncharacterized protein MGC2889	35.8955	5.16573	7.62E-08
ADAMTS20	ADAM metallopeptidase with thrombospondin type 1 motif_20	35.2102	5.13792	1.38E-08
HUNK	hormonally up-regulated Neu-associated kinase	34.6857	5.11627	3.50E-14
MTUS1	microtubule associated tumor suppressor 1	34.2018	5.096	3.01E-24
LOC101929086	NA	34.028	5.08865	8.77E-07
DACT2	dishevelled-binding antagonist of beta-catenin 2	33.744	5.07656	1.56E-06
ACTG2	actin_gamma 2_smooth muscle_enteric	33.0521	5.04667	1.30E-11
WNT2	wingless-type MMTV integration site family member 2	32.8017	5.0357	8.54E-08
TTR	transthyretin	32.3991	5.01788	2.02E-06
SFRP1	secreted frizzled-related protein 1	32.2615	5.01174	6.51E-40
GRPR	gastrin-releasing peptide receptor	32.2049	5.00921	3.28E-29
CCDC88C	coiled-coil domain containing 88C	32.1773	5.00797	8.98E-23
LOC440910	uncharacterized LOC440910	32.1351	5.00608	7.01E-06
CYP2S1	cytochrome P450_family 2_subfamily S_polypeptide 1	32.1307	5.00588	3.24E-59
LRRN1	leucine rich repeat neuronal 1	32.0926	5.00417	1.17E-06
C7	complement component 7	32.0613	5.00276	2.19E-13
NDRG2	NDRG family member 2	32.0118	5.00053	1.08E-55
ZDHHC8P1	zinc finger_DHHC-type containing 8 pseudogene 1	31.9831	4.99924	3.17E-14
LRFN5	leucine rich repeat and fibronectin type III domain containing 5	31.9362	4.99712	8.06E-09
NR0B1	nuclear receptor subfamily 0_group B_member 1	31.7781	4.98996	1.35E-05
FAM105A	family with sequence similarity 105_member A	31.7613	4.9892	2.11E-17
MMP1	matrix metallopeptidase 1	31.7026	4.98653	3.12E-12
GABRQ	gamma-aminobutyric acid (GABA) A receptor_theta	31.1647	4.96184	4.24E-07
C9orf47	chromosome 9 open reading frame 47	31.1247	4.95999	1.13E-14
HAND2	heart and neural crest derivatives expressed 2	30.8252	4.94604	7.86E-05
ARHGDIIB	Rho GDP dissociation inhibitor (GDI) beta	30.6697	4.93874	1.46E-162
KCNMB4	potassium channel subfamily M regulatory beta subunit 4	30.6622	4.93839	3.00E-36
LOC728392	uncharacterized LOC728392	30.6522	4.93792	1.84E-102
NUTM2F	NUT family member 2F	30.1029	4.91183	3.45E-07
GRIP1	glutamate receptor interacting protein 1	30.0545	4.90951	8.20E-33
AIM1L	absent in melanoma 1-like	29.8554	4.89992	5.19E-08
WT1-AS	WT1 antisense RNA	29.8471	4.89952	8.31E-07
PNMA3	paraneoplastic Ma antigen 3	29.7352	4.8941	4.99E-14
TPSG1	tryptase gamma 1	29.473	4.88132	9.37E-08
MOV10L1	Mov10 RISC complex RNA helicase like 1	29.1231	4.86409	5.72E-36
HOXD13	homeobox D13	29.089	4.8624	1.15E-08
KAL1	anosmin 1	29.0122	4.85859	2.64E-42
KNDC1	kinase non-catalytic C-lobe domain (KIND) containing 1	28.744	4.84519	3.37E-33
ADAM23	ADAM metallopeptidase domain 23	28.5026	4.83302	8.82E-19
TYRP1	tyrosinase-related protein 1	28.363	4.82594	1.51E-22

TABLE 3-continued

Genes more highly expressed in HMCs compared with BM-MSCs				
Gene Name	Description	Fold Change	Log Fold Change	p-Adj
SP140	SP140 nuclear body protein	28.3	4.82273	3.34E-28
LOC100652770	NA	28.1835	4.81678	1.28E-05
ZNF467	zinc finger protein 467	28.1178	4.81341	7.48E-14
GPR115	adhesion G protein-coupled receptor F4	27.9129	4.80286	1.95E-08
PNMT	phenylethanolamine N-methyltransferase	27.911	4.80276	1.28E-05
LINC00648	long intergenic non-protein coding RNA 648	27.9067	4.80254	8.86E-06
FAM95C	family with sequence similarity 95_member C	27.6934	4.79147	1.23E-06
LOC101928340	NA	27.633	4.78832	1.36E-05
FAM162B	family with sequence similarity 162_member B	27.3855	4.77534	4.42E-06
ASXL3	additional sex combs like transcriptional regulator 3	27.0169	4.75579	9.59E-06
EBI3	Epstein-Barr virus induced 3	26.9236	4.7508	8.48E-11
LYPLAL1-AS1	LYPLAL1 antisense RNA 1 (head to head)	26.8861	4.74879	2.75E-22
ANKRD18B	ankyrin repeat domain 18B	26.6734	4.73733	4.75E-11
LLGL2	lethal giant larvae homolog 2 (Drosophila)	26.6686	4.73707	5.18E-26
SRSF12	serine/arginine-rich splicing factor 12	26.1794	4.71036	1.89E-31
DLK1	delta-like 1 homolog (Drosophila)	26.1428	4.70834	1.22E-08
TMPRSS11B	transmembrane protease_serine 11B	26.0476	4.70308	1.68E-05
IGF2BP3	insulin-like growth factor 2 mRNA binding protein 3	26.0092	4.70095	1.08E-69
F11R	F11 receptor	25.9993	4.7004	2.83E-29
TNNI1	troponin I type 1 (skeletal_slow)	25.984	4.69955	1.41E-06
MAGEB17	melanoma antigen family B17	25.5824	4.67708	4.62E-06
PPARG	peroxisome proliferator-activated receptor gamma	25.1998	4.65534	1.06E-11
PLCB2	phospholipase C_beta 2	25.1225	4.65091	8.52E-26
HRASLS	HRAS-like suppressor	25.1096	4.65017	3.45E-05
JPH1	junctophilin 1	25.0058	4.64419	3.39E-06
EPHA7	EPH receptor A7	24.8508	4.63522	3.06E-05
PCYT1B	phosphate cytidylyltransferase 1_choline_beta	24.7382	4.62867	4.96E-06
KIAA1211	KIAA1211	24.6733	4.62488	5.54E-17
ARL14	ADP-ribosylation factor-like 14	24.6274	4.62219	5.67E-05
VIP	vasoactive intestinal peptide	24.5153	4.61561	1.86E-06
LHX2	LIM homeobox 2	24.445	4.61147	2.21E-08
C4BPB	complement component 4 binding protein_beta	24.4286	4.6105	1.18E-07
RSPO4	R-spondin 4	24.3298	4.60465	2.80E-14
YBX2	Y box binding protein 2	24.2681	4.60099	1.18E-07
THSD7A	thrombospondin_type I_domain containing 7A	24.2192	4.59808	2.09E-50
SDK2	sidekick cell adhesion molecule 2	24.0776	4.58962	1.10E-06
HS6ST2	heparan sulfate 6-O-sulfotransferase 2	23.8949	4.57863	3.22E-06
PCDHB2	protocadherin beta 2	23.8823	4.57787	1.41E-32
PCDH10	protocadherin 10	23.6912	4.56628	1.50E-07
ICOSLG	inducible T-cell co-stimulator ligand	23.6241	4.56219	5.57E-19
IGF2BP1	insulin-like growth factor 2 mRNA binding protein 1	23.6132	4.56152	4.59E-76
KCNF1	potassium channel_voltage gated modifier subfamily F_member 1	23.6097	4.56131	4.19E-11
GDF7	growth differentiation factor 7	23.5935	4.56032	9.44E-06
EFNA2	ephrin-A2	23.46	4.55213	3.31E-12
CXADR	coxsackie virus and adenovirus receptor	23.1897	4.53541	1.38E-08
GLB1L2	galactosidase_beta 1-like 2	23.1096	4.53042	4.28E-14
IGFBP5	insulin-like growth factor binding protein 5	22.9538	4.52066	8.23E-28
KRT79	keratin 79_type II	22.9042	4.51754	5.91E-08
IL33	interleukin 33	22.8265	4.51264	5.10E-05
CPA6	carboxypeptidase A6	22.6992	4.50457	1.90E-05
RGS1	regulator of G-protein signaling 1	22.6241	4.49979	0.000116
GPR63	G protein-coupled receptor 63	22.6204	4.49955	4.35E-10
DOC2GP	double C2-like	22.592	4.49774	1.08E-10
FAM110D	domains_gamma_pseudogene family with sequence similarity 110_member D	22.2782	4.47756	2.13E-08

TABLE 3-continued

Genes more highly expressed in HMCs compared with BM-MSCs				
Gene Name	Description	Fold Change	Log Fold Change	p-Adj
ART5	ADP-ribosyltransferase 5	22.0036	4.45967	6.14E-06
CD163L1	CD163 molecule-like 1	21.9861	4.45852	6.41E-25
ATCAY	ataxia_cerebellar_Cayman type	21.9716	4.45757	1.81E-05
CNTNS	contactin 5	21.7124	4.44045	0.000119
LONRF2	LON peptidase N-terminal domain and ring finger 2	21.3584	4.41673	3.34E-16
AFAP1L2	actin filament associated protein 1-like 2	21.2551	4.40974	1.28E-12
LRP1B	low density lipoprotein receptor-related protein 1B	21.1326	4.4014	0.000136
HOXA13	homeobox A13	21.1285	4.40112	1.71E-11
LCP1	lymphocyte cytosolic protein 1 (L-plastin)	21.0927	4.39867	1.38E-11
TNFSF4	tumor necrosis factor (ligand) superfamily_member 4	21.0743	4.39741	4.65E-65
AQP7P3	aquaporin 7 pseudogene 3	21.0438	4.39532	0.000248
METTL24	methyltransferase like 24	20.8515	4.38208	1.27E-05
SULT4A1	sulfotransferase family 4A_member 1	20.8356	4.38098	3.22E-20
PDE6B	phosphodiesterase 6B_cGMP-specific_rod_beta	20.8092	4.37915	5.14E-22
AQP7P1	aquaporin 7 pseudogene 1	20.7323	4.37381	9.27E-07
GUCY1A3	guanylate cyclase 1_soluble_alpha 3	20.6716	4.36958	3.47E-05
PCAT1	prostate cancer associated transcript 1 (non-protein coding)	20.6577	4.36861	0.000117
OTOS	otospiralin	20.6125	4.36545	3.94E-07
AQP5	aquaporin 5	20.6021	4.36472	5.95E-07
HES4	hes family bHLH transcription factor 4	20.5841	4.36346	5.75E-14
ADAMTS3	ADAM metallopeptidase with thrombospondin type 1 motif_3	20.527	4.35945	3.83E-34
C1orf94	chromosome 1 open reading frame 94	20.4524	4.3542	3.40E-05
LOC101928303	uncharacterized LOC101928303	20.4496	4.354	1.54E-05
MOB3B	MOB kinase activator 3B	20.3551	4.34732	1.05E-12
ITIH3	inter-alpha-trypsin inhibitor heavy chain 3	20.3247	4.34516	1.58E-13
SUCNR1	succinate receptor 1	20.1055	4.32952	0.000611
ST8SIA2	ST8 alpha-N-acetyl-neuraminiid alpha-2_8-sialyltransferase 2	19.9714	4.31986	1.02E-05
PCDHA11	protocadherin alpha 11	19.8527	4.31126	1.11E-07
S1PR5	sphingosine-1-phosphate receptor 5	19.7582	4.30438	5.60E-39
LRRK4C	leucine rich repeat containing 4C	19.7054	4.30052	3.88E-23
GPRIN2	G protein regulated inducer of neurite outgrowth 2	19.63	4.29499	1.04E-07
ANXA3	annexin A3	19.3198	4.27201	6.49E-38
UCP2	uncoupling protein 2 (mitochondrial_proton carrier)	19.1933	4.26253	9.86E-33
PRAC2	prostate cancer susceptibility candidate 2	18.9331	4.24284	0.000291
MAP3K9	mitogen-activated protein kinase kinase kinase 9	18.9294	4.24256	2.16E-25
MYH14	myosin_heavy chain 14_non-muscle	18.9226	4.24204	3.05E-09
SLITRK5	SLIT and NTRK-like family_member 5	18.887	4.23932	0.000287
RAMP2-AS1	RAMP2 antisense RNA 1	18.881	4.23886	2.61E-14
FRAS1	Fraser extracellular matrix complex subunit 1	18.7633	4.22984	7.69E-22
DCHS1	dachsous cadherin-related 1	18.7224	4.22669	1.91E-85
PCBP3	poly(rC) binding protein 3	18.6032	4.21748	5.50E-08
DENND2A	DENN/MADD domain containing 2A	18.5959	4.21691	2.08E-28
CYTH4	cytohesin 4	18.4855	4.20832	2.05E-05
SYT3	synaptotagmin III	18.4219	4.20335	4.79E-10
BEGAIN	brain-enriched guanylate kinase-associated	18.3092	4.1945	5.24E-14
SYT13	synaptotagmin XIII	18.3031	4.19402	1.84E-07
PRKQ	protein kinase C_theta	18.3006	4.19382	1.34E-08
ALPK3	alpha-kinase 3	18.0415	4.17325	8.05E-43
INPP5D	inositol polyphosphate-5-phosphatase D	18.0215	4.17165	1.99E-10
CLEC14A	C-type lectin domain family 14_member A	17.9653	4.16714	2.07E-10
GRAP	GRB2-related adaptor protein	17.9383	4.16497	9.76E-14
MYCT1	myc target 1	17.8007	4.15386	5.96E-17
SPINT1	serine peptidase inhibitor_Kunitz type 1	17.6879	4.14469	1.47E-10
LINC00951	long intergenic non-protein coding RNA 951	17.6694	4.14318	0.000391
SLC1A7	solute carrier family 1 (glutamate transporter)_member 7	17.6269	4.13971	5.10E-21
PLN	phospholamban	17.6175	4.13894	2.23E-05
CDH8	cadherin 8_type 2	17.6042	4.13785	5.23E-06
SCN2A	sodium channel_voltage gated_type II alpha subunit	17.5982	4.13736	1.84E-07

TABLE 3-continued

Genes more highly expressed in HMCs compared with BM-MSCs				
Gene Name	Description	Fold Change	Log Fold Change	p-Adj
OR2H2	olfactory receptor_family 2_subfamily H_member 2	17.4823	4.12782	5.83E-06
TNNI3	troponin I type 3 (cardiac)	17.2932	4.11213	8.76E-06
SNCB	synuclein_beta	17.2161	4.10569	2.97E-05
PRSS16	protease_serine_16 (thymus)	17.1239	4.09794	1.53E-05
NNAT	neuronatin	17.1189	4.09752	9.80E-78
ZBTB46	zinc finger and BTB domain containing 46	17.1106	4.09682	1.95E-29
SLC6A12	solute carrier family 6 (neurotransmitter transporter)_member 12	17.0269	4.08974	0.000365
EPB41L3	erythrocyte membrane protein band 4.1-like 3	17.0146	4.0887	0.001336
IL1A	interleukin 1_alpha	16.9791	4.08569	6.19E-09
GRIN2A	glutamate receptor_ionotropic_N-methyl D-aspartate 2A	16.9785	4.08564	2.15E-06
HBE1	hemoglobin_epsilon 1	16.9763	4.08545	3.06E-05
LIPH	lipase_member H	16.9375	4.08215	0.000383
EMCN	endomucin	16.9336	4.08182	1.72E-05
NTRK3	neurotrophic tyrosine kinase_receptor_type 3	16.9244	4.08103	4.31E-17
TMEFF2	transmembrane protein with EGF-like and two follistatin-like domains 2	16.918	4.08049	3.89E-06
N4BP3	NEDD4 binding protein 3	16.7396	4.06519	5.46E-10
LINC00460	long intergenic non-protein coding RNA 460	16.6098	4.05396	1.41E-09
SCARF1	scavenger receptor class F_member 1	16.605	4.05355	2.79E-51
SMCO3	single-pass membrane protein with coiled-coil domains 3	16.529	4.04693	1.48E-13
FBXL16	F-box and leucine-rich repeat protein 16	16.4858	4.04315	1.21E-14
SLC16A12	solute carrier family 16_member 12	16.4363	4.03881	2.11E-10
IRX4	iroquois homeobox 4	16.3644	4.03249	0.000015
F2RL1	coagulation factor II (thrombin) receptor-like 1	16.3467	4.03093	1.05E-12
PLCH2	phospholipase C_eta 2	16.2672	4.02389	1.91E-20
EPCAM	epithelial cell adhesion molecule	16.2263	4.02026	8.21E-19
TNFRSF9	tumor necrosis factor receptor superfamily_member 9	16.1981	4.01775	4.31E-20
CCDC3	coiled-coil domain containing 3	16.1881	4.01686	2.55E-20
SOX8	SRY (sex determining region Y)-box 8	16.1306	4.01173	3.37E-09
PTPN6	protein tyrosine phosphatase_non-receptor type 6	16.1207	4.01084	2.13E-21
PDGFR _L	platelet-derived growth factor receptor-like cerebellin 2 precursor	16.015	4.00135	1.75E-28
CBLN2	NLR family_pyrin domain containing 2	15.984	3.99856	0.001124
NLRP2	exophilin 5	15.9836	3.99852	2.37E-11
EXPH5	contactin 1	15.9414	3.99471	3.32E-10
CNTN1	acetylcholinesterase (Yt blood group)	15.9247	3.99319	9.80E-09
ACHE	adhesion G protein-coupled receptor G4	15.8565	3.987	2.21E-18
GPR112	family with sequence similarity 84_member B	15.7991	3.98177	5.31E-06
FAM84B	prostate androgen-regulated mucin-like protein 1	15.771	3.9792	2.10E-09
B3GNT5	RAB26_member RAS oncogene family	15.7637	3.97853	2.55E-29
MCF2L	coagulation factor X	15.7588	3.97809	6.13E-05
F10	olfactory receptor_family 51_subfamily E_member 2	15.7575	3.97797	3.70E-17
RAB26	annixin A13	15.7496	3.97724	1.59E-23
OR51E2	solute carrier family 12 (potassium/chloride transporter)_member 5	15.7274	3.97521	0.000128
ANXA13	Rho guanine nucleotide exchange factor (GEF) 26	15.6535	3.96841	0.000199
SLC12A5	high mobility group AT-hook 2	15.6414	3.9673	3.07E-10
ARHGEF26	synaptotagmin IX	15.637	3.96689	6.21E-18
CLDN1	cytochrome c oxidase subunit VIb	15.6055	3.96398	8.58E-16
HMGAA2	polypeptide 2 (testis)	15.5802	3.96164	3.74E-38
SYT9	solute carrier family 9_subfamily A (NHE4_cation proton antiporter 4)_member 4	15.5294	3.95693	0.000275
COX6B2	SLC9A4	15.4751	3.95188	3.39E-15
SLC9A4	solute carrier family 9_subfamily A (NHE4_cation proton antiporter 4)_member 4	15.4171	3.94646	0.00011

TABLE 3-continued

Genes more highly expressed in HMCs compared with BM-MSCs				
Gene Name	Description	Fold Change	Log Fold Change	p-Adj
SLTRK6	SLIT and NTRK-like family_member 6	15.4144	3.94621	0.001369
DOCK8	dedicator of cytokinesis 8	15.414	3.94617	0.000138
GPR126	adhesion G protein-coupled receptor G6	15.3514	3.9403	5.60E-39
LOC100130238	uncharacterized LOC100130238	15.2641	3.93207	2.52E-05
SULT1C2	sulfotransferase family_cytosolic_1C_member 2	15.2025	3.92624	4.89E-05
NIPAL1	NIPA-like domain containing 1	15.1915	3.92519	9.10E-12
GNA14	guanine nucleotide binding protein (G protein)_alpha 14	15.1356	3.91987	5.65E-26
PRKCQ-AS1	PRKCQ antisense RNA 1	15.0898	3.9155	2.20E-14
LOC102800447	uncharacterized LOC102800447	15.0873	3.91526	9.37E-06
KCNS1	potassium voltage-gated channel_modifier subfamily S_member 1	15.0747	3.91406	3.97E-16
LOC100126784	uncharacterized LOC100126784	15.0471	3.91141	1.38E-33
LPHN3	adhesion G protein-coupled receptor L3	14.9638	3.9034	0.000136
TMIGD2	transmembrane and immunoglobulin domain containing 2	14.9566	3.90271	0.001397
VSTM1	V-set and transmembrane domain containing 1	14.8319	3.89063	0.001267
CDH3	cadherin 3_type 1_P-cadherin (placental)	14.8271	3.89016	2.48E-20
PRKCZ	protein kinase C_zeta	14.7712	3.88472	2.05E-20
MAP2	microtubule-associated protein 2	14.7558	3.88321	4.24E-17
PIK3AP1	phosphoinositide-3-kinase adaptor protein 1	14.7409	3.88175	5.73E-06
TNFSF18	tumor necrosis factor (ligand) superfamily_member 18	14.7276	3.88045	0.001118
MIR4697HG	MIR4697 host gene	14.6591	3.87372	3.42E-07
GP6	glycoprotein VI (platelet)	14.6537	3.87319	0.000236
LINC01021	long intergenic non-protein coding RNA 1021	14.6366	3.87151	2.94E-08
PLAC8	placenta-specific 8	14.5941	3.86731	2.84E-39
TMEM88	transmembrane protein 88	14.5881	3.86672	9.16E-19
ENTPD8	ectonucleoside triphosphate diphosphohydrolase 8	14.5833	3.86625	0.000548
PPARGC1A	peroxisome proliferator-activated receptor gamma_coactivator 1 alpha	14.5566	3.8636	9.48E-07
SH3GL2	SH3-domain GRB2-like 2	14.4701	3.855	1.65E-06
SCN9A	sodium channel_voltage gated_type IX alpha subunit	14.4341	3.85141	9.10E-23
CPNE7	copine VII	14.4104	3.84904	1.53E-18
NRARP	NOTCH-regulated ankyrin repeat protein	14.4019	3.84819	6.33E-13
CERS4	ceramide synthase 4	14.3768	3.84567	1.43E-21
FCHO1	FCH domain only 1	14.3756	3.84555	1.82E-20
C19orf81	chromosome 19 open reading frame 81	14.3156	3.83952	4.03E-09
PGM5	phosphoglucomutase 5	14.3137	3.83932	5.56E-07
LINC01082	long intergenic non-protein coding RNA 1082	14.2988	3.83782	0.002369
HIST1H2BG	histone cluster 1_H2bg	14.2247	3.83033	5.47E-11
LOC100507006	uncharacterized LOC100507006	14.1543	3.82317	0.002106
LMTK3	lemur tyrosine kinase 3	14.1398	3.82169	2.65E-37
QPRT	quinolinate phosphoribosyltransferase	14.1045	3.81808	6.47E-60
TMEM35	transmembrane protein 35	14.0929	3.8169	7.46E-19
SEMA6B	sema domain_transmembrane domain (TM)_and cytoplasmic domain_(semaphorin) 6B	14.0663	3.81417	1.78E-13
AADACP1	arylacetamide deacetylase pseudogene 1	14.0634	3.81387	9.06E-05
CDH5	cadherin 5_type 2 (vascular endothelium)	14.0396	3.81143	3.35E-05
ZNF521	zinc finger protein 521	13.9425	3.80142	3.49E-07
ZYG11A	zyg-11 family member A_cell cycle regulator	13.8672	3.7936	3.38E-14
LINC00880	long intergenic non-protein coding RNA 880	13.826	3.78931	3.87E-06
DENN1C	DENN/MADD domain containing 1C	13.8021	3.78682	9.80E-07
LOC101927746	uncharacterized LOC101927746	13.6537	3.77122	1.42E-10
TRPV6	transient receptor potential cation channel_subfamily V_member 6	13.6524	3.77108	0.000789
CAMK1G	calcium/calmodulin-dependent protein kinase IG	13.5132	3.7563	8.50E-09
ELOVL2-AS1	ELOVL2 antisense RNA 1	13.4665	3.7513	0.000246
CYFIP2	cytoplasmic FMR1 interacting protein 2	13.3884	3.74291	8.57E-94
NOS1AP	nitric oxide synthase 1 (neuronal) adaptor protein	13.3866	3.74272	3.46E-07

TABLE 3-continued

Genes more highly expressed in HMCs compared with BM-MSCs				
Gene Name	Description	Fold Change	Log Fold Change	p-Adj
TRHDE	thyrotropin-releasing hormone degrading enzyme	13.2802	3.73121	1.32E-13
LSAMP-AS1	LSAMP antisense RNA 1	13.2538	3.72833	0.000305
SPOCK3	sparc/osteonectin_cwcw and kazal-like domains proteoglycan (testican) 3	13.2293	3.72566	0.0022
MPZL2	myelin protein zero-like 2	13.2262	3.72533	0.001202
LAMA5	laminin_alpha 5	13.2086	3.72341	1.87E-24
LOC101929690	NA	13.2059	3.72311	1.65E-16
F7	coagulation factor VII (serum prothrombin conversion accelerator)	13.1548	3.71752	0.001195
LOC101927482	uncharacterized LOC101927482	13.1233	3.71406	3.80E-09
ACSM4	acyl-CoA synthetase medium-chain family member 4	13.0723	3.70844	0.00141
KLHL6	kelch-like family member 6	13.0632	3.70744	0.000927
MUC22	mucin 22	13.0296	3.70372	0.001228
FGF13	fibroblast growth factor 13	13.018	3.70244	0.004351
F3	coagulation factor III (thromboplastin_tissue factor)	12.9766	3.69784	1.07E-10
TMSB15A	thymosin beta 15a	12.9458	3.69441	1.02E-14
KSR1	kinase suppressor of ras 1	12.9175	3.69125	1.82E-74
CERS1	ceramide synthase 1	12.9124	3.69068	5.47E-10
TNIK	TRAF2 and NCK interacting kinase	12.8675	3.68566	2.39E-15
PKIB	protein kinase (cAMP-dependent_catalytic) inhibitor beta	12.7595	3.6735	9.98E-05
C1orf226	chromosome 1 open reading frame 226	12.7485	3.67225	1.48E-05
DEF6	DEF6 guanine nucleotide exchange factor	12.7046	3.66728	3.26E-28
RCVRN	recoverin	12.6679	3.6631	0.001865
IL31RA	interleukin 31 receptor A	12.6668	3.66298	1.03E-08
SOWAHB	sosondowah ankyrin repeat domain family member B	12.6359	3.65946	5.40E-07
MIR2682	microRNA 2682	12.6238	3.65808	2.24E-37
SH2D5	SH2 domain containing 5	12.6064	3.65608	1.12E-31
ST6GALNAC5	ST6 (alpha-N-acetyl-neuraminy1-2_3-beta-galactosyl1-3)-N-acetylgalactosaminide alpha-2_6-sialyltransferase 5	12.5647	3.65131	6.63E-05
TNFRSF10C	tumor necrosis factor receptor superfamily member 10c_decoy without an intracellular domain	12.5125	3.6453	1.63E-21
GJA3	gap junction protein_alpha 3_46kDa	12.427	3.63541	2.24E-05
ELAVL2	ELAV like neuron-specific RNA binding protein 2	12.3924	3.63138	2.84E-06
ERC2	ELKS/RAB6-interacting/CAST family member 2	12.358	3.62737	3.63E-05
CAPN11	calpain 11	12.356	3.62714	0.0006
C7orf69	chromosome 7 open reading frame 69	12.3522	3.6267	1.28E-17
KIF17	kinesin family member 17	12.3375	3.62498	1.04E-21
ZBED2	zinc finger_BED-type containing 2	12.2674	3.61676	1.51E-06
TTYH2	weetie family member 2	12.2659	3.61658	1.79E-86
ST18	suppression of tumorigenicity 18_zinc finger	12.2605	3.61595	0.000105
GRB14	growth factor receptor-bound protein 14	12.2588	3.61574	2.43E-31
EDN2	endothelin 2	12.2511	3.61484	2.03E-06
KCP	kielin/chordin-like protein	12.2016	3.609	4.14E-05
MESTIT1	MEST intronic transcript 1_antisense RNA	12.1456	3.60236	0.000424
CLGN	calmegin	12.1193	3.59923	2.73E-09
IL18	interleukin 18	12.101	3.59706	6.08E-15
ANKRD18A	ankyrin repeat domain 18A	12.0977	3.59666	1.23E-05
UPB1	ureidopropionase_beta	12.0815	3.59473	0.000346
CARD11	caspase recruitment domain family_member 11	12.066	3.59287	4.03E-13
KLHL23	kelch-like family member 23	12.0564	3.59173	0.003407
ABCD2	ATP-binding cassette_sub-family D (ALD)_member 2	12.0107	3.58625	0.000115
ITGAX	integrin_alpha X (complement component 3 receptor 4 subunit)	11.9821	3.58281	0.003088
CDH18	cadherin 18_type 2	11.9667	3.58095	0.004769
NOX4	NADPH oxidase 4	11.9252	3.57594	7.16E-28
TMEM125	transmembrane protein 125	11.9135	3.57452	0.000735
PPARGC1B	peroxisome proliferator-activated receptor gamma_coactivator 1 beta	11.8045	3.56127	4.66E-06
F2	coagulation factor II (thrombin)	11.7803	3.5583	9.71E-05

TABLE 3-continued

Genes more highly expressed in HMCs compared with BM-MSCs				
Gene Name	Description	Fold Change	Log Fold Change	p-Adj
CAMSAP3	calmodulin regulated spectrin-associated protein family_member 3	11.777	3.5579	0.001984
LOC100996579	uncharacterized LOC100996579	11.7569	3.55544	0.000352
FBXO2	F-box protein 2	11.7289	3.55199	2.38E-28
ZNF663P	zinc finger protein 663_pseudogene	11.713	3.55004	1.20E-05
KCNK3	potassium channel_two pore domain subfamily K_member 3	11.7019	3.54867	9.68E-15
OGDHL	oxoglutarate dehydrogenase-like	11.6171	3.53818	1.44E-11
HTR1B	5-hydroxytryptamine (serotonin) receptor 1B_G protein-coupled	11.5855	3.53425	0.006255
NPW	neuropeptide W	11.5805	3.53363	8.71E-28
RND2	Rho family GTPase 2	11.5602	3.53109	2.29E-19
POU2F3	POU class 2 homeobox 3	11.4708	3.51989	0.000573
BAIAP3	BAI1-associated protein 3	11.4524	3.51758	4.89E-11
PCDH9A	protocadherin alpha 9	11.4289	3.51461	0.00541
INA	internexin neuronal intermediate filament protein_alpha	11.406	3.51172	1.76E-19
LINC01012	long intergenic non-protein coding RNA 1012	11.3526	3.50495	0.000134
FLT4	fms-related tyrosine kinase 4	11.3474	3.50429	9.13E-06
FAR2P2	fatty acyl CoA reductase 2 pseudogene	11.298	3.49799	1.10E-05
PALM3	paralemmin 3	11.2908	3.49708	3.25E-22
LINC00887	long intergenic non-protein coding RNA 887	11.2675	3.4941	9.65E-05
HSD17B14	hydroxysteroid (17-beta) dehydrogenase 14	11.261	3.49326	8.14E-10
ZNF853	zinc finger protein 853	11.2476	3.49155	5.44E-17
TYROBP	TYRO protein tyrosine kinase binding protein	11.2225	3.48832	0.004002
FCGBP	Fc fragment of IgG binding protein	11.193	3.48453	2.53E-08
LOC349160	uncharacterized LOC349160	11.1929	3.48451	0.00353
C10orf91	chromosome 10 open reading frame 91	11.1722	3.48184	1.42E-05
PCDH9	protocadherin 9	11.1083	3.47356	4.97E-14
CD101	CD101 molecule	11.0942	3.47174	3.83E-07
PCDH9A4	protocadherin alpha 4	11.0596	3.46723	7.10E-06
LINC00858	long intergenic non-protein coding RNA 858	11.0374	3.46433	0.007369
SPACA4	sperm acrosome associated 4	10.9188	3.44874	0.005785
C14orf39	chromosome 14 open reading frame 39	10.9121	3.44786	1.16E-15
JUP	junction plakoglobin	10.8918	3.44517	1.02E-41
KIF21B	kinesin family member 21B	10.847	3.43922	4.67E-31
NPPB	natriuretic peptide B	10.8154	3.43502	6.87E-06
GALNTL6	polypeptide N-acetylgalactosaminyltransferase-like 6	10.803	3.43336	0.001067
PCDHGB6	protocadherin gamma subfamily B_6	10.7364	3.42444	5.77E-09
KIAA1257	KIAA1257	10.7286	3.42339	0.00706
DNM1	dynamin 1	10.7235	3.42271	6.95E-21
CRB2	crumbs family member 2	10.6856	3.4176	7.06E-05
ECSCR	endothelial cell surface expressed chemotaxis and apoptosis regulator	10.64	3.41143	4.77E-18
SRRM4	serine/arginine repetitive matrix 4	10.595	3.40531	3.37E-08
SLC27A2	solute carrier family 27 (fatty acid transporter)_member 2	10.5673	3.40153	8.96E-05
ATRNL1	attractin-like 1	10.5349	3.39711	1.52E-13
PEG10	paternally expressed 10	10.4808	3.38968	2.60E-13
NFAM1	NFAT activating protein with ITAM motif 1	10.3784	3.37551	0.00437
BLACAT1	bladder cancer associated transcript 1 (non-protein coding)	10.3481	3.37129	0.000494
HSD17B2	hydroxysteroid (17-beta) dehydrogenase 2	10.3443	3.37077	0.006844
MEX3A	mex-3 RNA binding family member A	10.2924	3.36351	0.00E+00
LOC100129617	uncharacterized LOC100129617	10.2675	3.36001	7.93E-06
IGLON5	IgLON family member 5	10.2593	3.35886	4.35E-05
AQP1	aquaporin 1 (Colton blood group)	10.2493	3.35746	2.90E-52
ERBB4	erb-b2 receptor tyrosine kinase 4	10.2334	3.35521	0.003618
MGAT5B	mannosyl (alpha-1_6)-glycoprotein beta-1_6-N-acetyl-glucosaminyltransferase_isozyme B	10.2166	3.35284	1.50E-28
EPHB6	EPH receptor B6	10.2139	3.35246	6.39E-10
CTAGE11P	CTAGE family_member 11_pseudogene	10.2083	3.35167	0.000199
HOXB-AS3	HOXB cluster antisense RNA 3	10.1938	3.34962	6.77E-33
LOC102723854	uncharacterized LOC102723854	10.1809	3.3478	7.33E-06
KCNN3	potassium channel calcium activated intermediate/small conductance subfamily N alpha_member 3	10.1753	3.347	7.11E-05

TABLE 3-continued

Genes more highly expressed in HMCs compared with BM-MSCs				
Gene Name	Description	Fold Change	Log Fold Change	p-Adj
DCDC2	doublecortin domain containing 2	10.1005	3.33636	0.00503
ZFP92	ZFP92 zinc finger protein	10.0974	3.33591	4.67E-05
UPK1A-AS1	UPK1A antisense RNA 1	10.0951	3.33558	0.004621
HIST1H2BE	histone cluster 1_H2be	10.0917	3.3351	6.66E-05
RIMS2	regulating synaptic membrane exocytosis 2	10.0667	3.33152	0.001381
WSCD1	WSC domain containing 1	10.0653	3.33132	0.000557
LOC100507534	uncharacterized LOC100507534	10.0514	3.32933	2.13E-05
FSIP2	fibrous sheath interacting protein 2	10.0377	3.32735	4.93E-09
FGD4	FYVE_RhoGEF and PH domain containing 4	10.0126	3.32375	5.09E-57
CTSC	cathepsin C	10.0114	3.32357	3.86E-17
RASL10A	RAS-like_family 10_member A	10.0097	3.32333	3.46E-05
JSRP1	junctional sarcoplasmic reticulum protein 1	9.98879	3.32031	0.000419
ERVMER34-1	endogenous retrovirus group MER34_member 1	9.96811	3.31732	0.002564
ITGA2	integrin_alpha 2 (CD49B_alpha 2 subunit of VLA-2 receptor)	9.96486	3.31685	3.74E-13
LOC101927043	uncharacterized LOC101927043	9.94692	3.31425	5.99E-05
PROZ	protein Z_vitamin K-dependent plasma glycoprotein	9.93142	3.312	9.36E-09
NR2F2-AS1	NR2F2 antisense RNA 1	9.92254	3.31071	1.80E-45
PLAC1	placenta-specific 1	9.91313	3.30934	6.64E-08
NMNAT3	nicotinamide nucleotide adenyllyltransferase 3	9.90969	3.30884	1.04E-05
TMEM51	transmembrane protein 51	9.9007	3.30753	1.11E-35
ZIC2	Zic family member 2	9.89967	3.30738	0.006266
LOC100507600	uncharacterized LOC100507600	9.83537	3.29798	3.68E-35
AR	androgen receptor	9.7898	3.29128	3.71E-23
ALOX15	arachidonate 15-lipoxygenase	9.71686	3.28049	0.006396
ROR2	receptor tyrosine kinase-like orphan receptor 2	9.70407	3.27859	9.56E-11
MBP	myelin basic protein	9.66694	3.27306	5.54E-07
LEMD1-AS1	LEMD 1 antisense RNA 1	9.66353	3.27255	0.000186
TMEM151B	transmembrane protein 151B	9.66085	3.27215	0.000879
EGLN3	egl-9 family hypoxia-inducible factor 3	9.65482	3.27125	5.65E-06
SGIP1	SH3-domain GRB2-like (endophilin) interacting protein 1	9.64934	3.27043	1.12E-11
OVCH2	ovochymase 2 (gene/pseudogene)	9.61196	3.26483	4.28E-22
PRKAR2B	protein kinase_cAMP-dependent_regulatory_type II_beta	9.57233	3.25887	1.50E-16
PURG	purine-rich element binding protein G	9.549	3.25535	1.64E-07
KRT19	keratin 19_type I	9.51392	3.25004	3.57E-18
NFE2L3	nuclear factor_erythroid 2-like 3	9.51267	3.24985	7.63E-18
FILIP1	filamin A interacting protein 1	9.49936	3.24783	1.05E-06
MYOCD	myocardin	9.48028	3.24493	3.68E-49
KCNQ1	potassium channel_voltage gated KQT-like subfamily Q_member 1	9.44205	3.2391	0.003517
ACTBL2	actin_beta-like 2	9.43662	3.23827	3.82E-08
NUP62CL	nucleoporin 62kDa C-terminal like	9.4291	3.23712	0.007505
POTEF	POTE ankyrin domain family_member F	9.42244	3.2361	7.58E-23
FAM83E	family with sequence similarity 83_member E	9.41016	3.23422	0.000192
CPA4	carboxypeptidase A4	9.39003	3.23113	1.67E-160
FAM183A	family with sequence similarity 183_member A	9.38463	3.2303	0.000142
DUSP9	dual specificity phosphatase 9	9.37663	3.22907	1.19E-05
MYOM3	myomesin 3	9.30657	3.21825	4.91E-08
BCL11A	B-cell CLL/lymphoma 11A (zinc finger protein)	9.29523	3.21649	8.22E-07
GEM	GTP binding protein overexpressed in skeletal muscle	9.27688	3.21364	4.53E-64
TRABD2A	TraB domain containing 2A	9.25383	3.21005	3.80E-23
SPTBN2	spectrin_beta_non-erythrocytic 2	9.25318	3.20995	5.85E-33
ZP1	zona pellucida glycoprotein 1 (sperm receptor)	9.24959	3.20939	9.78E-05
VTRNA1-3	vault RNA 1-3	9.24312	3.20838	0.001629
FNDC9	fibronectin type III domain containing 9	9.23524	3.20715	0.004547
PPAP2C	phosphatidic acid phosphatase type 2C	9.21574	3.2041	1.87E-06
SERPINB7	serpin peptidase inhibitor_clade B (ovalbumin)_member 7	9.21146	3.20343	1.69E-16
LOC645752	golgin A6 family_member A pseudogene	9.19169	3.20033	0.0005

TABLE 3-continued

Genes more highly expressed in HMCs compared with BM-MSCs				
Gene Name	Description	Fold Change	Log Fold Change	p-Adj
SLC4A9	solute carrier family 4_sodium bicarbonate cotransporter_member 9	9.19029	3.20011	0.000273
SLC37A1	solute carrier family 37 (glucose-6-phosphate transporter)_member 1	9.18838	3.19981	3.01E-24
FSTL4	follistatin-like 4	9.12858	3.19039	0.009879
NTF4	neurotrophin 4	9.11094	3.1876	9.13E-10
DRP2	dystrophin related protein 2	9.0987	3.18566	6.82E-39
ILDR2	immunoglobulin-like domain containing receptor 2	9.06646	3.18054	0.001062
HBEGF	heparin-binding EGF-like growth factor	9.04249	3.17672	3.30E-40
MDFI	MyoD family inhibitor	9.03672	3.1758	3.42E-14
MED12L	mediator complex subunit 12-like	9.0187	3.17292	3.30E-16
TMCC3	transmembrane and coiled-coil domain family 3	8.99436	3.16902	2.07E-08
FBXL13	F-box and leucine-rich repeat protein 13	8.97206	3.16544	1.13E-16
LOC100652824	NA	8.96603	3.16447	2.05E-07
NSG1	neuron specific gene family member 1	8.91305	3.15592	8.80E-18
KRT18	keratin 18_type I	8.89023	3.15222	2.87E-11
DOC2A	double C2-like domains_alpha	8.88388	3.15119	1.98E-07
LOC642366	uncharacterized LOC642366	8.88142	3.15079	0.000859
NOS3	nitric oxide synthase 3 (endothelial cell)	8.85572	3.14661	1.46E-09
LPPR3	lipid phosphate phosphatase-related protein type 3	8.84382	3.14467	9.86E-23
DACH2	dachshund family transcription factor 2	8.83978	3.14401	0.008437
C16orf74	chromosome 16 open reading frame 74	8.82148	3.14102	8.22E-22
CAMK4	calcium/calmodulin-dependent protein kinase IV	8.81329	3.13968	6.34E-10
EMID1	EMI domain containing 1	8.80797	3.13881	8.00E-06
SSPO	SCO-spondin	8.79778	3.13714	1.54E-09
ST6GAL1	ST6 beta-galactosamide alpha-2_6-sialyltransferase 1	8.79705	3.13702	1.44E-24
RHOJ	ras homolog family member J	8.78103	3.13439	3.91E-10
ZBTB8B	zinc finger and BTB domain containing 8B	8.77744	3.1338	0.002569
PIK3R3	phosphoinositide-3-kinase_regulatory subunit 3 (gamma)	8.73344	3.12655	1.04E-59
TRPC5OS	TRPC5 opposite strand	8.72582	3.12529	0.003814
HS3ST1	heparan sulfate (glucosamine) 3-O-sulfotransferase 1	8.69744	3.12059	5.29E-07
LRMP	lymphoid-restricted membrane protein	8.64011	3.11105	9.22E-05
CASC9	cancer susceptibility candidate 9 (non-protein coding)	8.63556	3.11029	0.006985
EPPK1	epiplakin 1	8.63311	3.10988	1.71E-19
LGALS9	lectin_galactoside-binding_soluble_9	8.63095	3.10952	5.69E-10
TNNT1	troponin T type 1 (skeletal_slow)	8.59573	3.10362	2.35E-65
CASKIN1	CASK interacting protein 1	8.58239	3.10138	1.29E-09
EFNA1	ephrin-A1	8.58233	3.10137	1.97E-06
EPHA4	EPH receptor A4	8.53032	3.0926	8.89E-171
FUT1	fucosyltransferase 1 (galactoside 2-alpha-L-fucosyltransferase_H blood group)	8.52772	3.09216	2.02E-08
CD274	CD274 molecule	8.52725	3.09208	5.00E-85
ADAMTS15	ADAM metallopeptidase with thrombospondin type 1 motif_15	8.52394	3.09152	2.67E-62
MYH15	myosin_heavy chain 15	8.51272	3.08962	2.63E-11
ZBED9	zinc finger_BED-type containing 9	8.47087	3.08251	2.57E-06
ZFR2	zinc finger RNA binding protein 2	8.46688	3.08183	0.008776
SLC5A12	solute carrier family 5 (sodium/monocarboxylate cotransporter)_member 12	8.45837	3.08038	1.56E-12
HIST1H4E	histone cluster 1_H4e	8.45198	3.07929	3.48E-05
SLC28A3	solute carrier family 28 (concentrative nucleoside transporter)_member 3	8.43864	3.07701	5.17E-19
TLR2	toll-like receptor 2	8.42117	3.07402	1.85E-06
MIR450A2	microRNA 450a-2	8.42064	3.07393	0.009071
TRHDE-AS1	TRHDE antisense RNA 1	8.39482	3.0695	5.85E-07
FAM49A	family with sequence similarity 49_member A	8.39209	3.06903	4.98E-09

TABLE 3-continued

Genes more highly expressed in HMCs compared with BM-MSCs				
Gene Name	Description	Fold Change	Log Fold Change	p-Adj
DTX4	deltex 4_E3 ubiquitin ligase	8.35054	3.06187	7.50E-11
FRZB	frizzled-related protein	8.34771	3.06138	2.64E-24
LOC644838	uncharacterized LOC644838	8.33025	3.05836	0.000163
XKR6	XK_Kell blood group complex subunit-related family_member 6	8.3224	3.057	1.57E-09
SERTAD4	SERTA domain containing 4	8.32131	3.05681	9.53E-05
OR10A3	olfactory receptor_family 10_subfamily A_member 3	8.313	3.05537	0.000849
GNGT2	guanine nucleotide binding protein (G protein)_gamma transducing activity polypeptide 2	8.2804	3.0497	3.49E-05
MIR548AO	microRNA 548ao	8.26864	3.04765	4.29E-06
SLC29A2	solute carrier family 29 (equilibrative nucleoside transporter)_member 2	8.25295	3.04491	7.15E-27
BAI1	adhesion G protein-coupled receptor B1	8.24089	3.0428	2.23E-05
SAMD12	sterile alpha motif domain containing 12	8.23158	3.04117	7.76E-74
GUCA1A	guanylate cyclase activator 1A (retina)	8.22605	3.0402	4.66E-05
EFR3B	EFR3 homolog B	8.1885	3.0336	9.94E-28
LRCH2	leucine-rich repeats and calponin homology (CH) domain containing 2	8.18147	3.03236	5.11E-15
ZDHHC11	zinc finger_DHHC-type containing 11	8.15639	3.02793	9.38E-08
ICAM5	intercellular adhesion molecule 5_telencephalin	8.12	3.02148	3.39E-16
PYY2	peptide YY_2 (pseudogene)	8.11848	3.02121	2.82E-06
GNG4	guanine nucleotide binding protein (G protein)_gamma 4	8.10724	3.01921	0.0006
RASEF	RAS and EF-hand domain containing	8.09471	3.01698	1.21E-05
ANKRD1	ankyrin repeat domain 1 (cardiac muscle)	8.08955	3.01606	9.99E-26
SBK1	SH3 domain binding kinase 1	8.07314	3.01313	3.63E-07
KISS1	KiSS-1 metastasis-suppressor	8.05001	3.00899	8.23E-06
PTPN7	protein tyrosine phosphatase_non-receptor type 7	8.04404	3.00792	3.46E-05
KIAA1804	mixed lineage kinase 4	8.03986	3.00717	0.000206
LCT	lactase	8.03117	3.00561	0.002301
IQSEC3	IQ motif and Sec7 domain 3	8.01843	3.00332	0.000208
CXCL14	chemokine (C-X-C motif) ligand 14	7.97918	2.99624	4.67E-05
SLC6A16	solute carrier family 6_member 16	7.97901	2.99621	1.02E-14
PLCXD2	phosphatidylinositol-specific phospholipase C_X domain containing 2	7.96315	2.99334	0.000163
THBD	thrombomodulin	7.94661	2.99034	8.69E-13
NRGN	neurogranin (protein kinase C substrate_RC3)	7.94254	2.9896	6.09E-13
MAPK15	mitogen-activated protein kinase 15	7.91544	2.98467	1.72E-10
TSPEAR-AS1	TSPEAR antisense RNA 1	7.9002	2.98189	6.21E-08
TMEM52	transmembrane protein 52	7.89862	2.9816	2.09E-10
MIR503	microRNA 503	7.89796	2.98148	2.97E-09
FBP2	fructose-1_6-bisphosphatase 2	7.86867	2.97612	8.34E-08
OR5E1P	olfactory receptor_family 5_subfamily E_member 1 pseudogene	7.86818	2.97603	8.61E-06
GS1-24F.4.2	uncharacterized LOC100652791	7.85456	2.97353	7.22E-06
CX3CL1	chemokine (C-X3-C motif) ligand 1	7.85156	2.97298	0.00914
PLA2G3	phospholipase A2_group III	7.82435	2.96797	0.00959
STK32B	serine/threonine kinase 32B	7.81351	2.96597	1.02E-33
NR2F2	nuclear receptor subfamily 2_group F_member 2	7.81139	2.96558	1.03E-214
DPF3	D4_zinc and double PHD fingers_family 3	7.8095	2.96523	5.87E-13
MGARP	mitochondria-localized glutamic acid-rich protein	7.79257	2.9621	1.73E-30
BTBD11	BTB (POZ) domain containing 11	7.74567	2.95339	2.81E-07
SYNPO2L	synaptopodin 2-like	7.73698	2.95177	5.43E-09
SEP3	septin 3	7.66853	2.93895	3.40E-06
SORL1	sortilin-related receptor_L(DLR class) A repeats containing	7.65048	2.93555	1.07E-09
MYOZ3	myozenin 3	7.63792	2.93318	4.21E-27
MIR7851	microRNA 7851	7.62655	2.93103	0.007612
CNGA1	cyclic nucleotide gated channel alpha 1	7.61086	2.92806	0.002809
ZCCHC5	zinc finger_CCHC domain containing 5	7.60021	2.92604	1.23E-07
C14orf105	chromosome 14 open reading frame 105	7.59084	2.92426	0.009166
ZNF488	zinc finger protein 488	7.5507	2.91661	1.69E-05
HES7	hes family bHLH transcription factor 7	7.52379	2.91146	0.000368
CCDC81	coiled-coil domain containing 81	7.51863	2.91047	3.24E-22

TABLE 3-continued

Genes more highly expressed in HMCs compared with BM-MSCs				
Gene Name	Description	Fold Change	Log Fold Change	p-Adj
TCEAL7	transcription elongation factor A (SII)-like 7	7.5155	2.90987	2.66E-13
FRMPD4	FERM and PDZ domain containing 4	7.50957	2.90873	6.14E-17
CA11	carbonic anhydrase XI	7.49039	2.90504	4.39E-62
GAD1	glutamate decarboxylase 1 (brain_67 kDa)	7.48758	2.9045	1.51E-05
MARCHF3	membrane-associated ring finger (C3HC4) 3_E3 ubiquitin protein ligase	7.47296	2.90168	3.24E-35
MIR503HG	MIR503 host gene	7.46654	2.90044	8.97E-11
NRTN	neurturin	7.46587	2.90031	0.005609
PKNOX2	PBX/knotted 1 homeobox 2	7.43731	2.89478	2.23E-05
TMEM156	transmembrane protein 156	7.42052	2.89152	0.001671
HHX	hematopoietically expressed homeobox	7.41281	2.89002	1.56E-37
OBSCN	obscurin_cytoskeletal calmodulin and titin-interacting RhoGEF	7.37136	2.88193	4.80E-11
SDPR	serum deprivation response	7.36482	2.88065	2.55E-23
PKDCC	protein kinase domain containing_cytoplasmic	7.35375	2.87848	2.89E-30
LOC101926963	uncharacterized LOC101926963	7.30888	2.86965	1.84E-07
PPP1R9A	protein phosphatase 1 regulatory subunit 9A	7.30716	2.86931	0.00519
CAMK2N1	calcium/calmodulin-dependent protein kinase II inhibitor 1	7.29749	2.8674	9.32E-95
MTL5	metallothionein-like 5_testis-specific (tesmin)	7.29061	2.86604	1.26E-23
COLEC10	collectin sub-family member 10 (C-type lectin)	7.27986	2.86391	9.04E-10
MAMDC2	MAM domain containing 2	7.27224	2.8624	4.49E-08
CGN	cingulin	7.26227	2.86042	0.002144
KIF25	kinesin family member 25	7.2597	2.85991	0.005232
GFRA2	GDNF family receptor alpha 2	7.16685	2.84134	9.87E-06
TSPEAR	thrombospondin-type laminin G domain and EAR repeats	7.16581	2.84113	0.008624
HIST1H2AE	histone cluster 1_H2ae	7.15846	2.83965	7.07E-08
MAST1	microtubule associated serine/threonine kinase 1	7.10823	2.82949	7.37E-06
PCP2	Purkinje cell protein 2	7.10074	2.82797	0.000883
RAC3	ras-related C3 botulinum toxin substrate 3 (rho family_small GTP binding protein Rac3)	7.09951	2.82772	9.54E-62
JAG2	jagged 2	7.0975	2.82731	1.53E-11
AFF3	AF4/FMR2 family_member 3	7.08737	2.82525	2.06E-15
FGFBP3	fibroblast growth factor binding protein 3	7.0854	2.82485	8.65E-52
NAALAD2	N-acetylated alpha-linked acidic dipeptidase 2	7.07799	2.82334	5.08E-12
TMEM184A	transmembrane protein 184A	7.0749	2.82271	1.54E-20
PM20D2	peptidase M20 domain containing 2	7.06216	2.82011	5.26E-17
RAB38	RAB38_member RAS oncogene family	7.05771	2.8192	1.03E-08
RET	ret proto-oncogene	7.05135	2.8179	0.000163
HTRA4	HtrA serine peptidase 4	7.04583	2.81677	7.74E-07
LINC01096	long intergenic non-protein coding RNA 1096	7.04232	2.81605	0.008893
SRCRB4D	scavenger receptor cysteine rich family_4 domains	7.02593	2.81269	1.07E-17
SERTAD4-AS1	SERTAD4 antisense RNA 1	7.01377	2.81019	0.000178
AMN	amnion associated transmembrane protein	7.0109	2.8096	1.99E-05
NAP1L2	nucleosome assembly protein 1-like 2	7.00682	2.80876	6.17E-07
P2RX6P	purinergic receptor P2X_ligand gated ion channel_6 pseudogene	7.0057	2.80853	8.55E-05
PADI2	peptidyl arginine deiminase_type II	6.99644	2.80662	3.36E-09
NEDD4L	neural precursor cell expressed_developmentally down-regulated 4-like_E3 ubiquitin protein ligase	6.96899	2.80095	5.91E-83
RASGEF1A	RasGEF domain family_member 1A	6.96098	2.79929	0.001206
MIR3648	microRNA 3648-1	6.95794	2.79866	8.24E-06
MIR1204	microRNA 1204	6.93017	2.79289	1.30E-05
SNORD116-28	small nucleolar RNA_C/D box 116-28	6.92906	2.79266	1.24E-07
RBP7	retinol binding protein 7_cellular	6.87958	2.78232	3.79E-08
PIK3C2B	phosphatidylinositol-4-phosphate 3-kinase_catalytic subunit type 2 beta	6.85849	2.77789	1.86E-34
SLC4A11	solute carrier family 4_sodium borate transporter_member 11	6.83969	2.77393	3.99E-10
ISYNA1	inositol-3-phosphate synthase 1	6.83556	2.77306	1.30E-19

TABLE 3-continued

Genes more highly expressed in HMCs compared with BM-MSCs				
Gene Name	Description	Fold Change	Log Fold Change	p-Adj
SALL2	spalt-like transcription factor 2	6.82534	2.7709	4.21E-10
MIR3687	microRNA 3687-1	6.81026	2.76771	1.02E-06
SOX5	SRY (sex determining region Y)-box 5	6.76692	2.7585	0.001343
FOXL1	forkhead box L1	6.74075	2.75291	4.01E-101
AC093375.1	NA	6.73959	2.75266	0.000186
PLXDC1	plexin domain containing 1	6.7358	2.75185	3.23E-10
APOE	apolipoprotein E	6.71948	2.74835	8.58E-16
HID1	HID1 domain containing	6.71478	2.74734	1.31E-07
SSUH2	ssu-2 homolog (C. elegans)	6.71431	2.74724	0.006498
ABCA12	ATP-binding cassette_sub-family A (ABC1)_member 12	6.69391	2.74285	0.000933
OLFM2	olfactomedin 2	6.68636	2.74122	4.43E-22
GCA	grancalcin_EF-hand calcium binding protein	6.68066	2.73999	2.21E-23
MAGEL2	melanoma antigen family L2	6.67399	2.73855	6.63E-39
LINC00920	long intergenic non-protein coding RNA 920	6.67311	2.73836	7.44E-08
SLC40A1	solute carrier family 40 (iron-regulated transporter)_member 1	6.66535	2.73668	8.07E-16
MUC19	mucin 19_oligomeric	6.65242	2.73388	0.001879
GRAP2	GRB2-related adaptor protein 2	6.62458	2.72783	8.63E-06
HOXB6	homeobox B6	6.60748	2.7241	3.58E-47
ITPR1PL1	inositol 1_4_5-trisphosphate receptor interacting protein-like 1	6.59508	2.72139	4.78E-18
LOC100996351	uncharacterized LOC100996351	6.59097	2.72049	0.00819
F2RL2	coagulation factor II (thrombin) receptor-like 2	6.56193	2.71412	5.61E-09
WDR65	cilia and flagella associated protein 57	6.55112	2.71176	5.50E-05
AP1M2	adaptor-related protein complex 1_mu 2 subunit	6.55007	2.71151	4.62E-09
PLP1	proteolipid protein 1	6.54975	2.71144	3.53E-11
SLC6A17	solute carrier family 6 (neutral amino acid transporter)_member 17	6.54662	2.71075	2.30E-09
SALL1	spalt-like transcription factor 1	6.52818	2.70668	0.000106
TRIM17	tripartite motif containing 17	6.51882	2.70461	1.10E-25
CXorf57	chromosome X open reading frame 57	6.51832	2.7045	3.14E-11
ELF3	E74-like factor 3 (ets domain transcription factor_epithelial-specific)	6.46482	2.69261	0.000323
CNIH2	cornichon family AMPA receptor auxiliary protein 2	6.44915	2.68911	1.14E-22
C15orf48	chromosome 15 open reading frame 48	6.44795	2.68884	6.06E-08
LINGO1	leucine rich repeat and Ig domain containing 1	6.43861	2.68675	1.73E-08
CLDN11	claudin 11	6.42987	2.68479	8.10E-12
PLEKHG3	pleckstrin homology domain containing_family G (with RhoGef domain) member 3	6.42773	2.68431	4.08E-37
GPR132	G protein-coupled receptor 132	6.41763	2.68204	5.59E-06
LINC01239	long intergenic non-protein coding RNA 1239	6.4166	2.68181	1.45E-07
SPTB	spectrin_beta_erythrocytic	6.40669	2.67958	3.70E-15
LINC00649	long intergenic non-protein coding RNA 649	6.4051	2.67922	7.95E-05
ST6GALNAC1	ST6 (alpha-N-acetyl-neuraminyl-2_3-beta-galactosyl-1_3)-N-acetylgalactosaminide alpha-2_6-sialyltransferase 1	6.38785	2.67533	0.004035
STOX2	storkhead box 2	6.38108	2.6738	2.61E-05
HOXB5	homeobox B5	6.37811	2.67313	7.00E-11
HBQ1	hemoglobin_theta 1	6.37449	2.67231	0.003817
SORBS1	sorbin and SH3 domain containing 1	6.36597	2.67038	5.94E-12
DHDH	dihydrodiol dehydrogenase (dimeric)	6.35821	2.66862	0.000693
MYOZ2	myozinin 2	6.34034	2.66456	2.49E-07
MMP23A	matrix metallopeptidase 23A (pseudogene)	6.31994	2.65991	0.000145
PDE10A	phosphodiesterase 10A	6.31801	2.65947	4.38E-05
HEY1	hes-related family bHLH transcription factor with YRPW motif 1	6.30572	2.65666	1.47E-10
CTXN1	cortexin 1	6.30309	2.65606	2.29E-39
EDN1	endothelin 1	6.30056	2.65548	2.72E-51
PKD1L1	polycystic kidney disease 1 like 1	6.29078	2.65324	2.76E-09
LRRC7	leucine rich repeat containing 7	6.28608	2.65216	0.003815
LIMS3-LOC44089	LIMS3-LOC440895 readthrough	6.2829	2.65143	8.95E-10
PLEKHA6	pleckstrin homology domain containing_family A member 6	6.27972	2.6507	7.09E-06
POU3F1	POU class 3 homeobox 1	6.26698	2.64777	0.002473

TABLE 3-continued

Genes more highly expressed in HMCs compared with BM-MSCs				
Gene Name	Description	Fold Change	Log Fold Change	p-Adj
AMH	anti-Mullerian hormone	6.25002	2.64386	7.65E-10
PCLO	piccolo presynaptic cytomatrix protein	6.23941	2.64141	3.62E-08
MYOZ1	myozin 1	6.21502	2.63576	3.95E-05
CCDC78	coiled-coil domain containing 78	6.21145	2.63493	3.59E-10
CCDC85A	coiled-coil domain containing 85A	6.16961	2.62518	2.43E-05
PRKX	protein kinase_X-linked	6.1588	2.62265	1.00E-48
VEPH1	ventricular zone expressed PH domain-containing 1	6.15552	2.62188	7.39E-69
DDX26B	DEAD/H (Asp-Glu-Ala-Asp/His) box polypeptide 26B	6.12322	2.61429	2.74E-09
COCH	cochlin	6.1044	2.60985	0.000474
MYH10	myosin_heavy chain 10_non-muscle	6.09616	2.6079	3.63E-52
PDGF D	platelet derived growth factor D	6.08687	2.6057	4.95E-06
LINC00704	long intergenic non-protein coding RNA 704	6.08522	2.60531	5.99E-05
PHACTR1	phosphatase and actin regulator 1	6.07599	2.60312	0.000104
COL6A4P2	collagen_type VI_alpha 4 pseudogene 2	6.06232	2.59987	0.005576
TFAP2A	transcription factor AP-2 alpha (activating enhancer binding protein 2 alpha)	6.06161	2.5997	9.93E-06
COL17A1	collagen_type XVII_alpha 1	6.0569	2.59858	1.18E-08
LRP4	low density lipoprotein receptor-related protein 4	6.05648	2.59848	3.47E-20
DUSP4	dual specificity phosphatase 4	6.04855	2.59659	0.006571
MAP3K15	mitogen-activated protein kinase kinase kinase 15	6.03494	2.59334	2.05E-05
RAMP2	receptor (G protein-coupled) activity modifying protein 2	6.03469	2.59328	4.50E-09
DOK6	docking protein 6	6.0139	2.5883	4.14E-06
CELF2	CUGBP_Elav-like family member 2	6.00548	2.58628	4.06E-05
GRASP	GRP1 (general receptor for phosphoinositides 1)-associated scaffold protein	6.00448	2.58604	4.24E-16
ERICH5	glutamate-rich 5	6.00407	2.58594	3.75E-07
MFNG	MFNG O-fucosylpeptide 3-beta-N-acetylglucosaminyltransferase	5.99858	2.58462	0.001964
ETS2	v-ets avian erythroblastosis virus E26 oncogene homolog 2	5.99193	2.58302	1.91E-71
C21orf90	TSPEAR antisense RNA 2	5.99164	2.58295	2.26E-09
GABRA3	gamma-aminobutyric acid (GABA) A receptor_alpha 3	5.98931	2.58239	0.002658
FZD9	frizzled class receptor 9	5.9784	2.57976	2.07E-24
PGM5P2	phosphoglucomutase 5 pseudogene 2	5.96739	2.5771	1.46E-09
FAM179A	family with sequence similarity 179_member A	5.96437	2.57637	0.000582
GPR183	G protein-coupled receptor 183	5.9604	2.57541	2.09E-10
WFDC10B	WAP four-disulfide core domain 10B	5.95318	2.57366	0.007524
SP6	Sp6 transcription factor	5.94353	2.57132	2.26E-07
AMOT	angiomotin	5.94114	2.57074	1.51E-12
MAP2K6	mitogen-activated protein kinase kinase 6	5.93744	2.56984	2.54E-26
TMEFF1	transmembrane protein with EGF-like and two follistatin-like domains 1	5.92769	2.56747	0.001063
TPPP	tubulin polymerization promoting protein	5.92005	2.56561	2.81E-08
HIST1H3G	histone cluster 1_H3g	5.91648	2.56474	0.0055
RASL10B	RAS-like_family 10_member B	5.91378	2.56408	3.58E-48
TNFRSF18	tumor necrosis factor receptor superfamily_member 18	5.91054	2.56329	6.13E-10
ADAM19	ADAM metallopeptidase domain 19	5.90493	2.56192	3.09E-75
LOC400863	NA	5.90477	2.56188	0.00776
MLLT11	myeloid/lymphoid or mixed-lineage leukemia; translocated to_11	5.89863	2.56038	4.89E-56
NAV2	neuron navigator 2	5.89552	2.55962	5.06E-31
UPK1B	uroplakin 1B	5.88932	2.5581	0.001333
CORO1A	coronin_actin binding protein_1A	5.87232	2.55393	2.46E-16
AQP3	aquaporin 3 (Gill blood group)	5.86447	2.552	1.66E-18
OLFML2A	olfactomedin-like 2A	5.84118	2.54626	1.29E-12
CBX2	chromobox homolog 2	5.83693	2.54521	1.72E-76
KIT	v-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog	5.83693	2.54521	4.23E-07
CSDC2	cold shock domain containing C2_RNA binding	5.83673	2.54516	5.32E-26

TABLE 3-continued

Genes more highly expressed in HMCs compared with BM-MSCs				
Gene Name	Description	Fold Change	Log Fold Change	p-Adj
CXorf28	long intergenic non-protein coding RNA 1546	5.83592	2.54496	0.000425
TBX5	T-box 5	5.82909	2.54327	0.002357
CDKL2	cyclin-dependent kinase-like 2 (CDC2-related kinase)	5.82222	2.54157	3.15E-06
TLE4	transducin-like enhancer of split 4	5.79352	2.53444	7.60E-234
BRSK2	BR serine/threonine kinase 2	5.79187	2.53403	2.45E-11
MIR1206	microRNA 1206	5.79059	2.53371	0.009759
CHRNAS5	cholinergic receptor_nicotinic_alpha 5 (neuronal)	5.76748	2.52794	4.07E-05
DLL3	delta-like 3 (Drosophila)	5.75549	2.52494	9.19E-08
IL1B	interleukin 1_beta	5.73006	2.51855	4.35E-05
CDK18	cyclin-dependent kinase 18	5.69833	2.51054	2.31E-08
PODN	podocan	5.69782	2.51041	2.97E-22
MEIS2	Meis homeobox 2	5.69502	2.5097	9.78E-81
SLC35F2	solute carrier family 35_member F2	5.68338	2.50675	2.12E-11
MAP3K7CL	MAP3K7 C-terminal like	5.6811	2.50617	6.77E-23
LTK	leukocyte receptor tyrosine kinase	5.67763	2.50529	0.000247
FILIP1L	filamin A interacting protein 1-like	5.66777	2.50278	9.35E-14
CASC8	cancer susceptibility candidate 8 (non-protein coding)	5.664	2.50182	0.003796
ADM5	adrenomedullin 5 (putative)	5.64225	2.49627	4.68E-07
UNC13A	unc-13 homolog A (C. elegans)	5.61934	2.4904	4.82E-06
ZNF702P	zinc finger protein 702_pseudogene	5.57754	2.47963	1.14E-08
TFEC	transcription factor EC	5.56777	2.4771	0.006309
MAML3	mastermind-like transcriptional coactivator 3	5.55493	2.47377	2.57E-13
STMN3	stathmin-like 3	5.53717	2.46915	6.59E-20
GRIP2	glutamate receptor interacting protein 2	5.51064	2.46222	0.0023
RHOU	ras homolog family member U	5.50972	2.46198	2.42E-08
POU2F2	POU class 2 homeobox 2	5.49592	2.45836	9.51E-29
PMAIP1	phorbol-12-myristate-13-acetate-induced protein 1	5.49059	2.45696	3.86E-10
FRMD5	FERM domain containing 5	5.48929	2.45662	7.37E-40
PTN	pleiotrophin	5.48074	2.45437	1.09E-11
LOC101929555	uncharacterized LOC101929555	5.45251	2.44692	0.004989
ASRGL1	asparaginase like 1	5.44303	2.44441	7.07E-16
AZU1	azurocidin 1	5.43654	2.44269	0.000389
LINC00319	long intergenic non-protein coding RNA 319	5.4347	2.4422	0.002249
ST3GAL5	ST3 beta-galactoside alpha-2_3-sialyltransferase 5	5.43357	2.4419	3.42E-46
GDF6	growth differentiation factor 6	5.4242	2.43941	1.21E-06
MTRNR2L10	MT-RNR2-like 10	5.42292	2.43907	0.002039
CSRP2	cysteine and glycine-rich protein 2	5.41166	2.43607	2.13E-32
PRSS35	protease_serine_35	5.40914	2.4354	4.82E-10
CDCA7	cell division cycle associated 7	5.39476	2.43156	1.46E-12
RPS6KA1	ribosomal protein S6 kinase_90 kDa_polypeptide 1	5.38501	2.42895	1.51E-94
RUND3B	RUN domain containing 3B	5.34867	2.41918	2.30E-05
RGS2	regulator of G-protein signaling 2	5.34004	2.41685	3.99E-54
KRTAP5-1	keratin associated protein 5-1	5.33882	2.41652	0.006121
LINC01358	long intergenic non-protein coding RNA 1358	5.33737	2.41613	0.000225
PLS1	plastin 1	5.33723	2.41609	8.64E-12
RASGRP2	RAS guanyl releasing protein 2 (calcium and DAG-regulated)	5.33552	2.41563	2.81E-05
ALOXE3	arachidonate lipooxygenase 3	5.32968	2.41405	1.76E-06
TNFRSF21	tumor necrosis factor receptor superfamily_member 21	5.3223	2.41205	5.50E-09
SYNGR1	synaptogyrin 1	5.29258	2.40397	9.94E-21
RGS9	regulator of G-protein signaling 9	5.27003	2.39781	0.007409
ZMYND8	zinc finger_MYND-type containing 8	5.25281	2.39309	4.51E-28
CASS4	Cas scaffolding protein family member 4	5.25179	2.39281	0.001735
C20orf166-AS1	C20orf166 antisense RNA 1	5.23613	2.3885	0.002467
FGFR4	fibroblast growth factor receptor 4	5.22833	2.38635	7.16E-06
MARCKSL1	MARCKS-like 1	5.22101	2.38433	4.46E-162
TMEM179	transmembrane protein 179	5.21053	2.38143	0.006078
NPAS2	neuronal PAS domain protein 2	5.18732	2.37499	7.68E-06
LPPR4	lipid phosphate phosphatase-related protein type 4	5.15317	2.36546	3.99E-05
RGS20	regulator of G-protein signaling 20	5.15188	2.3651	5.03E-27
RPL13AP20	ribosomal protein L13a pseudogene 20	5.14696	2.36372	9.02E-08

TABLE 3-continued

Genes more highly expressed in HMCs compared with BM-MSCs				
Gene Name	Description	Fold Change	Log Fold Change	p-Adj
GPCR5C	G protein-coupled receptor_class C_group 5_member C	5.13644	2.36077	1.12E-15
PARD6G	par-6 family cell polarity regulator gamma	5.11031	2.35341	9.22E-67
SLC7A14	solute carrier family 7_member 14	5.09623	2.34943	4.24E-08
NES	nestin	5.09319	2.34857	4.94E-05
CADM4	cell adhesion molecule 4	5.07578	2.34363	4.33E-30
EBF4	early B-cell factor 4	5.07114	2.34231	4.29E-07
MEIS1-AS3	MEIS1 antisense RNA 3	5.0691	2.34173	0.006678
LYPD1	LY6/PLAUR domain containing 1	5.06204	2.33972	9.67E-12
DMRTA1	DMRT-like family A1	5.04649	2.33528	0.000332
MKRN7P	makorin ring finger protein 7_pseudogene	5.02265	2.32845	0.001418
CHRNB2	cholinergic receptor_nicotinic_beta 2 (neuronal)	5.0166	2.32671	0.002487
RTN4R	reticulon 4 receptor	5.01187	2.32535	1.61E-06
NUTM2G	NUT family member 2G	5.0032	2.32285	8.01E-13

TABLE 4

Genes more highly expressed in BM MSCs compared with HMCs				
Gene Name	Description	Fold Change	Log Fold Change	p-Adj
MEG3	maternally expressed 3 (non-protein coding)	-35629.9	-15.1208	7.46E-116
FLG	filaggrin	-6300.72	-12.6213	1.68E-64
DYNLT3	dynein_light_chain_Tctex-type 3	-4479.74	-12.1292	2.88E-63
CAT	catalase	-4286.84	-12.0657	2.94E-75
EMX2OS	EMX2 opposite strand/antisense RNA	-2329.98	-11.1861	5.58E-51
EYA2	EYA transcriptional coactivator and phosphatase 2	-2121.1	-11.0506	2.10E-69
CTSF	cathepsin F	-2093.35	-11.0316	1.29E-47
IRX3	iroquois homeobox 3	-2000.16	-10.9659	6.67E-128
FNDC1	fibronectin type III domain containing 1	-1635.26	-10.6753	1.84E-202
EMX2	empty spiracles homeobox 2	-1529.98	-10.5793	4.66E-55
EN1	engrailed homeobox 1	-1434.27	-10.4861	2.82E-42
COMP	cartilage oligomeric matrix protein	-1343.15	-10.3914	1.95E-89
S100A6	S100 calcium binding protein A6	-1267.09	-10.3073	1.14E-203
TEKT4P2	tektin 4 pseudogene 2	-1262.44	-10.302	1.48E-38
HSPB2	heat shock 27 kDa protein 2	-1165.07	-10.1862	1.34E-39
GSTT1	glutathione S-transferase theta 1	-1164.58	-10.1856	1.18E-39
LYNX1	Ly6/neurotoxin 1	-1153.42	-10.1717	4.51E-38
NFASC	neurofascin	-1132.03	-10.1447	3.32E-253
LINC00839	long intergenic non-protein coding RNA 839	-1026.77	-10.0039	1.19E-37
ZNF662	zinc finger protein 662	-965.023	-9.91442	9.55E-46
BHMT2	betaine-homocysteine S-methyltransferase 2	-925.315	-9.8538	5.90E-36
SCUBE1	signal peptide_CUB domain_EGF-like 1	-872.185	-9.76849	1.92E-39
FGFR2	fibroblast growth factor receptor 2	-810.535	-9.66273	1.40E-137
ANKRD20A5P	ankyrin repeat domain 20 family_member A5_pseudogene	-768.537	-9.58597	4.90E-33
CES1	carboxylesterase 1	-764.679	-9.57871	5.24E-33
CHI3L1	chitinase 3-like 1 (cartilage glycoprotein-39)	-703.37	-9.45814	8.98E-130
FLG-AS1	FLG antisense RNA 1	-667.864	-9.38341	1.10E-29
ISLR	immunoglobulin superfamily containing leucine-rich repeat	-627.765	-9.29408	0.00E+00
LOC400043	uncharacterized LOC400043	-617.438	-9.27015	6.34E-56
LINC01133	long intergenic non-protein coding RNA 1133	-608.212	-9.24843	8.34E-91
CYP4F35P	cytochrome P450_family 4_subfamily F_polypeptide 35_pseudogene	-601.512	-9.23245	4.19E-29
GREM2	gremlin 2_DAN family BMP antagonist	-598.256	-9.22462	2.08E-126
ANKRD30B	ankyrin repeat domain 30B	-579.225	-9.17798	1.31E-29
PPP1R14C	protein phosphatase 1_regulatory (inhibitor) subunit 14C	-552.557	-9.10998	2.51E-29
FPR1	formyl peptide receptor 1	-489.04	-8.93381	3.56E-27
LINC01268	long intergenic non-protein coding RNA 1268	-449.046	-8.81072	1.71E-74
KRT14	keratin 14_type I	-443.758	-8.79363	7.01E-63
TDRD9	tudor domain containing 9	-436.358	-8.76937	6.87E-26
ZNF300P1	zinc finger protein 300 pseudogene 1 (functional)	-420.677	-8.71657	1.01E-30

TABLE 4-continued

Genes more highly expressed in BM MSCs compared with HMCs				
Gene Name	Description	Fold Change	Log Fold Change	p-Adj
FAM225A	family with sequence similarity 225_member A (non-protein coding)	-400.542	-8.64581	1.47E-25
FAM180A	family with sequence similarity 180_member A	-380.312	-8.57104	7.93E-67
CCDC36	coiled-coil domain containing 36	-352.867	-8.46298	4.80E-24
CH25H	cholesterol 25-hydroxylase	-352.664	-8.46215	1.70E-23
CCKAR	cholecystokinin A receptor	-324.76	-8.34323	2.32E-22
KRBOX1	KRAB box domain containing 1	-322.749	-8.33427	4.54E-23
CCDC144B	coiled-coil domain containing 144B (pseudogene)	-315.525	-8.30161	6.20E-23
LINC00856	long intergenic non-protein coding RNA 856	-313.304	-8.29142	9.69E-23
CSTA	cystatin A (stefin A)	-310.748	-8.2796	1.38E-47
FAM225B	family with sequence similarity 225_member B (non-protein coding)	-301.418	-8.23562	2.28E-22
LINC00865	long intergenic non-protein coding RNA 865	-301.073	-8.23397	2.20E-22
CMKLR1	chemerin chemokine-like receptor 1	-281.601	-8.13751	4.31E-19
ENPP2	ectonucleotide pyrophosphatase/phosphodiesterase 2	-271.077	-8.08256	3.42E-71
FMOD	fibromodulin	-269.205	-8.07256	3.90E-23
SDR42E1	short chain dehydrogenase/reductase family 42E_member 1	-252.017	-7.97738	2.21E-20
ITGBL1	integrin_beta-like 1 (with EGF-like repeat domains)	-244.002	-7.93075	6.52E-295
IBSP	integrin-binding sialoprotein	-240.491	-7.90984	1.41E-19
FAM20A	family with sequence similarity 20_member A	-235.186	-7.87766	1.62E-85
MKRN3	makorin ring finger protein 3	-228.014	-7.83298	1.04E-19
NKAPL	NFKB activating protein-like	-218.076	-7.76869	2.56E-19
C5orf63	chromosome 5 open reading frame 63	-214.955	-7.74789	2.78E-24
MYBPH	myosin binding protein H	-214.733	-7.7464	6.31E-26
CPXM2	carboxypeptidase X (M14 family)_member 2	-211.34	-7.72342	4.82E-22
CECR7	cat eye syndrome chromosome region_candidate 7 (non-protein coding)	-207.364	-7.69602	2.50E-18
PCDHGB3	protocadherin gamma subfamily B_3	-206.449	-7.68964	2.56E-18
LINC00968	long intergenic non-protein coding RNA 968	-205.155	-7.68057	1.65E-129
FAM66B	family with sequence similarity 66_member B	-202.202	-7.65965	3.81E-18
PENK	proenkephalin	-200.898	-7.65032	3.99E-22
KIAA1644	KIAA1644	-194.503	-7.60365	9.45E-107
MEOX2	mesenchyme homeobox 2	-193.912	-7.59926	3.51E-16
COX7A1	cytochrome c oxidase subunit VIIa polypeptide 1 (muscle)	-191.832	-7.5837	2.42E-46
LOC284757	NA	-189.246	-7.56412	1.36E-21
SGCD	sarcoglycan_delta (35 kDa dystrophin-associated glycoprotein)	-183.534	-7.5199	1.79E-85
DDX43	DEAD (Asp-Glu-Ala-Asp) box polypeptide 43	-181.828	-7.50643	9.97E-20
LOC101927642	N	-181.224	-7.50163	3.36E-22
LRRK2	leucine-rich repeat kinase 2	-180.898	-7.49903	1.38E-17
NUPR1	nuclear protein_transcriptional regulator_1	-178.489	-7.47969	8.60E-126
LOC101929369	NA	-157.878	-7.30267	7.09E-25
DLX6-AS1	DLX6 antisense RNA 1	-154.645	-7.27282	2.04E-21
PCDHGA3	protocadherin gamma subfamily A_3	-154.162	-7.2683	5.13E-16
HAS1	hyaluronan synthase 1	-153.647	-7.26348	9.36E-40
M1AP	meiosis 1 associated protein	-150.851	-7.23698	9.94E-21
HLA-DPA1	major histocompatibility complex_class II_DP alpha 1	-147.269	-7.20231	3.20E-14
DNAJA4	DnaJ (Hsp40) homolog_subfamily A_member 4	-142.774	-7.15759	3.81E-82
PCDHGA12	protocadherin gamma subfamily A_12	-142.64	-7.15623	3.66E-41
MEG8	maternally expressed 8 (non-protein coding)	-142.207	-7.15185	1.69E-15
KRT16	keratin 16_type I	-140.972	-7.13926	3.82E-67
NRXN2	neurexin 2	-140.865	-7.13817	6.15E-187
PTGES	prostaglandin E synthase	-140.439	-7.1338	0.00E+00
C5AR2	complement component 5a receptor 2	-139.462	-7.12373	4.43E-15
ECM2	extracellular matrix protein 2_female organ and adipocyte specific	-138.933	-7.11825	6.04E-93
FGF7	fibroblast growth factor 7	-138.746	-7.1163	5.19E-71
SLC39A4	solute carrier family 39 (zinc transporter)_member 4	-138.362	-7.1123	7.14E-41
OAS2	2'-5'-oligoadenylate synthetase 2_69/71 kDa	-136.733	-7.09522	2.01E-31
HOXC-AS1	HOXC cluster antisense RNA 1	-135.946	-7.08689	8.21E-20
LINC00506	long intergenic non-protein coding RNA 506	-135.81	-7.08545	3.96E-15
CRYAB	crystallin_alpha B	-133.344	-7.05901	0.00E+00
CKM	creatine kinase_muscle	-131.62	-7.04023	5.91E-15

TABLE 4-continued

Genes more highly expressed in BM MSCs compared with HMCs				
Gene Name	Description	Fold Change	Log Fold Change	p-Adj
HYDIN	HYDIN_axonemal central pair apparatus protein	-130.426	-7.02709	8.10E-26
CYP1B1	cytochrome P450_family 1_subfamily B_polypeptide 1	-128.476	-7.00536	6.34E-95
LINC01018	long intergenic non-protein coding RNA 1018	-126.369	-6.9815	7.56E-52
NAALADL1	N-acetylated alpha-linked acidic dipeptidase-like 1	-126.097	-6.97839	8.44E-96
FMO3	flavin containing monooxygenase 3	-125.887	-6.97599	2.41E-17
KCNJ15	potassium channel_inwardly rectifying subfamily J_member 15	-125.648	-6.97324	5.50E-29
KRT34	keratin 34_type I	-123.593	-6.94945	1.45E-238
LSP1	lymphocyte-specific protein 1	-123.36	-6.94673	1.62E-77
ADAMTSL3	ADAMTS-like 3	-122.924	-6.94162	2.78E-14
LOC101927740	uncharacterized LOC101927740	-122.513	-6.93679	4.46E-31
LOC441666	zinc finger protein 91 pseudogene	-121.086	-6.91989	3.57E-14
LINC01114	long intergenic non-protein coding RNA 1114	-120.579	-6.91384	4.38E-14
SPESP1	sperm equatorial segment protein 1	-118.239	-6.88556	3.68E-13
LTF	lactotransferrin	-116.299	-6.8617	9.29E-14
ZNF572	zinc finger protein 572	-113.357	-6.82473	8.77E-14
ENPP4	ectonucleotide pyrophosphatase/phosphodiesterase 4 (putative)	-112.876	-6.81859	4.04E-25
ANKRD29	ankyrin repeat domain 29	-111.733	-6.80391	3.07E-41
ZNF736	zinc finger protein 736	-110.633	-6.78964	1.31E-13
COL10A1	collagen_type_X_alpha 1	-104.652	-6.70945	4.29E-16
DDO	D-aspartate oxidase	-103.847	-6.69832	4.62E-13
LOC400644	NA	-103.675	-6.69592	3.54E-13
PID1	phosphotyrosine interaction domain containing 1	-103.642	-6.69546	9.95E-50
LINC00654	long intergenic non-protein coding RNA 654	-103.64	-6.69544	6.70E-33
INSRR	insulin receptor-related receptor	-101.301	-6.6625	9.58E-13
FOXQ1	forkhead box Q1	-100.715	-6.65413	1.23E-12
LOC150381	NA	-100.34	-6.64875	1.90E-34
CRLF1	cytokine receptor-like factor 1	-98.9591	-6.62876	1.19E-124
ZNF208	zinc finger protein 208	-98.7165	-6.62522	1.48E-12
HOXD8	homeobox D8	-97.5297	-6.60777	1.81E-139
ZNF454	zinc finger protein 454	-97.3285	-6.60479	8.60E-21
GPNMB	glycoprotein (transmembrane) nmb	-97.0778	-6.60107	1.59E-129
NDNF	neuron-derived neurotrophic factor	-95.3473	-6.57512	1.41E-64
KRTAP1-5	keratin associated protein 1-5	-94.974	-6.56946	6.22E-138
HTR1F	5-hydroxytryptamine (serotonin) receptor 1F_G protein-coupled	-94.3421	-6.55983	1.89E-12
ZFP3	ZFP3 zinc finger protein	-93.8497	-6.55228	1.48E-85
FGF14	fibroblast growth factor 14	-93.5198	-6.5472	3.27E-59
HOXD-AS2	HOXD cluster antisense RNA 2	-92.3698	-6.52935	5.39E-47
FAM106A	family with sequence similarity 106_member A	-90.6541	-6.5023	3.74E-12
SFRP2	secreted frizzled-related protein 2	-90.2641	-6.49608	6.67E-12
WISP3	WNT1 inducible signaling pathway protein 3	-89.3459	-6.48133	1.32E-29
SORBS2	sorbin and SH3 domain containing 2	-85.5325	-6.4184	1.14E-65
HRNR	hornerin	-85.3134	-6.4147	1.35E-11
ANGPT4	angiopoietin 4	-85.0978	-6.41105	2.39E-14
PSG5	pregnancy specific beta-1-glycoprotein 5	-83.3795	-6.38162	4.75E-178
HOXD3	homeobox D3	-82.3393	-6.36351	2.07E-25
PAPPA2	pappalysin 2	-81.7037	-6.35233	2.07E-13
LOC728819	NA	-81.3742	-6.3465	1.77E-11
TGFA	transforming growth factor_alpha	-80.5845	-6.33243	4.10E-11
DEPTOR	DEP domain containing MTOR-interacting protein	-77.9318	-6.28414	2.95E-62
DMGDH	dimethylglycine dehydrogenase	-77.6697	-6.27928	4.55E-26
PTGDR	prostaglandin D2 receptor (DP)	-77.4445	-6.27509	4.87E-11
LOC102724678	NA	-77.2241	-6.27098	4.89E-14
C20orf197	chromosome 20 open reading frame 197	-75.3602	-6.23573	3.84E-36
RUNX3	runt-related transcription factor 3	-75.1822	-6.23232	5.89E-122
IRX5	iroquois homeobox 5	-75.1677	-6.23204	1.97E-163
TAS1R1	taste receptor_type 1_member 1	-75.1036	-6.23081	5.60E-11
ELANE	elastase_neutrophil expressed	-74.1873	-6.2131	8.13E-11
NINJ2	ninjurin 2	-72.5478	-6.18086	1.67E-36
FAM198A	family with sequence similarity 198_member A	-72.4965	-6.17984	1.80E-10
CXADR3	coxsackie virus and adenovirus receptor pseudogene 3	-72.3675	-6.17727	1.33E-10

TABLE 4-continued

Genes more highly expressed in BM MSCs compared with HMCs				
Gene Name	Description	Fold Change	Log Fold Change	p-Adj
COL14A1	collagen type XIV_alpha 1	-72.2227	-6.17438	1.61E-32
CLEC3B	C-type lectin domain family 3_member B	-71.9035	-6.16799	2.18E-42
TMEM178B	transmembrane protein 178B	-71.2387	-6.15459	3.10E-19
ITIHS	inter-alpha-trypsin inhibitor heavy chain family_member 5	-71.1864	-6.15353	5.61E-10
PRPH2	peripherin 2 (retinal degeneration_slow)	-70.98	-6.14934	4.07E-39
ELN	elastin	-70.9303	-6.14833	1.39E-152
KCTD12	potassium channel tetramerization domain containing 12	-70.8271	-6.14623	1.23E-114
DOK5	docking protein 5	-70.5136	-6.13983	1.22E-40
LOC100287846	patched 1 pseudogene	-70.372	-6.13693	1.78E-10
PTPN20B	protein tyrosine phosphatase_non-receptor type 20	-70.0489	-6.13029	1.79E-10
WISP2	WNT1 inducible signaling pathway protein 2	-69.2811	-6.11439	4.45E-40
DLX3	distal-less homeobox 3	-66.5059	-6.05541	1.41E-18
CCDC89	coiled-coil domain containing 89	-66.2524	-6.0499	1.20E-23
FPR2	formyl peptide receptor 2	-66.0346	-6.04515	3.24E-10
ITGB2	integrin_beta 2 (complement component 3 receptor 3 and 4 subunit)	-65.6849	-6.03749	1.16E-93
PPAPDC3	phosphatidic acid phosphatase type 2 domain containing 3	-65.2393	-6.02767	1.66E-153
ELOVL3	ELOVL fatty acid elongase 3	-65.1824	-6.02641	1.24E-28
SERPING1	serpin peptidase inhibitor_clade G (C1 inhibitor)_member 1	-64.6895	-6.01546	7.96E-157
ST8SIA1	ST8 alpha-N-acetyl-neuraminate alpha-2_8-sialyltransferase 1	-62.1154	-5.95688	1.66E-16
PCDHGA4	protocadherin gamma subfamily A_4	-61.6851	-5.94685	6.57E-22
TP53TG3D	TP53 target 3D	-61.6052	-5.94498	1.08E-09
PRSS30P	protease_serine_30_pseudogene	-61.4529	-5.94141	8.51E-10
GSTM5	glutathione S-transferase mu 5	-61.3317	-5.93856	5.36E-13
P2RY6	pyrimidinergic receptor P2Y_G-protein coupled_6	-60.6271	-5.92189	1.09E-69
EGFLAM	EGF-like_fibronectin type III and laminin G domains	-60.2517	-5.91293	5.44E-38
TNFRSF11B	tumor necrosis factor receptor superfamily_member 11b	-59.9164	-5.90488	1.45E-102
ALS2CR11	amyotrophic lateral sclerosis 2 (juvenile) chromosome region_candidate 11	-59.6645	-5.8988	8.62E-50
USP32P2	ubiquitin specific peptidase 32 pseudogene 2	-59.5653	-5.8964	1.88E-39
KRT81	keratin 81_type II	-59.3033	-5.89004	3.27E-15
DCHS2	dachshous cadherin-related 2	-59.2162	-5.88792	2.11E-11
XG	Xg blood group	-59.1707	-5.88681	2.16E-69
MAFB	v-maf avian musculoaponeurotic fibrosarcoma oncogene homolog B	-58.753	-5.87659	9.71E-55
LIPC	lipase_hepatic	-57.1242	-5.83603	1.35E-09
ZNF439	zinc finger protein 439	-56.9337	-5.83121	8.44E-49
SLC22A15	solute carrier family 22_member 15	-56.5498	-5.82145	6.31E-63
TDRD1	tudor domain containing 1	-56.2293	-5.81325	5.08E-09
GRM6	glutamate receptor_metabotropic 6	-56.1432	-5.81104	2.31E-11
P2RY2	purinergic receptor P2Y_G-protein coupled_2	-55.9967	-5.80727	1.68E-34
ACSM5	acyl-CoA synthetase medium-chain family member 5	-55.4867	-5.79407	2.02E-09
SPAG17	sperm associated antigen 17	-55.2572	-5.78809	2.69E-16
LOC101927468	uncharacterized LOC101927468	-54.9269	-5.77944	2.23E-09
SYT8	synaptotagmin VIII	-53.8752	-5.75155	2.03E-16
HOXC4	homeobox C4	-53.6672	-5.74597	6.76E-89
HOXC10	homeobox C10	-52.9838	-5.72748	1.87E-217
SNORD114-10	small nucleolar RNA C/D box 114-10	-52.8042	-5.72258	4.03E-09
BARX1	BARX homeobox 1	-52.6707	-5.71893	1.83E-10
LINC00664	long intergenic non-protein coding RNA 664	-52.6383	-5.71804	8.69E-09
RGL3	ral guanine nucleotide dissociation stimulator-like 3	-52.0505	-5.70184	3.35E-52
ZNF257	zinc finger protein 257	-51.9283	-5.69845	1.02E-08
AKR1C2	aldo-keto reductase family 1_member C2	-51.819	-5.69541	9.97E-51
HCAR1	hydroxycarboxylic acid receptor 1	-51.5214	-5.6871	1.14E-08
ZDHHC15	zinc_finger_DHHC-type containing 15	-51.0571	-5.67404	1.28E-08
HSPB7	heat shock 27 kDa protein family_member 7 (cardiovascular)	-50.9821	-5.67192	1.96E-97
IFI44L	interferon-induced protein 44-like	-50.8431	-5.66798	3.99E-46
POMC	proopiomelanocortin	-50.2343	-5.6506	4.12E-10
DLX5	distal-less homeobox 5	-50.0851	-5.64631	3.03E-53
EPGN	epithelial mitogen	-48.8136	-5.60921	2.21E-36

TABLE 4-continued

Genes more highly expressed in BM MSCs compared with HMCs				
Gene Name	Description	Fold Change	Log Fold Change	p-Adj
HAGLR	HOXD antisense growth-associated long non-coding RNA	-47.4406	-5.56805	2.98E-24
NOTUM	notum pectinacetyl esterase homolog (<i>Drosophila</i>)	-47.2843	-5.56329	7.00E-23
ISM1	isthmin 1_angiogenesis inhibitor	-46.9645	-5.5535	1.98E-17
SFRP4	secreted frizzled-related protein 4	-46.9411	-5.55278	4.74E-13
DLX6	distal-less homeobox 6	-46.9268	-5.55234	7.46E-74
CCL28	chemokine (C-C motif) ligand 28	-46.8501	-5.54998	7.28E-19
APBB1IP	amyloid beta (A4) precursor protein-binding family B_member 1 interacting protein	-46.7936	-5.54824	3.06E-66
NRN1	neuritin 1	-46.7933	-5.54823	2.76E-96
ATP1A2	ATPase_Na+/K+ transporting_alpha 2 polypeptide	-45.6518	-5.5126	6.32E-08
SLC2A5	solute carrier family 2 (facilitated glucose/fructose transporter)_member 5	-45.6069	-5.51118	2.46E-27
SAMD9L	sterile alpha motif domain containing 9-like epiphycan	-45.4488	-5.50617	7.48E-108
EPYC	RAS (RAD and GEM)-like GTP-binding 1	-45.3506	-5.50305	2.66E-08
REM1	cytochrome P450_family 19_subfamily A_polypeptide 1	-45.0583	-5.49372	3.23E-08
CYP19A1	cytochrome P450_family 19_subfamily A_polypeptide 1	-45.004	-5.49198	2.28E-08
SEPSECS-AS1	SEPSECS antisense RNA 1 (head to head)	-44.8986	-5.4886	2.63E-08
IFI30	interferon_gamma-inducible protein 30	-43.4309	-5.44065	2.99E-288
HOXC5	homeobox C5	-43.3641	-5.43843	2.23E-39
TMEM233	transmembrane protein 233	41.9538	-5.39073	1.91E-07
METTL7B	methyltransferase like 7B	-41.948	-5.39053	1.51E-23
DOK7	docking protein 7	-41.8052	-5.38561	2.21E-15
TNNT3	troponin T type 3 (skeletal_fast)	-41.6502	-5.38025	4.62E-16
LINC00944	long intergenic non-protein coding RNA 944	-41.6467	-5.38013	9.97E-08
HOXC8	homeobox C8	-40.9363	-5.35531	2.64E-147
RBP4	retinol binding protein 4_plasma	-40.7777	-5.34971	4.34E-23
FAM27A	family with sequence similarity 27_member C	-40.5416	-5.34133	7.17E-08
KRT86	keratin 86_type II	-40.3929	-5.33603	3.14E-18
IFI44	interferon-induced protein 44	-40.0664	-5.32432	2.25E-105
LCNL1	lipocalin-like 1	-39.8641	-5.31702	5.71E-20
HRCT1	histidine rich carboxyl terminus 1	-39.6602	-5.30962	4.53E-64
APOL1	apolipoprotein L_1	-39.6399	-5.30888	7.88E-165
ZIC4	Zic family member 4	-39.6291	-5.30849	4.67E-17
HCG4	HLA complex group 4 (non-protein coding)	-39.4647	-5.30249	1.68E-07
MRAP2	melanocortin 2 receptor accessory protein 2	-39.3374	-5.29783	1.34E-11
CABP1	calcium binding protein 1	-39.2854	-5.29592	3.55E-09
LOC100133445	NA	-39.1418	-5.29064	1.58E-07
SYN3	synapsin III	-39.0654	-5.28782	1.56E-07
C11orf70	chromosome 11 open reading frame 70	-38.8235	-5.27886	1.39E-124
LINC00482	long intergenic non-protein coding RNA 482	-38.7606	-5.27652	1.27E-07
ADAMTS5	ADAM metallopeptidase with thrombospondin type 1 motif 5	-37.5963	-5.23252	3.03E-51
APOC3	apolipoprotein C-III	-37.5229	-5.2297	2.14E-07
ERG	v-ets avian erythroblastosis virus E26 oncogene homolog	-37.4574	-5.22718	3.45E-16
PCDHGA6	protocadherin gamma subfamily A_6	-37.3744	-5.22398	2.20E-28
CIITA	class II_major histocompatibility complex_transactivator	-37.3343	-5.22243	9.56E-09
ADIRF	adipogenesis regulatory factor	-37.096	-5.21319	1.00E-21
SP7	Sp7 transcription factor	-36.5771	-5.19287	5.75E-07
PEG3	paternally expressed 3	-36.3802	-5.18508	3.42E-07
BHMT	betaine--homocysteine S-methyltransferase	-36.3023	-5.18199	3.42E-07
RARRES3	retinoic acid receptor responder (tazarotene induced) 3	-36.2603	-5.18032	3.07E-34
ERMN	ermn_ERM-like protein	-36.1008	-5.17396	6.53E-41
KRTAP1-1	keratin associated protein 1-1	-35.9286	-5.16706	3.30E-74
ABI3BP	ABI family_member 3 (NESH) binding protein	-35.9144	-5.16649	7.26E-68
ALX1	ALX homeobox 1	-35.5028	-5.14986	7.73E-28
HOMER2	homer scaffolding protein 2	-35.447	-5.14759	7.88E-50
HSD17B7P2	hydroxysteroid (17-beta) dehydrogenase 7 pseudogene 2	-35.1909	-5.13713	4.15E-18
IFITM10	interferon induced transmembrane protein 10	-35.0208	-5.13014	7.03E-87
PSG1	pregnancy specific beta-1-glycoprotein 1	-34.8641	-5.12367	1.04E-06
ASTL	astacin-like metallo-endopeptidase (M12 family)	-34.4342	-5.10577	1.51E-08
CTLA4	cytotoxic T-lymphocyte-associated protein 4	-34.2089	-5.0963	3.13E-10

TABLE 4-continued

Genes more highly expressed in BM MSCs compared with HMCs				
Gene Name	Description	Fold Change	Log Fold Change	p-Adj
TNFAIP8L3	tumor necrosis factor_alpha-induced protein 8-like 3	-34.1767	-5.09494	2.09E-38
CSF2RB	colony stimulating factor 2 receptor_beta_low-affinity (granulocyte-macrophage)	-34.0391	-5.08912	1.02E-25
SUSD3	sushi domain containing 3	-33.8605	-5.08153	4.41E-21
KLF8	Kruppel-like factor 8	-33.676	-5.07365	6.76E-09
KLF4	Kruppel-like factor 4 (gut)	-33.4045	-5.06197	3.52E-163
HAS2	hyaluronan synthase 2	-33.3869	-5.06121	1.19E-56
LOC100132891	NA	-33.1397	-5.05049	2.09E-48
EYA4	EYA transcriptional coactivator and phosphatase 4	-33.1124	-5.0493	5.02E-18
LOC100996609	NA	-33.0553	-5.04681	3.10E-06
C16orf54	chromosome 16 open reading frame 54	-32.8202	-5.03651	8.70E-07
ITGB2-AS1	ITGB2 antisense RNA 1	-32.6077	-5.02714	1.02E-25
LINC00884	long intergenic non-protein coding RNA 884	-32.4197	-5.0188	7.78E-09
PCDHGA7	protocadherin gamma subfamily A_7	-32.4112	-5.01842	3.70E-20
TMEM155	transmembrane protein 155	-31.9076	-4.99583	7.65E-43
ITGAL	integrin_alpha L (antigen CD11A (p180)_lymphocyte function-associated antigen 1; alpha polypeptide)	-31.8094	-4.99138	1.12E-06
SIX2	SIX homeobox 2	-31.7605	-4.98916	1.28E-134
ABCA8	ATP-binding cassette_sub-family A (ABC1)_member 8	-31.5103	-4.97775	1.79E-37
ZNF578	zinc finger protein 578	-30.6722	-4.93886	6.76E-29
OOEP	oocyte expressed protein	-30.5166	-4.93152	3.47E-06
DUXAP10	double homeobox A pseudogene 10	-30.303	-4.92139	4.16E-09
TEKT4	tektin 4	-29.2438	-4.87006	4.86E-06
SYNDIG1	synapse differentiation inducing 1	-29.2011	-4.86795	1.73E-31
ZIC1	Zic family member 1	-28.9793	-4.85695	8.42E-15
RFX8	RFX family member 8_lacking RFX DNA binding domain	-28.8092	-4.84846	4.93E-29
PTGDS	prostaglandin D2 synthase 21 kDa (brain)	-28.8045	-4.84822	2.95E-20
MR1	major histocompatibility complex_class I-related	-28.6716	-4.84155	3.59E-47
PCDHGA5	protocadherin gamma subfamily A_5	-28.5837	-4.83712	1.02E-25
LTBP2	latent transforming growth factor beta binding protein 2	-28.4538	-4.83055	7.30E-60
LINC00478	mir-99a-let-7c cluster host gene	-28.3982	-4.82773	5.37E-12
IL6	interleukin 6	-28.1909	-4.81716	7.58E-67
LINC00922	long intergenic non-protein coding RNA 922	-28.1849	-4.81685	7.58E-06
FBLN7	fibulin 7	-28.1669	-4.81593	8.77E-28
PAX8-AS1	PAX8 antisense RNA 1	-28.1127	-4.81315	9.03E-07
BRINP1	bone morphogenetic protein/retinoic acid inducible neural-specific 1	-28.0874	-4.81185	9.33E-111
IGJ	joining chain of multimeric IgA and IgM	-28.0393	-4.80938	5.41E-10
PCDHGA11	protocadherin gamma subfamily A_11	-28.0007	-4.80739	1.55E-40
KANK4	KN motif and ankyrin repeat domains 4	-27.9921	-4.80695	6.94E-06
C15orf54	chromosome 15 open reading frame 54	-27.7757	-4.79575	5.79E-13
ZNF492	zinc finger protein 492	-27.703	-4.79197	1.66E-07
SNTG2	syntrophin_gamma 2	-27.6039	-4.7868	5.38E-22
HOXC9	homeobox C9	-27.5876	-4.78595	9.32E-28
CPN2	carboxypeptidase N_polypeptide 2	-27.5662	-4.78483	2.28E-08
PP12613	uncharacterized LOC100192379	-27.2393	-4.76762	8.38E-08
ANGPTL1	angiopoietin-like 1	-27.2239	-4.7668	5.53E-11
PODNL1	podocan-like 1	-27.1105	-4.76078	3.88E-88
LOC101926935	uncharacterized LOC101926935	-27.0989	-4.76016	4.72E-06
LOC388849	uncharacterized LOC388849	-26.899	-4.74948	3.25E-48
CD300C	CD300c molecule	-26.7809	-4.74313	5.77E-06
ASB5	ankyrin repeat and SOCS box containing 5	-26.5086	-4.72839	1.84E-16
CCNYL2	cyclin Y-like 2_pseudogene	-26.4971	-4.72776	6.12E-06
ZFYVE28	zinc finger_FYVE domain containing 28	-26.4622	-4.72586	3.11E-64
SERINC2	serine incorporator 2	-26.3179	-4.71797	5.05E-126
COL15A1	collagen_type XV_alpha 1	-26.0413	-4.70273	9.51E-07
SLC30A3	solute carrier family 30 (zinc transporter)_member 3	-25.8968	-4.6947	2.23E-07
COL5A3	collagen_type V_alpha 3	-25.7264	-4.68518	1.17E-31
LOC100505718	NA	-25.717	-4.68465	7.80E-12
FLG2	filaggrin family member 2	-25.5466	-4.67506	1.48E-05
SYBU	syntabulin (syntaxin-interacting)	-25.4087	-4.66725	4.29E-21

TABLE 4-continued

Genes more highly expressed in BM MSCs compared with HMCs				
Gene Name	Description	Fold Change	Log Fold Change	p-Adj
LINC00578	long intergenic non-protein coding RNA 578	-25.2589	-4.65872	2.57E-07
SLC12A1	solute carrier family 12 (sodium/potassium/chloride transporter) _member 1	-25.254	-4.65844	9.59E-06
OASL	2'-5'-oligoadenylate synthetase-like	-25.1755	-4.65395	2.35E-07
OLAH	oleoyl-ACP hydrolase	-25.0589	-4.64725	8.67E-06
KRT9	keratin 9_type I	-25.0061	-4.64421	6.79E-07
PPAP2B	phosphatidic acid phosphatase type 2B	-24.7585	-4.62985	4.73E-24
TM4SF20	transmembrane 4 L six family member 20	-24.584	-4.61965	7.35E-16
PCDHGA2	protocadherin gamma subfamily A_2	-24.557	-4.61806	1.82E-17
AMPH	amphiphysin	-24.4871	-4.61395	3.66E-81
KCNK15	potassium channel_two pore domain subfamily K_member 15	-24.4564	-4.61214	2.64E-14
HOXA10-AS	HOXA10 antisense RNA	-24.4528	-4.61193	7.23E-30
INSC	inscuteable homolog (<i>Drosophila</i>)	-24.452	-4.61188	1.62E-05
MIR4257	microRNA 4257	-24.4166	-4.60979	1.11E-05
HOXC6	homeobox C6	-24.4007	-4.60885	1.41E-36
RTP4	receptor (chemosensory) transporter protein 4	-24.3581	-4.60633	1.95E-05
GAS1	growth arrest-specific 1	-24.0511	-4.58803	9.44E-50
EBF1	early B-cell factor 1	-23.9491	-4.5819	3.55E-143
SNTB1	syntrophin_beta 1 (dystrophin-associated protein A1_59 kDa_basic component 1)	-23.9123	-4.57968	1.73E-74
ANPEP	alanine (membrane) aminopeptidase	-23.8821	-4.57786	0.00E+00
C10orf105	chromosome 10 open reading frame 105	-23.8719	-4.57724	4.12E-07
PCDHGB1	protocadherin gamma subfamily B_1	-23.7715	-4.57116	4.31E-13
COMT	catechol-O-methyltransferase	-23.7198	-4.56802	8.63E-144
CYP7B1	cytochrome P450_family 7_subfamily B_poly peptide 1	-23.7073	-4.56726	5.30E-07
KLHL33	kelch-like family member 33	-23.6812	-4.56567	1.63E-05
KLHL13	kelch-like family member 13	-23.596	-4.56047	1.50E-44
RAET1E	retinoic acid early transcript 1E	-23.5653	-4.55859	1.34E-06
ABCC3	ATP-binding cassette_sub-family C (CFTR/MRP)_member 3	-23.5388	-4.55697	1.55E-32
PRR34	proline rich 34	-23.4808	-4.55341	5.23E-12
LOC100130992	uncharacterized LOC100130992	-23.2829	-4.5412	2.47E-26
ISLR2	immunoglobulin superfamily containing leucine-rich repeat 2	-23.2065	-4.53646	4.26E-05
PLAC9	placenta-specific 9	-23.1863	-4.5352	7.53E-79
ATE1-AS1	ATE1 antisense RNA 1	-22.9836	-4.52253	9.59E-06
ZMYND15	zinc finger_MYND-type containing 15	-22.9796	-4.52228	3.63E-15
PRL	prolactin	-22.9438	-4.52003	1.60E-05
GPAT2	glycerol-3-phosphate acyltransferase 2_mitochondrial	-22.8257	-4.51259	2.15E-15
SYT11	synaptotagmin XI	-22.6805	-4.50338	6.30E-20
RTN4RL1	reticulon 4 receptor-like 1	-22.6662	-4.50247	8.59E-07
PDK4	pyruvate dehydrogenase kinase_isozyme 4	-22.5842	-4.49724	6.18E-13
IGF1	insulin-like growth factor 1 (somatomedin C)	-22.4869	-4.49101	4.74E-21
COL8A2	collagen_type VIII_alpha 2	-22.4439	-4.48825	3.73E-22
C12orf56	chromosome 12 open reading frame 56	-22.4084	-4.48597	9.34E-08
CHRDLL2	chordin-like 2	-22.3783	-4.48403	1.55E-06
MIR10B	microRNA 10b	-22.2523	-4.47588	2.37E-05
IL18R1	interleukin 18 receptor 1	-22.2043	-4.47277	1.27E-08
OMD	osteomodulin	-22.1734	-4.47076	2.63E-05
C9orf170	chromosome 9 open reading frame 170	-22.1436	-4.46882	9.24E-07
HOXD4	homeobox D4	-22.1291	-4.46787	3.19E-29
LINC01060	long intergenic non-protein coding RNA 1060	-22.1154	-4.46698	4.42E-05
LOC100130539	NA	-22.0684	-4.46391	4.11E-14
ASPG	asparagine	-22.0317	-4.46151	3.52E-05
LOC729296	uncharacterized LOC729296	-21.9806	-4.45816	2.94E-05
SPATA41	spermatogenesis associated 41 (non-protein coding)	-21.9421	-4.45563	1.98E-06
LRRN4CL	LRRN4 C-terminal like	-21.936	-4.45523	4.64E-41
MYOC	myocilin_trabecular meshwork inducible glucocorticoid response	-21.9193	-4.45413	5.99E-05
POSTN	periostin_osteoblast specific factor	-21.9072	-4.45333	2.31E-13
FOXF2	forkhead box F2	-21.8768	-4.45133	2.78E-103
LYPD5	LY6/PLAUR domain containing 5	-21.8023	-4.44641	3.63E-05
ALX4	ALX homeobox 4	-21.7607	-4.44365	8.25E-14
HTR7	5-hydroxytryptamine (serotonin) receptor 7_adenylate cyclase-coupled	-21.6032	-4.43317	4.24E-12
MCOLN3	mucolipin 3	-21.5099	-4.42693	1.84E-11
NXF3	nuclear RNA export factor 3	-21.5056	-4.42667	9.32E-10

TABLE 4-continued

Genes more highly expressed in BM MSCs compared with HMCs				
Gene Name	Description	Fold Change	Log Fold Change	p-Adj
MFAP5	microfibrillar associated protein 5	-21.467	-4.42405	6.48E-64
MALRD1	MAM and LDL receptor class A domain containing 1	-21.4603	-4.4236	3.91E-05
ADAMTS4	ADAM metallopeptidase with thrombospondin type 1 motif_4	-21.4536	-4.42315	1.39E-43
ZNF528	zinc finger protein 528	-21.4192	-4.42083	8.50E-35
SLC8A3	solute carrier family 8 (sodium/calcium exchanger)_member 3	-21.3959	-4.41926	7.10E-05
NDUFA4L2	NADH dehydrogenase (ubiquinone) 1 alpha subcomplex_4-like 2	-21.3677	-4.41736	2.98E-19
TRABD2B	TraB domain containing 2B	-21.2105	-4.40671	1.19E-09
SIM1	single-minded family bHLH transcription factor 1	-21.2004	-4.40602	9.35E-06
FAM19A5	family with sequence similarity 19 (chemokine (C-C motif)-like)_member A5	-21.1652	-4.40362	3.42E-44
FAM50B	family with sequence similarity 50_member B	-21.0535	-4.39599	1.01E-50
KCNN4	potassium channel_calculm activated intermediate/small conductance subfamily N alpha_member 4	-20.9584	-4.38946	2.97E-46
HTR2A	5-hydroxytryptamine (serotonin) receptor 2A_G protein-coupled	-20.9571	-4.38937	0.00011
PM20D1	peptidase M20 domain containing 1	-20.5974	-4.36439	8.81E-05
LOC100506834	uncharacterized LOC100506834	-20.5877	-4.36371	6.39E-17
PLD5	phospholipase D family_member 5	-20.5811	-4.36325	0.000159
NR4A2	nuclear receptor subfamily 4_group A_member 2	-20.3715	-4.34848	1.39E-29
BACH2	BTB and CNC homology 1_basic leucine zipper transcription factor 2	-20.2688	-4.34119	2.14E-28
CRIP1	cysteine-rich protein 1 (intestinal)	-20.2183	-4.33759	1.77E-45
ANGPTL5	angiopoietin-like 5	-20.2061	-4.33672	7.79E-05
USP32P1	ubiquitin specific peptidase 32 pseudogene 1	-20.1748	-4.33448	6.91E-06
PLSCR4	phospholipid scramblase 4	-20.0422	-4.32497	1.83E-45
BACE2	beta-site APP-cleaving enzyme 2	-20.0121	-4.3228	5.29E-71
CYP1B1-AS1	CYP1B1 antisense RNA 1	-19.9626	-4.31923	2.92E-13
SLC14A2	solute carrier family 14 (urea transporter)_member 2	-19.7333	-4.30256	7.17E-05
POU5F1	POU class 5 homeobox 1	-19.6359	-4.29542	1.68E-08
KCND3	potassium channel_voltage gated Shal related subfamily D_member 3	-19.5189	-4.2868	1.65E-06
RHBDL2	rhomboid veinlet-like 2 (<i>Drosophila</i>)	-19.5079	-4.28599	2.69E-35
CCDC67	coiled-coil domain containing 67	-19.222	-4.26469	8.79E-05
ADAMTS2	ADAM metallopeptidase with thrombospondin type 1 motif_2	-19.1384	-4.2584	4.81E-197
ENTPD1-AS1	ENTPD1 antisense RNA 1	-19.1196	-4.25698	6.87E-05
MLKL	mixed lineage kinase domain-like	-19.1013	-4.2556	1.91E-88
BMPR1B	bone morphogenetic protein receptor_type IB	-18.9871	-4.24695	1.35E-21
LINC00028	long intergenic non-protein coding RNA 28	-18.9553	-4.24453	7.98E-05
MYOT	myotilin	-18.7318	-4.22742	4.74E-10
ADRA2C	adrenoceptor alpha 2C	-18.6355	-4.21998	3.71E-27
HOXC-AS2	HOXC cluster antisense RNA 2	-18.5603	-4.21415	1.91E-13
TIMP3	TIMP metallopeptidase inhibitor 3	-18.3901	-4.20086	7.89E-33
C21orf119	URB1 antisense RNA 1 (head to head)	-18.3392	-4.19686	6.85E-48
ANKRD7	ankyrin repeat domain 7	-18.2307	-4.1883	0.000179
ANKRD20A9P	ankyrin repeat domain 20 family_member A9_pseudogene	-18.175	-4.18388	0.000271
NFE2	nuclear factor_erythroid 2	-18.1645	-4.18305	1.53E-41
ASS1	argininosuccinate synthase 1	-18.1342	-4.18064	1.34E-73
BTILA	B and T lymphocyte associated	-18.1274	-4.1801	1.28E-05
SLC14A1	solute carrier family 14 (urea transporter)_member 1 (Kidd blood group)	-18.1032	-4.17817	4.65E-33
ANKRD6	ankyrin repeat domain 6	-18.0164	-4.17124	1.65E-85
DMBT1	deleted in malignant brain tumors 1	-17.9852	-4.16874	0.000133
LINC00271	long intergenic non-protein coding RNA 271	-17.9802	-4.16834	1.18E-05
OR2S2	olfactory receptor_family 2_subfamily S_member 2 (gene/pseudogene)	-17.9513	-4.16602	0.000215
SNED 1	sushi_nidogen and EGF-like domains 1	-17.8528	-4.15808	8.57E-101
LOC392232	transient receptor potential cation channel_subfamily A_member 1 pseudogene	-17.7659	-4.15104	0.000183
KCNT2	potassium channel sodium activated subfamily T_member 2	-17.5312	-4.13185	3.15E-18

TABLE 4-continued

Genes more highly expressed in BM MSCs compared with HMCs				
Gene Name	Description	Fold Change	Log Fold Change	p-Adj
RORA	RAR-related orphan receptor A	-17.4834	-4.12791	1.46E-114
TNFSF9	tumor necrosis factor (ligand) superfamily_member 9	-17.4353	-4.12394	2.78E-21
ADH1C	alcohol dehydrogenase 1C (class I)_gamma polypeptide	-17.4236	-4.12297	0.000163
FBXO39	F-box protein 39	-17.3262	-4.11488	0.000153
ZNF595	zinc finger protein 595	17.2323	-4.10704	1.79E-30
LMO7DN	LM07 downstream neighbor	-17.2099	-4.10517	2.90E-17
PI16	peptidase inhibitor 16	-17.1836	-4.10296	2.92E-11
EPDR1	ependymin related 1	-17.0851	-4.09467	8.65E-36
HLA-DRA	major histocompatibility complex_class II_DR alpha	-17.078	-4.09407	0.000417
C10orf54	chromosome 10 open reading frame 54	-17.0211	-4.08925	2.39E-93
ZNF311	zinc finger protein 311	-17.0103	-4.08834	2.37E-10
LINC01119	long intergenic non-protein coding RNA 1119	-16.956	-4.08372	7.58E-67
RASSF9	Ras association (RalGDS/AF-6) domain family (N-terminal) member 9	-16.9475	-4.083	4.43E-41
HLA-DRB1	major histocompatibility complex_class II_DR beta 1	-16.872	-4.07656	2.00E-08
HMOX1	heme oxygenase 1	-16.8711	-4.07648	2.77E-128
MIRLET7BHG	MIRLET7B host gene	-16.8548	-4.07509	2.54E-22
TRPM3	transient receptor potential cation channel_subfamily M_member 3	-16.8294	-4.07291	2.12E-13
CCDC64B	coiled-coil domain containing 64B	-16.8047	-4.07079	10.000407
HOXA9	homeobox A9	-16.7153	-4.0631	4.84E-53
BATF	basic leucine zipper transcription factor_ATF-like	-16.7105	-4.06268	0.000383
IGFBPL1	insulin-like growth factor binding protein-like 1	-16.6703	-4.05921	1.29E-35
KCNH1	potassium channel_voltage gated eag related subfamily H_member 1	-16.6561	-4.05798	2.27E-18
LPO	lactoperoxidase	-16.5886	-4.05212	1.79E-05
ADCY4	adenylate cyclase 4	-16.5671	-4.05025	4.41E-19
ANKRD65	ankyrin repeat domain 65	-16.3912	-4.03485	8.58E-49
OLFML1	olfactomedin-like 1	-16.3551	-4.03167	2.87E-21
C11orf96	chromosome 11 open reading frame 96	-16.2548	-4.02279	3.34E-22
TLE2	transducin-like enhancer of split 2	-16.2491	-4.02229	3.65E-36
LOC653602	uncharacterized LOC653602	-16.2049	-4.01836	2.06E-10
EVA1C	eva-1 homolog C (<i>C. elegans</i>)	-16.2023	-4.01813	2.64E-72
SATB2-AS1	SATB2 antisense RNA 1	-16.0753	-4.00677	0.000254
GBP5	guanylate binding protein 5	-16.0594	-4.00535	6.57E-06
IL1R1	interleukin 1 receptor_type I	-16.0375	-4.00338	5.75E-80
MIR656	microRNA 656	-15.983	-3.99847	0.000289
KCNK2	potassium channel_two pore domain subfamily K_member 2	-15.9332	-3.99396	2.10E-31
TNFRSF14	tumor necrosis factor receptor superfamily_member 14	-15.913	-3.99213	5.69E-44
PCDHGA1	protocadherin gamma subfamily A_1	-15.866	-3.98787	5.58E-09
CCL20	chemokine (C-C motif) ligand 20	-15.8653	-3.9878	6.53E-09
LOC284412	uncharacterized LOC284412	-15.8392	-3.98543	5.86E-07
TNFAIP6	tumor necrosis factor_alpha-induced protein 6	-15.7201	-3.97454	7.00E-12
ACAN	aggrecan	-15.6611	-3.96911	3.97E-83
VTRNA1-2	vault RNA 1-2	-15.6195	-3.96528	3.85E-10
RGN	regucalcin	-15.609	-3.96431	3.76E-23
NR4A1	nuclear receptor subfamily 4_group A_member 1	-15.5795	-3.96158	3.99E-95
TNS4	tensin 4	-15.5521	-3.95904	9.17E-22
CFB	complement factor B	-15.4426	-3.94884	5.90E-31
TMEM119	transmembrane protein 119	-15.4262	-3.94731	2.09E-59
MIR4271	microRNA 4271	-15.3448	-3.93968	0.000385
ABCC9	ATP-binding cassette_sub-family C (CFTR/MRP)_member 9	-15.294	-3.93489	6.82E-35
AGMO	alkylglycerol monooxygenase	-15.2848	-3.93403	0.000102
RIPK3	receptor-interacting serine-threonine kinase 3	-15.1926	-3.9253	1.71E-31
SLPI	secretory leukocyte peptidase inhibitor	-15.1322	-3.91955	0.000432
MIR23A	microRNA 23a	-15.1079	-3.91723	0.000424
EBF3	early B-cell factor 3	-15.0595	-3.9126	2.02E-102
RGS22	regulator of G-protein signaling 22	-15.059	-3.91255	7.45E-05
PRUNE2	prune homolog 2 (<i>Drosophila</i>)	-15.0164	-3.90847	3.38E-83
A2M	alpha-2-macroglobulin	-15.0025	-3.90713	4.18E-14
LRRC15	leucine rich repeat containing 15	-14.8862	-3.8959	1.94E-16
LOC101927650	uncharacterized LOC101927650	-14.8779	-3.8951	4.42E-05

TABLE 4-continued

Genes more highly expressed in BM MSCs compared with HMCs				
Gene Name	Description	Fold Change	Log Fold Change	p-Adj
LINC00870	long intergenic non-protein coding RNA 870	-14.8421	-3.89162	0.000319
LANCL3	LanC lantibiotic synthetase component C-like 3 (bacterial)	-14.8372	-3.89115	1.68E-08
SLC6A1	solute carrier family 6 (neurotransmitter transporter) member 1	-14.7885	-3.8864	0.000151
SNORD113-4	small nucleolar RNA_C/D box 113-4	-14.7598	-3.8836	0.000496
APOL6	apolipoprotein L_6	-14.7294	-3.88063	2.08E-62
CRIP3	cysteine-rich protein 3	-14.6825	-3.87603	5.54E-07
ADPRH	ADP-ribosylarginine hydrolase	-14.6571	-3.87353	6.54E-66
PLA2G5	phospholipase A2_group V	-14.6359	-3.87144	0.001334
LINC00877	long intergenic non-protein coding RNA 877	-14.4527	-3.85327	0.000505
FIBIN	fin bud initiation factor homolog (zebrafish)	-14.4064	-3.84864	2.26E-27
LIPI	lipase_member I	-14.3906	-3.84705	0.000612
LINC01121	long intergenic non-protein coding RNA 1121	-14.3857	-3.84656	0.000775
ABCA6	ATP-binding cassette_sub-family A (ABC1)_member 6	-14.3797	-3.84596	2.42E-16
LINC00961	long intergenic non-protein coding RNA 961	14.3653	-3.84452	4.16E-29
MLIP	muscular LMNA-interacting protein	-14.299	-3.83784	6.43E-05
TP63	tumor protein p63	-14.2856	-3.83649	4.77E-08
MEDAG	mesenteric estrogen-dependent adipogenesis	-14.2853	-3.83646	3.66E-98
FOSB	FBJ murine osteosarcoma viral oncogene homolog B	-14.261	-3.834	3.25E-18
CCDC144A	coiled-coil domain containing 144A	-14.2522	-3.83311	3.88E-05
ZNF704	zinc finger protein 704	-14.252	-3.83309	3.01E-11
FZD1	frizzled class receptor 1	-14.1041	-3.81804	2.20E-37
NPR3	natriuretic peptide receptor 3	-14.0506	-3.81256	2.04E-32
LRRC6	leucine rich repeat containing 6	-13.9759	-3.80487	1.02E-33
LAMA4	laminin_alpha 4	-13.9682	-3.80407	3.57E-32
FLJ22447	uncharacterized LOC400221	-13.9582	-3.80304	6.71E-23
ANKFN1	ankyrin-repeat and fibronectin type III domain containing 1	-13.9499	-3.80218	9.52E-11
LOC101927524	NA	-13.947	-3.80188	0.000913
C3	complement component 3	-13.9125	-3.79831	7.27E-21
TCHH	trichohyalin	-13.8398	-3.79075	0.000751
TMSB4Y	thymosin beta 4_Y-linked	-13.839	-3.79067	0.001604
PON3	paraoxonase 3	-13.7218	-3.7784	0.00108
KRT83	keratin 83_type II	-13.7094	-3.77709	0.00026
AGT	angiotensinogen (serpin peptidase inhibitor_clade A_member 8)	-13.702	-3.77631	2.67E-25
CEMIP	cell migration inducing protein_hyaluronan binding	-13.667	-3.77262	4.15E-30
MIR4297	microRNA 4297	-13.6626	-3.77216	0.001069
PSORS1C3	psoriasis susceptibility 1 candidate 3 (non-protein coding)	-13.5703	-3.76238	0.001055
ITGA8	integrin_alpha 8	-13.5429	-3.75946	2.41E-67
LOC102546299	uncharacterized LOC102546299	-13.5364	-3.75877	1.02E-06
GSTM1	glutathione S-transferase mu 1	-13.5248	-3.75754	0.001586
MIR6730	microRNA 6730	-13.49	-3.75382	9.36E-05
DHX58	DEXH (Asp-Glu-X-His) box polypeptide 58	-13.4889	-3.7537	5.11E-29
CXCL16	chemokine (C-X-C motif) ligand 16	-13.4676	-3.75142	1.20E-38
GJB5	gap junction protein_beta 5_31.1 kDa	-13.4535	-3.74991	0.000119
SCIN	scinderin	-13.4499	-3.74952	3.34E-08
CSGALNACT1	chondroitin sulfate N-acetylgalactosaminyltransferase 1	-13.4328	-3.74769	1.50E-70
LOC101928882	uncharacterized LOC101928882	-13.4233	-3.74667	0.001191
MSC	musculin	-13.4205	-3.74637	2.37E-56
WEE2	WEE1 homolog 2 (<i>S. pombe</i>)	-13.4086	-3.74509	0.001064
NR1I2	nuclear receptor subfamily 1_group L_member 2	-13.3169	-3.73519	0.000887
OAS1	2'-5'-oligoadenylate synthetase 1_40/46 kDa	-13.282	-3.7314	3.02E-07
LINC01116	long intergenic non-protein coding RNA 1116	-13.2627	-3.7293	2.01E-69
VMO1	vitelline membrane outer layer 1 homolog (chicken)	-13.2306	-3.72581	7.39E-16
CD4	CD4 molecule	-13.2111	-3.72368	9.20E-251
SLAMF9	SLAM family member 9	-13.208	-3.72334	5.08E-17
COL12A1	collagen_type XII_alpha 1	-13.1992	-3.72238	1.82E-30
TBX15	T-box 15	-13.1967	-3.7221	2.80E-169
LOC102724224	NA	-13.1605	-3.71814	3.31E-26
EYA1	EYA transcriptional coactivator and phosphatase 1	-13.1442	-3.71635	9.67E-11
HOXA1	homeobox A1	13.0858	-3.70993	3.29E-34
IL21R	interleukin 21 receptor	-13.0523	-3.70623	5.45E-25

TABLE 4-continued

Genes more highly expressed in BM MSCs compared with HMCs				
Gene Name	Description	Fold Change	Log Fold Change	p-Adj
AKR1C3	aldo-keto reductase family 1_member C3	-13.0514	-3.70613	4.31E-71
ELFN1-AS1	ELFN1 antisense RNA 1	-13.0005	-3.70049	0.001132
GIMAP2	GTPase_IMAP family member 2	-12.977	-3.69789	0.000193
EPHA3	EPH receptor A3	-12.9631	-3.69634	4.89E-09
AMDHD1	amidohydrolase domain containing 1	-12.8293	-3.68137	2.56E-06
DHRS3	dehydrogenase/reductase (SDR family) member 3	-12.8017	-3.67826	3.71E-99
HOTAIRM1	HOXA transcript antisense RNA_myeloid-specific 1	-12.6644	-3.66271	7.70E-17
LOC643733	caspase 4_apoptosis-related cysteine peptidase pseudogene	12.6634	-3.66259	0.001868
PLEKHS1	pleckstrin homology domain containing_S member 1	-12.6564	-3.6618	0.0018
ALDH3A1	aldehyde dehydrogenase 3 family_member A1	-12.5614	-3.65093	0.001122
FAM124A	family with sequence similarity 124A	-12.5491	-3.64951	3.37E-13
APOL4	apolipoprotein L_4	12.5159	-3.64569	4.34E-05
LOC344887	NmrA-like family domain containing 1 pseudogene	-12.445	-3.63749	8.59E-08
MKX	mohawk homeobox	-12.4443	-3.63741	3.59E-45
GPR1	G protein-coupled receptor 1	-12.4127	-3.63374	8.62E-69
C1S	complement component 1_s subcomponent	-12.3465	-3.62603	5.89E-122
WBP2NL	WBP2 N-terminal like	-12.3298	-3.62408	0.00032
ADAMTS1	ADAM metallopeptidase with thrombospondin type 1 motif_1	-12.2866	-3.61901	1.75E-51
PTPRQ	protein tyrosine phosphatase_receptor type_Q	-12.2197	-3.61114	6.07E-15
ADRA1D	adrenoceptor alpha 1D	-12.2063	-3.60955	3.37E-33
MIR4768	microRNA 4768	-12.1847	-3.607	5.42E-07
BPIFB4	BPI fold containing family B_member 4	-12.181	-3.60656	0.002036
GCNT1	glucosaminyl (N-acetyl) transferase 1_core 2	-12.1357	-3.60118	7.82E-213
THBS1	thrombospondin 1	-12.1223	-3.59959	8.45E-26
KLF15	Kruppel-like factor 15	-12.1204	-3.59936	5.06E-08
ICAM2	intercellular adhesion molecule 2	-12.0635	-3.59258	1.67E-16
LINC00264	long intergenic non-protein coding RNA 264	-12.0558	-3.59166	0.002903
HAR1B	highly accelerated region 1B (non-protein coding)	-12.0333	-3.58896	0.000378
KRT32	keratin 32_type I	-11.9989	-3.58483	0.000268
TRPA1	transient receptor potential cation channel_subfamily A_member 1	-11.9929	-3.58411	1.13E-09
CACNA1C-AS1	CACNA1C antisense RNA 1	-11.9457	-3.57842	3.11E-05
RXFP1	relaxin/insulin-like family peptide receptor 1	-11.9372	-3.57739	0.00163
HSPA7	heat shock 70 kDa protein 7 (HSP70B)	-11.9275	-3.57622	0.002637
ZSWIM2	zinc finger_SWIM-type containing 2	-11.9	-3.57289	5.58E-09
POM121L9P	POM121 transmembrane nucleoporin-like 9_pseudogene	-11.8915	-3.57186	2.42E-12
PLA2R1	phospholipase A2 receptor 1_180 kDa	-11.8505	-3.56687	6.96E-87
LOC100506258	uncharacterized LOC100506258	-11.8385	-3.56541	7.21E-08
MIR27A	microRNA 27a	-11.8194	-3.56308	0.00043
XAF1	XIAP associated factor 1	-11.8067	-3.56153	1.34E-19
C21orf15	cytochrome P450_family 4_subfamily F_polypeptide 29_pseudogene	-11.7779	-3.55801	0.00238
FIBCD1	fibrinogen C domain containing 1	-11.7398	-3.55333	1.37E-52
TLX2	T-cell leukemia homeobox 2	-11.7162	-3.55043	0.000158
PSG2	pregnancy specific beta-1-glycoprotein 2	-11.7126	-3.54999	0.001543
PCDHGB5	protocadherin gamma subfamily B_5	-11.6849	-3.54657	1.84E-09
RNF212	ring finger protein 212	-11.6282	-3.53956	1.92E-84
HERC2P10	hect domain and RLD 2 pseudogene 10	-11.6193	-3.53845	7.54E-07
SHCBP1L	SHC SH2-domain binding protein 1-like	-11.585	-3.53418	0.001762
FKBP9P1	FK506 binding protein 9 pseudogene 1	-11.5254	-3.52674	2.78E-17
MAB21L3	mab-21-like 3 (<i>C. elegans</i>)	-11.5082	-3.52459	0.002871
C9orf64	chromosome 9 open reading frame 64	-11.5027	-3.5239	1.20E-22
TDRD12	tudor domain containing 12	-11.4976	-3.52326	0.003909
FXYD3	FXYD domain containing ion transport regulator 3	-11.4449	-3.51663	0.002241
PCDHB15	protocadherin beta 15	-11.4199	-3.51348	4.29E-16
HTATSF1P2	HIV-1 Tat specific factor 1 pseudogene 2	-11.4056	-3.51167	1.54E-18
KRTAP1-3	keratin associated protein 1-3	-11.405	-3.5116	0.000615
ESR1	estrogen receptor 1	-11.4016	-3.51116	1.74E-09
TDRD6	tudor domain containing 6	-11.3952	-3.51035	5.09E-06
SLC4A4	solute carrier family 4 (sodium bicarbonate cotransporter)_member 4	-11.3712	-3.50731	6.76E-68
IL26	interleukin 26	-11.2376	-3.49026	1.05E-06

TABLE 4-continued

Genes more highly expressed in BM MSCs compared with HMCs				
Gene Name	Description	Fold Change	Log Fold Change	p-Adj
LIN7A	lin-7 homolog A (<i>C. elegans</i>)	-11.1763	-3.48237	1.60E-19
C2orf88	chromosome 2 open reading frame 88	-11.153	-3.47936	6.65E-36
PRRX2	paired related homeobox 2	-11.1516	-3.47918	4.79E-30
CASC1	cancer susceptibility candidate 1	-11.132	-3.47664	8.72E-06
HTR6	5-hydroxytryptamine (serotonin) receptor 6_G protein-coupled	-11.1213	-3.47525	9.95E-05
STAT4	signal transducer and activator of transcription 4	-11.0841	-3.47042	3.13E-15
MEIS3P1	Meis homeobox 3 pseudogene 1	-11.0567	-3.46685	5.16E-15
PCAT5	prostate cancer associated transcript 5 (non-protein coding)	-11.0216	-3.46226	0.003735
LEP	leptin	-10.9642	-3.45473	0.002439
SETBP1	SET binding protein 1	-10.9298	-3.4502	1.13E-13
CEACAM22P	carcinoembryonic antigen-related cell adhesion molecule 22_pseudogene	-10.913	-3.44797	0.003652
C4orf32	chromosome 4 open reading frame 32	-10.8864	-3.44445	2.30E-28
LINC00943	long intergenic non-protein coding RNA 943	-10.8536	-3.4401	0.004493
ZNF541	zinc finger protein 541	-10.8222	-3.43592	0.001083
CC2D2B	coiled-coil and C2 domain containing 2B	-10.8072	-3.43392	0.002733
LOC340113	uncharacterized LOC340113	-10.7923	-3.43193	0.003322
RAB3IL1	RAB3A interacting protein (rabin3)-like 1	-10.7393	-3.42483	1.25E-78
LEPR	leptin receptor	-10.7172	-3.42186	3.94E-24
CACNA1C	calcium channel_voltage-dependent_L type_alpha 1C subunit	-10.6935	-3.41866	8.21E-37
LMO7-AS1	LMO7 antisense RNA 1	-10.6495	-3.41271	8.67E-21
C1R	complement component 1_r subcomponent	-10.6162	-3.4082	3.20E-139
SLC9A9	solute carrier family 9_subfamily A (NHE9_cation proton antiporter 9)_member 9	-10.6078	-3.40705	3.19E-37
LOC102724927	uncharacterized LOC102724927	-10.5947	-3.40527	1.19E-20
DPT	dermatopontin	-10.5809	-3.40339	0.005268
EMP1	epithelial membrane protein 1	-10.5387	-3.39763	3.56E-26
ZNF676	zinc finger protein 676	-10.5336	-3.39693	0.00396
LIMCH1	LIM and calponin homology domains 1	-10.5325	-3.39678	3.84E-19
PLXNA4	plexin A4	-10.5205	-3.39513	1.94E-23
MT1M	metallothionein 1M	-10.5182	-3.39481	3.35E-15
TENM2	teneurin transmembrane protein 2	-10.5068	-3.39325	2.22E-96
WISP1	WNT1 inducible signaling pathway protein 1	-10.468	-3.38792	2.62E-25
LOC391322	D-dopachrome tautomerase-like	-10.3516	-3.37178	9.00E-12
CMAHP	cytidine monophospho-N-acetylneuraminic acid hydroxylase_pseudogene	-10.3496	-3.37151	5.26E-27
MIR92B	microRNA 92b	-10.3491	-3.37144	0.004725
IL7	interleukin 7	-10.3346	-3.36941	7.43E-15
KRT33B	keratin 33B_type I	-10.3158	-3.36678	3.78E-29
FAM109B	family with sequence similarity 109_member B	-10.2915	-3.36338	1.99E-239
TGM5	transglutaminase 5	-10.2562	-3.35843	0.006672
PAX8	paired box 8	-10.2492	-3.35744	0.000304
SOCS2	suppressor of cytokine signaling 2	-10.2112	-3.35208	2.28E-77
MEGF6	multiple EGF-like-domains 6	-10.2066	-3.35143	5.05E-52
ALOX15P1	arachidonate 15-lipoxygenase pseudogene 1	-10.2064	-3.3514	0.004495
LINC00982	long intergenic non-protein coding RNA 982	-10.1965	-3.35	3.29E-20
ZNF560	zinc finger protein 560	-10.1806	-3.34775	2.83E-07
FOS	FBJ murine osteosarcoma viral oncogene homolog	-10.1784	-3.34744	4.35E-15
ASPN	asporin	-10.1769	-3.34723	3.42E-05
CNTNAP2	contactin associated protein-like 2	-10.1411	-3.34214	4.27E-07
ESM1	endothelial cell-specific molecule 1	-10.1294	-3.34047	8.19E-14
CTSW	cathepsin W	-10.1277	-3.34023	0.000387
NFIX	nuclear factor I/X (CCAAT-binding transcription factor)	-9.99031	-3.32053	2.37E-35
GCKR	glucokinase (hexokinase 4) regulator	-9.97447	-3.31824	1.31E-20
HOXC11	homeobox C11	-9.96673	-3.31712	8.15E-41
B4GALNT1	beta-1_4-N-acetyl-galactosaminyl transferase 1	-9.96445	-3.31679	2.03E-47
LRRC2-AS1	LRRC2 antisense RNA 1	-9.9483	-3.31445	0.004436
ALDH1L2	aldehyde dehydrogenase 1 family_member L2	-9.92626	-3.31125	3.37E-31
DOCK9-AS2	DOCK9 antisense RNA 2 (head to head)	-9.92564	-3.31116	4.99E-08
ROCK1P1	Rho-associated_coiled-coil containing protein kinase 1 pseudogene 1	-9.8439	-3.29923	0.000897
LTC4S	leukotriene C4 synthase	-9.83353	-3.29771	4.10E-27
HOXA7	homeobox A7	-9.7738	-3.28892	5.73E-17
PCDHGA8	protocadherin gamma subfamily A_8	-9.76602	-3.28777	3.68E-30

TABLE 4-continued

Genes more highly expressed in BM MSCs compared with HMCs				
Gene Name	Description	Fold Change	Log Fold Change	p-Adj
TECTB	tectorin beta	-9.74931	-3.2853	0.006826
LINC00965	long intergenic non-protein coding RNA 965	-9.72515	-3.28172	0.005153
S100P	S100 calcium binding protein P	-9.7143	-3.28011	0.002216
TTTY10	testis-specific transcript_Y-linked 10 (non-protein coding)	-9.70481	-3.2787	0.008667
ALDH3B1	aldehyde dehydrogenase 3 family_member B1	-9.68338	-3.27551	8.63E-125
C1orf158	chromosome 1 open reading frame 158	-9.65944	-3.27194	0.006341
LOC101927755	uncharacterized LOC101927755	-9.65536	-3.27133	3.78E-06
MSR1	macrophage scavenger receptor 1	-9.65375	-3.27109	2.50E-11
TNFSF11	tumor necrosis factor (ligand) superfamily_member 11	-9.64439	-3.26969	0.004874
C5orf38	chromosome 5 open reading frame 38	-9.64305	-3.26949	2.16E-35
CFI	complement factor I	-9.63697	-3.26858	2.03E-37
TCF7	transcription factor 7 (T-cell specific_HMG-box)	-9.60729	-3.26413	4.99E-36
CD80	CD80 molecule	-9.60576	-3.2639	0.004995
MIR6071	microRNA 6071	-9.6027	-3.26344	0.007925
LCN1	lipocalin 1	-9.59651	-3.26251	2.06E-05
IL1R2	interleukin 1 receptor_type II	-9.58634	-3.26098	0.000578
LOC100506895	uncharacterized LOC100506895	-9.56291	-3.25745	1.66E-05
A2ML1	alpha-2-macroglobulin-like 1	-9.54662	-3.25499	0.0002
AFF2	AF4/FMR2 family_member 2	-9.53809	-3.2537	4.80E-45
NKG7	natural killer cell granule protein 7	-9.51933	-3.25086	0.002237
SIGLEC10	sialic acid binding Ig-like lectin 10	-9.46584	-3.24273	0.002419
TRIM4	tripartite motif containing 4	-9.44283	-3.23922	3.32E-58
ZG16B	zymogen granule protein 16B	-9.43708	-3.23834	8.22E-07
CCDC158	coiled-coil domain containing 158	-9.40514	-3.23345	3.13E-10
FGL2	fibrinogen-like 2	-9.40299	-3.23312	0.000861
LOC101927688	NA	-9.39908	-3.23252	9.42E-05
INHBB	inhibin_beta B	-9.38645	-3.23058	8.02E-123
HOXA10	homeobox A10	-9.35158	-3.22521	1.51E-123
FHAD1	forkhead-associated (FHA) phosphopeptide binding domain 1	-9.33345	-3.22241	1.89E-06
OSR2	odd-skipped related transcription factor 2	-9.30935	-3.21868	1.36E-05
SNORD11A-26	small nucleolar RNA_C/D box 11A-26	-9.27939	-3.21403	0.008533
NKX6-1	NK6 homeobox 1	-9.26352	-3.21156	1.76E-15
DNER	delta/notch-like EGF repeat containing	-9.25472	-3.21019	2.07E-06
LDHAL6B	lactate dehydrogenase A-like 6B	-9.24985	-3.20943	0.001253
C11orf86	chromosome 11 open reading frame 86	-9.24556	-3.20876	5.32E-05
VSTM4	V-set and transmembrane domain containing 4	-9.21485	-3.20396	2.42E-29
HOXA3	homeobox A3	-9.19985	-3.20161	1.76E-26
HOXC-AS3	HOXC cluster antisense RNA 3	-9.18303	-3.19897	4.60E-08
NPY6R	neuropeptide Y receptor Y6 (pseudogene)	-9.17883	-3.19831	0.009703
HSD11B1	hydroxysteroid (11-beta) dehydrogenase 1	-9.17323	-3.19743	0.008005
LINC01220	long intergenic non-protein coding RNA 1220	-9.16738	-3.19651	0.001771
MB21D1	Mab-21 domain containing 1	-9.16484	-3.19611	1.32E-26
RNF43	ring finger protein 43	-9.14802	-3.19346	0.001612
HEYL	hes-related family bHLH transcription factor with YRPW motif-like	-9.14321	-3.1927	0.000477
TNIP3	TNFAIP3 interacting protein 3	-9.14295	-3.19266	1.78E-12
SMCR9	NA	-9.12902	-3.19046	0.009476
SNORD11A-1	small nucleolar RNA_C/D box 11A-1	-9.11006	-3.18746	0.007346
CCRL2	chemokine (C-C motif) receptor-like 2	-9.04819	-3.17763	0.005581
GOLGA8O	golgin A8 family_member O	-9.00421	-3.1706	4.43E-05
MIR615	microRNA 615	-8.99835	-3.16966	0.009703
KLF17	Kruppel-like factor 17	-8.98289	-3.16718	3.70E-05
BST1	bone marrow stromal cell antigen 1	-8.96697	-3.16462	4.52E-64
MIR199A1	microRNA 199a-1	-8.87877	-3.15036	0.000581
SERP2	stress-associated endoplasmic reticulum protein family member 2	-8.87533	-3.1498	1.63E-47
S100B	S100 calcium binding protein B	-8.87514	-3.14977	9.46E-08
ZNF726	zinc finger protein 726	-8.84578	-3.14499	8.39E-07
COL16A1	collagen_type XVI_alpha 1	-8.83647	-3.14347	1.43E-59
TMEM30B	transmembrane protein 30B	-8.83133	-3.14263	1.45E-07
FLJ46906	uncharacterized LOC441172	-8.81866	-3.14056	1.58E-13
SCRT1	scratch family zinc finger 1	-8.77945	-3.13413	0.007849
GDAP1L1	ganglioside induced differentiation associated protein 1-like 1	-8.77622	-3.1336	0.000269
TRPM2	transient receptor potential cation channel_subfamily M_member 2	-8.76959	-3.13251	4.32E-08
CSMD1	CUB and Sushi multiple domains 1	-8.74592	-3.12861	0.00292

TABLE 4-continued

Genes more highly expressed in BM MSCs compared with HMCs				
Gene Name	Description	Fold Change	Log Fold Change	p-Adj
FTCDNL1	formiminotransferase cyclodeaminase N-terminal like	-8.73253	-3.1264	4.10E-05
RIMS1	regulating synaptic membrane exocytosis 1	-8.72987	-3.12596	5.39E-29
MIR409	microRNA 409	-8.70721	-3.12221	0.008342
RCN3	reticulocalbin 3_EF-hand calcium binding domain	-8.69955	-3.12094	3.55E-43
LOC101927354	uncharacterized LOC101927354	-8.68551	-3.11861	2.09E-06
PLA2G16	phospholipase A2_group XVI	-8.68226	-3.11807	8.21E-118
SLC1A3	solute carrier family 1 (glial high affinity glutamate transporter)_member 3	-8.64838	-3.11243	8.42E-16
CARD16	caspase recruitment domain family_member 16	-8.61225	-3.10639	2.92E-14
LOC101927667	NA	-8.61094	-3.10617	1.92E-05
DAPK1	death-associated protein kinase 1	-8.59746	-3.10391	1.87E-56
ANGPT1	angiopoietin 1	-8.57235	-3.09969	2.50E-11
ACOX2	acyl-CoA oxidase 2_branched chain	-8.56189	-3.09793	4.59E-28
GHDC	GH3 domain containing	-8.55483	-3.09674	3.85E-76
IGFBP1	insulin-like growth factor binding protein 1	-8.53103	-3.09272	0.004458
PDE7B	phosphodiesterase 7B	-8.52488	-3.09168	3.28E-45
MACROD2	MACRO domain containing 2	-8.51166	-3.08944	7.31E-06
RSPO2	R-spondin 2	-8.50788	-3.0888	0.009007
KCNJ9	potassium channel_inwardly rectifying subfamily J_member 9	-8.42934	-3.07542	0.003859
LOC101059948	uncharacterized LOC101059948	-8.42554	-3.07477	8.21E-06
GPR68	G protein-coupled receptor 68	-8.42543	-3.07475	5.26E-24
SOX9-AS1	SOX9 antisense RNA 1	-8.3768	-3.0664	0.001328
RDH5	retinol dehydrogenase 5 (11-cis/9-cis)	-8.36862	-3.06499	9.26E-19
NLRP3	NLR family_pyrin domain containing 3	-8.32102	-3.05676	1.57E-20
SLC22A3	solute carrier family 22 (organic cation transporter)_member 3	-8.31762	-3.05617	7.45E-15
G0S2	G0/G1 switch 2	-8.30817	-3.05453	4.71E-17
LOC100505739	NA	-8.29372	-3.05202	0.00648
C21orf167	long intergenic non-protein coding RNA 1547	-8.28844	-3.0511	1.50E-39
CHST15	carbohydrate (N-acetyl)galactosamine 4-sulfate 6-O sulfotransferase 15	-8.23107	-3.04108	4.79E-40
HOXD1	homeobox D1	-8.22674	-3.04032	0.005994
HOXA2	homeobox A2	-8.20418	-3.03636	3.98E-13
TRIB3	tribbles pseudokinase 3	-8.18805	-3.03352	3.54E-51
LOC100129722	NA	-8.18147	-3.03236	1.67E-05
CCIN	calicin	-8.17223	-3.03073	1.07E-17
ITGB8	integrin_beta 8	-8.16131	-3.0288	8.36E-29
HIST2H2BA	histone cluster 2_H2ba (pseudogene)	-8.13657	-3.02442	8.34E-11
PIWIL2	piwi-like RNA-mediated gene silencing 2	-8.13177	-3.02357	1.37E-05
ID4	inhibitor of DNA binding 4_dominant negative helix-loop-helix protein	-8.11865	-3.02124	7.49E-94
EVI2B	ecotropic viral integration site 2B	-8.11263	-3.02017	2.32E-16
LOC375196	uncharacterized LOC375196	-8.07711	-3.01384	3.53E-06
WEE2-AS1	WEE2 antisense RNA 1	-8.07107	-3.01276	2.72E-12
GYPE	glycophorin E (MNS blood group)	-8.04454	-3.00801	0.006375
OXT	oxytocin/neurophysin I prepropeptide	-8.04393	-3.0079	0.001064
LOC102724550	NA	-8.03317	-3.00597	1.79E-11
FAM87A	family with sequence similarity 87_member A	-8.0081	-3.00146	0.004949
VLDLR-AS1	VLDLR antisense RNA 1	-7.96365	-2.99343	8.01E-16
NECAB2	N-terminal EF-hand calcium binding protein 2	-7.9535	-2.99159	1.90E-11
ACSS3	acyl-CoA synthetase short-chain family member 3	-7.94006	-2.98915	1.83E-60
LOC284798	uncharacterized LOC284798	-7.92994	-2.98731	0.006819
MYO18B	myosin XVIIIB	-7.92143	-2.98576	0.004941
UBE2QL1	ubiquitin-conjugating enzyme E2Q family-like 1	-7.91692	-2.98494	2.09E-05
MFSD7	major facilitator superfamily domain containing 7	-7.85287	-2.97322	9.43E-57
PNMA2	paraneoplastic Ma antigen 2	-7.81074	-2.96546	8.09E-11
FXYD1	FXYD domain containing ion transport regulator 1	-7.79906	-2.9633	1.83E-11
PGF	placental growth factor	-7.75142	-2.95446	1.58E-176
RAD21-AS1	RAD21 antisense RNA 1	-7.75109	-2.9544	0.001458
ZFP57	ZFP57 zinc finger protein	-7.72037	-2.94867	0.002055
CRNDE	colorectal neoplasia differentially expressed (non-protein coding)	-7.70092	-2.94503	3.84E-139
BAALC	brain and acute leukemia_cytoplasmic leucine rich adaptor protein 1-like	-7.68764	-2.94254	2.92E-09
LURAP1L		-7.65939	-2.93723	1.58E-119

TABLE 4-continued

Genes more highly expressed in BM MSCs compared with HMCs				
Gene Name	Description	Fold Change	Log Fold Change	p-Adj
NOV	nephroblastoma overexpressed	-7.65419	-2.93625	3.00E-29
CALHM2	calcium homeostasis modulator 2	-7.65409	-2.93623	2.60E-57
TEC	tec protein tyrosine kinase	-7.64428	-2.93438	2.13E-10
LOC101928036	NA	-7.62586	-2.9309	3.39E-06
MACC1	metastasis associated in colon cancer 1	-7.61276	-2.92842	0.000151
FGR	proto-oncogene_Src family tyrosine kinase	-7.51472	-2.90972	0.007795
GPR85	G protein-coupled receptor 85	-7.50577	-2.908	3.58E-33
MIR24-2	microRNA 24-2	-7.48909	-2.90479	6.35E-05
HTRA1	HtrA serine peptidase 1	-7.43493	-2.89432	3.38E-46
CD97	adhesion G protein-coupled receptor E5	-7.39628	-2.8868	5.45E-18
OXCT1-AS1	OXCT1 antisense RNA 1	-7.39459	-2.88647	0.000781
LOC101928891	uncharacterized LOC101928891	-7.38977	-2.88553	6.18E-09
SVILP1	supervillin pseudogene 1	-7.37176	-2.88201	0.002022
LINC00619	long intergenic non-protein coding RNA 619	-7.36349	-2.88039	1.40E-11
PTX1	paired-like homeodomain 1	-7.33329	-2.87446	1.60E-40
DDIT4	DNA-damage-inducible transcript 4	-7.32445	-2.87272	2.85E-30
DAPK2	death-associated protein kinase 2	-7.3142	-2.8707	1.43E-19
PCDHGB2	protocadherin gamma subfamily B_2	-7.27169	-2.86229	2.78E-16
PDE2A	phosphodiesterase 2A cGMP-stimulated	-7.25291	-2.85856	3.93E-05
SLC38A5	solute carrier family 38_member 5	-7.21735	-2.85147	1.83E-60
TRPC6	transient receptor potential cation channel_subfamily C_member 6	-7.20945	-2.84989	7.86E-05
ITGA10	integrin_alpha 10	-7.19378	-2.84675	1.86E-15
CXCL3	chemokine (C-X-C motif) ligand 3	-7.19218	-2.84643	5.23E-06
CFD	complement factor D (adipsin)	-7.19049	-2.84609	3.15E-27
FAM78B	family with sequence similarity 78_member B	-7.18386	-2.84476	1.29E-05
C2orf73	chromosome 2 open reading frame 73	-7.17794	-2.84357	0.003713
ITGA7	integrin_alpha 7	-7.17232	-2.84244	5.49E-11
VDR	vitamin D (1,25-dihydroxyvitamin D3) receptor	-7.15926	-2.83981	4.27E-46
LOC100506188	uncharacterized LOC100506188	-7.15311	-2.83857	5.64E-11
LOC100240734	uncharacterized LOC100240734	-7.12801	-2.8335	0.004573
PRG4	proteoglycan 4	-7.11523	-2.83091	7.94E-17
LOC102723769	uncharacterized LOC102723769	-7.11064	-2.82998	0.008421
SLC30A2	solute carrier family 30 (zinc transporter)_member 2	-7.10237	-2.8283	0.000171
MISP	mitotic spindle positioning	-7.10183	-2.82819	7.07E-08
MTSS1	metastasis suppressor 1	-7.09096	-2.82598	1.40E-16
FAM178B	family with sequence similarity 178_member B	-7.09027	-2.82584	6.79E-05
C15orf59	chromosome 15 open reading frame 59	-7.08467	-2.8247	1.37E-32
FAM167A	family with sequence similarity 167_member A	-7.08197	-2.82415	2.71E-20
LOC101929234	uncharacterized LOC101929234	-7.06216	-2.82011	3.24E-07
CSF1R	colony stimulating factor 1 receptor	-7.04705	-2.81702	5.45E-12
PRSS12	protease_serine_12 (neurotrypsin_motopsin)	-7.04642	-2.81689	4.76E-14
HCG4B	HLA complex group 4B (non-protein coding)	-7.03246	-2.81403	0.000191
CYB561	cytochrome b561	-7.01533	-2.81051	5.12E-66
TMEM150C	transmembrane protein 150C	-6.98447	-2.80415	2.34E-33
LY75	lymphocyte antigen 75	-6.98326	-2.8039	0.003764
VCAM1	vascular cell adhesion molecule 1	-6.97542	-2.80228	6.95E-17
ZNF667-AS1	ZNF667 antisense RNA 1 (head to head)	-6.9484	-2.79668	1.23E-19
ALPK1	alpha-kinase 1	-6.94238	-2.79543	6.99E-35
ZNF354C	zinc finger protein 354C	-6.93824	-2.79457	2.95E-06
ZNF396	zinc finger protein 396	-6.93516	-2.79393	3.40E-07
NDRG1	N-myc downstream regulated 1	-6.93439	-2.79377	5.51E-30
ZNF829	zinc finger protein 829	-6.92479	-2.79177	2.09E-50
C10orf11	chromosome 10 open reading frame 11	-6.92354	-2.79151	9.83E-19
KRT31	keratin 31_type I	-6.92349	-2.7915	0.000395
NTRK1	neurotrophic tyrosine kinase_receptor_type 1	-6.91726	-2.7902	0.00105
PRDM6	PR domain containing 6	-6.89452	-2.78545	1.36E-05
KCNJ8	potassium channel_inwardly rectifying subfamily J_member 8	-6.89323	-2.78518	1.33E-44
FZD5	frizzled class receptor 5	-6.88306	-2.78305	1.81E-09
KLF9	Krppel-like factor 9	-6.87905	-2.78221	1.75E-17
GGT5	gamma-glutamyltransferase 5	-6.87896	-2.78219	1.66E-19
LOC115110	uncharacterized LOC115110	-6.8771	-2.7818	0.002611
SCRG1	stimulator of chondrogenesis 1	-6.86286	-2.77881	2.32E-19
OTUD7A	OTU deubiquitinase 7A	-6.86253	-2.77874	0.001651
C15orf65	chromosome 15 open reading frame 65	-6.85963	-2.77813	4.91E-26

TABLE 4-continued

Genes more highly expressed in BM MSCs compared with HMCs				
Gene Name	Description	Fold Change	Log Fold Change	p-Adj
AGBL2	ATP/GTP binding protein-like 2	-6.85255	-2.77664	1.04E-09
NR4A3	nuclear receptor subfamily 4_group A_member 3	-6.83504	-2.77295	6.82E-11
FOXC1	forkhead box C1	-6.78684	-2.76274	6.06E-51
VCAN	versican	-6.7773	-2.76071	6.67E-20
MILR1	mast cell immunoglobulin-like receptor 1	-6.74767	-2.75439	1.29E-07
KLF2	Kruppel-like factor 2	-6.74019	-2.75279	2.40E-150
ESPNL	espin-like	-6.73748	-2.75221	0.000167
JHDM1D-AS1	JHDM1D antisense RNA 1 (head to head)	-6.73137	-2.7509	5.34E-41
CFH	complement factor H	-6.70659	-2.74558	9.08E-17
MIR4664	microRNA 4664	-6.70241	-2.74468	0.002155
SLC1A1	solute carrier family 1 (neuronal/epithelial high affinity glutamate transporter_system Xag)_member 1	-6.69944	-2.74404	2.47E-45
HOXA-AS3	HOXA cluster antisense RNA 3	-6.67751	-2.73931	8.73E-21
RADIL	Ras association and DIL domains	-6.66867	-2.7374	2.59E-11
HOXA4	homeobox A4	-6.66258	-2.73608	6.22E-18
NAT2	N-acetyltransferase 2 (arylamine N-acetyltransferase)	-6.64993	-2.73334	0.001906
LINC00936	long intergenic non-protein coding RNA 936	-6.6138	-2.72548	1.61E-28
LINC00595	long intergenic non-protein coding RNA 595	-6.60954	-2.72455	7.72E-07
COLEC12	collectin sub-family member 12	-6.60904	-2.72444	1.14E-34
CST6	cystatin E/M	-6.59403	-2.72116	8.41E-10
SMOC1	SPARC related modular calcium binding 1	-6.58603	-2.71941	1.06E-12
BEX1	brain expressed_X-linked 1	-6.55884	-2.71344	1.73E-78
ADM2	adrenomedullin 2	-6.55079	-2.71167	2.80E-43
NXPH4	neurexophilin 4	-6.54045	-2.70939	3.69E-35
IL1RL2	interleukin 1 receptor-like 2	-6.52881	-2.70682	5.90E-11
LOC101060542	uncharacterized LOC101060542	-6.52261	-2.70545	0.001517
ENG	endoglin	-6.51701	-2.70421	3.07E-110
RNLS	renalase_FAD-dependent amine oxidase	-6.49167	-2.69859	3.94E-23
OLFML3	olfactomedin-like 3	-6.48659	-2.69746	1.13E-28
KLHDC7B	kelch domain containing 7B	-6.47549	-2.69499	3.22E-12
SLC38A3	solute carrier family 38_member 3	-6.47092	-2.69397	1.15E-10
CRISPLD2	cysteine-rich secretory protein LCCL domain containing 2	-6.43576	-2.68611	5.56E-22
DUSP2	dual specificity phosphatase 2	-6.41158	-2.68068	1.10E-41
PER3	period circadian clock 3	-6.39746	-2.6775	3.51E-25
TYMP	thymidine phosphorylase	-6.38732	-2.67521	3.10E-35
GSTO2	glutathione S-transferase omega 2	-6.38254	-2.67413	6.70E-56
LOC730102	quinone oxidoreductase-like protein 2 pseudogene	-6.37736	-2.67296	2.98E-80
STAC2	SH3 and cysteine rich domain 2	-6.37007	-2.67131	4.20E-16
PMP22	peripheral myelin protein 22	-6.35777	-2.66852	4.22E-47
CCR7	chemokine (C-C motif) receptor 7	-6.35495	-2.66788	4.47E-19
HECW1	HECT_C2 and WW domain containing E3 ubiquitin protein ligase 1	-6.33265	-2.66281	4.22E-09
PKP1	plakophilin 1	-6.32077	-2.6601	6.21E-08
BICC1	BiC family RNA binding protein 1	-6.30488	-2.65647	3.68E-11
C11orf87	chromosome 11 open reading frame 87	-6.27715	-2.65011	1.73E-10
ANKH	ANKH inorganic pyrophosphate transport regulator	-6.27311	-2.64918	2.02E-12
CCPG1	cell cycle progression 1	-6.25517	-2.64505	4.34E-25
NIM1K	NIM1 serine/threonine protein kinase	-6.23474	-2.64033	1.29E-12
ISL2	ISL LIM homeobox 2	-6.23427	-2.64022	3.68E-11
TLR3	toll-like receptor 3	-6.21748	-2.63633	5.43E-09
C2	complement component 2	-6.20031	-2.63234	2.07E-11
ERAP2	endoplasmic reticulum aminopeptidase 2	-6.19296	-2.63063	0.001254
ANKRD2	ankyrin repeat domain 2 (stretch responsive muscle)	-6.18177	-2.62802	1.59E-05
EPB41L4B	erythrocyte membrane protein band 4.1 like 4B	-6.18018	-2.62765	9.12E-16
WFDC1	WAP four-disulfide core domain 1	-6.17248	-2.62585	1.42E-09
PCK2	phosphoenolpyruvate carboxykinase 2 (mitochondrial)	-6.16803	-2.62481	3.91E-40
ENPP1	ectonucleotide pyrophosphatase/phosphodiesterase 1	-6.15146	-2.62093	2.52E-13
PRDM1	PR domain containing 1_with ZNF domain	-6.14605	-2.61966	1.49E-53
FAM149A	family with sequence similarity 149_member A	-6.14052	-2.61836	1.20E-10
MIR452	microRNA 452	-6.09565	-2.60778	0.000336
SLC22A23	solute carrier family 22_member 23	-6.09117	-2.60672	2.51E-12
LY6K	lymphocyte antigen 6 complex_locus K	-6.0611	-2.59958	1.18E-06

TABLE 4-continued

Genes more highly expressed in BM MSCs compared with HMCs				
Gene Name	Description	Fold Change	Log Fold Change	p-Adj
CLIC3	chloride intracellular channel 3	-6.05757	-2.59874	3.33E-15
RCAN2	regulator of calcineurin 2	-6.05401	-2.59789	3.03E-11
BEST1	bestrophin 1	-6.04964	-2.59685	1.30E-32
FRK	fyn-related Src family tyrosine kinase	-6.03846	-2.59418	0.002353
CEBPA	CCAAT/enhancer binding protein (C/EBP)_alpha	-6.03373	-2.59305	3.36E-13
MROH9	maestro heat-like repeat family member 9	-6.01986	-2.58973	0.000743
RRN3P2	RRN3 homolog_RNA polymerase I transcription factor pseudogene 2	-6.01819	-2.58933	2.73E-09
CASC2	cancer susceptibility candidate 2 (non-protein coding)	-6.01098	-2.5876	5.05E-20
TPD52L1	tumor protein D52-like 1	-5.99812	-2.58451	5.88E-10
C5orf49	chromosome 5 open reading frame 49	-5.98948	-2.58243	2.76E-12
SLC16A4	solute carrier family 16_member 4	-5.97807	-2.57968	4.74E-35
ACTC1	actin alpha cardiac muscle 1	-5.9597	-2.57524	4.39E-07
ZMYND12	zinc finger_MYND-type containing 12	-5.95437	-2.57395	3.45E-05
TEX41	testis expressed 41 (non-protein coding)	-5.94699	-2.57216	0.003728
ALPK2	alpha-kinase 2	-5.93591	-2.56947	6.22E-18
TIMP4	TIMP metallopeptidase inhibitor 4	-5.9332	-2.56881	1.17E-06
VEGFC	vascular endothelial growth factor C	-5.92954	-2.56792	2.29E-109
SNX29P2	sorting nexin 29 pseudogene 2	-5.92732	-2.56738	0.000105
DOK1	docking protein 1_62 kDa (downstream of tyrosine kinase 1)	-5.91866	-2.56527	1.07E-31
MEIOB	meiosis specific with OB domains	-5.91689	-2.56484	0.000871
CADPS2	Ca++-dependent secretion activator 2	-5.91427	-2.5642	2.11E-06
LOC729041	NA	-5.8972	-2.56003	5.46E-05
QPCT	glutaminyl-peptide cyclotransferase	-5.89426	-2.55931	1.37E-28
HOXA5	homeobox A5	-5.89393	-2.55923	1.56E-22
SOX18	SRY (sex determining region Y)-box 18	-5.88099	-2.55606	4.33E-11
GOLGA8S	golgin A8 family_member S	-5.87724	-2.55514	0.008437
EMR2	adhesion G protein-coupled receptor E2	-5.868	-2.55287	0.001436
GOLGA8M	golgin A8 family_member M	-5.86394	-2.55187	0.001897
LOXL3	lysyl oxidase-like 3	-5.85931	-2.55073	1.05E-25
CD70	CD70 molecule	-5.8535	-2.5493	0.000669
CRHR2	corticotropin releasing hormone receptor 2	-5.85204	-2.54894	0.004334
TUSC1	tumor suppressor candidate 1	-5.83742	-2.54533	4.43E-32
OPCML	opioid binding protein/cell adhesion molecule-like	-5.80964	-2.53845	7.19E-05
RASD1	RAS_dexamethasone-induced 1	-5.78987	-2.53353	2.46E-15
RASIP1	Ras interacting protein 1	-5.77736	-2.53041	0.003568
C8orf34	chromosome 8 open reading frame 34	-5.77396	-2.52956	2.92E-19
LINC00341	long intergenic non-protein coding RNA 341	-5.77043	-2.52868	2.78E-24
THPO	thrombopoietin	-5.72561	-2.51743	1.25E-05
KRT38	keratin 38_type I	-5.71245	-2.51411	0.008435
LOC100506746	uncharacterized LOC100506746	-5.69261	-2.50909	2.59E-10
ACTR3C	ARP3 actin-related protein 3 homolog C (yeast)	-5.68878	-2.50812	0.000316
GPR78	G protein-coupled receptor 78	-5.67866	-2.50555	0.002572
HAS2-AS1	HAS2 antisense RNA 1	-5.65148	-2.49863	9.77E-20
CACNA1G	calcium channel_voltage-dependent_T type_alpha 1G subunit	-5.62588	-2.49208	0.000806
C8orf31	chromosome 8 open reading frame 31	-5.62472	-2.49178	1.44E-19
DNAJC6	DnaJ (Hsp40) homolog_subfamily C_member 6	-5.60949	-2.48787	1.16E-20
PSTPIP1	proline-serine-threonine phosphatase interacting protein 1	-5.60114	-2.48572	1.32E-09
WDR96	cilia and flagella associated protein 43	-5.58242	-2.48089	1.59E-05
DMKN	dermokine	-5.58029	-2.48034	2.46E-06
ASIC4	acid sensing (proton gated) ion channel family member 4	-5.57596	-2.47922	8.95E-06
LOC100132352	NA	-5.56955	-2.47756	1.56E-18
CCDC170	coiled-coil domain containing 170	-5.55397	-2.47352	5.97E-15
VEGFA	vascular endothelial growth factor A	-5.53138	-2.46764	1.95E-13
SLC6A9	solute carrier family 6 (neurotransmitter transporter_glycine)_member 9	-5.53119	-2.46759	4.84E-36
EIF4EBP3	eukaryotic translation initiation factor 4E binding protein 3	-5.51362	-2.463	1.18E-06
MMP2	matrix metallopeptidase 2	-5.50976	-2.46199	6.16E-19
SLC15A3	solute carrier family 15 (oligopeptide transporter)_member 3	-5.50923	-2.46185	2.06E-21
MIR3074	microRNA 3074	-5.49504	-2.45813	0.000669

TABLE 4-continued

Genes more highly expressed in BM MSCs compared with HMCs				
Gene Name	Description	Fold Change	Log Fold Change	p-Adj
LINC00707	long intergenic non-protein coding RNA 707	-5.48766	-2.45619	0.004664
SNHG5	small nucleolar RNA host gene 5	-5.47478	-2.4528	6.87E-05
IRAK3	interleukin-1 receptor-associated kinase 3	-5.45792	-2.44835	7.59E-26
AK4	adenylate kinase 4	-5.44824	-2.44579	8.23E-19
GALNT1	polypeptide N-acetylgalactosaminyltransferase 1	-5.43526	-2.44235	5.15E-11
NR1D1	nuclear receptor subfamily 1_group D_member 1	-5.43255	-2.44163	3.99E-26
SOCS2-AS1	SOCS2 antisense RNA 1	-5.42758	-2.44031	3.48E-10
CLMP	CXADR-like membrane protein	-5.42382	-2.43931	9.55E-08
LOC101929125	uncharacterized LOC101929125	-5.40416	-2.43407	4.93E-05
ZNF568	zinc finger protein 568	-5.39982	-2.43291	4.37E-64
PTER	phosphotriesterase related	-5.39925	-2.43276	1.36E-11
GOLGA6L4	golgin A6 family-like 4	-5.39256	-2.43097	1.00E-05
CASP1	caspase 1_apoptosis-related cysteine peptidase	-5.39103	-2.43056	3.33E-15
LINC01152	long intergenic non-protein coding RNA 1152	-5.38774	-2.42968	0.000239
EFHD1	EF-hand domain family_member D1	-5.38662	-2.42938	0.000127
TMTC1	transmembrane and tetratricopeptide repeat containing 1	-5.37588	-2.4265	4.69E-09
HOTAIR	HOX transcript antisense RNA	-5.34882	-2.41922	2.75E-14
PRKDC1	protein kinase D1	-5.34804	-2.41901	1.67E-75
LOC102724316	NA	-5.31861	-2.41105	3.64E-148
FAM69A	family with sequence similarity 69_member A	-5.31555	-2.41022	1.23E-95
ODF3L2	outer dense fiber of sperm tails 3-like 2	-5.30963	-2.40861	1.50E-05
LOC101928414	uncharacterized LOC101928414	-5.29808	-2.40547	0.006814
PLCL1	phospholipase C-like 1	-5.29555	-2.40478	9.84E-08
NCF2	neutrophil cytosolic factor 2	-5.27361	-2.39879	2.58E-15
LOC101241902	chromosome 4 open reading frame 46 pseudogene	-5.27046	-2.39793	1.49E-06
PRR15	proline rich 15	-5.26802	-2.39726	1.01E-05
SERPINE2	serpin peptidase inhibitor_clade E (nexin_plasminogen activator inhibitor type 1)_member 2	-5.26685	-2.39694	5.29E-24
CYP4V2	cytochrome P450_family 4_subfamily V_polypeptide 2	-5.25992	-2.39504	1.24E-15
DENNND2C	DENN/MADD domain containing 2C	-5.2427	-2.39031	5.92E-07
SBSN	suprabasin	-5.24263	-2.39029	7.29E-08
PDGFRA	platelet-derived growth factor receptor_alpha polypeptide	-5.20862	-2.3809	2.21E-168
MYOM1	myomesin 1	-5.19942	-2.37835	4.14E-07
COL6A3	collagen_type VI_alpha 3	-5.19621	-2.37746	6.71E-55
MIR6775	microRNA 6775	-5.18477	-2.37428	0.000735
LINC00921	long intergenic non-protein coding RNA 921	-5.15046	-2.3647	1.26E-14
LINC01352	long intergenic non-protein coding RNA 1352	-5.13232	-2.35961	7.17E-06
NXPH3	neurexophilin 3	-5.12915	-2.35872	6.51E-10
LOC100507557	uncharacterized LOC100507557	-5.12826	-2.35847	7.49E-14
DHRS4L1	dehydrogenase/reductase (SDR family) member 4 like 1	-5.11906	-2.35588	0.004779
TXNRD2	thioredoxin reductase 2	-5.07937	-2.34465	1.58E-31
PCDHA3	protocadherin alpha 3	-5.07779	-2.3442	0.000773
ALDH1A3	aldehyde dehydrogenase 1 family_member A3	-5.0685	-2.34156	1.92E-06
PPFIA2	protein tyrosine phosphatase_receptor type_f polypeptide (PTPRF)_interacting protein (lirpin)_alpha 2	-5.06538	-2.34067	4.69E-05
TLE3	transducin-like enhancer of split 3	-5.06183	-2.33966	9.92E-78
CLDN23	claudin 23	-5.05927	-2.33893	0.000316
STEAP1	six transmembrane epithelial antigen of the prostate 1	-5.04544	-2.33498	3.27E-44
ADAMTS9-AS2	ADAMTS9 antisense RNA 2	-5.04177	-2.33393	4.23E-06
ANK2	ankyrin 2_neuronal	-5.03583	-2.33223	6.76E-28
FCRLA	Fc receptor-like A	-5.02004	-2.3277	8.25E-08
UNCSC	unc-5 netrin receptor C	-5.01017	-2.32486	1.67E-05
ATOH8	ataonal bHLH transcription factor 8	-5.0049	-2.32334	6.40E-56

TABLE 5

Genes more highly expressed in HMCs compared to UCB-MSCs				
Name	Description	Fold Change	Log Fold Change	p-Value
LRRN1	leucine rich repeat neuronal 1	3423.37	11.7412	7.84E-104
NKX2-5	NK2 homeobox 5	1581.96	10.6275	6.39E-97
IGFBP2	insulin-like growth factor binding protein 2_ 36 kDa	1184.37	10.2099	2.47E-103
DCC	DCC netrin 1 receptor	891.771	9.80053	1.60E-76
NETO1	neuropilin (NRP) and tolloid (TLL)-like 1	852.709	9.73591	3.52E-68
IGSF1	immunoglobulin superfamily_ member 1	611.14	9.25536	7.03E-52
LOC440416	NA	540.215	9.07739	3.70E-139
FLJ16779	uncharacterized LOC100192386	430.748	8.7507	3.08E-52
NKAIN4	Na+/K+ transporting ATPase interacting 4	369.492	8.5294	9.57E-49
OCA2	oculocutaneous albinism II	359.59	8.49021	2.24E-89
NLGN4X	neuroligin 4_ X-linked	350.92	8.455	1.14E-41
RSP04	R-spondin 4	313.369	8.29172	2.78E-76
LIN28B	lin-28 homolog B (C. elegans)	307.263	8.26333	2.37E-52
KCTD8	potassium channel tetramerization domain containing 8	297.083	8.21472	1.55E-48
IRX2	iroquois homeobox 2	237.351	7.89088	1.80E-48
PLAC8	placenta-specific 8	207.368	7.69605	2.30E-74
CLSTN2	calsyntenin 2	201.99	7.65814	4.29E-113
CACNG4	calcium channel_ voltage-dependent_ gamma subunit 4	174.326	7.44564	5.03E-71
PHOX2A	paired-like homeobox 2a	169.602	7.40601	2.70E-36
ITGA8	integrin_alpha 8	169.257	7.40307	4.76E-40
CHRD1	chordin-like 1	159.108	7.31386	2.02E-44
UNC5C	unc-5 netrin receptor C	150.173	7.23048	7.96E-46
NLRP2	NLR family_ pyrin domain containing 2	147.386	7.20346	3.25E-30
PRAC1	prostate cancer susceptibility candidate 1	136.827	7.09621	3.19E-25
PCDHB2	protocadherin beta 2	130.227	7.02488	3.62E-25
TRPC5	transient receptor potential cation channel_ subfamily C_ member 5	127.06	6.98937	3.76E-30
PPARGC1A	peroxisome proliferator-activated receptor_gamma_ coactivator 1 alpha	124.471	6.95967	4.68E-32
NRK	Nik related kinase	122.669	6.93863	5.98E-41
ABCB1	ATP-binding cassette_ sub-family B (MDR/TAP)_ member 1	122.107	6.932	2.34E-39
PALM	paralemmin	112.71	6.81647	2.44E-94
LRRTM1	leucine rich repeat transmembrane neuronal 1	112.66	6.81583	1.31E-68
LOC642366	uncharacterized LOC642366	109.152	6.77019	7.96E-38
KCNK3	potassium channel_ two pore domain subfamily K_ member 3	107.071	6.74242	5.85E-41
SIX1	SIX homeobox 1	105.882	6.72631	1.43E-71
SLC44A5	solute carrier family 44_ member 5	105.792	6.72509	3.28E-75
OVCH2	ovochymase 2 (gene/pseudogene)	105.433	6.72018	2.03E-45
PRDM16	PR domain containing 16	104.665	6.70963	2.54E-63
MGAM	maltase-glucosidase	100.991	6.65809	1.29E-46
GCNT2	glucosaminyl (N-acetyl) transferase 2_ I-branching enzyme (I blood group)	99.6577	6.63891	5.38E-48
TNRC6C-AS1	TNRC6C antisense RNA 1	99.3178	6.63398	1.80E-33
ANO1	anoctamin 1_calcium activated chloride channel	97.8208	6.61207	3.23E-44
GATA3-AS1	GATA3 antisense RNA 1	97.6731	6.60989	1.41E-29
EBF3	early B-cell factor 3	95.5471	6.57814	5.38E-33
SPINK5	serine peptidase inhibitor_ Kazal type 5	91.5539	6.51655	6.26E-18
FXYD6	FXYD domain containing ion transport regulator 6	86.0701	6.42744	1.97E-22
SLTRK1	SLT1 and NTRK-like family_ member 1	84.3333	6.39803	2.73E-28
DPPA4	developmental pluripotency associated 4	83.2928	6.38012	2.54E-16
NKX2-6	NK2 homeobox 6	77.2391	6.27126	9.65E-21
SYT13	synaptotagmin XIII	75.1088	6.23091	2.59E-17
LGR5	leucine-rich repeat containing G protein-coupled receptor 5	74.3515	6.21629	1.30E-16
LHX2	LIM homeobox 2	73.4001	6.19771	1.19E-30
CYTIP	cytogenetic interacting protein	72.9805	6.18944	4.02E-19
BMP2	bone morphogenetic protein 2	72.9274	6.18839	2.01E-33
CST1	cystatin SN	71.2699	6.15522	1.75E-18
AFF3	AF4/FMR2 family_ member 3	70.7339	6.14433	4.25E-45

TABLE 5-continued

Genes more highly expressed in HMCs compared to UCB-MSCs				
Name	Description	Fold Change	Log Fold Change	p-Value
TMEM132B	transmembrane protein 132B	66.6337	6.05818	1.53E-33
ADAMTS18	ADAM metallopeptidase with thrombospondin type 1 motif_ 18	65.9833	6.04403	1.11E-27
C8orf4	chromosome 8 open reading frame 4	65.9737	6.04382	5.03E-27
CDH10	cadherin 10_ type 2 (T2-cadherin)	64.672	6.01507	2.27E-20
PDE1C	phosphodiesterase 1C_ calmodulin-dependent 70 kDa	64.3452	6.00776	1.34E-91
PLCXD3	phosphatidylinositol-specific phospholipase C_ X domain containing 3	63.3025	5.98419	3.70E-17
SH2D3C	SH2 domain containing 3C	63.288	5.98386	5.85E-27
P2RY14	purinergic receptor P2Y_ G-protein coupled_ 14	62.0216	5.9547	7.33E-17
VIT	vitrin	61.9138	5.95219	1.55E-29
TLR4	toll-like receptor 4	61.5135	5.94283	1.08E-28
PKIB	protein kinase (cAMP-dependent_catalytic) inhibitor beta	61.1347	5.93392	5.81E-30
C5orf38	chromosome 5 open reading frame 38	60.5666	5.92045	3.12E-23
KCNA1	potassium channel_ voltage gated shaker related subfamily A_ member 1	60.5552	5.92018	9.27E-20
CDH3	cadherin 3_ type 1_ P-cadherin (placental)	58.9647	5.88178	4.90E-23
CD24	CD24 molecule	58.1703	5.86221	1.21E-27
PCDH12	protocadherin alpha 12	57.8257	5.85364	3.85E-17
LINC00491	long intergenic non-protein coding RNA 491	56.8741	5.8297	9.86E-16
COL22A1	collagen_ type XXII_ alpha 1	56.2589	5.81401	6.75E-16
LHX1	LIM homeobox 1	55.9249	5.80542	4.65E-21
CYP27C1	cytochrome P450_ family 27_ subfamily C_ polypeptide 1	55.3101	5.78947	1.14E-14
CRHBP	corticotropin releasing hormone binding protein	53.735	5.74779	3.46E-16
RERG	RAS-like_ estrogen-regulated_ growth inhibitor	53.574	5.74346	2.81E-21
LOC644919	uncharacterized LOC644919	52.9644	5.72695	1.01E-28
FRMPD3	FERM and PDZ domain containing 3	52.182	5.70548	6.36E-29
GABRG3	gamma-aminobutyric acid (GABA) A receptor_ gamma 3	51.9283	5.69845	8.06E-15
CHST15	carbohydrate (N-acetylgalactosamine 4-sulfate 6-O) sulfotransferase 15	51.5446	5.68775	9.64E-69
C14orf39	chromosome 14 open reading frame 39	51.4707	5.68568	1.34E-32
SLC5A12	solute carrier family 5 (sodium/monocarboxylate cotransporter)_ member 12	50.7533	5.66543	6.50E-28
ST8SIA2	ST8 alpha-N-acetyl-neuraminate alpha-2,8-sialyltransferase 2	50.7101	5.6642	2.57E-15
SFRP1	secreted frizzled-related protein 1	48.7693	5.6079	1.72E-51
SLCO6A1	solute carrier organic anion transporter family_ member 6A1	48.3763	5.59623	1.56E-13
KIAA0040	KIAA0040	48.2565	5.59265	3.37E-16
FBP2	fructose-1,6-bisphosphatase 2	48.0722	5.58713	1.41E-20
ANKRD1	ankyrin repeat domain 1 (cardiac muscle)	47.3197	5.56437	3.90E-29
TMEM40	transmembrane protein 40	47.1841	5.56023	1.11E-27
SLC1A7	solute carrier family 1 (glutamate transporter)_ member 7	46.3199	5.53356	6.47E-25
PODN	podocan	46.2856	5.53249	5.78E-87
SFMBT2	Scm-like with four mbt domains 2	46.1078	5.52694	2.44E-28
NKX3-2	NK3 homeobox 2	45.6483	5.51249	4.78E-22
SHC2	SHC (Src homology 2 domain containing) transforming protein 2	45.3695	5.50365	6.32E-54
SLCO2A1	solute carrier organic anion transporter family_ member 2A1	44.7573	5.48405	3.12E-23
MYCT1	myc target 1	44.739	5.48346	1.75E-22
FIRRE	firre intergenic repeating RNA element	43.2066	5.43318	2.76E-15
TNNI1	troponin I type 1 (skeletal_slow)	42.8853	5.42241	2.00E-23
BCL11B	B-cell CLL/lymphoma 11B (zinc finger protein)	42.833	5.42065	2.47E-14
ISL1	ISL LIM homeobox 1	42.4758	5.40857	2.02E-12
CLEC1A	C-type lectin domain family 1_ member A	42.2799	5.4019	5.81E-13

TABLE 5-continued

Genes more highly expressed in HMCs compared to UCB-MSCs				
Name	Description	Fold Change	Log Fold Change	p-Value
TSpan11	tetraspanin 11	41.6233	5.37932	1.52E-37
KRTAP1-1	keratin associated protein 1-1	41.5841	5.37796	1.11E-23
HS6ST2	heparan sulfate 6-O-sulfotransferase 2	41.4563	5.37352	1.08E-21
PCDHA4	protocadherin alpha 4	40.8944	5.35383	5.99E-17
WSCD1	WSC domain containing 1	40.5031	5.33996	6.93E-22
MED15P9	mediator complex subunit 15 pseudogene 9	39.4893	5.30339	3.88E-11
PLP1	proteolipid protein 1	39.4054	5.30032	4.24E-21
NIPAL4	NIPA-like domain containing 4	39.3494	5.29827	1.36E-59
FAR2P1	fatty acyl CoA reductase 2 pseudogene 1	39.2938	5.29623	4.11E-11
LINC01096	long intergenic non-protein coding RNA 1096	38.8828	5.28106	7.17E-14
MMP9	matrix metalloproteinase 9	38.4633	5.26541	1.22E-50
VAV3	vav 3 guanine nucleotide exchange factor	38.3209	5.26006	8.17E-19
C7	complement component 7	38.2986	5.25922	2.82E-18
TBX15	T-box 15	37.8573	5.2425	4.62E-19
CASC9	cancer susceptibility candidate 9 (non-protein coding)	37.6386	5.23414	3.36E-15
DIO2	deiodinase_ iodothyronine_type II	36.187	5.1774	2.13E-67
LIPG	lipase_endothelial	36.1381	5.17545	3.51E-58
GCNT4	glucosaminyl (N-acetyl) transferase 4_core 2	36.0191	5.17069	1.91E-24
MYH14	myosin_heavy chain 14_non-muscle	35.5979	5.15372	6.48E-15
A2M	alpha-2-macroglobulin	35.1412	5.13509	4.63E-16
LINC01021	long intergenic non-protein coding RNA 1021	34.8127	5.12154	2.04E-23
FAM65B	family with sequence similarity 65_member B	34.4156	5.10499	7.07E-43
GNA14	guanine nucleotide binding protein (G_protein)_alpha 14	34.2393	5.09758	2.18E-36
FAT3	FAT atypical cadherin 3	33.7873	5.07841	2.67E-22
LINC00982	long intergenic non-protein coding RNA 982	33.7057	5.07492	1.23E-12
TCEAL2	transcription elongation factor A (SII)-like 2	33.0111	5.04488	2.67E-17
ZCCHC16	zinc finger_CCHC domain containing 16	32.9462	5.04204	6.15E-12
GPR112	adhesion G protein-coupled receptor G4	32.5887	5.0263	2.27E-11
PCDHB4	protocadherin beta 4	31.9594	4.99817	3.18E-18
CACNA1H	calcium channel_voltage-dependent_T type_alpha 1H subunit	31.9406	4.99732	9.26E-41
SCARF1	scavenger receptor class F_member 1	31.5437	4.97928	3.39E-90
SHISA3	shisa family member 3	31.1437	4.96087	5.28E-15
KCNF1	potassium channel_voltage gated modified subfamily F_member 1	30.8845	4.94881	1.67E-15
B3GAT1	beta-1_3-glucuronyltransferase 1	30.6098	4.93592	3.57E-20
EXOC3L2	exocyst complex component 3-like 2	30.5731	4.93419	9.95E-36
TRIM55	tripartite motif containing 55	30.4766	4.92963	5.00E-118
PLXDC1	plexin domain containing 1	30.4333	4.92758	1.81E-26
TBX1	T-box 1	30.343	4.92329	8.72E-30
SMOC1	SPARC related modular calcium binding 1	30.1614	4.91463	2.44E-17
EFHD1	EF-hand domain family_member D1	29.6463	4.88978	4.18E-27
CD93	CD93 molecule	29.3736	4.87645	2.59E-14
KISS1	KiSS-1 metastasis-suppressor	28.5813	4.837	4.19E-12
OR10A3	olfactory receptor_family 10_subfamily A_member 3	28.1094	4.81298	4.22E-10
LRRC4C	leucine rich repeat containing 4C	27.9941	4.80705	7.72E-18
BEX1	brain expressed_X-linked 1	26.7397	4.74091	9.64E-24
TNNT2	troponin T type 2 (cardiac)	26.4701	4.72629	2.05E-21
RBM20	RNA binding motif protein 20	25.9298	4.69654	2.80E-25
TMC6	transmembrane channel-like 6	25.8548	4.69236	1.86E-27
TMEM200C	transmembrane protein 200C	25.7952	4.68903	2.92E-12
LINGO1	leucine rich repeat and Ig domain containing 1	25.5052	4.67272	1.30E-100
CNNM1	cyclin and CBS domain divalent metal cation transport mediator 1	25.5017	4.67252	1.63E-28

TABLE 5-continued

Genes more highly expressed in HMCs compared to UCB-MSCs					
Name	Description	Fold Change	Log Fold Change	p-Value	
PCDHA11	protocadherin alpha 11	24.9492	4.64092	7.22E-10	
FAM19A5	family with sequence similarity 19 (chemokine (C-C motif)-like) member A5	24.8579	4.63563	4.90E-20	
DACT2	dishevelled-binding antagonist of beta-catenin 2	24.8207	4.63347	2.24E-09	
BRINP1	bone morphogenetic protein/retinoic acid inducible neural-specific 1	24.5667	4.61863	4.07E-10	
CDH5	cadherin 5_type 2 (vascular endothelium)	24.4423	4.61131	1.18E-09	
ZMAT1	zinc finger_matin-type 1	24.4046	4.60908	6.07E-14	
SHISA2	shisa family member 2	24.293	4.60247	5.61E-17	
NUTM2F	NUT family member 2F	24.1311	4.59282	4.34E-10	
NNAT	neuronatin	23.7076	4.56728	1.98E-30	
LGII	leucine-rich_glioma inactivated 1	23.391	4.54788	5.91E-13	
MAP2	microtubule-associated protein 2	23.3814	4.54729	6.52E-74	
KC6	keratoconus gene 6	23.3338	4.54435	1.16E-14	
LPPR3	lipid phosphate phosphatase-related protein type 3	23.2252	4.53762	8.02E-25	
PARVG	parvin_gamma	22.8769	4.51582	6.30E-11	
EXTL_1	exostosin-like glycosyltransferase 1	22.7777	4.50955	3.33E-26	
BAI3	adhesion G protein-coupled receptor B3	22.6455	4.50115	1.26E-13	
ITIH3	inter-alpha-trypsin inhibitor heavy chain 3	22.6251	4.49985	1.71E-35	
LOC339166	uncharacterized LOC339166	22.4073	4.4859	5.90E-12	
GJA5	gap junction protein_alpha 5_40 kDa	22.3805	4.48417	2.27E-09	
TTR	transthyretin	22.3757	4.48386	4.57E-10	
LOC440910	uncharacterized LOC440910	22.3751	4.48382	1.60E-08	
NOVA1	neuro-oncological ventral antigen 1	22.1041	4.46624	4.48E-09	
PCDH17	protocadherin 17	22.0883	4.46521	1.44E-12	
ERP27	endoplasmic reticulum protein 27	21.8318	4.44836	2.90E-15	
SLC37A1	solute carrier family 37 (glucose-6-phosphate transporter)_member 1	21.6711	4.4377	1.39E-33	
MMP23B	matrix metalloproteinase 23B	21.3419	4.41562	7.23E-22	
SHOX2	short stature homeobox 2	21.0896	4.39846	6.22E-14	
PDE9A	phosphodiesterase 9A	20.9168	4.38659	8.62E-14	
GPR37	G protein-coupled receptor 37 (endothelin receptor type B-like)	20.6854	4.37054	2.43E-16	
KRTAP4-12	keratin associated protein 4-12	20.5994	4.36453	1.38E-09	
ABCB4	ATP-binding cassette_sub-family B (MDR/TAP)_member 4	20.596	4.36429	7.71E-14	
LOC283299	uncharacterized LOC283299	20.5908	4.36393	7.84E-11	
CXXC4	CXXC finger protein 4	20.5032	4.35778	4.39E-12	
LOC101928340	NA	20.221	4.33778	3.54E-08	
GRIN2A	glutamate receptor ionotropic_N-methyl D-aspartate 2A	20.0934	4.32865	7.56E-09	
FCGBP	Fc fragment of IgG binding protein	20.0563	4.32598	5.12E-16	
LOC102467080	uncharacterized LOC102467080	20.0368	4.32458	7.29E-32	
KIT	v-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog	19.7848	4.30632	1.51E-14	
ANOS	anoctamin 5	19.7803	4.30599	3.21E-08	
SALL1	spalt-like transcription factor 1	19.6367	4.29548	1.26E-19	
EMCN	endomucin	19.4577	4.28227	6.72E-10	
PLXNA4	plexin A4	19.3804	4.27653	7.04E-24	
NR0B1	nuclear receptor subfamily 0_group B_member 1	19.2784	4.26891	1.26E-08	
MDGA2	MAM domain containing glycosylphosphatidylinositol anchor 2	19.1619	4.26017	2.68E-24	
FAM49A	family with sequence similarity 49_member A	19.0858	4.25443	4.32E-58	
KSR2	kinase suppressor of ras 2	18.8714	4.23813	4.77E-09	
AIF1L	allograft inflammatory factor 1-like	18.8237	4.23448	2.05E-21	
DAAM2	dishevelled associated activator of morphogenesis 2	18.6607	4.22193	2.05E-45	
IGDCC3	immunoglobulin superfamily_DCC subclass_member 3	18.5723	4.21508	1.08E-10	
GDF7	growth differentiation factor 7	18.421	4.20328	3.48E-08	
MGAT4C	MGAT4 family_member C	18.3217	4.19548	1.72E-08	
LDB3	LIM domain binding 3	18.287	4.19275	1.11E-40	
DENNND2A	DENN/MADD domain containing 2A	18.2434	4.1893	3.62E-27	

TABLE 5-continued

Genes more highly expressed in HMCs compared to UCB-MSCs				
Name	Description	Fold Change	Log Fold Change	p-Value
OR5E1P	olfactory receptor_ family 5_ subfamily E_member 1 pseudogene	18.1705	4.18353	4.88E-09
SYT15	synaptotagmin-like 5	18.1419	4.18125	8.91E-19
TNFSF18	tumor necrosis factor (ligand) superfamily_member 18	18.1251	4.17992	1.85E-11
RELN	reelin	17.9466	4.16564	5.93E-14
IRX1	iroquois homeobox 1	17.9075	4.16249	1.27E-07
LARGE	like-glycosyltransferase	17.8339	4.15655	1.82E-39
FAM69B	family with sequence similarity 69_member B	17.7295	4.14808	1.72E-47
SULT1C4	sulfotransferase family_cytosolic_1C_member 4	17.4646	4.12636	2.56E-07
EMID1	EMI domain containing 1	17.2871	4.11162	1.05E-20
MGAT3	mannosyl (beta-1_4)-glycoprotein beta-1_4-N-acetylglucosaminyltransferase	17.2126	4.10539	9.53E-45
ILDR2	immunoglobulin-like domain containing receptor 2	16.8161	4.07177	4.49E-08
PLCB2	phospholipase C_beta 2	16.794	4.06987	9.31E-33
EPCAM	epithelial cell adhesion molecule	16.6721	4.05936	2.18E-19
EPB41L3	erythrocyte membrane protein band 4.1-like 3	16.6397	4.05656	6.17E-13
LICAM	L1 cell adhesion molecule	16.6355	4.05619	8.47E-30
BEX5	brain expressed_X-linked 5	16.586	4.05189	1.99E-07
GFRA2	GDNF family receptor alpha 2	16.5833	4.05166	1.29E-08
DLX5	distal-less homeobox 5	16.5784	4.05123	1.62E-07
DLX1	distal-less homeobox 1	16.5368	4.04761	7.18E-31
GRIA1	glutamate receptor_ionotropic_AMPA 1	16.5334	4.04731	7.77E-11
GRAP	GRB2-related adaptor protein	16.4563	4.04057	2.92E-19
BBOX1	butyrobetaine_(gamma)_2-oxoglutarate dioxygenase_(gamma-butyrobetaine hydroxylase) 1	16.3933	4.03503	7.12E-09
ADAMTS20	ADAM metallopeptidase with thrombospondin type 1 motif_20	16.3915	4.03488	7.59E-12
CXCL12	chemokine (C-X-C motif) ligand 12	16.3253	4.02904	4.11E-138
UNC13A	unc-13 homolog A (<i>C. elegans</i>)	16.2647	4.02367	1.32E-14
RGS1	regulator of G-protein signaling 1	16.2524	4.02258	5.09E-07
DLX6	distal-less homeobox 6	16.1897	4.017	5.02E-07
GRB14	growth factor receptor-bound protein 14	16.1678	4.01505	4.61E-15
HUNK	hormonally up-regulated Neu-associated kinase	15.9866	3.99879	6.11E-14
HEPH	hephaestin	15.8794	3.98908	4.82E-07
SLC6A16	solute carrier family 6_member 16	15.8359	3.98513	1.45E-22
RGMA	repulsive guidance molecule family member a	15.6927	3.97202	8.19E-18
GPR87	G protein-coupled receptor 87	15.6778	3.97065	8.41E-26
PADI2	peptidyl arginine deiminase_type II	15.645	3.96763	4.81E-15
PTPN6	protein tyrosine phosphatase_non-receptor type 6	15.6183	3.96517	2.28E-20
SUCNR1	succinate receptor 1	15.5191	3.95597	6.46E-07
PALMD	palmdelphin	15.5141	3.95551	1.40E-49
MERTK	MER proto-oncogene_tyrosine kinase	15.509	3.95503	5.72E-14
KCNC3	potassium channel_voltage gated Shaw related subfamily C_member 3	15.4779	3.95214	7.69E-11
PCDHB3	protocadherin beta 3	15.4368	3.9483	6.91E-09
CILP2	cartilage intermediate layer protein 2	15.2364	3.92945	1.66E-32
MAF	v-maf avian musculoaponeurotic fibrosarcoma oncogene homolog	15.2303	3.92887	8.06E-17
NTRK2	neurotrophic tyrosine kinase_receptor_type 2	15.1355	3.91986	1.08E-07
SEMA3E	sema domain_immunoglobulin domain (Ig)_short basic domain_secreted_(semaphorin) 3E	15.0925	3.91576	6.08E-10
C21orf90	TSPEAR antisense RNA 2	15.0718	3.91378	1.82E-12
PCDHB9	protocadherin beta 9	15.0096	3.90781	6.79E-14
SIX2	SIX homeobox 2	14.933	3.90043	1.73E-07
CALY	calcyon neuron-specific vesicular protein	14.8895	3.89622	9.05E-19

TABLE 5-continued

Genes more highly expressed in HMCs compared to UCB-MSCs				
Name	Description	Fold Change	Log Fold Change	p-Value
PCAT1	prostate cancer associated transcript 1 (non-protein coding)	14.6893	3.87669	4.25E-08
GPRC5C	G protein-coupled receptor_ class C_ group 5_member C	14.6602	3.87383	3.58E-07
NRN1	neuritin 1	14.6458	3.87242	1.36E-11
RIMS1	regulating synaptic membrane exocytosis 1	14.6198	3.86985	2.43E-22
LINC01012	long intergenic non-protein coding RNA 1012	14.5829	3.86621	6.92E-09
SH3GL2	SH3-domain GRB2-like 2	14.5492	3.86287	5.63E-09
SYT3	synaptotagmin III	14.5396	3.86192	3.33E-12
IL1RAPL1	interleukin 1 receptor accessory protein-like 1	14.538	3.86176	4.34E-13
PART1	prostate androgen-regulated transcript 1 (non-protein coding)	14.5131	3.85928	9.40E-12
PCDHB10	protocadherin beta 10	14.4383	3.85183	4.97E-17
SRSF12	serine/arginine-rich splicing factor 12	14.4059	3.84859	4.43E-16
TRH	thyrotropin-releasing hormone	14.405	3.8485	1.44E-06
EPHB1	EPH receptor B1	14.3437	3.84235	3.08E-13
CD70	CD70 molecule	14.1423	3.82194	1.66E-06
SPP1	secreted phosphoprotein 1	14.1278	3.82046	7.35E-19
DOC2GP	double C2-like domains_ gamma_pseudogene	14.0595	3.81347	4.24E-10
TSPEAR-AS1	TSPEAR antisense RNA 1	14.0479	3.81228	4.84E-31
THBD	thrombomodulin	14.0129	3.80868	1.12E-10
RGS5	regulator of G-protein signaling 5	14.0103	3.80842	1.90E-40
CYP26B1	cytochrome P450_ family 26_subfamily B_polypeptide 1	13.9621	3.80344	3.95E-15
LINC01139	long intergenic non-protein coding RNA 1139	13.882	3.79514	1.74E-20
NAPIL2	nucleosome assembly protein 1-like 2	13.8587	3.79272	2.85E-10
MTUS1	microtubule associated tumor suppressor 1	13.7747	3.78395	3.49E-09
DSP	desmoplakin	13.7042	3.77655	2.30E-31
AR	androgen receptor	13.6558	3.77144	1.35E-28
COL4A3	collagen_type IV_alpha 3 (Goodpasture antigen)	13.5989	3.76542	1.62E-19
PTH1R	parathyroid hormone 1 receptor	13.588	3.76426	3.24E-11
CELSR1	cadherin_EGF LAG seven-pass G-type receptor 1	13.4867	3.75347	6.06E-22
CCND2	cyclin D2	13.4595	3.75055	6.45E-07
LINC00951	long intergenic non-protein coding RNA 951	13.4392	3.74838	2.58E-06
AZU1	azurocidin 1	13.4366	3.7481	8.77E-10
SULT1C2	sulfotransferase family_cytosolic_1C_member 2	13.4353	3.74796	2.68E-06
LPAR4	lysophosphatidic acid receptor 4	13.4176	3.74606	8.11E-12
INA	internexin neuronal intermediate filament protein_alpha	13.3079	3.73421	5.90E-76
MYOZ3	myozenin 3	13.1452	3.71646	6.32E-75
AQP7P3	aquaporin 7 pseudogene 3	13.0872	3.71009	3.62E-07
FOXC1	forkhead box C1	13.0634	3.70746	2.10E-53
LRRK7	leucine rich repeat containing 7	13.0529	3.7063	1.25E-08
FZD3	frizzled class receptor 3	13.0287	3.70362	7.46E-27
NCALD	neurocalcin delta	12.9782	3.69802	4.24E-13
LSAMP-AS1	LSAMP antisense RNA 1	12.9224	3.6918	3.76E-06
IRX4	iroquois homeobox 4	12.8313	3.6816	1.79E-06
PURG	purine-rich element binding protein G	12.8256	3.68095	6.03E-10
AMH	anti-Mullerian hormone	12.7728	3.675	1.24E-21
RIPPLY3	ripply transcriptional repressor 3	12.6992	3.66667	2.22E-08
LOC101927482	uncharacterized LOC101927482	12.6952	3.66621	1.78E-15
C1orf94	chromosome 1 open reading frame 94	12.664	3.66266	8.39E-07
FOXA1	forkhead box A1	12.6375	3.65964	3.26E-07
FSTL5	follistatin-like 5	12.6272	3.65846	4.81E-08
KCNJ2	potassium channel_inwardly rectifying subfamily J_member 2	12.5831	3.65341	1.16E-07
XIRP1	xin actin binding repeat containing 1	12.4469	3.63772	1.58E-06
TMEM246	transmembrane protein 246	12.3385	3.62509	2.04E-11
LIPH	lipase_member H	12.2843	3.61874	5.47E-06

TABLE 5-continued

Genes more highly expressed in HMCs compared to UCB-MSCs				
Name	Description	Fold Change	Log Fold Change	p-Value
AQP7P1	aquaporin 7 pseudogene 1	12.1751	3.60586	2.31E-09
CASKIN1	CASK interacting protein 1	12.1053	3.59757	3.92E-15
ACHE	acetylcholinesterase (Yt blood group)	12.0642	3.59266	1.51E-17
C14orf105	chromosome 14 open reading frame 105	12.0171	3.58702	5.90E-06
TNFRSF10C	tumor necrosis factor receptor superfamily member 10c decoy without an intracellular domain	11.8486	3.56665	8.74E-46
FAM43B	family with sequence similarity 43 member B	11.7047	3.54901	5.63E-10
CBLN2	cerebellin 2 precursor	11.6961	3.54795	9.91E-06
FRZB	frizzled-related protein	11.6693	3.54465	2.01E-47
PTCHD4	patched domain containing 4	11.6421	3.54128	6.59E-16
DMRTA1	DMRT-like family A1	11.6186	3.53836	6.83E-16
ZSCAN1	zinc finger and SCAN domain containing 1	11.609	3.53717	4.18E-08
EPHA7	EPH receptor A7	11.5942	3.53533	3.06E-07
GABRA4	gamma-aminobutyric acid (GABA) A receptor_alpha 4	11.5797	3.53353	3.25E-06
AFAP1L2	actin filament associated protein 1-like 2	11.5445	3.52914	2.57E-11
RAPIGAP2	RAP1 GTPase activating protein 2	11.44	3.51602	4.39E-15
CSDC2	cold shock domain containing C2 RNA binding	11.4326	3.51508	5.86E-15
CGB8	chorionic gonadotropin_beta polypeptide 8	11.3511	3.50476	1.28E-08
ARHGEF16	Rho guanine nucleotide exchange factor (GEF) 16	11.3114	3.4997	2.42E-17
PCDH1	protocadherin 1	11.2726	3.49475	1.68E-17
NPPC	natriuretic peptide C	11.2664	3.49396	1.28E-06
ANGPTL4	angiopoietin-like 4	11.2516	3.49206	4.55E-35
ATP2B2	ATPase_Ca++ transporting_plasma membrane 2	11.1335	3.47684	9.53E-10
RNF182	ring finger protein 182	11.1267	3.47595	1.49E-10
CCDC160	coiled-coil domain containing 160	11.0566	3.46683	6.35E-12
DACH2	dachshund family transcription factor 2	11.0356	3.46409	2.10E-06
PTPRN2	protein tyrosine phosphatase_receptor type_N polypeptide 2	11.0305	3.46342	6.05E-07
IGFBP5	insulin-like growth factor binding protein 5	11.0117	3.46097	1.68E-06
COL4A4	collagen_type IV_alpha 4	11.0069	3.46033	6.39E-108
TMEM74B	transmembrane protein 74B	10.9141	3.44812	2.86E-09
OCLN	occludin	10.9085	3.44738	7.88E-18
PTGIS	prostaglandin I2 (prostacyclin) synthase	10.8909	3.44505	4.07E-17
CIDEA	cell death-inducing DFFA-like effector a	10.8757	3.44303	3.21E-07
VANGL2	VANGL planar cell polarity protein 2	10.8126	3.43464	2.88E-06
DOCK8	dedicator of cytokinesis 8	10.7905	3.43169	1.37E-06
CCDC88C	coiled-coil domain containing 88C	10.7762	3.42978	1.47E-08
NMNAT3	nicotinamide nucleotide adenyllyltransferase 3	10.7424	3.42524	1.21E-20
TCF15	transcription factor 15 (basic helix-loop-helix)	10.7253	3.42295	1.61E-07
ITGB6	integrin_beta 6	10.6645	3.41475	7.14E-08
SCUBE3	signal peptide_CUB domain_EGF-like 3	10.622	3.40899	5.25E-30
SOX17	SRY (sex determining region Y)-box 17	10.6119	3.40761	2.79E-06
IL2RB	interleukin 2 receptor_beta	10.6028	3.40637	7.12E-29
ATCAY	ataxia_cerebellar_Cayman type	10.5981	3.40573	8.13E-07
FMN1	formin 1	10.5973	3.40562	2.24E-36
EFNA2	ephrin-A2	10.5791	3.40314	1.56E-08
MAGEB17	melanoma antigen family B17	10.5548	3.39983	2.63E-06
CERS1	ceramide synthase 1	10.5375	3.39746	3.22E-09
DLK1	delta-like 1 homolog (Drosophila)	10.5276	3.39611	5.93E-11
DCHS1	dachsous cadherin-related 1	10.5002	3.39234	2.11E-108
SFTAIP	surfactant associated_1_pseudogene	10.3743	3.37494	1.05E-20
FOXP1	forkhead box G1	10.3464	3.37105	2.17E-05
ADAMTS7P1	ADAMTS7 pseudogene 1	10.3038	3.3651	2.14E-08
LEMD1-AS1	LEMD1 antisense RNA 1	10.2887	3.36299	6.84E-08

TABLE 5-continued

Genes more highly expressed in HMCs compared to UCB-MSCs				
Name	Description	Fold Change	Log Fold Change	p-Value
C6orf141	chromosome 6 open reading frame 141	10.1422	3.3423	1.99E-14
EDN1	endothelin 1	10.1099	3.3377	8.53E-77
RAB9B	RAB9B_ member RAS oncogene family	10.1049	3.33698	1.44E-32
SLC29A2	solute carrier family 29 (equilibrative nucleoside transporter)_ member 2	10.0911	3.33501	3.03E-28
GABRA5	gamma-aminobutyric acid (GABA) A receptor_alpha 5	10.09	3.33486	8.12E-06
RIMBP2	RIMS binding protein 2	10.0289	3.32609	4.37E-06
HTR1D	5-hydroxytryptamine (serotonin) receptor 1D_G protein-coupled	10.0216	3.32504	1.09E-17
GAL3ST3	galactose-3-O-sulfotransferase 3	9.99031	3.32053	4.84E-09
OXTR	oxytocin receptor	9.97952	3.31897	8.27E-11
SESN3	sestrin 3	9.97647	3.31853	8.95E-11
CCDC148	coiled-coil domain containing 148	9.92199	3.31063	1.51E-15
EPHA5	EPH receptor A5	9.84984	3.3001	4.99E-08
CTTNBP2	cortactin binding protein 2	9.84806	3.29984	1.31E-11
NLRP10	NLR family_pyrin domain containing 10	9.83285	3.29761	6.88E-08
ANO4	anoctamin 4	9.81113	3.29442	1.05E-10
KLHL6	kelch-like family member 6	9.78275	3.29024	4.00E-05
ALPK3	alpha-kinase 3	9.782	3.29013	1.59E-25
THRB	thyroid hormone receptor_beta	9.77116	3.28853	3.43E-05
TMEM63C	transmembrane protein 63C	9.76168	3.28713	1.95E-42
MLN	motilin	9.75086	3.28553	5.19E-06
LINC01082	long intergenic non-protein coding RNA 1082	9.74789	3.28509	3.83E-05
GBX2	gastrulation brain homeobox 2	9.63377	3.2681	1.35E-05
PCYT1B	phosphate cytidylyltransferase 1_choline_beta	9.59964	3.26298	8.46E-13
KRTAP4-9	keratin associated protein 4-9	9.55569	3.25636	5.02E-05
LOC90246	uncharacterized LOC90246	9.53148	3.2527	1.42E-28
PCDH19	protocadherin 19	9.51511	3.25022	1.59E-09
PCDHGB6	protocadherin gamma subfamily B_6	9.49593	3.24731	1.93E-10
FAM92B	family with sequence similarity 92_member B	9.43459	3.23796	1.44E-05
NTN4	netrin 4	9.42825	3.23699	6.41E-12
TPSG1	tryptase gamma 1	9.3604	3.22657	4.47E-05
PCDHAA9	protocadherin alpha 9	9.32536	3.22116	5.91E-05
FAM110D	family with sequence similarity 110_member D	9.3129	3.21923	1.47E-44
GATA3	GATA binding protein 3	9.25004	3.20946	2.07E-05
ELN	elastin	9.21082	3.20333	3.62E-29
NTNG1	netrin G1	9.15722	3.19491	6.47E-05
VIP	vasoactive intestinal peptide	9.13168	3.19088	6.52E-05
LHX9	LIM homeobox 9	9.10507	3.18667	8.09E-07
MYOZ1	myozinin 1	9.05729	3.17908	1.14E-07
FAM84A	family with sequence similarity 84_member A	9.04907	3.17777	9.59E-08
APOE	apolipoprotein E	9.04199	3.17664	2.45E-19
LOC102723344	uncharacterized LOC102723344	9.02815	3.17443	6.68E-08
RUND3B	RUN domain containing 3B	8.95349	3.16245	6.26E-06
C5orf46	chromosome 5 open reading frame 46	8.91071	3.15554	1.80E-27
LYVE1	lymphatic vessel endothelial hyaluronan receptor 1	8.90262	3.15423	7.29E-06
LINC00547	long intergenic non-protein coding RNA 547	8.88271	3.151	5.29E-05
SPINT2	serine peptidase inhibitor_Kunitz type_2	8.85505	3.1465	2.28E-25
GDF6	growth differentiation factor 6	8.82209	3.14112	1.43E-27
DACH1	dachshund family transcription factor 1	8.79004	3.13587	9.43E-05
HAP1	huntingtin-associated protein 1	8.77075	3.1327	5.15E-12
LOC149684	uncharacterized LOC149684	8.74792	3.12894	2.96E-06
BMP3	bone morphogenetic protein 3	8.74477	3.12842	1.07E-08
ALDH5A1	aldehyde dehydrogenase 5 family_member A1	8.72285	3.1248	1.65E-24
KIAA1211	KIAA1211	8.72013	3.12435	9.95E-10
MAP3K7CL	MAP3K7 C-terminal like	8.71361	3.12327	1.40E-59
AQP5	aquaporin 5	8.67359	3.11663	1.39E-06
LINC00887	long intergenic non-protein coding RNA	8.67191	3.11635	5.11E-07

TABLE 5-continued

Genes more highly expressed in HMCs compared to UCB-MSCs				
Name	Description	Fold Change	Log Fold Change	p-Value
ACSM4	acyl-CoA synthetase medium-chain family member 4	8.67101	3.1162	3.26E-05
SLC12A5	solute carrier family 12 (potassium/chloride transporter) member 5	8.66692	3.11552	1.95E-16
PPP1R14A	protein phosphatase 1_ regulatory (inhibitor) subunit 14A	8.62037	3.10775	6.73E-17
KCNMB1	potassium channel subfamily M regulatory beta subunit 1	8.61667	3.10713	2.55E-10
SLC5A4	solute carrier family 5 (glucose activated ion channel) member 4	8.5971	3.10385	4.58E-06
ZNF423	zinc finger protein 423	8.58459	3.10175	5.59E-15
CHRNA7	cholinergic receptor_nicotinic_alpha 7 (neuronal)	8.57015	3.09932	1.97E-05
FGF11	fibroblast growth factor 11	8.53766	3.09384	2.45E-58
CYTL1	cytokine-like 1	8.52908	3.09239	4.27E-35
GPR20	G protein-coupled receptor 20	8.52654	3.09196	1.94E-09
LOC100507600	uncharacterized LOC100507600	8.52406	3.09154	7.30E-09
SERTAD4	SERTA domain containing 4	8.52388	3.09151	5.96E-15
PROC	protein C (inactivator of coagulation factors Va and VIIa)	8.49091	3.08592	3.83E-07
JAM2	junctional adhesion molecule 2	8.48856	3.08552	7.86E-12
PCDHB16	protocadherin beta 16	8.48268	3.08452	7.41E-18
GRIK1-AS1	GRIK1 antisense RNA 1	8.45011	3.07897	2.75E-05
CGB2	chorionic gonadotropin_beta polypeptide 2	8.43343	3.07612	0.00012
CDH8	cadherin_8_type 2	8.4109	3.07226	8.44E-05
GPLD1	glycosylphosphatidylinositol specific phospholipase D1	8.40962	3.07204	5.72E-12
ZNF521	zinc finger protein 521	8.40507	3.07126	9.51E-26
FAM83E	family with sequence similarity 83_member E	8.38046	3.06703	6.69E-06
SBK3	SH3 domain binding kinase family_member 3	8.31767	3.05618	7.17E-05
WT1	Wilms tumor 1	8.30932	3.05473	4.77E-05
HID1	HID1 domain containing	8.25518	3.0453	1.09E-27
ERC2	ELKS/RAB6-interacting/CAST family member 2	8.21762	3.03872	1.91E-06
ESPN	espin	8.21625	3.03848	2.65E-06
WT1-AS	WT1 antisense RNA	8.19435	3.03463	6.39E-05
APBB1IP	amyloid beta (A4) precursor protein-binding_family B_member 1 interacting protein	8.191	3.03404	8.22E-12
PIEZ02	piezo-type mechanosensitive ion channel component 2	8.18754	3.03343	4.71E-09
AC093375.1	NA	8.15554	3.02778	0.000116
POTEF	POTE ankyrin domain family_member F	8.1373	3.02455	1.74E-28
JSRP1	junctional sarcoplasmic reticulum protein 1	8.12772	3.02285	4.78E-06
DRD1	dopamine receptor D1	8.11798	3.02112	5.53E-05
SYT9	synaptotagmin IX	8.04426	3.00796	7.24E-06
KRT7	keratin_7_type II	8.02866	3.00516	1.44E-64
LINC00858	long intergenic non-protein coding RNA 858	8.00705	3.00127	0.000153
ABCA13	ATP-binding cassette_sub-family A (ABC1)_member 13	7.98465	2.99723	3.12E-07
IGF1	insulin-like growth factor 1 (somatomedin C)	7.97768	2.99597	0.000181
PALD1	phosphatase domain containing_paladin 1	7.96188	2.99311	1.28E-08
SOWAHB	sosondowah ankyrin repeat domain family member B	7.95753	2.99232	3.29E-05
TMEM35	transmembrane protein 35	7.92494	2.9864	1.78E-38
ACTC1	actin_alpha_cardiac muscle 1	7.9239	2.98621	3.75E-16
CACNG6	calcium channel_voltage-dependent_gamma subunit 6	7.87156	2.97665	5.54E-34
PPL	periplakin	7.86982	2.97633	1.32E-14
TRPC5OS	TRPC5 opposite strand	7.86845	2.97608	0.00015
ABLIM1	actin binding LIM protein 1	7.82169	2.96748	2.65E-19

TABLE 5-continued

Genes more highly expressed in HMCs compared to UCB-MSCs				
Name	Description	Fold Change	Log Fold Change	p-Value
FOXL2	forkhead box L2	7.82115	2.96738	8.54E-08
TMOD1	tropomodulin 1	7.7731	2.95849	0.000143
FOXE3	forkhead box E3	7.72208	2.94899	5.15E-05
LINC00890	long intergenic non-protein coding RNA 890	7.70423	2.94565	9.71E-23
PLN	phospholamban	7.69819	2.94452	3.81E-08
CAPN11	calpain 11	7.69782	2.94445	4.09E-08
MAGEL2	melanoma antigen family L2	7.68668	2.94236	5.71E-12
LINC00622	long intergenic non-protein coding RNA 622	7.67023	2.93927	4.03E-13
RASL10A	RAS-like_ family 10_ member A	7.61561	2.92896	4.24E-05
C11orf87	chromosome 11 open reading frame 87	7.60006	2.92601	2.64E-06
LINC00840	long intergenic non-protein coding RNA 840	7.5575	2.91791	3.57E-06
SCG2	secretogranin II	7.55457	2.91735	7.95E-22
PXDNL	peroxidasin-like	7.5359	2.91378	8.38E-06
RASSF2	Ras association (RalGDS/AF-6) domain family member 2	7.49563	2.90605	3.11E-57
VGF	VGF nerve growth factor inducible	7.4909	2.90514	1.11E-12
NLGN1	neuroligin 1	7.46018	2.89921	7.92E-06
GRPR	gastrin-releasing peptide receptor	7.45051	2.89734	8.69E-29
ARL14	ADP-ribosylation factor-like 14	7.44819	2.89689	1.18E-05
RENBP	renin binding protein	7.40233	2.88798	2.31E-06
TRIML2	tripartite motif family-like 2	7.37534	2.88271	0.00029
FGD4	FYVE_ RhoGEF and PH domain containing 4	7.33934	2.87565	1.76E-20
BIRC7	baculoviral IAP repeat containing 7	7.33522	2.87484	0.000137
CADM4	cell adhesion molecule 4	7.33024	2.87386	9.04E-38
ANKS1B	ankyrin repeat and sterile alpha motif domain containing 1B	7.32308	2.87245	1.49E-05
LOC100130899	uncharacterized LOC100130899	7.31958	2.87176	0.00027
DCDC2	doublecortin domain containing 2	7.30194	2.86828	0.000282
CD101	CD101 molecule	7.30179	2.86825	3.82E-06
KIF21B	kinesin family member 21B	7.29992	2.86788	1.17E-68
EEF1A2	eukaryotic translation elongation factor 1 alpha 2	7.24763	2.85751	1.16E-22
CASC15	cancer susceptibility candidate 15 (non-protein coding)	7.23774	2.85554	6.66E-07
DCLK1	doublecortin-like kinase 1	7.22426	2.85285	2.25E-15
SOX18	SRY (sex determining region Y)-box 18	7.2107	2.85014	1.24E-08
CTNND2	catenin (cadherin-associated protein)_ delta 2	7.20676	2.84935	0.000304
NHS	Nance-Horan syndrome (congenital cataracts and dental anomalies)	7.20476	2.84895	5.32E-08
LOC100128531	uncharacterized LOC100128531	7.18551	2.84509	0.000395
RGS9	regulator of G-protein signaling 9	7.17555	2.84309	2.06E-15
NCF2	neutrophil cytosolic factor 2	7.16358	2.84068	1.39E-06
LINC00649	long intergenic non-protein coding RNA 649	7.15772	2.8395	2.36E-08
PCDHB8	protocadherin beta 8	7.13874	2.83567	7.07E-05
CLEC4GP1	C-type lectin domain family 4_ member G pseudogene 1	7.12243	2.83237	0.000363
PCBP3	poly(rC) binding protein 3	7.12199	2.83228	1.76E-13
CSMD3	CUB and Sushi multiple domains 3	7.11932	2.83174	5.68E-13
SERPINA9	serpin peptidase inhibitor_ clade A (alpha-1 antiproteinase_ antitrypsin)_ member 9	7.01897	2.81126	0.000456
ELAVL2	ELAV like neuron-specific RNA binding protein 2	7.01328	2.81009	8.89E-05
LBH	limb bud and heart development	6.9804	2.80331	5.82E-57
KCNN2	potassium channel_ calcium activated intermediate/small conductance subfamily N alpha_ member 2	6.96663	2.80046	4.14E-14
SEMA3F	sema domain_ immunoglobulin domain (Ig)_ short basic domain_ secreted_ (semaphorin) 3F	6.94267	2.79549	1.50E-60
BEND5	BEN domain containing 5	6.89538	2.78563	0.000319
P2RX6P	purinergic receptor P2X_ ligand gated ion channel_6 pseudogene	6.89509	2.78557	1.13E-07
LRMP	lymphoid-restricted membrane protein	6.89452	2.78545	9.07E-08
CNTNAP3B	contactin associated protein-like 3B	6.89089	2.78469	0.000117

TABLE 5-continued

Genes more highly expressed in HMCs compared to UCB-MSCs				
Name	Description	Fold Change	Log Fold Change	p-Value
ZCCHC18	zinc finger_ CCHC domain containing 18	6.88597	2.78366	2.72E-16
RASSF10	Ras association (RalGDS/AF-6) domain family (N-terminal) member 10	6.87391	2.78113	0.000516
ZIC2	Zic family member 2	6.86139	2.7785	0.000395
CYGB	cytoglobin	6.84267	2.77456	3.13E-31
TYROBP	TYRO protein tyrosine kinase binding protein	6.83154	2.77221	0.00043
LOC100507006	uncharacterized LOC100507006	6.81583	2.76889	0.000275
THSD7A	thrombospondin_ type I domain containing 7A	6.81361	2.76842	1.62E-06
MIR4321	microRNA 4321	6.7899	2.76339	0.000527
DYSF	dysferlin	6.78731	2.76284	6.21E-23
SYTL1	synaptotagmin-like 1	6.7575	2.75649	1.41E-09
ADCY10P1	adenylate cyclase 10 (soluble) pseudogene 1	6.74884	2.75464	2.20E-09
JAG2	jagged 2	6.73398	2.75146	1.38E-15
COL6A5	collagen_ type VI_ alpha 5	6.72302	2.74911	0.000601
PAQR6	progestin and adiponQ receptor family member VI	6.72195	2.74888	1.92E-09
FSTL4	follistatin-like 4	6.71483	2.74735	0.000619
UPB1	ureidopropionase_ beta	6.71129	2.74659	1.91E-06
LZTS1	leucine zipper_ putative tumor suppressor 1	6.70896	2.74609	9.30E-74
CNGA1	cyclic nucleotide gated channel alpha 1	6.70645	2.74555	1.88E-05
KCNH1	potassium channel_ voltage gated eag related subfamily H_ member 1	6.69549	2.74319	1.61E-09
RGPD1	RANBP2-like and GRIP domain containing 1	6.66165	2.73588	9.04E-06
SPINK1	serine peptidase inhibitor_ Kazal type 1	6.66082	2.7357	0.000649
ECSCR	endothelial cell surface expressed chemotaxis and apoptosis regulator	6.65985	2.73549	3.50E-17
MYL4	myosin_ light chain 4_ alkali; atrial_ embryonic	6.65547	2.73454	4.43E-07
ADCY4	adenylate cyclase 4	6.64339	2.73192	1.28E-05
ZMAT4	zinc finger_ matrin-type 4	6.62004	2.72684	6.04E-10
DUSP15	dual specificity phosphatase 15	6.59183	2.72068	0.000655
SHROOM2	shroom family member 2	6.57527	2.71705	1.20E-61
RAPGEF5	Rap guanine nucleotide exchange factor (GEF) 5	6.54952	2.71139	9.33E-06
CTAGE6	CTAGE family_ member 6	6.54925	2.71133	0.00016
Clorf106	chromosome 1 open reading frame 106	6.53003	2.70709	6.55E-41
TIE1	tyrosine kinase with immunoglobulin-like and EGF-like domains 1	6.49856	2.70012	4.16E-36
GZMA	granzyme A (granzyme 1_ cytotoxic T-lymphocyte-associated serine esterase 3)	6.47226	2.69427	0.000623
RHOV	ras homolog family member V	6.46433	2.6925	1.72E-06
LINC01002	long intergenic non-protein coding RNA 1002	6.42043	2.68267	2.59E-05
LEPREL1	prolyl 3-hydroxylase 2	6.40243	2.67862	8.05E-55
KRTAP5-1	keratin associated protein 5-1	6.40017	2.67811	0.000735
TLR2	toll-like receptor 2	6.37577	2.6726	0.000277
PALM2	paralemmin 2	6.34878	2.66648	3.95E-17
LINC00704	long intergenic non-protein coding RNA 704	6.317	2.65924	7.01E-06
LOC100652824	NA	6.31166	2.65802	3.63E-11
AADACP1	arylacetamide deacetylase pseudogene 1	6.301	2.65558	0.000388
TLL2	tolloid-like 2	6.29999	2.65535	2.58E-12
ENTPD3	ectonucleoside triphosphate diphosphohydrolase 3	6.28582	2.6521	4.00E-05
ATRN1	attractin-like 1	6.28468	2.65184	2.86E-06
LINC01239	long intergenic non-protein coding RNA 1239	6.2672	2.64782	1.04E-05
ZIC1	Zic family member 1	6.26702	2.64778	0.000977
UPK1A	uroplakin 1A	6.24976	2.6438	2.79E-05
LOC100507534	uncharacterized LOC100507534	6.2293	2.63907	1.20E-05
PDZD2	PDZ domain containing 2	6.22718	2.63858	3.38E-32
SEMA6B	sema domain_ transmembrane domain (TM)_ and cytoplasmic domain_ (semaphorin) 6B	6.21709	2.63624	9.15E-14
MEGF10	multiple EGF-like-domains 10	6.21063	2.63474	0.000763

TABLE 5-continued

Genes more highly expressed in HMCs compared to UCB-MSCs				
Name	Description	Fold Change	Log Fold Change	p-Value
LINC01197	long intergenic non-protein coding RNA 1197	6.20461	2.63334	0.000813
SPATA31E1	SPATA31 subfamily E_ member 1	6.19447	2.63098	0.000662
A2M-AS1	A2M antisense RNA 1 (head to head)	6.19176	2.63035	2.13E-05
CECR2	cat eye syndrome chromosome region_ candidate 2	6.19017	2.62998	0.000364
DNAH8	dynein_ axonemal_ heavy chain 8	6.18036	2.62769	0.000829
GPR183	G protein-coupled receptor 183	6.17916	2.62741	2.62E-18
PRICKLE1	prickle homolog 1	6.17192	2.62572	3.61E-10
MEI4	meiotic double-stranded break formation protein 4	6.16504	2.62411	0.000297
GNAO1	guanine nucleotide binding protein (G protein)_ alpha activating activity polypeptide O	6.16397	2.62386	1.09E-18
PCDHA2	protocadherin alpha 2	6.15846	2.62257	0.000939
FGFBP3	fibroblast growth factor binding protein 3	6.15599	2.62199	1.51E-120
PTPN7	protein tyrosine phosphatase_ non-receptor type 7	6.13465	2.61698	9.90E-05
BAALC	brain and acute leukemia_ cytoplasmic	6.12976	2.61583	5.89E-17
ZFHX2	zinc finger homeobox 2	6.12963	2.6158	1.58E-11
LAMC2	laminin_ gamma 2	6.12581	2.6149	6.63E-12
PPARG	peroxisome proliferator-activated receptor gamma	6.12428	2.61454	2.53E-11
LOC729737	uncharacterized LOC729737	6.11478	2.6123	3.85E-11
RASGRF1	Ras protein-specific guanine nucleotide-releasing factor 1	6.1072	2.61051	8.10E-24
ACVR1C	activin A receptor_type IC	6.08514	2.60529	1.32E-07
ST6GAL2	ST6 beta-galactosamidase alpha-2_6-sialyltranferase 2	6.08295	2.60477	1.66E-19
FAM162B	family with sequence similarity 162_member B	6.08193	2.60453	0.000742
MYOZ2	myozinin 2	6.07679	2.60331	2.14E-10
ZIC5	Zic family member 5	6.06955	2.60159	0.000829
SLC7A9	solute carrier family 7 (amino acid transporter light chain_ bo_+ system)_ member 9	6.05199	2.59741	5.05E-07
GPR143	G protein-coupled receptor 143	6.04486	2.59571	1.54E-18
WNT16	wingless-type MMTV integration site family_member 16	6.03971	2.59448	4.60E-08
LINC00222	long intergenic non-protein coding RNA 222	6.03009	2.59218	0.000545
PIFO	primary cilia formation	6.0247	2.59089	1.19E-09
MDFI	MyoD family inhibitor	6.02437	2.59081	4.67E-15
SGIP1	SH3-domain GRB2-like (endophilin) interacting protein 1	6.0134	2.58818	1.29E-15
FSIP2	fibrous sheath interacting protein 2	6.0124	2.58794	4.68E-06
ACAN	aggrecan	6.00973	2.5873	1.06E-08
LOC400863	NA	6.00885	2.58709	7.71E-05
C11orf88	chromosome 11 open reading frame 88	5.97741	2.57952	9.46E-15
TSPAN18	tetraspanin 18	5.96437	2.57637	9.71E-07
VSTM2L	V-set and transmembrane domain containing 2 like	5.96346	2.57615	1.08E-12
LINC00460	long intergenic non-protein coding RNA 460	5.95206	2.57339	6.68E-09
HOXB8	homeobox B8	5.94534	2.57176	7.30E-22
LINC00086	small integral membrane protein 10 like 2A	5.9242	2.56662	1.98E-08
CDHR1	cadherin-related family member 1	5.92223	2.56614	0.001148
BMF	Bcl2 modifying factor	5.92087	2.56581	2.33E-12
RUNX3	runt-related transcription factor 3	5.91292	2.56387	0.00036
SCNSA	sodium channel_voltage gated_type V alpha subunit	5.88809	2.5578	8.62E-07
GLRA4	glycine receptor_alpha 4	5.88793	2.55776	0.001253
PTPRR	protein tyrosine phosphatase_receptor type_R	5.87154	2.55374	1.05E-06

TABLE 5-continued

Genes more highly expressed in HMCs compared to UCB-MSCs				
Name	Description	Fold Change	Log Fold Change	p-Value
NTF4	neurotrophin 4	5.87053	2.55349	3.68E-12
MCF2	MCF.2 cell line derived transforming sequence	5.86829	2.55294	2.85E-05
TF	transferrin	5.84908	2.54821	3.31E-06
ATP2B3	ATPase_Ca++ transporting_plasma membrane 3	5.84714	2.54773	1.90E-06
CD37	CD37 molecule	5.83422	2.54454	7.82E-09
LAPTM5	lysosomal protein transmembrane 5	5.82008	2.54104	3.89E-31
RAMP2-AS1	RAMP2 antisense RNA 1	5.81049	2.53866	1.81E-09
IGLON5	IgLON family member 5	5.80401	2.53705	6.67E-05
SLC6A17	solute carrier family 6 (neutral amino acid transporter)_member 17	5.79641	2.53516	3.43E-15
GIPC3	GIPC PDZ domain containing family_member 3	5.7752	2.52987	6.08E-59
ASXL3	additional sex combs like transcriptional regulator 3	5.77324	2.52938	0.000148
PCDHAC1	protocadherin alpha subfamily C_1	5.77243	2.52918	0.001215
GRIK4	glutamate receptor_ionotropic_kainate 4	5.77079	2.52877	8.42E-06
IRF6	interferon regulatory factor 6	5.7632	2.52687	8.02E-09
KRT23	keratin 23_type I	5.75905	2.52583	2.56E-07
ST6GALNAC1	ST6 (alpha-N-acetyl-neuraminy-2-3-beta-galactosyl-1-3)-N-acetylgalactosaminide alpha-2-6-sialyltransferase 1	5.75581	2.52502	0.001081
CYP2E1	cytochrome P450_family 2_subfamily E_polypeptide 1	5.7484	2.52316	5.32E-07
SIPA1L2	signal-induced proliferation-associated 1 like 2	5.74103	2.52131	4.32E-53
CACNA2D3	calcium channel_voltage-dependent_alpha 2/delta subunit 3	5.73638	2.52014	2.26E-05
CCDC3	coiled-coil domain containing 3	5.72514	2.51731	1.02E-07
PTGS1	prostaglandin-endoperoxide synthase 1 (prostaglandin G/H synthase and cyclooxygenase)	5.72137	2.51636	6.83E-12
RGS7	regulator of G-protein signaling 7	5.71709	2.51528	1.57E-07
LINC01260	long intergenic non-protein coding RNA 1260	5.71614	2.51504	0.00024
LOC102724849	uncharacterized LOC102724849	5.71392	2.51448	2.09E-07
LRRN4	leucine rich repeat neuronal 4	5.71217	2.51404	4.42E-15
SP140	SP140 nuclear body protein	5.71063	2.51365	6.75E-14
C19orf81	chromosome 19 open reading frame 81	5.70956	2.51338	4.55E-05
KLHL4	kelch-like family member 4	5.69849	2.51058	1.19E-08
CD163L1	CD163 molecule-like 1	5.67893	2.50562	8.29E-08
TUBA3E	tubulin_alpha 3e	5.66777	2.50278	0.001189
FGF13	fibroblast growth factor 13	5.66568	2.50225	0.00092
GSC	goosecoid homeobox	5.66114	2.50116	1.08E-05
CGB5	chorionic gonadotropin_beta polypeptide 5	5.64166	2.49612	0.000597
PCDHB5	protocadherin beta 5	5.63693	2.49491	8.16E-06
SRCRB4D	scavenger receptor cysteine rich family_4 domains	5.63486	2.49438	2.65E-19
ZAP70	zeta-chain (TCR) associated protein	5.62596	2.4921	0.000113
CCDC81	kinase 70 kDa	5.6037	2.48638	6.86E-14
KIAA1456	coiled-coil domain containing 81	5.60048	2.48555	1.55E-20
NFATC2	KIAA1456	5.59757	2.4848	1.37E-19
MUC19	nuclear factor of activated T-cells_cytoplasmic_calcineurin-dependent 2	5.59536	2.48423	0.000489
KCNJ6	mucin 19_oligomeric	5.59284	2.48358	0.001973
MTRNR2L10	potassium channel_inwardly rectifying subfamily J_member 6	5.58513	2.48159	9.04E-05
ZBTB46	MT-RNR2-like 10	5.57495	2.47896	1.21E-23
PCDHB14	zinc finger and BTB domain containing 46	5.56515	2.47642	2.03E-06
IGSF3	immunoglobulin superfamily_member 3	5.56368	2.47604	1.39E-14
NOVA2	neuro-oncological ventral antigen 2	5.5601	2.47511	4.01E-06
DRP2	dystrophin related protein 2	5.54662	2.47161	1.49E-37
PRTG	protogenin	5.53752	2.46924	1.84E-09

TABLE 5-continued

Genes more highly expressed in HMCs compared to UCB-MSCs					
Name	Description	Fold Change	Log Fold Change	p-Value	
KIF26A	kinesin family member 26A	5.53717	2.46915	3.41E-08	
LINC01013	long intergenic non-protein coding RNA 1013	5.52759	2.46665	0.000302	
KNDC1	kinase non-catalytic C-lobe domain (KNCD) containing 1	5.52062	2.46483	1.87E-08	
PAK3	p21 protein (Cdc42/Rac)-activated kinase 3	5.51324	2.4629	5.54E-32	
TMEM52B	transmembrane protein 52B	5.51278	2.46278	0.002149	
HOXB13	homeobox B13	5.48937	2.45664	1.06E-05	
COL23A1	collagen_type XXIII_alpha 1	5.4837	2.45515	0.001602	
DNM3	dynamin 3	5.48298	2.45496	5.19E-11	
PAX9	paired box 9	5.46356	2.44984	0.002241	
SETBP1	SET binding protein 1	5.45784	2.44833	5.88E-06	
FGF16	fibroblast growth factor 16	5.4399	2.44358	0.002308	
DUSP26	dual specificity phosphatase 26 (putative)	5.43809	2.4431	0.002181	
BEX2	brain expressed X-linked 2	5.43259	2.44164	1.45E-09	
FAM84B	family with sequence similarity 84_member B	5.4242	2.43941	3.53E-13	
SDK2	sidekick cell adhesion molecule 2	5.40851	2.43523	1.06E-10	
KBTBD11	kelch repeat and BTB (POZ) domain containing 11	5.40671	2.43475	1.16E-10	
GRHL3	grainyhead-like transcription factor 3	5.40217	2.43354	8.32E-07	
ZBED2	zinc finger_BED-type containing 2	5.40094	2.43321	9.10E-07	
TMC8	transmembrane channel-like 8	5.3717	2.42538	0.001867	
C2CD4C	C2 calcium-dependent domain containing 4C	5.37103	2.4252	1.38E-10	
NBL1	neuroblastoma 1_DAN family BMP antagonist	5.3578	2.42164	0.000893	
ARL4C	ADP-ribosylation factor-like 4C	5.34848	2.41913	5.53E-19	
MS4A4A	membrane-spanning 4-domains_subfamily A_member 4A	5.33327	2.41502	0.001852	
GLB1L2	galactosidase_beta 1-like 2	5.32363	2.41241	3.97E-12	
FAM131B	family with sequence similarity 131_member B	5.31858	2.41104	1.09E-19	
LOC643542	uncharacterized LOC643542	5.31821	2.41094	0.00023	
TMEM151B	transmembrane protein 151B	5.30974	2.40864	0.002088	
LMO2	LIM domain only 2 (rhombotin-like 1)	5.30653	2.40777	0.000314	
IGDCC4	immunoglobulin superfamily_DCC subclass_member 4	5.29724	2.40524	5.68E-72	
OPCML	opioid binding protein/cell adhesion molecule-like	5.28436	2.40173	5.06E-05	
CACNG8	calcium channel_voltage-dependent_gamma subunit 8	5.27975	2.40047	1.83E-16	
RORB	RAR-related orphan receptor B	5.24415	2.39071	0.002129	
HAND1	heart and neural crest derivatives expressed 1	5.22167	2.38451	1.82E-06	
SULT4A1	sulfotransferase family 4A_member 1	5.21208	2.38186	1.47E-06	
HLA-B	major histocompatibility complex_class I_B	5.20569	2.38009	1.09E-26	
KCNN3	potassium channel_calcium activated intermediate/small conductance subfamily N alpha_member 3	5.20126	2.37886	0.000383	
CRLF1	cytokine receptor-like factor 1	5.15671	2.36645	1.13E-11	
ATP8A1	ATPase_aminocepholipid transporter (APLT)_class I_type 8A_member 1	5.15531	2.36606	1.96E-07	
TRIM9	tripartite motif containing 9	5.15374	2.36562	0.000187	
KCNA7	potassium channel_voltage gated shaker related subfamily A_member 7	5.15228	2.36521	2.72E-05	
TAGLN3	transgelin 3	5.14806	2.36403	4.16E-08	
PRKCG	protein kinase C_gamma	5.13449	2.36022	1.20E-05	
SPON1	spondin 1_extracellular matrix protein	5.12098	2.35642	5.19E-09	
PKD1L2	polycystic kidney disease 1-like 2 (gene/pseudogene)	5.12063	2.35632	0.000127	
PKNOX2	PBX/knotted 1 homeobox 2	5.11513	2.35477	0.000112	
LOC100129203	uncharacterized LOC100129203	5.10379	2.35157	0.001332	
DOK6	docking protein 6	5.07399	2.34312	4.34E-05	
TNFSF4	tumor necrosis factor (ligand) superfamily_member 4	5.05892	2.33883	1.26E-10	

TABLE 5-continued

Genes more highly expressed in HMCs compared to UCB-MSCs				
Name	Description	Fold Change	Log Fold Change	p-Value
CHDH	choline dehydrogenase	5.05647	2.33813	0.000408
CAMSAP3	calmodulin regulated spectrin-associated protein family member 3	5.04422	2.33463	0.000936
NEDD4L	neural precursor cell expressed developmentally down-regulated 4-like E3 ubiquitin protein ligase	5.03796	2.33284	8.36E-17
ZNF702P	zinc finger protein 702 pseudogene	5.02959	2.33044	2.26E-06
PPP1R1C	protein phosphatase 1 regulatory (inhibitor) subunit 1C	5.01083	2.32505	0.000132
CPE	carboxypeptidase E	5.00021	2.32199	2.22E-05

TABLE 6

Genes more highly expressed in UCB-MSCs compared to HMCs				
Name	Description	Fold Change	Log Fold Change	p-Value
MEG3	maternally expressed 3 (non-protein coding)	-17630.7	-14.1058	7.58E-194
CAT	catalase	-1511.12	-10.5614	1.14E-99
DYNLT3	dynein light chain Tctex-type 3	-1417.76	-10.4694	5.79E-88
ALDH1A1	aldehyde dehydrogenase 1 family member A1	-1170.82	-10.1933	5.05E-179
S100A6	S100 calcium binding protein A6	-895.544	-9.80662	5.29E-222
GSTT1	glutathione S-transferase theta 1	-681.793	-9.41319	2.12E-66
CTSF	cathepsin F	-302.374	-8.24019	7.74E-45
CMKLR1	chemerin chemokine-like receptor 1	-284.33	-8.15142	2.15E-43
FLG-AS1	FLG antisense RNA 1	-246.966	-7.94817	1.08E-41
KRBOX1	KRAB box domain containing 1	-229.441	-7.84198	4.89E-41
LYNX1	Ly6/neurotoxin 1	-199.238	-7.63835	7.06E-36
FMOD	fibromodulin	-191.276	-7.57951	1.15E-56
ZNF662	zinc finger protein 662	-174.724	-7.44893	1.18E-40
LMO3	LIM domain only 3 (rhombotin-like 2)	-170.074	-7.41002	8.31E-49
CNTN3	contactin 3 (plasmacytoma associated)	-162.07	-7.34047	1.38E-64
CXCL1	chemokine (C-X-C motif) ligand 1 (melanoma growth stimulating activity_alpha)	-149.21	-7.2212	2.41E-66
IRX3	iroquois homeobox 3	-148.228	-7.21167	1.60E-65
LINC01133	long intergenic non-protein coding RNA 1133	-143.929	-7.16921	8.35E-65
CCDC36	coiled-coil domain containing 36	-142.12	-7.15097	7.50E-32
LOC400043	uncharacterized LOC400043	-135.246	-7.07944	2.84E-43
CXCL6	chemokine (C-X-C motif) ligand 6	-134.778	-7.07444	4.76E-46
LOC101929369	NA	-133.058	-7.05591	2.42E-39
C5orf63	chromosome 5 open reading frame 63	-130.609	-7.02911	1.23E-35
ANGPTL1	angiopoietin-like 1	-129.967	-7.022	1.55E-47
MEG8	maternally expressed 8 (non-protein coding)	-128.676	-7.0076	1.67E-30
BHMT2	betaine-homocysteine S-methyltransferase 2	-114.938	-6.84471	8.37E-28
RTN1	reticulon 1	-109.648	-6.77673	6.25E-56
FLG	filaggrin	-100.449	-6.65032	8.20E-26
PCDHGA12	protocadherin gamma subfamily A_12	-99.7593	-6.64038	2.95E-35
P116	peptidase inhibitor 16	-98.0204	-6.61501	2.34E-34
FOXQ1	forkhead box Q1	-97.2354	-6.60341	5.15E-25
SLC39A4	solute carrier family 39 (zinc transporter)_member 4	-96.9111	-6.59859	2.72E-45
HOXC8	homeobox C8	-91.8113	-6.5206	3.45E-183
SDR42E1	short chain dehydrogenase/reductase family 42E_member 1	-88.1232	-6.46145	5.13E-25
ZNF300P1	zinc finger protein 300 pseudogene 1 (functional)	-86.6483	-6.4371	5.64E-28
PID1	phosphotyrosine interaction domain containing 1	-86.3803	-6.43263	1.87E-48
ABCA8	ATP-binding cassette_sub-family A (ABC1)_member 8	-82.6607	-6.36913	5.15E-87

TABLE 6-continued

Genes more highly expressed in UCB-MSCs compared to HMCs				
Name	Description	Fold Change	Log Fold Change	p-Value
NAALADL 1	N-acetylated alpha-linked acidic dipeptidase-like 1	-81.0517	-6.34077	5.70E-89
GSTM5	glutathione S-transferase mu 5	-78.262	-6.29024	7.38E-25
LOC150381	NA	-78.0664	-6.28663	2.48E-40
SPESP1	sperm equatorial segment protein 1	-75.344	-6.23542	7.37E-22
COX7A1	cytochrome c oxidase subunit VIIa polypeptide 1 (muscle)	-71.77	-6.16531	8.83E-41
CHI3L1	chitinase 3-like 1 (cartilage glycoprotein-39)	-71.6066	-6.16202	2.08E-36
PLD5	phospholipase D family_ member 5	-71.5604	-6.16109	3.57E-22
PAX8-AS1	PAX8 antisense RNA 1	-70.7006	-6.14365	6.52E-60
LINC00473	long intergenic non-protein coding RNA 473	-65.782	-6.03962	8.00E-37
TNFAIP6	tumor necrosis factor_ alpha-induced protein 6	-65.3624	-6.03039	6.10E-32
CCDC89	coiled-coil domain containing 89	-65.2389	-6.02766	3.85E-33
NKAPL	NFKB activating protein-like	-63.0638	-5.97874	1.55E-20
PTGES	prostaglandin E synthase	-61.3844	-5.9398	7.12E-283
IQGAP2	IQ motif containing GTPase activating protein 2	-61.2161	-5.93584	7.26E-46
HOXC-AS1	HOXC cluster antisense RNA 1	-61.0945	-5.93297	3.56E-23
CXCL3	chemokine (C-X-C motif) ligand 3	-60.7166	-5.92402	3.01E-21
DNAJA4	DnaJ (Hsp40) homolog_ subfamily A_ member 4	-59.1739	-5.88689	4.13E-60
LINC00654	long intergenic non-protein coding RNA 654	-54.5633	-5.76986	3.95E-29
MYH13	myosin_ heavy chain 13_ skeletal muscle	-53.4523	-5.74018	1.10E-19
CCDC144B	coiled-coil domain containing 144B (pseudogene)	-51.3236	-5.68155	5.35E-18
CXCL5	chemokine (C-X-C motif) ligand 5	-51.2493	-5.67946	9.87E-32
PCDHGB3	protocadherin gamma subfamily B_ 3	-51.168	-5.67717	4.94E-18
AARD	alanine and arginine rich domain containing protein	-50.3978	-5.65529	1.45E-27
CARD16	caspase recruitment domain family_ member 16	-50.1007	-5.64676	1.07E-63
GAS1	growth arrest-specific 1	-49.8734	-5.6402	4.77E-129
LOC100240735	uncharacterized LOC100240735	-49.8499	-5.63952	5.09E-18
CSF3	colony stimulating factor 3 (granulocyte)	-49.1343	-5.61866	1.33E-16
HOXC10	homeobox C10	-48.8217	-5.60945	2.74E-104
CXCL8	chemokine (C-X-C motif) ligand 8	-48.64	-5.60407	1.22E-37
NUPR1	nuclear protein_ transcriptional regulator_ 1	-48.4841	-5.59944	2.59E-81
ZNF572	zinc finger protein 572	-48.1552	-5.58962	1.69E-17
HSPB2	heat shock 27kDa protein 2	-47.9112	-5.58229	1.64E-17
HOXD8	homeobox D8	-47.1374	-5.5588	8.90E-63
GBP4	guanylate binding protein 4	-45.9041	-5.52055	4.74E-42
LRRK2	leucine-rich repeat kinase 2	-45.7497	-5.51569	6.91E-16
FAM66B	family with sequence similarity 66_ member B	-44.8352	-5.48656	1.09E-16
ISLR	immunoglobulin superfamily containing leucine-rich repeat	-44.685	-5.48172	1.83E-95
PCDHGA3	protocadherin gamma subfamily A_ 3	-44.2636	-5.46805	1.12E-16
ZNF736	zinc finger protein 736	-43.1447	-5.43111	3.45E-16
HSD17B7P2	hydroxysteroid (17-beta) dehydrogenase 7 pseudogene	-42.9582	-5.42486	2.52E-30
LRRTM3	leucine rich repeat transmembrane neuronal 3	-42.6848	-5.41565	4.82E-30
HGF	hepatocyte growth factor (hepatopoietin A; scatter factor)	-42.505	-5.40956	8.03E-36
ADAMTS4	ADAM metallopeptidase with thrombospondin type 1 motif_ 4	-42.3714	-5.40502	9.49E-138
ZNF257	zinc finger protein 257	-41.6912	-5.38167	4.49E-16
GRID2	glutamate receptor_ ionotropic_ delta 2	-41.5991	-5.37848	1.54E-18
FGF7	fibroblast growth factor 7	-41.044	-5.3591	1.97E-25
PRSS30P	protease_ serine_ 30_ pseudogene	-40.9168	-5.35462	1.00E-15
LINC00506	long intergenic non-protein coding RNA 506	-40.2244	-5.33	1.00E-15
HOXC5	homeobox C5	-37.8836	-5.2435	2.08E-41
ADIRF	adipogenesis regulatory factor	-37.6375	-5.2341	1.34E-31

TABLE 6-continued

Genes more highly expressed in UCB-MSCs compared to HMCs					
Name	Description	Fold Change	Log Fold Change	p-Value	
ZFP3	ZFP3 zinc finger protein	-37.3196	-5.22186	1.35E-56	
HYDIN	HYDIN_ axonemal central pair apparatus protein	-37.0798	-5.21256	8.40E-18	
TDO2	tryptophan 2_3-dioxygenase	-36.9156	-5.20616	2.68E-25	
CD200	CD200 molecule	-36.3481	-5.18381	0.00E+00	
HOXC4	homeobox C4	-36.3086	-5.18224	1.34E-75	
ANXA10	annexin A10	-35.674	-5.1568	2.34E-121	
LOC284757	NA	-35.3454	-5.14345	3.92E-16	
ZNF311	zinc finger protein 311	-34.811	-5.12147	4.19E-40	
CASP1	caspase 1_ apoptosis-related cysteine peptidase	-34.3279	-5.10131	1.32E-90	
C1QTNF7	C1q and tumor necrosis factor related protein 7	-33.2599	-5.05571	1.08E-13	
SNORD114-10	small nucleolar RNA_ C/D box 114-10	-32.3322	-5.0149	1.14E-13	
PCDHGA11	protocadherin gamma subfamily A_ 11	-32.1396	-5.00628	9.50E-53	
HOXD-AS2	HOXD cluster antisense RNA 2	-31.947	-4.99761	3.44E-26	
PITX1	paired-like homeodomain 1	-31.6427	-4.9838	1.10E-119	
ZNF492	zinc finger protein 492	-31.3026	-4.96821	1.68E-14	
HOXC6	homeobox C6	-31.295	-4.96786	4.21E-45	
HOXC9	homeobox C9	-31.2237	-4.96457	1.02E-30	
KCNJ13	potassium channel_ inwardly rectifying subfamily J_ member 13	-30.8716	-4.94821	4.29E-17	
IL1B	interleukin 1_ beta	-29.6829	-4.89156	1.93E-46	
C11orf86	chromosome 11 open reading frame 86	-29.6418	-4.88956	1.78E-20	
CSGALNACT1	chondroitin sulfate N-acetylgalactosaminyltransferase 1	-29.5941	-4.88724	2.37E-57	
FPR1	formyl peptide receptor 1	-29.0064	-4.8583	1.23E-12	
LOC728819	NA	-28.0926	-4.81212	2.57E-12	
MLC1	megalencephalic leukoencephalopathy with subcortical cysts 1	-28.0634	-4.81062	4.15E-21	
CXCL2	chemokine (C-X-C motif) ligand 2	-27.977	-4.80617	4.71E-24	
CEACAM22P	carcinoembryonic antigen-related cell adhesion molecule 22_ pseudogene	-27.7945	-4.79673	4.37E-12	
ZNF454	zinc finger protein 454	-27.2796	-4.76975	2.00E-15	
TDRD9	tudor domain containing 9	-26.7334	-4.74057	4.26E-12	
FAM198A	family with sequence similarity 198_ member A	-26.5826	-4.73241	8.07E-12	
IL21-AS1	IL21 antisense RNA 1	-26.2061	-4.71183	9.27E-12	
LINC00478	mir-99a-let-7c cluster host gene	-25.7904	-4.68876	1.29E-17	
ZNF439	zinc finger protein 439	-25.5938	-4.67772	2.02E-40	
KLHDC7B	kelch domain containing 7B	-25.3659	-4.66482	2.63E-32	
EN1	engrailed homeobox 1	-25.0474	-4.64659	1.53E-10	
SLC22A15	solute carrier family 22_ member 15	-24.8777	-4.63678	1.45E-62	
LOC283683	uncharacterized LOC283683	-24.4078	-4.60927	2.99E-14	
DOK5	docking protein 5	-24.0441	-4.58761	9.96E-25	
LINC00922	long intergenic non-protein coding RNA 922	-23.9592	-4.58251	4.59E-11	
LINC00865	long intergenic non-protein coding RNA 865	-23.941	-4.58141	3.99E-11	
PF4V1	platelet factor 4 variant 1	-23.5142	-4.55546	3.02E-10	
MLKL	mixed lineage kinase domain-like	-23.4787	-4.55328	3.66E-225	
HOXC-AS2	HOXC cluster antisense RNA 2	-23.2705	-4.54043	1.46E-23	
STAB1	stabilin 1	-23.2547	-4.53945	1.35E-19	
PTGFR	prostaglandin F receptor (FP)	-23.1644	-4.53384	1.80E-46	
HDC	histidine decarboxylase	-23.0207	-4.52486	1.88E-10	
IFI44	interferon-induced protein 44	-22.9589	-4.52098	1.56E-41	
LINC00578	long intergenic non-protein coding RNA 578	-22.9554	-4.52076	1.06E-12	
CSTA	cystatin A (stefin A)	-22.5737	-4.49657	1.31E-16	
GPNMB	glycoprotein (transmembrane) nmb	-22.3879	-4.48465	4.97E-49	
OR51E2	olfactory receptor_ family 51_ subfamily E_ member 2	-22.3769	-4.48394	6.76E-26	
LINC00856	long intergenic non-protein coding RNA 856	-22.3207	-4.48031	2.48E-10	
CFB	complement factor B	-21.9633	-4.45702	8.87E-137	
POMC	proopiomelanocortin	-21.6878	-4.43881	3.18E-11	
LOC101927468	uncharacterized LOC101927468	-21.205	-4.40633	3.00E-10	
CD7	CD7 molecule	-21.1331	-4.40143	4.15E-27	
BMPER	BMP binding endothelial regulator	-20.9432	-4.38841	4.46E-52	
GSDMA	gasdermin A	-20.921	-4.38688	1.37E-11	
SUSD3	sushi domain containing 3	-20.5652	-4.36213	1.29E-21	

TABLE 6-continued

Genes more highly expressed in UCB-MSCs compared to HMCs					
Name	Description	Fold Change	Log Fold Change	p-Value	
IL1A	interleukin 1_alpha	-20.5136	-4.35851	3.30E-31	
ELOVL3	ELOVL fatty acid elongase 3	-20.3658	-4.34808	3.34E-18	
PCDHGA6	protocadherin gamma subfamily A_6	-20.2761	-4.34171	6.62E-25	
IGJ	joining chain of multimeric IgA and IgM	-19.8671	-4.31231	3.70E-12	
SEPSECS-AS1	SEPSECS antisense RNA 1 (head to head)	-19.8668	-4.31229	1.20E-09	
PPP4R4	protein phosphatase 4_regulatory subunit 4	-19.4997	-4.28538	3.86E-40	
CCL20	chemokine (C-C motif) ligand 20	-19.484	-4.28422	1.44E-14	
DEPTOR	DEP domain containing MTOR-interacting protein	-19.4709	-4.28325	9.47E-33	
ANKRD7	ankyrin repeat domain 7	-19.4419	-4.2811	1.58E-09	
C3	complement component 3	-19.2979	-4.27037	2.08E-21	
APOL1	apolipoprotein L_1	-19.0488	-4.25163	3.81E-37	
ITGBL1	integrin_beta-like 1 (with EGF-like repeat domains)	-18.9388	-4.24327	1.78E-180	
PCDHGA4	protocadherin gamma subfamily A_4	-18.6151	-4.2184	1.07E-14	
SLC19A3	solute carrier family 19 (thiamine transporter)_member 3	-18.5448	-4.21294	5.33E-16	
CCL5	chemokine (C-C motif) ligand 5	-18.4312	-4.20408	2.95E-11	
MIR656	microRNA 656	-18.4149	-4.2028	3.88E-09	
MYH1	myosin_heavy chain 1_skeletal muscle_adult	-18.0365	-4.17285	5.52E-09	
PDPN	podoplanin	-17.8868	-4.16082	2.51E-17	
ZNF560	zinc finger protein 560	-17.6976	-4.14548	6.02E-17	
HRNR	hornerin	-17.6899	-4.14485	1.10E-08	
CNKS2R2	connector enhancer of kinase suppressor of Ras 2	-17.623	-4.13939	1.51E-09	
C21orf119	URB1 antisense RNA 1 (head to head)	-17.6194	-4.13909	2.07E-45	
SNORD114-1	small nucleolar RNA_C/D box 114-1	-17.5184	-4.1308	6.92E-09	
PCDHGA7	protocadherin gamma subfamily A_7	-17.5156	-4.13057	2.41E-19	
SLC22A3	solute carrier family 22 (organic cation transporter)_member 3	-17.5078	-4.12993	1.29E-63	
LOC100507540	NA	-17.3144	-4.1139	3.58E-11	
ZNF595	zinc finger protein 595	-17.2473	-4.1083	3.38E-37	
LOC100506834	uncharacterized LOC100506834	-17.2068	-4.10491	2.84E-25	
DDX43	DEAD (Asp-Glu-Ala-Asp) box polypeptide 43	-17.0631	-4.09281	1.50E-09	
SAMD9L	sterile alpha motif domain containing 9-like	-16.9705	-4.08496	9.90E-44	
ZNF578	zinc finger protein 578	-16.7751	-4.06825	6.41E-26	
FAM20A	family with sequence similarity 20_member A	-16.5262	-4.04668	3.43E-12	
ALDH1A3	aldehyde dehydrogenase 1 family_member A3	-16.4835	-4.04295	1.93E-28	
LINC00839	long intergenic non-protein coding RNA 839	-16.3055	-4.02729	6.19E-08	
LOC101926935	uncharacterized LOC101926935	-16.0385	-4.00347	2.44E-08	
HSPA2	heat shock 70kDa protein 2	-15.5047	-3.95463	1.15E-64	
SGCD	sarcoglycan_delta (35kDa dystrophin-associated glycoprotein)	-15.4663	-3.95106	8.53E-25	
AKR1C2	aldo-keto reductase family 1_member C2	-15.1928	-3.92532	5.86E-18	
FAM106A	family with sequence similarity 106_member A	-15.175	-3.92362	6.49E-08	
SPON2	spondin 2_extracellular matrix protein	-15.051	-3.91179	5.07E-25	
CNTNAP2	contactin associated protein-like 2	-14.8446	-3.89187	1.63E-17	
BRINP3	bone morphogenetic protein/retinoic acid inducible neural-specific 3	-14.776	-3.88518	3.70E-10	
ZNF280A	zinc finger protein 280A	-14.7238	-3.88008	1.26E-07	
SYT11	synaptotagmin XI	-14.71	-3.87873	2.65E-18	
IL13RA2	interleukin 13 receptor_alpha 2	-14.6618	-3.87399	7.77E-08	
HTR2A	5-hydroxytryptamine (serotonin) receptor 2A_G protein-coupled	-14.6491	-3.87274	9.16E-08	
FDCSP	follicular dendritic cell secreted protein	-14.606	-3.86849	1.59E-07	
PF4	platelet factor 4	-14.5247	-3.86044	1.20E-07	
LRRN4CL	LRRN4 C-terminal like	-14.4001	-3.84801	1.50E-36	
COMT	catechol-O-methyltransferase	-14.3741	-3.8454	4.90E-145	
HOXA1	homeobox A1	-14.3096	-3.83891	5.13E-52	
PDE7B	phosphodiesterase 7B	-14.2867	-3.8366	4.03E-98	

TABLE 6-continued

Genes more highly expressed in UCB-MSCs compared to HMCs					
Name	Description	Fold Change	Log Fold Change	p-Value	
RAD21-AS1	RAD21 antisense RNA 1	-14.2782	-3.83574	9.85E-11	
CBLC	Cbl proto-oncogene C_ E3 ubiquitin protein ligase	-14.2299	-3.83085	1.46E-08	
PRSS3	protease_serine_3	-14.22	-3.82985	2.89E-19	
STXBP5L	syntaxin binding protein 5-like	-14.064	-3.81393	3.06E-22	
AMPH	amphiphysin	-14.0368	-3.81114	9.92E-48	
FAM50B	family with sequence similarity 50_member B	-13.9849	-3.8058	9.58E-38	
MYH8	myosin_heavy chain 8_skeletal muscle_perinatal	-13.9336	-3.8005	3.09E-08	
PRPH2	peripherin 2 (retinal degeneration_slow)	-13.832	-3.78994	3.29E-13	
ARHGAP20	Rho GTPase activating protein 20	-13.8103	-3.78767	5.09E-20	
SPOCK3	sparc/osteonectin_cwcw and kazal-like domains proteoglycan (testican) 3	-13.79	-3.78555	1.19E-13	
HOXA10-AS	HOXA10 antisense RNA	-13.646	-3.77041	1.07E-23	
GREM2	gremlin 2_DAN family BMP antagonist	-13.637	-3.76945	7.24E-18	
C11orf70	chromosome 11 open reading frame 70	-13.5827	-3.7637	1.23E-56	
PCDHGA8	protocadherin gamma subfamily A_8	-13.484	-3.75318	2.54E-63	
SLC9A9	solute carrier family 9_subfamily A (NHE9_cation proton antiporter 9)_member 9	-13.3834	-3.74237	2.92E-41	
ZNF528	zinc finger protein 528	-13.3712	-3.74106	3.29E-35	
HOXC11	homeobox C11	-13.3183	-3.73534	5.42E-20	
HOTAIR	HOX transcript antisense RNA	-13.2446	-3.72733	1.66E-23	
HOXA9	homeobox A9	-12.9587	-3.69585	2.40E-46	
GALNT12	polypeptide N-acetylgalactosaminyltransferase 12	-12.9507	-3.69496	6.77E-23	
PDE2A	phosphodiesterase 2A_cGMP-stimulated	-12.9165	-3.69114	2.56E-12	
PRSS12	protease_serine_12 (neurotrypsin_motopsin)	-12.9162	-3.69111	2.60E-84	
LINC00707	long intergenic non-protein coding RNA 707	-12.9156	-3.69104	9.57E-21	
CHRD12	chordin-like 2	-12.9061	-3.68998	8.82E-08	
PCDHGA5	protocadherin gamma subfamily A_5	-12.7366	-3.67091	3.66E-17	
PPAPDC3	phosphatidic acid phosphatase type 2 domain containing 3	-12.6247	-3.65818	4.50E-56	
ST6GALNAC5	ST6 (alpha-N-acetyl-neuraminy1-2_3-beta-galactosyl1-3)-N-acetylgalactosaminide alpha-2_6-sialyltransferase 5	-12.604	-3.65581	1.09E-65	
LIN7A	lin-7 homolog A (<i>C. elegans</i>)	-12.5604	-3.65081	2.64E-53	
PTPRQ	protein tyrosine phosphatase_receptor type_Q	-12.554	-3.65008	5.16E-36	
FAM27A	family with sequence similarity 27_member C	-12.3804	-3.62999	9.74E-07	
CNTN5	contactin 5	-12.3042	-3.62108	8.87E-13	
IL1RN	interleukin 1 receptor antagonist	-12.2859	-3.61893	9.35E-07	
HS6ST3	heparan sulfate 6-O-sulfotransferase 3	-12.2168	-3.61079	9.07E-07	
SNORD113-4	small nucleolar RNA_C/D box 113-4	-12.116	-3.59884	9.47E-07	
PRSS21	protease_serine_21 (testisin)	-12.0628	-3.59249	1.80E-06	
TEKT4P2	tektin 4 pseudogene 2	-12.0135	-3.58658	2.77E-06	
SYBU	syntabulin (syntaxin-interacting)	-11.9685	-3.58117	1.77E-17	
P2RX1	purinergic receptor P2X_ligand gated ion channel_1	-11.86	-3.56803	1.82E-23	
IRX5	iroquois homeobox 5	-11.7574	-3.5555	1.53E-33	
ENTPD1-AS1	ENTPD1 antisense RNA 1	-11.7407	-3.55345	1.43E-06	
RBM47	RNA binding motif protein 47	-11.7375	-3.55305	6.27E-62	
RFX8	RFX family member 8_lacking RFX DNA binding domain	-11.7343	-3.55266	5.37E-18	
DHX58	DEXH (Asp-Glu-X-His) box polypeptide 58	-11.6685	-3.54455	1.82E-36	
ESPNL	espin-like	-11.6038	-3.53652	1.55E-21	
SPATA41	spermatogenesis associated 41 (non-protein coding)	-11.5983	-3.53584	2.01E-07	
SH3GL3	SH3-domain GRB2-like 3	-11.5783	-3.53335	5.54E-17	
NDUFA4L2	NADH dehydrogenase (ubiquinone) 1 alpha subcomplex_4-like 2	-11.5191	-3.52595	3.08E-25	
GGT5	gamma-glutamyltransferase 5	-11.506	-3.52432	1.42E-80	

TABLE 6-continued

Genes more highly expressed in UCB-MSCs compared to HMCs					
Name	Description	Fold Change	Log Fold Change	p-Value	
ASS1	argininosuccinate synthase 1	-11.4005	-3.51103	4.39E-41	
LOC645638	NA	-11.3763	-3.50796	8.68E-27	
SLPI	secretory leukocyte peptidase inhibitor	-11.303	-3.49863	2.64E-06	
AGBL2	ATP/GTP binding protein-like 2	-11.295	-3.49761	3.66E-16	
HOXD4	homeobox D4	-11.2388	-3.49041	1.49E-21	
TMEM155	transmembrane protein 155	-11.2145	-3.48729	1.59E-14	
SMM21	small integral membrane protein 21	-11.171	-3.48168	2.91E-06	
C9orf170	chromosome 9 open reading frame 170	-11.1377	-3.47738	4.33E-07	
ECM2	extracellular matrix protein 2_femail	-11.0978	-3.4722	1.52E-29	
	organ and adipocyte specific				
CHRNA9	cholinergic receptor_nicotinic_alpha 9 (neuronal)	-11.0708	-3.46869	6.89E-07	
PCDHGA2	protocadherin gamma subfamily A_2	-11.0172	-3.46168	8.04E-11	
NAT2	N-acetyltransferase 2 (arylamine N-acetyltransferase)	-10.9863	-3.45764	5.16E-10	
EMX2	empty spiracles homeobox 2	-10.9733	-3.45593	3.76E-07	
PDIA2	protein disulfide isomerase family A_member 2	-10.9385	-3.45134	6.66E-10	
OGN	osteoglycin	-10.9193	-3.44881	1.20E-07	
LTF	lactotransferrin	-10.8719	-3.44253	4.86E-06	
GRM6	glutamate receptor_metabotropic 6	-10.8433	-3.43873	1.06E-06	
PRR34	proline rich 34	-10.8229	-3.43601	9.05E-09	
USP32P2	ubiquitin specific peptidase 32_pseudogene 2	-10.7465	-3.42579	1.18E-07	
GPAT2	glycerol-3-phosphate acyltransferase_2_mitochondrial	-10.6944	-3.41879	1.94E-10	
PTGS2	prostaglandin-endoperoxide synthase 2 (prostaglandin G/H synthase and cyclooxygenase)	-10.678	-3.41657	4.22E-30	
C9orf64	chromosome 9 open reading frame 64	-10.6157	-3.40813	5.46E-28	
LINC00884	long intergenic non-protein coding RNA 884	-10.5556	-3.39994	8.61E-07	
GUCY1B3	guanylate cyclase 1_soluble_beta 3	-10.5296	-3.39638	6.23E-36	
DMRT2	doublesex and mab-3 related transcription factor 2	-10.4519	-3.3857	9.81E-06	
GBP5	guanylate binding protein 5	-10.4326	-3.38302	4.00E-07	
MYOT	myotilin	-10.3531	-3.37199	4.38E-10	
PCDHGB1	protocadherin gamma subfamily B_1	-10.3161	-3.36682	8.50E-10	
EPGN	epithelial mitogen	-10.2797	-3.36172	3.50E-09	
MME	membrane metallo-endopeptidase	-10.2755	-3.36114	5.88E-25	
ST3GAL6-AS1	ST3GAL6 antisense RNA 1	-10.269	-3.36023	1.58E-12	
ATP8B4	ATPase_class I_type 8B_member 4	-10.242	-3.35643	9.62E-16	
TSTD1	thiosulfate sulfurtransferase (rhodanese)-like domain containing 1	-10.231	-3.35488	2.07E-13	
LOC102724927	uncharacterized LOC102724927	-10.1447	-3.34265	1.27E-18	
LIPC	lipase_hepatic	-10.1202	-3.33917	9.64E-06	
RAETIE	retinoic acid early transcript 1E	-10.1052	-3.33702	4.21E-07	
EMX2OS	EMX2 opposite strand/antisense RNA	-10.0321	-3.32655	1.01E-05	
LINC00540	long intergenic non-protein coding RNA 540	-9.99412	-3.32108	1.10E-05	
RSPO2	R-spondin 2	-9.98734	-3.3201	9.05E-06	
PDE4B	phosphodiesterase 4B_cAMP-specific	-9.96763	-3.31725	4.87E-44	
LCNL1	lipocalin-like 1	-9.96645	-3.31708	4.54E-26	
HOTAIRM1	HOXA transcript antisense RNA_myeloid-specific 1	-9.94899	-3.31455	2.93E-11	
DMGDH	dimethylglycine dehydrogenase	-9.88328	-3.30499	4.90E-09	
SIGLEC10	sialic acid binding Ig-like lectin 10	-9.87917	-3.30439	1.40E-06	
ELANE	elastase_neutrophil expressed	-9.78058	-3.28992	1.22E-05	
CD55	CD55 molecule_decay accelerating factor for complement (Cromer blood group)	-9.66681	-3.27304	1.09E-17	
TNFRSF8	tumor necrosis factor receptor superfamily_member 8	-9.66205	-3.27233	3.99E-08	
MB21D1	Mab-21 domain containing 1	-9.5886	-3.26132	2.18E-34	
IL1R1	interleukin 1 receptor type_I	-9.54616	-3.25492	5.60E-97	
SNTG2	syntrophin_gamma 2	-9.4908	-3.24653	5.86E-14	
ANPEP	alanyl (membrane) aminopeptidase	-9.46866	-3.24316	1.64E-113	
HP09025	uncharacterized LOC100652929	-9.45076	-3.24043	1.87E-05	
PAX8	paired box 8	-9.40977	-3.23416	5.17E-15	
IL1R2	interleukin 1 receptor_type II	-9.39713	-3.23222	4.46E-07	

TABLE 6-continued

Genes more highly expressed in UCB-MSCs compared to HMCs					
Name	Description	Fold Change	Log Fold Change	p-Value	
HOXA10	homeobox A10	-9.37189	-3.22834	2.63E-96	
ST8SIA4	ST8 alpha-N-acetyl-neuraminate alpha-2_8-sialyltransferase 4	-9.36728	-3.22763	1.55E-42	
PIWIL2	piwi-like RNA-mediated gene silencing 2	-9.31522	-3.21959	1.57E-10	
COL14A1	collagen_type XIV_alpha 1	-9.30515	-3.21803	2.33E-09	
DHRS3	dehydrogenase/reductase (SDR family) member 3	-9.29774	-3.21688	2.28E-115	
MR1	major histocompatibility complex_class I-related	-9.27785	-3.21379	5.21E-24	
HOXA11	homeobox A11	-9.21868	-3.20456	5.28E-303	
VTN	vitronectin	-9.19685	-3.20114	6.40E-52	
C1QTNF1	C1q and tumor necrosis factor related protein 1	-9.16344	-3.19589	1.36E-28	
ABCA6	ATP-binding cassette_sub-family A (ABC1)_member 6	-9.06131	-3.17972	9.25E-09	
CHRM3	cholinergic receptor_muscarinic 3	-9.03134	-3.17494	2.72E-05	
GPR85	G protein-coupled receptor 85	-9.02571	-3.17404	7.36E-43	
CCL7	chemokine (C-C motif) ligand 7	-9.01627	-3.17253	1.82E-13	
KLF4	Kruppel-like factor 4 (gut)	-8.9928	-3.16877	2.83E-34	
MALRD1	MAM and LDL receptor class A domain containing 1	-8.91837	-3.15678	3.50E-05	
SLC27A2	solute carrier family 27 (fatty acid transporter)_member 2	-8.91108	-3.1556	1.64E-10	
DIRAS3	DIRAS family_GTP-binding RAS-like 3	-8.838	-3.14372	9.46E-137	
CRYAB	crystallin_alpha B	-8.83359	-3.143	1.22E-23	
LINC00968	long intergenic non-protein coding RNA 968	-8.82888	-3.14223	2.73E-11	
LAMA2	laminin_alpha 2	-8.81329	-3.13968	1.53E-37	
MCTP2	multiple C2 domains_transmembrane 2	-8.79577	-3.13681	2.25E-19	
MIR199A1	microRNA 199a-1	-8.77312	-3.13309	2.25E-06	
FGF14	fibroblast growth factor 14	-8.76655	-3.13201	2.54E-13	
PIWIL3	piwi-like RNA-mediated gene silencing 3	-8.74695	-3.12878	4.15E-05	
PRG2	proteoglycan 2_bone marrow (natural killer cell activator_eosinophil granule major basic protein)	-8.69683	-3.12049	3.14E-08	
NMU	neuromedin U	-8.66945	-3.11594	4.96E-05	
PTPN20B	protein tyrosine phosphatase_non-receptor type 20	-8.55964	-3.09755	4.66E-05	
XAF1	XIAP associated factor 1	-8.55869	-3.09739	3.21E-18	
ABCC3	ATP-binding cassette_sub-family C (CFTR/MRP)_member 3	-8.55857	-3.09737	3.88E-29	
HSPA7	heat shock 70kDa protein 7 (HSP70B)	-8.55436	-3.09666	4.67E-05	
SYN3	synapsin III	-8.54843	-3.09566	4.78E-05	
JAKMIP2	janus kinase and microtubule interacting protein 2	-8.53996	-3.09423	2.50E-07	
TMCC3	transmembrane and coiled-coil domain family 3	-8.52719	-3.09207	1.37E-26	
IL22RA1	interleukin 22 receptor_alpha 1	-8.46823	-3.08206	1.47E-05	
ATE1-AS1	ATE1 antisense RNA 1	-8.42987	-3.07551	5.34E-05	
KCND2	potassium channel_voltage gated Shal related subfamily D_member 2	-8.41096	-3.07227	1.61E-10	
MIR410	microRNA 410	-8.40927	-3.07198	5.23E-05	
LINC00664	long intergenic non-protein coding RNA 664	-8.4	-3.07039	5.69E-05	
MKRN3	makorin ring finger protein 3	-8.37959	-3.06688	6.58E-05	
ANKRD2	ankyrin repeat domain 2 (stretch responsive muscle)	-8.36891	-3.06504	2.42E-14	
COL8A2	collagen_type VIII_alpha 2	-8.26996	-3.04788	8.49E-24	
CFHR1	complement factor H-related 1	-8.24809	-3.04406	7.97E-12	
TRPV3	transient receptor potential cation channel_subfamily V_member 3	-8.2018	-3.03594	8.67E-13	
GAL3ST1	galactose-3-O-sulfotransferase 1	-8.17971	-3.03205	7.89E-05	
PCDHGB5	protocadherin gamma subfamily B_5	-8.17002	-3.03034	3.34E-09	
TFPI2	tissue factor pathway inhibitor 2	-8.1526	-3.02726	4.98E-24	
LPO	lactoperoxidase	-8.10836	-3.01941	1.89E-05	
EVI2B	ecotropic viral integration site 2B	-8.07532	-3.01352	5.75E-10	
FRMPD1	FERM and PDZ domain containing 1	-8.0519	-3.00933	3.56E-05	

TABLE 6-continued

Genes more highly expressed in UCB-MSCs compared to HMCs				
Name	Description	Fold Change	Log Fold Change	p-Value
B4GALNT1	beta-1_4-N-acetyl-galactosaminyl transferase 1	-8.04934	-3.00887	1.81E-22
TRPA1	transient receptor potential cation channel_ subfamily A_ member 1	-8.02538	-3.00457	1.88E-06
ASB2	ankyrin repeat and SOCS box containing 2	-7.95317	-2.99153	5.28E-17
HOXD3	homeobox D3	-7.92077	-2.98564	8.03E-07
POM121L9P	POM121 transmembrane nucleoporin-like 9_ pseudogene	-7.87866	-2.97795	1.58E-09
PSG5	pregnancy specific beta-1-glycoprotein 5	-7.82847	-2.96873	1.32E-09
LOC654342	lymphocyte-specific protein 1 pseudogene	-7.8218	-2.9675	3.42E-73
HOXA3	homeobox A3	-7.76922	-2.95777	1.04E-15
HOXC-AS3	HOXC cluster antisense RNA 3	-7.75002	-2.9542	6.68E-09
CDSN	corneodesmosin	-7.74895	-2.954	7.46E-07
PLEKHA7	pleckstrin homology domain containing_ family A member 7	-7.71957	-2.94852	1.05E-16
GRIK2	glutamate receptor_ ionotropic_ kainate 2	-7.70925	-2.94659	2.40E-44
FXYD1	FXYD domain containing ion transport regulator 1	-7.67911	-2.94094	3.54E-13
TRIM4	tripartite motif containing 4	-7.65127	-2.9357	3.26E-64
PP12613	uncharacterized LOC100192379	-7.61931	-2.92966	3.85E-05
KDR	kinase insert domain receptor	-7.59337	-2.92474	1.08E-31
MIR10B	microRNA 10b	-7.59337	-2.92474	0.000142
TSPAN32	tetraspanin 32	-7.56594	-2.91952	7.50E-09
TRPM3	transient receptor potential cation channel_ subfamily M_ member 3	-7.55714	-2.91784	3.49E-09
RGL3	ral guanine nucleotide dissociation stimulator-like 3	-7.55567	-2.91756	7.95E-09
CXCL14	chemokine (C-X-C motif) ligand 14	-7.54181	-2.91491	5.44E-10
RBM46	RNA binding motif protein 46	-7.53465	-2.91354	0.000159
KCNQ3	potassium channel_ voltage gated KQT-like subfamily Q_ member 3	-7.52817	-2.9123	4.08E-20
FAM225A	family with sequence similarity 225_ member A (non-protein coding)	-7.51587	-2.90994	0.000168
TRIM29	tripartite motif containing 29	-7.49381	-2.9057	4.35E-15
PRDM1	PR domain containing 1_ with ZNF domain	-7.48966	-2.9049	5.11E-33
HIST2H2BA	histone cluster 2_ H2ba (pseudogene)	-7.48011	-2.90306	1.97E-12
SUSD2	sushi domain containing 2	-7.47804	-2.90266	2.34E-06
HPD	4-hydroxyphenylpyruvate dioxygenase	-7.46064	-2.8993	4.25E-10
GPR115	adhesion G protein-coupled receptor F4	-7.46028	-2.89923	2.61E-26
PHYHIP	phytanoyl-CoA 2-hydroxylase interacting protein	-7.44742	-2.89674	6.50E-21
SPN	sialophorin	-7.40741	-2.88897	1.04E-09
FAM109B	family with sequence similarity 109_ member B	-7.38363	-2.88433	1.52E-90
LOC101926892	uncharacterized LOC101926892	-7.34595	-2.87695	0.000183
CASC1	cancer susceptibility candidate 1	-7.33019	-2.87385	4.51E-06
PRND	prion protein 2 (dublet)	-7.32328	-2.87249	0.000189
KCNT2	potassium channel_ sodium activated subfamily T_ member 2	-7.26433	-2.86083	3.16E-13
GBP7	guanylate binding protein 7	-7.24964	-2.85791	0.000204
TYMP	thymidine phosphorylase	-7.24643	-2.85727	1.99E-51
P4HA3	prolyl 4-hydroxylase_ alpha polypeptide III	-7.23127	-2.85425	1.01E-28
MX2	MX dynamin-like GTPase 2	-7.22406	-2.85281	1.96E-43
ATP6V0A4	ATPase_ H+ transporting_ lysosomal V0 subunit a4	-7.16531	-2.84103	3.08E-06
IL6	interleukin 6	-7.16268	-2.8405	6.92E-09
SCRG1	stimulator of chondrogenesis 1	-7.14171	-2.83627	3.06E-33
ENPP4	ectonucleotide pyrophosphatase/phosphodiesterase 4 (putative)	-7.11247	-2.83035	2.30E-06

TABLE 6-continued

Genes more highly expressed in UCB-MSCs compared to HMCs					
Name	Description	Fold Change	Log Fold Change	p-Value	
GCH1	GTP cyclohydrolase 1	-7.09022	-2.82583	2.11E-20	
LOC102724224	NA	-7.07054	-2.82182	5.08E-15	
ZNF726	zinc finger protein 726	-7.05854	-2.81937	2.09E-07	
TNFRSF11B	tumor necrosis factor receptor superfamily member 11b	-7.05683	-2.81902	6.55E-11	
ZNF829	zinc finger protein 829	-7.04715	-2.81704	2.15E-54	
TULP2	tubby like protein 2	-7.04485	-2.81657	1.07E-05	
LOC101929319	uncharacterized LOC101929319	-7.03261	-2.81406	0.000119	
HSPB6	heat shock protein alpha-crystallin-related B6	-7.01854	-2.81117	1.15E-21	
LAMA1	laminin alpha 1	-7.0143	-2.8103	9.37E-45	
LUZP2	leucine zipper protein 2	-7.00954	-2.80932	7.61E-31	
LOC101928161	uncharacterized LOC101928161	-7.00255	-2.80788	6.81E-24	
CCDC64B	coiled-coil domain containing 64B	-6.98897	-2.80508	0.000297	
CRHR2	corticotropin releasing hormone receptor 2	-6.98839	-2.80496	1.30E-06	
TIMP3	TIMP metallopeptidase inhibitor 3	-6.988	-2.80488	2.42E-17	
OASL	2'-5'-oligoadenylate synthetase-like	-6.98369	-2.80399	0.000202	
SGCG	sarcoglycan gamma (35kDa dystrophin-associated glycoprotein)	-6.94816	-2.79663	9.02E-14	
GYPE	glycophorin E (MNS blood group)	-6.91309	-2.78933	0.000146	
TMEM215	transmembrane protein 215	-6.8823	-2.78289	0.00033	
RADIL	Ras association and DIL domains	-6.86181	-2.77859	2.72E-30	
LRRIQ3	leucine-rich repeats and IQ motif containing 3	-6.8524	-2.77661	1.68E-06	
NR5A2	nuclear receptor subfamily 5 group A member 2	-6.85041	-2.77619	0.00012	
PABPC4L	poly(A) binding protein cytoplasmic 4-like	-6.84818	-2.77572	4.78E-29	
PLSCR4	phospholipid scramblase 4	-6.843	-2.77463	9.90E-72	
LOC100132891	NA	-6.83817	-2.77361	1.07E-10	
LOC100240734	uncharacterized LOC100240734	-6.83201	-2.77231	1.59E-05	
PRDM6	PR domain containing 6	-6.76711	-2.75854	3.35E-06	
DNAJC12	DnaJ (Hsp40) homolog subfamily C member 12	-6.76134	-2.75731	4.24E-23	
ADAM33	ADAM metallopeptidase domain 33	-6.74519	-2.75386	6.75E-10	
ANXA8	annexin A8	-6.73118	-2.75086	2.82E-18	
ZFYVE28	zinc finger FYVE domain containing 28	-6.72083	-2.74864	3.30E-17	
RRN3P2	RRN3 homolog RNA polymerase I transcription factor pseudogene 2	-6.70557	-2.74536	3.86E-14	
LINC00271	long intergenic non-protein coding RNA 271	-6.69285	-2.74262	0.000178	
LINC01116	long intergenic non-protein coding RNA 1116	-6.69169	-2.74237	1.07E-40	
KCNIP3	Kv channel interacting protein 3 calsenilin	-6.68459	-2.74084	4.54E-17	
SLC30A3	solute carrier family 30 (zinc transporter) member 3	-6.68237	-2.74036	0.000188	
KCNE4	potassium channel voltage gated subfamily E regulatory beta subunit 4	-6.67672	-2.73914	2.01E-26	
LOC101927650	uncharacterized LOC101927650	-6.66004	-2.73553	0.000222	
MEG9	maternally expressed 9 (non-protein coding)	-6.64975	-2.7333	1.07E-11	
SPAG17	spERM associated antigen 17	-6.63263	-2.72958	2.02E-05	
RNF112	ring finger protein 112	-6.62601	-2.72814	4.94E-13	
BACH2	BTB and CNC homology 1 basic leucine zipper transcription factor 2	-6.60624	-2.72383	3.20E-09	
M1AP	meiosis 1 associated protein	-6.59279	-2.72089	0.000184	
HOXA7	homeobox A7	-6.5864	-2.71949	7.83E-11	
PPP1R14C	protein phosphatase 1 regulatory (inhibitor) subunit 14C	-6.57354	-2.71667	0.000573	
LINC01081	long intergenic non-protein coding RNA 1081	-6.53252	-2.70764	0.000487	
MOCOS	molybdenum cofactor sulfurase	-6.52985	-2.70705	4.40E-12	
HOXA4	homeobox A4	-6.49257	-2.69879	4.09E-14	
ATP2B1	ATPase Ca++ transporting plasma membrane 1	-6.48124	-2.69627	8.06E-35	
ALDH3B1	aldehyde dehydrogenase 3 family member B1	-6.47078	-2.69394	9.21E-80	
NKG7	natural killer cell granule protein 7	-6.43206	-2.68528	0.000222	

TABLE 6-continued

Genes more highly expressed in UCB-MSCs compared to HMCs					
Name	Description	Fold Change	Log Fold Change	p-Value	
S100A4	S100 calcium binding protein A4	-6.42248	-2.68313	3.30E-18	
LOC441666	zinc finger protein 91 pseudogene	-6.41349	-2.68111	0.00069	
CRISPLD2	cysteine-rich secretory protein LCCL domain containing 2	-6.38028	-2.67362	2.78E-11	
SLC38A5	solute carrier family 38 member 5	-6.37595	-2.67264	7.82E-40	
KRT34	keratin 34 type I	-6.35852	-2.66869	2.57E-05	
APOL6	apolipoprotein L_6	-6.33252	-2.66278	1.01E-35	
DPP10	dipeptidyl-peptidase 10 (non-functional)	-6.31845	-2.65957	7.29E-06	
KLF15	Kruppel-like factor 15	-6.30523	-2.65655	6.85E-06	
IL33	interleukin 33	-6.28503	-2.65192	1.04E-11	
HOXA-AS3	HOXA cluster antisense RNA 3	-6.27515	-2.64965	1.92E-19	
MIR541	microRNA 541	-6.22835	-2.63885	0.000695	
ANXA8L1	annexin A8-like 1	-6.21916	-2.63672	9.58E-20	
STRA6	stimulated by retinoic acid 6	-6.21395	-2.63551	3.82E-20	
PM20D1	peptidase M20 domain containing 1	-6.20921	-2.63441	0.000794	
GPR1	G protein-coupled receptor 1	-6.19666	-2.63149	2.05E-28	
IL21R	interleukin 21 receptor	-6.16645	-2.62444	2.53E-09	
LOC284889	NA	-6.15198	-2.62105	2.12E-09	
FLJ45974	NA	-6.10766	-2.61062	0.000858	
ABCA9	ATP-binding cassette sub-family A (ABC1) member 9	-6.09827	-2.6084	8.73E-07	
C12orf56	chromosome 12 open reading frame 56	-6.09688	-2.60807	0.000122	
AKRIB10	aldo-keto reductase family 1 member B10 (aldose reductase)	-6.09206	-2.60693	1.09E-07	
MYBPH	myosin binding protein H	-6.06324	-2.60009	0.000347	
HSD11B1	hydroxysteroid (11-beta) dehydrogenase 1	-6.05896	-2.59907	0.001014	
LOC391322	D-dopachrome tautomerase-like	-6.05149	-2.59729	1.82E-07	
LIP1	lipase member 1	-6.03465	-2.59327	0.000958	
ICAM4	intercellular adhesion molecule 4 (Landsteiner-Wiener blood group)	-6.03072	-2.59233	1.43E-11	
RTP4	receptor (chemosensory) transporter protein 4	-5.97637	-2.57927	0.00098	
LOC100507642	uncharacterized LOC100507642	-5.96305	-2.57605	2.82E-29	
C4BPB	complement component 4 binding protein_beta	-5.95421	-2.57391	5.64E-14	
EVA1C	eva-1 homolog C (<i>C. elegans</i>)	-5.94217	-2.57099	2.18E-23	
MIR615	microRNA 615	-5.8772	-2.55513	0.001088	
ASIC5	acid sensing (proton gated) ion channel family member 5	-5.87676	-2.55502	0.001107	
TRIM61	tripartite motif containing 61	-5.85513	-2.5497	1.21E-16	
OLFML3	olfactomedin-like 3	-5.84576	-2.54739	2.66E-32	
ALPK1	alpha-kinase 1	-5.8373	-2.5453	4.75E-37	
LINC00936	long intergenic non-protein coding RNA 936	-5.81396	-2.53952	1.41E-32	
LINC00570	long intergenic non-protein coding RNA 570	-5.80852	-2.53817	0.001211	
LOC340515	NA	-5.80538	-2.53739	0.001211	
GALNT18	polypeptide N-acetylgalactosaminyltransferase 18	-5.78501	-2.53232	1.74E-19	
HOXA11-AS	HOXA11 antisense RNA	-5.778	-2.53057	4.63E-102	
HRCT1	histidine rich carboxyl terminus 1	-5.77227	-2.52914	9.88E-32	
RASIP1	Ras interacting protein 1	-5.75398	-2.52456	8.49E-17	
FPR2	formyl peptide receptor 2	-5.74597	-2.52255	0.001275	
IFI44L	interferon-induced protein 44-like	-5.74306	-2.52182	9.82E-09	
CCDC147-AS1	CFAP58 antisense RNA 1 (head to head)	-5.73952	-2.52093	4.88E-09	
LDHAL6B	lactate dehydrogenase A-like 6B	-5.7328	-2.51924	0.000211	
KCTD12	potassium channel tetramerization domain containing 12	-5.71221	-2.51405	6.98E-12	
GNG2	guanine nucleotide binding protein (G protein)_gamma 2	-5.71055	-2.51363	8.51E-23	
KLHL33	kelch-like family member 33	-5.70418	-2.51202	0.001368	
ADAMTS1	ADAM metallopeptidase with thrombospondin type 1 motif_1	-5.69596	-2.50994	5.60E-24	
SCIN	scinderin	-5.69008	-2.50845	3.26E-08	
INSC	inscuteable homolog (<i>Drosophila</i>)	-5.68555	-2.5073	0.001391	
DLGAP1	discs large (<i>Drosophila</i>) homolog-associated protein 1	-5.66922	-2.50315	0.000493	
ZNF354C	zinc finger protein 354C	-5.66871	-2.50302	2.85E-06	

TABLE 6-continued

Genes more highly expressed in UCB-MSCs compared to HMCs					
Name	Description	Fold Change	Log Fold Change	p-Value	
ODAM	odontogenic_ ameloblast assosciated	-5.65223	-2.49882	0.001552	
LPXN	leupaxin	-5.65203	-2.49877	1.59E-27	
NOV	nephroblastoma overexpressed	-5.63045	-2.49325	3.30E-06	
HAND2-AS1	HAND2 antisense RNA 1 (head to head)	-5.60856	-2.48763	2.11E-115	
BCL2A1	BCL2-related protein A1	-5.60848	-2.48761	0.000262	
ENPP2	ectonucleotide pyrophosphatase/phosphodiesterase 2	-5.60393	-2.48644	9.74E-09	
CKM	creatine kinase_ muscle	-5.5897	-2.48277	0.001639	
PTGDR	prostaglandin D2 receptor (DP)	-5.57391	-2.47869	0.001624	
SLC7A7	solute carrier family 7 (amino acid transporter light chain_ y + L system)_ member 7	-5.57314	-2.47849	9.34E-50	
DAW1	dynein assembly factor with WDR repeat domains 1	-5.55902	-2.47483	1.25E-12	
OVCH1-AS1	OVCH1 antisense RNA 1	-5.55493	-2.47377	0.001707	
LRRTM2	leucine rich repeat transmembrane neuronal 2	-5.53203	-2.46781	3.28E-08	
KCNE3	potassium channel_ voltage gated subfamily E regulatory beta subunit 3	-5.51951	-2.46454	1.51E-14	
IRAK3	interleukin-1 receptor-associated kinase 3	-5.51068	-2.46223	3.63E-10	
OGFRL 1	opioid growth factor receptor-like 1	-5.50247	-2.46008	1.39E-99	
HOXA6	homeobox A6	-5.50015	-2.45947	8.54E-12	
C1S	complement component 1_ s subcomponent	-5.47793	-2.45363	2.03E-35	
CYSLTR2	cysteinyl leukotriene receptor 2	-5.47489	-2.45283	0.000616	
PODNL1	podocan-like 1	-5.47322	-2.45239	5.63E-51	
RBM11	RNA binding motif protein 11	-5.4681	-2.45104	0.001847	
NID2	nidogen 2 (osteonidogen)	-5.45103	-2.44653	3.65E-43	
BTBD11	BTB (POZ) domain containing 11	-5.44775	-2.44566	4.29E-45	
KIF6	kinesin family member 6	-5.44126	-2.44394	0.000483	
LYPD5	LY6/PLAUR domain containing 5	-5.42409	-2.43938	0.001979	
GCNT1	glucosaminyl (N-acetyl) transferase 1_ core 2	-5.42224	-2.43889	2.28E-139	
LOC375196	uncharacterized LOC375196	-5.42074	-2.43849	7.01E-06	
LOC101928200	NA	-5.3954	-2.43173	6.53E-14	
ADAMTS9	ADAM metallopeptidase with thrombospondin type 1 motif_ 9	-5.39529	-2.4317	1.31E-12	
LINC00870	long intergenic non-protein coding RNA 870	-5.3923	-2.4309	0.002006	
MIR6730	microRNA 6730	-5.39211	-2.43085	0.000806	
CP	ceruloplasmin (ferroxidase)	-5.37483	-2.42622	0.001242	
SULT1E1	sulfotransferase family 1E_ estrogen-preferring_ member 1	-5.35869	-2.42188	8.47E-05	
ROR2	receptor tyrosine kinase-like orphan receptor 2	-5.35832	-2.42178	2.45E-10	
MFSD7	major facilitator superfamily domain containing 7	-5.34533	-2.41828	1.30E-20	
NECAB2	N-terminal EF-hand calcium binding protein 2	-5.33837	-2.4164	3.15E-09	
IP6K3	inositol hexakisphosphate kinase 3	-5.33649	-2.41589	3.69E-24	
INHBE	inhibin_ beta E	-5.3237	-2.41243	5.12E-18	
ALDH1L2	aldehyde dehydrogenase 1 family_ member L2	-5.30804	-2.40818	1.83E-18	
HOXA2	homeobox A2	-5.30253	-2.40668	3.64E-08	
RCN3	reticulocalbin 3_ EF-hand calcium binding domain	-5.29984	-2.40595	2.01E-34	
NOL4	nucleolar protein 4	-5.2921	-2.40384	0.001181	
ISLR2	immunoglobulin superfamily containing leucine-rich repeat 2	-5.28928	-2.40307	0.002359	
DHRS4L1	dehydrogenase/reductase (SDR family) member 4 like 1	-5.27818	-2.40004	7.20E-08	
HOXA5	homeobox A5	-5.27503	-2.39918	7.07E-11	
EHHADH	enoyl-CoA_ hydratase/3-hydroxyacyl CoA dehydrogenase	-5.26119	-2.39539	1.38E-16	
LOC101928891	uncharacterized LOC101928891	-5.25839	-2.39462	4.53E-08	
MGC27382	uncharacterized MGC27382	-5.25791	-2.39449	0.002301	
SLC12A8	solute carrier family 12_ member 8	-5.24943	-2.39216	1.29E-29	
CTHRC1	collagen triple helix repeat containing 1	-5.23947	-2.38942	1.59E-40	

TABLE 6-continued

Genes more highly expressed in UCB-MSCs compared to HMCs					
Name	Description	Fold Change	Log Fold Change	p-Value	
SNORD127	small nucleolar RNA_ C/D box 127	-5.22474	-2.38536	0.001157	
BST1	bone marrow stromal cell antigen 1	-5.2242	-2.38521	6.04E-21	
APOA1	apolipoprotein A-I	-5.2238	-2.3851	1.64E-06	
LINC01169	long intergenic non-protein coding RNA 1169	-5.21414	-2.38243	0.001091	
LINC00163	long intergenic non-protein coding RNA 163	-5.21393	-2.38237	0.000343	
FHAD1	forkhead-associated (FHA) phosphopeptide binding domain 1	-5.1735	-2.37114	3.98E-12	
PDC	phosducin	-5.16569	-2.36896	0.001012	
HMOX1	heme oxygenase 1	-5.15739	-2.36664	5.29E-29	
FAM27E3	family with sequence similarity 27_member E3	-5.15367	-2.3656	9.91E-07	
HAS1	hyaluronan synthase 1	-5.14635	-2.36355	9.44E-07	
LINC00052	long intergenic non-protein coding RNA 52	-5.13691	-2.3609	5.40E-09	
EYA2	EYA transcriptional coactivator and phosphatase 2	-5.12816	-2.35844	0.000837	
CABP1	calcium binding protein 1	-5.1219	-2.35668	0.001407	
PCDHGA1	protocadherin gamma subfamily A_ 1	-5.11598	-2.35501	6.54E-05	
TXNRD2	thioredoxin reductase 2	-5.10008	-2.35052	2.65E-45	
USP32P1	ubiquitin specific peptidase 32 pseudogene 1	-5.02757	-2.32986	0.001626	
DPP4	dipeptidyl-peptidase 4	-5.00486	-2.32333	2.66E-16	

Example 7—In Vivo Middle Cerebral Artery Occlusion (MCAO) Stroke Model

[0355] The HMCs and HMC-EVs of the presently disclosed subject matter were tested in an *in vivo* model of middle cerebral artery occlusion (MCAO) stroke.

[0356] HMCs were generated from the same bank of frozen hemangioblasts described in Example 1.

[0357] For HMC-EVs, early passage (passage 4) HMCs were thawed, washed, counted, and plated in Corning Cell-BIND flasks at a density of 5,000 cells/cm² in RoosterBio RoosterNourish-MSC-XF media. Cells were grown for 96 hours to a confluence of approximately 70-90% for acclimation to the media and cell expansion. At 96 hours, cells were removed from flasks with TripLE dissociation, live cells were counted, and replated at 5,000 cells/cm² in new flasks and fresh media at passage 5. At this passage media can be collected after 96 hours for EV isolation. Cells can be passaged again up to passage 7 for larger volumes of media collection. After media was harvested for EV isolation, it was clarified to remove cells and debris with differential, low-speed centrifugation at 300×g for 10 minutes and 2,000×g for 20 minutes followed by 0.2 μm vacuum filtration. EVs were isolated from the clarified media using tangential flow filtration (TFF) on the Repligen KR2i system outfitted with a hollow fiber, 300 kDa pore, mPES membrane filter. The approximately 100 nm pore size of filter removed small impurities and retained the EVs. Combined, the clarification and TFF parameters were such that particles between 100 nm and 200 nm in size were isolated. The media was first concentrated by a factor of approximately 10x before it was diafiltered with DPBS to improve sample purity and remove non-EV associated proteins during the TFF process. The diafiltered media was further concentrated so that the final product was concentrated by a factor of approximately 100x. The resulting isolated and concentrated EVs in DPBS were

then ready for downstream analyses and could also be further purified using chromatography techniques.

In Vivo Effects of HMCs and HMC-EVs on Locomotor Skills

[0358] MCAO animal models were generated as described herein. Briefly, one day prior to surgical injury, the Body Swing Test was performed to establish the baseline performance using male Sprague-Dawley rats (300-400 g). For each, the rat was held approximately one inch from the base of its tail. It was then elevated to an inch above a surface of a table. The rat was held in the vertical axis, defined as no more than 100 to either the left or the right side. A swing was recorded whenever the rat moved its head out of the vertical axis to either side. The rat must have returned to the vertical position for the next swing to be counted. Thirty total swings were counted. A normal rat typically has an equal number of swings to either side. Following focal ischemia, the rat tends to swing to the contralateral (left) side. After one day of testing, focal cerebral infarcts were made by permanent occlusion of the proximal right middle cerebral artery (MCA) using a modification of the method of Tamura et al. The rats were anesthetized with 1-3% isoflurane in the mixture of N₂O:O₂ (2:1), and were maintained with 1.5-2% isoflurane in the mixture of N₂O:O₂ (2:1). The temporalis muscle was bisected and reflected through an incision made midway between the eye and the eardrum canal. The proximal MCA was exposed through a subtemporal craniectomy without removing the zygomatic arch and without transecting the facial nerve. The artery was then occluded by micro bipolar coagulation from just proximal to the olfactory tract to the inferior cerebral vein. Body temperature was maintained at 37.0±1° C. throughout the entire procedure. Cefazolin (40 mg/kg) was given intraperitoneally (i.p.) before MCAO to prevent infections. Buprenorphine, s.c., (~0.1 mg/kg Simbadol) was given before the MCAO surgery

as analgesia. For Sham conditions, animals underwent the same procedure described above without the middle cerebral artery being coagulated.

[0359] Treatments were administered on day 1 and day 7 after the MCAO surgery (24 hours and 7 days \pm 10%). For HMC treatments, the cells were stored in liquid nitrogen until the day of use. Cells were thawed in a 37° C. water bath, counted, and diluted in the vehicle, Plasma-Lyte A. For HMC-EV treatments, EV aliquots were stored at -80° C. until the day of use. EVs were thawed on ice and either diluted in the vehicle, DPBS, or used as prepared.

[0360] On day 1 and day 7 after the MCAO (24 hours and 7 days \pm 10%), animals were anesthetized with 1-3% isoflurane in the O2 and were maintained with 1.5-2% isoflurane in O2. Jugular vein injections were performed by using a 1 ml syringe with a 25G (3/4") needle attached, 0.5 ml vehicle or cells were injected into the jugular vein. The injection site was compressed for about 1 minute to ensure there was no bleeding. Local injection were performed by using a 50 microliter Hamilton syringe with a 26G needle attached, 10 microliters of vehicle, cells, or EVs were injected to the peri infarct area in 3 locations at 3 to 4 microliters per site. Intrathecal injections were performed using a 25G hypodermic needle and an insulin syringe (0.5 mL), 40 microliters of vehicle, cells, or EVs were injected between the last lumbar vertebra and the 1st sacral vertebrae (L6-S1).

[0361] The Body Swing Test was performed on day 1, 7, 14, 21, and 28 post-injury, and animals were sacrificed after testing 28 days post-injury. At twenty-eight days (Day 28) after MCAO, rats were anesthetized deeply with ketamine/xylazine (91 mg/kg ketamine, 9 mg/kg xylazine, respectively). After the rats were in the deep anesthetized stage, they were perfused transcardially with normal saline (with heparin 2 unit/ml) followed by 4% paraformaldehyde. Brains were removed and stored in 4% paraformaldehyde for 24 hours then changed to 1xPBS and stored in 0-4° C. All data were expressed as mean \pm S.E.M. The Body Swing Test data was analyzed by two-way ANOVA and Tukey's multiple comparison test. Significance is represented as *p<0.05, **p<0.01, ***p<0.001, ****p<0.0001.

[0362] The effects of the HMCs and HMC-EVs of the presently disclosed subject matter on locomotion were evaluated in MCAO models.

[0363] HMC cells were injected via three routes of administrations including intravenous (IV), intracerebral (IC) and intrathecal (IT) administration. Cells were dosed at 4 million in 0.5 mL per IV injection; 400,000 in 10 microliters per IC injection; and 500,000 or 1 million in 40 microliters per IT injection. As shown in FIG. 20, all treatment groups demonstrated improvement in recovering deficits in the Body Swing Test, with the IV and IC treatments having the most significance.

[0364] In another study, animals were subjected to the MCAO injury as described above. Cell treatments were administered on day 1 and day 7 after the MCAO surgery (24 hours and 7 days \pm 10%) using HMCs, specifically HMCs derived from C-GS1 cells (C-GS1-HMC) and N-lot QR57 cells (N-HMC). The dosing of the cells was 4 million in 0.5 mL per IV injection. Extracellular vesicle (EV) treatments were administered on day 1 and day 7 after the MCAO surgery (24 hours and 7 days \pm 10%) using EVs derived from N-HMCs (N-HMC-EVs). The dosing of the EVs was 10 \times 10¹⁰ for intracerebral and intracisternal. All

treatment groups demonstrated significant improvement in the limb placement tests (FIG. 21). In the Body Swing Test, all treatment groups provided recovery, with the C-GS1-HMCs, N-HMCs, and N-HMC-EVs via intracerebral injections demonstrating significant increases.

[0365] In a separate study, treatments were administered on day 1 and day 7 after the MCAO surgery (24 hours and 7 days \pm 10%) using N-HMC-EVs (N-lot p6 and p7 treated with IFNgamma for 96 hours at 50 ng/ml). The dosing of the EVs was 10 \times 10¹⁰ or 30 \times 10¹⁰ total for N-HMC-EVs (stimulated N-lot) via intracisternal injections. All groups provided significant improvement in all three behavioral tests, with the most significant improvement demonstrated in the forelimb placement test and the body swing test (FIG. 22).

[0366] In yet another study, treatments were administered on day 1 and day 7 after the MCAO surgery (24 hours and 7 days \pm 10%) using HMC-EVs (N-lot) or HE-VPC-EVs. The dosing of the exosomes was 10 \times 10¹⁰, 30 \times 10¹⁰, and 10 \times 10¹¹ for HMC-EVs and 10 \times 10¹⁰ for VPC-EVs via intrathecal injections. HMC-EV depleted injections were performed as a negative control. All groups provided significant improvement in all three behavioral tests, with the most significant improvement demonstrated in the forelimb placement test and the body swing test (FIG. 23).

[0367] Accordingly, the HMCs of the presently disclosed subject matter and HMC-EVs were efficacious in an MCAO stroke model via intravenous, intrathecal, intracerebral and/or intracisternal administrations, and both HMC and EV treatments provided improved locomotor recovery in behavioral tests.

In Vivo Effects of HMC on Histopathological Outcome

[0368] The effects of the HMCs of the presently disclosed subject matter on histopathological outcome were assessed. Specifically, animals were subjected to the MCAO injury as described above. Cell treatments were administered on day 1 and day 7 after the MCAO surgery (24 hours and 7 days \pm 10%) using HMCs, specifically HMCs derived from C-GS1 cells (C-GS1-HMCs) and N-lot QR57 cells (N-HMCs). The dosing of the cells was 4 million in 0.5 mL per IV injection.

[0369] Sham, vehicle, and cell treatment groups were prepared for histopathological analysis for white matter loss (MBP), and markers for neuroinflammation such as microglial activation (Iba-1) and astrocyte activation (GFAP).

[0370] FIG. 24 shows preservation of myelin with HMC cell treatment in striatum. Specifically, for MBP, there was a statistically significant difference between the sham and vehicle, but there was no statistically significant difference between the vehicle and treatment groups in the ipsi part of the cortex. There was a statistically significant difference between the vehicle and N-line cell treatment groups in the contralateral cortex, however, there was no statistically significant difference between the groups in the ipsi and as well as sham and vehicle in the contra part of the cortex. There was a statistically significant difference between the sham and vehicle for both ipsi and contra in striatum, vehicle and both cell treatment groups only in ipsi part of the striatum. There was no statistically significant difference between the groups in the contra part of striatum.

[0371] FIG. 25 shows reduced microglial activation following HMC administration. Specifically, for Iba-1, there was a statistically significant difference between the sham and for both ipsi and contra part of cortex, vehicle and cell

treatment groups only in ipsi part of cortex. There was no statistically significant difference between the vehicle and treatment groups in the contra part of cortex. There was a statistically significant difference between the sham and vehicle for both ipsi and contra part of striatum, vehicle and C-GS1 cell treatment groups in the ipsi part of striatum. There was no statistically significant difference between the vehicle and treatment groups in the contra part of striatum.

[0372] FIG. 26 shows reduction of astrocyte reactivity upon HMC treatment. Specifically, for GFAP, there was a statistically significant difference between the sham and vehicle as well as vehicle and cell treatment groups for both ipsi and contra part of cortex. There was a statistically significant difference between the sham and vehicle as well as vehicle and cell treatment groups for both ipsi and contra part of striatum.

[0373] Accordingly, these results demonstrated that the MSCs of the presently disclosed subject matter not only increased preservation of myelin, thus white matter, but also resulted in robust reduction of neuroinflammation markers by reducing the number of reactive astrocytes and microglia.

In vivo effects of HMC-EVs on histopathological outcome

[0374] The effects of HMC-EVs on histopathological outcome were also assessed. Specifically, animals were subjected to the MCAO injury as described above. Treatments were administered on day 1 and day 7 after the MCAO surgery (24 hours and 7 days+/-10%) using HMC-EVs (N-lot p6 and p7 treated with IFNgamma for 96 hours at 50 ng/ml). The dosing of the EVs was 10×10^{10} or 30×10^{10} total for HMC-EVs (stimulated N-lot) via intracisternal injections.

[0375] Sham, vehicle, and cell treatment groups were prepared for histopathological analysis for MBP, Iba-1, GFAP, Olig-2, and NG2. FIG. 27 shows preservation of myelin with intracisternal delivery of EVs. Specifically, MBP IF staining showed a stable stained area in all treatment groups in the range of 0.81-0.88. The mean ratio of the vehicle group was the lowest (0.64). The differences between the vehicle group and all the treatment groups were significant.

[0376] FIG. 28 shows the effects of HMC-EV treatment on microglial activation. Specifically, Iba-1 IF staining showed the same mean ratio (R/L) of the number of positive cells in the vehicle group and in the HMC-EV 10^{10} and HMC-EV 30^{10} treatment groups (~2.5).

[0377] FIG. 29 shows the effects of intracisternal HMC-EV delivery on astrocyte reactivity. Specifically, GFAP IF staining did not reveal any differences between the control and all treatment groups and showed stable mean ratios (R/L) of the number of positive stained cells.

[0378] FIG. 30 shows that intracisternal delivery of HMC-EVs increased oligodendrocytes. Specifically, Olig-2 IF staining revealed highest mean ratio (R/L) of positive stained cells in all exosome treatment groups (compare to the vehicle group). The differences between the Vehicle group and HMC-EV 10^{10} and HMC-EV 30^{10} were significant.

[0379] FIG. 31 shows that intracisternal delivery of HMC-EVs increased oligodendrocyte precursor cells. Specifically, NG2 IF staining revealed a statistically significant increase in the mean ratio (R/L) of positive stained area in HMC-EV 10^{10} and HMC-EV 30^{10} compared to the vehicle group.

[0380] Accordingly, these results demonstrated that HMC-EVs increased preservation of myelin. In addition, EV treatment also increased oligodendrocytes and oligodendrocyte-precursor cells.

Example 8—In Vitro Oxygen Glucose Deprivation Stroke Model

[0381] The neuroprotective effect of MSCs of the presently disclosed subject matter was examined in vitro. An oxygen glucose deprivation (OGD) assay which combines hypoxic conditions with glucose-deprived media was used to model stroke in vitro.

[0382] The overview of the assay is shown in FIG. 32. For primary neuronal culture, embryonic day 18 (E18) rat cortex samples (#SDECX), sourced from Sprague Dawley rats, were ordered from Brain Bits, LLC (Springfield, IL.). The cortices were washed in dissection media (DM) three times. DM consists of 50 mL 10xHBSS (w/o Ca and Mg; Gibco 14185-052), 500 μ L Gentamicin, 5 mL pyruvate (Gibco: 11360070), 5 mL Hepes (Gibco 15630080) 10 mM final, 15 mL Glucose 30 mM Final (1M stock), and 425 mL water. After washing, DM was aspirated and the tissue was then minced into equal sized pieces with scalpel. A DM, papain, and DNase I solution was prepared while washing tissue by measuring 1 mL DM, 40 μ L papain (Worthington LS003126), and 2.5 μ L DNase I (DNase (Sigma #DN-25) per brain; activating the papain with incubation in a 37°C water bath for 30 minutes; and sterile filter using a 0.22 micron filter. The DM, activated papain, and DNase I solution was added to the cortex samples and incubated at 37°C for 30 minutes to dissociate the tissue.

[0383] During this time, neuronal media (NMO) was also prepared and incubated at 37°C. NMO consists of Neurobasal plus media with 1x B27 plus added fresh (Neurobasal Plus and B27; Life Tech Corp A3653401), 1x Glutamax (Gibco #35050-061), and gentamycin sulfate (MP Biomedical #0916760-CF). Dissociation pipets were prepared by fire polishing Pasteur pipets with sequentially smaller tip diameters (1=just flame polish, 2=3/4 of original diameter, 3=1/2 of original diameter). After the 30 minutes incubation, the tissue was removed from the water bath. The DM/papain/DNase I solution was gently aspirated and 5 mL of pre-warmed NMO with freshly added B27 was added. The tissue was allowed to settle, and the NMO was gently pipetted off. The tissue was washed again with 5 mL fresh NMO (with B27), and this was repeated for a total of 3 washes. After the last wash, the NMO was removed. The tissue was dissociated by gently triturating the brain tissue through a fire-polished Pasteur pipet, starting with the largest pipet. This was performed by adding 3 mL of NMO, gently triturate 4-5X, and dispensing tissue against wall of tube to prevent bubble formation as neurons trapped in bubbles will die. After the remaining tissue settled, the supernatant was removed and added to a fresh 50 mL falcon tube. This was repeated for all pipet sizes and the cell mixture was then passed through a 70 micron cell strainer. Cells were counted and diluted to 600,000 cells per mL. Cells were plated on tissue culture plates precoated with poly-D-lysine (PDL). For a 6-well plate, 2 mL was added for a total of 1.2 million cells per well. For a 24-well plate, 0.5 mL was added for a total of 300,000 cells per well. Cultures were then fed with 1/2 media changes every 3rd day to prevent metabolic byproduct accumulation. After one week, the cells were then subjected to the OGD assay.

[0384] Five days before the endpoint processing for the neurons, N-lot HMC were thawed in a 37° C. water bath with gentle swirling. Once thawed, cells were pipetted dropwise into pre-warmed MSC media (alpha MEM without nucleosides (Hyclone, #SH30568.01), 20% Defined FBSHeat Inactivated (Hyclone, #SH30070.03HI), 1× Glutamax (Gibco #35050-061), 1×MEM NEAA (Gibco #11140-050), 1× Pen/Strep (Gibco #15140-120)). Cells were then centrifuged at 300×g for 5 min, resuspended, and counted. 1 million MSCs were plated in a T225 flask using 50 mL of MSC media and allowed to persist in culture for 4 days. HMCs were then harvested by first aspirating the media. The flask was washed with 10 mL of PBS, the PBS was aspirated, 3 mL of TrypLE Express (Gibco, #12604021) was added, and the cells were incubated at 37° C. for 4-6 minutes. Following the incubation, the cells were washed with MSC media, collected into a 50 mL conical tube, the plate was washed with MSC media to remove remaining cells, the cells were centrifuged for 5 minutes at 300×g. The cells were then resuspended in MSC media and counted. HMCs were then plated in transwell inserts in MSC media to achieve a 1:10 ratio of HMCs to neurons (for 6-well transwell inserts, 120,000 HMCs were plated per well, and for 24-well transwell inserts, 30,000 HMCs were plated per well). The HMCs were allowed to recover for 24 hours, and the MSC media was replaced with NMO to remove traces of FBS. The HMCs were incubated in NMO media for 24 hours until their use for recovery in the oxygen glucose deprivation (OGD) assay.

[0385] For the OGD assay, OGD media was used to deprive the neurons of glucose. OGD media consisted of 1 mM CaCl₂, 5 mM KCl, 137 mM NaCl, 0.4 mM KH₂PO₄, 0.3 mM Na₃HPO₄, 0.5 mM MgCl₂, 0.4 mM MgSO₄, 25 mM HEPES, 4 mM NaHCO₃, 1× Pen/Strep diluted in 450 mL DI water. The pH was adjusted to 7.3 and water was added for a final volume of 500 mL. The media was then sterile filtered using a 0.2 μm filter. One day prior to initiating the OGD experiment, OGD media was placed in T75 vented flasks and incubated in a hypoxia chamber (C-Chamber with ProOx C21 Oxygen CO₂ Single Chamber Controller, Bio-Spherix, Parish, NY) overnight to allow for diffusion of oxygen out of the media. The next day, the OGD media was removed from hypoxia chamber and neurons were washed once with OGD media to remove traces of NMO. OGD media was removed and a complete media change with OGD media was performed just prior to adding cells to chamber, i.e. media for 3 hr OGD duration was changed, but media for 2 hr time point was not changed until just before adding cells to chamber, etc. This ensures that the recovery time was the same for all conditions. Neurons were incubated in the hypoxia chamber with OGD media for 1, 2, or 3 hours. Once finished, the neurons were removed and complete media change with NMO media (+B27) was performed. For noninjured controls, NMO was replaced with OGD media, but neurons were not incubated in hypoxia chamber. OGD media in the non-injured controls was replaced with NMO at the same time as the injured cells. HMC co-culture conditions were performed for both non-injured controls and injured cells. Immediately after the OGD media was replaced with NMO, the transwell inserts with HMCs were added in the co-culture conditions. Recovery from the OGD injury was allowed to persist for 24 hours in an incubator under normal cell culture conditions. The

neurons were either collected for RNA isolation, or fixed and subjected to TUNEL staining.

In Vitro OGD Assay TUNEL Analysis

[0386] Primary neuronal culture was generated from embryonic day 18 (E18) rat cortex samples, sourced from Sprague Dawley rats, that were ordered from Brain Bits, LLC (Springfield, IL) as described above. HMC co-culture conditions using a transwell insert (no direct contact) at a ratio of 1:10 HMCs to neurons were performed using N-lot cells, and initiated immediately after OGD injury for a total duration of 24 hrs.

[0387] To assess the effects of HMC co-culture to prevent neuronal cell death caused by the OGD assay, TUNEL staining, imaging, and quantification was performed. After the OGD assay, the transwells were removed in co-culture conditions, and the neurons were first fixed with 4% paraformaldehyde. To fix the cells, the NMO was removed and 4% paraformaldehyde was applied to each well and incubated at room temperature for 10 minutes. After the fixation, the cells were then washed 3× with PBS and permeabilized with 0.02% Triton-X in PBS for 10 minutes at room temperature. The cells were then washed 3× with PBS. The positive control was designated and treated with DNase I (Sigma #4536282001) in DNase I Reaction Buffer (20 mM Tris-HCl, pH 8.4, 2 mM MgCl₂, 50 mM KCl) for 30 minutes at room temperature at 370 for 30 minutes. The positive control was then washed 3× in PBS.

[0388] To achieve TUNEL staining, the TUNEL Label Mix (Sigma #11767291910) and TUNEL Enzyme kit (Sigma #11767305001) was used according to the manufacturer's protocol with slight variation. In general, two kits were used per experiment and diluted in PBS to accommodate the larger volume for 24-well plates. The instructions suggest to use the kit directly with a volume of 50 μL per well, but to ensure coverage of a 24-well plate, PBS was used to dilute the sample for 150 μL per well. For negative control, TUNEL labeling reagent without TUNEL enzyme diluted in PBS was used. For all samples, 200 μL of DAPI staining solution (VWR #10791-650) was added to the combined solution. TUNEL labeling reagent with TUNEL enzyme dilution was added to desired wells, and samples were incubated for 1 hr at 37° C. Samples were washed 3× with PBS. Imaging was performed on the Leica DMi8 microscope and quantification was performed using the Leica LAS X Navigation software. For each condition, 3 wells were stained and 9 images per well were taken and quantified, producing 27 images per condition to be analyzed. TUNEL staining and analysis demonstrated significant increase in cell death with increasing OGD injury duration.

[0389] As shown in FIG. 33, HMC co-culture prevented cell death in primary rat neurons following OGD injury. Neuroprotective effects of HMC cells in ischemic injury do not require direct contact with neurons, function via paracrine effect onto target neurons.

[0390] Accordingly, the in vitro analysis demonstrated that HMCs of the presently disclosed subject matter can protect from ischemic injury (i.e., oxygen glucose deprivation) in isolated neuronal culture preparations, demonstrating a benefit of direct access to central nervous system in stroke.

RNAseq Analysis of Oxygen-Glucose Deprived Rat Neurons

[0391] Primary rat neuronal culture was subjected to oxygen glucose deprivation (OGD) for various durations (e.g., 0, 1, 2 and 3 hours injury duration). Neurons were subsequently co-cultured with HMCs for 24 hours after OGD treatment. RNA samples were collected 24 hours after OGD treatment. RNA-seq analysis was performed to examine transcriptome and pathway enrichment following OGD in vivo injury with or without subsequent HMC co-culture.

[0392] For RNA isolation, neurons were collected by washing with PBS, scraping, and centrifuging in a microcentrifuge tube at 500 g for 5 minutes. The PBS was aspirated and the cell pellet was either snap frozen and placed at -80° C. or immediately processed through the RNeasy RNA isolation kit (Qiagen #74104) following the manufacturer's protocol. RNA was quantified using a Nano Drop and all samples were normalized to 50 ng/uL and 1 ug total was submitted to GeneWiz for RNAseq analysis with the goal of analyzing the changes in gene expression in response to the OGD injury and HMC co-culture. The conditions were Control, Control with HMCs, 1 hr OGD, 1 hr OGD with MSCs, 2 hr OGD, 2 hr OGD with MSCs, 3 hr OGD, and 3 hr OGD with HMCs. For each condition, 3 biological replicates were provided.

[0393] Library preparation was performed using the NEB Ultra II RNA library preparation kit followed by Illumina sequencing. For each sample, 20-30 million reads were achieved. Bioinformatic analysis was performed, and RNAseq data was analyzed. Reads were trimmed using cutadapt1. Quality scores were assessed using FastQC2. Reads were aligned to the *Rattus norvegicus* genome build rn6 using STAR3. Individual sample reads were quantified using HTseq4 and normalized via Relative Log Expression (RLE) using DESeq2 R library5. Read Distribution percentages, violin plots, identity heatmaps, and sample MDS plots were generated as part of the QC step using RSQC6. DEseq2 was also used to calculate fold changes and p-values and perform optional covariate correction. Clustering of genes for the final heatmap of differentially expressed genes was done using the PAM (Partitioning Around Medoids) method using the fpc R library7. Hypergeometric distribution was used to analyze the enrichment of pathways, gene ontology, domain structure, and other ontologies. The topGO R library8, was used to determine local similarities and dependencies between GO terms in order to perform Elim pruning correction. Several database sources were referenced for enrichment analysis, including Interpro, NCBI, MSigDB REACTOME, WikiPathways. Enrichment was calculated relative to a set of background genes relevant for the experiment. Although numerous gene expression changes were observed, genes involved in neuroprotection were highlighted.

[0394] The therapeutic effect of HMC-enriched culture for OGD neuron growth was observed for neurons subjected to 3 hours of OGD damage. Pathway enrichment analysis of the differential expression between neurons subjected to 3 hours of OGD damage and grown on HMC-enriched and control media was performed using Qiagen Ingenuity Pathway Analysis framework. As shown in FIGS. 34A-C, pathways enriched by this differential expression include (a) STAT3 pathway (p -value: 4×10^{-11}), deactivated in HMC-cultured OGD neurons, (b) CREB signaling in neurons (p -value: 4.4×10^{-8}), and (c) numerous inflammatory activity

pathways downregulated in HMC-cultured OGD neurons (e.g., IL-6 signaling, IL-10 signaling, Th1/2 activation pathway).

[0395] Enriching differential expression between OGD neurons grown on HMC-enriched and control media for Gene Ontologyterms (FIGS. 34C-F) in turn shows increase in cell viability of OGD neurons grown on HMC-enriched culture (FIG. 34C), direct neuroprotective effect (FIG. 34C, genes involved in upregulation of neuroprotection are presented on FIG. 34D) and upregulation of pathways involved in synaptic transmission (FIG. 34C). Simultaneously, pathways involved in apoptosis (FIG. 34E, genes downregulated by the effect of HMC-enriched growth culture are presented on FIG. 34F) and general response to cell death are strongly downregulated. This reflects the relation between full differential expression and the displacement of the molecular marker of OGD damage induced by the presence of HMC-enriched growth medium.

[0396] To validate these increases in gene expression, the same RNA samples used for RNAseq analysis were used for qPCR analysis. To perform qPCR analysis, Taqman probes (ThermoFisher Scientific) were designed and used with the Taqman Fast Advanced Master Mix (ThermoFisher Scientific #4444556) and samples were analyzed on the QuantStudio Flex 7 RT-PCR system (Applied Biosystems #4485698). The three biological replicates for each sample were run in duplicate, and the analysis demonstrates the similar increase in gene expression with the presence of HMCs. Statistical significance was achieved through 2-way ANOVA and Sidak multiple comparison test (* $p < 0.05$, ** $p < 0.01$, **** $p < 0.0001$).

[0397] As shown in FIG. 35, qPCR analysis verified RNAseq results of genes involved in cell viability and neuroprotection. Specifically, HMC cells stimulated expression of neuroprotective genes in neuron undergoing ischemic injury, such as heat shock protein family B member 1 (HSPB1), insulin-like growth factor 1 (IGF2), and secreted phosphoprotein 1 (SPP1), also known as osteopontin.

Example 9—In Vitro Oxidative Damage Model

[0398] The HMC-EVs of the presently disclosed subject matter were tested in an in vitro oxidative damage model. Briefly, neurons were subject to H₂O₂ oxidative damage, and treated with HMC-EVs at a dose of about 10,000, 30,000 or 100,000 EVs/cells. Percentage of cell death was determined as the number of propidium iodide (PI)-positive cells out of the total cell number.

[0399] As shown in FIG. 36, HMC-EV treatment resulted in a dose-dependent attenuation of cell death. A significant rescue from cell death by HMC-EVs was observed at 30K and 100K doses. The overall cell death rate was about 44% lower than the control group without EV treatment.

[0400] Accordingly, these results demonstrated that HMC-EVs can prevent oxidative injury in neurons.

Example 10—In vitro Glutamate Excitotoxicity Model

[0401] The HMC-EVs of the presently disclosed subject matter were tested in an in vitro glutamate excitotoxicity (high doses of L-glutamate) model. Briefly, neurons were exposed to various concentrations of L-glutamate (about 0, 30, 300 and 3000 uM), and treated with HMC-EVs at a dose

of about 50,000 EVs/cells. Percentage of cell death was determined as the number of propidium iodide (PI)+ cells out of the total cell number.

[0402] As shown in FIG. 37, HMC-EV treatment sustained cells in the nuclear swelling stage after glutamate-induced injury and maintained viability. Staining with TMRM (cell permeant dye that accumulates in active mitochondria with intact membrane potentials) showed that HMC-EV treatment also maintained mitochondrial activity in injured cells.

[0403] Accordingly, these results demonstrated that HMC-EVs prevent neuronal death due to glutamate excitotoxic injury.

Example 11—RNAseq analysis of HMCs vs Bone Marrow-MSC vs Adipose Tissue-MSC

[0404] RNAseq analysis was performed for the HMCs of the presently disclosed subject matter under both basal and stimulated conditions. HMCs were generated from both N-line (N-HMCs) and GMP-1 (GMP-HMCs) cell line, and 3 technical replicate samples were prepared for each condition. MSCs isolated from adipose tissue and bone marrow were also analyzed and compared with the HMCs of the presently disclosed subject matter. AD-MSCs were collected from 3 different adult donors, and 2 technical replicate samples were prepared for each biological replicate. BM-MSCs were also collected from 3 different adult donors.

HMCs Vs. Adipose Tissue Derived MSCs

[0405] Principal component analysis of transcriptomes of HMCs (obtained from the N-cell line) and AD-MSCs shows that HMCs are distinct from the latter in both basal and interferon-gamma stimulated state (FIG. 38). The first principal component largely describes the effect of stimulation with gamma interferon, while the second principal component describes the difference between HMCs and AD-MSCs.

[0406] Weights of different genes contributing to the second principal component which determines the variance between HMCs and AD-MSCs. Of a particular note is down-regulation of collagen genes (COL1A1, COL3A1 etc.), mitochondrial function genes and TGF Beta 1 (one of the main factors promoting angiogenesis) in HMCs as compared to AD-MSCs demonstrating a certain degree of immaturity of HMCs (FIG. 39).

[0407] Hierarchical clustering demonstrates similarity between biological/technical replicate samples of the same biological type as well as clear difference between HMCs and AD-MSCs, in both basal cell states and cell states stimulated with gamma interferon (FIG. 40).

[0408] As shown in FIG. 41, genes in this cluster were up-regulated in HMCs (both basal and INFN gamma-stimulated) as compared to AD-MSCs. The genes included: CALR, UBB, PKM, CXCL8, C15orf48, PSME2, TPM3, ANKRD1, PFN1, SRGN, ACTB, MDK, TAGLN2, CFL1, HSP90AA1, HSPA8, CXCL12, UCHL1, HMGA2, HMGA1, HN1, PTMA, SP90AB1, PRDX1, GSTP1, KRT18, IGFBP4, CALD1, COL4A1, COL4A2 and GAPDH. Differential expression of these genes between HMCs and AD-MSCs was consistent across biological and technical replicates according to the hierarchical clustering map.

[0409] Functional annotation of biological pathways enriched in the cluster on FIG. 41 was performed using Reactome (<https://reactome.org/>). The top pathway enriched by the corresponding genes was associated with axon guid-

ance. Other significantly enriched pathways included cellular stress response and developmental biology (related to the relative immaturity of HMCs).

[0410] As shown in FIG. 42, genes in this cluster were down-regulated in HMCs (both basal and INFN gamma-stimulated) as compared to AD-MSCs. The genes included: SERPINE1, ACTA2, TPM2, CTGF, SERPINE2, CRYAB, ELN, MFGE8, ANXA2, POSTN, VIM, MFAP5, ISLR, THBS1, TIMP3, DKK1, COL6A3, COL6A1, TPT1, BCYRN1, COL1A1, SPARC, TPM1, BGN, COL1A2, COL3A1, TGFB1, CRLF1, COMP, NEAT1, MT-CO3, MT-CO2, MT-ATP8, MT-CYB, MT-CO1, MT-ATP6, MT-ND4, MT-ND4L, MT-ND5, MT-ND6, MT-ND3, MT-ND1, MT-ND2, GREM1, TMSB4X, ITGB1, LMNA, H2AFZ, FTL, EEF1G, NPM1, EEF1A1, RACK1, ACTG1, and TPM4. Differential expression of these genes between HMCs and AD-MSCs was consistent across biological and technical replicates according to the hierarchical clustering map.

[0411] Functional annotation of biological pathways enriched in the cluster on FIG. 42 was performed using Reactome (<https://reactome.org/>). The top pathways enriched by the corresponding genes were associated with respiratory electron transport and mitochondrial function in general as well as collagen biosynthesis.

[0412] Canonical pathway enrichment of differential gene expression signature between HMCs and AD-MSCs shows noticeable HMC-specific up-regulation of several pathways (denoted by red arrows) involved in the development of neuronal lineage including axon guidance, CREB signaling in neurons, synaptogenesis signaling etc. (FIG. 43). These results suggest that HMCs have a distinct expression profile when compared to AD-MSCs, and HMCs may confer neuroprotective effects, and provide neurotrophic factors, factors involved in supporting neuronal health and recovery.

[0413] Lists of genes-contributors to the activated pathways establishing this difference are shown in FIGS. 44-47.

[0414] FIG. 44 depicts the top 15 most strongly differentially expressed genes contributing to activation of neuronal CREB signaling in HMCs. Expr Log Ratio denotes base 10 logarithm of the fold change between average TPM expression of a gene in HMCs and its average TPM expression in adipose tissue-derived MSCs, i.e., the Expr Log Ratio higher than 2 implies gene expression increase by a factor larger than 100.

[0415] FIG. 45 depicts the top 15 most strongly upregulated genes contributing to the enrichment of axon guidance pathway in HMCs. Although activation pattern of axonal guidance signaling pathway has not been determined by Qiagen Ingenuity Pathway Analysis, the pathway was enriched with p-value ~1.38e-4 in HMCs as compared to AD-MSCs.

[0416] FIG. 46 depicts the top 15 most strongly expressed genes contributing to activation of synaptogenesis signaling pathway in HMCs. Enrichment p-value 1.14e-3, activation pattern z-score 3.578, the highest among all pathways differentially upregulated in HMCs.

[0417] FIG. 47 depicts the top 15 most up-regulated genes out of contributing to activation of neuroinflammation signaling pathway in HMCs. Pathway enrichment p-value 4.97e-3, activation z-score 1.508.

[0418] HMCs were also generated from a different pluripotent stem cell, i.e., GMP1 cells. Principal component analysis of transcriptomes of GMP1-HMC was also per-

formed and compared with HMC derived from N-line cells (N-HMCs) and AD-MSCs under both basal and stimulated conditions (FIG. 48).

[0419] Hierarchical clustering analysis showed that GMP1-HMCs had similar profiles to the N-HMCs (FIG. 49). As shown in FIG. 50, genes in this cluster were up-regulated in N-HMCs and GMP1-HMCs (both basal and INFN gamma-stimulated) as compared to AD-MSCs. The genes included: TMSB4X, ACTG1, GSTP1, KRT18, IGFBP5, NPY, KRT8, PRDX6, MDK, DKK3, UCHL1, TUBB3, HN1, PTMA, HSP90AB1, HMGA1, HSPA8, TAGLN2, ANKRD1, PFN1, CYBA, and UBB. Differential expression of these genes between N-HMC, GMP1-HMC, and adipose tissue-derived MSC lines was consistent across biological and technical replicates according to the hierarchical clustering map.

[0420] Functional annotation of biological pathways enriched in the cluster on FIG. 50 was performed using Reactome (<https://reactome.org/>). The top pathway enriched by the corresponding genes was associated with axon guidance. Other significantly enriched pathways included cellular stress response and developmental biology.

[0421] As shown in FIG. 51, genes in this cluster were down-regulated in N-HMCs and GMP1-HMCs in basal condition as compared to AD-MSCs. The genes included: SERPINE1, S100A6, CD59, POSTN, VIM, MFAP5, ISLR, THBS1, COL6A3, TIMP3, ELN, ANXA2, COL1A1, BCYRN1, CCDC80, COL6A1, COL6A2, BGN, COL1A2, COL3A1, TGFB1, CRLF1, COMP, and GREM1. Differential expression of these genes between N-HMC, GMP1-HMC, and AD-MSC lines was consistent across biological and technical replicates according to the hierarchical clustering map.

[0422] As shown in FIG. 52, genes in this cluster were down-regulated in N-HMCs and GMP1-HMCs in INFN gamma-stimulated condition as compared to AD-MSCs. The genes included: MT1X, MT1G, TMSB10, CCL8, INHBA, CTSB, SERPINB2, ADM, APOL1, FTH1, CCL2, CCL5, CSF1, IL1B, IGFBP3, P4HB, DCN, FSTL1, ANXA5, LOX, CD63, CTSZ, FN1, LGALS1, LDHA, RCN3, MMP2, and TIMP1. Differential expression of these genes between N-HMC, GMP1-HMC, and AD-MSC lines was consistent across biological and technical replicates according to the hierarchical clustering map.

[0423] Functional annotation of biological pathways enriched in the cluster on FIGS. 51 and 52 was performed using Reactome (<https://reactome.org/>). The top pathways enriched by the corresponding genes were associated with extracellular matrix organization in general as well as collagen biosynthesis.

[0424] Similarly, canonical pathway enrichment of differential gene expression signature between N-HMCs, GMP1-HMCs, and AD-MSCs shows noticeable HMC-specific up-regulation of several pathways (denoted by red arrows) involved in the development of neuronal lineage including axon guidance, CREB signaling in neurons, synaptogenesis signaling etc. (FIGS. 53A-C and 54A-C). Thus, N-HMC and GMP1-HMCs shared a similar profile and both showed axon guidance enrichment.

[0425] Accordingly, it is concluded that the HMCs of the presently disclosed subject matter are distinct from AD-MSCs. Specifically, the MSCs of the presently disclosed subject matter have a distinct expression profile when compared to AD-MSCs, and may confer neuroprotective effects, provide neurotrophic factors, i.e., factors involved in supporting neuronal survival, growth, health and recovery. HMC Vs. Bone Marrow Derived MSC

[0426] Principal component analysis of transcriptomes of HMCs (obtained from N-cell line) and BM-MSCs shows

that HMCs are distinct from the latter in both basal and INFN-gamma stimulated state. The 1st principal component largely describes the effect of stimulation with gamma interferon, while the 2nd principal component describes the difference between HMCs and BM-MSCs (FIG. 55).

[0427] Weights of different genes contributing to the 2nd principal component which determines the variance between HMCs and BM-MSCs. Of a particular note is down-regulation of collagen genes (COL1A1, COL1A2, COL3A1, COL6A2 etc.), mitochondrial function genes and TGF Beta 1 (one of the main factors promoting angiogenesis) in HMCs as compared to BM-MSCs demonstrating a certain degree of immaturity of HMCs as compared to the latter (FIG. 56).

[0428] Hierarchical clustering demonstrates similarity between biological replicate samples of the same type as well as clear difference between HMCs and BM-MSCs, in both basal cell states and cell states stimulated with gamma interferon (FIG. 57).

[0429] Genes in this cluster were up-regulated in HMCs (both basal and INFN gamma-stimulated) as compared to BM-MSCs (FIG. 58). The genes included: PP1A, NPM1, HNRNPA1, IGFBP5, KRT19, KRT18, GSTP1, TUBB, TUBA1B, KRT8, HN1, PTMA, TUBA1C, HSPA8, HMGA1, CFL1, MYL6, ACTB, UCHL1, TAGLN2, MDK, GREM1, MMP1, and CTSC. Differential expression of these genes between HMCs and BM-MSCs was consistent across biological and technical replicates according to the hierarchical clustering map.

[0430] Functional annotation of biological pathways enriched in the cluster on FIG. 58 was performed using Reactome (<https://reactome.org/>). Among the top pathways enriched by the corresponding genes there is axon guidance. Other significantly enriched pathways included cellular stress response and developmental biology (related to the relative immaturity of HMCs).

[0431] Genes in this cluster were down-regulated in HMCs (both basal and INFN gamma-stimulated) as compared to BM-MSCs (FIG. 59). The genes included: ANXA2, TPT1, VIM, COL6A1, BGN, COL6A2, CTGF, TIMP3, ACTA2, COL3A1, SPARC, ITGB1, SERPINH1, TPM2, TGFBI, COL1A1, TPM1, COL6A3, TPM4, SERPINE2, CALD1, COL1A2, TAGLN, MYL9, MT-RNR2, POSTN. Differential expression of these genes between HMCs and BM-MSCs was consistent across biological and technical replicates according to the hierarchical clustering map.

[0432] Functional annotation of biological pathways enriched in the cluster on FIG. 59 was performed using Reactome (<https://reactome.org/>). The top pathways enriched by the corresponding genes were associated with collagen biosynthesis/assembly (demonstrating similarities between BM-MSCs and AD-MSCs).

[0433] Canonical pathway enrichment of differential gene expression signature between HMCs and BM-MSCs again shows an HMC-specific up-regulation of pathways involved in the development of neuronal lineage such as CREB signaling in neurons (FIG. 60).

[0434] FIG. 61 depicts the top 15 most strongly differentially expressed genes contributing to activation of neuronal CREB signaling in HMCs as compared to BM-MSCs. FIG. 62. depicts the top 15 most strongly upregulated genes contributing to activation of synaptogenesis signaling in HMCs as compared to BM-MSCs.

[0435] Accordingly, it is concluded that, the HMCs of the presently disclosed subject matter are distinct from BM-MSCs. Specifically, the HMCs of the presently disclosed subject matter have a distinct expression profile, and provide neuroprotective effects when compared to BM-MSCs.

TABLE 7

Genes more highly expressed in HMCs compared with AD-MSCs				
Gene name	Description	Fold Change	Log Fold Change	p-Adj
LOC400655	uncharacterized LOC400655	298.97	8.2239	2.40E-39
BAI3	adhesion G protein-coupled receptor B3	234.52	7.8735	2.09E-44
SHISA2	shisa family member 2	197.93	7.6288	9.51E-133
CYYR1	cysteine/tyrosine-rich 1	190.66	7.5749	1.02E-30
PAX7	paired box 7	181.34	7.5025	4.73E-29
SYT14	synaptotagmin XIV	181.02	7.5000	1.15E-39
ELAVL2	ELAV like neuron-specific RNA binding protein 2	158.73	7.3105	4.28E-80
DCC	DCC netrin 1 receptor	157.22	7.2966	3.12E-59
WDR72	WD repeat domain 72	156.71	7.2920	6.07E-32
TMEM40	transmembrane protein 40	137.10	7.0991	3.16E-33
TTTY15	testis-specific transcript_Y-linked 15 (non-protein coding)	123.88	6.9528	1.15E-131
HRH2	histamine receptor H2	112.31	6.8114	2.57E-22
CA8	carbonic anhydrase VIII	103.90	6.6990	3.78E-28
TFAP2A	transcription factor AP-2 alpha (activating enhancer binding protein 2 alpha)	101.18	6.6608	1.12E-48
ZDHHC8P1	zinc finger_DHHC-type containing 8 pseudogene 1	97.79	6.6115	2.23E-75
DENND2A	DENN/MADD domain containing 2A	83.16	6.3778	2.98E-72
HOPX	HOP homeobox	78.67	6.2978	1.14E-29
SYT13	synaptotagmin XIII	72.13	6.1726	1.68E-29
KC6	keratoconus gene 6	71.51	6.1602	1.97E-21
KDM5D	lysine (K)-specific demethylase 5D	68.12	6.0899	1.32E-90
UTY	ubiquitously transcribed tetratricopeptide repeat containing_Y-linked	67.39	6.0744	1.17E-124
SULT1C4	sulfotransferase family_cytosolic_1C_member 4	67.28	6.0721	1.62E-18
MAB21L2	mab-21-like 2 (<i>C. elegans</i>)	64.72	6.0161	1.10E-13
ZIC2	Zic family member 2	64.55	6.0124	5.67E-45
LOC644919	uncharacterized LOC644919	63.85	5.9965	5.51E-22
USP9Y	ubiquitin specific peptidase 9_Y-linked	62.40	5.9634	5.67E-57
MSX2	msh homeobox 2	60.69	5.9233	1.33E-41
GATA3	GATA binding protein 3	59.60	5.8973	2.70E-62
RIPK4	receptor-interacting serine-threonine kinase 4	59.03	5.8833	1.18E-61
PKIB	protein kinase (cAMP-dependent_catalytic) inhibitor beta	58.55	5.8717	1.61E-22
GAL3ST3	galactose-3-O-sulfotransferase 3	58.19	5.8627	1.39E-21
CASC9	cancer susceptibility candidate 9 (non-protein coding)	56.08	5.8095	1.34E-24
TGFB2	transforming growth factor_beta 2	53.17	5.7324	2.52E-45
L1CAM	L1 cell adhesion molecule	53.09	5.7305	2.84E-117
TXLNGY	taxilin gamma pseudogene_Y-linked	50.60	5.6610	3.79E-98
EIF1AY	eukaryotic translation initiation factor 1A_Y-linked	50.17	5.6487	3.91E-55
RPS4Y1	ribosomal protein S4_Y-linked 1	48.25	5.5925	6.04E-33
PCDHA2	protocadherin alpha 2	47.12	5.5582	5.20E-33
LINC00648	long intergenic non-protein coding RNA 648	46.20	5.5298	2.25E-16
SNRPN	small nuclear ribonucleoprotein polypeptide N	45.49	5.5075	2.85E-23
PRKY	protein kinase_Y-linked_pseudogene	44.67	5.4813	5.09E-58
TTTY14	testis-specific transcript_Y-linked 14 (non-protein coding)	44.52	5.4764	3.51E-12
PCDHB5	protocadherin beta 5	43.99	5.4592	7.71E-125
SDK2	sidekick cell adhesion molecule 2	43.14	5.4310	3.20E-46
CDH3	cadherin 3_type 1_P-cadherin (placental)	43.08	5.4289	7.17E-39
FZD10-AS1	FZD10 antisense RNA 1 (head to head)	42.97	5.4251	2.77E-12
CD24	CD24 molecule	41.69	5.3818	2.94E-211
C7orf69	chromosome 7 open reading frame 69	40.57	5.3422	1.20E-33

TABLE 7-continued

Genes more highly expressed in HMCs compared with AD-MSCs				
Gene name	Description	Fold Change	Log Fold Change	p-Adj
NETO1	neuropilin (NRP) and tolloid (TLL)-like 1	40.16	5.3277	1.29E-66
SOX11	SRY (sex determining region Y)-box 11	40.07	5.3244	5.46E-13
SLC7A2	solute carrier family 7 (cationic amino acid transporter_y + system)_member 2	39.40	5.3002	3.79E-13
NLGN4X	neuroligin 4_X-linked	38.78	5.2773	2.05E-11
MDFI	MyoD family inhibitor	38.75	5.2762	1.58E-226
GABRB1	gamma-aminobutyric acid (GABA) A receptor_beta 1	38.15	5.2535	1.20E-15
LOC100507600	uncharacterized LOC100507600	36.76	5.1999	1.30E-19
DDX3Y	DEAD (Asp-Glu-Ala-Asp) box helicase 3_Y-linked	36.52	5.1908	1.14E-21
IGF2-AS	IGF2 antisense RNA	35.47	5.1486	1.14E-10
GPRC5C	G protein-coupled receptor_class C_group 5_member C	35.30	5.1415	3.14E-44
MSLN	mesothelin	35.29	5.1412	1.09E-10
LPAR4	lysophosphatidic acid receptor 4	35.24	5.1392	2.90E-22
EFNA1	ephrin-A1	34.82	5.1217	2.55E-31
MUM1L1	melanoma associated antigen (mutated) 1-like 1	33.17	5.0516	1.14E-10
C7	complement component 7	32.85	5.0377	1.03E-09
NLGN4Y	neuroligin 4_Y-linked	32.76	5.0340	1.43E-14
PCDHA12	protocadherin alpha 12	32.56	5.0249	1.18E-11
TFAP2A-AS1	TFAP2A antisense RNA 1	32.47	5.0211	1.24E-17
CDH18	cadherin 18_type 2	32.36	5.0160	6.15E-13
DPY19L2P1	DPY19L2 pseudogene 1	31.57	4.9804	2.43E-15
GABRA3	gamma-aminobutyric acid (GABA) A receptor_alpha 3	30.86	4.9475	4.71E-18
CLDN1	claudin 1	30.81	4.9454	8.36E-18
CYP27C1	cytochrome P450_family 27_subfamily C_polypeptide 1	30.78	4.9439	1.65E-17
IGSF9B	immunoglobulin superfamily_member 9B	30.52	4.9316	8.19E-25
C5orf46	chromosome 5 open reading frame 46	30.22	4.9175	1.02E-09
C1orf94	chromosome 1 open reading frame 94	30.16	4.9148	1.70E-10
NEDD4L	neural precursor cell expressed_developmentally down-regulated 4-like_E3 ubiquitin protein ligase	29.64	4.8895	4.58E-81
MLC1	megalecephalic leukoencephalopathy with subcortical cysts 1	29.14	4.8650	2.64E-10
DLX1	distal-less homeobox 1	29.04	4.8601	3.14E-116
PAX3	paired box 3	28.76	4.8457	6.05E-156
PCDHAC2	protocadherin alpha subfamily C_2	28.62	4.8388	2.47E-22
MAGEL2	melanoma antigen family L2	28.59	4.8374	4.18E-21
PLCH2	phospholipase C_eta 2	28.36	4.8256	3.33E-11
NR0B1	nuclear receptor subfamily 0_group B_member 1	28.35	4.8253	3.16E-17
CCNLJ	cyclin J-like	28.31	4.8232	5.67E-16
SORCS1	sortilin-related VPS10 domain containing receptor 1	27.98	4.8064	6.23E-10
VANGL2	VANGL planar cell polarity protein 2	27.96	4.8054	3.88E-14
SALL1	spalt-like transcription factor 1	27.92	4.8035	1.31E-18
LOC102467080	uncharacterized LOC102467080	27.08	4.7594	9.43E-11
CRISPLD1	cysteine-rich secretory protein LCCL domain containing 1	26.77	4.7424	1.83E-16
TMEM132D	transmembrane protein 132D	26.14	4.7082	9.35E-11
PRKCQ-AS1	PRKCQ antisense RNA 1	25.48	4.6711	2.53E-17
CACNG4	calcium channel_voltage-dependent_gamma subunit 4	25.36	4.6644	1.76E-08
KIAA1211	KIAA1211	25.20	4.6553	2.27E-31
ANXA3	annexin A3	25.16	4.6532	2.77E-46
NMNNAT3	nicotinamide nucleotide adenyllyltransferase 3	25.10	4.6493	3.46E-09
SLAMF7	SLAM family member 7	24.98	4.6427	8.99E-13
GPR20	G protein-coupled receptor 20	24.72	4.6275	9.88E-11
OLFML2A	olfactomedin-like 2A	24.60	4.6206	4.62E-40

TABLE 7-continued

Genes more highly expressed in HMCs compared with AD-MSCs				
Gene name	Description	Fold Change	Log Fold Change	p-Adj
IP6K3	inositol hexakisphosphate kinase 3	24.54	4.6172	1.08E-10
LMX1B	LIM homeobox transcription factor 1_beta	24.37	4.6070	7.25E-15
IGF2	insulin-like growth factor 2	24.24	4.5992	3.10E-08
KCNK3	potassium channel_two pore domain subfamily K_member 3	24.24	4.5991	3.99E-08
ZFY	zinc finger protein_Y-linked	23.97	4.5833	1.42E-09
CLSTN2	calsyntenin 2	23.89	4.5781	6.01E-11
GNAZ	guanine nucleotide binding protein (G protein)_alpha z polypeptide	23.80	4.5728	1.11E-90
GCNT2	glucosaminyl (N-acetyl) transferase 2_I-branching enzyme (I blood group)	23.61	4.5616	2.98E-28
PCDHB15	protocadherin beta 15	23.53	4.5564	2.81E-46
PCDHA10	protocadherin alpha 10	23.47	4.5527	3.83E-16
C11orf88	chromosome 11 open reading frame 88	23.47	4.5527	3.83E-11
MGAT5B	mannosyl (alpha-1_6)-glycoprotein beta-1_6-N-acetyl-glucosaminyltransferase_isozyme B	23.21	4.5366	6.99E-73
OVCH2	ovochymase 2 (gene/pseudogene)	23.17	4.5344	2.35E-11
ATRN1L	attractin-like 1	23.05	4.5266	8.08E-18
TEX15	testis expressed 15	22.84	4.5138	2.28E-12
SHROOM2	shroom family member 2	22.83	4.5131	4.36E-10
ECEL1P2	endothelin converting enzyme-like 1_pseudogene 2	22.60	4.4985	6.48E-10
SDK1	sidekick cell adhesion molecule 1	22.28	4.4780	1.76E-24
EPHB2	EPH receptor B2	22.27	4.4773	2.63E-18
MIR4697HG	MIR4697 host gene	22.12	4.4675	2.04E-17
ABCA13	ATP-binding cassette_sub-family A (ABC1)_member 13	21.72	4.4407	2.93E-17
C21orf88	B3GALT5 antisense RNA 1	21.46	4.4238	1.23E-09
LIN28B	lin-28 homolog B (<i>C. elegans</i>)	21.46	4.4233	1.04E-19
LINC01158	long intergenic non-protein coding RNA 1158	21.14	4.4018	1.41E-08
RASGRF1	Ras protein-specific guanine nucleotide-releasing factor 1	21.12	4.4004	1.98E-13
GRIA1	glutamate receptor_ionotropic_AMPA 1	20.59	4.3639	6.29E-25
LINC00491	long intergenic non-protein coding RNA 491	20.56	4.3619	1.12E-08
PCDHB2	protocadherin beta 2	20.19	4.3355	1.69E-71
ZNF853	zinc finger protein 853	19.98	4.3202	6.14E-46
SERPINA5	serpin peptidase inhibitor_clade A (alpha-1_antiproteinase_antitrypsin)_member 5	19.89	4.3138	1.54E-10
CA3	carbonic anhydrase III	19.47	4.2832	1.71E-07
PLEKHA6	pleckstrin homology domain containing_family A member 6	19.34	4.2734	1.17E-22
LOC283299	uncharacterized LOC283299	19.22	4.2642	2.33E-08
NRK	Nik related kinase	18.95	4.2444	2.17E-47
LINC00460	long intergenic non-protein coding RNA 460	18.91	4.2414	3.71E-08
MYO5C	myosin VC	18.88	4.2390	1.38E-12
ANK1	ankyrin_1_erythrocytic	18.61	4.2182	1.01E-25
NIPAL4	NIPA-like domain containing 4	18.46	4.2066	8.70E-10
SAMD5	sterile alpha motif domain containing 5	18.35	4.1981	6.95E-07
SOWAHD	sosondowah ankyrin repeat domain family member D	18.22	4.1874	3.96E-18
CIDEA	cell death-inducing DFFA-like effector a	18.04	4.1732	1.37E-06
SHF	Src homology 2 domain containing F	17.93	4.1643	9.93E-91
GABRQ	gamma-aminobutyric acid (GABA) A receptor theta	17.93	4.1639	8.84E-09
NFE2L3	nuclear factor_erythroid 2-like 3	17.87	4.1596	4.45E-50
CRHBP	corticotropin releasing hormone binding protein	17.49	4.1285	2.10E-08
SPTBN2	spectrin_beta_non-erythrocytic 2	17.41	4.1219	3.91E-106
INA	internexin neuronal intermediate filament protein_alpha	17.37	4.1188	1.25E-22

TABLE 7-continued

Genes more highly expressed in HMCs compared with AD-MSCs				
Gene name	Description	Fold Change	Log Fold Change	p-Adj
VAX1	ventral anterior homeobox 1	17.32	4.1144	8.06E-07
CDKL2	cyclin-dependent kinase-like 2 (CDC2-related kinase)	17.11	4.0971	2.86E-12
GLIS1	GLIS family zinc finger 1	17.08	4.0943	6.84E-149
IRF6	interferon regulatory factor 6	16.81	4.0711	7.61E-11
POU3F3	POU class 3 homeobox 3	16.77	4.0680	1.72E-10
LOC339975	uncharacterized LOC339975	16.72	4.0639	3.00E-08
RASL10B	RAS-like_family_10_member B	16.67	4.0590	1.14E-52
KLHL4	kelch-like family member 4	16.57	4.0502	7.55E-23
EN2	engrailed homeobox 2	16.46	4.0405	3.11E-07
FBXO2	F-box protein 2	16.33	4.0291	9.42E-23
CADM1	cell adhesion molecule 1	16.17	4.0152	1.30E-11
SIPA1L2	signal-induced proliferation-associated 1 like 2	16.14	4.0125	1.24E-23
PAK3	p21 protein (Cdc42/Rac)-activated kinase 3	16.08	4.0071	3.73E-38
EPHAS5-AS1	EPHAS5 antisense RNA 1	15.99	3.9993	2.38E-06
OPRD1	opioid receptor_delta 1	15.91	3.9915	6.44E-06
NIPAL1	NIPA-like domain containing 1	15.83	3.9846	1.07E-09
SRSF12	serine/arginine-rich splicing factor 12	15.68	3.9709	2.27E-10
NNAT	neuronatin	15.59	3.9623	2.99E-19
FAM69B	family with sequence similarity 69_member B	15.49	3.9532	1.53E-83
DUSP8	dual specificity phosphatase 8	15.45	3.9493	7.39E-44
MAMDC2-AS1	MAMDC2 antisense RNA 1	15.38	3.9433	1.48E-08
MEX3A	mex-3 RNA binding family member A	15.32	3.9375	9.15E-96
PLEKHG4B	pleckstrin homology domain containing_family G (with RhoGef domain) member 4B	15.18	3.9241	2.31E-23
EYA1	EYA transcriptional coactivator and phosphatase 1	15.07	3.9137	1.31E-09
TIE1	tyrosine kinase with immunoglobulin-like and EGF-like domains 1	15.03	3.9096	1.41E-17
ARSE	arylsulfatase E (chondrodysplasia punctata 1)	14.84	3.8914	1.74E-36
FAM110D	family with sequence similarity 110_member D	14.73	3.8807	1.42E-17
PLCXD3	phosphatidylinositol-specific phospholipase C_X domain containing 3	14.68	3.8759	1.26E-05
SLC44A5	solute carrier family 44_member 5	14.68	3.8753	1.15E-06
PCSK1N	proprotein convertase subtilisin/kexin type 1 inhibitor	14.66	3.8737	1.93E-06
IL31RA	interleukin 31 receptor A	14.62	3.8701	1.26E-08
PCDHGB6	protocadherin gamma subfamily B_6	14.54	3.8620	5.59E-70
WSCD1	WSC domain containing 1	14.47	3.8555	6.83E-06
KLHL23	kelch-like family member 23	14.36	3.8442	8.90E-08
KCNF1	potassium channel_voltage gated modifier subfamily F_member 1	14.35	3.8430	2.97E-06
TFAP2C	transcription factor AP-2 gamma (activating enhancer binding protein 2 gamma)	14.26	3.8339	9.30E-08
CD163L1	CD163 molecule-like 1	14.13	3.8202	9.04E-28
RAMP1	receptor (G protein-coupled) activity modifying protein 1	13.96	3.8033	1.04E-07
C10orf126	chromosome 10 open reading frame 126	13.61	3.7662	2.35E-05
CPXM1	carboxypeptidase X (M14 family)_member 1	13.60	3.7657	1.95E-58
SPINK5	serine peptidase inhibitor_Kazal type 5	13.56	3.7614	4.59E-06
NCRNA00185	testis-specific transcript_Y-linked 14 (non-protein coding)	13.51	3.7558	2.44E-05
JAKMIP2	janus kinase and microtubule interacting protein 2	13.39	3.7428	7.95E-12
SLC7A14	solute carrier family 7_member 14	13.38	3.7415	1.86E-30
B4GALNT4	beta-1_4-N-acetyl-galactosaminyl transferase 4	13.35	3.7385	2.93E-10

TABLE 7-continued

Genes more highly expressed in HMCs compared with AD-MSCs				
Gene name	Description	Fold Change	Log Fold Change	p-Adj
ETNK2	ethanolamine kinase 2	13.22	3.7248	1.53E-135
SH2D3C	SH2 domain containing 3C	13.17	3.7196	8.57E-08
MAP3K9	mitogen-activated protein kinase kinase kinase 9	12.93	3.6923	2.32E-23
SHC2	SHC (Src homology 2 domain containing) transforming protein 2	12.84	3.6829	1.46E-08
PTGER4	prostaglandin E receptor 4 (subtype EP4)	12.81	3.6794	1.54E-59
EPHA5	EPH receptor A5	12.70	3.6673	1.03E-18
LINC01012	long intergenic non-protein coding RNA 1012	12.64	3.6596	9.52E-06
IL2RB	interleukin 2 receptor_beta	12.64	3.6595	1.10E-07
GATA3-AS1	GATA3 antisense RNA 1	12.62	3.6581	2.67E-06
RIMS2	regulating synaptic membrane exocytosis 2	12.60	3.6551	2.86E-22
ADAMTS3	ADAM metallopeptidase with thrombospondin type 1 motif_3	12.60	3.6549	1.02E-64
PIEZ02	piezo-type mechanosensitive ion channel component 2	12.55	3.6495	2.89E-08
GLP2R	glucagon-like peptide 2 receptor	12.46	3.6393	3.38E-06
GPRC5D	G protein-coupled receptor_class C_group 5_member D	12.45	3.6382	4.22E-06
GBX2	gastrulation brain homeobox 2	12.44	3.6366	1.28E-07
TMEM255A	transmembrane protein 255A	12.34	3.6257	8.27E-14
LOC100506314	uncharacterized LOC100506314	12.33	3.6240	5.74E-19
LHX8	LIM homeobox 8	12.31	3.6221	4.39E-06
NOMO3	NODAL modulator 3	12.30	3.6210	8.51E-148
LINC00858	long intergenic non-protein coding RNA 858	12.25	3.6152	5.74E-05
C2CD4C	C2 calcium-dependent domain containing 4C	12.22	3.6110	4.68E-14
COL4A6	collagen_typeIV_alpha 6	12.20	3.6084	4.19E-05
CD6	CD6 molecule	12.18	3.6059	8.90E-07
EFNB2	ephrin-B2	12.06	3.5922	1.23E-06
FOXF1	forkhead box F1	11.99	3.5840	9.88E-22
B3GNT5	UDP-GlcNAc:betaGal beta-1→3-N-acetylglucosaminyltransferase 5	11.97	3.5812	6.07E-128
LINC00470	long intergenic non-protein coding RNA 470	11.89	3.5720	4.17E-07
ADARB2	adenosine deaminase_RNA-specific_B2 (non-functional)	11.83	3.5640	2.75E-05
IGFBP2	insulin-like growth factor binding protein 2_36 kDa	11.82	3.5635	5.62E-05
LRP1B	low density lipoprotein receptor-related protein 1B	11.82	3.5626	5.67E-05
DUSP4	dual specificity phosphatase 4	11.81	3.5624	2.18E-42
TRHDE-AS1	TRHDE antisense RNA 1	11.78	3.5588	1.62E-05
TFAP2B	transcription factor AP-2 beta (activating enhancer binding protein 2 beta)	11.77	3.5565	1.86E-05
BIRC7	baculoviral IAP repeat containing 7	11.72	3.5505	3.89E-05
TMCC3	transmembrane and coiled-coil domain family 3	11.70	3.5482	4.68E-07
LINC00649	long intergenic non-protein coding RNA 649	11.69	3.5470	3.31E-20
GDF5	growth differentiation factor 5	11.64	3.5409	3.92E-09
BEND5	BEN domain containing 5	11.55	3.5293	3.37E-09
AFAP1L2	actin filament associated protein 1-like 2	11.44	3.5157	1.02E-16
SALL2	spalt-like transcription factor 2	11.40	3.5109	3.93E-27
FZD10	frizzled class receptor 10	11.35	3.5045	6.53E-05
DPPA4	developmental pluripotency associated 4	11.30	3.4989	1.23E-04
MECOM	MDS1 and EVI1 complex locus	11.26	3.4925	7.73E-06
RBP1	retinol binding protein 1_cellular	11.22	3.4885	9.69E-27
PPARGC1A	peroxisome proliferator-activated receptor gamma_coactivator 1 alpha	11.21	3.4872	5.02E-05
TMEM200C	transmembrane protein 200C	11.15	3.4784	1.09E-04
PCDHA11	protocadherin alpha 11	11.14	3.4777	8.36E-07
PCDHA3	protocadherin alpha 3	11.13	3.4768	2.60E-10
LRFN5	leucine rich repeat and fibronectin type III domain containing 5	11.07	3.4686	5.35E-09

TABLE 7-continued

Genes more highly expressed in HMCs compared with AD-MSCs				
Gene name	Description	Fold Change	Log Fold Change	p-Adj
SCGB3A2	secretoglobin_family 3A_member 2	10.82	3.4361	1.56E-04
SCN2B	sodium channel_voltage gated_type II beta subunit	10.81	3.4348	1.58E-04
HMGAA2	high mobility group AT-hook 2	10.78	3.4309	4.79E-14
TLL1	tolloid-like 1	10.77	3.4296	3.71E-22
PM20D2	peptidase M20 domain containing 2	10.77	3.4292	2.19E-22
PURG	purine-rich element binding protein G	10.72	3.4228	1.15E-06
KLHL38	kelch-like family member 38	10.68	3.4173	2.07E-06
HIST1H2BH	histone cluster 1_H2bh	10.68	3.4170	1.17E-12
ITGB6	integrin_beta 6	10.56	3.4000	9.77E-09
AFF3	AF4/FMR2 family_member 3	10.55	3.3986	3.23E-81
ZBED2	zinc finger_BED-type containing 2	10.49	3.3907	1.64E-06
TRHDE	thyrotropin-releasing hormone degrading enzyme	10.40	3.3789	5.13E-05
APBA2	amyloid beta (A4) precursor protein-binding_family A_member 2	10.39	3.3775	2.69E-08
PCDHA4	protocadherin alpha 4	10.36	3.3733	2.60E-08
SMIM1	small integral membrane protein 1 (Vel blood group)	10.27	3.3608	6.15E-07
PIK3R3	phosphoinositide-3-kinase_regulatory subunit 3 (gamma)	10.19	3.3496	2.71E-34
KALRN	kalirin_RhoGEF kinase	10.03	3.3267	1.54E-34
LOC728463	NA	10.01	3.3241	2.74E-04
PTN	pleiotrophin	9.96	3.3165	2.92E-06
CLDN6	claudin 6	9.95	3.3142	3.72E-07
ASXL3	additional sex combs like transcriptional regulator 3	9.93	3.3111	1.05E-04
KBTBD11	kelch repeat and BTB (POZ) domain containing 11	9.86	3.3023	2.00E-06
GALNT14	polypeptide N-acetylgalactosaminyltransferase 14	9.86	3.3022	1.82E-09
LOC440173	uncharacterized LOC440173	9.86	3.3022	1.39E-04
TLE4	transducin-like enhancer of split 4	9.85	3.2996	2.87E-71
NOX4	NADPH oxidase 4	9.81	3.2948	1.77E-23
EPHX4	epoxide hydrolase 4	9.73	3.2823	1.50E-05
DIO2	deiodinase_iodothyronine_type_II	9.68	3.2755	2.14E-05
DNAJC6	DnaJ (Hsp40) homolog_subfamily C_member 6	9.60	3.2634	7.55E-24
SLC16A12	solute carrier family 16_member 12	9.60	3.2630	2.76E-06
BCL11A	B-cell CLL/lymphoma 11A (zinc finger protein)	9.49	3.2467	4.04E-15
ZNF608	zinc finger protein 608	9.45	3.2402	2.33E-16
PPAP2C	phosphatidic acid phosphatase type 2C	9.37	3.2285	1.22E-17
IGSF3	immunoglobulin superfamily_member 3	9.29	3.2164	2.26E-38
COL18A1	collagen_type XVIII_alpha 1	9.20	3.2021	2.63E-16
ZNF732	zinc finger protein 732	9.18	3.1988	3.05E-16
NAALAD2	N-acetylated alpha-linked acidic dipeptidase 2	9.18	3.1979	4.47E-06
EXOC3L2	exocyst complex component 3-like 2	9.16	3.1959	8.87E-09
JUP	junction plakophilin	9.14	3.1926	3.22E-24
MSR1	macrophage scavenger receptor 1	9.12	3.1888	4.36E-07
TRIM58	tripartite motif containing 58	9.03	3.1745	3.32E-25
TMSB15A	thymosin beta 15a	9.02	3.1728	2.04E-17
MAPK15	mitogen-activated protein kinase 15	9.00	3.1707	1.35E-05
CELSR1	cacherin_EGF LAG seven-pass G-type receptor 1	9.00	3.1705	1.83E-15
SEMA3D	sema domain_immunoglobulin domain_(Ig)_short basic domain_secrated_(semaphorin) 3D	8.96	3.1630	2.81E-06
SH3RF2	SH3 domain containing ring finger 2	8.93	3.1586	5.06E-16
MYPN	myopalladin	8.81	3.1391	5.10E-11
PKD1L1	polycystic kidney disease 1 like 1	8.80	3.1377	1.21E-05
PCDHA13	protocadherin alpha 13	8.76	3.1317	4.55E-04
PKNOX2	PBX/knotted 1 homeobox 2	8.76	3.1317	7.68E-07
ZIC5	Zic family member 5	8.74	3.1277	3.70E-05

TABLE 7-continued

Genes more highly expressed in HMCs compared with AD-MSCs				
Gene name	Description	Fold Change	Log Fold Change	p-Adj
LOC90246	uncharacterized LOC90246	8.72	3.1251	4.62E-14
SLC12A5	solute carrier family 12 (potassium/chloride transporter)___member 5	8.68	3.1175	1.98E-09
PCDHB10	protocadherin beta 10	8.67	3.1168	2.00E-16
TMEM63C	transmembrane protein 63C	8.65	3.1130	1.86E-09
LYN	LYN proto-oncogene_Src family tyrosine kinase	8.65	3.1127	9.22E-41
CHMP4C	charged multivesicular body protein 4C	8.61	3.1057	6.67E-06
GPRIN2	G protein regulated inducer of neurite outgrowth 2	8.56	3.0977	1.13E-05
TNS3	tensin 3	8.56	3.0972	3.01E-30
DOCK3	dedicator of cytokinesis 3	8.55	3.0955	4.29E-21
CPA4	carboxypeptidase A4	8.54	3.0935	1.85E-05
C1orf106	chromosome 1 open reading frame 106	8.53	3.0928	6.67E-10
LOC339862	uncharacterized LOC339862	8.51	3.0891	2.74E-04
SLC6A6	solute carrier family 6 (neurotransmitter transporter)___member 6	8.47	3.0819	6.02E-44
LPPR3	lipid phosphate phosphatase-related protein type 3	8.43	3.0762	2.23E-10
BMF	Bcl2 modifying factor	8.43	3.0758	4.14E-79
MDK	midkine (neurite growth-promoting factor 2)	8.43	3.0749	3.83E-52
SBK1	SH3 domain binding kinase 1	8.38	3.0668	8.81E-06
ZNF676	zinc finger protein 676	8.36	3.0643	2.95E-04
SIM2	single-minded family bHLH transcription factor 2	8.32	3.0570	6.97E-17
COL24A1	collagen_type XXIV_alpha 1	8.31	3.0555	2.37E-06
C14orf39	chromosome 14 open reading frame 39	8.29	3.0520	9.36E-04
RTL1	retrotransposon-like 1	8.29	3.0513	2.60E-06
TUBB2B	tubulin_beta 2B class IIb	8.29	3.0508	1.38E-04
PDZD2	PDZ domain containing 2	8.23	3.0409	1.60E-15
SEMA6B	sema domain_transmembrane domain (TM)_and cytoplasmic domain_(semaphorin) 6B	8.22	3.0388	2.53E-15
KCTD8	potassium channel tetramerization domain containing 8	8.21	3.0380	8.62E-04
FAM213A	family with sequence similarity 213_member A	8.19	3.0336	3.82E-06
HRASLS	HRAS-like suppressor	8.18	3.0326	2.51E-07
TRIML2	tripartite motif family-like 2	8.14	3.0253	8.36E-16
CNIH2	cornichon family AMPA receptor auxiliary protein 2	8.09	3.0166	1.42E-47
OCA2	oculocutaneous albinism II	8.01	3.0011	4.47E-04
RNF165	ring finger protein 165	8.01	3.0010	2.48E-04
PTPRN2	protein tyrosine phosphatase_receptor type_N polypeptide 2	8.00	3.0000	3.98E-34
PIK3C2B	phosphatidylinositol-4-phosphate 3-kinase_catalytic subunit type 2 beta	7.99	2.9979	4.89E-53
NFE2	nuclear factor_cythroid 2	7.96	2.9927	1.85E-04
PRND	prion protein 2 (dublet)	7.95	2.9901	1.26E-03
EGLN3	egl-9 family hypoxia-inducible factor 3	7.91	2.9828	7.72E-07
SLC38A3	solute carrier family 38_member 3	7.88	2.9781	6.75E-04
IGF2BP3	insulin-like growth factor 2 mRNA binding protein 3	7.87	2.9762	5.96E-05
RAB27B	RAB27B_member RAS oncogene family	7.84	2.9712	1.03E-11
LINC00333	long intergenic non-protein coding RNA 333	7.84	2.9702	4.05E-04
CYTL1	cytokine-like 1	7.81	2.9650	3.54E-05
FENDRR	FOXF1 adjacent non-coding developmental regulatory RNA	7.78	2.9597	5.21E-04
WNK3	WNK lysine deficient protein kinase 3	7.76	2.9568	6.00E-09
CDH10	cadherin 10_type 2 (T2-cadherin)	7.73	2.9498	2.09E-11
GPRIN3	GPRIN family member 3	7.71	2.9468	1.31E-03
DOK2	docking protein 2_56 kDa	7.70	2.9440	2.85E-05

TABLE 7-continued

Genes more highly expressed in HMCs compared with AD-MSCs				
Gene name	Description	Fold Change	Log Fold Change	p-Adj
TTYH2	tweety family member 2	7.70	2.9440	1.49E-48
SLC2A12	solute carrier family 2 (facilitated glucose transporter)_member 12	7.66	2.9377	3.75E-16
DYSF	dysferlin	7.65	2.9362	6.16E-12
NRARP	NOTCH-regulated ankyrin repeat protein	7.65	2.9355	6.67E-10
CELSR2	cadherin_EGF LAG seven-pass G-type receptor 2	7.65	2.9354	4.02E-13
RAD21L1	RAD21 cohesin complex component like 1	7.65	2.9350	4.40E-04
RAP1GAP2	RAP1 GTPase activating protein 2	7.63	2.9309	1.35E-09
OGDHL	oxoglutarate dehydrogenase-like	7.56	2.9179	1.33E-16
IGFBP7-AS1	IGFBP7 antisense RNA 1	7.51	2.9092	7.05E-06
PIANP	PILR alpha associated neural protein	7.46	2.8994	2.59E-15
TRABD2A	TraB domain containing 2A	7.46	2.8991	7.41E-83
FSIP2	fibrous sheath interacting protein 2	7.46	2.8986	1.04E-03
RASSF4	Ras association (RalGDS/AF-6) domain family member 4	7.42	2.8915	7.70E-31
ABCA4	ATP-binding cassette_sub-family A (ABC1)_member 4	7.34	2.8764	8.46E-09
PPP1R3A	protein phosphatase 1_regulatory subunit 3A	7.33	2.8734	2.01E-03
ZBTB46	zinc finger and BTB domain containing 46	7.32	2.8724	1.25E-30
CYP2S1	cytochrome P450_family 2_subfamily S_polypeptide 1	7.29	2.8668	2.98E-09
DIRC3	disrupted in renal carcinoma 3	7.26	2.8600	9.57E-08
COL9A3	collagen_type IX_alpha 3	7.24	2.8559	4.41E-10
MAMDC2	MAM domain containing 2	7.20	2.8474	5.15E-18
GIPC3	GIPC PDZ domain containing family_member 3	7.20	2.8471	6.98E-09
DPYSL4	dihydropyrimidinase-like 4	7.18	2.8445	3.72E-06
DLX2	distal-less homeobox 2	7.17	2.8429	1.60E-37
TRIM67	tripartite motif containing 67	7.16	2.8401	5.57E-07
ADAMTS18	ADAM metallopeptidase with thrombospondin type 1 motif_18	7.13	2.8348	1.91E-03
IGDCC4	immunoglobulin superfamily_DCC subclass_member 4	7.12	2.8317	2.14E-18
EFNA2	ephrin-A2	7.12	2.8313	1.23E-04
CPVL	carboxypeptidase_vitellogenin-like	7.11	2.8292	1.50E-08
PCDHHA8	protocadherin alpha 8	7.09	2.8261	1.57E-03
DBNDD1	dysbindin (dystrobrevin binding protein 1) domain containing 1	7.09	2.8253	2.34E-11
DNER	delta/notch-like EGF repeat containing	7.08	2.8239	7.46E-15
NPW	neuropeptide W	7.07	2.8226	7.31E-25
GNGT2	guanine nucleotide binding protein (G protein)_gamma transducing activity polypeptide 2	7.03	2.8129	8.59E-07
CDC42BPG	CDC42 binding protein kinase gamma (DMPK-like)	7.02	2.8124	4.40E-12
FBN2	fibrillin 2	7.01	2.8089	1.27E-29
TPSG1	tryptase gamma 1	6.97	2.8020	1.48E-03
KCND1	potassium channel_voltage gated Shal related subfamily D_member 1	6.96	2.7996	8.82E-34
KRT80	keratin 80_type II	6.95	2.7979	1.69E-16
ST6GAL1	ST6 beta-galactosamide alpha-2_-6-sialyltransferase 1	6.90	2.7872	3.42E-59
EPPK1	epiplakin 1	6.89	2.7849	2.02E-06
HS6ST2	heparan sulfate 6-O-sulfotransferase 2	6.89	2.7836	2.41E-03
OBSCN	obscurin_cytoskeletal calmodulin and titin-interacting RhoGEF	6.88	2.7826	2.91E-28
CCDC68	coiled-coil domain containing 68	6.88	2.7825	1.73E-22
ZNF185	zinc finger protein 185 (LIM domain)	6.87	2.7805	1.15E-04
PCDHB9	protocadherin beta 9	6.84	2.7748	1.21E-09
SH3GL2	SH3-domain GRB2-like 2	6.84	2.7736	3.07E-03
LINC00707	long intergenic non-protein coding RNA 707	6.81	2.7680	5.48E-04
GABRA5	gamma-aminobutyric acid (GABA) A receptor_alpha 5	6.78	2.7620	2.28E-24

TABLE 7-continued

Genes more highly expressed in HMCs compared with AD-MSCs				
Gene name	Description	Fold Change	Log Fold Change	p-Adj
KRT8	keratin 8_type II	6.78	2.7605	1.07E-07
RNF43	ring finger protein 43	6.76	2.7576	3.24E-03
SLC35F3	solute carrier family 35_member F3	6.74	2.7536	7.42E-05
SNCA	synuclein_alpha (non A4 component of amyloid precursor)	6.68	2.7395	2.22E-03
CGN	cingulin	6.65	2.7323	3.68E-05
LOC100131289	uncharacterized LOC100131289	6.62	2.7260	1.55E-03
LOC100128885	uncharacterized LOC100128885	6.60	2.7219	8.13E-11
LOC653712	intraflagellar transport 122 homolog (<i>Chlamydomonas</i>) pseudogene	6.59	2.7198	5.35E-18
LLGL2	lethal giant larvae homolog 2 (<i>Drosophila</i>)	6.58	2.7171	2.79E-10
TRIM62	tripartite motif containing 62	6.54	2.7097	7.99E-154
AMZ1	archaelysin family metallopeptidase 1	6.54	2.7088	1.81E-70
PDE3B	phosphodiesterase 3B_cGMP-inhibited	6.54	2.7085	2.17E-05
IGDCC3	immunoglobulin superfamily_DCC subclass_member 3	6.51	2.7021	1.17E-03
RAB38	RAB38_member RAS oncogene family	6.48	2.6951	2.73E-05
SFMBT2	Scm-like with four mbt domains 2	6.47	2.6930	1.62E-13
MEST	mesoderm specific transcript	6.42	2.6817	3.56E-05
MAP2K6	mitogen-activated protein kinase kinase 6	6.31	2.6583	5.33E-06
TOX	thymocyte selection-associated high mobility group box	6.21	2.6352	1.98E-05
GARNL3	GTPase activating Rap/RanGAP domain-like 3	6.21	2.6336	2.42E-05
TRIM16L	tripartite motif containing 16-like	6.20	2.6334	1.13E-18
ABI3	ABI family_member 3	6.20	2.6330	3.20E-33
SHC4	SHC (Src homology 2 domain containing) family_member 4	6.20	2.6326	3.82E-11
BFSP1	beaded filament structural protein 1_filensin	6.17	2.6255	3.20E-22
FAXC	failed axon connections homolog	6.17	2.6251	2.70E-16
TBX1	T-box 1	6.16	2.6234	1.74E-03
PLS1	plastin 1	6.15	2.6195	8.36E-16
RGS9	regulator of G-protein signaling 9	6.14	2.6177	9.91E-08
NLRP3	NLR family_pyrin domain containing 3	6.13	2.6164	2.52E-04
LOC101928775	uncharacterized LOC101928775	6.13	2.6148	5.43E-03
FAM84B	family with sequence similarity 84_member B	6.09	2.6074	4.97E-08
VSTM1	V-set and transmembrane domain containing 1	6.09	2.6073	5.51E-03
RNF150	ring finger protein 150	6.09	2.6064	1.69E-03
KIF21B	kinesin family member 21B	6.06	2.6002	2.72E-25
ZNF702P	zinc finger protein 702_pseudogene	6.05	2.5959	1.47E-10
ITPR1PL1	inositol 1_4_5-trisphosphate receptor interacting protein-like 1	6.04	2.5955	1.98E-19
ANKRD18B	ankyrin repeat domain 18B	6.02	2.5907	1.70E-03
SIX1	SIX homeobox 1	6.02	2.5889	8.50E-09
RUNX3	runt-related transcription factor 3	6.00	2.5848	1.62E-12
TNFRSF21	tumor necrosis factor receptor superfamily_member 21	5.98	2.5803	2.24E-24
SUSD5	sushi domain containing 5	5.98	2.5795	1.27E-03
GRIP1	glutamate receptor interacting protein 1	5.96	2.5744	5.40E-05
MEGF10	multiple EGF-like-domains 10	5.94	2.5704	5.12E-03
MGC2889	uncharacterized protein MGC2889	5.94	2.5696	4.80E-03
EDARADD	EDAR-associated death domain	5.92	2.5663	2.25E-13
FBXO16	F-box protein 16	5.91	2.5642	6.29E-08
VASH2	vasohibin 2	5.90	2.5606	5.92E-08
PCDHAC1	protocadherin alpha subfamily C_1	5.88	2.5560	3.37E-03
ADM5	adrenomedullin 5 (putative)	5.88	2.5552	4.05E-10
FAM160A1	family with sequence similarity 160 member A1	5.86	2.5510	2.61E-03
EFNB3	ephrin-B3	5.86	2.5500	5.60E-13
STK32B	serine/threonine kinase 32B	5.85	2.5482	1.91E-83
MYOZ1	myozinin 1	5.82	2.5412	4.63E-04
EGF	epidermal growth factor	5.82	2.5398	8.06E-07

TABLE 7-continued

Genes more highly expressed in HMCs compared with AD-MSCs				
Gene name	Description	Fold Change	Log Fold Change	p-Adj
FRRS1L	ferri-chelate reductase 1-like	5.81	2.5387	5.23E-03
CSR P2	cysteine and glycine-rich protein 2	5.81	2.5386	1.37E-56
FAM83F	family with sequence similarity 83_member F	5.78	2.5323	2.50E-03
LOC101929690	NA	5.78	2.5321	1.50E-03
EPB41L4B	erythrocyte membrane protein band 4.1 like 4B	5.78	2.5303	1.25E-26
APOE	apolipoprotein E	5.76	2.5265	5.10E-11
PCDHGC4	protocadherin gamma subfamily C_4	5.76	2.5249	8.40E-12
GPR162	G protein-coupled receptor 162	5.72	2.5166	1.36E-08
SLC29A2	solute carrier family 29 (equilibrative nucleoside transporter)_member 2	5.71	2.5131	7.20E-15
GULP1	GULP_engulfment adaptor PTB domain containing 1	5.70	2.5107	9.81E-17
AC093375.1	NA	5.69	2.5079	6.38E-03
PIFO	primary cilia formation	5.68	2.5048	3.68E-03
GALNT3	polypeptide N-acetylgalactosaminyltransferase 3	5.67	2.5039	1.41E-05
CBX2	chromobox homolog 2	5.67	2.5031	4.47E-37
PROC	protein C (inactivator of coagulation factors Va and VIIIa)	5.67	2.5029	8.18E-07
CHD7	chromodomain helicase DNA binding protein 7	5.66	2.5004	1.63E-18
VAC14-AS1	VAC14 antisense RNA 1	5.66	2.5001	3.38E-05
ISYNA1	inositol-3-phosphate synthase 1	5.65	2.4986	1.68E-21
FBXL16	F-box and leucine-rich repeat protein 16	5.64	2.4961	1.63E-07
NKAIN4	Na+/K+ transporting ATPase interacting 4	5.64	2.4951	3.47E-03
HID1	HID1 domain containing	5.63	2.4927	1.59E-04
SYT12	synaptotagmin XII	5.62	2.4907	4.24E-03
BEGAIN	brain-enriched guanylate kinase-associated	5.61	2.4875	1.29E-07
OCIAD2	OCIA domain containing 2	5.60	2.4850	9.91E-54
FSD1	fibronectin type III and SPRY domain containing 1	5.59	2.4817	1.01E-24
SCD5	stearoyl-CoA desaturase 5	5.58	2.4813	1.61E-13
PTCHD4	patched domain containing 4	5.57	2.4767	6.76E-04
OR2W3	olfactory receptor_family 2_subfamily W_member 3	5.55	2.4735	4.87E-07
PNMT	phenylethanolamine N-methyltransferase	5.55	2.4733	3.44E-03
ZNF208	zinc finger protein 208	5.51	2.4630	1.91E-04
MYOZ3	myozinin 3	5.50	2.4595	1.47E-20
CPT1B	ceramite palmitoyltransferase 1B (muscle)	5.50	2.4587	5.67E-03
KCNMA1	potassium channel_calcium activated large conductance subfamily M alpha_member 1	5.48	2.4541	1.81E-67
PALMD	palmidelphin	5.47	2.4521	8.82E-05
SYNGR1	synaptogyrin 1	5.46	2.4485	1.69E-91
DRP2	dystrophin related protein 2	5.46	2.4482	5.80E-23
CAPN14	calpain 14	5.42	2.4384	3.28E-03
SOX17	SRY (sex determining region Y)-box 17	5.39	2.4314	8.94E-03
PTGES3L	prostaglandin E synthase 3 (cytosolic)-like	5.39	2.4308	2.45E-04
KCTD4	potassium channel tetramerization domain containing 4	5.38	2.4287	2.05E-04
PCDHA6	protocadherin alpha 6	5.38	2.4282	3.90E-03
LOC101927497	uncharacterized LOC101927497	5.37	2.4259	7.44E-07
TMEM184A	transmembrane protein 184A	5.35	2.4201	5.40E-18
DOCK4	dedicator of cytokinesis 4	5.35	2.4184	6.49E-25
THEMIS	thymocyte selection associated	5.34	2.4177	1.06E-02
HEY1	hes-related family bHLH transcription factor with YRPW motif 1	5.34	2.4169	1.31E-06

TABLE 7-continued

Genes more highly expressed in HMCs compared with AD-MSCs				
Gene name	Description	Fold Change	Log Fold Change	p-Adj
MKRN3	makorin ring finger protein 3	5.34	2.4156	9.13E-13
JAG2	jagged 2	5.33	2.4144	2.59E-09
LOC101927482	uncharacterized LOC101927482	5.33	2.4137	2.19E-04
RND2	Rho family GTPase 2	5.32	2.4121	2.31E-15
DSC2	desmocollin 2	5.32	2.4107	1.56E-03
CTXN1	cortexin 1	5.31	2.4095	1.48E-11
LOC100128076	protein tyrosine phosphatase pseudogene	5.31	2.4080	2.30E-04
KCNS1	potassium voltage-gated channel_modifier subfamily S_member 1	5.30	2.4048	1.77E-19
KCNMB4	potassium channel subfamily M regulatory beta subunit 4	5.29	2.4042	4.48E-16
MCTP1	multiple C2 domains_transmembrane 1	5.28	2.4012	5.81E-06
SLC2A14	solute carrier family 2 (facilitated glucose transporter)_member 14	5.26	2.3962	5.86E-04
MTL5	metallothionein-like 5_testis-specific (tesmin)	5.25	2.3921	1.23E-09
SLC16A4	solute carrier family 16_member 4	5.24	2.3905	2.14E-63
CARD10	caspase recruitment domain family_member 10	5.23	2.3856	3.39E-28
TMEM108	transmembrane protein 108	5.21	2.3821	2.63E-05
NETO2	neuropilin (NRP) and tolloid (TLL)-like 2	5.19	2.3764	5.94E-37
CLDN16	claudin 16	5.16	2.3679	1.34E-02
SLC29A4	solute carrier family 29 (equilibrative nucleoside transporter)_member 4	5.15	2.3656	1.71E-23
ZBED9	zinc finger_BED-type containing 9	5.15	2.3652	6.60E-10
SLC22A31	solute carrier family 22_member 31	5.15	2.3641	3.24E-03
CCND2	cyclin D2	5.13	2.3600	2.48E-26
BEX1	brain expressed_X-linked 1	5.13	2.3592	1.18E-02
PPM1H	protein phosphatase_Mg2+/Mn2+ dependent_1H	5.13	2.3592	5.26E-07
C7orf61	chromosome 7 open reading frame 61	5.13	2.3588	7.21E-06
RGPD1	RANBP2-like and GRIP domain containing 1	5.13	2.3586	4.05E-03
GPR143	G protein-coupled receptor 143	5.13	2.3576	9.43E-03
TNFRSF10C	tumor necrosis factor receptor superfamily_member 10c_decoy without an intracellular domain	5.10	2.3515	4.48E-07
MSI2	musashi RNA-binding protein 2	5.10	2.3502	1.21E-79
HIST1H3F	histone cluster 1_H3f	5.09	2.3485	1.42E-02
TRIM55	tripartite motif containing 55	5.07	2.3425	9.83E-05
LPAR3	lysophosphatidic acid receptor 3	5.07	2.3411	5.33E-03
LEPREL1	prolyl 3-hydroxylase 2	5.03	2.3313	5.14E-05
KCNN3	potassium channel_calcium activated intermediate/small conductance subfamily N alpha_member 3	5.01	2.3251	7.84E-06

TABLE 8

Genes more highly expressed in AD-MSCs compared with HMCs				
Gene name	Description	Fold Change	Log Fold Change	p-Adj
TWIST2	twist family bHLH transcription factor 2	-615.13	-9.265	2.6E-153
FGL2	fibrinogen-like 2	-521.90	-9.028	1.5E-52
PI116	peptidase inhibitor 16	-505.64	-8.982	1.6E-78
EMX2OS	EMX2 opposite strand/antisense RNA	-429.80	-8.748	4.3E-56
XIST	X inactive specific transcript (non-protein coding)	-416.10	-8.701	2.3E-269
ISLR	immunoglobulin superfamily containing leucine-rich repeat	-316.46	-8.306	1.1E-26

TABLE 8-continued

Genes more highly expressed in AD-MSCs compared with HMCs					
Gene name	Description	Fold Change	Log Fold Change	p-Adj	
MEOX2	mesenchyme homeobox 2	-302.76	-8.242	2.2E-45	
HAGLR	HOXD antisense growth-associated long non-coding RNA	-273.46	-8.095	7.7E-39	
FAM180A	family with sequence similarity 180_member A	-260.12	-8.023	3.2E-51	
LINC00856	long intergenic non-protein coding RNA 856	-254.50	-7.992	2.9E-36	
EMX2	empty spiracles homeobox 2	-246.43	-7.945	9.7E-54	
TNXB	tenascin XB	-240.63	-7.911	7.3E-140	
HAS1	hyaluronan synthase 1	-233.59	-7.868	4.5E-47	
HAS2	hyaluronan synthase 2	-209.41	-7.710	8.3E-139	
TBX5-AS1	TBX5 antisense RNA 1	-202.78	-7.664	1.8E-41	
BHMT2	betaine--homocysteine S-methyltransferase 2	-195.84	-7.614	8.1E-82	
HOXC5	homeobox C5	-185.04	-7.532	1.1E-52	
COMP	cartilage oligomeric matrix protein	-182.83	-7.514	3.3E-35	
DOK5	docking protein 5	-182.49	-7.512	2.7E-154	
CSTA	cystatin A (stefin A)	-181.14	-7.501	5.4E-32	
CCDC36	coiled-coil domain containing 36	-179.59	-7.489	3.7E-42	
TPTEP1	transmembrane phosphatase with tensin homology pseudogene 1	-175.65	-7.457	1.4E-29	
XG	Xg blood group	-174.60	-7.448	1.6E-37	
KRT14	keratin 14_type I	-170.06	-7.410	9.0E-29	
NDNF	neuron-derived neurotrophic factor	-169.92	-7.409	1.6E-46	
HTR2A	5-hydroxytryptamine (serotonin) receptor 2A_G protein-coupled	-160.86	-7.330	1.2E-34	
PSG5	pregnancy specific beta-1-glycoprotein 5	-160.55	-7.327	8.1E-76	
DCLK3	doublecortin-like kinase 3	-158.45	-7.308	3.7E-29	
KCND2	potassium channel_voltage gated Shal related subfamily D_member 2	-148.30	-7.212	4.1E-28	
LINC01133	long intergenic non-protein coding RNA 1133	-139.87	-7.128	1.6E-31	
CNTN3	contactin 3 (plasmacytoma associated)	-137.81	-7.107	1.3E-66	
GPAT2	glycerol-3-phosphate acyltransferase 2_mitochondrial	-137.06	-7.099	5.4E-37	
HOXC6	homeobox C6	-136.95	-7.098	0.0E+00	
KRBOX1	KRAB box domain containing 1	-136.24	-7.090	9.5E-54	
ITGBL1	integrin_beta-like 1 (with EGF-like repeat domains)	-135.06	-7.077	0.0E+00	
PCDHGA12	protocadherin gamma subfamily A_12	-134.87	-7.075	1.8E-210	
DMGDH	dimethylglycine dehydrogenase	-130.82	-7.031	5.0E-36	
SGCG	sarcoglycan_gamma (35 kDa dystrophin-associated glycoprotein)	-130.78	-7.031	1.1E-29	
HOXD3	homeobox D3	-130.60	-7.029	3.0E-26	
HOXD8	homeobox D8	-127.97	-7.000	8.4E-156	
EGFLAM	EGF-like_fibronectin type III and laminin G domains	-127.49	-6.994	2.4E-43	
HOXD9	homeobox D9	-118.10	-6.884	1.1E-41	
MASP1	mannan-binding lectin serine peptidase 1 (C4/C2 activating component of Reactive factor)	-115.18	-6.848	3.1E-29	
OLFM1	olfactomedin 1	-113.80	-6.830	2.5E-110	
ADRA2A	adrenoceptor alpha 2A	-109.79	-6.779	2.0E-49	
HOXD4	homeobox D4	-109.17	-6.770	1.2E-47	
ARHGAP20	Rho GTPase activating protein 20	-108.16	-6.757	2.8E-48	
PRR15	proline rich 15	-107.72	-6.751	2.2E-148	
PENK	proenkephalin	-103.97	-6.700	1.4E-30	
MMP3	matrix metallopeptidase 3	-101.89	-6.671	7.5E-36	
SFRP4	secreted frizzled-related protein 4	-100.96	-6.658	1.1E-22	
SIM1	single-minded family bHLH transcription factor 1	-100.64	-6.653	6.4E-36	
TEKT4P2	tektin 4 pseudogene 2	-98.84	-6.627	1.6E-37	
MYH2	myosin_heavy chain 2_skeletal muscle_adult	-98.26	-6.619	9.2E-25	
EN1	engrailed homeobox 1	-98.11	-6.616	7.5E-95	
TBX5	T-box 5	-94.95	-6.569	7.2E-31	
HOXC10	homeobox C10	-94.63	-6.564	1.4E-43	
ABCC9	ATP-binding cassette_sub-family C (CFTR/MRP)_member 9	-89.87	-6.490	7.9E-81	
HOXC-AS2	HOXC cluster antisense RNA 2	-89.25	-6.480	1.4E-29	

TABLE 8-continued

Genes more highly expressed in AD-MSCs compared with HMCs					
Gene name	Description	Fold Change	Log Fold Change	p-Adj	
USP32P1	ubiquitin specific peptidase 32 pseudogene 1	-87.52	-6.452	3.3E-25	
FMOD	fibromodulin	-87.47	-6.451	1.1E-75	
ABCA8	ATP-binding cassette_ sub-family A (ABC1)_ member 8	-87.45	-6.450	3.1E-33	
PDE1A	phosphodiesterase 1A_ calmodulin-dependent	-86.65	-6.437	3.6E-56	
COL15A1	collagen_ type XV_ alpha 1	-86.33	-6.432	1.7E-142	
HOXC4	homeobox C4	-85.68	-6.421	4.2E-84	
GSC	goosecoid homeobox	-85.63	-6.420	2.9E-28	
IL13RA2	interleukin 13 receptor_ alpha 2	-84.87	-6.407	1.1E-21	
LINC00968	long intergenic non-protein coding RNA 968	-83.09	-6.377	4.8E-35	
HOXD-AS2	HOXD cluster antisense RNA 2	-82.83	-6.372	1.6E-67	
PAPPA2	pappalysin 2	-82.24	-6.362	6.6E-35	
HOXC8	homeobox C8	-81.56	-6.350	0.0E+00	
CCDC144B	coiled-coil domain containing 144B (pseudogene)	-79.34	-6.310	5.6E-35	
TMEM233	transmembrane protein 233	-74.43	-6.218	2.6E-19	
HOXC9	homeobox C9	-74.28	-6.215	2.5E-275	
FAM225B	family with sequence similarity 225_ member B (non-protein coding)	-74.15	-6.212	1.9E-18	
FGF7	fibroblast growth factor 7	-72.94	-6.189	8.8E-55	
C2orf88	chromosome 2 open reading frame 88	-69.58	-6.121	5.1E-41	
NFASC	neurofascin	-67.27	-6.072	2.8E-158	
HSPB2	heat shock 27 kDa protein 2	-66.67	-6.059	1.7E-95	
HOXA10-AS	HOXA10 antisense RNA	-64.54	-6.012	5.4E-28	
HOXA7	homeobox A7	-63.72	-5.994	1.8E-32	
USP32P2	ubiquitin specific peptidase 32 pseudogene 2	-63.62	-5.991	3.0E-24	
MCF2L	MCF.2 cell line derived transforming sequence-like	-62.47	-5.965	6.2E-44	
DCN	decorin	-60.95	-5.929	9.3E-243	
PRSS12	protease_ serine_ 12 (neurotrypsin_ motopsin)	-59.56	-5.896	6.0E-143	
LAMA2	laminin_ alpha 2	-59.38	-5.892	2.7E-151	
RARRES2	retinoic acid receptor responder (tazarotene induced) 2	-59.19	-5.887	8.3E-25	
EYA2	EYA transcriptional coactivator and phosphatase 2	-58.85	-5.879	4.3E-18	
LINC01018	long intergenic non-protein coding RNA 1018	-58.61	-5.873	3.3E-16	
CLEC11A	C-type lectin domain family 11_ member A	-58.21	-5.863	0.0E+00	
CRLF1	cytokine receptor-like factor 1	-57.83	-5.854	7.2E-39	
TRH	thyrotropin-releasing hormone	-57.47	-5.845	6.7E-16	
LOC400043	uncharacterized LOC400043	-56.54	-5.821	4.9E-49	
ASPN	asporin	-56.26	-5.814	2.0E-26	
PRG4	proteoglycan 4	-56.25	-5.814	3.7E-24	
LYNX1	Ly6/neurotoxin 1	-56.17	-5.812	5.7E-40	
HOTAIRM1	HOXA transcript antisense RNA_ myeloid-specific 1	-55.20	-5.787	1.6E-63	
NUPR1	nuclear protein_ transcriptional regulator_ 1	-53.82	-5.750	2.4E-182	
CECR7	cat eye syndrome chromosome region_ candidate 7 (non-protein coding)	-53.72	-5.747	9.2E-17	
GREM2	gremlin 2_ DAN family BMP antagonist	-52.48	-5.714	5.2E-78	
ADAMTSL3	ADAMTS-like 3	-52.02	-5.701	2.5E-16	
KCNE4	potassium channel_ voltage gated subfamily E regulatory beta subunit 4	-51.90	-5.698	2.1E-145	
PODN	podocan	-51.36	-5.683	7.4E-182	
PRDM6	PR domain containing 6	-50.92	-5.670	2.9E-21	
HOXA9	homeobox A9	-50.65	-5.663	1.7E-69	
HSPB7	heat shock 27 kDa protein family_ member 7 (cardiovascular)	-50.60	-5.661	0.0E+00	
MFAP5	microfibrillar associated protein 5	-47.76	-5.578	2.6E-241	
WISP2	WNT1 inducible signaling pathway protein 2	-46.57	-5.541	3.2E-16	
PPAPDC3	phosphatidic acid phosphatase type 2 domain containing 3	-46.47	-5.538	9.0E-97	

TABLE 8-continued

Genes more highly expressed in AD-MSCs compared with HMCs					
Gene name	Description	Fold Change	Log Fold Change	p-Adj	
KCNJ8	potassium channel_ inwardly rectifying subfamily J_ member 8	-46.17	-5.529	1.5E-148	
PRSS30P	protease_ serine_ 30_ pseudogene	-46.12	-5.527	3.5E-14	
NINJ2	ninjurin 2	-45.86	-5.519	2.8E-29	
TECTB	tectorin beta	-44.68	-5.482	1.1E-13	
IRX5	iroquois homeobox 5	-44.28	-5.468	8.4E-64	
CADPS	Ca++-dependent secretion activator	-44.19	-5.466	2.2E-24	
LIMCH1	LIM and calponin homology domains 1	-44.02	-5.460	7.0E-23	
NR3C2	nuclear receptor subfamily 3_ group C_ member 2	-44.00	-5.459	3.2E-17	
CCDC89	coiled-coil domain containing 89	-43.76	-5.452	7.3E-53	
DUXAP10	double homeobox A pseudogene 10	-43.60	-5.446	1.3E-63	
S1PR1	sphingosine-1-phosphate receptor 1	-43.42	-5.440	1.0E-30	
FNDC1	fibronectin type III domain containing 1	-43.32	-5.437	7.2E-18	
HOXA6	homeobox A6	-43.04	-5.428	1.5E-16	
MIRLET7BHG	MIRLET7B host gene	-42.02	-5.393	1.7E-61	
IRX3	iroquois homeobox 3	-41.92	-5.390	2.6E-99	
WNT2	wingless-type MMTV integration site family member 2	-41.90	-5.389	4.3E-12	
HAS2-AS1	HAS2 antisense RNA 1	-41.88	-5.388	2.6E-25	
LOC643355	uncharacterized LOC643355	-41.85	-5.387	1.2E-13	
SYBU	syntabulin (syntaxin-interacting)	-41.62	-5.379	7.3E-101	
MB	myoglobin	-41.60	-5.378	1.8E-13	
GYPE	glycophorin E (MNS blood group)	-41.46	-5.374	3.2E-17	
CLEC2B	C-type lectin domain family 2 member B	-41.02	-5.358	1.1E-17	
HOXC-AS1	HOXC cluster antisense RNA 1	-40.92	-5.355	4.6E-20	
MALL	mal_ T-cell differentiation protein-like	-40.81	-5.351	6.2E-43	
HOXA11	homeobox A11	-40.54	-5.341	3.4E-48	
RFX8	RFX family member 8_ lacking RFX DNA binding domain	-40.47	-5.339	1.3E-55	
BMPER	BMP binding endothelial regulator	-39.88	-5.318	1.2E-59	
KCTD12	potassium channel tetramerization domain containing 12	-39.69	-5.311	2.0E-40	
CH25H	cholesterol 25-hydroxylase	-39.23	-5.294	5.3E-13	
ERG	v-ets avian erythroblastosis virus E26 oncogene homolog	-38.73	-5.275	3.9E-13	
CCL26	chemokine (C-C motif) ligand 26	-38.66	-5.273	3.4E-27	
HOXA10	homeobox A10	-38.54	-5.268	1.7E-144	
POMC	propiomelanocortin	-38.34	-5.261	9.8E-12	
LOC100996609	NA	-38.33	-5.260	1.6E-17	
TDRD9	tudor domain containing 9	-38.08	-5.251	1.9E-13	
LOC100506834	uncharacterized LOC100506834	-37.86	-5.243	2.5E-12	
HOXB7	homeobox B7	-37.72	-5.237	5.8E-95	
KRT34	keratin 34_ type I	-37.35	-5.223	7.0E-63	
FRMPD1	FERM and PDZ domain containing 1	-37.23	-5.218	1.9E-12	
BHMT	betaine--homocysteine S-methyltransferase	-37.16	-5.216	3.8E-12	
FAM198A	family with sequence similarity 198_ member A	-36.59	-5.194	1.9E-12	
PSTPIP1	proline-serine-threonine phosphatase interacting protein 1	-36.30	-5.182	3.6E-19	
HOXB-AS3	HOXB cluster antisense RNA 3	-35.85	-5.164	7.0E-51	
TRABD2B	TrAB domain containing 2B	-35.59	-5.153	1.7E-13	
GALNT12	polypeptide N-acetylgalactosaminyltransferase 12	-34.90	-5.125	6.8E-63	
C8orf31	chromosome 8 open reading frame 31	-34.72	-5.118	1.0E-23	
ZNF300P1	zinc finger protein 300 pseudogene 1 (functional)	-34.71	-5.117	2.1E-51	
TNFRSF11B	tumor necrosis factor receptor superfamily_ member 11b	-34.56	-5.111	2.2E-27	
PLBD1	phospholipase B domain containing 1	-34.51	-5.109	7.9E-33	
PPP1R14C	protein phosphatase 1_ regulatory (inhibitor) subunit 14C	-34.18	-5.095	1.5E-18	
MROH9	maestro heat-like repeat family member 9	-34.17	-5.095	1.7E-11	
HOXD1	homeobox D1	-34.15	-5.094	7.3E-15	
HOXA4	homeobox A4	-33.55	-5.068	2.5E-30	
LUM	lumican	-33.14	-5.050	1.5E-72	

TABLE 8-continued

Genes more highly expressed in AD-MSCs compared with HMCs					
Gene name	Description	Fold Change	Log Fold Change	p-Adj	
HOXB5	homeobox B5	-33.04	-5.046	2.2E-39	
MR1	major histocompatibility complex__ class I-related	-32.88	-5.039	3.7E-63	
TSKS	testis-specific serine kinase substrate	-32.74	-5.033	6.0E-15	
SPATA22	spermatogenesis associated 22	-32.55	-5.025	1.9E-11	
GIPC2	GIPC PDZ domain containing family__ member 2	-32.43	-5.019	3.5E-34	
FGF14	fibroblast growth factor 14	-31.99	-5.000	6.2E-30	
HOXB6	homeobox B6	-31.84	-4.993	1.9E-126	
HOXB4	homeobox B4	-31.80	-4.991	3.2E-58	
BAIAP2L2	BAI1-associated protein 2-like 2	-31.62	-4.983	5.1E-35	
HOXB3	homeobox B3	-31.37	-4.971	2.0E-77	
TP53TG3D	TP53 target 3D	-31.36	-4.971	6.5E-11	
HOXA3	homeobox A3	-31.31	-4.969	2.0E-13	
POSTN	periostin__ osteoblast specific factor	-30.78	-4.944	1.8E-38	
IRAK3	interleukin-1 receptor-associated kinase 3	-30.66	-4.938	6.7E-68	
TNFSF9	tumor necrosis factor (ligand) superfamily__ member 9	-30.57	-4.934	3.9E-47	
BEAN1	brain expressed__ associated with NEDD4__ 1	-30.15	-4.914	2.3E-12	
HOXC11	homeobox C11	-29.68	-4.891	5.8E-12	
LRRK2	leucine-rich repeat kinase 2	-29.57	-4.886	2.4E-26	
NRN1	neuritin 1	-29.56	-4.886	2.1E-133	
LOC388780	uncharacterized LOC388780	-29.54	-4.884	1.1E-10	
C3orf80	chromosome 3 open reading frame 80	-29.33	-4.874	1.7E-18	
PINLYP	phospholipase A2 inhibitor and LY6/PLAUR domain containing	-29.27	-4.871	1.9E-27	
PLAC9	placenta-specific 9	-29.00	-4.858	7.1E-184	
CHST8	carbohydrate (N-acetylgalactosamine 4-O) sulfotransferase 8	-28.41	-4.828	1.1E-11	
LOC100240735	uncharacterized LOC100240735	-28.35	-4.825	1.5E-12	
TSHZ2	teashirt zinc finger homeobox 2	-28.01	-4.808	6.3E-14	
PRR34	proline rich 34	-27.65	-4.789	3.7E-10	
DNASE1L3	deoxyribonuclease I-like 3	-27.53	-4.783	2.5E-09	
COL10A1	collagen__ type X__ alpha 1	-27.42	-4.777	7.4E-12	
FPR1	formyl peptide receptor 1	-27.04	-4.757	2.4E-12	
KCND3	potassium channel__ voltage gated Shal related subfamily D__ member 3	-26.98	-4.754	7.2E-41	
MRAP2	melanocortin 2 receptor accessory protein 2	-26.90	-4.750	2.8E-09	
MIR10B	microRNA 10b	-26.66	-4.737	5.5E-10	
DLX3	distal-less homeobox 3	-26.66	-4.737	2.4E-18	
PCSK9	proprotein convertase subtilisin/kexin type 9	-26.34	-4.719	2.0E-20	
ANGPTL1	angiopoietin-like 1	-26.14	-4.708	6.3E-15	
CLIC3	chloride intracellular channel 3	-26.07	-4.704	4.0E-17	
OSR2	odd-skipped related transcription factor 2	-26.05	-4.703	8.5E-19	
SORCS2	sorbin-related VPS10 domain containing receptor 2	-25.91	-4.696	5.3E-28	
HOXB2	homeobox B2	-25.67	-4.682	1.6E-154	
LOC728613	programmed cell death 6 pseudogene	-25.51	-4.673	2.8E-41	
ADAMTS4	ADAM metallopeptidase with thrombospondin type 1 motif__ 4	-25.45	-4.670	1.8E-57	
NGFR	nerve growth factor receptor	-25.08	-4.648	3.5E-13	
KCNK2	potassium channel__ two pore domain subfamily K__ member 2	-24.80	-4.632	8.3E-98	
GAS1	growth arrest-specific 1	-24.65	-4.623	1.3E-61	
ABCA9	ATP-binding cassette__ sub-family A (ABC1)__ member 9	-24.63	-4.622	6.9E-09	
THRB	thyroid hormone receptor__ beta	-24.45	-4.612	4.6E-19	
M1AP	meiosis 1 associated protein	-24.10	-4.591	3.3E-14	
SLC7A8	solute carrier family 7 (amino acid transporter light chain__ L system)__ member 8	-24.02	-4.586	2.4E-12	
ENPP2	ectonucleotide pyrophosphatase/phosphodiesterase 2	-23.98	-4.584	2.7E-26	
LOC102724224	NA	-23.97	-4.583	2.7E-28	
GABBR2	gamma-aminobutyric acid (GABA) B receptor__ 2	-23.97	-4.583	3.3E-09	

TABLE 8-continued

Genes more highly expressed in AD-MSCs compared with HMCs					
Gene name	Description	Fold Change	Log Fold Change	p-Adj	
RASSF9	Ras association (RalGDS/AF-6) domain family (N-terminal) member 9	-23.96	-4.583	4.4E-22	
TRIM29	tripartite motif containing 29	-23.93	-4.581	6.4E-09	
GGT8P	gamma-glutamyltransferase 8 pseudogene	-23.83	-4.574	5.7E-09	
FBLN5	fibulin 5	-23.70	-4.567	0.0E+00	
HOXA5	homeobox A5	-23.63	-4.563	1.1E-12	
EYA4	EYA transcriptional coactivator and phosphatase 4	-23.47	-4.553	2.6E-11	
GPC3	glypican 3	-23.38	-4.547	1.5E-10	
HTR1F	5-hydroxytryptamine (serotonin) receptor 1F_G protein-coupled	-23.32	-4.543	1.6E-08	
LOC101928370	uncharacterized LOC101928370	-23.01	-4.525	7.4E-10	
HOXA2	homeobox A2	-23.01	-4.524	1.3E-09	
LOC102800310	NA	-22.91	-4.518	2.1E-08	
RHBDL2	rhomboid_veinlet-like 2 (Drosophila)	-22.89	-4.517	7.4E-46	
ACTC1	actin_alpha_cardiac muscle 1	-22.82	-4.512	1.5E-88	
ACOX2	acyl-CoA oxidase 2_branched chain	-22.68	-4.503	3.9E-55	
RAET1E	retinoic acid early transcript 1E	-22.54	-4.494	1.5E-13	
TNFAIP8L3	tumor necrosis factor_alpha-induced protein 8-like 3	-22.53	-4.494	4.3E-87	
LRRC15	leucine rich repeat containing 15	-22.43	-4.487	1.4E-10	
IL33	interleukin 33	-22.38	-4.484	2.2E-12	
PTPN20B	protein tyrosine phosphatase_non-receptor type 20	-22.28	-4.477	1.3E-08	
RIPK3	receptor-interacting serine-threonine kinase 3	-22.28	-4.477	5.6E-19	
CHI3L1	chitinase 3-like 1 (cartilage glycoprotein-39)	-22.22	-4.474	8.4E-13	
CNKSRS2	connector enhancer of kinase suppressor of Ras 2	-22.19	-4.472	1.5E-19	
ZFYVE28	zinc finger_FYVE domain containing 28	-22.16	-4.470	3.9E-42	
HMOX1	heme oxygenase 1	-22.07	-4.464	3.1E-113	
FLG-AS1	FLG antisense RNA 1	-22.02	-4.461	3.8E-08	
SGCD	sarcoglycan_delta (35 kDa dystrophin-associated glycoprotein)	-21.92	-4.454	4.1E-20	
CD36	CD36 molecule (thrombospondin receptor)	-21.67	-4.437	4.8E-08	
GPR133	adhesion G protein-coupled receptor D1	-21.65	-4.436	1.1E-59	
PTGIS	prostaglandin I2 (prostacyclin) synthase	-21.63	-4.435	9.9E-125	
PCDHGA4	protocadherin gamma subfamily A_4	-21.59	-4.432	4.0E-22	
RAI2	retinoic acid induced 2	-21.54	-4.429	5.9E-10	
LCN1	lipocalin 1	-21.52	-4.428	3.8E-09	
ANKRD6	ankyrin repeat domain 6	-21.48	-4.425	1.2E-26	
ADIRF	adipogenesis regulatory factor	-21.09	-4.398	1.3E-21	
ISLR2	immunoglobulin superfamily containing leucine-rich repeat 2	-21.04	-4.395	1.1E-26	
FLG	filaggrin	-21.04	-4.395	2.0E-08	
IBSP	integrin-binding sialoprotein	-20.92	-4.387	1.0E-07	
ELN	elastin	-20.70	-4.371	1.1E-56	
SALL4	salt-like transcription factor 4	-20.68	-4.370	1.2E-13	
TRPV3	transient receptor potential cation channel_subfamily V_member 3	-20.62	-4.366	3.7E-28	
PTGS1	prostaglandin-endoperoxide synthase 1 (prostaglandin G/H synthase and cyclooxygenase)	-20.61	-4.365	0.0E+00	
FGF18	fibroblast growth factor 18	-20.56	-4.361	2.0E-17	
ZNF662	zinc finger protein 662	-20.47	-4.356	3.3E-35	
KCNJ15	potassium channel_inwardly rectifying subfamily J_member 15	-20.33	-4.346	1.0E-35	
LINC01354	long intergenic non-protein coding RNA 1354	-20.07	-4.327	1.1E-09	
LGI2	leucine-rich repeat LGI family_member 2	-20.02	-4.323	5.3E-13	
TIMP3	TIMP metallopeptidase inhibitor 3	-19.80	-4.308	4.6E-92	
EDA	ectodysplasin A	-19.58	-4.292	7.3E-24	
FAM225A	family with sequence similarity 225_member A (non-protein coding)	-19.26	-4.267	1.1E-11	

TABLE 8-continued

Genes more highly expressed in AD-MSCs compared with HMCs					
Gene name	Description	Fold Change	Log Fold Change	p-Adj	
ALS2CR11	amyotrophic lateral sclerosis 2 (juvenile) chromosome region candidate 11	-19.16	-4.260	8.9E-24	
COX7A1	cytochrome c oxidase subunit VIIa polypeptide 1 (muscle)	-19.02	-4.249	1.1E-46	
HCG4	HLA complex group 4 (non-protein coding)	-18.90	-4.240	1.3E-07	
KLF14	Kruppel-like factor 14	-18.65	-4.221	2.2E-07	
APOD	apolipoprotein D	-18.62	-4.219	1.8E-07	
NOV	nephroblastoma overexpressed	-18.58	-4.215	2.0E-49	
CLEC14A	C-type lectin domain family 14 member A	-18.57	-4.215	2.3E-07	
CGREF1	cell growth regulator with EF-hand domain 1	-18.43	-4.204	5.5E-55	
NTF3	neurotrophin 3	-18.40	-4.201	9.1E-29	
FOLR3	folate receptor 3 (gamma)	-18.29	-4.193	1.6E-09	
LOC100132077	uncharacterized LOC100132077	-18.27	-4.192	1.8E-25	
WNT11	wingless-type MMTV integration site family member 11	-18.08	-4.177	6.9E-15	
CLIC6	chloride intracellular channel 6	-17.89	-4.161	8.0E-17	
PRSS3	protease_serine_3	-17.80	-4.154	1.5E-09	
PSG2	pregnancy specific beta-1-glycoprotein 2	-17.77	-4.152	5.8E-07	
MFSD7	major facilitator superfamily domain containing 7	-17.75	-4.150	3.3E-51	
PIWI4	piwi-like RNA-mediated gene silencing 4	-17.71	-4.147	1.3E-23	
MEGF6	multiple EGF-like-domains 6	-17.69	-4.145	9.3E-50	
LINC01116	long intergenic non-protein coding RNA 1116	-17.69	-4.145	3.0E-41	
TLX2	T-cell leukemia homeobox 2	-17.25	-4.108	7.0E-10	
GRID1	glutamate receptor ionotropic_delta 1	-17.25	-4.108	6.6E-07	
DLGAP1	discs large (Drosophila) homolog-associated protein 1	-17.21	-4.105	4.3E-07	
SPESP1	sperm equatorial segment protein 1	-17.05	-4.092	1.2E-09	
NAALADL1	N-acetylated alpha-linked acidic dipeptidase-like 1	-16.94	-4.083	1.2E-101	
IL22RA1	interleukin 22 receptor_alpha 1	-16.93	-4.081	6.4E-07	
SNORD114-10	small nucleolar RNA_C/D box 114-10	-16.91	-4.080	5.8E-07	
PSG1	pregnancy specific beta-1-glycoprotein 1	-16.89	-4.078	7.5E-07	
LOC100130872	uncharacterized LOC100130872	-16.85	-4.075	4.2E-26	
LPXN	leupaxin	-16.83	-4.073	2.6E-133	
GSTM5	glutathione S-transferase mu 5	-16.82	-4.072	1.5E-13	
NDUFA4L2	NADH dehydrogenase (ubiquinone) 1 alpha subcomplex_4-like 2	-16.80	-4.071	6.2E-10	
MYH13	myosin_heavy chain 13_skeletal muscle	-16.76	-4.067	1.1E-06	
PCDHGA2	protocadherin gamma subfamily A_2	-16.75	-4.066	2.3E-29	
HOXB-AS1	HOXB cluster antisense RNA 1	-16.48	-4.043	3.4E-24	
ZFP92	ZFP92 zinc finger protein	-16.47	-4.042	1.1E-08	
GLYATL2	glycine-N-acyltransferase-like 2	-16.44	-4.039	9.7E-10	
LIPC	lipase_hepatic	-16.34	-4.031	9.3E-07	
BMPR1B	bone morphogenetic protein receptor_type IB	-16.32	-4.029	4.9E-22	
PTGES	prostaglandin E synthase	-16.31	-4.028	1.5E-35	
S100P	S100 calcium binding protein P	-16.14	-4.013	1.4E-06	
LINC00595	long intergenic non-protein coding RNA 595	-16.01	-4.001	7.2E-08	
SLC1A2	solute carrier family 1 (glial high affinity glutamate transporter)_member 2	-15.96	-3.996	9.5E-08	
AGMO	alkylglycerol monooxygenase	-15.91	-3.992	1.7E-07	
BMP6	bone morphogenetic protein 6	-15.87	-3.988	7.5E-15	
SLC1A1	solute carrier family 1 (neuronal/epithelial high affinity glutamate transporter_system Xag)_member 1	-15.85	-3.987	8.9E-14	
IGF1	insulin-like growth factor 1 (somatomedin C)	-15.78	-3.980	5.4E-11	
IFNE	interferon_epsilon	-15.73	-3.976	1.1E-14	

TABLE 8-continued

Genes more highly expressed in AD-MSCs compared with HMCs					
Gene name	Description	Fold Change	Log Fold Change	p-Adj	
SHCBP1L	SHC SH2-domain binding protein 1-like	-15.70	-3.972	1.2E-06	
OPCML	opioid binding protein/cell adhesion molecule-like	-15.69	-3.972	1.3E-13	
DKK1	dickkopf WNT signaling pathway inhibitor 1	-15.64	-3.967	1.5E-120	
ASTL	astacin-like metallo-endopeptidase (M12 family)	-15.62	-3.965	1.6E-06	
LDLRAD4	low density lipoprotein receptor class A domain containing 4	-15.61	-3.964	1.1E-19	
P2RY6	pyrimidinergic receptor P2Y_G-protein coupled_6	-15.57	-3.960	2.6E-11	
FAM87B	family with sequence similarity 87_member B	-15.49	-3.953	1.2E-15	
PLEKHH2	pleckstrin homology domain containing_family H (with MyTH4 domain) member 2	-15.47	-3.952	2.2E-64	
ALK	anaplastic lymphoma receptor tyrosine kinase	-15.46	-3.951	1.8E-06	
MKX	mohawk homeobox	-15.44	-3.948	3.9E-07	
MT1A	metallothionein 1A	-15.39	-3.944	3.1E-16	
SHANK1	SH3 and multiple ankyrin repeat domains 1	-15.31	-3.937	2.7E-18	
LOC150381	NA	-15.30	-3.936	1.4E-30	
ZNF503	zinc finger protein 503	-14.98	-3.905	8.3E-59	
ZMYND12	zinc finger_MYND-type containing 12	-14.96	-3.903	8.4E-10	
A4GALT	alpha 1_4-galactosyltransferase	-14.91	-3.898	4.6E-49	
HOXA1	homeobox A1	-14.87	-3.894	1.0E-21	
ADRA2C	adrenoceptor alpha 2C	-14.85	-3.892	2.6E-15	
GALNT13	polypeptide N-acetylgalactosaminyltransferase 13	-14.70	-3.878	4.4E-06	
RASIP 1	Ras interacting protein 1	-14.68	-3.875	2.8E-21	
CCDC85A	coiled-coil domain containing 85A	-14.61	-3.869	2.0E-10	
PLCL1	phospholipase C-like 1	-14.56	-3.864	8.5E-11	
KLF8	Kruppel-like factor 8	-14.54	-3.862	1.3E-15	
FAM20A	family with sequence similarity 20_member A	-14.53	-3.861	1.4E-18	
HOXA-AS3	HOXA cluster antisense RNA 3	-14.51	-3.859	2.2E-10	
LMO3	LIM domain only 3 (rhombotin-like 2)	-14.44	-3.852	2.8E-07	
LOC100133669	uncharacterized LOC100133669	-14.39	-3.847	7.4E-10	
SLC22A3	solute carrier family 22 (organic cation transporter)_member 3	-14.37	-3.845	4.1E-18	
SSTR1	somatostatin receptor 1	-14.28	-3.835	1.7E-08	
SBSN	suprabasin	-14.27	-3.835	1.1E-43	
LY96	lymphocyte antigen 96	-14.24	-3.832	1.9E-48	
FAM46C	family with sequence similarity 46_member C	-14.18	-3.826	1.1E-08	
ATP8B4	ATPase_class I_type 8B_member 4	-14.07	-3.814	5.2E-06	
LINC00702	long intergenic non-protein coding RNA 702	-14.02	-3.810	3.3E-16	
ANPEP	alanyl (membrane) aminopeptidase	-14.00	-3.807	1.8E-57	
MIR31HG	MIR31 host gene	-13.99	-3.806	1.7E-100	
ESPNL	espin-like	-13.85	-3.791	1.8E-09	
FLJ12825	uncharacterized LOC440101	-13.84	-3.791	3.6E-11	
KLF4	Kruppel-like factor 4 (gut)	-13.73	-3.779	1.2E-61	
KCNK15	potassium channel_two pore domain subfamily K_member 15	-13.67	-3.773	3.9E-08	
IL1RN	interleukin 1 receptor antagonist	-13.65	-3.771	2.0E-07	
CACNB4	calcium channel_voltage-dependent_beta 4 subunit	-13.65	-3.771	8.5E-07	
PPAP2B	phosphatidic acid phosphatase type 2B	-13.65	-3.770	1.3E-64	
NEFM	neurofilament_medium polypeptide	-13.53	-3.758	1.3E-06	
KLF17	Kruppel-like factor 17	-13.51	-3.756	1.1E-07	
CNGA3	cyclic nucleotide gated channel alpha 3	-13.50	-3.755	9.6E-10	
ROS1	ROS proto-oncogene 1 _receptor tyrosine kinase	-13.44	-3.749	4.4E-09	
PTX3	pentraxin 3_long	-13.36	-3.740	4.2E-21	
BRINP1	bone morphogenetic protein/retinoic acid inducible neural-specific 1	-13.33	-3.736	1.0E-05	

TABLE 8-continued

Genes more highly expressed in AD-MSCs compared with HMCs					
Gene name	Description	Fold Change	Log Fold Change	p-Adj	
RGL3	ral guanine nucleotide dissociation stimulator-like 3	-13.23	-3.726	8.6E-06	
DEPTOR	DEP domain containing MTOR-interacting protein	-13.21	-3.723	1.2E-48	
ADH1C	alcohol dehydrogenase 1C (class I) gamma polypeptide	-13.16	-3.718	1.1E-05	
ADAMTS2	ADAM metallopeptidase with thrombospondin type 1 motif_2	-13.14	-3.716	3.0E-156	
CASP10	caspase 10_apoptosis-related cysteine peptidase	-13.13	-3.715	2.2E-31	
LINC00398	long intergenic non-protein coding RNA 398	-13.13	-3.714	9.1E-06	
TFPI2	tissue factor pathway inhibitor 2	-13.09	-3.710	7.5E-08	
PLXDC2	plexin domain containing 2	-13.07	-3.708	1.7E-08	
SYT7	synaptotagmin VII	-12.97	-3.697	1.5E-22	
GPC6	glypican 6	-12.96	-3.696	4.6E-51	
GGT5	gamma-glutamyltransferase 5	-12.94	-3.694	9.6E-10	
INMT	indoethylamine N-methyltransferase	-12.89	-3.688	6.5E-06	
PTGDS	prostaglandin D2 synthase 21 kDa (brain)	-12.86	-3.685	3.5E-09	
CHRD	chordin	-12.79	-3.677	1.0E-38	
PLA2G5	phospholipase A2_group V	-12.73	-3.670	7.8E-08	
PTGER3	prostaglandin E receptor 3 (subtype EP3)	-12.66	-3.662	3.5E-15	
RGS22	regulator of G-protein signaling 22	-12.64	-3.660	1.4E-05	
CARD6	caspase recruitment domain family_member 6	-12.59	-3.654	5.0E-75	
ANKRD30B	ankyrin repeat domain 30B	-12.58	-3.653	4.9E-07	
NPY4R	neuropeptide Y receptor Y4	-12.46	-3.639	9.9E-07	
P2RY2	purinergic receptor P2Y_G-protein coupled_2	-12.42	-3.635	1.2E-06	
HRCT1	histidine rich carboxyl terminus 1	-12.41	-3.634	1.9E-08	
CCDC144A	coiled-coil domain containing 144A	-12.37	-3.629	1.8E-07	
MEIS1	Meis homeobox 1	-12.33	-3.624	5.6E-85	
DLEU7	deleted in lymphocytic leukemia_7	-12.30	-3.620	8.7E-07	
ZNF385D	zinc finger protein 385D	-12.27	-3.617	3.7E-16	
HOXB8	homeobox B8	-12.26	-3.616	9.9E-27	
PCDHGA9	protocadherin gamma subfamily A_9	-12.25	-3.614	3.0E-23	
DHRS3	dehydrogenase/reductase (SDR family) member 3	-12.17	-3.605	2.7E-43	
C4BPB	complement component 4 binding protein_beta	-12.16	-3.604	3.4E-05	
ANKRD2	ankyrin repeat domain 2 (stretch responsive muscle)	-12.15	-3.603	2.0E-19	
PHYHIP	phytanoyl-CoA 2-hydroxylase interacting protein	-12.15	-3.603	3.2E-10	
PPP2R2C	protein phosphatase 2_regulatory subunit B_gamma	-12.11	-3.598	5.3E-07	
AKR1C2	aldo-keto reductase family 1_member C2	-12.09	-3.596	3.6E-174	
THNSL2	threonine synthase-like 2 (<i>S. cerevisiae</i>)	-12.08	-3.594	5.4E-27	
PID1	phosphotyrosine interaction domain containing 1	-12.07	-3.593	1.8E-117	
PSORS1C1	psoriasis susceptibility 1 candidate 1	-12.03	-3.588	9.8E-07	
CPXM2	carboxypeptidase X (M14 family)_member 2	-11.97	-3.581	6.1E-11	
TNFAIP6	tumor necrosis factor_alpha-induced protein 6	-11.96	-3.580	4.6E-09	
DMRT2	doublesex and mab-3 related transcription factor 2	-11.93	-3.577	1.1E-08	
PCDHGB3	protocadherin gamma subfamily B_3	-11.87	-3.569	7.2E-18	
TMTc2	transmembrane and tetratricopeptide repeat containing 2	-11.84	-3.566	2.1E-61	
C2orf81	chromosome 2 open reading frame 81	-11.84	-3.565	7.5E-65	
KANK4	KN motif and ankyrin repeat domains 4	-11.81	-3.562	2.8E-05	
SEL1L2	sel-1 suppressor of lin-12-like 2 (<i>C. elegans</i>)	-11.80	-3.561	3.2E-05	

TABLE 8-continued

Genes more highly expressed in AD-MSCs compared with HMCs					
Gene name	Description	Fold Change	Log Fold Change	p-Adj	
HOXC13	homeobox C13	-11.80	-3.561	4.5E-05	
NR4A2	nuclear receptor subfamily 4_group A_member 2	-11.74	-3.554	1.2E-18	
FLRT2	fibronectin leucine rich transmembrane protein 2	-11.74	-3.553	3.3E-14	
SCRG1	stimulator of chondrogenesis 1	-11.71	-3.550	1.5E-41	
LTBP2	latent transforming growth factor beta binding protein 2	-11.70	-3.549	9.9E-194	
SPON1	spondin 1_extracellular matrix protein	-11.65	-3.543	1.8E-84	
SYNDIG1	synapse differentiation inducing 1	-11.63	-3.540	2.2E-09	
MMRN2	multimerin 2	-11.57	-3.532	6.7E-17	
EDNRB	endothelin receptor type B	-11.55	-3.530	4.5E-05	
GRIA3	glutamate receptor_ ionotropic_AMPA 3	-11.54	-3.528	2.1E-38	
SOD3	superoxide dismutase 3_extracellular	-11.53	-3.527	1.7E-09	
SAMD3	sterile alpha motif domain containing 3	-11.37	-3.507	9.7E-08	
SUSD3	sushi domain containing 3	-11.32	-3.500	3.7E-30	
PCOLCE2	procollagen C-endopeptidase enhancer 2	-11.28	-3.496	7.1E-65	
C1QL3	complement component 1_q subcomponent-like 3	-11.23	-3.489	6.5E-11	
SUSD2	sushi domain containing 2	-11.21	-3.487	1.5E-06	
C1S	complement component 1_s subcomponent	-11.20	-3.485	5.1E-125	
PRELP	proline/arginine-rich end leucine-rich repeat protein	-11.17	-3.481	8.7E-25	
CDA	cytidine deaminase	-11.15	-3.479	2.5E-53	
PTPRD	protein tyrosine phosphatase_receptor type_D	-11.09	-3.471	5.5E-07	
ZDHHC15	zinc finger_DHHC-type containing 15	-10.98	-3.456	6.4E-06	
APOA1	apolipoprotein A-I	-10.96	-3.454	1.2E-08	
FHAD1	forkhead-associated (FHA) phosphopeptide binding domain 1	-10.96	-3.454	2.0E-08	
HIST1H1E	histone cluster 1_H1e	-10.93	-3.450	5.6E-05	
LOC100507642	uncharacterized LOC100507642	-10.92	-3.449	3.1E-13	
CFD	complement factor D (adipsin)	-10.91	-3.448	2.5E-23	
LOC100507540	NA	-10.91	-3.447	4.6E-20	
RTN1	reticulon 1	-10.90	-3.447	4.4E-07	
ADH1B	alcohol dehydrogenase 1B (class I)_beta polypeptide	-10.85	-3.440	7.8E-05	
CCL28	chemokine (C-C motif) ligand 28	-10.83	-3.437	1.6E-05	
HOTAIR	HOX transcript antisense RNA	-10.79	-3.432	3.2E-06	
LOC100505718	NA	-10.76	-3.427	1.3E-08	
RNF212	ring finger protein 212	-10.63	-3.411	2.9E-16	
FIBCD1	fibrinogen C domain containing 1	-10.61	-3.407	1.3E-28	
EFCAB1	EF-hand calcium binding domain 1	-10.60	-3.406	2.2E-08	
LOC101059948	uncharacterized LOC101059948	-10.56	-3.400	9.5E-06	
PCDH18	protocadherin 18	-10.53	-3.397	1.0E-39	
CPNE8	copine VIII	-10.51	-3.394	1.5E-80	
TIMP1	TIMP metallopeptidase inhibitor 1	-10.49	-3.390	0.0E+00	
TINAGL 1	tubulointerstitial nephritis antigen-like 1	-10.39	-3.377	7.6E-06	
C10orf11	chromosome 10 open reading frame 11	-10.27	-3.360	2.1E-06	
PCDHGB5	protocadherin gamma subfamily B_5	-10.25	-3.358	3.2E-102	
P2RX1	purinergic receptor P2X_ligand gated ion channel_1	-10.24	-3.356	2.2E-05	
RPLP0P2	ribosomal protein_large_P0 pseudogene 2	-10.22	-3.353	2.0E-07	
HOXA11-AS	HOXA11 antisense RNA	-10.22	-3.353	1.2E-11	
COL21A1	collagen_type XXI_alpha 1	-10.22	-3.353	5.8E-05	
ESM1	endothelial cell-specific molecule 1	-10.20	-3.351	1.5E-06	
FAM106A	family with sequence similarity 106_member A	-10.19	-3.350	1.1E-04	
GHDC	GH3 domain containing	-10.17	-3.347	6.2E-96	
LOC654342	lymphocyte-specific protein 1 pseudogene	-10.15	-3.344	6.6E-147	
GAS7	growth arrest-specific 7	-10.07	-3.332	2.5E-36	
FAM124A	family with sequence similarity 124A	-10.06	-3.331	1.3E-05	
ITGB2-AS1	ITGB2 antisense RNA 1	-10.06	-3.330	1.1E-06	

TABLE 8-continued

Genes more highly expressed in AD-MSCs compared with HMCs					
Gene name	Description	Fold Change	Log Fold Change	p-Adj	
ZNF280A	zinc finger protein 280A	-10.04	-3.328	1.4E-04	
MEDAG	mesenteric estrogen-dependent adipogenesis	-10.04	-3.327	5.5E-17	
DNAH2	dynein_axonemal_heavy chain 2	-9.99	-3.320	4.8E-05	
WNT4	wingless-type MMTV integration site family_member 4	-9.96	-3.317	4.4E-05	
COL12A1	collagen_type XII_alpha 1	-9.89	-3.306	8.1E-35	
DMKN	dermokine	-9.87	-3.303	6.9E-14	
SLC1A7	solute carrier family 1 (glutamate transporter)_member 7	-9.83	-3.297	3.5E-06	
COL8A2	collagen_type VIII_alpha 2	-9.80	-3.292	6.4E-09	
MYOM3	myomesin 3	-9.77	-3.288	9.5E-28	
EPDR1	ependymin related 1	-9.76	-3.287	2.2E-30	
TMEM155	transmembrane protein 155	-9.71	-3.279	1.1E-08	
PODNL1	podocan-like 1	-9.71	-3.279	5.8E-47	
PITX1	paired-like homeodomain 1	-9.68	-3.275	2.3E-25	
IL20RA	interleukin 20 receptor_alpha	-9.68	-3.274	5.1E-05	
GPR4	G protein-coupled receptor 4	-9.67	-3.274	5.5E-05	
GPX3	glutathione peroxidase 3	-9.67	-3.273	5.3E-09	
C5orf27	long intergenic non-protein coding RNA 1554	-9.67	-3.273	2.3E-05	
CYP1B1	cytochrome P450_family 1_subfamily B_polypeptide 1	-9.64	-3.269	3.2E-14	
TEK	TEK tyrosine kinase_endothelial	-9.63	-3.267	1.4E-61	
KRT13	keratin 13_type I	-9.60	-3.263	5.5E-06	
NEFL	neurofilament_light polypeptide	-9.58	-3.260	4.5E-07	
BDKRB1	bradykinin receptor B1	-9.55	-3.256	7.0E-39	
LINC01140	long intergenic non-protein coding RNA 1140	-9.53	-3.253	4.2E-17	
SEMA7A	semaphorin_7A_GPI membrane anchor (John Milton Hagen blood group)	-9.53	-3.252	2.6E-85	
PCDHGA7	protocadherin gamma subfamily A_7	-9.47	-3.244	3.5E-20	
ZNF503-AS2	ZNF503 antisense RNA 2	-9.44	-3.239	5.5E-25	
MMP12	matrix metallopeptidase 12	-9.43	-3.238	2.5E-05	
ANKRD37	ankyrin repeat domain 37	-9.43	-3.238	3.0E-38	
KRT81	keratin 8_type II	-9.40	-3.233	4.2E-26	
AADAC	arylacetamide deacetylase	-9.40	-3.232	6.1E-05	
PARP15	poly (ADP-ribose) polymerase family_member 15	-9.33	-3.223	9.8E-08	
FAM90A1	family with sequence similarity 90_member A1	-9.33	-3.222	2.4E-04	
OXCT2	3-oxoacid CoA transferase 2	-9.33	-3.222	4.6E-06	
SLC22A15	solute carrier family 22_member 15	-9.29	-3.215	1.2E-47	
SAA1	serum amyloid A1	-9.26	-3.212	2.6E-04	
ANKRD65	ankyrin repeat domain 65	-9.25	-3.210	6.6E-07	
UBE2QL1	ubiquitin-conjugating enzyme E2Q_family-like 1	-9.24	-3.208	5.9E-05	
LHB	luteinizing hormone beta polypeptide	-9.22	-3.205	5.5E-06	
SLC9A9	solute carrier family 9_subfamily A (NHE9_cation proton antiporter 9)_member 9	-9.19	-3.200	3.1E-26	
PRDM8	PR domain containing 8	-9.18	-3.198	5.7E-119	
MAGOH2	mago homolog_2_pseudogene	-9.17	-3.197	3.2E-04	
ICAM2	intercellular adhesion molecule 2	-9.16	-3.195	1.2E-07	
NECAB2	N-terminal EF-hand calcium binding protein 2	-9.13	-3.191	1.1E-06	
MDGA1	MAM domain containing glycosylphosphatidylinositol anchor 1	-9.13	-3.191	9.3E-99	
BCL6B	B-cell CLL/lymphoma 6_member B	-9.09	-3.185	1.6E-05	
HSD11B1	hydroxysteroid (11-beta) dehydrogenase 1	-9.09	-3.184	1.2E-05	
DIRAS3	DIRAS family_GTP-binding RAS-like 3	-9.05	-3.177	7.7E-06	
MOB3B	MOB kinase activator 3B	-9.03	-3.175	6.7E-19	
ITM2A	integral membrane protein 2A	-9.02	-3.173	3.8E-04	
CRYAB	crystallin_alpha B	-9.01	-3.171	1.1E-11	
HLA-F-AS1	HLA-F antisense RNA 1	-9.00	-3.170	2.2E-17	
LINC00578	long intergenic non-protein coding RNA 578	-8.99	-3.168	3.2E-04	
DUSP2	dual specificity phosphatase 2	-8.95	-3.163	6.4E-84	

TABLE 8-continued

Genes more highly expressed in AD-MSCs compared with HMCs					
Gene name	Description	Fold Change	Log Fold Change	p-Adj	
FAM228A	family with sequence similarity 228_member A	-8.94	-3.161	1.2E-04	
PLSCR4	phospholipid scramblase 4	-8.94	-3.160	1.0E-65	
CD97	adhesion G protein-coupled receptor E5	-8.87	-3.148	3.3E-70	
KCNE1	potassium channel_voltage gated subfamily E regulatory beta subunit 1	-8.84	-3.144	1.2E-07	
PCSK1	proprotein convertase subtilisin/kexin type 1	-8.79	-3.135	3.2E-06	
ZNF558	zinc finger protein 558	-8.78	-3.134	1.3E-52	
CXCL6	chemokine (C-X-C motif) ligand 6	-8.77	-3.132	3.5E-05	
KCNS3	potassium voltage-gated channel_modifier subfamily S_member 3	-8.73	-3.125	7.4E-13	
CD14	CD14 molecule	-8.67	-3.116	4.4E-07	
FLJ38576	uncharacterized LOC651430	-8.66	-3.114	6.1E-05	
VTN	vitronectin	-8.65	-3.113	4.3E-04	
EBF2	early B-cell factor 2	-8.64	-3.111	7.4E-20	
MIR503	microRNA 503	-8.61	-3.107	1.4E-11	
CHRDLL2	chordin-like 2	-8.57	-3.099	5.2E-04	
ACADL	acyl-CoA dehydrogenase_long chain	-8.56	-3.098	5.3E-04	
HCRTTR1	hypocretin (orexin) receptor 1	-8.54	-3.095	3.8E-05	
KCNC4-AS1	KCNC4 antisense RNA 1 (head to head)	-8.51	-3.088	7.1E-05	
PVRL4	poliovirus receptor-related 4	-8.49	-3.085	1.0E-07	
FRY	furry homolog (<i>Drosophila</i>)	-8.47	-3.082	7.6E-11	
ITIH5	inter-alpha-trypsin inhibitor heavy chain family_member 5	-8.45	-3.080	6.6E-04	
GSTO2	glutathione S-transferase omega 2	-8.42	-3.075	3.8E-22	
LOC101927524	NA	-8.42	-3.074	6.3E-04	
PODXL	podocalyxin-like	-8.37	-3.065	2.3E-09	
STXBP5L	syntaxin binding protein 5-like	-8.36	-3.063	1.1E-04	
NR4A1	nuclear receptor subfamily 4_group A_member 1	-8.36	-3.063	2.6E-72	
CD55	CD55 molecule_decay accelerating factor for complement (Cromer blood group)	-8.32	-3.057	2.0E-67	
FMO3	flavin containing monooxygenase 3	-8.28	-3.049	2.1E-04	
ZG16B	zymogen granule protein 16B	-8.26	-3.047	5.1E-05	
CHN2	chimerin 2	-8.24	-3.043	7.0E-12	
FPR2	formyl peptide receptor 2	-8.18	-3.033	2.0E-04	
COL5A3	collagen_type V_alpha 3	-8.18	-3.032	3.6E-13	
TNFRSF14	tumor necrosis factor receptor superfamily_member 14	-8.18	-3.031	5.1E-10	
PAQR9	progesterin and adiponectin receptor family member IX	-8.17	-3.031	2.5E-05	
LOC101927229	uncharacterized LOC101927229	-8.17	-3.030	5.0E-04	
MME	membrane metallo-endopeptidase	-8.12	-3.022	1.3E-12	
FZD1	frizzled class receptor 1	-8.11	-3.020	6.2E-29	
COL6A6	collagen_type VI_alpha 6	-8.11	-3.020	2.1E-04	
PRG2	proteoglycan_2_bone marrow (natural killer cell activator_eosinophil granule major basic protein)	-8.11	-3.020	5.6E-04	
PLD5	phospholipase D family_member 5	-8.09	-3.016	9.1E-04	
CCDC64B	coiled-coil domain containing 64B	-8.06	-3.011	7.9E-04	
MIR503HG	MIR503 host gene	-8.05	-3.010	9.4E-18	
SULF1	sulfatase 1	-8.05	-3.009	1.7E-31	
SDHAP3	succinate dehydrogenase complex_subunit A_flavoprotein pseudogene 3	-8.05	-3.009	9.2E-13	
DACT1	dishevelled-binding antagonist of beta-catenin 1	-8.05	-3.009	3.6E-50	
C3	complement component 3	-8.02	-3.004	3.9E-15	
ABI3BP	ABI family_member 3 (NESH) binding protein	-8.00	-3.001	4.3E-87	
ANKH	ANKH inorganic pyrophosphate transport regulator	-7.97	-2.994	6.5E-31	
RADIL	Ras association and DIL domains	-7.96	-2.992	1.5E-25	
ZNF454	zinc finger protein 454	-7.93	-2.987	2.7E-06	
KRTAP1-5	keratin associated protein 1-5	-7.93	-2.986	4.6E-05	
SUPT20HL1	suppressor of Ty 20 homolog (<i>S. cerevisiae</i>)-like 1	-7.92	-2.986	4.5E-04	
DPT	dermatopontin	-7.88	-2.979	1.1E-03	

TABLE 8-continued

Genes more highly expressed in AD-MSCs compared with HMCs					
Gene name	Description	Fold Change	Log Fold Change	p-Adj	
CHST15	carbohydrate (N-acetylgalactosamine 4-sulfate 6-O) sulfotransferase 15	-7.88	-2.978	1.1E-22	
OLFML1	olfactomedin-like 1	-7.86	-2.974	5.2E-07	
MT1M	metallothionein 1M	-7.85	-2.973	1.3E-28	
AKR1C1	aldo-keto reductase family 1 member C1	-7.84	-2.971	2.0E-88	
TLE2	transducin-like enhancer of split 2	-7.84	-2.970	5.6E-41	
PIGZ	phosphatidylinositol glycan anchor biosynthesis class Z	-7.83	-2.969	5.9E-32	
KRT16	keratin 16_type I	-7.82	-2.967	2.2E-09	
CAPN3	calpain 3	-7.78	-2.960	3.0E-18	
LOC100506385	NA	-7.78	-2.960	4.5E-14	
TBX18	T-box 18	-7.74	-2.952	3.1E-119	
SOCS2-AS1	SOCS2 antisense RNA 1	-7.73	-2.950	7.4E-13	
DLX4	distal-less homeobox 4	-7.71	-2.947	1.1E-03	
PF4V1	platelet factor 4 variant 1	-7.71	-2.947	1.1E-03	
LOC729041	NA	-7.70	-2.944	4.7E-04	
XYLT1	xylosyltransferase I	-7.69	-2.944	7.1E-65	
C1R	complement component 1_r subcomponent	-7.69	-2.942	2.3E-23	
XAF1	XIAP associated factor 1	-7.68	-2.940	1.7E-30	
RBPMS2	RNA binding protein with multiple splicing 2	-7.67	-2.939	2.0E-22	
SLC22A23	solute carrier family 22_member 23	-7.67	-2.938	1.0E-29	
RAB3IL1	RAB3A interacting protein (rabin3)-like 1	-7.66	-2.937	4.6E-55	
MPV17L	MPV17 mitochondrial membrane protein-like	-7.64	-2.933	7.0E-07	
CSF3	colony stimulating factor 3 (granulocyte)	-7.64	-2.933	1.2E-03	
TRPM2	transient receptor potential cation channel_subfamily M_member 2	-7.62	-2.931	3.4E-05	
KRT33B	keratin 33B_type I	-7.61	-2.929	1.3E-14	
EID3	EP300 interacting inhibitor of differentiation 3	-7.60	-2.927	2.7E-30	
CES1	carboxylesterase 1	-7.59	-2.925	9.9E-04	
ACSL5	acyl-CoA synthetase long-chain family member 5	-7.59	-2.924	3.7E-14	
CTSK	cathepsin K	-7.58	-2.922	1.6E-18	
LINC00654	long intergenic non-protein coding RNA 654	-7.54	-2.914	2.0E-26	
F8	coagulation factor VIII_procoagulant component	-7.53	-2.913	2.6E-23	
MAGEB17	melanoma antigen family B17	-7.52	-2.911	1.5E-03	
SLIT3	slit guidance ligand 3	-7.52	-2.911	4.7E-230	
ZXDA	zinc finger_X-linked duplicated A	-7.52	-2.911	1.3E-44	
HAR1A	highly accelerated region 1A (non-protein coding)	-7.49	-2.905	2.9E-04	
IFI27	interferon_alpha-inducible protein 27	-7.47	-2.902	4.2E-34	
SPOCK1	spark/osteonectin_cwcw and kazal-like domains proteoglycan (testican) 1	-7.47	-2.901	3.8E-50	
FLJ43879	FLJ43879 protein	-7.46	-2.900	1.4E-03	
GPR150	G protein-coupled receptor 150	-7.46	-2.898	1.1E-13	
DDO	D-aspartate oxidase	-7.45	-2.898	1.6E-03	
JOSD2	Josephin domain containing 2	-7.44	-2.895	1.4E-100	
ANKRD35	ankyrin repeat domain 35	-7.43	-2.893	2.1E-41	
LINC00482	long intergenic non-protein coding RNA 482	-7.41	-2.889	1.5E-03	
TDRD1	tudor domain containing 1	-7.38	-2.883	6.7E-04	
VCAN	versican	-7.37	-2.882	3.8E-166	
OGN	osteoglycin	-7.37	-2.882	8.3E-04	
S100A4	S100 calcium binding protein A4	-7.35	-2.878	5.2E-09	
SHANK2	SH3 and multiple ankyrin repeat domains 2	-7.35	-2.877	1.8E-35	
POU5F1	POU class 5 homeobox 1	-7.35	-2.877	3.4E-13	
CALB2	calbindin 2	-7.34	-2.876	3.3E-04	
ECM2	extracellular matrix protein 2_female	-7.34	-2.875	3.9E-08	
WNT9A	organ and adipocyte specific wingless-type MMTV integration site family_member 9A	-7.32	-2.872	9.3E-05	
LCE2A	late cornified envelope 2A	-7.32	-2.872	1.8E-03	

TABLE 8-continued

Genes more highly expressed in AD-MSCs compared with HMCs					
Gene name	Description	Fold Change	Log Fold Change	p-Adj	
IGFBP3	insulin-like growth factor binding protein 3	-7.32	-2.871	8.2E-48	
ANK2	ankyrin 2_ neuronal	-7.28	-2.864	9.4E-61	
ELOVL3	ELOVL fatty acid elongase 3	-7.28	-2.863	5.0E-07	
MAB21L1	mab-21-like 1 (<i>C. elegans</i>)	-7.27	-2.863	9.4E-28	
ADCY4	adenylyl cyclase 4	-7.27	-2.862	2.0E-07	
RORA	RAR-related orphan receptor A	-7.27	-2.861	1.2E-17	
MFAP4	microfibrillar-associated protein 4	-7.25	-2.857	1.3E-27	
ZDHHC23	zinc finger_ DHHC-type containing 23	-7.22	-2.852	9.9E-25	
SLC2A9	solute carrier family 2 (facilitated glucose transporter)_ member 9	-7.20	-2.848	5.5E-11	
SLC14A1	solute carrier family 14 (urea transporter)_ member 1 (Kidd blood group)	-7.19	-2.847	1.8E-03	
LRRC6	leucine rich repeat containing 6	-7.17	-2.842	1.2E-08	
C15orf59	chromosome 15 open reading frame 59	-7.16	-2.839	2.0E-08	
PRRX2	paired related homeobox 2	-7.15	-2.838	6.5E-295	
C11orf91	chromosome 11 open reading frame 91	-7.15	-2.838	2.6E-16	
LRRN4CL	LRRN4 C-terminal like	-7.12	-2.832	7.3E-09	
FLRT1	fibronectin leucine rich transmembrane protein 1	-7.12	-2.832	4.3E-13	
PSG3	pregnancy specific beta-1-glycoprotein 3	-7.11	-2.830	1.9E-03	
CR1L	complement component (3b/4b) receptor 1-like	-7.11	-2.829	8.4E-04	
ABCA6	ATP-binding cassette_ sub-family A (ABC1)_ member 6	-7.06	-2.820	1.5E-04	
ADRA2B	adrenoceptor alpha 2B	-7.06	-2.819	2.0E-03	
TPTE2P6	transmembrane phosphoinositide 3-phosphatase and tensin homolog 2 pseudogene 6	-7.05	-2.817	2.1E-03	
MYH15	myosin_ heavy chain 15	-7.04	-2.815	9.5E-13	
ZFP3	ZFP3 zinc finger protein	-7.03	-2.813	2.4E-44	
THEM6	thioesterase superfamily member 6	-7.02	-2.811	1.5E-13	
MOXD1	monooxygenase_ DBH-like 1	-7.01	-2.809	5.1E-14	
FBLN7	fibulin 7	-7.00	-2.808	9.6E-18	
LOC728819	NA	-7.00	-2.808	8.2E-05	
EPHA1-AS1	EPHA1 antisense RNA 1	-6.99	-2.806	2.2E-03	
PRL	prolactin	-6.99	-2.805	2.3E-03	
PSG4	pregnancy specific beta-1-glycoprotein 4	-6.96	-2.799	1.3E-03	
LOC646762	uncharacterized LOC646762	-6.96	-2.798	4.4E-40	
MIR497HG	mir-497-195 cluster host gene	-6.95	-2.796	9.7E-10	
PTER	phosphotriesterase related	-6.94	-2.795	3.8E-37	
ADAM12	ADAM metallopeptidase domain 12	-6.94	-2.794	2.2E-231	
ADH6	alcohol dehydrogenase 6 (class V)	-6.93	-2.794	1.3E-04	
FAM66D	family with sequence similarity 66_ member D	-6.91	-2.790	1.3E-07	
GUCY1A2	guanylate cyclase 1_ soluble_ alpha 2	-6.90	-2.787	8.6E-04	
MAPK13	mitogen-activated protein kinase 13	-6.87	-2.781	3.9E-55	
PLCL2	phospholipase C-like 2	-6.87	-2.780	1.7E-41	
POU3F2	POU class 3 homeobox 2	-6.86	-2.778	9.8E-04	
DDX43	DEAD (Asp-Glu-Ala-Asp) box polypeptide 43	-6.84	-2.774	2.6E-05	
HIST2H2BA	histone cluster 2_ H2ba (pseudogene)	-6.84	-2.774	1.8E-12	
IVL	involucrin	-6.83	-2.772	2.7E-03	
DOK7	docking protein 7	-6.82	-2.770	1.7E-04	
MUC13	mucin 13_ cell surface associated	-6.81	-2.767	2.8E-03	
FAM198B	family with sequence similarity 198_ member B	-6.79	-2.763	2.1E-31	
TRAPPCL	trafficking protein particle complex 3-like	-6.78	-2.761	2.7E-03	
PIWI2	piwi-like RNA-mediated gene silencing 2	-6.77	-2.760	1.3E-03	
RNF112	ring finger protein 112	-6.76	-2.757	5.0E-11	
LINC01060	long intergenic non-protein coding RNA 1060	-6.75	-2.756	2.7E-12	
PCDHGB8P	protocadherin gamma subfamily B_ 8 pseudogene	-6.75	-2.754	5.8E-04	

TABLE 8-continued

Genes more highly expressed in AD-MSCs compared with HMCs				
Gene name	Description	Fold Change	Log Fold Change	p-Adj
SOST	sclerostin	-6.74	-2.753	1.8E-03
FAM167B	family with sequence similarity 167_member B	-6.72	-2.749	2.2E-17
IL21R	interleukin 21 receptor	-6.72	-2.748	4.0E-64
DDIT4L	DNA-damage-inducible transcript 4-like	-6.71	-2.746	2.3E-05
C19orf81	chromosome 19 open reading frame 81	-6.71	-2.745	2.8E-03
AGTR1	angiotensin II receptor_type 1	-6.70	-2.745	1.8E-09
SCUBE3	signal peptide_CUB domain_EGF-like 3	-6.69	-2.742	9.5E-81
PDE2A	phosphodiesterase 2A_cGMP-stimulated	-6.69	-2.742	3.8E-04
MMP8	matrix metalloproteinase 8	-6.67	-2.739	5.0E-04
SHOX2	short stature homeobox 2	-6.66	-2.737	6.0E-41
DPY19L2P3	DPY19L2 pseudogene 3	-6.64	-2.731	3.0E-03
NPAS1	neuronal PAS domain protein 1	-6.63	-2.730	4.2E-17
FAM87A	family with sequence similarity 87_member A	-6.63	-2.729	3.3E-03
CEMIP	cell migration inducing protein_hyaluronan binding	-6.61	-2.725	3.4E-07
C1QTNF3	C1q and tumor necrosis factor related protein 3	-6.58	-2.718	1.0E-05
ADAMTSL1	ADAMTS-like 1	-6.58	-2.718	5.1E-33
TSPEAR-AS1	TSPEAR antisense RNA 1	-6.55	-2.713	1.1E-03
ASCL2	achaete-scute family bHLH transcription factor 2	-6.52	-2.705	5.9E-04
MYH3	myosin_heavy chain 3_skeletal muscle_embryonic	-6.51	-2.703	3.2E-13
RPSAP52	ribosomal protein SA pseudogene 52	-6.50	-2.701	4.2E-06
KCNJ2-AS1	KCNJ2 antisense RNA 1 (head to head)	-6.49	-2.697	3.6E-03
LINC00961	long intergenic non-protein coding RNA 961	-6.47	-2.695	2.7E-08
LINC01123	long intergenic non-protein coding RNA 1123	-6.45	-2.689	1.1E-06
TBX15	T-box 15	-6.44	-2.688	4.9E-09
MCOLN3	mucolipin 3	-6.43	-2.686	3.8E-03
ROR2	receptor tyrosine kinase-like orphan receptor 2	-6.43	-2.684	2.4E-04
DPP4	dipeptidyl-peptidase 4	-6.40	-2.678	2.3E-07
GPC4	glypican 4	-6.39	-2.677	4.1E-08
RBP4	retinol binding protein 4_plasma	-6.39	-2.675	1.6E-06
CDH1	cadherin 1_type 1	-6.37	-2.671	3.0E-05
COL14A1	collagen_type XIV_alpha 1	-6.37	-2.671	6.3E-05
SNCG	synuclein_gamma (breast cancer-specific protein 1)	-6.36	-2.669	2.5E-08
TSPAN2	tetraspanin 2	-6.35	-2.667	4.0E-13
PSG7	pregnancy specific beta-1-glycoprotein 7 (gene/pseudogene)	-6.35	-2.667	3.9E-03
LINC00161	long intergenic non-protein coding RNA 161	-6.34	-2.664	4.4E-03
ANXA8L1	annexin A8-like 1	-6.33	-2.662	5.9E-07
FAM129A	family with sequence similarity 129_member A	-6.31	-2.658	3.5E-51
GPR1	G protein-coupled receptor 1	-6.30	-2.656	5.4E-55
TEX36	testis expressed 36	-6.28	-2.650	4.5E-03
CCL20	chemokine (C-C motif) ligand 20	-6.28	-2.650	1.6E-03
LOC101929234	uncharacterized LOC101929234	-6.27	-2.648	2.3E-03
ANXA8	annexin A8	-6.25	-2.644	7.9E-08
ANO1	anoctamin 1_calcium activated chloride channel	-6.24	-2.641	3.2E-05
MFSD6	major facilitator superfamily domain containing 6	-6.22	-2.638	1.6E-28
LOC101929369	NA	-6.22	-2.637	7.4E-08
ARHGEF35	Rho guanine nucleotide exchange factor (GEF) 35	-6.21	-2.635	3.3E-19
GPAM	glycerol-3-phosphate acyltransferase_mitochondrial	-6.21	-2.634	6.0E-09
PRSS35	protease_serine_35	-6.20	-2.632	7.7E-07
IFI44	interferon-induced protein 44	-6.19	-2.630	1.1E-22
TACR1	tachykinin receptor 1	-6.18	-2.627	4.8E-03

TABLE 8-continued

Genes more highly expressed in AD-MSCs compared with HMCs				
Gene name	Description	Fold Change	Log Fold Change	p-Adj
COL16A1	collagen_type XVI_alpha 1	-6.17	-2.624	1.7E-108
FAIM2	Fas apoptotic inhibitory molecule 2	-6.16	-2.623	2.6E-07
TULP2	tubby like protein 2	-6.15	-2.621	1.6E-03
HERC3	HECT and RLD domain containing E3 ubiquitin protein ligase 3	-6.14	-2.618	1.5E-34
SLC47A1	solute carrier family 47 (multidrug and toxin extrusion)_member 1	-6.12	-2.614	4.4E-05
SLC30A3	solute carrier family 30 (zinc transporter)_member 3	-6.11	-2.612	1.7E-03
LOX	lysyl oxidase	-6.10	-2.609	1.2E-104
ACE	angiotensin I converting enzyme	-6.10	-2.608	1.7E-15
PPP4R4	protein phosphatase 4_regulatory subunit 4	-6.09	-2.605	1.1E-03
RDH5	retinol dehydrogenase 5 (11-cis/9-cis)	-6.08	-2.604	1.3E-05
CTD-2258A20.5	BEAN1 antisense RNA 1	-6.08	-2.604	5.1E-03
OTOF	otoferlin	-6.08	-2.604	1.1E-03
ZFP42	ZFP42 zinc finger protein	-6.08	-2.603	1.8E-04
PCSK6	proprotein convertase subtilisin/kexin type 6	-6.07	-2.601	3.4E-08
FAM13A-AS1	FAM13A antisense RNA 1	-6.06	-2.600	7.2E-06
HS3ST3A1	heparan sulfate (glucosamine) 3-O-sulfotransferase 3A1	-6.06	-2.599	3.0E-17
PRKG2	protein kinase_cGMP-dependent_type II	-6.06	-2.598	3.3E-03
KCNT2	potassium channel_sodium activated subfamily T_member 2	-6.05	-2.597	1.4E-07
PAMR1	peptidase domain containing associated with muscle regeneration 1	-6.05	-2.596	2.5E-09
MEG3	maternally expressed 3 (non-protein coding)	-6.03	-2.593	1.5E-24
NFIX	nuclear factor I/X (CCAAT-binding transcription factor)	-6.03	-2.591	1.6E-91
EPHA3	EPH receptor A3	-6.02	-2.590	5.2E-04
MAP3K8	mitogen-activated protein kinase kinase kinase 8	-6.02	-2.590	6.3E-21
LINC01204	long intergenic non-protein coding RNA 1204	-6.00	-2.585	9.8E-22
PTGIR	prostaglandin I2 (prostacyclin) receptor (IP)	-6.00	-2.584	1.7E-93
LOR	loricrin	-5.99	-2.582	5.9E-03
NTNG1	netrin G1	-5.98	-2.580	1.1E-05
LMO7DN	LMO7 downstream neighbor	-5.98	-2.579	2.1E-03
UNC13A	unc-13 homolog A (<i>C. elegans</i>)	-5.97	-2.579	1.6E-08
FREM1	FRAS1 related extracellular matrix 1	-5.97	-2.578	3.2E-03
CYP26B1	cytochrome P450_family 26_subfamily B_poly peptide 1	-5.97	-2.577	9.4E-05
LRRC38	leucine rich repeat containing 38	-5.96	-2.576	6.1E-03
PDPN	podoplanin	-5.95	-2.574	1.3E-03
RECK	reversion-inducing-cysteine-rich protein with kazal motifs	-5.94	-2.571	1.1E-165
UNC5B	unc-5 netrin receptor B	-5.94	-2.570	1.4E-06
GOLGA8K	golgin A8 family_member K	-5.93	-2.569	6.0E-03
ADAMTS1	ADAM metallopeptidase with thrombospondin type 1 motif_1	-5.93	-2.568	2.0E-06
C3orf55	PQ loop repeat containing 2-like	-5.92	-2.566	5.6E-27
NR1D1	nuclear receptor subfamily 1_group D_member 1	-5.91	-2.564	1.5E-82
HERC2P4	hect domain and RLD 2 pseudogene 4	-5.91	-2.563	2.2E-10
ADD2	adducin 2 (beta)	-5.90	-2.561	6.5E-03
SLC1A3	solute carrier family 1 (glial high affinity glutamate transporter)_member 3	-5.89	-2.559	5.4E-12
KLHL33	kelch-like family member 33	-5.89	-2.558	1.2E-04
ANGPTL4	angiopoietin-like 4	-5.89	-2.558	7.5E-09
MILR1	mast cell immunoglobulin-like receptor 1	-5.89	-2.557	8.7E-04
SLC17A9	solute carrier family 17 (vesicular nucleotide transporter)_member 9	-5.88	-2.556	4.0E-34
HSPB6	heat shock protein_alpha-crystallin-related_B6	-5.88	-2.556	1.1E-209

TABLE 8-continued

Genes more highly expressed in AD-MSCs compared with HMCs					
Gene name	Description	Fold Change	Log Fold Change	p-Adj	
MIR3613	microRNA 3613	-5.87	-2.554	6.3E-03	
TSIX	TSIX transcript_ XIST antisense RNA	-5.86	-2.552	6.5E-03	
P2RX5	purinergic receptor P2X_ ligand gated ion channel_ 5	-5.81	-2.540	9.3E-06	
CRIP1	cysteine-rich protein 1 (intestinal)	-5.81	-2.540	7.2E-122	
CALHM3	calcium homeostasis modulator 3	-5.81	-2.537	6.7E-03	
TIMP4	TIMP metallopeptidase inhibitor 4	-5.79	-2.533	4.2E-17	
C11orf70	chromosome 11 open reading frame 70	-5.77	-2.528	7.6E-23	
PDGFRA	platelet-derived growth factor receptor_ alpha polypeptide	-5.77	-2.527	3.2E-11	
TBX4	T-box 4	-5.76	-2.527	1.3E-03	
SORCS3	sortilin-related VPS10 domain containing receptor 3	-5.75	-2.524	7.3E-03	
SPATA41	spermatogenesis associated 41 (non-protein coding)	-5.72	-2.516	3.4E-03	
LOC101927905	uncharacterized LOC101927905	-5.72	-2.516	5.5E-07	
ANKRD20A5P	ankyrin repeat domain 20 family_ member A5_ pseudogene	-5.70	-2.512	2.7E-03	
IL1R1	interleukin 1 receptor_ type I	-5.70	-2.511	1.1E-64	
LURAP1L	leucine rich adaptor protein 1-like	-5.70	-2.511	4.5E-16	
GDNF-AS1	GDNF antisense RNA 1 (head to head)	-5.69	-2.509	2.5E-18	
LOC100505739	NA	-5.69	-2.509	7.6E-03	
MRO	maestro	-5.68	-2.506	7.6E-03	
RAP1GAP	RAP1 GTPase activating protein	-5.68	-2.505	2.6E-05	
PDE4C	phosphodiesterase 4C_ cAMP-specific	-5.68	-2.505	7.3E-05	
HSD3B7	hydroxy-delta-5-steroid dehydrogenase_ 3 beta- and steroid delta-isomerase 7	-5.67	-2.504	3.0E-57	
PRLR	prolactin receptor	-5.66	-2.501	3.2E-03	
ADAMTSL2	ADAMTS-like 2	-5.66	-2.500	2.3E-03	
SLC38A5	solute carrier family 38_ member 5	-5.66	-2.500	3.7E-60	
C4BPA	complement component 4 binding protein_ alpha	-5.65	-2.499	7.9E-03	
SLC38A4	solute carrier family 38_ member 4	-5.65	-2.498	2.4E-27	
MESP2	mesoderm posterior bHLH transcription factor 2	-5.64	-2.496	6.0E-05	
LINC01268	long intergenic non-protein coding RNA 1268	-5.63	-2.494	4.5E-03	
NPR1	natriuretic peptide receptor 1	-5.63	-2.494	2.7E-03	
COL3A1	collagen_ type III_ alpha 1	-5.63	-2.493	4.8E-26	
FAM107A	family with sequence similarity 107_ member A	-5.62	-2.490	2.5E-03	
FAM149A	family with sequence similarity 149_ member A	-5.61	-2.489	1.6E-26	
HCG4B	HLA complex group 4B (non-protein coding)	-5.61	-2.488	4.9E-04	
CHN1	chimerin 1	-5.61	-2.488	7.7E-47	
TMTC1	transmembrane and tetratricopeptide repeat containing 1	-5.60	-2.486	1.6E-10	
NEAT1	nuclear paraspeckle assembly transcript 1 (non-protein coding)	-5.59	-2.484	8.4E-11	
IGFL3	IGF-like family member 3	-5.59	-2.482	8.7E-03	
MFAP3L	microfibrillar-associated protein 3-like	-5.58	-2.480	1.9E-93	
PTGS2	prostaglandin-endoperoxide synthase 2 (prostaglandin G/H synthase and cyclooxygenase)	-5.58	-2.479	2.1E-05	
LINC00312	long intergenic non-protein coding RNA 312	-5.56	-2.476	1.5E-04	
PLA2G2A	phospholipase A2_ group IIA (platelets_ synovial fluid)	-5.55	-2.473	9.1E-03	
RGMA	repulsive guidance molecule family member a	-5.54	-2.470	1.0E-05	
CCDC158	coiled-coil domain containing 158	-5.53	-2.468	4.2E-03	
EMP1	epithelial membrane protein 1	-5.53	-2.468	1.3E-33	
MT1G	metallothionein 1G	-5.53	-2.467	4.5E-10	
ITGB8	integrin_ beta 8	-5.53	-2.467	4.5E-10	
ZNF311	zinc finger protein 311	-5.53	-2.466	2.1E-09	
HSD3B1	hydroxy-delta-5-steroid dehydrogenase_ 3 beta- and steroid delta-isomerase 1	-5.50	-2.458	9.6E-03	
F10	coagulation factor X	-5.48	-2.454	1.1E-08	

TABLE 8-continued

Genes more highly expressed in AD-MSCs compared with HMCs					
Gene name	Description	Fold Change	Log Fold Change	p-Adj	
LINC00478	mir-99a-let-7c cluster host gene	-5.47	-2.453	5.2E-04	
DOK6	docking protein 6	-5.46	-2.450	2.5E-08	
MIR193A	microRNA 193a	-5.46	-2.448	6.1E-04	
RASL11B	RAS-like_ family 11_ member B	-5.45	-2.446	7.0E-05	
AKR1C3	aldo-keto reductase family 1_ member C3	-5.44	-2.445	5.2E-11	
FAS	Fas cell surface death receptor	-5.44	-2.444	1.8E-61	
KY	kypboscoliosis peptidase	-5.44	-2.443	3.2E-15	
AGAP11	ankyrin repeat and GTPase domain Arf GTPase activating protein 11	-5.43	-2.442	9.8E-06	
PRRG4	proline rich Gla (G-carboxyglutamic acid) 4 (transmembrane)	-5.43	-2.441	2.1E-04	
MUC12	mucin 12_ cell surface associated	-5.43	-2.441	6.6E-03	
CYP21A2	cytochrome P450_ family 21_ subfamily A_ polypeptide 2	-5.42	-2.439	1.0E-02	
IL6	interleukin 6	-5.41	-2.436	1.2E-05	
ANKRD29	ankyrin repeat domain 29	-5.40	-2.433	1.7E-05	
NFIA	nuclear factor I/A	-5.39	-2.431	8.0E-25	
TENM2	teneurin transmembrane protein 2	-5.39	-2.430	1.3E-03	
LOC101928200	NA	-5.38	-2.427	3.0E-05	
CAMK2B	calcium/calmodulin-dependent protein kinase II beta	-5.37	-2.426	8.0E-03	
CDC20B	cell division cycle 20B	-5.35	-2.420	1.1E-02	
FPR3	formyl peptide receptor 3	-5.35	-2.419	1.1E-02	
MIR10A	microRNA 10a	-5.33	-2.415	1.1E-02	
TTC3P1	tetratricopeptide repeat domain 3 pseudogene 1	-5.33	-2.414	4.5E-08	
LY86	lymphocyte antigen 86	-5.33	-2.414	1.1E-02	
HRNR	hornerin	-5.32	-2.412	1.1E-02	
SERPING1	serpin peptidase inhibitor_ clade G (C1 inhibitor)_ member 1	-5.31	-2.409	1.4E-15	
NRG1	neuregulin 1	-5.31	-2.409	7.4E-09	
ALDH1A3	aldehyde dehydrogenase 1 family_ member A3	-5.31	-2.408	3.9E-05	
IL20RB	interleukin 20 receptor beta	-5.30	-2.407	1.7E-11	
MMP10	matrix metalloproteinase 10	-5.30	-2.406	5.2E-05	
ZNF704	zinc finger protein 704	-5.29	-2.403	1.2E-04	
OR2S2	olfactory receptor_ family 2_ subfamily S_ member 2 (gene/pseudogene)	-5.29	-2.403	2.4E-03	
RSPO3	R-spondin 3	-5.27	-2.398	7.5E-04	
BEND7	BEN domain containing 7	-5.27	-2.397	9.5E-22	
C21orf90	TSPEAR antisense RNA 2	-5.26	-2.396	1.2E-02	
SBSPON	somatomedin B and thrombospondin_ type 1 domain containing	-5.26	-2.395	9.7E-04	
EEF1DP3	eukaryotic translation elongation factor 1 delta pseudogene 3	-5.26	-2.395	3.2E-04	
LY6K	lymphocyte antigen 6 complex_ locus K	-5.25	-2.392	5.2E-03	
ENPP4	ectonucleotide pyrophosphatase/phosphodiesterase 4_ (putative)	-5.25	-2.392	5.9E-10	
EVPL	envoplakin	-5.24	-2.390	9.7E-03	
SFN	stratifin	-5.23	-2.386	8.8E-03	
CYP4V2	cytochrome P450_ family 4 subfamily V_ polypeptide 2	-5.22	-2.385	4.0E-15	
GJB5	gap junction protein beta 5 31.1 kDa	-5.22	-2.384	1.2E-02	
SERPINB2	serpin peptidase inhibitor_ clade B (ovalbumin)_ member 2	-5.21	-2.382	5.0E-05	
C2	complement component 2	-5.21	-2.382	2.0E-06	
LMO2	LIM domain only 2 (rhomboitin-like 1)	-5.21	-2.381	5.2E-05	
ELTD1	adhesion G protein-coupled receptor L4	-5.20	-2.379	1.3E-48	
ESR1	estrogen receptor 1	-5.20	-2.378	1.3E-02	
MYH8	myosin_ heavy chain 8_ skeletal muscle_ perinatal	-5.20	-2.378	1.2E-02	
GDNF	glial cell derived neurotrophic factor	-5.19	-2.376	9.7E-59	
KRT222	keratin 22_ type II	-5.18	-2.374	1.2E-02	
SNTB1	syntrophin_ beta 1 (dystrophin-associated protein A1_ 59 kDa_ basic component 1)	-5.18	-2.372	1.0E-05	

TABLE 8-continued

Genes more highly expressed in AD-MSCs compared with HMCs					
Gene name	Description	Fold Change	Log Fold Change	p-Adj	
PRUNE2	prune homolog 2 (<i>Drosophila</i>)	-5.17	-2.371	5.6E-03	
PCDHGA5	protocadherin gamma subfamily A_5	-5.16	-2.368	1.2E-05	
LBX2	ladybird homeobox 2	-5.16	-2.367	2.8E-09	
LINC01119	long intergenic non-protein coding RNA 1119	-5.16	-2.367	2.6E-11	
SLC4A4	solute carrier family 4 (sodium bicarbonate cotransporter)_ member 4	-5.15	-2.365	4.2E-83	
SEL1L3	sel-1 suppressor of lin-12-like 3 (<i>C. elegans</i>)	-5.15	-2.364	1.7E-90	
HSPA7	heat shock 70 kDa protein 7 (HSP70B)	-5.14	-2.363	3.1E-04	
PRKD1	protein kinase D1	-5.13	-2.358	2.6E-50	
ADPRH	ADP-ribosylarginine hydrolase	-5.13	-2.358	5.5E-30	
GPR116	adhesion G protein-coupled receptor F5	-5.11	-2.354	1.4E-02	
NKPD1	NTPase_KAP family P-loop domain containing 1	-5.11	-2.354	7.5E-03	
CNTD2	cyclin N-terminal domain containing 2	-5.11	-2.354	1.1E-04	
GAL	galanin/GMAP prepropeptide	-5.10	-2.351	7.0E-16	
ENPP1	ectonucleotide pyrophosphatase/phosphodiesterase 1	-5.09	-2.349	6.2E-07	
SERINC2	serine incorporator 2	-5.09	-2.347	4.9E-18	
ASS1	argininosuccinate synthase 1	-5.08	-2.344	5.7E-09	
PITX2	paired-like homeodomain 2	-5.07	-2.343	7.4E-05	
LINC00933	long intergenic non-protein coding RNA 933	-5.07	-2.342	4.4E-03	
C11orf96	chromosome 11 open reading frame 96	-5.06	-2.340	2.3E-03	
APOBEC3G	apolipoprotein B mRNA editing enzyme_catalytic polypeptide-like 3G	-5.04	-2.332	7.4E-21	
MBP	myelin basic protein	-5.02	-2.329	5.9E-14	
RGS7BP	regulator of G-protein signaling 7 binding protein	-5.02	-2.329	1.5E-02	
ACKR4	atypical chemokine receptor 4	-5.02	-2.327	7.8E-05	
TYMP	thymidine phosphorylase	-5.01	-2.324	2.4E-31	
MAB21L3	mab-21-like 3 (<i>C. elegans</i>)	-5.01	-2.324	1.5E-02	
DENN2DC	DENN/MADD domain containing 2C	-5.00	-2.323	2.7E-07	
FLJ46906	uncharacterized LOC441172	-5.00	-2.321	6.7E-21	
PSG11	pregnancy specific beta-1-glycoprotein 11	-5.00	-2.321	1.5E-02	

Example 12. miRNA Nanostring nCounter Analysis of HMC-EVs Vs BM-MSC-EVs Vs UCB-MSC-EVs Vs AD-MSC-EVs

[0436] HMCs were generated from the same bank of frozen hemangioblasts described in Example 1. HMCs were generated and passaged up to six passages (P6) according to the method described in Example 1. Extracellular vesicles (EVs) were purified from HMCs (HMC-EVs) by tangential flow filtration (TFF). miRNA profiling was performed using Nanostring nCounter Analysis system for three lots of HMC-EVs under basal conditions. EVs isolated from bone marrow (BM-MSC-EVs) (3 lots), umbilical cord blood (UCB-MSC-EVs) (3 lots), and adipose tissue (AD-MSC-EVs) under basal conditions were used as controls.

[0437] Table 9 shows miRNAs that were more highly expressed in the HMC-EVs compared with UCB-MSC-EVs. Table 10 shows miRNAs that were more highly expressed in UCB-MSC-EVs compared with the HMC-EVs. Table 11 shows miRNAs that were highly expressed in HMC-EVs compared with BM-MSC-EVs. Table 12 shows miRNAs that were more highly expressed in BM-MSC-EVs compared with the HMC-EVs. Table 13 shows miRNAs that were highly expressed in HMC-EVs compared with AD-MSC-EVs. Table 14 shows miRNAs that were more highly

expressed in AD-MSC-EVs compared with the HMC-EVs. HMC-EVs of the presently disclosed subject matter may be selected or purified based on one of the miRNAs that are differentially expressed.

TABLE 9

miRNAs with higher expression in HMC-EVs compared to UCB-MSC-EVs		
miRNA ID	Fold Difference	p-Value
hsa-miR-125b-5p	3.90	0.000
hsa-miR-100-5p	3.50	0.004
hsa-miR-21-5p	2.59	0.025
hsa-miR-199a-3p + hsa-miR-199b-3p	2.57	0.000
hsa-miR-23a-3p	2.37	0.013
hsa-miR-181a-5p	2.16	0.007
hsa-miR-199b-5p	2.07	0.000
hsa-miR-125a-5p	2.05	0.008
hsa-miR-1204	1.96	0.035
hsa-miR-106a-5p + hsa-miR-17-5p	1.73	0.013
hsa-let-7e-5p	1.68	0.017
hsa-miR-450a-5p	1.67	0.014

TABLE 10

miRNAs with higher expression in UCB- MSC-EVs compared to HMC-EVs		
miRNA ID	Fold Difference	p-Value
hsa-miR-1252-5p	-2.04	0.00
hsa-miR-376c-3p	-2.00	0.01
hsa-miR-196b-5p	-1.93	0.02
hsa-miR-4755-5p	-1.83	0.00
hsa-miR-211-3p	-1.81	0.05
hsa-miR-548d-3p	-1.66	0.05
hsa-miR-671-3p	-1.66	0.03
hsa-miR-1297	-1.56	0.01
hsa-miR-134-5p + hsa-miR-6728-5p	-1.55	0.05
hsa-mir-498	-1.52	0.01
hsa-miR-128-1-5p	-1.52	0.01
hsa-miR-1269b	-1.51	0.01

TABLE 11

miRNAs with higher expression in HMC-EVs compared to BM-MSC-EVs		
miRNA ID	Fold Difference	p-Value
hsa-miR-320e	13.68	0.035
hsa-miR-125b-5p	4.81	0.000
hsa-miR-100-5p	4.38	0.001
hsa-miR-181a-5p	3.42	0.007
hsa-miR-23a-3p	3.03	0.006
hsa-miR-21-5p	2.95	0.012
hsa-miR-199a-3p + hsa-miR-199b-3p	2.86	0.007
hsa-let-7a-5p	2.30	0.032
hsa-miR-221-3p	2.18	0.005
hsa-miR-199b-5p	2.07	0.000
hsa-miR-29a-3p	1.67	0.019
hsa-miR-125a-5p	1.64	0.034
hsa-let-7g-5p	1.54	0.025

TABLE 12

miRNAs with higher expression in BM- MSC-EVs compared to HMC-EVs		
miRNA ID	Fold Difference	p-Value
hsa-miR-1469	-2.34	0.026
hsa-miR-892b	-2.29	0.004
hsa-miR-664b-5p	-2.27	0.003
hsa-miR-151b	-2.20	0.012
hsa-miR-219a-2-3p	-2.16	0.035
hsa-miR-485-3p	-2.14	0.010
hsa-miR-134-5p + hsa-miR-6728-5p	-2.07	0.008
hsa-miR-195-5p	-2.05	0.014
hsa-miR-508-3p	-2.03	0.004
hsa-miR-5010-5p	-2.01	0.032
hsa-miR-629-5p	-1.99	0.018
hsa-miR-518d-3p	-1.99	0.035
hsa-miR-18b-5p	-1.98	0.037
hsa-miR-147a	-1.92	0.048
hsa-miR-196b-5p	-1.90	0.013
hsa-miR-486-3p	-1.88	0.032
hsa-miR-1258	-1.85	0.023
hsa-miR-548aa + hsa-miR-548t-3p	-1.81	0.034
hsa-miR-584-5p	-1.81	0.047
hsa-miR-3202	-1.80	0.012
hsa-miR-663a	-1.80	0.034
hsa-miR-517a-3p	-1.80	0.013
hsa-miR-329-3p	-1.80	0.019
hsa-miR-1248	-1.76	0.035
hsa-miR-628-3p	-1.76	0.013
hsa-miR-499b-5p	-1.75	0.038

TABLE 12-continued

miRNAs with higher expression in BM- MSC-EVs compared to HMC-EVs		
miRNA ID	Fold Difference	p-Value
hsa-miR-1279	-1.74	0.017
hsa-miR-873-3p	-1.74	0.048
hsa-miR-514a-5p	-1.73	0.008
hsa-miR-127-5p	-1.72	0.048
hsa-miR-491-3p	-1.71	0.019
hsa-miR-548k	-1.71	0.013
hsa-miR-566	-1.70	0.036
hsa-miR-520c-3p	-1.69	0.036
hsa-miR-591	-1.68	0.012
hsa-miR-129-5p	-1.67	0.013
hsa-miR-6503-3p	-1.66	0.011
hsa-miR-1183	-1.65	0.003
hsa-miR-1178-3p	-1.65	0.046
hsa-miR-885-3p	-1.65	0.019
hsa-miR-6721-5p	-1.62	0.013
hsa-miR-4536-5p	-1.61	0.033
hsa-miR-617	-1.61	0.027
hsa-miR-510-5p	-1.59	0.031
hsa-mir-498	-1.59	0.017
hsa-miR-142-5p	-1.59	0.006
hsa-miR-378d	-1.58	0.014
hsa-miR-3131	-1.58	0.016
hsa-miR-578	-1.57	0.041
hsa-miR-450a-2-3p	-1.57	0.002
hsa-miR-620	-1.57	0.024
hsa-miR-3613-3p	-1.57	0.012
hsa-miR-1234-3p	-1.57	0.049
hsa-miR-1269b	-1.57	0.029
hsa-miR-940	-1.56	0.007
hsa-miR-4787-5p	-1.55	0.019
hsa-miR-378h	-1.55	0.005
hsa-miR-654-5p	-1.53	0.028
hsa-miR-92b-3p	-1.51	0.044

TABLE 13

miRNAs with higher expression in HMC-EVs compared to AD-MSC-EVs		
miRNA ID	Fold Difference	p-Value
hsa-miR-125b-5p	5.73	0.004
hsa-miR-4454 + hsa-miR-7975	4.31	0.001
hsa-miR-100-5p	4.03	0.002
hsa-miR-181a-5p	3.39	0.001
hsa-miR-21-5p	3.20	0.021
hsa-miR-199a-3p + hsa-miR-199b-3p	3.06	0.011
hsa-miR-23a-3p	2.69	0.007
hsa-miR-125a-5p	2.22	0.024
hsa-miR-29a-3p	2.14	0.024
hsa-miR-450a-5p	2.11	0.004
hsa-miR-25-3p	2.02	0.000
hsa-miR-221-3p	1.99	0.009
hsa-miR-106a-5p + hsa-miR-17-5p	1.79	0.001
hsa-miR-199b-5p	1.76	0.027
hsa-miR-214-3p	1.65	0.034

TABLE 14

miRNAs with higher expression in AD-MSC EVs compared to HMC-EVs		
miRNA ID	Fold Difference	p-Value
hsa-miR-194-5p	-2.54	0.023
hsa-miR-665	-2.05	0.025
hsa-miR-219a-2-3p	-1.95	0.046

TABLE 14-continued

miRNAs with higher expression in AD-MSC EVs compared to HMC-EVs		
miRNA ID	Fold Difference	p-Value
hsa-miR-4536-3p	-1.91	0.049
hsa-miR-18b-5p	-1.87	0.039
hsa-miR-124-3p	-1.83	0.042
hsa-miR-127-5p	-1.83	0.016
hsa-miR-628-3p	-1.83	0.026
hsa-miR-2110	-1.80	0.022
hsa-miR-566	-1.77	0.027
hsa-miR-4755-5p	-1.76	0.025
hsa-miR-509-3p	-1.76	0.003
hsa-miR-578	-1.71	0.029
hsa-miR-1248	-1.66	0.030
hsa-miR-1252-5p	-1.63	0.034
hsa-miR-28-5p	-1.63	0.005
hsa-miR-128-1-5p	-1.62	0.014
hsa-miR-1183	-1.62	0.004
hsa-miR-1296-3p	-1.61	0.045
hsa-miR-1285-5p	-1.61	0.015
hsa-miR-485-3p	-1.60	0.032
hsa-miR-514a-5p	-1.59	0.039
hsa-miR-498	-1.58	0.024
hsa-miR-330-5p	-1.56	0.020
hsa-miR-10a-5p	-1.55	0.038
hsa-miR-888-5p	-1.55	0.013
hsa-miR-183-5p	-1.52	0.049
hsa-miR-760	-1.51	0.016
hsa-miR-6721-5p	-1.51	0.019
hsa-miR-664b-5p	-1.50	0.025

Example 13. Proteome Profiling for HMC-EVs Vs BM-MSC-EVs Vs UCB-MSC-EVs Vs AD-MSC-EVs

[0438] HMCs were generated from the same bank of frozen hemangioblasts described in Example 1. HMCs were generated and passaged up to six passages (P6) according to the method described in Example 1. Extracellular vesicles (EVs) were purified from HMCs (HMC-EVs) by tangential flow filtration (TFF). Proteome profiling by standard mass spectrometry analysis was performed for three lots of HMC-EVs under basal conditions. EVs isolated from bone marrow (BM-MSC-EVs) (3 lots), umbilical cord blood (UCB-MSC-EVs) (3 lots), and adipose tissue (AD-MSC-EVs) under basal conditions were used as controls.

[0439] T-test statistical analysis was used to identify proteins with significant differences in abundance between EV types. Table 15 shows proteins that were more highly abundant in the HMC-EVs compared with UCB-MSC-EVs. Table 16 shows proteins that were more highly abundant in UCB-MSC-EVs compared with the HMC-EVs. Table 17 shows proteins that were more highly abundant in HMC-EVs compared with BM-MSC-EVs. Table 18 shows proteins that were more highly abundant in BM-MSC-EVs compared with the HMC-EVs. Table 19 shows proteins that were more highly abundant in HMC-EVs compared with AD-MSC-EVs. Table 20 shows proteins that were more highly abundant in AD-MSC-EVs compared with the HMC-EVs. HMC-EVs of the presently disclosed subject matter may be selected or purified based on any of the proteins that are differentially abundant.

[0440] The proteomics data was subsequently analysed to determine how the overall protein expression profile may affect different signaling pathways. FIG. 63A depicts the pathway enrichment of differential expression pattern

between HMC-EVs and BM-MSC-EVs. FIG. 64A depicts the pathway enrichment of differential expression pattern between HMC-EVs and AD-MSC-EVs. FIG. 65A depicts the pathway enrichment of differential expression pattern between HMC-EVs and EVs secreted from umbilical cord blood-derived MSCs (UCB-MSC-EVs). As shown in FIGS. 63A, 64A and 65A, certain pathways are up-regulated (see orange bars) in HMC-EVs as compared to EVs secreted from other tissue-derived MSCs, such as pathways involved in LXR/RXR activation, acute phase response signaling, B cell receptor signaling, and systemic lupus erythematosus in B cell signaling pathway. In addition, proteins contributing to certain pathways, for example, IL-15 signaling, claritin-mediated endocytosis signaling, and FXR/RXR activation, are also enriched (see white and gray bars). etc

[0441] Diseases or functional annotation of proteins that are differentially expressed in HMC-EVs and EVs secreted from tissue-derived MSCs are also analyzed. FIG. 63B depicts the functional annotation of proteins that are upregulated in HMC-EVs when compared to BM-MSC-EVs. FIG. 63C depicts the functional annotation of proteins that are downregulated in HMC-EVs when compared to BM-MSC-EVs. FIG. 64B depicts the functional annotation of proteins that are upregulated in HMC-EVs when compared to AD-MSC-EVs. FIG. 64C depicts the functional annotation of proteins that are downregulated in HMC-EVs when compared to AD-MSC-EVs. FIG. 65B depicts the functional annotation of proteins that are upregulated in HMC-EVs when compared to UCB-MSC-EVs. FIG. 65C depicts the functional annotation of proteins that are downregulated in HMC-EVs when compared to UCB-MSC-EVs. An activation z-score above 2 or below -2 is considered as the threshold value. The analysis suggests that proteins involved in cell viability/survival, cellular movement, cell-to-cell signalizing and interaction pathways are upregulated in HMC-EVs, whereas proteins involved in cell death or apoptosis are downregulated in HMC-EVs.

TABLE 15

Proteins significantly more abundant in HMC-EVs compared to UCB-MSC EVs		
Name	log 2 fold difference	p-value
SLC2A1	5.55	1.62E-05
MFGE8	5.07	2.17E-04
MAMDC2	4.72	2.05E-03
H3-3A	4.31	2.35E-04
MARCKSL1	4.11	1.78E-04
KIF11	4.08	3.76E-05
PRSS23	3.97	2.13E-02
SLC3A2	3.95	2.18E-03
CD81	3.85	2.02E-03
TSPAN14	3.84	7.49E-05
CD99	3.79	3.63E-03
MDGA1	3.78	1.66E-03
RPS18	3.76	5.81E-04
CAV1	3.70	1.10E-03
KRT4	3.69	3.30E-04
MVP	3.57	7.81E-04
KPNA2	3.47	1.25E-03
HLA-A	3.47	1.10E-02
TRIM5	3.46	6.75E-04
KRAS	3.46	1.36E-04
ANXA5	3.35	2.75E-03
GNG12	3.32	8.10E-05
S100A11	3.31	2.61E-03
H4-16	3.22	2.39E-05

TABLE 15-continued

Proteins significantly more abundant in HMC-EVs compared to UCB-MSC EVs		
Name	log 2 fold difference	p-value
PCDH1	3.19	2.16E-03
ITGAV	3.17	1.55E-03
H3-7	3.11	7.29E-04
TNC	3.09	2.30E-02
VAT1	3.09	2.25E-04
RAP2A	3.06	2.12E-03
UCHL1	3.01	3.08E-03
FDPS	3.01	2.08E-03
H2AC20	3.01	4.80E-03
RPS4X	3.00	4.96E-03
BASP1	2.99	2.49E-06
CKM	2.97	1.41E-03
B2M	2.89	1.16E-02
TSPAN9	2.89	8.06E-04
RPS3A	2.83	3.59E-03
RPS13	2.82	4.48E-03
MMP14	2.78	2.06E-06
GNAI2	2.77	2.88E-05
YWHAQ	2.77	4.56E-03
PDIA3	2.75	7.76E-03
RALA	2.75	5.45E-03
RPS3	2.74	1.77E-03
EPB41L3	2.70	1.75E-03
SLC44A1	2.70	2.09E-03
ARL8A	2.69	5.53E-03
H1-3	2.69	1.27E-03
NIBAN2	2.64	2.11E-05
ITGA2	2.63	5.60E-06
TUBB3	2.63	1.77E-02
BBS1	2.62	5.29E-03
MAPK3	2.61	4.10E-03
YWHAB	2.58	5.14E-03
H2BC15	2.58	1.87E-05
TRPM2	2.52	9.52E-03
GALE	2.49	2.26E-04
CA2	2.49	2.81E-04
H2AC21	2.48	1.22E-02
TTYH3	2.45	1.23E-05
PDGFRB	2.44	2.84E-05
CD47	2.41	5.97E-05
DTD1	2.41	3.62E-03
GP9	2.39	2.26E-03
TAGLN2	2.38	1.02E-02
GNAQ	2.37	4.97E-03
PPP2R1A	2.37	2.16E-02
ALDOC	2.36	1.08E-03
RPS15A	2.35	8.55E-03
MERTK	2.35	4.34E-03
MDH1	2.34	1.63E-05
TPT1	2.27	1.35E-03
EIF5A	2.21	2.70E-02
LYN	2.20	2.74E-02
VCAN	2.18	7.73E-09
CYFIP1	2.18	5.89E-03
APBB2	2.18	1.93E-02
SDCBP	2.16	1.56E-06
LAP3	2.16	2.08E-02
KRT13	2.15	3.25E-02
LRRC59	2.13	5.62E-03
RPL13	2.13	4.00E-04
CD36	2.12	2.49E-05
SRSF8	2.08	2.45E-05
TSPAN33	2.03	4.53E-03
TPTE2	2.03	2.17E-02
HLA-A	2.02	1.02E-02
EPHB2	1.93	9.56E-03
FAH	1.93	4.25E-03
FUCA1	1.90	3.24E-04
MARCKS	1.89	2.79E-05
GP1BB	1.88	2.91E-04
CD276	1.88	1.48E-03
ACLY	1.86	2.15E-02

TABLE 15-continued

Proteins significantly more abundant in HMC-EVs compared to UCB-MSC EVs		
Name	log 2 fold difference	p-value
YWHAE	1.86	1.50E-02
PLAA	1.85	2.05E-02
UBE2L3	1.85	2.75E-02
WARS1	1.83	9.19E-04
AOC3	1.83	3.71E-05
BGN	1.82	1.55E-07
AGRN	1.82	8.24E-06
SLC44A2	1.78	3.13E-02
RPL11	1.77	1.77E-02
FARP1	1.73	5.55E-03
ITGA3	1.72	6.48E-07
ANXA2	1.71	3.90E-05
STX11	1.71	4.14E-05
TBC1D2	1.71	1.96E-02
PGAP1	1.71	5.86E-06
RPL14	1.68	1.27E-02
RPL10A	1.66	9.01E-06
CD63	1.66	5.06E-05
CPN2	1.63	4.56E-06
RPS25	1.62	8.88E-03
BLVRA	1.62	3.32E-03
PPP2CB	1.62	2.58E-04
LGALS1	1.59	1.48E-05
S100A6	1.51	2.82E-07
MEIOB	1.51	4.95E-06
NME2	1.51	2.23E-03
OSMR	1.50	2.78E-02
SEPTIN5	1.49	6.58E-03
MYL12B	1.49	1.38E-03
FN3KRP	1.49	9.63E-03
CDH5	1.48	4.17E-05
ITGA2B	1.48	1.11E-05
HLA-B	1.47	1.33E-04
BMP1	1.46	4.26E-02
CLIC4	1.45	1.31E-03
BST1	1.45	1.05E-03
ITGB1	1.45	6.19E-11
STRADB	1.44	2.93E-04
MOB1B	1.43	5.59E-03
SDC1	1.43	4.81E-03
B4GALT1	1.42	3.27E-03
ITGA6	1.38	2.40E-09
RPL4	1.36	3.19E-02
ITGA4	1.33	4.40E-04
COL4A2	1.33	3.97E-07
PDCD6IP	1.32	1.34E-07
MSN	1.32	1.34E-07
PF4	1.32	2.10E-03
STXBPA2	1.31	1.64E-02
ARF6	1.30	3.43E-02
EDIL3	1.29	1.12E-02
COTL1	1.29	1.54E-02
ITGA5	1.28	1.34E-05
QSOX1	1.28	3.43E-04
RALB	1.28	1.71E-04
NAGLU	1.28	6.87E-04
GNB1	1.28	3.11E-03
PDE4DIP	1.27	2.47E-04
CBR1	1.27	3.98E-03
ROBO4	1.26	8.58E-04
FBLN1	1.25	1.33E-02
STOM	1.25	2.40E-05
SRPX	1.25	4.98E-04
GSTM2	1.24	1.05E-04
ZNF607	1.23	7.88E-05
KIT	1.21	8.09E-05
LAMP1	1.21	7.48E-03
SEPTIN2	1.21	3.37E-04
CDC42	1.20	2.49E-03
ANXA6	1.19	3.38E-05
TANK	1.17	1.89E-05
UBA52	1.17	2.31E-04

TABLE 15-continued

Proteins significantly more abundant in HMC-EVs compared to UCB-MSC EVs		
Name	log 2 fold difference	p-value
COL18A1	1.17	1.41E-02
PAFAH1B1	1.15	3.38E-02
NUTF2	1.15	5.64E-04
TPI1	1.14	3.11E-07
LRP1	1.14	1.21E-04
SERPINA10	1.14	8.66E-03
MYO1F	1.13	2.84E-03
VNN1	1.12	1.99E-04
RPSA	1.12	1.82E-04
ARPC5	1.12	2.29E-02
CTBS	1.11	1.26E-07
MON2	1.11	1.38E-05
LUM	1.10	1.24E-03
RPS12	1.08	5.10E-03
PGLYRP2	1.08	5.38E-05
APOC4	1.08	9.84E-04
BANF1	1.08	1.55E-02
PRG4	1.07	3.13E-02
SERPINE2	1.07	1.26E-02
AHSG	1.07	2.87E-07
DYNLL1	1.06	3.53E-06
RAC1	1.06	3.65E-04
PRKAR1A	1.06	2.75E-03
SH3BGRL3	1.05	1.10E-03
CD9	1.04	7.31E-08
CLPP	1.04	9.54E-03
DEFA3	1.03	2.28E-02
CCT4	1.03	1.79E-04
HSPA4L	1.03	5.99E-04
EFEMP1	1.02	2.90E-02
GLIPR2	1.02	1.07E-03
ITGB3	1.02	1.86E-05
FUCA2	1.01	1.66E-02
PROCR	1.01	9.71E-05
CFHR1	1.00	1.67E-04
YWHAZ	1.00	3.72E-06

TABLE 16

Proteins significantly more abundant in UCB-MSC EVs compared to HMC-EVs		
Name	log 2 fold difference	p-value
TMEM198	-5.16	3.92E-10
CAT	-5.16	1.45E-06
SPON2	-4.11	5.60E-05
DOK4	-4.09	3.21E-05
LRAT	-3.88	3.31E-05
ADIPOQ	-3.85	3.79E-04
PTX3	-3.69	7.69E-06
CHST9	-3.52	5.30E-07
CEP290	-3.46	3.05E-03
FAM151B	-3.41	1.76E-02
IGHV1-45	-3.36	1.71E-02
MSH6	-3.22	7.41E-03
SNTG1	-3.11	4.29E-06
AKAP9	-2.92	3.94E-06
MUC16	-2.91	2.71E-03
ALB	-2.87	5.77E-04
LRRTM2	-2.79	8.46E-05
SURF1	-2.77	1.45E-02
CDSN	-2.76	1.11E-02
PSMA6	-2.73	7.91E-05
F11	-2.68	4.35E-08
ALOX5	-2.63	3.36E-06
SEMA7A	-2.52	1.92E-02
TAS2R33	-2.50	2.27E-03
IGHV3-38-3	-2.48	1.14E-03

TABLE 16-continued

Proteins significantly more abundant in UCB-MSC EVs compared to HMC-EVs		
Name	log 2 fold difference	p-value
TYMP	-2.47	7.15E-06
MMRN2	-2.47	1.11E-02
PAK6	-2.46	4.81E-03
LDLR	-2.46	1.24E-02
KRT17	-2.45	3.78E-02
CCIN	-2.45	1.39E-03
RGS14	-2.39	5.06E-03
TRIM4	-2.38	7.42E-03
CFHR5	-2.38	1.71E-02
AP3B2	-2.34	1.05E-02
TIMP3	-2.34	3.57E-04
L1CAM	-2.31	3.56E-06
IGHV3OR16-13	-2.27	3.03E-02
AB13	-2.24	1.71E-03
BLMH	-2.20	3.37E-03
S100A9	-2.19	3.76E-06
LAMB4	-2.16	1.42E-02
LTF	-2.15	2.62E-02
ERC1	-2.14	1.10E-02
APLP2	-2.12	6.31E-03
ZSWIM9	-2.11	7.12E-03
OLFML3	-2.10	1.82E-02
CTHRC1	-2.10	1.79E-05
CD109	-2.07	1.92E-02
IGLV6-57	-2.04	4.16E-04
REG1A	-2.02	1.27E-02
CCBE1	-2.02	1.36E-02
OAF	-2.01	2.28E-05
NEO1	-1.97	2.41E-02
NBEAL2	-1.92	1.99E-02
PIWIL2	-1.84	3.95E-05
SBSN	-1.82	4.12E-02
CAPN5	-1.80	1.04E-08
TRIM7	-1.76	1.08E-06
ZNF804B	-1.73	1.35E-03
LYVE1	-1.72	4.57E-04
ACTR1A	-1.70	1.16E-02
IGHG2	-1.67	9.34E-10
DSC1	-1.66	2.60E-04
PDZK1P1	-1.63	8.47E-04
FHL1	-1.61	1.39E-02
PSMA7	-1.58	1.94E-07
DBH	-1.55	1.42E-03
IGHV3-74	-1.53	2.05E-05
PRXL2B	-1.53	2.10E-07
C18orf63	-1.51	5.55E-06
IGHG1	-1.48	2.23E-09
PSMA4	-1.45	3.77E-03
UBTD1	-1.45	2.11E-06
PIEZ01	-1.44	1.14E-05
MYCBP2	-1.43	1.76E-02
NYAP2	-1.43	2.19E-06
CCDC110	-1.42	1.18E-05
ZNF800	-1.41	1.95E-07
VEGFA	-1.41	3.31E-02
FBRSL1	-1.41	1.61E-04
GTF2IRD2	-1.39	1.99E-06
PPM1F	-1.39	4.41E-02
HGFAC	-1.37	5.90E-03
IGLV3-1	-1.36	8.16E-04
CD99L2	-1.36	6.57E-06
L1TD1	-1.35	4.40E-11
KRT16	-1.34	2.76E-03
XPNPEP2	-1.34	2.62E-05
IGHA2	-1.32	7.71E-04
ADA	-1.30	2.88E-07
ALB	-1.30	1.22E-02
IGLV2-18	-1.29	2.05E-02
IGHV4-4	-1.28	2.45E-09
COLEC11	-1.27	1.39E-02
PKP1	-1.24	1.57E-03
MYH3	-1.23	4.39E-02

TABLE 16-continued

Proteins significantly more abundant in UCB-MSC EVs compared to HMC-EVs		
Name	log 2 fold difference	p-value
TGFB1	-1.23	2.74E-06
IGHV1-69	-1.23	1.28E-04
IGLV3-21	-1.22	2.11E-08
DDX55	-1.20	9.05E-10
IGHA1	-1.20	5.28E-11
ANO7	-1.20	1.08E-07
MPP1	-1.19	1.11E-03
GPR179	-1.19	4.94E-06
WDR46	-1.19	1.08E-04
SYMPK	-1.18	2.74E-05
TNFAIP6	-1.13	1.92E-06
RACK1	-1.13	2.93E-04
LOXL2	-1.12	3.21E-02
A2M	-1.12	3.96E-07
S100A8	-1.11	4.92E-06
IGKV3D-20	-1.11	6.86E-06
ITIH1	-1.10	1.87E-09
GDI1	-1.09	9.12E-06
IGHV5-10-1	-1.06	4.68E-05
CYLC2	-1.05	2.35E-05
IGHD	-1.04	1.81E-04
VTI1B	-1.04	8.83E-04
VCP	-1.03	9.97E-07
USP4	-1.03	1.72E-04
ATAD2	-1.03	1.41E-05
TF	-1.03	4.24E-08
F13B	-1.03	7.08E-05
ITIH3	-1.02	1.71E-06
IGLV3-25	-1.02	1.38E-07
CCT6A	-1.01	1.46E-02
CFH	-1.00	2.81E-06
IGLV3-27	-1.00	2.68E-06

TABLE 17

Proteins significantly more abundant in HMC-EVs compared to BM-MSC EVs		
Name	log 2 fold difference	p-value
GDF10	9.24	9.5E-08
L1TD1	7.45	0.004719
CD82	7.27	6.06E-07
ZNF607	7.18	6.84E-07
KRT78	6.83	2.14E-07
H2AC20	6.53	1.75E-06
IGKV1-17	6.46	5.34E-05
GATA5	6.34	2.64E-06
H3-3A	6.10	5.68E-05
GOLGB1	5.73	4.16E-06
CCT4	5.39	4.42E-06
DYNLL1	5.38	0.000324
ARHGDI1	5.36	0.000256
B4GALT1	5.26	2.07E-05
LTBP3	5.17	0.008415
CORO1A	5.15	6.22E-10
ADGRG6	5.14	1.64E-07
PRDM5	5.11	3.57E-06
STAC2	5.10	4.11E-05
IGLV2-14	5.10	0.000465
ROBO4	5.04	7.26E-09
MBTD1	5.03	8.28E-06
CHMP4B	4.98	0.002437
IGHV5-10-1	4.93	0.000306
FAM76A	4.93	2.98E-06
C4B_2	4.86	0.000418
OBSCN	4.81	5.91E-05
N4BP1	4.79	0.002836
VCP	4.76	0.000141

TABLE 17-continued

Proteins significantly more abundant in HMC-EVs compared to BM-MSC EVs		
Name	log 2 fold difference	p-value
MYEF2	4.65	0.014568
EXOC1	4.62	1.8E-07
IGHV4-4	4.61	0.000758
SLC2A1	4.38	4.24E-06
SPARC	4.33	6.11E-08
FBLN1	4.32	2.04E-07
NBPF4	4.30	0.014757
BASP1	4.29	0.002139
MYO1F	4.22	4.22E-06
PIK3CA	4.14	0.000126
STRADB	4.11	0.00015
MERTK	4.10	7.49E-05
DENND1B	4.08	0.000505
COL4A1	4.08	8.57E-05
SLTM	4.05	1.03E-05
LGALS1	4.03	0.010051
CFHR1	4.03	3.92E-05
TSPAN14	3.92	3.45E-05
MARCKSL1	3.91	1.26E-05
CAV1	3.83	7.42E-05
ZNF879	3.81	5.73E-05
MIF	3.78	0.00036
MVP	3.78	2.82E-06
STXBP2	3.77	2.93E-05
TAGLN2	3.77	2.81E-11
MOB1B	3.77	0.000694
TSKU	3.76	0.001976
PMVK	3.72	0.000187
TNC	3.71	0.000233
GPX3	3.68	2E-06
GOT1L1	3.68	6.05E-06
EDIL3	3.68	1.24E-06
SNX14	3.63	0.00065
MYL12B	3.63	0.000851
KRT4	3.61	0.000113
COL5A2	3.59	0.002899
PRAMEF10	3.57	2.37E-05
ITGA2	3.51	1E-05
CDH5	3.48	0.000121
APBB2	3.48	0.005607
CCN2	3.47	0.000961
ALOX12	3.45	0.001648
SLC3A2	3.45	0.000745
IGLV1-40	3.44	0.000266
YWHAH	3.44	0.002303
H3-7	3.42	0.004263
TIMP1	3.42	0.008573
GNB2	3.41	0.009415
VAT1	3.40	4.14E-05
PLCH1	3.39	1.03E-07
IGKV1D-16	3.39	0.000314
SMG1	3.38	9.29E-08
CALR	3.38	0.005623
RPS18	3.37	0.000232
CYP11B1	3.37	0.00017
RPSA	3.35	0.008587
IGHV3-64	3.33	0.001246
CDH13	3.31	8.2E-09
PDIA3	3.30	0.000169
MMP14	3.26	0.026749
PCDH1	3.25	9.86E-05
MFGE8	3.23	0.00748
IGHV1-18	3.22	3.63E-06
IGHG4	3.21	0.000498
TSPAN9	3.21	0.000157
ALDOC	3.21	5.46E-07
BIN2	3.20	0.035938
STN1	3.19	0.00191
GNAQ	3.18	0.002647
GANAB	3.17	6.5E-05
ADA	3.14	0.030644
PF4	3.13	7.99E-08

TABLE 17-continued

Proteins significantly more abundant in HMC-EVs compared to BM-MSC EVs		
Name	log 2 fold difference	p-value
ARPC5	3.09	0.000116
HLA-A	3.09	0.006161
APRT	3.07	0.000978
PAFAH1B1	3.07	1.37E-05
PGAP1	3.06	8.7E-05
PRG4	3.06	1.28E-05
CAP1	3.02	1.92E-08
COL18A1	3.02	0.015049
ATP6V1E1	3.02	0.004046
IGLV2-18	3.01	0.000485
KPNA2	3.01	0.001586
ANXA6	3.00	7E-06
TRIM5	2.97	0.006958
CD99	2.96	0.001694
HSPB1	2.92	0.000978
PXDN	2.92	1.47E-06
H4-16	2.92	8.26E-05
PON3	2.91	2.32E-05
BLVRA	2.90	0.016521
CLIC4	2.88	0.001057
RPL18	2.87	4.68E-05
YWHAE	2.87	0.001475
EEF1D	2.87	0.001449
UCHL1	2.85	0.00102
SDCBP	2.85	6.09E-07
KIF3B	2.84	0.000319
APOC4	2.83	2.48E-05
GPR108	2.83	0.000693
MDGA1	2.79	0.013423
SFRP1	2.79	0.035069
LCP2	2.79	4.89E-05
ANXA5	2.78	5.76E-05
FGD6	2.77	0.001047
DSP	2.76	2.7E-05
TTYH3	2.76	0.005149
MMP2	2.75	0.001
AEBP1	2.75	0.00897
RPS3A	2.74	2.67E-06
RPLP2	2.74	0.000334
GNG12	2.72	0.003946
FDPS	2.72	0.013411
DSG1	2.72	3.89E-07
YWHAQ	2.71	0.001864
IGKV1-16	2.69	0.006457
LAMP1	2.69	0.003596
ENG	2.68	0.000983
TPM3	2.67	1.31E-06
MYO3A	2.67	0.022487
CAPN1	2.67	0.004755
MAMDC2	2.64	0.014581
MYH13	2.63	0.010167
CCDC110	2.61	0.025959
UNC13D	2.61	6.39E-05
AZGP1	2.59	8.12E-08
IGLV7-46	2.59	2.12E-05
MFAP2	2.58	0.000225
KRAS	2.57	0.000972
ESD	2.57	0.005135
DSTN	2.54	0.006875
BST1	2.52	0.018602
CNTFR	2.51	0.006624
IGHV1-46	2.50	1.45E-05
MYLK	2.49	0.000117
H2AC21	2.47	0.001132
HSP90AA1	2.45	1.04E-08
COL9A1	2.44	0.003595
ARPC1B	2.44	0.002084
TGM2	2.43	0.00205
SLC44A2	2.43	0.012886
TPP1	2.41	0.002061
EPB41L1	2.39	0.026857
PACSIN2	2.38	3.55E-05

TABLE 17-continued

Proteins significantly more abundant in HMC-EVs compared to BM-MSC EVs		
Name	log 2 fold difference	p-value
CCNB3	2.36	0.001287
FHL1	2.36	0.002402
GP9	2.35	0.003498
SDC4	2.35	6.41E-05
COP1	2.33	0.000435
S100A13	2.32	0.00412
GMPR	2.32	0.006239
RAB8B	2.31	0.001874
CKM	2.31	0.011772
TMC8	2.31	0.026692
RAC2	2.27	3.6E-10
F13A1	2.26	2.5E-07
CD34	2.25	0.002686
PLOD1	2.25	0.000714
ARHGAP1	2.24	0.009884
CCT7	2.24	0.007496
LRRC59	2.23	0.006427
GNB1	2.21	8.13E-05
TSPAN33	2.21	0.014502
TUBA8	2.20	0.00438
GDI2	2.20	0.001214
GPX1	2.19	4.02E-05
UBE2D3	2.19	0.019397
AGRN	2.19	1.05E-05
HIP1	2.18	0.013348
DNAH14	2.18	0.034721
PTPRJ	2.17	0.010632
EPB41L3	2.17	0.004269
KIT	2.17	1.47E-07
EEF1G	2.16	0.001644
COMP	2.15	0.000843
COPS5	2.15	0.006709
CROCC	2.14	0.017985
PDGFRB	2.14	0.024622
MARCKS	2.13	9.55E-05
SEPTIN7	2.12	0.029813
TRIM7	2.11	0.017447
MPP1	2.11	0.028828
ARF3	2.11	4.97E-05
PEBP1	2.11	7.82E-05
RPL4	2.11	0.015036
CD81	2.11	0.022106
UTRN	2.10	0.013306
PARVB	2.07	3.93E-06
UBA1	2.07	0.00192
FLT1	2.07	0.000237
FGA	2.06	3.05E-08
STX11	2.05	0.005538
SYMPK	2.05	0.029327
RPS4X	2.05	0.000531
ACTN4	2.03	0.000159
ENO1	2.03	1.17E-07
RPL13	2.02	0.036252
TGFBI	2.02	0.010422
IGKV3D-15	2.01	0.03058
MTHFD1	1.98	0.033147
PDCD6IP	1.98	9.8E-05
LOXL2	1.98	0.002378
RALA	1.97	0.030452
ITGB1	1.96	8E-11
LAMC2	1.95	0.000129
VASN	1.95	1.91E-06
CAPZA2	1.95	0.001251
IDE	1.95	6.78E-05
EIF5A	1.95	0.000575
ACTR2	1.94	6.37E-07
RPL14	1.94	0.001723
LAP3	1.94	5.36E-05
PLAA	1.92	0.003494
CYFIP1	1.92	0.025712
CAMP	1.91	0.023111
UBE2L3	1.90	0.011389

TABLE 17-continued

Proteins significantly more abundant in HMC-EVs compared to BM-MSC EVs		
Name	log 2 fold difference	p-value
ZNF800	1.90	0.022228
RPS25	1.90	0.00532
RPL11	1.89	0.012891
CD63	1.88	0.001159
IGFALS	1.88	1.01E-05
IGHV3-20	1.87	0.002723
YWHAZ	1.86	0.001333
SAR1A	1.85	0.003235
CALU	1.85	0.000369
DNAJB2	1.84	0.016971
GAPDH	1.84	7.75E-06
EGFR	1.83	9.58E-05
IGKV6D-21	1.80	0.017376
ITGA3	1.80	2.31E-09
KRT16	1.80	0.006106
IGLV8-61	1.76	0.00018
CAPNS1	1.75	0.016719
RPS3	1.74	0.005878
NT5E	1.74	0.013852
PKM	1.71	0.002702
FLNA	1.70	5.52E-07
TUBB3	1.70	0.017002
ANXA7	1.66	0.004786
IGHV2-5	1.66	0.001333
HRNR	1.65	0.00186
RPS15A	1.65	0.003786
ARF6	1.62	0.005927
PDIA3	1.62	0.001716
H2BC15	1.61	0.000244
FUCA1	1.60	8.36E-06
C1QA	1.60	0.00089
GLIPR2	1.60	0.000144
DDX55	1.59	0.035084
PDLIM7	1.59	1.72E-05
SERPINE1	1.59	0.00105
CALM3	1.59	0.026876
NPTX1	1.58	0.023521
NIBAN2	1.58	0.007383
PPBP	1.57	0.000391
HK1	1.57	0.031509
FCN3	1.57	0.000268
MYL6	1.57	0.000755
PTGES3	1.56	0.023852
GPR179	1.55	0.004002
PRDX6	1.55	7.44E-05
VCAN	1.54	0.003195
MSN	1.54	1.34E-05
C1RL	1.52	4.62E-07
RAB8A	1.52	0.000118
HTRA1	1.51	0.027976
C1QB	1.51	0.000215
S100A4	1.51	0.034502
IGHV3-64D	1.51	0.001005
DTD1	1.50	0.007098
THBS2	1.50	0.023918
PATJ	1.50	5.49E-05
CFH	1.50	0.00065
HSPA5	1.49	2.24E-05
UBA52	1.49	0.006603
HLA-A	1.49	0.027277
IGKV3-7	1.49	6.84E-05
RAP2A	1.48	0.01951
CNTNAP5	1.48	0.020994
APOA1	1.47	7.05E-05
CD59	1.46	0.017075
TGFBI	1.46	0.000145
EHD3	1.45	6.79E-07
TMT2C	1.45	0.000856
CD276	1.45	0.003687
IGLV3-21	1.45	6.09E-05
PLXDC2	1.43	2.54E-06
SP5	1.43	0.033692

TABLE 17-continued

Proteins significantly more abundant in HMC-EVs compared to BM-MSC EVs		
Name	log 2 fold difference	p-value
AHCY	1.42	0.010938
IGHG3	1.41	0.003373
PTPRG	1.41	5.65E-06
SERPINC1	1.40	1.47E-05
C1R	1.40	0.000988
HABP2	1.40	0.000584
FN1	1.40	0.0248
C1S	1.40	2.03E-05
FBN1	1.38	5.52E-05
CDC42	1.38	1.69E-05
INF2	1.37	0.007261
HBA1	1.37	2.11E-05
PCYOX1	1.37	0.015589
HBD	1.37	0.00225
SELENOP	1.37	3.88E-05
C8B	1.36	0.000264
C9	1.36	1.91E-05
TUBB1	1.36	1.06E-05
PII6	1.35	0.000586
EMILIN1	1.35	0.027038
LYN	1.35	0.008809
VPS13A	1.33	0.001477
IGLV1-47	1.32	0.001108
COTL1	1.31	0.018812
CLTC	1.31	0.00392
IGHV3-33	1.31	0.005984
CPB2	1.30	1.11E-06
F12	1.30	8.18E-05
TUBA1B	1.30	3.08E-09
IGLV4-69	1.29	0.000486
RAB7A	1.29	0.016284
NAA25	1.28	0.001563
F2	1.28	0.000124
CLEC3B	1.28	0.01992
C1QC	1.25	0.000596
APP	1.24	0.001311
SERPINA1	1.23	2.47E-07
DENNDA2A	1.21	0.033105
GSTP1	1.20	4.84E-07
NID2	1.20	0.014748
RNASE11	1.19	0.03571
COL6A2	1.19	0.020663
NUTTF2	1.19	0.000436
YWHAG	1.18	9.65E-06
PEPD	1.18	3.67E-06
PPP1CA	1.17	0.017239
ILK	1.16	0.022235
EHD1	1.15	0.001047
APCS	1.15	1.05E-05
RALB	1.15	4.1E-05
IGHV3-73	1.14	0.00507
IGHA2	1.13	0.000613
CD36	1.12	8E-07
HRG	1.12	9.25E-05
GALE	1.12	0.034543
VASP	1.11	0.002503
ACE	1.09	4.32E-05
TUBB	1.09	0.000838
TPI1	1.09	3.71E-05
RAC1	1.07	0.000549
ANXA2	1.07	8.86E-08
FAH	1.07	0.023699
TUBB4B	1.06	4.98E-06
GSN	1.06	2.88E-06
EIF4A1	1.05	4.7E-06
COL5A1	1.04	5.41E-05
FERMT3	1.03	4.1E-07
ITGA2B	1.03	0.001339
PROS1	1.02	0.002371
HSP90B1	1.00	0.015352
LGALS3BP	1.00	0.003375

TABLE 18

Proteins significantly more abundant in BM-MSC EVs compared to HMC-EVs		
Name	log 2 fold difference	p-value
DMXL1	-9.78	4.91E-13
PXYLP1	-7.74	1.34E-08
PTGFRN	-7.55	1.38E-14
CSSH1	-4.51	6.52E-03
RNH1	-4.24	3.53E-02
AASS	-3.91	7.86E-03
APOL1	-3.85	4.66E-12
RPL15	-3.72	8.13E-03
IRF6	-3.48	1.71E-02
TMEM198	-3.29	1.49E-03
RAB1B	-3.10	8.69E-03
ASPM	-2.91	2.21E-02
SULT1A1	-2.79	1.21E-08
GP5	-2.69	5.64E-08
CAT	-2.63	3.53E-02
KYAT3	-2.54	6.63E-06
CCT2	-2.46	1.87E-07
TAS2R33	-2.41	3.11E-03
FGG	-2.33	3.66E-10
ABI3BP	-2.30	7.93E-08
ARMCX5	-2.25	2.54E-02
IGLV6-57	-2.23	2.66E-03
ADIPOQ	-2.23	2.36E-02
WNT5B	-2.23	2.45E-02
IGKV1D-39	-2.18	1.61E-05
CUX1	-2.10	1.19E-02
LILRA3	-2.06	2.74E-03
PPM1F	-2.01	1.70E-02
GM2A	-2.01	1.32E-02
CEP290	-2.01	2.08E-02
IGLV3-1	-2.01	6.15E-03
CTSK	-1.94	1.70E-02
IGHV3-38	-1.78	1.08E-03
CCDC80	-1.77	1.88E-02
DOCK9	-1.72	1.45E-04
LAMA4	-1.71	1.52E-02
NAP1L4	-1.60	1.91E-04
APOA2	-1.59	3.14E-04
NBEAL2	-1.58	2.65E-02
KRT81	-1.48	2.99E-02
AASDHPPPT	-1.46	1.29E-02
PAICS	-1.45	2.47E-06
FBLN5	-1.45	6.53E-04
MUC16	-1.44	3.66E-02
PRXL2C	-1.42	1.97E-05
IGLV4-60	-1.40	3.26E-02
AKR7A2	-1.39	2.67E-04
SRR	-1.30	1.57E-02
CYLC2	-1.26	1.37E-05
COL3A1	-1.20	3.78E-03
GMFG	-1.19	2.10E-02
PDLIM1	-1.16	8.70E-05
SPOCK1	-1.04	1.69E-04
ITIH1	-1.00	1.51E-02

TABLE 19

Proteins significantly more abundant in HMC-EVs compared to AD-MSC EVs		
Name	log 2 fold difference	P-Value
SEPTIN5	6.88	3.98E-08
B2M	6.71	1.29E-07
H3-3A	6.61	9.60E-04
PRSS23	6.46	1.73E-08
SLC2A1	5.40	1.62E-07
IGKV3D-20	5.14	9.44E-05
RAB6B	5.13	2.00E-04

TABLE 19-continued

Proteins significantly more abundant in HMC-EVs compared to AD-MSC EVs		
Name	log 2 fold difference	P-Value
APBB2	5.11	1.32E-06
LTBP3	5.01	3.28E-03
PGAP1	5.00	1.75E-04
TAGLN2	4.69	1.16E-10
CD81	4.64	6.54E-07
SRSF8	4.55	3.60E-05
BSG	4.54	1.65E-02
ENG	4.52	6.54E-05
NT5E	4.49	2.13E-03
RPS3A	4.39	1.21E-06
S100A11	4.38	3.93E-05
CA2	4.30	8.95E-04
CD99	4.29	2.10E-07
ESD	4.24	1.58E-03
TSPAN14	4.20	7.38E-05
RPS4X	4.13	1.15E-04
CAV1	4.13	1.15E-05
FSCN1	4.12	2.04E-02
ARF4	4.10	2.53E-03
ITGA2	4.10	4.84E-05
ANXA5	4.08	1.59E-04
RPS18	4.07	1.04E-03
BLVRA	4.07	2.14E-03
VAT1	4.06	1.27E-04
MAMDC2	4.05	3.48E-03
KIF11	4.00	8.93E-03
GNAQ	3.99	4.47E-05
CKM	3.99	2.49E-03
YWHAQ	3.99	1.25E-02
CD36	3.99	8.04E-04
MARCKSL1	3.94	2.00E-05
ARHGDIB	3.90	8.12E-03
RAB27B	3.89	2.15E-03
GNAI2	3.88	3.08E-03
H3-7	3.85	2.02E-03
KRAS	3.77	1.12E-03
ARIHGDI	3.69	3.75E-03
MFGE8	3.63	1.01E-07
MEIOB	3.63	3.25E-03
CDC42	3.63	6.84E-05
SH3BGRL3	3.62	2.31E-03
STXBP2	3.59	4.95E-04
STX11	3.58	8.41E-05
ARL8A	3.56	2.66E-06
TRPM2	3.53	6.82E-04
CCN2	3.52	4.52E-04
H2BC15	3.48	3.02E-07
MERTK	3.46	2.22E-03
YWHAB	3.46	8.75E-03
ALDOC	3.44	1.72E-07
TUBB3	3.44	2.51E-03
FDPS	3.40	2.12E-03
SFRP1	3.39	1.70E-03
TSPAN33	3.39	1.54E-04
PCDH1	3.38	1.50E-02
MBTD1	3.37	3.98E-02
SLTM	3.37	8.65E-03
COL4A2	3.35	1.76E-06
MARCKS	3.34	5.03E-06
FUCA1	3.34	5.42E-08
TSPAN9	3.33	3.04E-04
CD47	3.31	1.77E-04
DTD1	3.29	4.19E-05
KPN2A	3.29	5.32E-05
MDGA1	3.27	5.41E-04
BCL9	3.24	6.32E-03
HIP1	3.23	2.83E-03
IGLV2-23	3.23	2.68E-02
TTYH3	3.23	1.38E-04
TNC	3.22	4.36E-02
LAMP1	3.21	3.34E-03
HLA-A	3.18	1.74E-02

TABLE 19-continued

Proteins significantly more abundant in HMC-EVs compared to AD-MSC EVs		
Name	log 2 fold difference	P-Value
PPP2R1A	3.18	2.11E-03
MDH1	3.17	3.10E-04
MYO3A	3.14	1.89E-02
PGD	3.13	3.38E-02
RPS12	3.12	4.41E-04
PXDN	3.11	5.32E-06
YWHAE	3.10	1.50E-03
PRXL2C	3.10	1.99E-02
GNG12	3.10	1.59E-03
ARPC5	3.08	4.69E-03
LRRC59	3.05	2.84E-03
PF4	3.05	2.00E-06
SLC44A1	3.05	1.83E-07
TPII	3.03	6.86E-06
CCNB3	3.03	1.22E-03
CD63	3.02	1.40E-05
GP9	3.01	5.73E-04
PSTPIP2	2.99	5.92E-06
HP	2.97	8.61E-04
PPP2CB	2.96	8.89E-03
H2AC20	2.96	1.77E-02
BST1	2.96	1.45E-02
SLC3A2	2.94	4.64E-02
ACACA	2.94	4.53E-03
MTPN	2.93	1.85E-02
EPB4L3	2.93	2.63E-03
MMP14	2.89	2.18E-05
RPS3	2.87	1.26E-03
BMP1	2.87	3.15E-02
FCGR3A	2.86	4.72E-03
COP1	2.86	3.04E-02
UCHL1	2.85	1.26E-05
PEBP1	2.85	6.66E-04
SLC44A2	2.85	5.32E-03
SDCBP	2.82	1.40E-06
PLXDC2	2.81	2.13E-04
RAB11FIP1	2.80	1.23E-04
RNASE11	2.80	9.39E-03
MYL12B	2.77	1.88E-03
RPL10A	2.76	3.20E-05
SMG1	2.75	2.02E-08
ITGA3	2.73	2.01E-05
PDIA3	2.72	3.30E-03
H4-16	2.71	5.73E-04
AGRN	2.71	3.35E-05
AOC3	2.71	4.15E-04
ARPC2	2.69	1.06E-02
ITGA2B	2.69	3.15E-06
VCAN	2.69	1.80E-05
COTL1	2.67	1.88E-03
RPL13	2.66	1.16E-02
RICTOR	2.64	1.71E-02
DYNLL1	2.64	8.64E-04
H1-3	2.63	1.03E-03
H2AC21	2.63	1.64E-02
TPP1	2.62	7.50E-03
RAB14	2.61	4.68E-04
PDGFRB	2.61	2.90E-02
RPL14	2.61	3.28E-05
TUBA8	2.59	4.67E-03
ADGRG6	2.59	4.04E-03
KRT4	2.58	7.61E-03
MYO1F	2.57	1.00E-02
EPHB2	2.56	1.62E-03
RALA	2.56	4.82E-04
RPS25	2.55	1.54E-02
MAPK3	2.55	7.18E-03
STOM	2.53	4.63E-05
CTBS	2.51	6.65E-05
SERPINA10	2.50	1.92E-02
GNB4	2.50	2.35E-02
ANXA6	2.49	1.01E-05

TABLE 19-continued

Proteins significantly more abundant in HMC-EVs compared to AD-MSC EVs		
Name	log 2 fold difference	P-Value
CD276	2.49	2.99E-03
GLIPR2	2.49	6.02E-05
BBS1	2.48	2.48E-02
BASP1	2.48	4.27E-02
MVP	2.47	3.35E-02
FAH	2.47	8.09E-03
CD34	2.47	2.04E-03
NAGLU	2.47	4.76E-04
PTPRG	2.47	1.09E-03
THY1	2.45	1.37E-06
PRG4	2.42	8.78E-06
RPS15A	2.42	1.07E-02
FREM3	2.42	1.08E-04
MOB1B	2.42	9.08E-03
FLG2	2.42	2.52E-02
SEPTIN2	2.39	1.29E-04
PTGDS	2.38	1.39E-03
IL1RAP	2.38	4.95E-04
NIBAN2	2.38	2.82E-04
LGALS1	2.37	1.45E-06
GSTM1	2.37	6.30E-03
EEF1D	2.36	3.60E-06
SPARC	2.35	3.57E-02
UBE2L3	2.34	5.48E-03
CBR1	2.34	4.64E-02
RAP2A	2.34	7.67E-03
TANK	2.34	1.89E-05
S100A6	2.32	5.70E-03
CRISP3	2.29	3.53E-05
ANXA2	2.28	2.47E-07
MON2	2.28	6.21E-06
APOC4	2.28	4.38E-04
MTHFD1	2.27	3.08E-02
DEFA3	2.27	5.03E-03
NPM1	2.26	1.08E-02
C1QA	2.25	5.27E-05
ACLY	2.24	3.88E-02
ITGB3	2.24	4.84E-07
CPN2	2.23	5.77E-08
RPS13	2.22	3.10E-03
ARIHAP1	2.20	4.63E-02
HYOU1	2.20	2.88E-02
IGLV7-43	2.19	3.58E-02
GNB1	2.19	2.91E-05
ZNF607	2.19	7.60E-04
TGM2	2.18	9.01E-03
CORO1A	2.18	4.53E-05
CD9	2.18	2.71E-06
STRADB	2.16	3.17E-02
GATA5	2.16	3.73E-05
YBX3	2.16	4.51E-02
EHD1	2.15	2.63E-03
LUM	2.13	5.69E-05
CNDP2	2.12	3.00E-03
ITGA4	2.10	5.79E-04
RNF149	2.09	2.50E-04
SRPX	2.09	1.32E-09
HSP90AB1	2.09	4.04E-05
LAP3	2.08	4.83E-04
ITGB1	2.05	1.72E-07
HSPA4L	2.05	1.89E-04
TPTE2	2.05	1.85E-02
QSOX1	2.04	3.25E-04
PLOD1	2.04	5.58E-02
SERPINAA11	2.04	1.85E-02
EEF1G	2.02	8.25E-03
DENNDA2A	2.01	5.43E-03
RPSA	2.01	7.73E-06
PRKAR1A	2.01	3.58E-03
LCAT	2.01	9.99E-08
C1QB	2.00	1.60E-05
PROCR	2.00	4.29E-06

TABLE 19-continued

Proteins significantly more abundant in HMC-EVs compared to AD-MSC EVs		
Name	log 2 fold difference	P-Value
MYH13	1.98	1.77E-02
NME2	1.95	1.43E-03
PGLYRP2	1.95	7.91E-09
SDC4	1.94	2.60E-03
PTPN6	1.94	2.68E-04
C1RL	1.93	1.91E-04
AFM	1.92	4.17E-06
B4GALT1	1.92	9.83E-03
CNTFR	1.92	4.02E-04
HSPE1-MOB4	1.92	3.09E-02
COL18A1	1.91	1.23E-02
ARF6	1.91	7.99E-03
ACOT7	1.91	4.52E-04
ROBO4	1.90	1.22E-03
CAPZA2	1.90	5.23E-02
CLIC4	1.90	3.52E-03
RAB8B	1.89	1.57E-02
PFN1	1.89	5.10E-06
APRT	1.88	1.18E-02
RBP4	1.87	4.24E-04
ACTR3	1.87	2.56E-02
MYL6	1.86	2.32E-04
CD82	1.86	1.27E-03
PDCD6IP	1.86	3.88E-06
ARHGAP6	1.86	2.73E-02
ADCY5	1.86	1.09E-04
SDC1	1.85	3.15E-05
C1QC	1.85	1.71E-04
ITGA6	1.82	6.75E-06
GMPR	1.82	2.99E-02
VNN1	1.82	2.85E-05
TUBA4A	1.82	7.14E-03
GPNMB	1.81	1.32E-02
GGH	1.81	6.85E-05
NUTF2	1.80	6.20E-04
CDH5	1.79	3.11E-04
INF2	1.79	2.52E-02
OSMR	1.78	2.41E-04
AHSG	1.77	2.67E-07
RPL4	1.76	2.48E-02
PDE4DIP	1.75	1.35E-07
RALB	1.74	1.20E-05
TBC1D2	1.74	2.92E-02
EHD3	1.73	1.45E-04
EIF3K	1.73	1.38E-02
C1R	1.73	5.18E-05
IGHG4	1.71	3.10E-04
LGALSL	1.71	1.49E-06
LIPT1	1.71	4.62E-02
WDR48	1.70	4.83E-05
FARP1	1.70	8.11E-03
RAB11B	1.69	2.80E-02
UNC13D	1.69	2.60E-02
PAFAH1B1	1.69	9.85E-04
IGKV6D-21	1.68	5.48E-04
ARPC1B	1.67	3.51E-03
LCP2	1.67	9.04E-03
TUBB1	1.67	5.82E-04
CDH13	1.64	3.23E-03
AHCY	1.64	1.06E-02
SLC22A23	1.64	3.11E-04
GANAB	1.63	3.25E-06
SELL	1.63	2.53E-07
PRPH2	1.63	2.30E-05
PYGB	1.62	1.12E-04
CLIC1	1.62	3.58E-04
MYO15A	1.60	1.45E-04
TMС8	1.60	1.06E-02
LOXL2	1.60	8.00E-04
APOE	1.58	3.45E-04
RPL11	1.57	1.32E-02
RAP1B	1.57	2.29E-03

TABLE 19-continued

Proteins significantly more abundant in HMC-EVs compared to AD-MSC EVs		
Name	log 2 fold difference	P-Value
FGA	1.56	8.45E-05
RAB8A	1.56	4.90E-03
GSTO1	1.56	1.40E-03
LRG1	1.55	1.69E-04
UBA52	1.54	7.44E-05
HLA-A	1.54	4.79E-02
CD14	1.54	3.09E-04
CALM3	1.53	1.38E-04
RHOA	1.53	8.42E-05
ITGA5	1.51	2.00E-06
HPX	1.51	5.50E-05
APOA2	1.50	2.40E-02
NEBL	1.50	6.28E-03
CCT4	1.50	1.65E-04
LRP1	1.49	1.91E-04
TEX35	1.49	1.11E-04
ARPC4	1.48	2.63E-04
LPA	1.48	7.69E-05
OBSCN	1.47	3.86E-03
ACE	1.47	6.26E-03
CALR	1.46	9.54E-03
HP	1.46	4.00E-04
TUBB4B	1.45	4.15E-07
MAPRE2	1.45	6.84E-04
ILK	1.43	1.31E-06
LAMC2	1.43	1.05E-02
YWHAQ	1.43	1.25E-03
SERPINA6	1.42	8.01E-07
FUCA2	1.41	3.97E-04
PCOLCE	1.41	2.17E-03
POTEJ	1.40	9.12E-04
MCAM	1.40	6.43E-05
MYH9	1.40	1.46E-05
LBP	1.40	2.72E-03
DSTN	1.38	7.18E-05
DYNC1H1	1.38	1.11E-05
YWHAZ	1.38	1.22E-06
FERMT3	1.37	6.62E-06
PPIA	1.37	6.55E-05
APMAP	1.35	1.77E-02
PII6	1.34	7.66E-07
A1BG	1.33	5.52E-08
DNAJB2	1.33	2.80E-02
EDIL3	1.33	2.07E-03
PSMB4	1.33	3.52E-02
APP	1.33	4.69E-05
CAP1	1.33	1.24E-04
PRKDC	1.31	1.33E-04
CACNA2D1	1.31	1.64E-03
SYK	1.31	5.47E-03
AKR7A2	1.30	2.85E-04
COL1A2	1.29	4.13E-03
FN1	1.29	2.43E-03
ZNF879	1.29	1.30E-02
RAB10	1.27	1.34E-04
SRC	1.26	2.09E-03
PVR	1.26	2.61E-03
APCS	1.26	1.19E-04
WARS1	1.26	5.38E-02
CNN2	1.25	2.34E-02
PKM	1.25	1.66E-03
PFKP	1.25	2.58E-04
GAPDH	1.25	3.31E-03
IGFALS	1.24	2.59E-02
ALDOA	1.23	4.07E-05
BCHE	1.23	1.05E-04
ALOX12	1.23	4.37E-02
HSPB1	1.23	9.90E-04
CD59	1.23	4.25E-04
CSF1R	1.22	3.24E-03
PRDX6	1.22	1.01E-03
MIF	1.22	2.05E-04

TABLE 19-continued

Proteins significantly more abundant in HMC-EVs compared to AD-MSC EVs		
Name	log 2 fold difference	P-Value
COL6A2	1.22	6.03E-06
MTAP	1.21	5.61E-03
COL6A3	1.21	1.03E-04
F10	1.21	1.34E-03
BANF1	1.21	8.40E-04
F13A1	1.19	1.39E-04
APOA4	1.19	9.01E-06
FGG	1.18	6.87E-07
SAR1A	1.17	9.11E-03
ARPC3	1.17	7.77E-04
ADAMTS12	1.16	4.03E-02
EEF2	1.15	7.16E-05
VTN	1.15	5.04E-04
C1S	1.15	1.22E-06
CETP	1.15	4.16E-03
ADH5	1.14	5.04E-03
HABP2	1.14	2.65E-02
SYNE1	1.13	5.60E-04
TIMM13	1.13	6.67E-05
APOC4-APOC2	1.13	2.40E-02
APOC3	1.13	1.88E-02
HP	1.13	1.14E-04
SPP2	1.12	2.41E-05
PPBP	1.12	2.83E-05
CC2D2B	1.12	1.48E-02
COL1A1	1.12	8.40E-04
AHNAK	1.12	2.44E-03
TPX2	1.11	4.00E-03
FBN2	1.11	1.06E-02
APOC1	1.11	1.22E-03
IGHM	1.11	1.29E-03
MASP2	1.10	3.47E-03
PGK1	1.10	1.05E-03
DIAPH1	1.09	4.53E-02
AGT	1.09	4.53E-06
CCT3	1.09	3.36E-02
DPP4	1.08	1.78E-06
CPB2	1.08	4.46E-03
PEPD	1.07	5.39E-09
BGN	1.07	6.47E-05
IDE	1.07	4.31E-05
DNAJC12	1.06	1.42E-04
PTGES3	1.06	4.09E-02
APOH	1.05	6.15E-06
CCT2	1.05	9.47E-04
ACTB	1.05	6.98E-08
MTA2	1.05	6.42E-03
MRC2	1.05	1.19E-02
TUBA1B	1.03	2.86E-04
CD5L	1.02	3.55E-04
CFHR1	1.02	1.07E-03
CTSD	1.01	1.49E-03
FCGBP	1.01	9.17E-04
ARF3	1.00	6.70E-04
CAPZB	1.00	1.91E-03

TABLE 20

Proteins significantly more abundant in AD-MSC EVs compared to HMC-EVs		
Name	log 2 fold difference	P-Value
TMEM198	-6.91	6.10E-12
ARMCX5	-6.41	1.83E-02
SH3BGRL	-4.93	2.45E-06
CAT	-4.70	4.13E-07
CEP290	-4.35	2.28E-09
TAS2R33	-4.18	4.86E-03

TABLE 20-continued

Proteins significantly more abundant in AD-MSC EVs compared to HMC-EVs		
Name	log 2 fold difference	P-Value
ALB	-4.13	3.11E-05
KRT81	-4.04	2.94E-07
ADIPOQ	-3.99	3.32E-04
SEMA7A	-3.95	5.59E-07
SPON2	-3.94	3.38E-04
CHST9	-3.93	2.60E-08
IGHV1-45	-3.90	7.40E-03
CD109	-3.78	2.49E-09
NEO1	-3.70	5.61E-06
IQGAP2	-3.68	4.59E-07
SURF1	-3.66	3.77E-09
SEPTIN6	-3.58	2.10E-08
LTF	-3.57	6.82E-03
ZNF800	-3.56	8.17E-09
ERC1	-3.46	6.65E-05
ITPR3	-3.44	7.92E-07
MSH6	-3.37	2.76E-03
OLFM3	-3.30	7.36E-03
ALB	-3.24	8.12E-06
HAUS6	-3.23	1.89E-03
PAK6	-3.16	2.33E-03
PRDX2	-3.16	1.33E-05
AKAP9	-3.12	5.02E-04
HAUS8	-3.11	9.58E-07
ALOX5	-3.08	9.38E-07
PRKACB	-3.07	5.34E-03
CDSN	-3.05	2.49E-03
SLC9A4	-3.04	1.49E-08
LRRTM2	-3.00	1.13E-04
ALX4	-2.99	1.46E-06
GPR179	-2.97	1.08E-07
CYLC2	-2.93	5.87E-07
DSC1	-2.91	2.21E-08
NBEAL2	-2.90	4.83E-05
DDX55	-2.78	7.01E-11
SYMPK	-2.77	7.34E-08
L1TD1	-2.77	5.98E-08
QDPR	-2.76	1.82E-04
C6	-2.76	2.19E-12
RGS14	-2.72	2.47E-03
CNDP1	-2.68	4.27E-10
LRAT	-2.62	5.70E-03
LAMB4	-2.61	1.47E-04
F11	-2.59	9.76E-08
RPS6KA4	-2.55	7.87E-03
MOGS	-2.51	3.62E-02
IGLV6-57	-2.50	6.55E-03
CCDC178	-2.50	9.07E-03
ATP10A	-2.49	1.15E-04
SLC24A4	-2.49	7.62E-03
PHF24	-2.47	1.84E-05
SNX14	-2.44	3.37E-06
DCN	-2.43	2.90E-04
IGHV1-8	-2.43	1.58E-02
VCP	-2.41	9.84E-06
OAF	-2.39	1.15E-03
COG2	-2.39	3.26E-02
TRIM4	-2.38	7.87E-03
GTF2IRD2	-2.37	1.81E-08
TRIM7	-2.35	4.33E-06
NID2	-2.33	3.79E-06
RPL13A	-2.30	3.89E-02
TNFAIP6	-2.30	1.08E-05
IGLL1	-2.25	1.61E-03
GMFG	-2.21	4.87E-03
DBH	-2.21	3.65E-02
SERPINB12	-2.20	3.30E-02
PSMA7	-2.18	1.94E-08
TIMP2	-2.17	1.70E-03
IGHV5-51	-2.11	3.25E-07
RACK1	-2.09	8.66E-06
APLP2	-2.05	5.38E-03

TABLE 20-continued

Proteins significantly more abundant in AD-MSC EVs compared to HMC-EVs		
Name	log 2 fold difference	P-Value
IGHV1-69D	-2.02	6.38E-03
KRT16	-2.02	1.24E-04
IGHV2-26	-2.00	7.32E-05
CAPN5	-2.00	6.65E-07
PSMA6	-1.97	5.32E-02
IGHG1	-1.97	1.83E-07
IGHG2	-1.95	2.21E-07
CCT6A	-1.93	3.26E-05
GP6	-1.93	1.75E-02
C18orf63	-1.88	9.55E-06
ANO7	-1.88	3.89E-08
IGLV4-60	-1.87	3.29E-02
XYLT1	-1.84	3.86E-03
FAM180A	-1.81	7.96E-04
LYVE1	-1.81	1.23E-02
ERFL	-1.78	2.65E-09
CRTAP	-1.78	1.15E-02
MYCBP2	-1.76	4.22E-03
SCIN	-1.75	6.38E-08
FBLN5	-1.73	1.16E-02
ITGAV	-1.73	1.17E-04
KIF5C	-1.71	5.47E-09
ZNF488	-1.70	1.01E-04
ITIH1	-1.70	1.95E-06
PDZK1P1	-1.70	7.05E-04
SBSN	-1.69	1.58E-02
FBRSL1	-1.68	1.87E-04
CHL1	-1.67	3.00E-04
TF	-1.66	1.67E-05
COL3A1	-1.66	5.22E-02
MMP1	-1.63	4.10E-04
GRIN2C	-1.62	2.48E-02
CAMP	-1.61	4.54E-05
BLMH	-1.58	5.24E-04
ADA	-1.55	2.61E-06
ALB	-1.54	3.86E-07
TIMP3	-1.53	1.81E-03
HK1	-1.49	9.51E-07
LCN1	-1.47	4.32E-03
TGM1	-1.44	4.86E-02
COMP	-1.44	1.07E-05
SLC26A11	-1.40	2.30E-03
IGLV3-9	-1.39	8.77E-08
IGLV3-21	-1.39	4.11E-07
VPS13A	-1.37	2.81E-05
IGHV1-69	-1.35	4.84E-05
PRXL2B	-1.34	2.79E-02
IGHA2	-1.33	3.04E-03
CPQ	-1.33	1.19E-08
PAICS	-1.31	2.83E-04
ABCC4	-1.28	5.62E-07
IGHV3-74	-1.28	6.09E-05
IGKV1D-16	-1.26	2.09E-03
DNAH11	-1.26	1.07E-04
IGKV1D-39	-1.25	2.39E-02
ZGRF1	-1.24	1.53E-06
TGFB1	-1.21	1.31E-04
DCD	-1.20	1.97E-04
KRT9	-1.20	4.97E-09
IGHV4-4	-1.20	9.57E-03
XPNPEP2	-1.19	3.50E-03
PKP1	-1.16	9.92E-05
RASGRP2	-1.16	8.93E-04
CLEC3B	-1.15	9.25E-04
LRP1B	-1.14	3.59E-02
IGKV3D-15	-1.13	2.04E-05
ATAD2	-1.13	2.38E-03
IGHV5-10-1	-1.12	6.47E-05
TPM4	-1.11	3.11E-06
KRT2	-1.10	9.67E-08
IGHD	-1.10	8.57E-06
IGHV3-43	-1.09	2.07E-04

TABLE 20-continued

Proteins significantly more abundant in AD-MSC EVs compared to HMC-EVs		
Name	log 2 fold difference	P-Value
PATJ	-1.09	9.49E-03
ZNF425	-1.08	5.60E-02
IGHV1OR15-1	-1.08	3.68E-03
CCCD180	-1.04	1.48E-04
EIF4A1	-1.03	3.56E-04
IGLV3-25	-1.03	1.36E-06
F13B	-1.02	2.69E-02
MSN	-1.01	3.22E-06
CSTA	-1.01	6.82E-07
FAM47E-STBD1	-1.00	4.16E-05

Example 14. smRNAseq Profiling for HMC Cells Vs HMC-EVs

[0442] HMCs were generated from the same bank of frozen hemangioblasts described in Example 1. HMCs were generated and passaged up to six passages (P6) according to the method described in Example 1. Extracellular vesicles (EVs) were purified from HMCs (HMC-EVs) by tangential flow filtration (TFF). smRNAseq profiling was performed for HMC-EVs (n=3) and HMCs (n=3).

[0443] Table 21 shows smRNAs that were more highly abundant in the HMC-EVs compared with HMCs. Table 22 shows smRNAs that were more highly abundant in the HMCs compared with HMC-EVs.

TABLE 21

miRNAs with higher levels in HMC-EVs compared to HMCs		
miRNA ID	Fold difference	P value
hsa-miR-1290	-3237.80	0
hsa-miR-122-5p	-2697.49	6.83E-40
hsa-miR-223-3p	-1451.47	1.70E-20
hsa-miR-338-5p	-1191.28	1.44E-19
hsa-miR-451a	-672.00	3.99E-26
hsa-miR-320c	-513.86	0
hsa-miR-1246	-485.03	0
hsa-miR-320d	-447.23	0
hsa-miR-9-3p	-333.60	1.98E-12
hsa-miR-139-3p	-282.32	4.45E-12
hsa-miR-150-5p	-268.41	8.85E-12
hsa-miR-423-5p	-253.84	0
hsa-miR-4516	-241.56	4.44E-11
hsa-miR-4433b-5p	-235.62	5.88E-11
hsa-miR-223-5p	-222.70	9.27E-11
hsa-miR-3138	-213.62	3.87E-17
hsa-miR-4433b-3p	-184.67	9.31E-10
hsa-miR-11400	-170.22	1.16E-09
hsa-miR-486-5p	-159.91	0
hsa-miR-4738-3p	-135.10	7.01E-10
hsa-miR-5010-5p	-130.91	1.30E-08
hsa-miR-144-3p	-126.67	2.43E-08
hsa-miR-664a-5p	-124.89	0
hsa-miR-432-5p	-122.75	0
hsa-miR-6809-5p	-117.30	1.35E-07
hsa-miR-320b	-110.63	0
hsa-miR-4659b-3p	-99.06	2.55E-06
hsa-miR-139-5p	-89.21	4.42E-08
hsa-miR-142-5p	-82.36	0
hsa-miR-320e	-79.30	4.88E-14
hsa-miR-363-3p	-76.09	2.75E-27
hsa-miR-1273h-5p	-75.36	2.36E-06
hsa-miR-3679-5p	-67.01	2.62E-24
hsa-miR-584-5p	-63.66	0

TABLE 21-continued

miRNAs with higher levels in HMC-EVs compared to HMCs		
miRNA ID	Fold difference	P value
hsa-miR-2110	-62.37	0
hsa-miR-6877-5p	-59.41	5.22E-05
hsa-miR-6862-5p	-58.09	4.50E-05
hsa-miR-766-5p	-55.73	2.21E-08
hsa-miR-4446-3p	-51.85	6.66E-06
hsa-miR-5187-5p	-49.91	0.000222
hsa-miR-544b	-47.93	0.000163
hsa-miR-320a-3p	-47.66	0
hsa-miR-6515-5p	-46.42	1.83E-05
hsa-miR-342-5p	-43.34	2.57E-20
hsa-miR-338-3p	-43.19	0.000301
hsa-miR-3154	-41.01	0.000725
hsa-miR-193b-5p	-40.02	0
hsa-miR-628-3p	-39.55	0
hsa-miR-4429	-36.37	0.000548
hsa-miR-6837-5p	-36.33	7.33E-05
hsa-miR-7849-3p	-35.48	0.004653
hsa-miR-122-3p	-34.71	0.001147
hsa-miR-6866-5p	-32.18	0.001507
hsa-miR-6735-5p	-31.29	0.00492
hsa-miR-4743-5p	-30.88	0.001291
hsa-miR-3177-3p	-30.77	5.76E-21
hsa-miR-7854-3p	-28.89	1.52E-05
hsa-miR-6852-5p	-28.85	5.35E-12
hsa-miR-126-5p	-28.31	0
hsa-miR-1908-5p	-26.94	2.76E-17
hsa-miR-323b-3p	-26.80	0
hsa-miR-2276-3p	-26.68	0.005841
hsa-miR-142-3p	-26.63	0.000857
hsa-miR-3175	-26.50	0.002484
hsa-miR-5189-5p	-26.30	0.001287
hsa-miR-616-3p	-26.22	2.88E-05
hsa-miR-144-5p	-26.09	0.000808
hsa-miR-4667-5p	-25.94	0.000963
hsa-miR-483-5p	-25.40	0
hsa-miR-877-5p	-23.99	0
hsa-miR-204-3p	-23.92	0.012059
hsa-miR-126-3p	-23.32	0
hsa-miR-7856-5p	-23.28	0.004825
hsa-miR-1273h-3p	-23.10	0.004919
hsa-let-7b-5p	-22.10	0
hsa-miR-433-3p	-21.75	1.59E-09
hsa-miR-3161	-20.29	0.010391
hsa-miR-146a-5p	-20.17	0
hsa-miR-1-3p	-20.10	0
hsa-miR-6131	-19.93	0.010871
hsa-miR-1262	-18.98	1.96E-18
hsa-miR-10399-5p	-18.72	5.36E-15
hsa-miR-5584-5p	-18.07	0.013828
hsa-miR-3126-5p	-17.58	7.88E-06
hsa-miR-4804-5p	-17.11	1.74E-05
hsa-miR-335-5p	-17.04	0
hsa-miR-95-3p	-16.80	0.005371
hsa-miR-148a-3p	-16.41	0
hsa-miR-23b-5p	-15.34	6.38E-39
hsa-miR-10b-3p	-15.11	0.002094
hsa-miR-3125	-14.93	0.001865
hsa-miR-3187-3p	-14.48	7.00E-05
hsa-miR-760	-14.46	1.14E-07
hsa-miR-942-3p	-14.12	1.30E-06
hsa-miR-10526-3p	-13.89	0.008759
hsa-miR-548j-3p	-13.31	0.014203
hsa-miR-3960	-13.13	0.004868
hsa-miR-5189-3p	-13.00	0.011457
hsa-miR-4647	-12.61	0.004701
hsa-miR-3622a-5p	-12.43	0.001639
hsa-miR-4662a-5p	-12.21	2.37E-08
hsa-miR-1299	-12.13	0.000244
hsa-miR-10a-3p	-10.83	5.92E-08
hsa-miR-1270	-10.52	6.89E-38
hsa-let-7c-5p	-10.37	0
hsa-miR-3944-5p	-9.06	0.00445
hsa-miR-3605-5p	-8.98	2.29E-17

TABLE 21-continued

miRNAs with higher levels in HMC-EVs compared to HMCs		
miRNA ID	Fold difference	P value
hsa-miR-3120-3p	-8.97	0.003762
hsa-miR-1180-3p	-8.79	7.93E-34
hsa-miR-758-5p	-8.33	2.17E-05
hsa-miR-3928-3p	-8.18	6.01E-05
hsa-miR-7706	-8.02	2.68E-21
hsa-miR-10399-3p	-7.86	0.012167
hsa-miR-182-5p	-7.30	0
hsa-miR-485-5p	-7.05	1.78E-11
hsa-miR-574-5p	-6.67	0
hsa-miR-505-5p	-6.42	2.25E-07
hsa-miR-1843	-6.34	3.29E-18
hsa-miR-3934-5p	-6.20	7.24E-07
hsa-miR-543	-6.20	6.64E-15
hsa-miR-654-5p	-5.92	1.94E-06
hsa-miR-421	-5.90	1.68E-44
hsa-miR-23a-5p	-5.90	0.002561
hsa-miR-548e-3p	-5.88	1.03E-24
hsa-miR-4645-3p	-5.71	0.010916
hsa-miR-25-5p	-5.55	1.87E-12
hsa-miR-196b-5p	-5.35	0.009427
hsa-miR-3140-3p	-5.18	0.010278
hsa-miR-1301-3p	-5.16	2.63E-36
hsa-miR-4435	-5.13	0.006987
hsa-miR-889-3p	-5.02	0
hsa-miR-744-5p	-5.01	0
hsa-miR-148a-5p	-4.74	8.33E-05
hsa-miR-486-3p	-4.74	0.005596
hsa-miR-125a-3p	-4.61	7.80E-30
hsa-miR-323a-3p	-4.60	1.49E-25
hsa-miR-1292-5p	-4.44	0.000159
hsa-miR-10b-5p	-4.38	0
hsa-miR-365b-5p	-4.37	0.000148
hsa-miR-193a-5p	-4.35	2.27E-29
hsa-miR-10527-5p	-4.35	0.002016
hsa-miR-134-5p	-4.20	2.31E-25
hsa-miR-423-3p	-4.02	2.84E-34
hsa-miR-3129-5p	-4.00	8.78E-05
hsa-miR-942-5p	-3.96	7.75E-05
hsa-miR-16-2-3p	-3.80	1.32E-22
hsa-miR-101-3p	-3.75	0
hsa-miR-495-3p	-3.74	1.64E-07
hsa-miR-92b-5p	-3.67	0.000132
hsa-miR-369-3p	-3.62	5.98E-06
hsa-miR-1197	-3.51	0.003072
hsa-miR-382-5p	-3.49	2.65E-15
hsa-miR-1285-3p	-3.42	7.67E-06
hsa-miR-30a-3p	-3.13	3.03E-18
hsa-miR-656-3p	-3.10	2.82E-05
hsa-miR-589-5p	-2.99	0
hsa-miR-128-3p	-2.99	0
hsa-miR-409-3p	-2.95	0
hsa-miR-215-5p	-2.83	0.000243
hsa-miR-378i	-2.81	0.003797
hsa-miR-382-3p	-2.78	4.02E-08
hsa-miR-185-5p	-2.52	0
hsa-let-7d-5p	-2.50	5.51E-43
hsa-let-7e-5p	-2.48	0
hsa-miR-576-3p	-2.45	9.25E-09
hsa-miR-652-3p	-2.41	4.86E-09
hsa-miR-10a-5p	-2.34	3.29E-25
hsa-miR-1304-3p	-2.29	1.16E-05
hsa-miR-28-3p	-2.25	0
hsa-miR-92a-3p	-2.15	6.94E-09
hsa-let-7d-3p	-2.15	0.000249
hsa-miR-330-3p	-2.07	3.20E-11
hsa-miR-629-5p	-1.84	0.000424
hsa-miR-424-3p	-1.82	5.89E-08

TABLE 21-continued

miRNAs with higher levels in HMC-EVs compared to HMCs		
miRNA ID	Fold difference	P value
hsa-miR-30e-3p	-1.78	2.84E-06
hsa-miR-378a-3p	-1.78	7.49E-23
hsa-miR-146b-5p	-1.71	2.30E-20
hsa-miR-654-3p	-1.68	4.70E-19
hsa-miR-224-5p	-1.64	1.42E-13
hsa-miR-106b-3p	-1.59	1.10E-08

TABLE 22

miRNAs with higher levels in HMC cells compared to HMC-EVs		
miRNA ID	Fold difference	P value
hsa-miR-5701	347.64	9.55E-14
hsa-miR-500a-5p	93.58	3.69E-08
hsa-miR-145-5p	78.86	0
hsa-miR-7974	76.40	2.30E-11
hsa-miR-4521	71.20	3.38E-07
hsa-miR-137-3p	55.66	1.57E-09
hsa-miR-152-5p	54.93	2.47E-06
hsa-miR-1260a	46.60	0
hsa-miR-483-3p	44.67	1.22E-05
hsa-miR-12135	42.22	2.94E-05
hsa-miR-548i	42.02	2.14E-05
hsa-miR-140-5p	41.64	1.64E-13
hsa-miR-5100	36.65	5.81E-05
hsa-miR-190a-5p	31.23	0.000258
hsa-miR-153-3p	31.17	0.000223
hsa-miR-27a-5p	29.93	4.85E-28
hsa-miR-500b-5p	27.87	0.000394
hsa-let-7c-3p	27.31	0.000354
hsa-miR-4286	25.72	1.00E-34
hsa-miR-374b-3p	25.68	0.000161
hsa-miR-218-5p	24.79	1.43E-13
hsa-miR-331-3p	19.83	9.12E-41
hsa-miR-301b-3p	19.57	0.002357
hsa-miR-188-3p	19.51	0.002865
hsa-miR-18a-5p	18.74	4.22E-10
hsa-miR-874-5p	18.67	0.003373
hsa-miR-105-5p	18.22	0.003366
hsa-miR-31-3p	17.35	3.79E-06
hsa-let-7a-2-3p	16.87	0.001668
hsa-miR-21-3p	16.43	9.09E-13
hsa-miR-210-5p	16.37	0.005401
hsa-miR-2277-5p	16.24	0.002077
hsa-miR-450a-1-3p	15.87	0.007502
hsa-miR-296-5p	15.50	0.008142
hsa-miR-1260b	14.94	0
hsa-miR-193a-3p	14.50	0.009837
hsa-miR-212-3p	14.40	0.010622
hsa-miR-130a-5p	14.39	0.000405
hsa-miR-542-3p	14.09	5.25E-39
hsa-miR-125a-5p	13.32	0
hsa-miR-7-5p	13.03	0
hsa-miR-4497	13.02	0.015303
hsa-miR-454-3p	12.59	1.99E-08
hsa-miR-21-5p	12.45	0
hsa-miR-570-3p	11.59	0.009332
hsa-miR-424-5p	11.54	0
hsa-miR-132-5p	11.48	4.52E-07
hsa-miR-125b-5p	11.40	0
hsa-miR-7977	11.37	3.36E-44
hsa-miR-34b-3p	11.18	0.010197
hsa-miR-93-5p	10.73	0
hsa-miR-199a-5p	10.58	0
hsa-miR-197-3p	10.19	3.63E-29
hsa-miR-210-3p	9.66	2.56E-05
hsa-miR-221-5p	9.28	0
hsa-miR-582-5p	9.09	1.82E-10
hsa-miR-99b-5p	8.87	0

TABLE 22-continued

miRNAs with higher levels in HMC cells compared to HMC-EVs		
miRNA ID	Fold difference	P value
hsa-miR-3940-3p	8.72	0.000688
hsa-miR-103a-3p	8.70	0
hsa-miR-34a-5p	8.49	4.14E-33
hsa-miR-143-5p	8.47	3.58E-38
hsa-miR-31-5p	8.34	0
hsa-miR-24-2-5p	8.30	2.00E-22
hsa-miR-452-5p	8.25	6.71E-22
hsa-miR-874-3p	8.15	9.71E-42
hsa-miR-145-3p	8.03	0
hsa-miR-143-3p	7.80	0
hsa-miR-365a-3p	7.70	0
hsa-miR-365b-3p	7.70	0
hsa-miR-3613-5p	7.52	2.97E-06
hsa-miR-33b-3p	7.50	0.001136
hsa-miR-708-5p	7.45	0
hsa-miR-17-3p	7.22	8.22E-05
hsa-miR-1296-5p	7.12	2.14E-05
hsa-miR-27a-3p	7.11	0
hsa-miR-17-5p	6.83	0
hsa-miR-2682-5p	6.75	1.73E-06
hsa-miR-148b-5p	6.70	6.49E-05
hsa-let-7a-3p	6.38	4.34E-42
hsa-miR-576-5p	6.38	0.000384
hsa-miR-181a-3p	6.36	0
hsa-miR-665	6.33	9.58E-06
hsa-miR-3130-5p	6.30	0.015272
hsa-let-7i-3p	6.19	0.010866
hsa-miR-30e-5p	5.99	0
hsa-miR-30a-5p	5.99	0
hsa-let-7i-5p	5.79	0
hsa-let-7g-5p	5.79	0
hsa-miR-335-3p	5.60	0
hsa-miR-425-5p	5.56	0
hsa-miR-4454	5.55	6.45E-30
hsa-miR-20a-5p	5.46	0
hsa-miR-34a-3p	5.45	0.010285
hsa-miR-29a-3p	5.42	0
hsa-miR-362-5p	5.39	1.42E-15
hsa-miR-708-3p	5.37	9.33E-20
hsa-miR-342-3p	5.25	0
hsa-miR-193b-3p	5.19	1.77E-23
hsa-miR-301a-5p	5.12	3.39E-05
hsa-miR-15b-5p	5.08	0
hsa-miR-34c-5p	5.07	0
hsa-miR-345-5p	5.06	1.40E-45
hsa-miR-4636	4.99	0.010845
hsa-miR-374b-5p	4.80	1.90E-33
hsa-miR-12136	4.80	0.012744
hsa-miR-4326	4.71	1.35E-05
hsa-miR-374a-3p	4.69	1.22E-39
hsa-miR-29c-5p	4.54	0.01528
hsa-miR-15a-5p	4.46	1.46E-11
hsa-miR-103a-2-5p	4.43	7.59E-06
hsa-miR-450a-5p	4.42	0
hsa-miR-411-5p	4.31	3.39E-35
hsa-miR-3158-3p	4.22	0.000646
hsa-miR-3117-3p	4.20	0.00018
hsa-miR-409-5p	4.16	0
hsa-miR-548w	4.11	0.007376
hsa-miR-532-3p	4.06	1.86E-05
hsa-miR-106a-5p	4.06	0.000408
hsa-miR-374a-5p	4.03	1.22E-19
hsa-miR-9903	4.03	0.014869
hsa-miR-181b-3p	3.99	1.83E-09
hsa-miR-214-3p	3.83	0
hsa-miR-99a-5p	3.83	0
hsa-miR-671-5p	3.80	5.71E-07
hsa-let-7e-3p	3.76	0.00696
hsa-miR-100-5p	3.74	0
hsa-miR-106b-5p	3.71	1.27E-09
hsa-miR-339-5p	3.70	1.04E-08
hsa-miR-16-5p	3.69	0
hsa-miR-376c-3p	3.63	0.007115

TABLE 22-continued

miRNAs with higher levels in HMC cells compared to HMC-EVs		
miRNA ID	Fold difference	P value
hsa-miR-582-3p	3.52	0.007728
hsa-miR-561-5p	3.51	0.000356
hsa-miR-30b-5p	3.50	0
hsa-miR-500a-3p	3.24	3.86E-32
hsa-miR-381-3p	3.17	9.94E-05
hsa-miR-130b-5p	3.17	0
hsa-miR-130a-3p	3.09	3.31E-07
hsa-let-7f-1-3p	3.09	0.008094
hsa-miR-194-5p	3.08	3.68E-11
hsa-miR-502-3p	3.08	4.76E-14
hsa-miR-32-5p	3.07	0.015461
hsa-miR-5094	3.06	0.007148
hsa-miR-125b-2-3p	2.98	1.04E-07
hsa-miR-625-3p	2.95	1.48E-11
hsa-miR-379-5p	2.91	1.68E-09
hsa-miR-484	2.82	0
hsa-miR-138-5p	2.80	1.76E-16
hsa-miR-148b-3p	2.78	0
hsa-miR-27b-3p	2.75	0
hsa-miR-19b-3p	2.66	1.11E-19
hsa-miR-30c-5p	2.63	3.60E-34
hsa-miR-22-3p	2.63	3.16E-33
hsa-miR-221-3p	2.62	0
hsa-miR-183-5p	2.58	0.000322
hsa-miR-214-5p	2.56	3.02E-05
hsa-miR-2355-5p	2.55	0.000159
hsa-miR-29b-3p	2.48	2.65E-05
hsa-miR-149-5p	2.40	2.02E-05
hsa-miR-4677-3p	2.34	6.76E-06
hsa-miR-98-5p	2.32	1.53E-19
hsa-miR-361-3p	2.30	3.19E-06
hsa-miR-181a-2-3p	2.29	2.46E-17
hsa-miR-370-3p	2.26	4.89E-07
hsa-miR-140-3p	2.19	1.90E-25
hsa-miR-574-3p	2.16	2.43E-06
hsa-miR-127-3p	2.13	1.73E-28
hsa-miR-28-5p	2.11	8.76E-18
hsa-miR-181c-3p	2.03	8.80E-09
hsa-miR-24-3p	2.02	1.08E-28
hsa-miR-136-3p	2.00	1.84E-06
hsa-miR-107	2.00	0.000144
hsa-miR-199b-5p	1.99	7.66E-26
hsa-miR-26b-5p	1.91	1.80E-17
hsa-miR-191-5p	1.87	1.08E-22
hsa-miR-450b-5p	1.81	1.76E-07
hsa-miR-30d-5p	1.69	2.65E-42
hsa-miR-339-3p	1.66	0.008601
hsa-miR-23b-3p	1.64	3.63E-18
hsa-miR-769-5p	1.51	0.000511

[0444] While the foregoing description and figures represent exemplary embodiments of the present disclosure, it will be understood that various additions, modifications and substitutions may be made therein without departing from the spirit and scope and range of equivalents of the accompanying claims. In particular, it will be clear to those skilled in the art that the presently disclosed subject matter may be embodied in other forms, structures, arrangements, and with other elements, materials, and components, without departing from the spirit or essential characteristics thereof. In addition, numerous variations in the methods/processes described herein may be made within the scope of the present disclosure without departing from the principles described herein. The presently disclosed embodiments are therefore to be considered in all respects as illustrative and not restrictive. The appended claims should be construed broadly, to include other variants and embodiments of the disclosure, which may be made by those skilled in the art without departing from the scope and range of equivalents.

1. A method of treating a brain injury in a subject suffering from, or suspected of suffering from, a brain injury, the method comprising administering to the subject an effective amount of extracellular vesicles (EVs) secreted from mesenchymal stem cells (HMCs) obtained by in vitro differentiation of pluripotent stem cells, thereby treating the brain injury in the subject.

2. The method of claim 1, wherein the brain injury is selected from the group consisting of stroke, optic neuropathy, traumatic brain injury, cerebral palsy, acquired brain injury, anoxic brain injury, diffuse axonal brain injury, focal brain injury, subdural hematoma, brain aneurysm, and coma.

3. The method of claim 2, wherein the brain injury is stroke.

4. The method of any one of claims 1-3, wherein the method comprises increasing oligodendrocyte and precursor cells in the brain following administration of the EVs secreted from the HMCs (HMC-EVs) into the subject.

5. The method of any one of claims 1-3, wherein the method comprises preserving myelin in the brain following administration of the HMC-EVs into the subject.

6. The method of any one of claims 1-3, wherein the method comprises preventing oxidative damage in neurons following administration of the HMC-EVs into the subject.

7. The method of any one of claims 1-3, wherein the method comprises preventing neuronal death due to glutamate excitotoxicity injury following administration of the HMC-EVs into the subject.

8. The method of any one of claims 1-3, wherein the method comprises reducing tissue loss in the brain following administration of the HMC-EVs into the subject.

9. The method of any one of claims 1-3, wherein the method comprises reducing cell death in the brain following administration of the HMC-EVs into the subject.

10. The method of any one of claims 1-3, wherein the method comprises stimulating pathways involved in the development of neuronal lineage following administration of the HMC-EVs into the subject.

11. The method of any one of claims 1-10, wherein the HMC-EVs are administered systemically.

12. The method of any one of claims 1-10, wherein the HMC-EVs are administered intracerebrally.

13. The method of any one of claims 1-10, wherein the HMC-EVs are administered intrathecally.

14. The method of any one of claims 1-10, wherein the HMC-EVs are administered intracisternally.

15. The method of any one of claims 1-10, wherein the HMC-EVs are administered intraperitoneally.

16. The method of any one of claims 1-15, wherein the subject is a human.

17. The method of any one of claims 1-16, wherein the HMCs are obtained by in vitro differentiation of human pluripotent stem cells.

18. The method of any one of claims 1-17, wherein the pluripotent stem cells are further differentiated into hemangioblasts.

19. The method of any one of claims 1-18, wherein the pluripotent stem cells are embryonic stem cells.

20. The method of any one of claims 1-18, wherein the pluripotent stem cells are induced pluripotent stem cells.

21. The method of claim 20, wherein the induced pluripotent stem cells are produced by contacting a cell with one or more reprogramming factors.

22. The method of any one of claims **1-21**, wherein the HMC-EVs express at least one of the miRNA in Table 9 at a higher level compared to EVs secreted from umbilical cord blood-derived mesenchymal stem cells (UCB-MSC-EVs).

23. The method of any one of claims **1-22**, wherein the HMC-EVs express at least one of the miRNA in Table 10 at a lower level compared to UCB-MSC-EVs.

24. The method of any one of claims **1-23**, wherein the HMC-EVs express at least one of the miRNA in Table 11 at a higher level compared to EVs secreted from bone marrow-derived mesenchymal stem cells (BM-MSC-EVs).

25. The method of any one of claims **1-24**, wherein the HMC-EVs express at least one of the miRNA in Table 12 at a lower level compared to BM-MSC-EVs.

26. The method of any one of claims **1-25**, wherein the HMC-EVs express at least one of the miRNA in Table 13 at a higher level compared to EVs secreted from adipose tissue-derived mesenchymal stem cells (AD-MSC-EVs).

27. The method of any one of claims **1-26**, wherein the HMC-EVs express at least one of the miRNA in Table 14 at a lower level compared to AD-MSC-EVs.

28. The method of any one of claims **1-27**, wherein the HMC-EVs express at least one of the proteins in Table 15 at a higher level compared to UCB-MSC-EVs.

29. The method of any one of claims **1-28**, wherein the HMC-EVs express at least one of the proteins in Table 16 at a lower level compared to UCB-MSC-EVs.

30. The method of any one of claims **1-29**, wherein the HMC-EVs express at least one of the proteins in Table 17 at a higher level compared to BM-MSC-EVs.

31. The method of any one of claims **1-30**, wherein the HMC-EVs express at least one of the proteins in Table 18 at a lower level compared to BM-MSC-EVs.

32. The method of any one of claims **1-31**, wherein the HMC-EVs express at least one of the proteins in Table 19 at a higher level compared to AD-MSC-EVs.

33. The method of any one of claims **1-32**, wherein the HMC-EVs express at least one of the proteins in Table 20 at a lower level compared to AD-MSC-EVs.

34. The method of any one of claims **1-33**, wherein the HMC-EVs express at least one of the miRNA in Table 21 at a higher level compared to the HMCs.

35. The method of any one of claims **1-34**, wherein the HMC-EVs express at least one of the miRNA in Table 22 at a lower level compared to the HMCs.

36. The method of any one of claims **1-35**, wherein the HMC-EVs express at least one of the miRNAs selected from the group consisting of hsa-miR-125b-5p, hsa-miR-181a-5p, hsa-miR-199b-5p, hsa-miR-21-5p, hsa-miR-23a-3p, hsa-miR-125a-5p, hsa-miR-106a-5p+hsa-miR-17-5p and hsa-miR-221-3p at a higher level compared to BM-MSC-EVs, UCB-MSC-EVs, and/or AD-MSC-EVs.

37. The method of any one of claims **1-36**, wherein the HMC-EVs express at least one of the proteins selected from the group consisting of ALDOC, ANXA5, APBB2, BASP1, CAV1, CD81, CD99, CKM, EPB41L3, FDPS, GNAQ, GNG12, GP9, H2AC20, H2AC21, H3-3A, H3-7, H4-16, HLA-A, ITGA2, KPNA2, KRAS, KRT4, LRRK59, MAMDC2, MARCKSL1, MDGA1, MERTK, MFGE8, MMP14, MVP, PCDH1, PDGFRB, PDIA3, RPL13, RPS18, RPS3A, RPS4X, SDCBP, SLC2A1, SLC3A2, TAGLN2, TNC, TSPAN14, TSPAN33, TSPAN9, TTYH3, UCHL1, VAT1, YWHAQ, and YWHAQ at a higher level compared to BM-MSC-EVs, UCB-MSC-EVs, and/or AD-MSC-EVs.

38. The method of any one of claims **1-37**, wherein the HMC-EVs express at least one of the proteins selected from the group consisting of ADGRG6, AGRN, ANXA6, APOC4, ARHGAP1, ARGHdia, ARL8A, ARPC5, B2M, BBS1, BLVRA, BST1, CA2, CCN2, CCNB3, CD34, CD36, CD47, CORO1A, DTD1, EEF1D, EEF1G, ENG, ESD, GNAI2, GNB1, H1-3, H2BC15, HIP1, KIF11, LAMP1, LAP3, LGALS1, LTBP3, MAPK3, MARCKS, MBTD1, MDH1, MOB1B, MYL12B, MYO1F, MYO3A, NIBAN2, PEBP1, PF4, PGAP1, PLD1, PPP2R1A, PRSS23, PXDN, RALA, RAP2A, RPS13, RPS3, RPSA, S100A11, SLC44A1, SLC44A2, SLTM, SMG1, SPARC, SRSF8, STRADB, STX11, STXBP2, TGM2, TPP1, TPTE2, TRIM5, TRPM2, TUBA8, TUBB3, VCAN, YWHAE, and ZFN607 at a higher level compared to BM-MSC-EVs, UCB-MSC-EVs, and/or AD-MSC-EVs.

39. The method of any one of claims **1-38**, wherein the HMC-EVs express at least one of the proteins selected from the group consisting of ADIPOQ, CAT, CEP290, IGLV6-57, TAS2R33, and TMEM198 at a lower level compared to BM-MSC-EVs, UCB-MSC-EVs, and/or AD-MSC-EVs.

40. The method of any one of claims **1-39**, wherein the HMC-EVs express at least one of the proteins selected from the group consisting of AKAP9, ALB, ALOX5, APLP2, CD109, CDSN, CHST9, ERC1, F11, ARMCX5, LAMB4, LRRTM2, LTF, MSH6, OAF, OLML3, PAK6, RGS14, SEMA7A, SURF1, and TRIM4 at a lower level compared to BM-MSC-EVs, UCB-MSC-EVs, and/or AD-MSC-EVs.

41. The method of any one of claims **1-40**, wherein about 1×10^6 to about 1×10^3 HMC-EVs are administered to the subject.

42. The method of any one of claims **1-41**, wherein about 10×10^{10} or about 30×10^{10} HMC-EVs are administered to the subject.

43. The method of any one of claims **1-42**, wherein the HMC-EVs are administered in a pharmaceutical composition.

44. The method of claim **43**, wherein the pharmaceutical composition comprises

(a) a buffer, maintaining the solution at a physiological pH;

(b) at least 2 mM or at least 0.05% (w/v) glucose; and

(c) an osmotically active agent maintaining the solution at a physiological osmolarity.

45. The method of claim **44**, wherein the glucose is D-glucose (Dextrose).

46. The method of claim **44**, wherein the osmotically active agent is a salt.

47. The method of claim **46**, wherein the salt is sodium chloride.

48. The method of any one of claims **1-47**, further comprising administering to the subject an effective amount of HMCs obtained by in vitro differentiation of pluripotent stem cells.

49. A method of treating a brain injury in a subject suffering from, or suspected of suffering from, a brain injury, the method comprising administering to the subject an effective amount of mesenchymal stem cells (HMCs) obtained by in vitro differentiation of pluripotent stem cells, thereby treating the brain injury in the subject.

50. The method of claim **49**, wherein the brain injury is selected from the group consisting of stroke, optic neuropathy, traumatic brain injury, cerebral palsy, acquired brain

injury, anoxic brain injury, diffuse axonal brain injury, focal brain injury, subdural hematoma, brain aneurysm, and coma.

51. The method of claim **50**, wherein the brain injury is stroke.

52. The method of any one of claims **49-51**, wherein the method comprises preserving myelin in the brain following administration of the HMCs into the subject.

53. The method of any one of claims **49-51**, wherein the method comprises suppressing neuroinflammatory responses following administration of the HMCs into the subject.

54. The method of any one of claims **49-51**, wherein the method comprises reducing microglial and astrocyte activation in the brain following administration of the HMCs into the subject.

55. The method of any one of claims **49-51**, wherein the method comprises stimulating pathways involved in cell survival following administration of the HMCs into the subject.

56. The method of any one of claims **49-51**, wherein the method comprises stimulating expression of a neuroprotective gene in the brain following administration of the HMCs into the subject.

57. The method of claim **56**, wherein the neuroprotective gene is selected from the group consisting of heat shock protein family B member 1 (HSPB1), insulin-like growth factor 1 (IGF2), and secreted phosphoprotein 1 (SPP1).

58. The method of any one of claims **49-51**, wherein the method comprises stimulating pathways involved in synaptic transmission in the brain following administration of the HMCs into the subject.

59. The method of any one of claims **49-51**, wherein the method comprises stimulating pathways involved in the development of neuronal lineage following administration of the HMCs into the subject.

60. The method of any one of claims **49-51**, wherein the method comprises reducing apoptosis following administration of the HMCs into the subject.

61. The method of claim **50**, wherein the brain injury is traumatic brain injury.

62. The method of claim **61**, wherein the method comprises reducing tissue loss in the brain following administration of the HMCs into the subject.

63. The method of claim **61** or **62**, wherein the method comprises reducing cell death in the brain following administration of the HMCs into the subject.

64. The method of any one of claims **61-63**, wherein the method comprises increasing neurogenesis following the administration of the HMCs into the subject.

65. The method of any one of claims **61-64**, wherein the method comprises reducing the presence of microglia and macrophages in the cortex and striatum following the administration of the HMCs into the subject.

66. The method of any one of claims **61-65**, wherein the method comprises reducing inflammation of the spleen following the administration of the HMCs into the subject.

67. The method of any one of claims **61-66**, wherein the method comprises migration of HMCs across the blood-brain barrier to the cortex, striatum, and/or hippocampus.

68. The method of claim **50**, wherein the brain injury is cerebral palsy.

69. The method of claim **68**, wherein the method comprises reducing apoptosis in the brain following administration of the HMCs into the subject.

70. The method of claim **68** or **69**, wherein the method comprises reducing lesion size in the brain following administration of the HMCs into the subject.

71. The method of any one of claims **68-70**, wherein the method comprises reducing microglial and astrocyte activation in the brain following administration of the HMCs into the subject.

72. The method of any one of claims **68-71**, wherein the method comprises preserving myelin of the corpus callosum following administration of the HMCs into the subject.

73. The method of any one of claims **68-72**, wherein the method comprises at least a partial rescue of Olig2 in the brain following administration of the HMCs into the subject.

74. The method of any one of claims **49-73**, wherein the HMCs are administered systemically.

75. The method of any one of claims **49-73**, wherein the HMCs are administered intracerebrally.

76. The method of any one of claims **49-73**, wherein the HMCs are administered intrathecally.

77. The method of any one of claims **49-73**, wherein the HMCs are administered intracisternally.

78. The method of any one of claims **49-73**, wherein the HMCs are administered intraperitoneally.

79. The method of any one of claims **49-78**, wherein the mesenchymal stem cells are human cells.

80. The method of any one of claims **49-79**, wherein the subject is a human.

81. The method of any one of claims **49-80**, wherein the pluripotent stem cells are further differentiated into hemangioblasts.

82. The method of any one of claims **49-81**, wherein the pluripotent stem cells are embryonic stem cells.

83. The method of any one of claims **49-82**, wherein the pluripotent stem cells are induced pluripotent stem cells.

84. The method of any one of claims **49-83**, wherein the pluripotent stem cells are human pluripotent stem cells.

85. The method of any one of claims **49-84**, wherein the HMCs have been passaged no more than 5 times in vitro before administration into the subject.

86. The method of any one of claims **49-85**, wherein the HMCs express at least one of the genes in Table 3 at a higher level compared to bone marrow-derived MSCs (BM-MSCs).

87. The method of any one of claims **49-85**, wherein the HMCs express at least one of the genes in Table 4 at a lower level compared to BM-MSCs.

88. The method of any one of claims **49-85**, wherein the HMCs express at least one of the genes in Table 5 at a higher level compared to umbilical cord blood-derived MSCs (UCB-MSCs).

89. The method of any one of claims **49-85**, wherein the HMCs express at least one of the genes in Table 6 at a lower level compared to UCB-MSCs.

90. The method of any one of claims **49-85**, wherein the HMCs express at least one of the genes in Table 7 at a higher level compared to adipose tissue-derived MSCs (AD-MSCs).

91. The method of any one of claims **49-85**, wherein the HMCs express at least one of the genes in Table 8 at a lower level compared to AD-MSCs.

92. The method of any one of claims **49-85**, wherein the HMCs express, in a basal state, mRNA encoding interleukin-6 (IL-6) at a level less than ten percent of the IL-6 mRNA level expressed by BM-MSCs in a basal state and

wherein the HMCs express, in a basal state, mRNA encoding CD24 at a level that is greater than the CD24 mRNA level expressed by BM-MSCs in a basal state.

93. The method of any one of claims **49-85**, wherein the HMCs express at least one of the genes selected from the group consisting of CALR, UBB, PKM, CXCL8, C15orf48, PSME2, TPM3, ANKRD1, PFN1, SRGN, ACTB, MDK, TAGLN2, CFL1, HSP90AA1, HSPA8, CXCL12, UCHL1, HMGA2, HMGA1, HN1, PTMA, SP90AB1, PRDX1, GSTP1, KRT18, IGFBP4, CALD1, COL4A1, COL4A2, and GAPDH at a higher level compared to AD-MSCs.

94. The method of any one of claims **49-85**, wherein the HMCs express at least one of the genes selected from the group consisting of TMSB4X, ACTG1, GSTP1, KRT18, IGFBP5, NPY, KRT8, PRDX6, MDK, DKK3, UCHL1, TUBB3, HN1, PTMA, HSP90AB1, HMGA1, HSPA8, TAGLN2, ANKRD1, PFN1, CYBA, and UBB at a higher level compared to AD-MSCs.

95. The method of any one of claims **49-85**, wherein the HMCs express at least one of the genes selected from the group consisting of SERPINE1, ACTA2, TPM2, CTGF, SERPINE2, CRYAB, ELN, MFGE8, ANXA2, POSTN, VIM, MFAP5, ISLR, THBS1, TIMP3, DKK1, COL6A3, COL6A1, TPT1, BCYRN1, COL1A1, SPARC, TPM1, BGN, COL1A2, COL3A1, TGFB1, CRLF1, COMP, NEAT1, MT-CO3, MT-CO2, MT-ATP8, MT-CYB, MT-CO1, MT-ATP6, MT-ND4, MT-ND4L, MT-ND5, MT-ND6, MT-ND3, MT-ND1, MT-ND2, GREM1, TMSB4X, ITGB1, LMNA, H2AFZ, FTL, EEF1G, NPM1, EEF1A1, RACK1, ACTG1, and TPM4 at a lower level compared to AD-MSCs.

96. The method of any one of claims **49-85**, wherein the HMCs express at least one of the genes selected from the group consisting of SERPINE1, S100A6, CD59, POSTN, VIM, MFAP5, ISLR, THBS1, COL6A3, TIMP3, ELN, ANXA2, COL1A1, BCYRN1, CCDC80, COL6A1, COL6A2, BGN, COL1A2, COL3A1, TGFB1, CRLF1, COMP, and GREM1 at a lower level compared to AD-MSCs.

97. The method of any one of claims **49-85**, wherein the HMCs express at least one of the genes selected from the group consisting of MT1X, MT1G, TMSB10, CCL8, INHBA, CTSB, SERPINB2, ADM, APOL1, FTH1, CCL2, CCL5, CSF1, IL1B, IGFBP3, P4HB, DCN, FSTL1, ANXA5, LOX, CD63, CTSZ, FN1, LGALS1, LDHA, RCN3, MMP2, and TIMP1 at a lower level compared to AD-MSCs.

98. The method of any one of claims **49-85**, wherein the HMCs express at least one of the genes selected from the group consisting of PP1A, NPM1, HNRNPA1, IGFBP5, KRT19, KRT18, GSTP1, TUBB, TUBA1B, KRT8, HN1, PTMA, TUBA1C, HSPA8, HMGA1, CFL1, MYL6, ACTB, UCHL1, TAGLN2, MDK, GREM1, MMP1, and CTSC at a higher level compared to BM-MSCs.

99. The method of any one of claims **49-85**, wherein the HMCs express at least one of the genes selected from the group consisting of ANXA2, TPT1, VIM, COL6A1, BGN, COL6A2, CTGF, TIMP3, ACTA2, COL3A1, SPARC, ITGB1, SERPINH1, TPM2, TGFB1, COL1A1, TPM1, COL6A3, TPM4, SERPINE2, CALD1, COL1A2, TAGLN, MYL9, MT-RNR2, POSTN at a lower level compared to BM-MSCs.

100. The method of any one of claims **49-85**, wherein the HMCs express at least one of the miRNA in Table 21 at a lower level compared to the HMC-EVs.

101. The method of any one of claims **49-85**, wherein the HMCs express at least one of the miRNA in Table 22 at a higher level compared to the HMC-EVs.

102. The method of any one of claims **49-101**, wherein about 1×10^6 to about 1×10^{13} HMCs are administered to the subject.

103. The method of any one of claims **49-102**, wherein the HMCs are administered in a pharmaceutical composition.

104. The method of claim **103**, wherein the pharmaceutical composition comprises

- (a) a buffer, maintaining the solution at a physiological pH;
- (b) at least 2 mM or at least 0.05% (w/v) glucose; and
- (c) an osmotically active agent, maintaining the solution at a physiological osmolarity.

105. The method of claim **104**, wherein the glucose is D-glucose (Dextrose).

106. The method of claim **104**, wherein the osmotically active agent is a salt.

107. The method of claim **106**, wherein the salt is sodium chloride.

108. A composition comprising HMCs obtained by in vitro differentiation of pluripotent stem cells, wherein the HMCs express at least one of the genes selected from the group consisting of CALR, UBB, PKM, CXCL8, C15orf48, PSME2, TPM3, ANKRD1, PFN1, SRGN, ACTB, MDK, TAGLN2, CFL1, HSP90AA1, HSPA8, CXCL12, UCHL1, HMGA2, HMGA1, HN1, PTMA, SP90AB1, PRDX1, GSTP1, KRT18, IGFBP4, CALD1, COL4A1, COL4A2, and GAPDH at a higher level compared to AD-MSCs.

109. A composition comprising HMCs obtained by in vitro differentiation of pluripotent stem cells, wherein the HMCs express at least one of the genes selected from the group consisting of TMSB4X, ACTG1, GSTP1, KRT18, IGFBP5, NPY, KRT8, PRDX6, MDK, DKK3, UCHL1, TUBB3, HN1, PTMA, HSP90AB1, HMGA1, HSPA8, TAGLN2, ANKRD1, PFN1, CYBA, and UBB at a higher level compared to AD-MSCs.

110. A composition comprising HMCs obtained by in vitro differentiation of pluripotent stem cells, wherein the HMCs express at least one of the genes selected from the group consisting of PP1A, NPM1, HNRNPA1, IGFBP5, KRT19, KRT18, GSTP1, TUBB, TUBA1B, KRT8, HN1, PTMA, TUBA1C, HSPA8, HMGA1, CFL1, MYL6, ACTB, UCHL1, TAGLN2, MDK, GREM1, MMP1, and CTSC at a higher level compared to BM-MSCs.

111. A composition comprising HMCs obtained by in vitro differentiation of pluripotent stem cells, wherein the HMCs express at least one of the genes selected from the group consisting of SERPINE1, ACTA2, TPM2, CTGF, SERPINE2, CRYAB, ELN, MFGE8, ANXA2, POSTN, VIM, MFAP5, ISLR, THBS1, TIMP3, DKK1, COL6A3, COL6A1, TPT1, BCYRN1, COL1A1, SPARC, TPM1, BGN, COL1A2, COL3A1, TGFB1, CRLF1, COMP, NEAT1, MT-CO3, MT-CO2, MT-ATP8, MT-CYB, MT-CO1, MT-ATP6, MT-ND4, MT-ND4L, MT-ND5, MT-ND6, MT-ND3, MT-ND1, MT-ND2, GREM1, TMSB4X, ITGB1, LMNA, H2AFZ, FTL, EEF1G, NPM1, EEF1A1, RACK1, ACTG1, and TPM4 at a lower level compared to AD-MSCs.

112. A composition comprising HMCs obtained by in vitro differentiation of pluripotent stem cells, wherein the HMCs express at least one of the genes selected from the group consisting of SERPINE1, S100A6, CD59, POSTN, VIM, MFAP5, ISLR, THBS1, COL6A3, TIMP3, ELN,

ANXA2, COL1A1, BCYRN1, CCDC80, COL6A1, COL6A2, BGN, COL1A2, COL3A1, TGFB1, CRLF1, COMP, and GREM1 at a lower level compared to AD-MSCs.

113. A composition comprising HMCs obtained by in vitro differentiation of pluripotent stem cells, wherein the HMCs express at least one of the genes selected from the group consisting of MT1X, MT1G, TMSB10, CCL8, INHBA, CTSB, SERPINB2, ADM, APOL1, FTH1, CCL2, CCL5, CSF1, IL1B, IGFBP3, P4HB, DCN, FSTL1, ANXA5, LOX, CD63, CTSZ, FN1, LGALS1, LDHA, RCN3, MMP2, and TIMP1 at a lower level compared to AD-MSCs.

114. A composition comprising HMCs obtained by in vitro differentiation of pluripotent stem cells, wherein the HMCs express at least one of the genes selected from the group consisting of ANXA2, TPT1, VIM, COL6A1, BGN, COL6A2, CTGF, TIMP3, ACTA2, COL3A1, SPARC, ITGB1, SERPINH1, TPM2, TGFB1, COL1A1, TPM1, COL6A3, TPM4, SERPINE2, CALD1, COL1A2, TAGLN, MYL9, MT-RNR2, POSTN at a lower level compared to BM-MSCs.

115. The composition of any one of claims **108-114**, wherein the HMCs further express at least one of the genes in Table 3 at a higher level compared to BM-MSCs.

116. The composition of any one of claims **108-114**, wherein the HMCs further express at least one of the genes in Table 4 at a lower level compared to BM-MSCs.

117. The composition of any one of claims **108-114**, wherein the HMCs further express at least one of the genes in Table 5 at a higher level compared to UCB-MSCs.

118. The composition of any one of claims **108-114**, wherein the HMCs further express at least one of the genes in Table 6 at a lower level compared to UCB-MSCs.

119. The composition of any one of claims **108-114**, wherein the HMCs further express at least one of the genes in Table 7 at a higher level compared to AD-MSCs.

120. The composition of any one of claims **108-114**, wherein the HMCs further express at least one of the genes in Table 8 at a lower level compared to AD-MSCs.

121. A pharmaceutical composition comprising the HMCs of any one of claims **108-114**, and a pharmaceutically acceptable carrier.

122. A population of HMC-EVs of any one of claims **108-114**.

123. The population of EVs of claim **122**, wherein the HMC-EVs express at least one of the miRNA in Table 9 at a higher level compared UCB-MSC-EVs.

124. The population of EVs of claim **122 or 123**, wherein the HMC-EVs express at least one of the miRNA in Table 10 at a lower level compared to UCB-MSC-EVs.

125. The population of EVs of any one of claims **122-124**, wherein the HMC-EVs express at least one of the miRNA in Table 11 at a higher level compared to BM-MSC-EVs.

126. The population of EVs of any one of claims **122-125**, wherein the HMC-EVs express at least one of the miRNA in Table 12 at a lower level compared to BM-MSC-EVs.

127. The population of EVs of any one of claims **122-126**, wherein the HMC-EVs express at least one of the miRNA in Table 13 at a higher level compared to AD-MSC-EVs.

128. The population of EVs of any one of claims **122-127**, wherein the HMC-EVs express at least one of the miRNA in Table 14 at a lower level compared to AD-MSC-EVs.

129. The population of EVs of any one of claims **122-128**, wherein the HMC-EVs express at least one of the proteins in Table 15 at a higher level compared to UCB-MSC-EVs.

130. The population of EVs of any one of claims **122-129**, wherein the HMC-EVs express at least one of the proteins in Table 16 at a lower level compared to UCB-MSC-EVs.

131. The population of EVs of any one of claims **122-130**, wherein the HMC-EVs express at least one of the proteins in Table 17 at a higher level compared to BM-MSC-EVs.

132. The population of EVs of any one of claims **122-131**, wherein the HMC-EVs express at least one of the proteins in Table 18 at a lower level compared to BM-MSC-EVs.

133. The population of EVs of any one of claims **122-132**, wherein the HMC-EVs express at least one of the proteins in Table 19 at a higher level compared to AD-MSC-EVs.

134. The population of EVs of any one of claims **122-133**, wherein the HMC-EVs express at least one of the proteins in Table 20 at a lower level compared to AD-MSC-EVs.

135. The population of EVs of any one of claims **122-134**, wherein the HMC-EVs express at least one of the miRNA in Table 21 at a higher level compared to the HMCs.

136. The population of EVs of any one of claims **122-135**, wherein the HMC-EVs express at least one of the miRNA in Table 22 at a lower level compared to the HMCs.

137. The population of EVs of any one of claims **122-136**, wherein the HMC-EVs express at least one of the miRNAs selected from the group consisting of hsa-miR-125b-5p, hsa-miR-181a-5p, hsa-miR-199b-5p, hsa-miR-21-5p, hsa-miR-23a-3p, hsa-miR-125a-5p, hsa-miR-106a-5p+hsa-miR-17-5p and hsa-miR-221-3p at a higher level compared to BM-MSC-EVs, UCB-MSC-EVs, and/or AD-MSC-EVs.

138. The population of EVs of any one of claims **122-137**, wherein the HMC-EVs express at least one of the proteins selected from the group consisting of ALDOC, ANXA5, APBB2, BASP1, CAV1, CD81, CD99, CKM, EPB41L3, FDPS, GNAQ, GNG12, GP9, H2AC20, H2AC21, H3-3A, H3-7, H4-16, HLA-A, ITGA2, KPNA2, KRAS, KRT4, LRRK59, MAMDC2, MARCKSL1, MDGA1, MERTK, MGFE8, MMP14, MVP, PCDH1, PDGFRB, PDIA3, RPL13, RPS18, RPS3A, RPS4X, SDCBP, SLC2A1, SLC3A2, TAGLN2, TNC, TSPAN14, TSPAN33, TSPAN9, TTYH3, UCHL1, VAT1, YWHAB, and YWHAQ at a higher level compared to BM-MSC-EVs, UCB-MSC-EVs, and/or AD-MSC-EVs.

139. The population of EVs of any one of claims **122-138**, wherein the HMC-EVs express at least one of the proteins selected from the group consisting of ADGRG6, AGRN, ANXA6, APOC4, ARHGAP1, ARGHIDIA, ARL8A, ARPC5, B2M, BBS1, BLVRA, BST1, CA2, CCN2, CCNB3, CD34, CD36, CD47, CORO1A, DTD1, EEF1D, EEF1G, ENG, ESD, GNAI2, GNB1, H1-3, H2BC15, HIP1, KIF11, LAMP1, LAP3, LGALS1, LTBP3, MAPK3, MARCKS, MBTD1, MDH1, MOB1B, MYL12B, MYO1F, MYO3A, NIBAN2, PEBP1, PF4, PGAP1, PLOD1, PPP2R1A, PRSS23, PXDN, RALA, RAP2A, RPS13, RPS3, RPSA, S100A 11, SLC44A 1, SLC44A2, SLTM, SMG1, SPARC, SRSF8, STRADB, STX11, STXBP2, TGM2, TPP1, TPTE2, TRIM5, TRPM2, TUBA8, TUBB3, VCAN, YWHAE, and ZFN607 at a higher level compared to BM-MSC-EVs, UCB-MSC-EVs, and/or AD-MSC-EVs.

140. The population of HMC-EVs of any one of claims **122-139**, wherein the HMC-EVs express at least one of the proteins selected from the group consisting of ADIPOQ,

CAT, CEP290, IGLV6-57, TAS2R33, and TMEM198 at a lower level compared to BM-MSC-EVs, UCB-MSC-EVs, and/or AD-MSC-EVs.

141. The population of HMC-EVs of any one of claims **122-140**, wherein the HMC-EVs express at least one of the proteins selected from the group consisting of AKAP9, ALB, ALOX5, APLP2, CD109, CDSN, CHST9, ERC1, F11, ARMCX5, LAMB4, LRRTM2, LTF, MSH6, OAF, OLFML3, PAK6, RGS14, SEMA7A, SURF1, and TRIM4 at a lower level compared to BM-MSC-EVs, UCB-MSC-EVs, and/or AD-MSC-EVs.

142. A pharmaceutical composition comprising the HMC-EVs of any one of claims **122-141**, and a pharmaceutically acceptable carrier.

143. A population of HMC-EVs obtained by in vitro differentiation of pluripotent stem cells, wherein the HMC-EVs express at least one of the miRNAs in Table 9 at a higher level compared to UCB-MSC-EVs.

144. A population of HMC-EVs obtained by in vitro differentiation of pluripotent stem cells, wherein the HMC-EVs express at least one of the miRNAs in Table 10 at a lower level compared to UCB-MSC-EVs.

145. A population of HMC-EVs obtained by in vitro differentiation of pluripotent stem cells, wherein the HMC-EVs express at least one of the miRNAs in Table 11 at a higher level compared to BM-MSC-EVs.

146. A population of HMC-EVs obtained by in vitro differentiation of pluripotent stem cells, wherein the HMC-EVs express at least one of the miRNAs in Table 12 at a lower level compared to BM-MSC-EVs.

147. A population of HMC-EVs obtained by in vitro differentiation of pluripotent stem cells, wherein the HMC-EVs express at least one of the miRNAs in Table 13 at a higher level compared to AD-MSC-EVs.

148. A population of HMC-EVs obtained by in vitro differentiation of pluripotent stem cells, wherein the HMC-EVs express at least one of the miRNA in Table 14 at a lower level compared to AD-MSC-EVs.

149. A population of HMC-EVs obtained by in vitro differentiation of pluripotent stem cells, wherein the HMC-EVs express at least one of the proteins in Table 15 at a higher level compared to UCB-MSC-EVs.

150. A population of HMC-EVs obtained by in vitro differentiation of pluripotent stem cells, wherein the HMC-EVs express at least one of the proteins in Table 16 at a lower level compared to UCB-MSC-EVs.

151. A population of HMC-EVs obtained by in vitro differentiation of pluripotent stem cells, wherein the HMC-EVs express at least one of the proteins in Table 17 at a higher level compared to (BM-MSC-EVs).

152. A population of HMC-EVs obtained by in vitro differentiation of pluripotent stem cells, wherein the HMC-EVs express at least one of the proteins in Table 18 at a lower level compared to BM-MSC-EVs.

153. A population of HMC-EVs obtained by in vitro differentiation of pluripotent stem cells, wherein the HMC-EVs express at least one of the proteins in Table 19 at a higher level compared to AD-MSC-EVs.

154. A population of HMC-EVs obtained by in vitro differentiation of pluripotent stem cells, wherein the HMC-EVs express at least one of the proteins in Table 20 at a lower level compared to AD-MSC-EVs.

155. A population of HMC-EVs obtained by in vitro differentiation of pluripotent stem cells, wherein the HMC-

EVs express at least one of the miRNAs selected from the group consisting of hsa-miR-125b-5p, hsa-miR-181a-5p, hsa-miR-199b-5p, hsa-miR-21-5p, hsa-miR-23a-3p, hsa-miR-125a-5p, hsa-miR-106a-5p+hsa-miR-17-5p and hsa-miR-221-3p at a higher level compared to BM-MSC-EVs, UCB-MSC-EVs, and/or AD-MSC-EVs.

156. A population of HMC-EVs obtained by in vitro differentiation of pluripotent stem cells, wherein the HMC-EVs express at least one of the proteins selected from the group consisting of ALDOC, ANXA5, APBB2, BASP1, CAV1, CD81, CD99, CKM, EPB41L3, FDPS, GNAQ, GNG12, GP9, H2AC20, H2AC21, H3-3A, H3-7, H4-16, HLA-A, ITGA2, KPNA2, KRAS, KRT4, LRRC59, MAMDC2, MARCKSL1, MDGA1, MERTK, MGFE8, MMP14, MVP, PCDH1, PDGFRB, PDIA3, RPL13, RPS18, RPS3A, RPS4X, SDCBP, SLC2A1, SLC3A2, TAGLN2, TNC, TSPAN14, TSPAN33, TSPAN9, TTYH3, UCHL1, VAT1, YWHAQ, and YWHAQ at a higher level compared to BM-MSC-EVs, UCB-MSC-EVs, and/or AD-MSC-EVs.

157. A population of HMC-EVs obtained by in vitro differentiation of pluripotent stem cells, wherein the HMC-EVs express at least one of the proteins selected from the group consisting of ADGRG6, AGRN, ANXA6, APOC4, ARHGAP1, ARGHEDIA, ARL8A, ARPC5, B2M, BBS1, BLVRA, BST1, CA2, CCN2, CCNB3, CD34, CD36, CD47, CORO1A, DTD1, EEF1D, EEF1G, ENG, ESD, GNAI2, GNB1, H1-3, H2BC15, HIP1, KIF11, LAMP1, LAP3, LGALS1, LTBP3, MAPK3, MARCKS, MBTD1, MDH1, MOB1B, MYL12B, MYO1F, MYO3A, NIBAN2, PEBP1, PF4, PGAP1, PLD1, PPP2R1A, PRSS23, PXDN, RALA, RAP2A, RPS13, RPS3, RPSA, S100A11, SLC44A1, SLC44A2, SLTM, SMG1, SPARC, SRSF8, STRADB, STX11, STXBP2, TGM2, TPP1, TPTE2, TRIM5, TRPM2, TUBA8, TUBB3, VCAN, YWHAE, and ZFN607 at a higher level compared to BM-MSC-EVs, UCB-MSC-EVs, and/or AD-MSC-EVs.

158. A population of HMC-EVs obtained by in vitro differentiation of pluripotent stem cells, wherein the HMC-EVs express at least one of the proteins selected from the group consisting of ADIPOQ, CAT, CEP290, IGLV6-57, TAS2R33, and TMEM198 at a lower level compared to BM-MSC-EVs, UCB-MSC-EVs, and/or AD-MSC-EVs.

159. A population of HMC-EVs obtained by in vitro differentiation of pluripotent stem cells, wherein the HMC-EVs express at least one of the proteins selected from the group consisting of AKAP9, ALB, ALOX5, APLP2, CD109, CDSN, CHST9, ERC1, F11, ARMCX5, LAMB4, LRRTM2, LTF, MSH6, OAF, OLFML3, PAK6, RGS14, SEMA7A, SURF1, and TRIM4 at a lower level compared to BM-MSC-EVs, UCB-MSC-EVs, and/or AD-MSC-EVs.

160. A population of HMC-EVs obtained by in vitro differentiation of pluripotent stem cells, wherein the HMC-EVs express at least one of the miRNA in Table 21 at a higher level compared to the HMCs.

161. A population of HMC-EVs obtained by in vitro differentiation of pluripotent stem cells, wherein the HMC-EVs express at least one of the miRNA in Table 22 at a lower level compared to the HMCs.

162. A pharmaceutical composition comprising the HMC-EVs of any one of claims **143-161**, and a pharmaceutically acceptable carrier.

163. A method of determining neurite outgrowth of an HMC population comprising:

- (a) preparing a mixed neuronal culture from an isolated cerebral cortex;
- (b) plating the HMC population on a permeable membrane;
- (c) applying strain on the mixed neuronal culture;
- (d) overlaying the strained mixed neuronal culture with the permeable membrane of step (b); and
- (e) measuring neurite outgrowth of the mixed neuronal culture.

164. The method of claim 163, further determining gene expression of the mixed neuronal culture in the presence and absence of the HMC population.

165. The method of claim 163, wherein the strain is a physical scratch made in the mixed neuronal culture.

166. The method of claim 163, wherein the strain is vacuum pressure and positive air pressure applied to the mixed neuronal culture.

167. The method of claim 163, wherein the strain is applied at 15% to 0% stretching oscillations.

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