CL:0000037 hematopoietic stem cell

(Unique DEGs among top-100 found by the distance-based method, 52 genes)
6 genes are specifically directly related to hematopoietic stem cell
5 additional genes are related to hematopoietic stem cell

mndal: **myeloid nuclear differentiation** antigen like:
Suppresses cell growth when expressed ectopically.

ctgf: connective tissue growth factor:
Major connective tissue mitoattractant secreted by vascular endothelial cells. Promotes proliferation and differentiation of chondrocytes. Mediates heparin- and divalent cation-dependent cell adhesion in many cell types including fibroblasts, myofibroblasts, endothelial and epithelial cells. Enhances fibroblast growth factor-induced DNA synthesis.

hspb1: heat shock protein 1:
Involved in stress resistance and actin organization.

ins2: insulin II:
This gene **encodes insulin**, a peptide hormone that plays a vital role in the regulation of carbohydrate and lipid metabolism. The encoded precursor protein undergoes proteolytic cleavage to produce a disulfide-linked heterodimeric functional protein that is stored in secretory granules. An increase in blood glucose levels, among others, induces the release of insulin from the secretory granules.
Insulin decreases blood glucose concentration. It increases cell permeability to monosaccharides, amino acids and fatty acids. It accelerates glycolysis, the pentose phosphate cycle, and glycogen synthesis in liver.

ajuba: ajuba LIM protein:

pcsk2: proprotein convertase subtilisin/kexin type 2 :
Involved in the processing of hormone and other protein precursors at sites comprised of pairs of basic amino acid residues. **Responsible for the release of glucagon from proglucagon in pancreatic A cells**.

pgam1: phosphoglycerate mutase 1:
Interconversion of 3- and 2-phosphoglycerate with 2,3- bisphosphoglycerate as the primer of the reaction. Can also catalyze the reaction of EC 5.4.2.4 (synthase) and EC 3.1.3.13 (phosphatase), but with a reduced activity.

sparc: secreted acidic cysteine rich glycoprotein:
Appears to **regulate cell growth through interactions with the extracellular matrix and cytokines**. Binds calcium and copper, several types of collagen, albumin, thrombospondin, **PDGF** and cell membranes. There are two calcium binding sites; an acidic domain that binds 5 to 8 Ca(2+) with a low affinity and an EF-hand loop that binds a Ca(2+) ion with a high affinity.

tdgf1: teratocarcinoma-derived growth factor 1:
Could play a role in the determination of the epiblastic cells that subsequently give rise to the **mesoderm**.

utf1: undifferentiated embryonic cell transcription factor 1:
Acts as a transcriptional coactivator of ATF2.

zfp42: zinc finger protein 42:
Involved in the **reprogramming of X-chromosome inactivation during the acquisition of pluripotency**. Required for efficient elongation of TSIX, a non-coding RNA antisense to XIST. Binds DXPas34 enhancer within the TSIX promoter. Involved in ES cell self-renewal.

dbpht2: DNA binding protein with his-thr domain.

dppa5a: developmental pluripotency associated 5A:
Involved in the **maintenance of embryonic stem (ES) cell pluripotency**. Dispensable for self-renewal of pluripotent ES cells and establishment of germ cells. Associates with specific target mRNAs.

cldn6: claudin 6:
This gene encodes a member of the claudin family. Claudins are integral membrane proteins and components of tight junction strands. Tight junction strands serve as a physical barrier to prevent solutes and water from passing freely through the paracellular space between epithelial or endothelial cell sheets, and also play critical roles in maintaining cell polarity and signal transductions. The protein encoded by this gene is **essential for blastocyst formation in preimplantation mouse embryos**, and is invloved in and is crucial for the formation and maintenance of the epidermal permeability barrier. Plays a **major role in tight junction-specific obliteration of the intercellular space**, through calcium- independent cell-adhesion activity.

mapk8ip2: mitogen-activated protein kinase 8 interacting protein 2:
The JNK-interacting protein (JIP) group of scaffold proteins selectively mediates JNK signaling by aggregating specific components of the MAPK cascade to form a functional JNK signaling module. JIP2 **inhibits IL1 beta-induced apoptosis in insulin-secreting cells**.

dusp26: dual specificity phosphatase 26 (putative):
Inactivates MAPK1 and MAPK3 which leads to **dephosphorylation of heat shock factor protein 4** and a reduction in its DNA-binding activity.

cnn3: calponin 3, acidic:
Thin filament-associated protein that is implicated in the **regulation and modulation of smooth muscle contraction**. It is capable of binding to actin, calmodulin, troponin C and

tropomyosin. The interaction of calponin with actin inhibits the actomyosin Mg-ATPase activity.

zcchc12: zinc finger, CCHC domain containing 12:
Transcriptional coactivator in **the bone morphogenetic protein (BMP)-signaling pathway**. It positively modulates BMP signaling by interacting with SMAD1 and associating with CBP in the transcription complex. It contributes to the BMP-induced enhancement of cholinergic-neuron-specific gene expression.

tubb2b: tubulin, beta 2B class IIB:
Tubulin is the major constituent of microtubules. It binds two moles of GTP, one at an exchangeable site on the beta chain and one at a non-exchangeable site on the alpha chain (By similarity). TUBB2B is implicated in neuronal migration.

chpf: chondroitin polymerizing factor:
Has both beta-1,3-glucuronic acid and beta-1,4-N- acetylgalactosamine transferase activity. Transfers glucuronic acid (GlcUA) from UDP-GlcUA and N-acetylgalactosamine (GalNAc) from UDP-GalNAc to the non-reducing end of the elongating chondroitin polymer (By similarity). Isoform 2 may facilitate PARK2 transport into the mitochondria. In collaboration with PARK2, isoform 2 may **enhance cell viability and protect cells from oxidative stress**.

prss23: protease, serine 23.

shisa4: shisa family member 4:

bhlhe41: basic helix-loop-helix family, member e41:
This gene encodes a basic helix-loop-helix protein expressed in various tissues. The encoded protein can interact with Arntl or compete for E-box binding sites in the promoter of Per1 and repress Clock/Arntl's transactivation of Per1. This gene is believed to be involved in **the control of circadian rhythm and cell differentiation**. Defects in this gene are associated with the short sleep phenotype.
Transcriptional repressor involved in the **regulation of the circadian rhythm** by negatively **regulating the activity of the clock genes and clock-controlled genes**. Acts as the negative limb of a novel autoregulatory feedback loop (DEC loop) which differs from the one formed by the PER and CRY transcriptional repressors (PER/CRY loop). Both these loops are interlocked as it represses the expression of PER1 and in turn is repressed by PER1/2 and CRY1/2. Represses the activity of the circadian transcriptional activator-CLOCK-ARNTL/BMAL1 heterodime.

tmem132a: transmembrane protein 132A:
May **play a role in embryonic and postnatal development of the brain**. Increased resistance to cell death induced by serum starvation in cultured cells. Regulates cAMP-induced GFAP gene expression via STAT3 phosphorylation

sall4: spalt like transcription factor 4:

This gene belongs to the spalt family of zinc finger transcription factors. In mouse, functions for this gene have been described in many embryonic developmental processes, including brain, heart, and limb development. In addition, this gene is **an important pluripotency factor that is required for stem cell maintenance**. Homozygous mutant mice display embryonic lethality, while conditional knock-out in embryonic germ cells results in failure to establish a robust stem cell population.
Transcription factor with **a key role in the maintenance and self-renewal of embryonic and hematopoietic stem cells**.

cldn9: claudin 9:

This intronless gene encodes a member of the claudin family. Claudins are integral membrane proteins and components of tight junction strands. Tight junction strands serve as a physical barrier to prevent solutes and water from passing freely through the paracellular space between epithelial or endothelial cell sheets, and also play critical roles in maintaining cell polarity and signal transductions. This gene is developmentally regulated; it is expressed in neonate kidney, but disappers by adulthood. It is required for the preservation of sensory cells in the hearing organ and the gene deficiency is associated with deafness.
Plays a major role in tight junction-specific obliteration of the intercellular space, through calcium- independent cell-adhesion activity.

ddr1: discoidin domain receptor family, member 1:

Tyrosine kinase that functions as cell surface **receptor for fibrillar collagen and regulates cell attachment to the extracellular matrix, remodeling of the extracellular matrix, cell migration, differentiation, survival and cell proliferation**. Collagen binding triggers a signaling pathway that involves SRC and leads to the activation of MAP kinases. Regulates remodeling of the extracellular matrix by up-regulation of the matrix metalloproteinases MMP2, MMP7 and MMP9, and thereby facilitates cell migration and wound healing.

pyy: peptide YY:

This gut peptide **inhibits exocrine pancreatic secretion**, has a vasoconstrictory action and inhibitis jejunal and colonic mobility.

sox2: SRY (sex determining region Y)-box 2:

This intronless gene encodes a member of the SRY-related HMG-box (SOX) family of transcription factors involved in the **regulation of embryonic development and in the determination of cell fate**. The product of this gene is **required for stem-cell maintenance in the central nervous system, and also regulates gene expression in the stomach**. Mutations in a similar gene in human have been associated with optic nerve hypoplasia and with syndromic microphthalmia, a severe form of structural eye malformation. This gene lies within an intron of another gene called SOX2 overlapping transcript (Sox2ot).
Transcription factor that forms a trimeric complex with OCT4 on DNA and controls the expression of a number of genes involved in embryonic development such as YES1, FGF4, UTF1 and ZFP206. **Critical for early embryogenesis and for embryonic stem cell**

pluripotency. May function as a switch in neuronal development. Downstream SRRT target that **mediates the promotion of neural stem cell self-renewal**. Keeps neural cells undifferentiated by counteracting the activity of proneural proteins and suppresses neuronal differentiation.

sept3: septin 3:
Filament-forming cytoskeletal GTPase. May play a role in cytokinesis (Potential).

zfp185: zinc finger protein 185:
May be involved in the **regulation of cellular proliferation and/or differentiation**.

pcbp4: poly(rC) binding protein 4:
Single-stranded nucleic acid binding protein that binds preferentially to oligo dC.

col6a2: collagen, type VI, alpha 2:
Collagen VI acts as a cell-binding protein.

gmfg: glia maturation factor, gamma.

elf3: E74-like factor 3:
Transcriptional activator that binds and transactivates ETS sequences containing the consensus nucleotide core sequence GGA[AT]. Acts synergistically with POU2F3 to transactivate the SPRR2A promoter and with RUNX1 to transactivate the ANGPT1 promoter. Also **transactivates collagenase**, CCL20, CLND7, FLG, KRT8, NOS2, PTGS2, SPRR2B, TGFBR2 and TGM3 promoters. Represses KRT4 promoter activity. Involved in **mediating vascular inflammation**. May **play an important role in epithelial cell differentiation and tumorigenesis**.

col6a1: collagen, type VI, alpha 1:
Collagen VI acts as a cell-binding protein.

sparcl1: SPARC-like 1.

mafb: v-maf musculoaponeurotic fibrosarcoma oncogene family, protein B (avian):
Acts as a transcriptional activator or repressor. Plays a **pivotal role in regulating lineage-specific hematopoiesis by repressing ETS1-mediated transcription of erythroid-specific genes in myeloid cells**. Required for monocytic, macrophage, osteoclast, podocyte and islet beta cell differentiation. Involved in renal tubule survival and F4/80 maturation. Activates the insulin and glucagon promoters. Together with PAX6, transactivates weakly the glucagon gene promoter through the G1 element. SUMO modification control

scg5: secretogranin V:
Acts as **a molecular chaperone for PCSK2/PC2, preventing its premature activation in the regulated secretory pathway**. Binds to inactive PCSK2 in the endoplasmic reticulum and facilitates its transport from there to later compartments of the secretory pathway where it is proteolytically matured and activated. Also required for cleavage of PCSK2 but

does not appear to be involved in its folding. **Plays a role in regulating pituitary hormone secretion**. The C-terminal peptide inhibits PCSK2 in vitro.

atp6v0e2: ATPase, H+ transporting, lysosomal V0 subunit E2:

Vacuolar ATPase is responsible for acidifying a variety of intracellular compartments in eukaryotic cells.

cldn4: claudin 4:

This gene encodes a member of the claudin family. **Claudins are integral membrane proteins and components of tight junction strands**. Tight junction strands serve as a physical barrier to prevent solutes and water from passing freely through the paracellular space between epithelial or endothelial cell sheets, and also play critical roles in maintaining cell polarity and signal transductions. The protein encoded by this gene is a high-affinity receptor for clostridium perfringens enterotoxin (CPE) produced by the bacterium Clostridium perfringens, and the interaction with CPE results in increased membrane permeability by forming small pores in plasma membrane. This protein augments alveolar epithelial barrier function and is induced in acute lung injury. It is highly expressed in pancreatic and ovarian cancers.
Plays a major role in tight junction-specific obliteration of the intercellular space, through calcium- independent cell-adhesion activity.

cacnb3: calcium channel, voltage-dependent, beta 3 subunit:

The beta subunit of voltage-dependent calcium channels **contributes to the function of the calcium channel** by increasing peak calcium current, shifting the voltage dependencies of activation and inactivation, **modulating G protein inhibition** and controlling the alpha-1 subunit membrane targeting.

gpr62: G protein-coupled receptor 62:

Orphan receptor.

gjc1: gap junction protein, gamma 1:

One **gap junction** consists of a cluster of closely packed pairs of transmembrane channels, the connexons, through which materials of low MW diffuse from one cell to a neighboring cell.

gcg: glucagons:

This gene **encodes glucagon**, **a pancreatic hormone that counteracts the action of insulin in the bloodstream**. The encoded protein is processed to generate glucagon and two other glucagon-like peptides, GLP1 and GLP2. Glucagon stimulates gluconeogenesis, glycogenolysis and lipolysis. GLP1 induces secretion of insulin, suppresses glucagon secretion and inhibits feeding. GLP2 **induces intestinal absorption of glucose** by **stimulating the growth of intestinal cells** and preventing apoptosis.
Glicentin may **modulate gastric acid secretion and gastro-pyloro-duodenal activity**.

timp1: tissue inhibitor of metalloproteinase 1:

Metalloproteinase inhibitor that functions by forming one to one complexes with **target metalloproteinases, such as collagenases, and irreversibly inactivates them** by binding to their catalytic zinc cofactor. Acts on MMP1, MMP2, MMP3, MMP7, MMP8, MMP9, MMP10, MMP11, MMP12, MMP13 and MMP16. Does not act on MMP14. Also functions **as a growth factor that regulates cell differentiation**, migration and cell death and activates cellular signaling cascades via CD63 and ITGB1. Plays a role in integrin signaling.

sall1: spalt like transcription factor 1:

Transcriptional repressor **involved in organogenesis**. **Essential for ureteric bud invasion in kidney development.** Homozygous deletion of SALL1 results in an incomplete ureteric bud outgrowth, a failure of tubule formation in the **mesenchyme** and an apoptosis of the **mesenchyme**.

gas2l1: growth arrest-specific 2 like 1:

This gene encodes a member of the Gas2 family, **actin-associated proteins** expressed at high levels in growth-arrested cells. The gene expression is negatively regulated by serum and growth factors.
Seems to be **involved in the cross-linking of microtubules and microfilaments**.

st8sia3: ST8 alpha-N-acetyl-neuraminide alpha-2,8-sialyltransferase 3:

Catalyzes the transfer of sialic acid from a CMP-linked sialic acid donor onto the terminal sialic acid of an acceptor through alpha-2,8-linkages. Is active with alpha-2,3-linked, alpha-2,6-linked and alpha-2,8-linked sialic acid of **N-linked oligosaccharides of glycoproteins and glycolipids**. Displays preference for substrates with alpha-2,3-linked terminal sialic acid. It can form polysialic acid in vitro directly on alpha-2,3-, alpha-2,6-, or alpha-2,8-linked sialic acid.

pacsin1: protein kinase C and casein kinase substrate in neurons 1:

Binds to membranes via its F-BAR domain and **mediates membrane tubulation**. **Plays a role in the reorganization of the microtubule cytoskeleton** via its interaction with MAPT; this decreases microtubule stability and inhibits MAPT-induced microtubule polymerization. **Plays a role in cellular transport processes** by recruiting DNM1, DNM2 and DNM3 to membranes. **Plays a role in the reorganization of the actin cytoskeleton and in neuron morphogenesis** via its interaction with COBL and WASL, and by recruiting COBL to the cell cortex.

tram1l1: translocation associated membrane protein 1-like 1:

Stimulatory or required for the **translocation of secretory proteins across the ER membrane**.

caly: calcyon neuron-specific vesicular protein:

Interacts with clathrin light chain A and **stimulates clathrin self-assembly and clathrin-mediated endocytosis**.