CL:0002319 neural cell

(Unique DEGs among top-100 found by the distance-based method, 44 genes)
15 genes are specifically directly related to neural cell
4 additional genes are related to neural cell

dynlt1c: dynein light chain Tctex-type 1C.

ccl21b: chemokine (C-C motif) ligand 21B (leucine).

klhl3: kelch-like 3:

Substrate-specific adapter of a BCR (BTB-CUL3-RBX1) E3 ubiquitin ligase complex that acts as **a regulator of ion transport in the distal nephron**. The BCR(KLHL3) complex acts by mediating ubiquitination of WNK4, an inhibitor of potassium channel KCNJ1, leading to WNK4 degradation.

gm10591: predicted gene 10591.

gm13304: predicted gene 13304.

gm21541: predicted gene, 21541.

dock9: dedicator of cytokinesis 9:

Guanine nucleotide-exchange factor (GEF) that activates CDC42 by exchanging bound GDP for free GTP. Overexpression induces filopodia formation.

lgals2: lectin, galactose-binding, soluble 2:

This protein binds beta-galactoside. Its physiological function is not yet known.

grm7: glutamate receptor, metabotropic 7:

G-protein coupled receptor for glutamate. Ligand binding causes a conformation change that triggers signaling via guanine nucleotide-binding proteins (G proteins) and modulates the activity of down-stream effectors, such as adenylate cyclase. Signaling inhibits adenylate cyclase activity.

npy: neuropeptide Y:

NPY is implicated in the **control of feeding and in secretion of gonadotrophin-release hormone**.

akr7a5: aldo-keto reductase family 7, member A5 (aflatoxin aldehyde reductase):

Catalyzes the NADPH-dependent reduction of succinic semialdehyde to gamma-hydroxybutyrate. May have an important role in producing the neuromodulator gamma-hydroxybutyrate (GHB). Has broad substrate specificity. Can reduce the dialdehyde protein- binding form of aflatoxin B1 (AFB1) to the non-binding AFB1 dialcohol. May be involved in protection of liver against the toxic and carcinogenic effects of AFB1, a potent hepatocarcinogen.

adam15: a disintegrin and metallopeptidase domain 15 (metargidin):

This gene encodes a member of a disintegrin and metalloprotease (ADAM) family of endoproteases that play important roles in various biological processes including **cell signaling**, **adhesion and migration**. This gene is prominently **expressed in vascular cells**, **the endocardium**, **hypertrophic cells in developing bone**, **and specific areas of hippocampus and cerebellum**. The encoded preproprotein undergoes proteolytic processing to generate a mature, functional protein. Mice lacking the encoded protein have increased bone mass resulting from osteoblast proliferation, and exhibit reduced neovascularization in a mouse model for retinopathy.

Active metalloproteinase with gelatinolytic and collagenolytic activity. Plays a role in the wound healing process. Mediates both heterotypic intraepithelial cell/T-cell interactions and homotypic T-cell aggregation. Inhibits beta-1 integrin-mediated cell adhesion and migration of airway smooth muscle cells. Suppresses cell motility on or towards fibronectin possibly by driving alpha-v/beta-1 integrin (ITAGV-ITGB1) cell surface expression via ERK1/2 inactivation. Cleaves E-cadherin in response to growth factor deprivation.

adra1a: adrenergic receptor, alpha 1a:

This gene encodes one of several multipass transmembrane proteins that function as G protein-coupled receptors. The encoded protein binds to epinephrine and norepinephrine to **mediate signaling in cells of the cardiac, nervous, and other organ systems.**This alpha-adrenergic receptor mediates its action by association with G proteins that activate a phosphatidylinositol- calcium second messenger system. Its effect is mediated by G(q) and G(11) proteins. Nuclear ADRA1A-ADRA1B heterooligomers regulate phenylephrine (PE)-stimulated ERK signaling in cardiac myocytes.

anxa7: annexin A7:

Calcium/phospholipid-binding protein which **promotes membrane fusion** and **is involved in exocytosis**.

apoc1: apolipoprotein C-I:

This gene encodes a precursor plasma protein that is cleaved to yield a signal peptide and two alternatively processed mature peptides. The encoded protein, which is a component of chylomicrons, very low density lipoproteins and high density lipoproteins, **transports lipids from the intestines to other locations** in the body. This protein binds to free fatty acids preventing their uptake by cells. This protein is a **cofactor for lecithin cholesterol acyltransferase**, an enzyme that **catalyzes the conversion of free cholesterol to cholesteryl esters**. The encoded protein inhibits the activity of the cholesteryl ester transfer protein which promotes the exchange of neutral lipids between lipoproteins. This gene is clustered with three other apolipoprotein genes on chromosome 7. Inhibitor of lipoprotein binding to the low density lipoprotein (LDL) receptor, LDL receptor-related protein, and very low density lipoprotein (VLDL) receptor. Associates with high density lipoproteins (HDL) and the triacylglycerol-rich lipoproteins in the plasma and makes up about 10% of the protein of the VLDL and 2% of that of HDL. Appears to **interfere directly with fatty acid uptake** and is also the **major plasma**

inhibitor of cholesteryl ester transfer protein (CETP). Modulates the interaction of APOE with beta-migrating VLDL

<u>neurod6</u>: **neurogenic** differentiation 6:

Activates E box-dependent transcription in collaboration with TCF3/E47. May be a trans-acting factor involved in the development and maintenance of the mammalian nervous system. Transactivates the promoter of its own gene.

bcan: brevican:

May play a role in the terminally differentiating and the adult nervous system during postnatal development. Could stabilize interactions between hyaluronan (HA) and brain proteoglycans

<u>cspg4</u>: chondroitin sulfate proteoglycan 4:

Proteoglycan playing a role in cell proliferation and migration which stimulates endothelial cells motility during microvascular morphogenesis. May also **inhibit neurite outgrowth and growth cone collapse during axon regeneration.** Cell surface receptor for collagen alpha 2(VI) which may confer cells ability to migrate on that substrate. Binds through its extracellular N- terminus growth factors, extracellular matrix proteases modulating their activity. May regulate MPP16-dependent degradation and invasion of type I collagen participating in melanoma.

<u>fabp7</u>: fatty acid binding protein 7, brain:

B-FABP could be involved in the transport of a so far unknown hydrophobic ligand with potential morphogenic activity during CNS development. It is required for the **establishment of the radial glial fiber system** in developing brain, **a system that is necessary for the migration of immature neurons to establish cortical layers**.

camk2b: calcium/calmodulin-dependent protein kinase II, beta.

cd38: CD38 antigen:

This gene encodes a non-lineage-restricted, type II transmembrane glycoprotein that synthesizes and hydrolyzes cyclic adenosine 5'-diphosphate-ribose, an intracellular calcium ion mobilizing messenger. The release of soluble protein and the ability of membrane-bound protein to become internalized indicate both extracellular and intracellular functions for the protein. This protein has an N-terminal cytoplasmic tail, a single membrane-spanning domain, and a C-terminal extracellular region with four N-glycosylation sites.

Synthesizes the second messagers cyclic ADP-ribose and nicotinate-adenine dinucleotide phosphate, the former a second messenger for glucose-induced insulin secretion. Also has cADPr hydrolase activity.

cd83: CD83 antigen:

May play a significant role in **antigen presentation** or the **cellular interactions** that follow **lymphocyte activation**.

chgb: chromogranin B:

Secretogranin-1 is **a neuroendocrine secretory granule protein**, which may be the precursor for other biologically active peptide.

chil1: chitinase-like 1.

cldn3: claudin 3:

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 low-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 is highly overexpressed in uterine carcinosarcoma. This protein is also predominantly present in brain endothelial cells, where it plays a specific role in the establishment and maintenance of blood brain barrier tight junction morphology.

Plays a major role in tight junction-specific obliteration of the intercellular space, through calcium- independent cell-adhesion activity.

cntn1:

Contactins **mediate cell surface interactions during nervous system development**. Involved in the formation of paranodal axo-glial junctions in myelinated peripheral nerves and in the signaling between axons and myelinating glial cells via its association with CNTNAP1. Participates in oligodendrocytes generation by acting as a ligand of NOTCH1. Its association with NOTCH1 promotes NOTCH1 activation through the released notch intracellular domain (NICD) and subsequent translocation to the nucleus. **Interaction with TNR induces a repulsion of neurons and an inhibition of neurit**.

<u>dok2</u>: docking protein 2:

DOK proteins are enzymatically inert adaptor or scaffolding proteins. They **provide a docking platform for the assembly of multimolecular signaling complexes**. DOK2 may modulate the cellular proliferation induced by IL-4, as well as IL-2 and IL-3. May be involved in modulating Bcr-Abl signaling. Attenuates EGF-stimulated MAP kinase activation.

sparcl1: SPARC-like 1.

<u>eno2</u>: enolase 2, gamma neuronal:

Has neurotrophic and neuroprotective properties on a broad spectrum of central nervous system (CNS) neurons. Binds, in a calcium-dependent manner, to cultured neocortical neurons and promotes cell survival

ephx2: epoxide hydrolase 2, cytoplasmic:

The C-terminal domain has epoxide hydrolase activity and acts on epoxides (alkene oxides, oxiranes) and arene oxides. **Plays a role in xenobiotic metabolism** by degrading

potentially toxic epoxides. Also determines steady-state levels of physiological mediators. The N-terminal domain has lipid phosphatase activity, with the highest activity towards threo- 9,10-phosphonooxy-hydroxy-octadecanoic acid, followed by erythro- 9,10-phosphonooxy-hydroxy-octadecanoic acid, 12-phosphonooxy- octadec-9Z-enoic acid, 12-phosphonooxy-octadec-9E-eno.

bcl11a: B cell CLL/lymphoma 11A (zinc finger protein)

ezh2: enhancer of zeste 2 polycomb repressive complex 2 subunit:

Polycomb group (PcG) protein. Catalytic subunit of the PRC2/EED-EZH2 complex, which methylates (H3K9me) and 'Lys-27' (H3K27me) of histone H3, leading to transcriptional repression of the affected target gene. Able to mono-, di- and trimethylate 'Lys-27' of histone H3 to form H3K27me1, H3K27me2 and H3K27me3, respectively. Compared to EZH2-containing complexes, it is more abundant in embryonic stem cells and plays a major role in forming H3K27me3, which is required for embryonic stem cell identity and proper differentiation. The PRC2/EED-EZH2 ...

myh7: myosin, heavy polypeptide 7, cardiac muscle, beta: Muscle contraction.

acsl1: acyl-CoA synthetase long-chain family member 1:

Activation of long-chain fatty acids for both synthesis of cellular lipids, and degradation via beta-oxidation. Preferentially uses oleate, arachidonate, eicosapentaenoate and docosahexaenoate as substrates

fhl2: four and a half LIM domains 2:

This gene encodes a member of the four-and-a-half-LIM-only protein family. The encoded protein functions as a regulator in numerous signaling pathways and cellular processes in development and cellular differentiation, including development and maintenance of the cardiovascular system and striated muscles. This gene also plays a role in bone formation and regulates and bone mineral content and bone mineral density. May function as a molecular transmitter linking various signaling pathways to transcriptional regulation. Negatively regulates the transcriptional repressor E4F1 and may function in cell growth. Inhibits the transcriptional activity of FOXO1 and its apoptotic function by enhancing the interaction of FOXO1 with SIRT1 and FOXO1 deacetylation

lpin1: lipin 1:

Plays important roles in **controlling the metabolism of fatty acids** at differents levels. Acts as a magnesium-dependent phosphatidate phosphatase enzyme which catalyzes the conversion of phosphatidic acid to diacylglycerol during triglyceride, phosphatidylcholine and phosphatidylethanolamine biosynthesis. Acts also as nuclear transcriptional coactivator for PPARGC1A/PPARA regulatory pathway to modulate lipid metabolism gene expression. Is involved in adipocyte differentiation. Isoform 1 is

recruited at the mitochondrion outer membrane and is involved in mitochondrial fission by...

fos: FBJ osteosarcoma oncogene:

Nuclear phosphoprotein which forms a tight but non- covalently linked complex with the JUN/AP-1 transcription factor. On TGF-beta activation, forms a multimeric SMAD3/SMAD4/JUN/FOS complex, at the AP1/SMAD-binding site to regulate TGF-beta- mediated signaling (By similarity). Has a critical function in regulating the development of cells destined to form and maintain the skeleton. It is thought to **have an important role in signal transduction**, cell proliferation and differentiation. In growing cells, activates phospholipid synthesis, possibly by activating CD...

fosb: FBJ osteosarcoma oncogene B:

FosB interacts with Jun proteins enhancing their DNA binding activity.

ftl1: ferritin light polypeptide 1.

gaa: glucosidase, alpha, acid:

This gene encodes a lysosomal acid glucosidase that is involved in the degradation of glycogen. The encoded preproprotein undergoes proteolytic processing to generate a mature enzyme that cleaves alpha-1-4 and alpha-1-6 glycosidic bonds of glycogen, maltose and intermediate oligosaccharides within the lysosome.

Essential for the degradation of glygogen to glucose in lysosomes.

gabra1: gamma-aminobutyric acid (GABA) A receptor, subunit alpha 1:

Component of the heteropentameric receptor for GABA, the major inhibitory neurotransmitter in the vertebrate brain. Functions also as histamine receptor and mediates cellular responses to histamine. Functions as receptor for diazepines and various anesthetics, such as pentobarbital; these are bound at a separate allosteric effector binding site. Functions as ligand- gated chloride channel

gabrg1: gamma-aminobutyric acid (GABA) A receptor, subunit gamma 1:

GABA, the major inhibitory neurotransmitter in the vertebrate brain, mediates neuronal inhibition by binding to the GABA/benzodiazepine receptor and opening an integral chloride channel.

gad1: glutamate decarboxylase 1:

Catalyzes the production of GABA.

gal: galanin:

This gene **encodes a neuroendocrine peptide** that is principally produced by a subpopulation of lactotrophs in the pituitary gland. The encoded protein is a precursor that is proteolytically processed to generate two mature peptides: galanin and galanin message-associated peptide (GMAP).

Endocrine hormone of the central and peripheral nervous systems that binds and activates the G protein-coupled receptors GALR1, GALR2, and GALR3. This small

neuropeptide may regulate diverse physiologic functions including contraction of smooth muscle of the gastrointestinal and genitourinary tract, growth hormone and insulin release and adrenal secretion.