# SUPPLEMENTARY DATA ONLINE

## In utero gene expression in the *Slc39a8(neo/neo)* knockdown mouse

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**TABLE S1.** Differentially-expressed genes — using a *P*-value <0.05 and absolute fold-change >2 — when comparing *Slc39a8(neo/neo)* knockdown with *Slc39a8(+/+)* wild-type

**GD13.5 YOLK SAC**

| **Gene symbol**[a] | **Official gene name** | **Average expression (RPKM)** | **Fold-Change** | **log$_2$ Fold-Change** | ***P*-value** |
|---|---|---|---|---|---|
| ***Gm10377*** | predicted gene 10377 | 2.1 | NA | **+10** | 0.038077 |
| ***Ccdc170*** | coiled-coil domain containing 170 | 2.7 | NA | 10 | 0.003263 |
| ***Ghrh*** | growth hormone releasing hormone | 3.3 | NA | 10 | 0.001096 |
| ***Hdac11*** | histone deacetylase 11 | 1.7 | NA | 10 | 0.027588 |
| ***Gbp1***[b] | guanylate-binding protein 1 | 15.1 | 19.23 | 4.27 | 5.00E-05 |
| ***Stc2*** | stanniocalcin 2 | 28.3 | 15.37 | 3.94 | 1.25E-12 |
| ***Ano2*** | anoctamin 2 | 2.9 | 14.37 | 3.84 | 0.017375 |
| ***2610528A11Rik*** | RIKEN cDNA 2610528A11 gene | 20.3 | 14.2 | 3.83 | 7.79E-10 |
| ***Etnk2*** | ethanolamine kinase 2 | 2.5 | 11.84 | 3.57 | 0.039089 |
| ***Gng4*** | guanine nucleotide-binding protein (G protein), γ4 | 2.3 | 11.35 | 3.5 | 0.038245 |
| ***Gprc5a*** | G-protein-coupled receptor, family C, group 5, member A | 4.1 | 9.68 | 3.28 | 0.007207 |
| ***Gm853*** | predicted gene 853 | 17.5 | 9.21 | 3.2 | 1.74E-07 |
| ***Sema7a*** | sema domain, immunoglobulin domain (Ig), and GPI-membrane anchor, 7A | 3.3 | 8.03 | 3.01 | 0.027538 |
| ***Kcna4*** | potassium voltage-gated channel, shaker-related subfamily, member 4 | 8.5 | 7.85 | 2.97 | 0.019251 |
| ***Aox4*** | aldehyde oxidase 4 | 18.3 | 7.75 | 2.95 | 0.000224 |
| ***Efhc2*** | EF-hand domain (C-terminal) containing 2 | 33.3 | 7.52 | 2.91 | 0.040932 |
| ***Igfbp1***[c] | insulin-like growth factor-binding protein 1 | 248.6 | 7.48 | 2.9 | 2.08E-14 |
| ***Adh7*** | alcohol dehydrogenase 7 (class IV), mu or sigma polypeptide | 41.1 | 7.29 | 2.87 | 1.67E-10 |
| ***Ercc2*** | excision-repair cross-complemntng repair deficiency, complemntation group 2 | 4.8 | 7.27 | 2.86 | 0.009128 |
| ***Zbtb8b*** | zinc finger- and BTB domain-containing 8b | 22.7 | 6 | 2.58 | 2.51E-05 |
| ***Bmp6*** | bone morphogenetic protein 6 | 15.3 | 5.71 | 2.51 | 0.001397 |
| ***Aim1l*** | absent in melanoma 1-like | 3.7 | 5.5 | 2.46 | 0.032743 |
| ***H2-Ab1*** | histocompatibility 2, class II antigen A, β1 | 6.1 | 5.47 | 2.45 | 0.008387 |
| ***Cyp1b1*** | cytochrome P450, family 1, subfamily b, polypeptide 1 | 8.5 | 5.37 | 2.43 | 0.03492 |
| ***Mgarp*** | mitochondrial-localized glutamic acid-rich protein | 5.8 | 4.96 | 2.31 | 0.011293 |
| ***Pkhd1l1*** | polycystic kidney and hepatic disease 1-like 1 | 246.1 | 4.88 | 2.29 | 1.09E-12 |
| ***Esm1*** | endothelial cell-specific molecule 1 | 583.3 | 4.62 | 2.21 | 0.000122 |
| ***Ntm*** | Neurotrimin | 5.2 | 4.48 | 2.16 | 0.032329 |
| ***Lancl3*** | LanC lantibiotic synthetase component C-like 3 (*bacterial*) | 24 | 4.44 | 2.15 | 2.22E-05 |
| ***Reln*** | Reelin | 63.4 | 4.44 | 2.15 | 7.02E-05 |
| ***Egln3*** | EGL nine homolog 3 (*C. elegans*) | 97.8 | 4.22 | 2.08 | 4.61E-09 |
| ***Mapt*** | microtubule-associated protein τ | 5.7 | 4.04 | 2.01 | 0.028332 |
| ***Sp6*** | *trans*-acting transcription factor 6 | 4.7 | 4.02 | 2.01 | 0.038992 |
| ***Col25a1*** | collagen, type XXV, α1 | 4.8 | 4 | 2.00 | 0.049798 |
| ***Hemgn*** | hemogen | 56 | 3.83 | 1.94 | 5.02E-07 |
| ***Pitpnm2*** | phosphatidylinositol transfer protein, membrane-associated 2 | 10.5 | 3.6 | 1.85 | 0.013494 |
| ***Slc30a10*** | solute carrier family 30, member 10 | 38.1 | 3.59 | 1.84 | 2.38E-05 |
| ***Snap91*** | synaptosomal-associated protein 91 | 6.1 | 3.55 | 1.83 | 0.028576 |
| ***Ank1*** | ankyrin 1, erythroid | 25.8 | 3.53 | 1.82 | 0.0124 |
| ***Ap2a1*** | adaptor-related protein complex 2, α1 subunit | 11.1 | 3.49 | 1.8 | 0.005272 |
| ***Ccdc102a*** | coiled-coil domain-containing 102A | 5.9 | 3.45 | 1.79 | 0.049812 |
| ***Synpo2*** | synaptopodin 2 | 63.7 | 3.29 | 1.72 | 0.00697 |
| ***Cnpy3*** | canopy 3 homolog (*zebrafish*; *Danio rerio*) | 7.3 | 3.26 | 1.71 | 0.028175 |
| ***Thoc6*** | THO complex 6 homolog (*Drosophila*) | 8 | 3.25 | 1.7 | 0.028794 |
| ***Ccdc164*** | coiled-coil domain containing 164 | 8 | 3.15 | 1.66 | 0.032467 |
| ***Slc16a3*** | solute carrier family 16 (monocarboxylic acid transporters), member 3 | 13.3 | 3.11 | 1.64 | 0.035615 |
| ***Capn5*** | calpain 5 | 66.5 | 3.07 | 1.62 | 0.03789 |
| ***Kcne3*** | potassium voltage-gated channel, Isk-related subfamily, gene 3 | 17.3 | 3.07 | 1.62 | 0.003336 |
| ***Gm14047*** | predicted gene 14047 | 7.7 | 3.07 | 1.62 | 0.031458 |
| ***Gch1*** | GTP cyclohydrolase 1 | 14.7 | 3.06 | 1.62 | 0.005759 |

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|---|---|---|---|---|---|
| ***Fscn1*** | fascin homolog 1, actin bundling protein (*Strongylocentrotus purpuratus*) | 17 | 3.06 | 1.61 | 0.003526 |
| ***Vldlr*** | very low-density lipoprotein receptor | 278.3 | 3.01 | 1.59 | 2.19E-07 |
| ***Fetub*** | fetuin β | 31.1 | 3 | 1.59 | 0.00862 |
| ***Ermap*** | erythroblast membrane-associated protein | 132.9 | 2.99 | 1.58 | 0.006552 |
| ***Pde2a*** | phosphodiesterase 2A, cGMP-stimulated | 10.6 | 2.98 | 1.58 | 0.020801 |
| ***Mthfd2*** | MTHF dehydrogenase (NAD+ dependent), methenyltetrahydrofolate cyclohydrolase | 24.9 | 2.97 | 1.57 | 0.001119 |
| ***Krt19*** | keratin 19 | 100.7 | 2.87 | 1.52 | 0.000943 |
| ***Bcl11a*** | B-cell CLL/lymphoma 11A (zinc-finger protein) | 16.6 | 2.84 | 1.51 | 0.006931 |
| ***A930005H10Rik*** | RIKEN cDNA A930005H10 gene | 13.1 | 2.83 | 1.5 | 0.017392 |
| ***Pcdh20*** | protocadherin 20 | 9.5 | 2.82 | 1.5 | 0.048775 |
| ***Isg20*** | interferon-stimulated protein | 29.7 | 2.79 | 1.48 | 0.011065 |
| ***Hsd3b6*** | hydroxy-Δ-5-steroid dehydrogenase, 3β- and steroid Δ-isomerase 6 | 470.9 | 2.75 | 1.46 | 0.008695 |
| ***Spry4*** | sprouty homolog 4 (*Drosophila*) | 31.4 | 2.74 | 1.45 | 0.038453 |
| ***Sulf2*** | sulfatase 2 | 28.1 | 2.68 | 1.42 | 0.014406 |
| ***Stk32b*** | serine/threonine kinase 32B | 19.6 | 2.68 | 1.42 | 0.005446 |
| ***Igfbp3***[c] | insulin-like growth factor-binding protein 3 | 134.6 | 2.67 | 1.41 | 0.00298 |
| ***Mmp19*** | matrix metallopeptidase 19 | 9 | 2.61 | 1.39 | 0.04751 |
| ***Stc1*** | stanniocalcin 1 | 11.7 | 2.61 | 1.38 | 0.024014 |
| ***Gdpd2*** | glycerophosphodiester phosphodiesterase domain-containing 2 | 10.9 | 2.6 | 1.38 | 0.0356 |
| ***Asns*** | asparagine synthetase | 70.7 | 2.56 | 1.36 | 0.000127 |
| ***Slc2a1*** | solute carrier family 2 (facilitated glucose transporters), member 1 | 469.5 | 2.55 | 1.35 | 0.000473 |
| ***Rhag*** | Rhesus blood group-associated A glycoprotein | 60.2 | 2.52 | 1.33 | 0.000338 |
| ***Slc2a3*** | solute carrier family 2 (facilitated glucose transporters), member 3 | 671.1 | 2.5 | 1.32 | 0.005112 |
| ***Gpr50*** | G-protein-coupled receptor 50 | 17.8 | 2.49 | 1.32 | 0.020918 |
| ***Yif1a*** | Yip1-interacting factor homolog A (*S. cerevisiae*) | 11.3 | 2.48 | 1.31 | 0.04979 |
| ***Ndnl2*** | necdin-like 2 | 12.6 | 2.47 | 1.31 | 0.028845 |
| ***Adra2b*** | adrenergic receptor α2b | 16.5 | 2.46 | 1.3 | 0.013904 |
| ***Sdc1*** | syndecan 1 | 11.6 | 2.39 | 1.26 | 0.04787 |
| ***Bhlhe41*** | basic helix-loop-helix family, member e41 | 84.6 | 2.37 | 1.25 | 0.010568 |
| ***Aldoa*** | aldolase A, fructose-bisphosphate | 275.7 | 2.35 | 1.24 | 0.031794 |
| ***Mvd*** | mevalonate (diphospho)decarboxylase | 25.5 | 2.34 | 1.23 | 0.006026 |
| ***Mif*** | macrophage migration inhibitory factor | 18.4 | 2.34 | 1.23 | 0.021821 |
| ***Zfp94*** | zinc-finger protein 94 | 12 | 2.32 | 1.22 | 0.041933 |
| ***Apoc3*** | apolipoprotein C-III | 12.6 | 2.31 | 1.21 | 0.045566 |
| ***Eno1*** | enolase 1α, non-neuronal | 269.7 | 2.3 | 1.2 | 0.014886 |
| ***Cdh3*** | cadherin 3 | 70 | 2.26 | 1.18 | 0.001717 |
| ***Hk1*** | hexokinase 1 | 26.6 | 2.25 | 1.17 | 0.024595 |
| ***Map1b*** | microtubule-associated protein 1B | 391 | 2.23 | 1.16 | 0.001862 |
| ***Tgfb3*** | transforming growth factor, β3 | 29.3 | 2.22 | 1.15 | 0.008699 |
| ***Basp1*** | brain-abundant, membrane-attached signal protein 1 | 64.8 | 2.22 | 1.15 | 0.001918 |
| ***Bhlhe40*** | basic helix-loop-helix family, member e40 | 161.5 | 2.21 | 1.14 | 0.006853 |
| ***Apln*** | Apelin | 71.5 | 2.18 | 1.12 | 0.011892 |
| ***Gm5506*** | predicted gene 5506 | 483.6 | 2.17 | 1.12 | 0.024416 |
| ***Plekha2*** | pleckstrin homol. domain-containing, family A ($IP_3$-binding specific), memb 2 | 52.4 | 2.16 | 1.11 | 0.003497 |
| ***Pm20d2*** | peptidase M20 domain-containing 2 | 15.5 | 2.15 | 1.11 | 0.04351 |
| ***Myadm*** | myeloid-associated differentiation marker | 2123.3 | 2.14 | 1.1 | 0.037611 |
| ***Tubb2b*** | tubulin β, class IIB | 19.2 | 2.14 | 1.1 | 0.031801 |
| ***Dio2*** | deiodinase, iodothyronine, type II | 21.9 | 2.14 | 1.1 | 0.038542 |
| ***Slc38a1*** | solute carrier family 38, member 1 | 353.5 | 2.13 | 1.09 | 0.0003 |
| ***H2-K1*** | histocompatibility 2, K1, K region | 156.7 | 2.13 | 1.09 | 0.00061 |
| ***Ak4*** | adenylate kinase 4 | 326.9 | 2.13 | 1.09 | 0.000395 |
| ***Slc1a4*** | solute carrier family 1 (glutamate/neutral amino acid transporters), member 4 | 47.9 | 2.12 | 1.08 | 0.004676 |
| ***Lss*** | lanosterol synthase | 404 | 2.09 | 1.07 | 0.00208 |
| ***Psca*** | prostate stem-cell antigen | 26.5 | 2.09 | 1.07 | 0.018211 |
| ***Hmgcl*** | 3-hydroxy-3-methylglutaryl-Coenzyme A lyase | 26.5 | 2.09 | 1.07 | 0.024636 |
| ***Ppp1r9b*** | protein phosphatase 1, regulatory subunit 9B | 34 | 2.09 | 1.06 | 0.048548 |
| ***Lgals3*** | lectin, galactose-binding, soluble 3 | 21.8 | 2.08 | 1.05 | 0.049121 |

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|---|---|---|---|---|---|
| ***Pdgfa*** | platelet-derived growth factor α | 50.3 | 2.07 | 1.05 | 0.007183 |
| ***Pkm*** | pyruvate kinase, muscle | 371.6 | 2.06 | 1.05 | 0.003951 |
| ***8430408G22Rik*** | RIKEN cDNA 8430408G22 gene | 113.9 | 2.06 | 1.04 | 0.002176 |
| ***Prelid2*** | PRELI domain-containing 2 | 54.1 | 2.06 | 1.04 | 0.005484 |
| ***Cited2*** | Cbp/p300-interacting transactivator, Glu/Asp-rich COOH-terminal domain, 2 | 315.1 | 2.06 | 1.04 | 0.000622 |
| ***Atp5d*** | ATP synthase, H+ transporting, mito F1 complex, Δ subunit | 25.1 | 2.06 | 1.04 | 0.025065 |
| ***Trf*** | transferrin | 19653.8 | 2.05 | 1.04 | 0.013549 |
| ***Hif3a*** | hypoxia-inducible factor 3, α subunit | 924.9 | 2.04 | 1.03 | 0.000368 |
| ***Cryl1*** | crystallin, λ1 | 27.1 | 2.04 | 1.03 | 0.029265 |
| ***Map7d1*** | MAP7 domain-containing 1 | 25.4 | 2.03 | 1.02 | 0.039494 |
| ***Stambp*** | STAM-binding protein | 27.2 | 2.03 | 1.02 | 0.023061 |
| ***Hsd3b2*** | hydroxy-Δ-5-steroid dehydrogenase, 3β- and steroid Δ-isomerase 2 | 138.3 | 2.02 | 1.02 | 0.018028 |
| ***Mt2*** | metallothionein 2 | 346.4 | 2.02 | 1.02 | 0.000935 |
| ***Gpr116*** | G protein-coupled receptor 116 | 191.8 | 2.02 | 1.02 | 0.00775 |
| ***Hunk*** | hormonally-upregulated Neu-associated kinase | 70.7 | 2.01 | 1.01 | 0.016569 |
| ***Eda2r*** | ectodysplasin A2 receptor | 55.6 | 0.5 | –1.00 | 0.021863 |
| ***4932411N23Rik*** | RIKEN cDNA 4932411N23 gene | 99.7 | 0.5 | -1.01 | 0.005988 |
| ***Aadac*** | arylacetamide deacetylase (esterase) | 210.9 | 0.49 | -1.03 | 0.031819 |
| ***Rimklb*** | ribosomal-modification protein rimK-like family member B | 148.3 | 0.48 | -1.06 | 0.001323 |
| ***Prodh2*** | proline dehydrogenase (oxidase) 2 | 19.4 | 0.48 | -1.07 | 0.028371 |
| ***Dnajc6*** | DnaJ (Hsp40) homolog, subfamily C, member 6 | 122.7 | 0.47 | -1.07 | 0.001134 |
| ***Hba-a1*** | hemoglobin alpha, adult chain 1 | 2545.6 | 0.46 | –1.11 | 0.026408 |
| ***Hba-a2*** | hemoglobin alpha, adult chain 2 | 2546 | 0.46 | –1.11 | 0.026455 |
| ***Slc8a3*** | solute carrier family 8 (sodium/calcium exchangers), member 3 | 26.4 | 0.46 | –1.11 | 0.014213 |
| ***C030030A07Rik*** | RIKEN cDNA C030030A07 gene | 28 | 0.46 | -1.13 | 0.01204 |
| ***Bhmt*** | betaine-homocysteine methyltransferase | 70.7 | 0.45 | -1.14 | 0.000949 |
| ***Clec4a3*** | C-type lectin domain family 4, member a3 | 13.8 | 0.44 | -1.18 | 0.042468 |
| ***Fam220a*** | family with sequence similarity 220, member A | 16.7 | 0.44 | -1.18 | 0.025718 |
| ***Marcksl1-ps4*** | MARCKS-like 1, pseudogene 4 | 28.5 | 0.44 | -1.19 | 0.007226 |
| ***Tlr7*** | toll-like receptor 7 | 20.7 | 0.44 | -1.2 | 0.013775 |
| ***Aadat*** | aminoadipate aminotransferase | 31.3 | 0.43 | -1.22 | 0.005303 |
| ***1810062O18Rik*** | RIKEN cDNA 1810062O18 gene | 10.8 | 0.43 | -1.22 | 0.04315 |
| ***Cfh*** | complement component factor h | 203 | 0.41 | -1.3 | 0.014087 |
| ***Pxmp2*** | peroxisomal-membrane protein 2 | 8.7 | 0.35 | -1.51 | 0.03088 |
| ***Magea5*** | melanoma antigen, family A, 5 | 6.3 | 0.33 | -1.61 | 0.049439 |
| ***Slc6a15*** | solute carrier family 6 (neurotransmitter transporters), member 15 | 7.2 | 0.32 | –1.65 | 0.037471 |
| ***Grm7*** | glutamate receptor, metabotropic 7 | 6.2 | 0.31 | -1.69 | 0.035742 |
| ***Clec5a*** | C-type lectin-domain family 5, member a | 5.8 | 0.31 | -1.7 | 0.04088 |
| ***Slc5a11*** | solute carrier family 5 (sodium/glucose cotransporters), member 11 | 5.7 | 0.31 | –1.70 | 0.041006 |
| ***Hbb-y*** | hemoglobin Y, β-like embryonic chain | 19218.6 | 0.31 | –1.71 | 2.09E-06 |
| ***Gm101*** | predicted gene 101 | 7.2 | 0.31 | -1.71 | 0.019502 |
| ***BC049635*** | cDNA sequence BC049635 | 6.1 | 0.29 | -1.78 | 0.035888 |
| ***Esrrb*** | estrogen-related receptor β | 9.4 | 0.28 | -1.85 | 0.005738 |
| ***Gm6642*** | ubiquitin-like 5 pseudogene | 6.6 | 0.28 | -1.85 | 0.033137 |
| ***Vmn2r12*** | vomeronasal 2, receptor 12 | 8 | 0.27 | -1.91 | 0.011006 |
| ***Gabra1*** | γ-aminobutyric acid (GABA) A receptor, subunit α1 | 14.5 | 0.27 | -1.91 | 0.00112 |
| ***2900002K06Rik*** | RIKEN cDNA 2900002K06 gene | 6 | 0.25 | -1.99 | 0.025151 |
| ***Elavl2*** | ELAV (embryonic lethal, abnormal vision, *Drosophila*)-like 2 (Hu antigen B) | 6.2 | 0.25 | -2.01 | 0.019532 |
| ***Slc39a8*** | solute carrier family 39 (metal ion transporters), member 8 | 981 | 0.25 | –2.02 | 0.003534 |
| ***Dgkb*** | diacylglycerol kinase, β | 17.3 | 0.24 | -2.04 | 0.003267 |
| ***Hbb-b1*** | hemoglobin, beta adult major chain | 7608.1 | 0.21 | –2.23 | 0.01473 |
| ***Hbb-b2*** | hemoglobin, beta adult minor chain | 7608.1 | 0.21 | –2.23 | 0.01473 |
| ***Beta-s*** | hemoglobin subunit β1-like | 6346.6 | 0.21 | –2.27 | 0.01333 |
| ***Olfr857*** | olfactory receptor 857 | 11.4 | 0.14 | -2.79 | 0.020188 |
| ***Ifi202b*** | interferon-activated gene 202B | 20.7 | 0.04 | -4.48 | 0.006328 |
| ***Kdm5d*** | lysine (K)-specific demethylase 5D | 213 | NA | -10 | 0.033431 |
| ***Gpr111*** | G protein-coupled receptor 111 | 1.3 | NA | -10 | 0.048708 |
| ***Ccdc81*** | coiled-coil domain-containing 81 | 1.5 | NA | -10 | 0.030022 |
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**GD13.5 PLACENTA**

| **Gene symbol** | **Official gene name** | **Average expression (RPKM)** | **Fold-Change** | **log$_2$ Fold-Change** | ***P*-value** |
|---|---|---|---|---|---|
| ***Slc43a1*** | solute carrier family 43, member 1 | 2.6 | 21.8 | +4.45 | 0.029887 |
| ***Hemgn*** | Hemogen | 72.1 | 18.87 | 4.24 | 2.15E-06 |
| ***Slc10a6*** | solute carrier family 10 (sodium/bile acid cotransporter family), member 6 | 3.4 | 13.63 | 3.77 | 0.030592 |
| ***Tmem229a*** | transmembrane protein 229A | 2.8 | 13.5 | 3.75 | 0.02237 |
| ***Gm16617*** | predicted gene, 16617 | 3 | 8.42 | 3.07 | 0.0404 |
| ***Ank1*** | ankyrin 1, erythroid | 5.4 | 7.76 | 2.96 | 0.00739 |
| ***Vamp1*** | vesicle-associated membrane protein 1 | 3.5 | 7.23 | 2.85 | 0.045509 |
| ***Gbp1*** | guanylate-binding protein 1 | 51.3 | 5.69 | 2.51 | 6.52E-06 |
| ***Fam196b*** | family with sequence similarity 196, member B | 6.8 | 4.88 | 2.29 | 0.019586 |
| ***D330022K07Rik*** | RIKEN cDNA D330022K07 gene | 230 | 4.55 | 2.19 | 0.007746 |
| ***Bcl11a*** | B-cell CLL/lymphoma 11A (zinc-finger protein) | 21.5 | 4.28 | 2.1 | 0.000456 |
| ***Dusp14*** | dual-specificity phosphatase 14 | 7.9 | 4.08 | 2.03 | 0.009089 |
| ***Nxpe2*** | neurexophilin and PC-esterase domain family, member 2 | 35.5 | 3.76 | 1.91 | 0.002373 |
| ***Msl3l2*** | male-specific lethal 3-like 2 (*Drosophila*) | 9.3 | 3.37 | 1.75 | 0.017999 |
| ***Oit3*** | oncoprotein-induced transcript 3 | 9.8 | 3.29 | 1.72 | 0.022152 |
| ***Tal1*** | T-cell acute lymphocytic leukemia 1 | 16.1 | 3.15 | 1.65 | 0.038062 |
| ***Prl8a2*** | prolactin family 8, subfamily a, member 2 | 1908.2 | 2.97 | 1.57 | 0.012757 |
| ***Gm15713*** | predicted gene 15713 | 16.1 | 2.94 | 1.55 | 0.012836 |
| ***Rgs18*** | regulator of G-protein signaling 18 | 30.7 | 2.85 | 1.51 | 0.003008 |
| ***1500015A07Rik*** | RIKEN cDNA 1500015A07 gene | 12.7 | 2.77 | 1.47 | 0.022345 |
| ***Slc25a2*** | solute carrier family 25 (mitochondrial carrier, ornithine transporter) member 2 | 9.8 | 2.71 | 1.44 | 0.041635 |
| ***St8sia6*** | ST8 α-*N*-acetyl-neuraminide α-2,8-sialyltransferase 6 | 26.1 | 2.64 | 1.4 | 0.03219 |
| ***Gbp3*** | guanylate-binding protein 3 | 53.2 | 2.48 | 1.31 | 0.004881 |
| ***Malat1*** | metastasis-associated lung adenocarcinoma transcript 1 (non-coding RNA) | 264438.1 | 2.44 | 1.29 | 0.027408 |
| ***Tmc7*** | transmembrane channel-like gene family 7 | 60.8 | 2.39 | 1.26 | 0.007686 |
| ***Ctsk*** | cathepsin K | 592.6 | 2.39 | 1.26 | 0.04233 |
| ***Atp8a1*** | ATPase, aminophospholipid transporter (APLT), class I, type 8A, member 1 | 262.3 | 2.37 | 1.25 | 0.003137 |
| ***Cep128*** | centrosomal protein 128 | 64.8 | 2.36 | 1.24 | 0.004782 |
| ***Sulf1*** | sulfatase 1 | 25.2 | 2.34 | 1.23 | 0.046307 |
| ***Mns1*** | meiosis-specific nuclear structural protein 1 | 17 | 2.33 | 1.22 | 0.030083 |
| ***Dhrs9*** | dehydrogenase/reductase (SDR family) member 9 | 89 | 2.33 | 1.22 | 0.004546 |
| ***Usp53*** | ubiquitin-specific peptidase 53 | 1441.3 | 2.29 | 1.19 | 0.049738 |
| ***Rrm2*** | ribonucleotide reductase M2 | 464 | 2.26 | 1.18 | 0.023818 |
| ***Ikzf1*** | IKAROS family zinc-finger 1 | 32 | 2.24 | 1.17 | 0.033308 |
| ***Cped1*** | cadherin-like and PC-esterase domain-containing 1 | 104.5 | 2.21 | 1.14 | 0.043615 |
| ***Trim30d*** | tripartite motif-containing 30D | 57.8 | 2.18 | 1.12 | 0.00915 |
| ***Lyve1*** | lymphatic-vessel endothelial hyaluronan receptor 1 | 135.2 | 2.17 | 1.12 | 0.007705 |
| ***Gpx8*** | glutathione peroxidase 8 (putative) | 139 | 2.11 | 1.08 | 0.006049 |
| ***Atp13a2*** | ATPase type 13A2 | 78.1 | 2.08 | 1.06 | 0.01376 |
| ***Adal*** | adenosine deaminase-like | 37.9 | 2.07 | 1.05 | 0.023871 |
| ***E230016K23Rik*** | RIKEN cDNA E230016K23 gene | 47.9 | 2.04 | 1.03 | 0.041235 |
| ***Gm14057*** | Ppp1r14c pseudogene | 28.9 | 2.03 | 1.02 | 0.044186 |
| ***Pet100*** | PET100 homolog (*S. cerevisiae*) | 104.4 | 0.5 | –1.01 | 0.010124 |
| ***Pld5*** | phospholipase D family, member 5 | 31.2 | 0.5 | -1.01 | 0.043083 |
| ***Cdh1*** | cadherin 1 | 331.7 | 0.49 | -1.02 | 0.007064 |
| ***Pde6a*** | phosphodiesterase 6A, cGMP-specific, rod, α | 36 | 0.49 | -1.03 | 0.033413 |
| ***Rpl41*** | ribosomal protein L41 | 976.6 | 0.48 | -1.07 | 0.028875 |
| ***Rpl19*** | ribosomal protein L19 | 134.4 | 0.48 | -1.07 | 0.024411 |
| ***Fau*** | Finkel-Biskis-Reilly murine sarcoma virus (FBR-MuSV) ubiquitously-expressd | 311.8 | 0.48 | -1.07 | 0.017805 |
| ***1500004A13Rik*** | RIKEN cDNA 1500004A13 gene | 56.7 | 0.47 | -1.08 | 0.036297 |
| ***Rps16*** | ribosomal protein S16 | 69.3 | 0.47 | -1.1 | 0.026093 |
| ***Pskh1*** | protein serine kinase H1 | 37.4 | 0.46 | -1.13 | 0.017623 |
| ***Rps15*** | ribosomal-protein S15 | 121.1 | 0.45 | -1.15 | 0.01362 |
| ***Gjb5*** | gap-junction protein, β5 | 33.3 | 0.42 | -1.24 | 0.009968 |
| ***Epn3*** | epsin 3 (target of *Trp53*) | 40 | 0.42 | -1.26 | 0.004879 |

| | | | | | |
|---|---|---|---|---|---|
| ***Hbb-b1*** | hemoglobin, beta adult major chain | 1242.6 | 0.4 | –1.34 | 0.028901 |
| ***Hbb-b2*** | hemoglobin, beta adult minor chain | 1242.6 | 0.4 | –1.34 | 0.028901 |
| ***Rps11*** | ribosomal-protein S11 | 95 | 0.39 | -1.35 | 0.009822 |
| ***Smarca1*** | SWI/SNF-related, matrix-associated, actin-dependent regulator of chromatin, subfamily a, member 1 | 82.8 | 0.39 | -1.37 | 0.017411 |
| ***Maz*** | MYC-associated zinc-finger protein (purine-binding transcription factor) | 18.8 | 0.38 | -1.38 | 0.046655 |
| ***Ano3*** | anoctamin 3 | 10.2 | 0.38 | -1.39 | 0.04212 |
| ***Tubb3*** | tubulin, β3 class III | 13.5 | 0.38 | -1.4 | 0.021319 |
| ***Pla2g12a*** | phospholipase $A_2$, group XIIA | 17.2 | 0.38 | -1.41 | 0.03545 |
| ***Col11a1*** | collagen, type XI, α1 | 78.4 | 0.38 | -1.41 | 0.03266 |
| ***Rab9b*** | RAB9B, member RAS oncogene family | 8.9 | 0.35 | -1.52 | 0.047809 |
| ***Csf1*** | colony-stimulating factor 1 (macrophage) | 20.8 | 0.34 | -1.55 | 0.004804 |
| ***A430089I19Rik*** | RIKEN cDNA A430089I19 gene | 8 | 0.34 | -1.56 | 0.04584 |
| ***Lrsam1*** | Leu-rich repeat and sterile α-motif-containing 1 | 10.3 | 0.34 | -1.56 | 0.02876 |
| ***Slc39a8*** | solute carrier family 39 (metal ion transporter), member 8 | 109 | 0.31 | –1.71 | 1.94E-05 |
| ***Mrps28*** | mitochondrial-ribosomal protein S28 | 6.6 | 0.3 | -1.74 | 0.045011 |
| ***Gaa*** | glucosidase, α, acid | 8.4 | 0.3 | -1.76 | 0.027864 |
| ***Efnb1*** | ephrin B1 | 8.8 | 0.29 | -1.76 | 0.016407 |
| ***2810001G20Rik*** | RIKEN cDNA 2810001G20 gene | 6.6 | 0.28 | -1.85 | 0.035636 |
| ***Ppargc1a*** | peroxisome proliferative-activated receptor-γ, coactivator 1α | 23 | 0.27 | -1.91 | 0.002026 |
| ***Gm21637*** | predicted gene, 21637 | 5.2 | 0.24 | -2.04 | 0.036323 |
| ***Gm14354*** | predicted gene 14354 | 5.2 | 0.24 | -2.04 | 0.036323 |
| ***Ifitm10*** | interferon-induced transmembrane protein 10 | 5.3 | 0.23 | -2.13 | 0.035472 |
| ***Ict1*** | immature colon carcinoma transcript 1 | 5.2 | 0.22 | -2.18 | 0.031189 |
| ***Rmrp*** | RNA component of mitochondrial RNAase P | 11.2 | 0.22 | -2.18 | 0.034409 |
| ***Prol1*** | proline rich, lacrimal 1 | 11.8 | 0.21 | -2.22 | 0.048119 |
| ***Cacna1e*** | calcium channel, voltage-dependent, R type, α 1E subunit | 4 | 0.19 | -2.38 | 0.045875 |
| ***Gm6150*** | predicted gene 6150 | 4.2 | 0.19 | -2.43 | 0.031557 |
| ***Rpph1*** | ribonuclease P RNA component H1 | 44 | 0.18 | -2.47 | 0.021699 |
| ***Gm15023*** | predicted gene 15023 | 4.4 | 0.17 | -2.6 | 0.021963 |
| ***AV320801*** | expressed sequence AV320801 | 4.4 | 0.17 | -2.6 | 0.021963 |
| ***Neurog2*** | neurogenin 2 | 48.6 | 0.14 | -2.85 | 2.63E-05 |
| ***Nudt11*** | nudix (nucleoside diphosphate linked moiety X)-type motif 11 | 4.2 | 0.13 | -2.98 | 0.012352 |
| ***Gpr81*** | G-protein-coupled receptor 81 | 2.3 | 0.09 | -3.55 | 0.046167 |
| ***Olfml2b*** | olfactomedin-like 2B | 2.4 | 0.07 | -3.78 | 0.049678 |
| ***Trhde*** | TRH-degrading enzyme | 2.5 | 0.07 | -3.83 | 0.02367 |
| ***Acot4*** | acyl-CoA thioesterase 4 | 2.5 | 0.06 | -3.99 | 0.023963 |
| ***Tacr3*** | tachykinin receptor 3 | 3.8 | 0.05 | -4.47 | 0.029893 |
| ***Cbfa2t3*** | core-binding factor, runt domain, α-subunit 2, translocated to, 3 (human) | 4 | 0.04 | -4.55 | 0.006988 |
| ***Rps19bp1*** | ribosomal-protein S19-binding protein 1 | 1.6 | NA | -10 | 0.047475 |

## GD16.5 LIVER

| **Gene symbol** | **Official gene name** | **Average expression (RPKM)** | **Fold-Change** | **log$_2$ Fold-Change** | ***P*-value** |
|---|---|---|---|---|---|
| ***Anks1*** | ankyrin repeat and SAM domain-containing 1 | 3.8 | NA | **+10** | 0.034196 |
| ***B430319G15Rik*** | RIKEN cDNA B430319G15 gene | 8.7 | 6.42 | 2.68 | 0.041893 |
| ***Gbp1*** | guanylate-binding protein 1 | 23.5 | 6.35 | 2.67 | 0.003716 |
| ***Mir1906-1*** | microRNA 1906-1 | 10.5 | 5.43 | 2.44 | 0.046248 |
| ***Mir1906-2*** | microRNA 1906-2 | 10.5 | 5.43 | 2.44 | 0.046248 |
| ***Epor*** | erythropoietin receptor | 18.5 | 3.66 | 1.87 | 0.035935 |
| ***Slc6a9*** | solute carrier family 6 (neurotransmitter transporter, glycine), member 9 | 53.4 | 3.1 | 1.63 | 0.021275 |
| ***Frat2*** | frequently-rearranged in advanced T-cell lymphomas 2 | 40.3 | 2.72 | 1.44 | 0.041021 |
| ***Lars2*** | leucyl-tRNA synthetase, mitochondrial | 4976.1 | 2.69 | 1.43 | 0.006643 |
| ***Grina*** | glutamate receptor, ionotropic, N-$CH_3$-D-Asp-associated protein 1 (Glx-binding) | 60 | 2.62 | 1.39 | 0.042098 |
| ***Ip6k1*** | inositol hexaphosphate kinase 1 | 116.7 | 2.37 | 1.25 | 0.037276 |
| ***Acer2*** | alkaline ceramidase 2 | 77.5 | 2.33 | 1.22 | 0.037935 |
| ***Fads1*** | fatty-acid desaturase 1 | 555.8 | 2.3 | 1.2 | 0.022541 |
| ***Glipr2*** | GLI pathogenesis-related 2 | 132.8 | 2.21 | 1.14 | 0.04476 |

| | | | | | |
|---|---|---|---|---|---|
| ***Supt4a*** | suppressor of Ty 4A | 345.5 | 2.18 | 1.13 | 0.049975 |
| ***Garem*** | GRB2-associated, regulator of MAPK1 | 185.8 | 2.14 | 1.1 | 0.042327 |
| ***Pdcd5*** | programmed cell death 5 | 777.1 | 0.45 | -1.15 | 0.023395 |
| ***Bhmt*** | betaine-homocysteine methyltransferase | 964.9 | 0.44 | -1.17 | 0.030857 |
| ***Cyp3a11*** | **cytochrome P450, family 3, subfamily a, polypeptide 11** | 505.2 | 0.43 | –1.20 | 0.029067 |
| ***Cth*** | cystathionase (cystathionine γ-lyase) | 451.3 | 0.43 | -1.22 | 0.023948 |
| ***Cisd2*** | CDGSH iron-sulfur domain 2 | 489.5 | 0.43 | -1.22 | 0.015569 |
| ***2810004N23Rik*** | RIKEN cDNA 2810004N23 gene | 199.3 | 0.42 | -1.24 | 0.046931 |
| ***Psmc3*** | proteasome (prosome, macropain) 26S subunit, ATPase 3 | 362.8 | 0.42 | -1.26 | 0.017579 |
| ***Pon1*** | paraoxonase 1 | 88.4 | 0.41 | -1.28 | 0.01868 |
| ***Fabp2*** | fatty-acid-binding protein 2, intestinal | 254.9 | 0.4 | -1.33 | 0.013452 |
| ***Gm3500*** | predicted gene 3500 | 78.5 | 0.4 | -1.34 | 0.036891 |
| ***Med21*** | mediator complex subunit 21 | 165.8 | 0.39 | -1.36 | 0.01525 |
| ***Gm3696*** | predicted gene 3696 | 43.1 | 0.38 | -1.38 | 0.045917 |
| ***Chpt1*** | choline phosphotransferase 1 | 294.9 | 0.37 | -1.43 | 0.00517 |
| ***Dcaf12l1*** | DDB1- and CUL4-associated factor 12-like 1 | 36.6 | 0.33 | -1.59 | 0.031118 |
| ***Ugt3a1*** | UDP glycosyltransferase 3 family, polypeptide A1 | 41.4 | 0.31 | -1.68 | 0.009639 |
| ***Actn2*** | actinin α2 | 1294.9 | 0.31 | -1.7 | 0.000942 |
| ***Gsg1l*** | GSG1-like | 451.6 | 0.3 | -1.74 | 0.001029 |
| ***Ces1c*** | carboxylesterase 1C | 67.7 | 0.25 | -1.98 | 0.031081 |
| ***Car3*** | carbonic anhydrase 3 | 442.3 | 0.23 | -2.14 | 0.013403 |
| ***Eya1*** | eyes absent 1 homolog (*Drosophila*) | 12.1 | 0.21 | -2.27 | 0.025619 |
| ***Pcdh15*** | protocadherin 15 | 13 | 0.2 | -2.32 | 0.025444 |
| ***Ugt3a2*** | UDP glycosyltransferase 3 family, polypeptide A2 | 70.8 | 0.19 | -2.37 | 0.004476 |
| ***6030408B16Rik*** | RIKEN cDNA 6030408B16 gene | 693.3 | 0.18 | -2.48 | 3.07E-06 |
| ***Gm10413*** | predicted gene 10413 | 8.9 | 0.13 | -2.9 | 0.030739 |
| ***Gm5795*** | predicted gene 5795 | 8.9 | 0.13 | -2.9 | 0.030739 |
| ***Fam13c*** | family with sequence similarity 13, member C | 5.9 | 0.08 | -3.66 | 0.032405 |
| ***Phyhipl*** | phytanoyl-CoA hydroxylase-interacting protein-like | 4.5 | 0.04 | -4.63 | 0.048457 |
| ***Col6a5*** | collagen, type VI, α5 | 5.6 | 0.03 | -4.96 | 0.016125 |
| ***Mup15*** | major urinary protein 15 | 11.9 | NA | -10 | 0.035407 |
| ***Gm15085*** | predicted gene 15085 | 5.5 | NA | -10 | 0.004892 |
| ***Lmo3*** | LIM domain only 3 | 3.7 | NA | -10 | 0.02402 |
| ***Mep1a*** | meprin 1α | 3.1 | NA | -10 | 0.044104 |
| ***Mup2*** | major urinary protein 2 | 21.6 | NA | -10 | 0.042211 |
| ***Ott*** | ovary testis transcribed | 5.5 | NA | -10 | 0.004892 |
| ***Slc5a1*** | solute carrier family 5 (Na/glucose cotransporter), member 1 | 6.8 | NA | –10.00 | 0.024828 |
| ***Abca16*** | ATP-binding cassette, sub-family A (ABC1), member 16 | 3.4 | NA | -10 | 0.038952 |
| ***Gm6367*** | predicted gene 6367 | 3.4 | NA | -10 | 0.038952 |
| ***Clca6*** | chloride channel calcium-activated 6 | 3.8 | NA | -10 | 0.022852 |

**GD16.5 KIDNEY**

| **Gene symbol** | **Official gene name** | **Average expression (RPKM)** | **Fold-Change** | **$\log_2$ Fold-Change** | ***P*-value** |
|---|---|---|---|---|---|
| ***Fbp1*** | fructose bisphosphatase 1 | 8.9 | 7.39 | **+2.88** | 0.043426 |
| ***Defb1*** | defensin β1 | 9.9 | 6.68 | 2.74 | 0.041522 |
| ***Slc22a19*** | solute carrier family 22 (organic anion transporter), member 19 | 28.1 | 6.65 | 2.73 | 0.013501 |
| ***Cndp1*** | carnosine dipeptidase 1 (metallopeptidase M20 family) | 19.8 | 5.68 | 2.51 | 0.018248 |
| ***Ppp1r42*** | protein phosphatase 1, regulatory subunit 42 | 17 | 5.25 | 2.39 | 0.027867 |
| ***Gsdmc3*** | gasdermin C3 | 83.5 | 5.23 | 2.39 | 0.01128 |
| ***Mcoln3*** | mucolipin 3 | 19.8 | 5.07 | 2.34 | 0.010291 |
| ***Gsdmc4*** | gasdermin C4 | 34.5 | 4.7 | 2.23 | 0.019218 |
| ***Abca13*** | ATP-binding cassette, sub-family A (ABC1), member 13 | 133.2 | 4.59 | 2.2 | 0.010566 |
| ***Gsdmc2*** | gasdermin C2 | 87.6 | 4.55 | 2.19 | 0.011279 |
| ***Slc12a1*** | solute carrier family 12, member 1 | 970.6 | 4.14 | 2.05 | 0.002836 |
| ***Cldn16*** | claudin 16 | 16.6 | 3.99 | 2 | 0.034985 |
| ***Col4a4*** | collagen, type IV, α4 | 27.8 | 3.86 | 1.95 | 0.018653 |
| ***Esm1*** | endothelial cell-specific molecule 1 | 151.8 | 3.74 | 1.9 | 0.001607 |
| ***Pkhd1*** | polycystic kidney and hepatic disease 1 | 569.6 | 3.72 | 1.9 | 0.001486 |
| ***4930442L01Rik*** | RIKEN cDNA 4930442L01 gene | 20.2 | 3.7 | 1.89 | 0.037006 |
| ***1700109F18Rik*** | RIKEN cDNA 1700109F18 gene | 45.3 | 3.6 | 1.85 | 0.011631 |
| ***Cfhr2*** | complement factor H-related 2 | 532.7 | 3.58 | 1.84 | 0.001066 |

| | | | | | |
|---|---|---|---|---|---|
| ***Nphs2*** | nephrosis 2 homolog, podocin (human) | 168.4 | 3.51 | 1.81 | 0.004109 |
| ***Rsad2*** | radical *S*-adenosyl methionine domain-containing 2 | 199.9 | 3.47 | 1.8 | 0.002213 |
| ***Fmo2*** | flavin-containing monooxygenase 2 | 43.9 | 3.4 | 1.76 | 0.023056 |
| ***4930533B01Rik*** | RIKEN cDNA 4930533B01 gene | 23.8 | 3.39 | 1.76 | 0.047078 |
| ***Sostdc1*** | sclerostin domain-containing 1 | 283.9 | 3.39 | 1.76 | 0.001895 |
| ***Plscr2*** | phospholipid scramblase 2 | 75.9 | 3.37 | 1.75 | 0.025821 |
| ***Mep1b*** | meprin 1β | 62.9 | 3.37 | 1.75 | 0.031021 |
| ***Cldn11*** | claudin 11 | 164.2 | 3.21 | 1.68 | 0.002362 |
| ***Plau*** | plasminogen activator, urokinase | 91.5 | 3.18 | 1.67 | 0.007402 |
| ***Cubn*** | cubilin (intrinsic factor-cobalamin receptor) | 422.6 | 3.12 | 1.64 | 0.017264 |
| ***Neat1*** | nuclear paraspeckle assembly transcript 1 (non-protein coding) | 502.5 | 3.11 | 1.64 | 0.030174 |
| ***Nkx3-1*** | NK-3 transcription factor, locus 1 (*Drosophila*) | 28.9 | 3.11 | 1.64 | 0.03619 |
| ***Tinag*** | tubulointerstitial-nephritis antigen | 38.8 | 3.08 | 1.62 | 0.028105 |
| ***Lrp2*** | low-density lipoprotein receptor-related protein 2 | 2651.6 | 3.05 | 1.61 | 0.0124 |
| ***Cfh*** | complement component factor h | 4429.2 | 3.02 | 1.59 | 0.0028 |
| ***Cldn8*** | claudin 8 | 467.7 | 3 | 1.59 | 0.003548 |
| ***Btnl9*** | butyrophilin-like 9 | 68.1 | 2.99 | 1.58 | 0.02331 |
| ***Slco1a4*** | solute carrier organic anion transporter family, member 1a4 | 51 | 2.95 | 1.56 | 0.029147 |
| ***Gm4788*** | predicted gene 4788 | 441.4 | 2.9 | 1.54 | 0.005177 |
| ***Ehf*** | ets homologous factor | 492 | 2.88 | 1.53 | 0.004413 |
| ***Atp6v0a4*** | ATPase, H+ transporting, lysosomal V0 subunit A4 | 134.7 | 2.86 | 1.52 | 0.048821 |
| ***1110028F11Rik*** | RIKEN cDNA 1110028F11 gene | 38.4 | 2.85 | 1.51 | 0.03568 |
| ***Hoxd3*** | homeobox D3 | 120.1 | 2.82 | 1.5 | 0.009016 |
| ***Npr3***[d] | natriuretic-peptide receptor 3 | 515.9 | 2.77 | 1.47 | 0.007925 |
| ***Mme*** | membrane metallo endopeptidase | 1285.3 | 2.73 | 1.45 | 0.01965 |
| ***Samd9l*** | sterile α-motif domain-containing 9-like | 365 | 2.72 | 1.44 | 0.011491 |
| ***Cyp7b1*** | **cytochrome P450, family 7, subfamily b, polypeptide 1** | 72.8 | 2.66 | 1.41 | 0.024117 |
| ***AI314831*** | expressed sequence AI314831 | 86.8 | 2.64 | 1.4 | 0.019515 |
| ***D030045P18Rik*** | RIKEN cDNA D030045P18 gene | 53 | 2.63 | 1.4 | 0.048051 |
| ***Ly6a*** | lymphocyte antigen 6 complex, locus A | 206.3 | 2.59 | 1.37 | 0.017636 |
| ***Tmem52b*** | transmembrane-protein 52B | 231.5 | 2.59 | 1.37 | 0.014651 |
| ***Alx1*** | ALX homeobox 1 | 107.5 | 2.58 | 1.37 | 0.013814 |
| ***Nabp1*** | nucleic acid-binding protein 1 | 263.4 | 2.58 | 1.37 | 0.024406 |
| ***Cth*** | cystathionase (cystathionine γ-lyase) | 92.7 | 2.56 | 1.36 | 0.045199 |
| ***Ace2***[e] | angiotensin I-converting enzyme (peptidyl-dipeptidase A) 2 | 699.3 | 2.54 | 1.34 | 0.012319 |
| ***Tm4sf1*** | transmembrane 4 superfamily member 1 | 178.1 | 2.51 | 1.33 | 0.025193 |
| ***Slc47a1*** | solute carrier family 47, member 1 | 94.2 | 2.44 | 1.28 | 0.038417 |
| ***Snord22*** | small nucleolar RNA, C/D box 22 | 98.5 | 2.43 | 1.28 | 0.042851 |
| ***Tmprss2*** | transmembrane protease, serine 2 | 82.8 | 2.41 | 1.27 | 0.028147 |
| ***Hoxa10*** | homeobox A10 | 180.7 | 2.4 | 1.26 | 0.018985 |
| ***Eya4*** | eyes absent 4 homolog (*Drosophila*) | 427 | 2.39 | 1.26 | 0.017776 |
| ***Mir17hg*** | Mir17 host gene 1 (non-protein coding) | 447.5 | 2.38 | 1.25 | 0.02446 |
| ***Hrsp12*** | heat-responsive protein 12 | 380.7 | 2.37 | 1.25 | 0.036323 |
| ***9130206I24Rik*** | RIKEN cDNA 9130206I24 gene | 63.6 | 2.36 | 1.24 | 0.048052 |
| ***Ocln*** | Occludin | 101.8 | 2.35 | 1.23 | 0.045698 |
| ***Hoxd10*** | homeobox D10 | 183.3 | 2.34 | 1.23 | 0.021565 |
| ***BC021891*** | cDNA sequence BC021891 | 77 | 2.34 | 1.23 | 0.044348 |
| ***Mctp2*** | multiple C2 domains, transmembrane 2 | 299.4 | 2.33 | 1.22 | 0.02828 |
| ***Wt1*** | Wilms tumor 1 homolog | 837.5 | 2.31 | 1.21 | 0.026022 |
| ***Met*** | met proto-oncogene | 517.8 | 2.3 | 1.2 | 0.022918 |
| ***Ros1*** | Ros1 proto-oncogene | 272 | 2.28 | 1.19 | 0.020944 |
| ***Rnf128*** | ring-finger protein 128 | 259.7 | 2.26 | 1.18 | 0.042698 |
| ***Cyp1b1*** | **cytochrome P450, family 1, subfamily b, polypeptide 1** | 284.5 | 2.26 | 1.17 | 0.032379 |
| ***Hoxd11*** | homeobox D11 | 664.7 | 2.25 | 1.17 | 0.021077 |
| ***Epcam*** | epithelial cell adhesion molecule | 409 | 2.25 | 1.17 | 0.020497 |
| ***Aim1*** | absent in melanoma 1 | 176.2 | 2.25 | 1.17 | 0.031708 |
| ***Hoxd8*** | homeobox D8 | 132.7 | 2.24 | 1.17 | 0.043709 |
| ***Cdc14a*** | CDC14 cell-division cycle 14A | 339.9 | 2.23 | 1.16 | 0.038619 |
| ***Gimap4*** | GTPase, IMAP family member 4 | 616.1 | 2.23 | 1.16 | 0.032168 |
| ***Leprel1*** | leprecan-like 1 | 252.7 | 2.23 | 1.16 | 0.041677 |
| ***Hmcn1*** | hemicentin 1 | 2504.1 | 2.19 | 1.13 | 0.025176 |
| ***Shcbp1*** | Shc SH2-domain-binding protein 1 | 504.2 | 2.17 | 1.12 | 0.04345 |
| ***Dcdc2a*** | doublecortin domain-containing 2a | 1358.4 | 2.14 | 1.10 | 0.037054 |

| | | | | | |
|---|---|---|---|---|---|
| ***Gm10664*** | predicted gene 10664 | 141.5 | 2.13 | 1.09 | 0.036868 |
| ***Mecom*** | MDS1 and EVI1 complex locus | 1279.5 | 2.11 | 1.08 | 0.035085 |
| ***Tfcp2l1*** | transcription factor CP2-like 1 | 1897.8 | 2.1 | 1.07 | 0.032161 |
| ***Hoxb7*** | homeobox B7 | 273.1 | 2.08 | 1.06 | 0.047805 |
| ***Heph*** | hephaestin | 374.3 | 2.07 | 1.05 | 0.039407 |
| ***Calb1*** | calbindin 1 | 1117.2 | 2.07 | 1.05 | 0.04244 |
| ***Frem1*** | Fras1-related extracellular-matrix protein 1 | 2090.7 | 2.05 | 1.03 | 0.040591 |
| ***Ptn*** | pleiotrophin | 1262.8 | 0.48 | –1.05 | 0.044521 |
| ***Map4*** | microtubule-associated protein 4 | 1191 | 0.46 | -1.12 | 0.038893 |
| ***Gm15800*** | predicted gene 15800 | 502.4 | 0.46 | -1.13 | 0.043195 |
| ***Lss*** | lanosterol synthase | 154.1 | 0.44 | -1.19 | 0.046385 |
| ***Tuba1c*** | tubulin, α1C | 1779.9 | 0.44 | -1.19 | 0.037291 |
| ***Timp2*** | tissue inhibitor of metalloproteinase 2 | 294.8 | 0.44 | -1.2 | 0.04697 |
| ***Tmsb10*** | thymosin, β10 | 473.7 | 0.43 | -1.22 | 0.04194 |
| ***Fdft1*** | farnesyl diphosphate farnesyl transferase 1 | 312.1 | 0.43 | -1.22 | 0.03784 |
| ***Hsbp1*** | heat shock factor-binding protein 1 | 362.8 | 0.43 | -1.22 | 0.033025 |
| ***Arrb1*** | arrestin, β1 | 297.2 | 0.43 | -1.22 | 0.031968 |
| ***Igdcc4*** | immunoglobulin superfamily, DCC subclass, member 4 | 182.2 | 0.42 | -1.24 | 0.036855 |
| ***Trak1*** | trafficking protein, kinesin-binding 1 | 279 | 0.41 | -1.28 | 0.047585 |
| ***Usp13*** | ubiquitin-specific peptidase 13 (isopeptidase T-3) | 85.7 | 0.41 | -1.3 | 0.041395 |
| ***Gm6682*** | tubulin, α1C pseudogene | 673.2 | 0.41 | -1.3 | 0.026988 |
| ***Ptgfrn*** | prostaglandin $F_2$ receptor negative regulator | 229.2 | 0.39 | -1.36 | 0.042508 |
| ***Asns*** | asparagine synthetase | 119.7 | 0.39 | -1.37 | 0.019912 |
| ***Rnf187*** | ring-finger protein 187 | 126.5 | 0.38 | -1.41 | 0.037146 |
| ***Wbscr17*** | Williams-Beuren syndrome chromosome region 17 homolog (*human*) | 44.7 | 0.35 | -1.5 | 0.041549 |
| ***Clip3*** | CAP-GLY domain-containing linker protein 3 | 196.3 | 0.35 | -1.51 | 0.013397 |
| ***Sulf2*** | sulfatase 2 | 187.1 | 0.35 | -1.53 | 0.027623 |
| ***Bpgm***[f] | 2,3-*bis*-phosphoglycerate mutase | 378.1 | 0.35 | -1.53 | 0.026492 |
| ***Fam210b*** | family with sequence similarity 210, member B | 61.8 | 0.35 | -1.53 | 0.025588 |
| ***Pid1*** | phosphotyrosine interaction domain-containing 1 | 182.1 | 0.34 | -1.54 | 0.022869 |
| ***Ankrd44*** | ankyrin-repeat domain 44 | 501.4 | 0.34 | -1.57 | 0.0437 |
| ***Xk*** | Kell blood group precursor (McLeod phenotype) homolog | 128.4 | 0.33 | –1.60 | 0.016258 |
| ***Endod1*** | endonuclease domain-containing 1 | 55.8 | 0.33 | -1.61 | 0.015329 |
| ***Scd1*** | stearoyl-Coenzyme A desaturase 1 | 82.6 | 0.33 | -1.62 | 0.015271 |
| ***Tnc*** | tenascin C | 514.9 | 0.32 | -1.63 | 0.032698 |
| ***Grina*** | glutamate receptor, ionotropic, N-$CH_3$-D-Asp-assoc protein 1 (Glx binding) | 31.9 | 0.31 | -1.68 | 0.035333 |
| ***Gpr173*** | G-protein-coupled receptor 173 | 25.5 | 0.3 | -1.72 | 0.041552 |
| ***Tmem56*** | transmembrane-protein 56 | 181.8 | 0.3 | -1.73 | 0.032215 |
| ***Epb4.1l3*** | erythrocyte protein band 4.1-like 3 | 379.8 | 0.3 | –1.73 | 0.011557 |
| ***Prune2*** | prune homolog 2 (*Drosophila*) | 72.8 | 0.29 | -1.76 | 0.045509 |
| ***Palmd*** | palmdelphin | 39.3 | 0.28 | -1.81 | 0.012063 |
| ***Stim1*** | stromal-interaction molecule 1 | 44 | 0.28 | -1.81 | 0.027134 |
| ***Lair1*** | leukocyte-associated Ig-like receptor 1 | 18.5 | 0.28 | -1.84 | 0.040326 |
| ***Amy2a5*** | amylase 2a5 | 52 | 0.28 | -1.86 | 0.022358 |
| ***Nkain1*** | Na+/K+ transporting ATPase-interacting 1 | 50.1 | 0.27 | -1.9 | 0.039634 |
| ***Masp1*** | mannan-binding lectin serine peptidase 1 | 33.6 | 0.26 | -1.94 | 0.014467 |
| ***Ddc*** | DOPA decarboxylase | 52.6 | 0.26 | -1.95 | 0.019292 |
| ***Ndrg2*** | N-myc downstream-regulated gene 2 | 460.2 | 0.25 | -1.99 | 0.046684 |
| ***Vat1*** | vesicle amine-transport protein 1 homolog (*T. californica*) | 40.6 | 0.25 | -2.01 | 0.00859 |
| ***Paqr9*** | progestin and adipoQ receptor family member IX | 81.8 | 0.25 | -2.02 | 0.02769 |
| ***Galnt16*** | UDP-*N*-acetyl-α-D-galactosamine:polypeptide *N*-acetyl-galactosamine transferase 16 | 53.8 | 0.24 | -2.06 | 0.025983 |
| ***Mageb16-ps1*** | melanoma antigen family B, 16, pseudogene 1 | 50.5 | 0.24 | -2.06 | 0.038005 |
| ***Ajap1*** | adherens junction-associated protein 1 | 15.7 | 0.24 | -2.07 | 0.045122 |
| ***Hspb6*** | heat-shock protein, α-crystallin-related, B6 | 16.7 | 0.24 | -2.08 | 0.046724 |
| ***Speer8-ps1*** | spermatogenesis-associated glutamate (E)-rich protein 8, pseudogene 1 | 13.8 | 0.22 | -2.17 | 0.040374 |
| ***Mras*** | muscle and microspikes RAS | 71.6 | 0.22 | -2.21 | 0.024459 |
| ***Me1*** | malic enzyme 1, NADP(+)-dependent, cytosolic | 149 | 0.21 | -2.23 | 0.031703 |
| ***Slc1a4*** | solute carrier family 1 (glutamate/neutral amno acid transporter), member 4 | 81.4 | 0.21 | –2.25 | 0.024939 |

| | | | | | |
|---|---|---|---|---|---|
| ***Tox*** | thymocyte selection-associated high-mobility group box | 60.1 | 0.2 | -2.3 | 0.006862 |
| ***Tal1*** | T-cell acute lymphocytic leukemia 1 | 52.2 | 0.2 | –2.30 | 0.010111 |
| ***Slc2a3*** | solute carrier family 2 (facilitated glucose transporters), member 3 | 169.1 | 0.2 | –2.31 | 0.030869 |
| ***Myh8*** | myosin, heavy polypeptide 8, skeletal muscle, perinatal | 15.5 | 0.19 | -2.43 | 0.031745 |
| ***Sptb*** | spectrin β, erythrocytic | 62.5 | 0.18 | –2.46 | 0.01178 |
| ***Mirg*** | miRNA-containing gene | 23.9 | 0.18 | -2.5 | 0.025552 |
| ***Tmcc2*** | transmembrane and coiled-coil domains 2 | 26.7 | 0.17 | -2.52 | 0.019628 |
| ***Atp7b*** | ATPase, Cu++ transporting, β polypeptide | 8.8 | 0.17 | -2.54 | 0.046861 |
| ***6430411K18Rik*** | RIKEN cDNA 6430411K18 gen | 35.1 | 0.17 | -2.56 | 0.047039 |
| ***Zcchc16*** | zinc-finger, CCHC domain-containing 16 | 8.3 | 0.16 | -2.62 | 0.042393 |
| ***Rian*** | RNA-imprinted and -accumulated in nucleus | 1973.2 | 0.16 | -2.62 | 0.025825 |
| ***Col19a1*** | collagen, type XIX, α1 | 17.1 | 0.16 | -2.63 | 0.036613 |
| ***Mab21l2*** | mab-21-like 2 (*C. elegans*) | 36.2 | 0.16 | -2.67 | 0.013764 |
| ***Slc22a4*** | solute carrier family 22 (organic cation transporter), member 4 | 19.5 | 0.15 | –2.70 | 0.022468 |
| ***Aldh1l2*** | aldehyde dehydrogenase family 1, member L2 | 239 | 0.15 | -2.74 | 0.025841 |
| ***Tmem132c*** | transmembrane-protein 132C | 17.9 | 0.15 | -2.78 | 0.014959 |
| ***Rundc3a*** | RUN domain-containing 3A | 8.1 | 0.14 | -2.81 | 0.042826 |
| ***Qpct*** | glutaminyl-peptide cyclotransferase (glutaminyl cyclase) | 30.1 | 0.14 | -2.82 | 0.022509 |
| ***Snca*** | synuclein, α | 153.6 | 0.14 | -2.86 | 0.010375 |
| ***AF357425*** | snoRNA AF357425 | 96.9 | 0.14 | -2.88 | 0.042269 |
| ***Aldh1a1*** | aldehyde dehydrogenase family 1, subfamily A1 | 183.2 | 0.14 | -2.88 | 0.011707 |
| ***DQ267100*** | snoRNA DQ267100 | 112.1 | 0.14 | -2.88 | 0.023599 |
| ***Rpp25*** | ribonuclease P/MRP 25 subunit | 8.2 | 0.12 | -3.01 | 0.032914 |
| ***AF357359*** | snoRNA AF357359 | 58.1 | 0.12 | -3.04 | 0.023706 |
| ***Aff2*** | AF4/FMR2 family, member 2 | 185.6 | 0.12 | -3.1 | 0.012867 |
| ***Optc*** | Opticin | 7.2 | 0.11 | -3.2 | 0.02907 |
| ***Mageb16*** | melanoma-antigen family B, 16 | 137.7 | 0.09 | -3.42 | 0.013263 |
| ***Grem2*** | gremlin 2 homolog, cysteine-knot superfamily (*Xenopus laevis*) | 46.9 | 0.09 | -3.47 | 0.017832 |
| ***Pex5l*** | peroxisomal biogenesis factor 5-like | 13.2 | 0.08 | -3.6 | 0.022658 |
| ***A2m*** | α2-macroglobulin | 39.7 | 0.08 | -3.68 | 0.048256 |
| ***Mir1906-1*** | microRNA 1906-1 | 7.9 | 0.08 | -3.71 | 0.011924 |
| ***Mir1906-2*** | microRNA 1906-2 | 7.9 | 0.08 | -3.71 | 0.011924 |
| ***Ank1*** | ankyrin 1, erythroid | 81.8 | 0.08 | –3.73 | 0.017692 |
| ***2810459M11Rik*** | RIKEN cDNA 2810459M11 gene | 10.1 | 0.07 | -3.81 | 0.036795 |
| ***Slc30a10*** | solute carrier family 30, member 10 | 117.8 | 0.06 | –4.06 | 0.01406 |
| ***E130309D14Rik*** | RIKEN cDNA E130309D14 gene | 7.9 | 0.03 | -5.03 | 0.00286 |
| ***Otof*** | Otoferlin | 6.5 | 0.03 | -5.23 | 0.011119 |
| ***Zfhx4*** | zinc-finger homeodomain 4 | 805.6 | 0.02 | -5.66 | 0.007916 |
| ***Nrn1*** | neuritin 1 | 139.2 | 0.02 | -5.76 | 0.032328 |
| ***Itgbl1*** | integrin, β-like 1 | 39.9 | 0.02 | -5.99 | 0.008509 |
| ***Cpne4*** | copine IV | 26.5 | 0 | -7.81 | 0.022175 |
| ***Darc*** | Duffy blood group, chemokine receptor | 17.1 | NA | –10.00 | 0.02699 |
| ***Slc17a6*** | solute carrier fam 17 (Na-dependent inorganic phosphate cotransporter), member 6 | 485.5 | NA | –10.00 | 0.042424 |
| ***Gpr50*** | G-protein-coupled receptor 50 | 9.4 | NA | -10 | 0.049046 |
| ***Lrrc73*** | Leucine-rich repeat-containing 73 | 3.8 | NA | -10 | 0.048763 |
| ***Cdh7*** | cadherin 7, type 2 | 126.4 | NA | -10 | 0.038507 |
| ***Gpr158*** | G-protein-coupled receptor 158 | 75.4 | NA | -10 | 0.049454 |
| ***Cacng3*** | calcium channel, voltage-dependent, γ subunit 3 | 7.3 | NA | -10 | 0.024119 |
| ***Stmn4*** | stathmin-like 4 | 113 | NA | -10 | 0.038829 |
| ***Snord116*** | small nucleolar RNA, C/D box 116 | 83.1 | NA | -10 | 0.036871 |
| ***Snord116l1*** | small nucleolar RNA, C/D box 116-like 1 | 83.1 | NA | -10 | 0.036871 |
| ***Snord116l2*** | small nucleolar RNA, C/D box 116-like 2 | 83.1 | NA | -10 | 0.036871 |
| ***2610100L16Rik*** | RIKEN cDNA 2610100L16 gene | 139 | NA | -10 | 0.036769 |
| ***Klhl1*** | kelch-l like | 82.5 | NA | -10 | 0.047351 |

**GD16.5 LUNG**

| Gene symbol | Official gene name | Average expression (RPKM) | Fold-Change | log$_2$ Fold-Change | *P*-value |
|---|---|---|---|---|---|
| ***Gbp1*** | guanylate-binding protein 1 | 5.9 | 28.81 | **+4.85** | 0.036787 |
| ***Wnt7a*** | wingless-related MMTV integration site 7A | 3.1 | 19.46 | 4.28 | 0.027765 |

| | | | | | |
|---|---|---|---|---|---|
| ***Myh3*** | myosin, heavy polypeptide 3, skeletal muscle, embryonic | 70.2 | 8.32 | 3.06 | 0.034623 |
| ***Cngb1*** | cyclic nucleotide-gated channel β1 | 6.8 | 7.31 | 2.87 | 0.006094 |
| ***Tslp*** | thymic stromal lymphopoietin | 12.4 | 6.85 | 2.78 | 0.001705 |
| ***Tceal7*** | transcription elongation factor A (SII)-like 7 | 13.2 | 5.55 | 2.47 | 0.013361 |
| ***Atp1b4*** | ATPase, (Na+)/K+ transporting, β4 polypeptide | 23.6 | 5.53 | 2.47 | 0.03129 |
| ***Krt15*** | keratin 15 | 14.7 | 3.5 | 1.81 | 0.008463 |
| ***Sftpc*** | surfactant-associated protein C | 736.4 | 3.48 | 1.8 | 0.043302 |
| ***Egfem1*** | EGF-like and EMI domain-containing 1 | 109.6 | 3.37 | 1.75 | 0.018341 |
| ***Ccdc158*** | coiled-coil domain-containing 158 | 31.4 | 2.8 | 1.49 | 0.007803 |
| ***Poln*** | DNA polymerase N | 22.1 | 2.63 | 1.4 | 0.019689 |
| ***Fas*** | Fas (TNF receptor superfamily member 6) | 18.6 | 2.56 | 1.36 | 0.028566 |
| ***Ppp1r3c*** | protein phosphatase 1, regulatory (inhibitor) subunit 3C | 737.2 | 2.53 | 1.34 | 0.004868 |
| ***Frrs1l*** | ferric-chelate reductase 1-like | 62.5 | 2.45 | 1.29 | 0.006612 |
| ***Rab38*** | RAB38, member of RAS oncogene family | 55.1 | 2.41 | 1.27 | 0.036639 |
| ***Ager*** | advanced glycosylation end product-specific receptor | 20.5 | 2.34 | 1.23 | 0.038365 |
| ***Slc26a9*** | solute carrier family 26, member 9 | 31.2 | 2.31 | 1.21 | 0.035034 |
| ***Cebpa*** | CCAAT/enhancer binding protein (C/EBP), α | 19.8 | 2.29 | 1.19 | 0.037194 |
| ***Dpt*** | dermatopontin | 118.5 | 2.28 | 1.19 | 0.038236 |
| ***Abcb1a*** | ATP-binding cassette, sub-family B (MDR/TAP), member 1A | 66.7 | 2.24 | 1.16 | 0.018031 |
| ***Lgr6*** | Leu-rich repeat-containing G-protein-coupled receptor 6 | 25 | 2.22 | 1.15 | 0.018926 |
| ***Myh14*** | myosin, heavy polypeptide 14 | 26.1 | 2.2 | 1.14 | 0.018232 |
| ***Scn3b*** | sodium channel, voltage-gated, type III, β | 76.5 | 2.2 | 1.13 | 0.001647 |
| ***AF357359*** | snoRNA AF357359 | 54 | 2.16 | 1.11 | 0.004584 |
| ***Pirt*** | phosphoinositide-interacting regulator of transient-receptor potential channels | 49.1 | 2.01 | 1.01 | 0.03256 |
| ***Lpcat1*** | lysophosphatidylcholine acyltransferase 1 | 217.3 | 2 | 1 | 0.012104 |
| ***4930570G19Rik*** | RIKEN cDNA 4930570G19 gene | 27.3 | 0.47 | –1.09 | 0.043599 |
| ***Cyp2s1*** | **cytochrome P450, family 2, subfamily s, polypeptide 1** | 25.9 | 0.46 | 1.11 | 0.026306 |
| ***Negr1*** | neuronal growth regulator 1 | 181.9 | 0.45 | -1.14 | 0.011947 |
| ***Zfp641*** | zinc-finger protein 641 | 24.2 | 0.45 | -1.15 | 0.044072 |
| ***Epb4.2*** | erythrocyte protein band 4.2 | 29.6 | 0.43 | -–1.21 | 0.027399 |
| ***Tuba4a*** | tubulin, α 4A | 27.4 | 0.42 | -1.24 | 0.021661 |
| ***Frrs1*** | ferric-chelate reductase 1 | 44.8 | 0.42 | -1.25 | 0.012293 |
| ***Rgn*** | Regucalcin | 52.7 | 0.4 | -1.31 | 0.000861 |
| ***Capn5*** | calpain 5 | 18.9 | 0.39 | -1.35 | 0.049831 |
| ***F11*** | coagulation factor XI | 9.8 | 0.39 | -1.35 | 0.049162 |
| ***Cfb*** | complement factor B | 37.7 | 0.39 | -1.36 | 0.006608 |
| ***Ppargc1b*** | peroxisome proliferative-activated receptor γ, coactivator 1β | 19 | 0.38 | -1.38 | 0.031338 |
| ***Slc4a1***[g] | solute carrier family 4 (anion exchanger), member 1 | 173 | 0.38 | –1.41 | 0.034826 |
| ***Cyp3a16*** | **cytochrome P450, family 3, subfamily a, polypeptide 16** | 8.8 | 0.36 | –1.46 | 0.03581 |
| ***Got1*** | glutamate oxaloacetate transaminase 1, soluble | 65.9 | 0.36 | -1.47 | 0.017347 |
| ***Ermap*** | erythroblast membrane-associated protein | 109.8 | 0.36 | –1.48 | 0.023993 |
| ***Rbp4*** | retinol-binding protein 4, plasma | 29.5 | 0.35 | -1.53 | 0.001504 |
| ***Gys2*** | glycogen synthase 2 | 12.5 | 0.34 | -1.57 | 0.012228 |
| ***Acpp*** | acid phosphatase, prostate | 22.7 | 0.33 | -1.59 | 0.026206 |
| ***C8b*** | complement component 8, β polypeptide | 18.7 | 0.33 | -1.6 | 0.002955 |
| ***Itih2*** | inter-α trypsin inhibitor, heavy chain 2 | 138.9 | 0.33 | -1.61 | 0.000457 |
| ***Syt9*** | synaptotagmin IX | 11.9 | 0.32 | -1.66 | 0.049333 |
| ***Cps1*** | carbamoyl-phosphate synthetase 1 | 26.9 | 0.31 | -1.68 | 0.012572 |
| ***Prr15*** | proline-rich 15 | 11.1 | 0.3 | -1.73 | 0.041482 |
| ***Tdrd5*** | tudor domain-containing 5 | 21.7 | 0.3 | -1.74 | 0.03502 |
| ***Trf*** | transferrin | 244.4 | 0.29 | –1.78 | 0.001129 |
| ***F13b*** | coagulation factor XIII, β subunit | 16.8 | 0.29 | -1.78 | 0.002825 |
| ***Alb*** | albumin | 2289.8 | 0.28 | -1.81 | 0.000304 |
| ***Otc*** | ornithine transcarbamylase | 11.1 | 0.28 | -1.85 | 0.007028 |
| ***Tmem56*** | transmembrane-protein 56 | 78.6 | 0.27 | -1.88 | 7.98E-05 |
| ***Gc*** | group-specific component | 25 | 0.27 | -1.89 | 0.000189 |
| ***Slc22a4*** | solute carrier family 22 (organic cation transporter), member 4 | 9.7 | **0.27** | **–1.91** | **0.036427** |
| ***Edaradd*** | EDAR (ectodysplasin-A receptor)-associated death domain | 46 | 0.27 | -1.91 | 0.021752 |
| ***Gsta3*** | glutathione *S*-transferase, a3 | 28.6 | 0.27 | -1.92 | 0.002929 |
| ***Bhmt*** | betaine-homocysteine methyltransferase | 15.3 | 0.26 | -1.92 | 0.002084 |
| ***Cyp2c67*** | **cytochrome P450, family 2, subfamily c, polypeptide 67** | 7.4 | 0.26 | –1.93 | 0.026034 |
| ***Apob*** | apolipoprotein B | 717.9 | 0.26 | -1.93 | 0.00013 |

|  |  |  |  |  |  |
|---|---|---|---|---|---|
| ***Apoh*** | apolipoprotein H | 10.6 | 0.26 | -1.96 | 0.006327 |
| ***Afp*** | α-fetoprotein | 569.1 | 0.26 | -1.96 | 5.30E-06 |
| ***Klkb1*** | kallikrein B, plasma 1 | 8.1 | 0.26 | -1.97 | 0.02064 |
| ***F5*** | coagulation factor V | 40 | 0.25 | -1.99 | 0.000185 |
| ***Slco5a1*** | solute carrier organic anion transporter family, member 5A1 | 40.3 | 0.25 | –1.99 | 0.047989 |
| ***Aldh8a1*** | aldehyde dehydrogenase 8 family, member A1 | 7.3 | 0.25 | -2.01 | 0.025139 |
| ***Hemgn*** | hemogen | 133 | 0.25 | –2.02 | 0.008414 |
| ***Ahsg*** | α2-HS-glycoprotein | 68.3 | 0.24 | -2.05 | 6.85E-07 |
| ***Cyp2c40*** | **cytochrome P450, family 2, subfamily c, polypeptide 40** | 10.1 | 0.24 | –2.08 | 0.006742 |
| ***Apoa2*** | apolipoprotein A-II | 25.3 | 0.24 | -2.09 | 0.001639 |
| ***Serpina1d*** | serine (or cysteine) peptidase inhibitor, clade A, member 1D | 20.3 | 0.24 | -2.09 | 0.000281 |
| ***Pzp*** | pregnancy-zone protein | 121.7 | 0.23 | -2.09 | 2.53E-06 |
| ***Akr1d1*** | aldo-keto reductase family 1, member D1 | 6.4 | 0.23 | -2.12 | 0.036532 |
| ***Apoa1*** | apolipoprotein A-I | 59.8 | 0.23 | -2.15 | 8.22E-05 |
| ***Serpina1c*** | serine (or cysteine) peptidase inhibitor, clade A, member 1C | 25.8 | 0.22 | -2.16 | 2.67E-05 |
| ***Hsd17b2*** | hydroxysteroid (17β) dehydrogenase 2 | 5.5 | 0.21 | -2.22 | 0.028871 |
| ***Serpina1e*** | serine (or cysteine) peptidase inhibitor, clade A, member 1E | 18.6 | 0.21 | -2.23 | 0.000263 |
| ***Pklr*** | pyruvate kinase liver and red blood cell | 6.5 | 0.21 | –2.24 | 0.027325 |
| ***Rab11fip4*** | RAB11 family-interacting protein 4 (class II) | 7.5 | 0.21 | -2.25 | 0.029383 |
| ***Fgg*** | fibrinogen γ chain | 125.3 | 0.21 | -2.25 | 1.10E-08 |
| ***Serpina1b*** | serine (or cysteine) preptidase inhibitor, clade A, member 1B | 40.9 | 0.21 | -2.25 | 4.19E-07 |
| ***Ttr*** | Transthyretin | 61.2 | 0.21 | -2.25 | 8.56E-08 |
| ***Fn3k*** | Fructosamine-3 kinase | 14.1 | 0.21 | -2.25 | 0.020082 |
| ***Rprm*** | reprimo, TRP53-dependent G$_2$ arrest mediator candidate | 12.8 | 0.21 | -2.27 | 0.025739 |
| ***Timd2*** | T-cell immunoglobulin- and mucin domain-containing 2 | 9.1 | 0.2 | -2.29 | 0.010745 |
| ***Vtn*** | Vitronectin | 8.3 | 0.2 | -2.33 | 0.006947 |
| ***Kng1*** | kininogen 1 | 41.5 | 0.2 | -2.35 | 9.57E-08 |
| ***Fgb*** | fibrinogen β-chain | 96.2 | 0.2 | -2.36 | 1.06E-10 |
| ***C3*** | complement component 3 | 60.7 | 0.19 | -2.37 | 0.000239 |
| ***Fga*** | fibrinogen α chain | 90.3 | 0.19 | -2.39 | 3.55E-10 |
| ***Olfr78*** | olfactory receptor 78 | 5.4 | 0.19 | -2.39 | 0.044948 |
| ***Slc14a1*** | solute carrier family 14 (urea transporter), member 1 | 7.8 | 0.19 | –2.39 | 0.01236 |
| ***Plg*** | plasminogen | 15.7 | 0.18 | -2.44 | 0.000143 |
| ***Cyp2c68*** | **cytochrome P450, family 2, subfamily c, polypeptide 68** | 14.7 | 0.18 | –2.51 | 0.000346 |
| ***Slc30a10*** | solute carrier family 30, member 10 | 30.6 | 0.17 | –2.52 | 0.023084 |
| ***Serpina6*** | serine (or cysteine) peptidase inhibitor, clade A, member 6 | 72.8 | 0.17 | -2.55 | 4.07E-09 |
| ***Dsc2*** | desmocollin 2 | 70.1 | 0.16 | -2.67 | 0.034503 |
| ***Mcoln2*** | mucolipin 2 | 7.6 | 0.16 | -2.67 | 0.018071 |
| ***Fabp1*** | fatty-acid binding-protein 1, liver | 6.4 | 0.15 | -2.69 | 0.013204 |
| ***Aadac*** | arylacetamide deacetylase (esterase) | 33 | 0.15 | -2.75 | 0.00991 |
| ***C8a*** | complement component 8, α polypeptide | 6.3 | 0.14 | -2.81 | 0.00857 |
| ***Ugt2b34*** | UDP glycosyltransferase 2 family, polypeptide B34 | 51.9 | 0.13 | -2.89 | 0.007348 |
| ***Dpp10*** | dipeptidylpeptidase 10 | 7.2 | 0.13 | -2.95 | 0.01963 |
| ***Abcb11*** | ATP-binding cassette, sub-family B (MDR/TAP), member 11 | 5 | 0.09 | -3.46 | 0.008631 |
| ***Ambp*** | α1 microglobulin/bikunin | 15.3 | 0.09 | -3.5 | 3.98E-06 |
| ***Dmrt2*** | doublesex- and mab-3-related transcription factor 2 | 3.9 | 0.09 | -3.53 | 0.039071 |
| ***Itih3*** | inter-α trypsin inhibitor, heavy chain 3 | 25.2 | 0.08 | -3.56 | 2.61E-08 |
| ***Uroc1*** | urocanase domain-containing 1 | 3.1 | 0.08 | -3.57 | 0.033389 |
| ***Skap1*** | Src family-associated phosphoprotein 1 | 4.3 | 0.08 | -3.69 | 0.03618 |
| ***Spp2*** | secreted phosphoprotein 2 | 15.1 | 0.08 | -3.71 | 0.045364 |
| ***Amy2b*** | amylase 2b | 2.8 | 0.06 | -3.95 | 0.0494 |
| ***Ctse*** | cathepsin E | 23.2 | 0.06 | -4.03 | 0.004886 |
| ***Slc5a9*** | solute carrier family 5 (sodium/glucose cotransporters), member 9 | 10.3 | 0.01 | –6.21 | 0.044942 |
| ***Thy1*** | thymus cell antigen 1, Θ | 13.3 | 0.01 | -6.59 | 0.007509 |
| ***Hoxd11*** | homeobox D11 | 137.9 | NA | -10 | 0.040832 |
| ***Itih1*** | inter-α trypsin inhibitor, heavy chain 1 | 2.2 | NA | -10 | 0.035079 |
| ***Acot12*** | acyl-CoA thioesterase 12 | 2.5 | NA | -10 | 0.025818 |

**GD16.5 HEART**

| **Gene symbol** | **Official gene name** | **Average expression (RPKM)** | **Fold-Change** | **log$_2$ Fold-Change** | ***P*-value** |
|---|---|---|---|---|---|

| | | | | | |
|---|---|---|---|---|---|
| ***AU018829*** | expressed sequence AU018829 | 1.8 | NA | **+10** | 0.026286 |
| ***Gm3286*** | predicted gene 3286 | 2.5 | NA | 10 | 0.008466 |
| ***Ager*** | advanced glycosylation end product-specific receptor | 4.9 | NA | 10 | 3.29E-05 |
| ***Scgb3a2*** | secretoglobin, family 3A, member 2 | 2.6 | NA | 10 | 0.041262 |
| ***Cbr2*** | carbonyl reductase 2 | 3.4 | NA | 10 | 0.017131 |
| ***Crabp2*** | cellular retinoic acid-binding protein II | 1.6 | NA | 10 | 0.047249 |
| ***Cyp2f2*** | **cytochrome P450, family 2, subfamily f, polypeptide 2** | 4.8 | NA | 10 | 0.021909 |
| ***Cd74*** | CD74 antigen (invariant polypeptide of MHC, class II antigen-associated) | 16.1 | NA | 10 | 0.001655 |
| ***Inmt*** | indolethylamine *N*-methyltransferase | 3.9 | NA | 10 | 0.044646 |
| ***Scgb1a1*** | secretoglobin, family 1A, member 1 (uteroglobin) | 62.6 | NA | 10 | 0.000148 |
| ***Cd52*** | CD52 antigen | 2.8 | NA | 10 | 0.045474 |
| ***Gm16367*** | predicted gene 16367 | 1.6 | NA | 10 | 0.047249 |
| ***Sftpc*** | surfactant-associated protein C | 27.4 | 46.49 | 5.54 | 0.009319 |
| ***Gbp1*** | guanylate-binding protein 1 | 4.5 | 24.03 | 4.59 | 0.036024 |
| ***Slc34a2*** | solute carrier family 34 (sodium phosphate), member 2 | 2.7 | 17.77 | 4.15 | 0.031583 |
| ***H2-Eb1*** | histocompatibility 2, class II antigen E β1 | 7.4 | 13.67 | 3.77 | 0.019073 |
| ***Psmb8*** | proteasome (prosome, macropain) subunit, β type 8 (multifunctnl peptidase 7) | 6.1 | 9.82 | 3.3 | 0.022277 |
| ***Mir682*** | microRNA 682 | 4.3 | 8.97 | 3.17 | 0.042703 |
| ***Vill*** | villin-like | 4.3 | 8.91 | 3.16 | 0.009913 |
| ***Gpr97*** | G-protein-coupled receptor 97 | 3.9 | 5.38 | 2.43 | 0.045928 |
| ***Itga2b*** | integrin α2b | 4.7 | 4.32 | 2.11 | 0.028463 |
| ***Dbc1*** | deleted in bladder cancer 1 (*human*) | 6.5 | 3.7 | 1.89 | 0.020692 |
| ***Dab1*** | disabled 1 | 8.1 | 3.61 | 1.85 | 0.022708 |
| ***2700089I24Rik*** | RIKEN cDNA 2700089I24 gene | 7.9 | 3.39 | 1.76 | 0.017813 |
| ***BC024139*** | cDNA sequence BC024139 | 10.3 | 3.36 | 1.75 | 0.011219 |
| ***Usp43*** | ubiquitin-specific peptidase 43 | 7.6 | 3.29 | 1.72 | 0.030229 |
| ***Lgals3bp*** | lectin, galactoside-binding, soluble, 3 binding protein | 7.4 | 3.15 | 1.66 | 0.026976 |
| ***AI837181*** | expressed sequence AI837181 | 7.1 | 2.87 | 1.52 | 0.049133 |
| ***Acap1*** | ArfGAP with coiled-coil, ankyrin repeat and PH domains 1 | 6.8 | 2.84 | 1.51 | 0.029801 |
| ***Zfpm1*** | zinc-finger protein, multitype 1 | 8.2 | 2.8 | 1.49 | 0.037439 |
| ***Ephx1*** | epoxide hydrolase 1, microsomal | 14.5 | 2.73 | 1.45 | 0.011254 |
| ***Shb*** | Src homology 2 domain-containing transforming protein B | 13.2 | 2.55 | 1.35 | 0.014603 |
| ***Ybx2*** | Y-box protein 2 | 17.5 | 2.49 | 1.31 | 0.007175 |
| ***Sftpb*** | surfactant-associated protein B | 25.1 | 2.46 | 1.3 | 0.042026 |
| ***Emc10*** | ER-membrane protein complex subunit 10 | 17.7 | 2.43 | 1.28 | 0.005151 |
| ***Zfhx2*** | zinc-finger homeobox 2 | 16.1 | 2.33 | 1.22 | 0.015254 |
| ***Hoxb4*** | homeobox B4 | 19.4 | 2.24 | 1.17 | 0.02096 |
| ***Ust*** | uronyl-2-sulfotransferase | 10.5 | 2.22 | 1.15 | 0.048486 |
| ***Syp*** | Synaptophysin | 18.5 | 2.19 | 1.13 | 0.019403 |
| ***Ddx49*** | DEAD (Asp-Glu-Ala-Asp) box polypeptide 49 | 14.1 | 2.18 | 1.13 | 0.019958 |
| ***Bud13*** | BUD13 homolog (*yeast*) | 25.2 | 2.12 | 1.08 | 0.005948 |
| ***Erdr1*** | erythroid differentiation regulator 1 | 111.2 | 2.05 | 1.04 | 0.046802 |
| ***Gpr65*** | G-protein-coupled receptor 65 | 31.2 | 0.5 | –1.01 | 0.007421 |
| ***Slc25a37***$^{h}$ | solute carrier family 25, member 37 | 2057.6 | 0.45 | –1.14 | 3.49E-05 |
| ***Fam46c*** | family with sequence similarity 46, member C | 70.2 | 0.45 | -1.16 | 0.022372 |
| ***Cldn11*** | claudin 11 | 24.1 | 0.44 | -1.2 | 0.048754 |
| ***Hsd3b6*** | hydroxy-Δ-5-steroid dehydrogenase, 3β- and steroid Δ-isomerase 6 | 10.7 | 0.35 | -1.49 | 0.019907 |
| ***Sowaha*** | sosondowah-ankyrin repeat-domain family member A | 12.6 | 0.35 | -1.53 | 0.023357 |
| ***Isg20*** | interferon-stimulated protein | 10.8 | 0.33 | -1.62 | 0.039091 |
| ***Mirlet7d*** | microRNA let7d | 4.9 | 0.29 | -1.81 | 0.028989 |
| ***4930570G19Rik*** | RIKEN cDNA 4930570G19 gene | 4.3 | 0.15 | -2.71 | 0.013752 |
| ***Il1rapl2*** | interleukin 1 receptor accessory protein-like 2 | 5 | 0.15 | -2.74 | 0.003039 |
| ***Ms4a2*** | membrane-spanning 4-domains, subfamily A, member 2 | 3 | 0.07 | -3.77 | 0.018637 |

**GD16.5 CEREBELLUM**

| Gene symbol | Official gene name | Average expression (RPKM) | Fold-Change | $\log_2$ Fold-Change | *P*-value |
|---|---|---|---|---|---|
| ***Btbd11*** | BTB (POZ) domain-containing 11 | 58.1 | 2.58 | **+1.37** | 0.04094 |
| ***Cyp1b1*** | **cytochrome P450, family 1, subfamily b, polypeptide 1** | 52 | 0.4 | –1.31 | 0.034512 |

| | | | | | |
|---|---|---|---|---|---|
| ***Naa38*** | *N*-α-acetyltransferase 38, NatC auxiliary subunit | 129.4 | 0.38 | -1.4 | 0.043117 |
| ***Spta1*** | spectrin α, erythrocytic 1 | 28 | 0.29 | -1.78 | 0.025538 |
| ***Mrc1*** | mannose receptor, C-type 1 | 111.1 | 0.27 | -1.87 | 0.036005 |
| ***Cfhr2*** | complement factor H-related 2 | 34.9 | 0.25 | -2.01 | 0.04028 |
| ***Apob*** | apolipoprotein B | 86.2 | 0.23 | -2.1 | 0.035616 |
| ***Cfh*** | complement-component factor h | 284.3 | 0.23 | -2.11 | 0.018478 |
| ***Dcn*** | decorin | 49.1 | 0.19 | -2.38 | 0.001055 |
| ***Lum*** | lumican | 14.7 | 0.14 | -2.87 | 0.000786 |
| ***Vamp5*** | vesicle-associated membrane protein 5 | 11.1 | 0.1 | -3.37 | 0.017568 |
| ***Tlr7*** | toll-like receptor 7 | 5.8 | 0.09 | -3.52 | 0.015934 |
| ***Aoah*** | acyloxyacyl hydrolase | 3.3 | 0.04 | -4.67 | 0.045123 |
| ***Tspan8*** | tetraspanin 8 | 202.2 | NA | -10 | 0.046697 |
| ***Il21r*** | interleukin 21 receptor | 2.6 | NA | -10 | 0.02836 |
| | | | | | |

[a] More than 80 genes in ***bolded red font*** denote hematopoiesis- and hypoxia-related genes, including iron transport**;** these include all platelet and white cell types and functions because all are derived from hematopoietic stem cells. Yolk sac and lung had the most hematopoiesis- and hypoxia-related genes (about two dozen each)**;** liver showed the least, only three genes. Genes in ***bolded blue font*** include those in the solute carrier (*Slc*) superfamily and other transporter and channel families. Genes in ***bolded green font*** are members of the cytochrome P450 (*Cyp*) gene superfamily.

[b] Two *Gbp* genes coding for guanylate-binding proteins were strikingly up-regulated in six *Slc39a8(neo/neo)* tissues**:** *Gbp1* in yolk sac, placenta, liver, lung and heart**;** *Gbp3* in placenta. GBPs play pivotal roles in many critical-life processes including inflammatory and innate immune functions**;** the GBP family comprises seven members and is a subset within the dynamin-related large GTPases that are expressed in response to interferons and other pro-inflammatory cytokines[1]. In addition to GBPs being induced by interferon, and protecting against intracellular pathogens, a growing number of GBPs are not directly related to pathogen protection[2]. Our discovery of dramatically up-regulated *Gbp* genes in five of seven *Slc39a8(neo/neo)* tissues examined — would support this view that GBPs are involved in much more than just defense against inflammation.

[c] Insulin-like growth factor (IGF)-binding proteins were up-regulated in yolk sac. Hypoxia is known to induce IGF-binding proteins and stimulate erythropoietin formation.

[d] *Npr3* (natriuretic peptide receptor-3) is up-regulated, and this finding is relevant to another investigation in this laboratory. In a *Sglt2>Cre>Slc39a8(flox/neo)* conditional knockout in which renal epithelial ZIP8 was ablated, atrial natriuretic peptide (ANP) levels were markedly decreased (Jorge-Nebert L, Soleimani M, and Nebert DW, *unpublished*). Atrial natriuretic peptides (ANPs) are known to dilate blood vessels and stimulate natriuresis and diuresis — rsulting in lowered blood pressure and blood volume**;** in part, ANPs counterbalance actions of the renin-angiotensin-aldosterone and neurohormonal systems, and play a pivotal role in cardiovascular regulation[3]. In liver, *Ace2* (angiogenesis I-converting enzyme) was also up-regulated, contributing perhaps to the potential clinical role of *SLC39A8* and heart disease.

A genome-wide association study (GWAS) of coronary artery disease in almost 104,000 participants (cases vs controls) from eight populations[4] found a significant association ($P \leq 5.0$ x $10^{-8}$) between a putatively functional single-nucleotide variant in the *SLC39A8* gene and serum levels of high-density-lipoprotein cholesterol. In the human and mouse genomes, there are three *ANP* genes and three natriuretic peptide receptor genes (*NPR1*, *NPR2*, *NPR3*). If ZIP8 deficiency results in ANP depletion, it seems plausible that up-regulation of the receptor *Npr3* might follow. We speculate that enhanced renal *Npr3* in the *Slc39a8(neo/neo)* fetus might therefore be relevant to the GWAS — implicating a relationship between the *SLC39A8* variant and coronary heart disease.

[e] *Ace2* (angiotensin I-converting enzyme A2) is up-regulated in kidney**;** ACE2 has been associated with the induction of erythrocyte formation.

[f] *Bpgm* encodes BPGM (2,3-*bis*-phosphoglycerate mutase) catalyzes 2,3-diphosphogylycerate — which regulates the affinity of hemoglobin for oxygen. Several variant mutations gene are known clinically to cause hemolytic anemia and affect erythrocyte metabolism**;** this is this case in the Luebering-Rapaport pathway. BPGM, together with GSH and pyruvate, are affected as the result of adaptation of erythrocytes during anemia. Erythrocytes, due to lack of mitochondria, obtain their energy only through anaerobic glycolysis.

[g] *Slc4a1* encodes a red blood cell solute carrier family 4, member 1, a chloride/bicarbonate anion exchanger. One null mutation in *SLC4A1* causes severe anemia, and other mutations are known to detabilize the red cell membrane [*reviewed in Ref. 5*].

[h] *Slc25a37*, down-regulated in heart, encodes a solute carrier that moves $Fe^{2+}$ into the mitochondrion, and is important for synthesis of mitochondrial heme in immature erythrocytes.

**Differentially-expressed cytochrome P450 (Cyp) genes.** We found nine cytochrome P450 (*Cyp*) genes (***green font***) — *Cyp1b1* differentially-expressed in yolk sac, kidney and cerebellum, whereas the other eight *Cyp* genes were each found in only one tissue. Except for *Cyp7b1* (oxysterol metabolism) and *Cyp1b1*, the remaining seven *Cyp* genes are members of the *Cyp2* and *Cyp3* families.

In the mouse genome there are 103 *Cyp* genes in 18 families — with the *Cyp2*, *Cyp3* and *Cyp4* families greatly expanded — compared with the human genome that has 57 *CYP* genes in 18 families[6,7]. *Slc39a8(neo/neo) Cyp1b1* was up-regulated in yolk sac and kidney, but down-regulated in cerebellum. The results were also mixed with the other eight *Cyp* genes.

How can these data be explained? CYP monooxygenases (in particular, members of *Cyp1*, *Cyp2*, *Cyp3* and *Cyp4* families) participate in the second-messenger lipid-mediator (LM) cascade**;** LMs play important roles in virtually every critical-life function [*reviewed in Refs. 7,8*]. In support of this, zymosan-induced peritonitis in *Cyp1(–/–)* triple-knockout mice resulted in alteration of eight distinct LM metabolic steps, suggesting that one or more of the three CYP1 enzymes contribute to the local metabolite profile of LMs that regulate inflammation[9].

Hence, defective ZIP8-mediated function evokes changes in hepatic *Cyp3a11*, pulmonary *Cyp2s1*, *Cyp3a16*, *Cyp2c67*, *Cyp2c40*, and *Cyp2c68*, and cardiac *Cyp2f2* expression levels — which, in turn, will modify cell-specific LM metabolites that regulate numerous critical-life processes. On the other hand, deficient ZIP8-mediated stimulation of *Cyp7b1*, coding for oxysterol 7α-hydroxylase[7], is most likely associated with dysregulation of fatty-acid and steroid homeostasis. Except for *Cyp7b1*, the other eight *Cyp* genes are known to be regulated by AHR/ARNT heterodimeric binding to the AHRE casettte**;** involvement of the AHR/CYP1 axis as “early first-responders to various types of stress signals” has recently been reviewed[10].

**Differentially-expressed solute-carrier (Slc) genes.** Excluding *Slc39a8*, there were 27 other genes in the solute-carrier (*Slc*) transporter superfamily (***blue font***), some found in two or three of the seven tissues, but most of them differentially-expressed in just one tissue**;** 18 various *Slc* genes were up-regulated and 12 down-regulated, in no discernible pattern. Twenty-one of the 52 known *Slc* gene families were represented, and none of the fourteen genes in the *Slc39* family (other than *Slc39a8*) was differentially-expressed.

The *Slc* gene superfamily contains 57 gene families encoding at least 395 protein-coding genes [https://www.genenames.org/]. SLC proteins include passive transporters, symporters and antiporters, located in all cellular and organelle membranes. Transport substrates include**:** amino acids and oligopeptides, glucose and other sugars, innumerable inorganic cations and anions, bile salts, carboxylate and other organic anions, acetyl coenzyme A, biogenic amines, neurotransmitters, vitamins, fatty acids and lipids, nucleosides, ammonium, choline, thyroid hormone, and urea [*reviewed in Ref. 11*].

In our RNA-seq analysis, besides *Slc39a8* down-regulation, we found *Slc30a10* (as the only one of ten *Slc30* family members) up-regulated in yolk sac and down-regulated in kidney and lung (*vide supra*). SLC30 (ZnT) zinc transporters move $Zn^{2+}$ out of the cell whereas ZIP8 moves $Zn^{2+}$ into the cell, providing a balance between intracellular and extracellular $Zn^{2+}$ concentrations[12]. Other than *Slc39a8* and *Slc30a10* — diminished ZIP8 function resulted in 17 other *Slc* genes up-regulated and 11 other *Slc* genes down-regulated in one or another of the tissues — except for cerebellum. To understand these effects of ZIP8 deficiency on regulation of all these other SLC transporters will require further study. Of interest, other differentially-expressed channel genes (*e.g.* $Ca^{2+}$ and $Na^{+}$) were also seen in substantial numbers (*vide supra).*

**TABLE S2.** Genes differentially-expressed in more than one of the seven tissues examined

| **Genes differentially regulated in at least three tissues** | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | **Fold-change, comparing *Slc39a8(neo/neo)* with *Slc39a8(+/+)*** | | | | | | |
| **Gene symbol**[a] | **Official gene name** | **Yolk sac** | **Placenta** | **Liver** | **Kidney** | **Lung** | **Heart** | **Cerebellum** |
| ***Gbp1*** | guanylate-binding protein 1 | +19.23 | +5.69 | +6.35 | | +28.81 | +24.03 | |
| ***Cyp1b1*** | cytochrome P450, family 1, subfamily b, polypeptide 1 | +5.37 | | | +2.26 | | | –2.49 |
| ***Hemgn*** | hemogen | +3.83 | +18.87 | | | –4.05 | | |
| ***Slc30a10*** | solute carrier family 30, member 10 | +3.59 | | | –16.64 | –5.74 | | |
| ***Ank1*** | ankyrin 1, erythroid | +3.53 | +7.76 | | –13.28 | | | |
| ***Bhmt*** | betaine-homocysteine methyltransferase | –2.20 | | –2.25 | | –3.78 | | |
| ***Cfh*** | complement-component factor h | –2.46 | | | +3.02 | | | –4.32 |

| **Genes differentially regulated in at least two tissues** | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | **Fold-change, comparing *Slc39a8(neo/neo)* with *Slc39a8(+/+)*** | | | | | | |
| **Gene symbol** | **Official gene name** | **Yolk sac** | **Placenta** | **Liver** | **Kidney** | **Lung** | **Heart** | **Cerebellum** |
| ***Gbp1*** | guanylate-binding protein 1 | +19.23 | +5.69 | +6.35 | | +28.81 | +24.03 | |
| ***Cyp1b1*** | cytochrome P450, family 1, subfamily b, polypeptide 1 | +5.37 | | | +2.26 | | | –2.49 |
| ***Esm1*** | endothelial cell-specific molecule 1 | +4.62 | | | +3.74 | | | |
| ***Hemgn*** | hemogen | +3.83 | +18.87 | | | –4.05 | | |
| ***Slc30a10*** | solute carrier family 30, member 10 | +3.59 | | | –16.64 | –5.74 | | |
| ***Ank1*** | ankyrin 1, erythroid | +3.53 | +7.76 | | –13.28 | | | |
| ***Capn5*** | calpain 5 | +3.07 | | | | –2.55 | | |
| ***Ermap*** | erythroblast membrane-associated protein | +2.99 | | | | –2.79 | | |
| ***Bcl11a*** | B-cell CLL/lymphoma 11A (zinc-finger protein) | +2.84 | +4.28 | | | | | |
| ***Isg20*** | interferon-stimulated protein | +2.79 | | | | | –3.07 | |
| ***Hsd3b6*** | HO-Δ-5-steroid dehydrogenase, 3β- and steroid-Δ-isomerase 6 | +2.75 | | | | | –2.82 | |
| ***Sulf2*** | sulfatase 2 | +2.68 | | | –2.88 | | | |
| ***Asns*** | asparagine synthetase | +2.56 | | | –2.58 | | | |
| ***Slc2a3*** | solute carrier family 2 (facilitated glucose transporters), member 3 | +2.50 | | | –4.96 | | | |
| ***Gpr50*** | G-protein-coupled receptor 50 | +2.49 | | | | | | |
| ***Slc1a4*** | solute carrier family 1 (Glx/neutral amino acid transporter), member 4 | +2.12 | | | –4.77 | | | |
| ***Lss*** | lanosterol synthase | +2.09 | | | –2.28 | | | |
| ***Trf*** | transferrin | +2.05 | | | | –3.43 | | |
| ***Aadac*** | arylacetamide deacetylase (esterase) | –2.04 | | | | –6.72 | | |
| ***Bhmt*** | betaine-homocysteine methyltransferase | –2.20 | | –2.25 | | –3.78 | | |
| ***Tlr7*** | toll-like receptor 7 | –2.29 | | | | | | –11.46 |
| ***Cfh*** | complement-component factor h | –2.46 | | | +3.02 | | | –4.32 |
| ***Slc39a8*** | solute carrier family 39 (metal ion transporter), member 8 | –4.06 | –3.27 | | | | | |
| ***Hbb-b1*** | hemoglobin, beta adult major chain | –4.69 | –2.53 | | | | | |
| ***Hbb-b2*** | hemoglobin, beta adult minor chain | –4.69 | –2.53 | | | | | |
| ***4930570G19Rik*** | RIKEN cDNA 4930570G19 gene | | | | | –2.12 | –6.53 | |
| ***AF357359*** | snoRNA AF357359 | | | | –8.22 | +2.16 | | |
| ***Ager*** | advanced glycosylation end-product-specific receptor | | | | | +2.34 | | |
| ***Apob*** | apolipoprotein B | | | | | –3.80 | | –4.28 |
| ***Cfhr2*** | complement-factor H-related 2 | | | | +3.58 | | | –4.04 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| ***Cldn11*** | claudin 11 | | | | **+3.21** | | **–2.29** | |
| ***Cth*** | cystathionase (cystathionine γ-lyase) | | | **-2.32** | **+2.56** | | | |
| ***Grina*** | glutamate receptor, ionotropic, N-methyl-*D*-aspartate-associated protein 1 (Glx- binding) | | | **+2.62** | **–3.21** | | | |
| ***Hoxd11*** | homeobox D11 | | | | **+2.25** | | | |
| ***Mir1906-1*** | microRNA 1906-1 | | | **+5.43** | **–13.05** | | | |
| ***Mir1906-2*** | microRNA 1906-2 | | | **+5.43** | **–13.05** | | | |
| ***Sftpc*** | surfactant-associated protein C | | | | | **+3.48** | **+46.49** | |
| ***Slc22a4*** | solute carrier family 22 (organic cation transporter), member 4 | | | | **–6.49** | **–3.77** | | |
| ***Tal1*** | T-cell acute lymphocytic leukemia 1 | | **+3.15** | | **–4.93** | | | |
| ***Tmem56*** | transmembrane-protein 56 | | | | **–3.31** | **–3.68** | | |

[a] Genes are ranked by the degree of differential change in yolk sac. Those with no change seen in yolk sac — are then listed alphabetically below. In the seven *columns* at *right*, up-regulation is denoted in ***red***, down-regulation in ***blue***.

**TABLE S3.** Significant differentially-expressed genes — using a FDR-adjusted meta-*P*-value <0.1 — that were identified across all tissues by meta-analysis

| **Gene symbol**[a] | **Official gene name** | ***P*-values for Fisher test FDR down-regulated genes**[b,c] | ***P*-values for Fisher test FDR up-regulated genes**[b,c] |
|---|---|---|---|
| ***Slc39a8*** | solute carrier family 39 (metal ion transporter), member 8 | 0.00035 | 1.00000 |
| ***Bhmt*** | betaine-homocysteine methyltransferase | 0.00713 | 1.00000 |
| ***Hbb-b1*** | hemoglobin, beta adult major chain | 0.00713 | 1.00000 |
| ***Hbb-b2*** | hemoglobin, beta adult minor chain | 0.00713 | 1.00000 |
| ***Psmc3*** | proteasome (prosome, macropain) 26S subunit, ATPase 3 | 0.01182 | 1.00000 |
| ***Hbb-bs*** | hemoglobin subunit beta-1-like | 0.01235 | 1.00000 |
| ***Apob*** | apolipoprotein B | 0.01235 | 1.00000 |
| ***Bpgm***[d] | 2,3-*bis*-phosphoglycerate mutase | 0.02678 | 1.00000 |
| ***Cisd2*** | CDGSH iron sulfur domain 2 | 0.03351 | 1.00000 |
| ***Slc25a37*** | solute carrier family 25, member 37 | 0.03451 | 1.00000 |
| ***Fgb*** | fibrinogen β-chain | 0.03540 | 1.00000 |
| ***Hba-a2*** | hemoglobin alpha, adult chain 2 | 0.03540 | 1.00000 |
| ***Ahsg*** | α2-HS-glycoprotein | 0.03540 | 1.00000 |
| ***Fabp2*** | fatty-acid-binding protein 2, intestinal | 0.03540 | 1.00000 |
| ***Hba-a1*** | hemoglobin alpha, adult chain 1 | 0.03540 | 1.00000 |
| ***Ovca2*** | candidate tumor suppressor in ovarian cancer 2 | 0.03540 | 1.00000 |
| ***Snca*** | synuclein, α | 0.03930 | 0.99406 |
| ***Fgg*** | fibrinogen γ-chain | 0.03930 | 1.00000 |
| ***A530054K11Rik*** | RIKEN cDNA A530054K11 gene | 0.03997 | 1.00000 |
| ***Cth*** | cystathionase (cystathionine γ-lyase) | 0.04105 | 0.98646 |
| ***Hbb-y*** | hemoglobin Y, beta-like embryonic chain | 0.04105 | 1.00000 |
| ***Lum*** | Lumican | 0.04105 | 1.00000 |
| ***Gsg1l*** | GSG1-like | 0.04105 | 1.00000 |
| ***Usmg5*** | up-regulated during skeletal muscle growth 5 | 0.05303 | 1.00000 |
| ***Slc4a1*** | solute carrier family 4 (anion exchangers), member 1 | 0.05759 | 0.97794 |
| ***Dgkb*** | diacylglycerol kinase, β | 0.06022 | 0.98156 |
| ***Dnajc6*** | DnaJ (Hsp40) homolog, subfamily C, member 6 | 0.06022 | 0.99234 |
| ***Gm14305*** | predicted gene 14305 | 0.06022 | 1.00000 |
| ***Zfp758*** | zinc-finger protein 758 | 0.06866 | 1.00000 |
| ***Gm14308*** | predicted gene 14308 | 0.07221 | 1.00000 |
| ***Cps1*** | carbamoyl-phosphate synthetase 1 | 0.07221 | 1.00000 |
| ***Fam166a*** | family with sequence similarity 166, member A | 0.07221 | 1.00000 |
| ***6030408B16Rik*** | RIKEN cDNA 6030408B16 gene | 0.07221 | 1.00000 |
| ***Actn2*** | actinin α2 | 0.07403 | 1.00000 |
| ***Slc8a1*** | solute carrier family 8 (sodium/calcium exchangers), member 1 | 0.07403 | 1.00000 |
| ***Neto2*** | neuropilin (NRP) & tolloid (TLL)-like 2 | 0.07403 | 1.00000 |
| ***Gpr65*** | G-protein-coupled receptor 65 | 0.08457 | 1.00000 |
| ***Gucy1a2*** | guanylate cyclase 1, soluble, α2 | 0.08457 | 1.00000 |
| ***Cdr2***[e] | cerebellar degeneration-related 2 | 0.08709 | 0.99898 |
| ***Gm14432*** | predicted gene 14432 | 0.08709 | 1.00000 |
| ***Xlr*** | X-linked lymphocyte-regulated complex | 0.09410 | 1.00000 |
| ***Tomm5*** | translocase of outer mitochondrial membrane 5 homolog (*Saccharomyces*) | 0.09410 | 1.00000 |
| ***Paqr9*** | progestin and adipoQ receptor fam member IX | 0.09568 | 0.97794 |
| ***Dcn*** | decorin | 0.09568 | 1.00000 |
| ***Otc*** | ornithine transcarbamylase | 0.09568 | 1.00000 |
| | | | |
| ***Gbp1*** | guanylate-binding protein 1 | 1.00000 | **<0.00001** |
| ***Esm1*** | endothelial cell-specific molecule 1 | 1.00000 | **0.00725** |

[a] Genes in ***bolded blue font*** denote members of the solute carrier (*Slc*) superfamily. Genes in ***bolded red font*** denote hematopoiesis-related genes and genes in other blood cell types and functions.

[b] The last two columns list false discovery rate (FDR)-adjusted *P*-values for down- and up-regulation, respectively. Using this method of analysis, there are 45 genes having an FDR of <0.1 for ***down***-regulation, with *Slc39a8* as the most highly significant *P*-value. Only the last two rows (*Gbp1* and *Esm1* genes) show an FDR of <0.1 for ***up***-regulation.

[c] This meta-analysis combines *P*-values from all tissues into a single *P*-value. In **Step 1**, the genes are ranked from low to high — based on their assigned differential-expression *P*-values in each tissue separately. For example, the rank order of *Slc39a8* in each tissue was**:**

| **Yolk sac** | **Placenta** | **Liver** | **Kidney** | **Lung** | **Heart** | **Cerebellum** |
|---|---|---|---|---|---|---|
| 12th | 1st | 121st | 4404th | 4783rd | 482nd | 323rd |

In **Step 2**, these rank orders are then converted to empirical *P*-values by dividing the rank by the total number of genes (17,163 in our case), which gives us the *P*-value in each tissue**:**

| **Yolk sac** | **Placenta** | **Liver** | **Kidney** | **Lung** | **Heart** | **Cerebellum** |
|---|---|---|---|---|---|---|
| 6.99e-04 | 5.83e-05 | 7.05-03 | 2.57e-01 | 2.79e-01 | 2.81e-02 | 1.88e-02 |

In **Step 3**, "Fisher's combined probability test" then combines these empirical *P*-values into a single *P*-value. For *Slc39a8*, the combined *P*-value is 2.03e–08. After the FDR adjustment, the combined *P*-value is 0.00035. This *P*-value specifies how likely it is to see, by chance alone, a gene with such a low rank order in seven tissues. Because the genes were ranked from "low" to "high" in **Step 1**, this is a test for "consistent down-regulation" in all seven tissues.

The rank order of genes from "high" to "low" was then calculated by repeating **Steps 1 to 3** in order to create the *P*-values for "consistent up-regulation" in all tissues**;** only the last two genes (*Gbp1*, *Esm1*) in the table are of this category.

This meta-analysis considers all tissues together, and not for any individual tissue. This technique of meta-analysis is widely used in genome-wide association studies and is less commonly used to combine rank-based empirical *P*-values**;** in this case, however, we have used it in combination with ToppGene.

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[d] It is worth noting that *Bpgm* encodes 2,3-*bis*-phosphoglycerate mutase (BPGM). Clinically, BPGM enzyme deficiency is known to increase the affinity of hemoglobin for oxygen[13].

[e] Intriguingly, the cerebellar degeneration-related-2 gene (*Cdr2*) was down-regulated**;** this finding might be clinically relevant to studies demonstrating cerebellar atrophy and mental retardation in children having a mutant *SLC39A8* allele putatively causing ZIP8 function to be markedly impaired[14,15].

**TABLE S4.** Known TAL1-downstream target genes found in the present study — comparing *Slc39a8(neo/neo)* with *Slc39a8(+/+)* wild-type.

*P*-value of <0.05 and absolute fold-change >2 were used as the cut-off values.

| | | | | | | |
|---|---|---|---|---|---|---|
| **GD13.5 YOLK SAC *P* = 1.178e–5**[a] | | | | | | |
| **Gene symbol**[b] | **Official gene name** | **Fold-Change** | **log$_2$ Fold-Change** | ***P*val** | **$P_{adj}$** | **TAL1 effect on transcription** |
| ***Egln3*** | EGL nine homolog 3 (*C. elegans*) | 4.218064 | +2.076581 | 4.61E-09 | 1.51E-05 | Activation |
| ***Hemgn*** | hemogen | 3.825722 | 1.935732 | 5.02E-07 | 0.001095 | Activation |
| ***Ank1*** | ankyrin 1, erythroid | 3.527797 | 1.818768 | 0.0124 | 1.00000 | Activation |
| ***Ermap*** | erythroblast membrane-associated protein | 2.990613 | 1.580441 | 0.006552 | 1.00000 | Undetectable |
| ***Rhag*** | Rhesus blood group-associated A glycoprotein | 2.515802 | 1.331018 | 0.000338 | 0.331496 | Undetectable |
| ***Slc2a3*** | solute carrier family 2 (facilitated glucose transporter), member 3 | 2.499126 | 1.321424 | 0.005112 | 1.00000 | Repression |
| ***Hbb-b2*** | hemoglobin, beta adult minor chain | 0.213027 | –2.23089 | 0.01473 | 1.00000 | Repression |
| | | | | | | |
| **GD13.5 PLACENTA *P* = 4.982e–6** | | | | | | |
| **Gene symbol** | **Official gene name** | **Fold-Change** | **log$_2$ Fold-Change** | ***P*val** | **$P_{adj}$** | **TAL1 effect on transcription** |
| ***Hemgn*** | Hemogen | 18.87205 | +4.238179 | 2.15E-06 | 0.045538 | Activation |
| ***Ank1*** | ankyrin 1, erythroid | 7.760406 | 2.956132 | 0.00739 | 1.00000 | Activation |
| ***Tal1***[c] | T cell acute lymphocytic leukemia 1 | 3.145147 | 1.653127 | 0.038062 | 1.00000 | Undetectable |
| ***Ikzf1*** | IKAROS family zinc-finger 1 | 2.244527 | 1.166411 | 0.033308 | 1.00000 | Undetectable |
| ***Hbb-b2*** | hemoglobin, beta adult minor chain | 0.395638 | –1.33775 | 0.028901 | 1.00000 | Repression |
| ***Cbfa2t3*** | core-binding factor, runt domain, α-subunit 2, translocated to, 3 (*human*) | 0.042822 | -4.54552 | 0.006988 | 1.00000 | Undetectable |
| | | | | | | |
| **GD16.5 LIVER *P* = 0.2233** | | | | | | |
| **Gene symbol** | **Official gene name** | **Fold-Change** | **log$_2$ Fold-Change** | ***P*val** | **$P_{adj}$** | **TAL1 effect on transcription** |
| ***Epor*** | erythropoietin receptor | 3.657651 | +1.870917 | 0.035935 | 1.00000 | Activation |
| | | | | | | |
| **GD16.5 KIDNEY *P* = 0.06134** | | | | | | |
| **Gene symbol** | **Official gene name** | **Fold-Change** | **log$_2$ Fold-Change** | ***P*val** | **$P_{adj}$** | **TAL1 effect on transcription** |
| ***Tal1***[c] | T-cell acute lymphocytic leukemia 1 | 0.202956 | –2.30076 | 0.010111 | 1.00000 | Undetectable |
| ***Slc2a3*** | solute carrier family 2 (facilitated glucose transporter), member 3 | 0.20156 | -2.31072 | 0.030869 | 1.00000 | Repression |
| ***Ank1*** | ankyrin 1, erythroid | 0.075312 | –3.73098 | 0.017692 | 1.00000 | Activation |
| | | | | | | |
| **GD16.5 LUNG *P* = 0.01895** | | | | | | |

| Gene symbol | Official gene name | Fold-Change | $\log_2$ Fold-Change | *P*val | $P_{\text{adj}}$ | TAL1 effect on transcription |
|---|---|---|---|---|---|---|
| ***Slc4a1*** | solute carrier family 4 (anion exchanger), membr 1 | 0.375952 | –1.41138 | 0.034826 | 1.00000 | Activation |
| ***Ermap*** | erythroblast membrane-associated protein | 0.358182 | -1.48124 | 0.023993 | 1.00000 | Undetectable |
| ***Hemgn*** | Hemogen | 0.246722 | -2.01904 | 0.008414 | 1.00000 | Activation |
| | | | | | | |
| **GD16.5 HEART *P* = 0.2196** | | | | | | |
| **Gene symbol** | **Official gene name** | **Fold-Change** | **$\log_2$ Fold-Change** | ***P*val** | **$P_{\text{adj}}$** | **TAL1 effect on transcription** |
| ***Zfpm1*** | zinc-finger protein, multitype 1 | 2.801525 | +1.486213 | 0.037439 | 1.00000 | Undetectable |
| | | | | | | |
| **GD16.5 CEREBELLUM *P* = 0.06771** | | | | | | |
| **Gene symbol** | **Official gene name** | **Fold-Change** | **$\log_2$ Fold-Change** | ***P*val** | **$P_{\text{adj}}$** | **TAL1 effect on transcription** |
| ***Spta1*** | spectrin α, erythrocytic 1 | 0.291331 | –1.77927 | 0.025538 | 1.00000 | Undetectable |
| | | | | | | |

[a] This file contains the Fisher's exact test *P*-values in each tissue, testing for enrichment of TAL1-downstream targets in differentially-expressed genes.

[b] Genes in ***bolded red font*** denote hematopoiesis-related genes and genes in all other blood cell types and functions. Genes in ***bolded blue font*** denote members of the solute carrier (*Slc*) superfamily.

[c] One might ask "How can a gene (*e.g. Tal1*) regulate itself?" Actually, this is not that uncommon in genetic pathways and networks. The gene product (*e.g.* TAL1) participates as a TF that binds upstream in a regulatory module of the gene (*Tal1*) from which it is derived. This phenomenon represents a negative feedback regulatory loop. The effects of TAL1 on downstream targets have been reported[16].

**TABLE S5.** Known GATA1-downstream target genes found in the present study — comparing *Slc39a8(neo/neo)* with *Slc39a8(+/+)* wild-type. *P*-value of <0.05 and absolute fold-change >2 were used as the cut-off values.

**GD13.5 YOLK SAC** ***P* = 0.001369**[a]

| Gene symbol[b] | Official gene name | Fold-Change | $\log_2$ Fold-Change | *P*val | $P_{adj}$ |
|---|---|---|---|---|---|
| ***Hdac11*** | histone deacetylase 11 | NA | +10.00 | 0.02759 | 1.0000 |
| ***Reln*** | reelin | 4.44 | 2.15 | 7.02E-05 | 0.092 |
| ***Hemgn*** | hemogen | 3.83 | +1.94 | 5.02E-07 | 0.001 |
| ***Slc30a10*** | solute carrier family 30, member 10 | 3.59 | +1.84 | 2.38E-05 | 0.038 |
| ***Capn5*** | calpain 5 | 3.07 | 1.62 | 0.03789 | 1.0000 |
| ***Ermap*** | erythroblast membrane-associated protein | 2.99 | +1.58 | 0.00655 | 1.0000 |
| ***Mthfd2*** | methylenetetrahydrofolate dehydrogenase ($NAD^+$-dependent), methenyltetrahydrofolate cyclohydrolase | 2.97 | 1.57 | 0.00112 | 0.635 |
| ***Asns*** | asparagine synthetase | 2.56 | 1.36 | 0.00013 | 0.147 |
| ***Rhag*** | Rhesus blood group-associated A glycoprotein | 2.52 | +1.33 | 0.00034 | 0.331 |
| ***Aldoa*** | aldolase A, fructose-bisphosphate | 2.35 | 1.24 | 0.03179 | 1.0000 |
| ***Hbb-y*** | hemoglobin Y, beta-like embryonic chain | 0.31 | –1.71 | 2.09E-06 | 0.004 |
| ***BC049635*** | cDNA sequence BC049635 | 0.29 | -1.78 | 0.03589 | 1.0000 |
| ***Slc39a8*** | solute carrier family 39 (metal ion transporter), member 8 | 0.25 | –2.02 | 0.00353 | 1.0000 |
| ***Hbb-b1*** | hemoglobin, beta adult major chain | 0.21 | –2.23 | 0.01473 | 1.0000 |

**GD13.5 PLACENTA** ***P* = 0.02229**

| Gene symbol | Official gene name | Fold-Change | $\log_2$ Fold-Change | *P*val | $P_{adj}$ |
|---|---|---|---|---|---|
| ***Slc43a1*** | solute carrier family 43, member 1 | 21.80 | +4.45 | 0.02989 | 1.0000 |
| ***Hemgn*** | Hemogen | 18.87 | 4.24 | 2.15E-06 | 0.046 |
| ***Tal1*** | T-cell acute lymphocytic leukemia 1 | 3.15 | 1.65 | 0.03806 | 1.0000 |
| ***Mns1*** | meiosis-specific nuclear structural protein 1 | 2.33 | 1.22 | 0.03008 | 1.0000 |
| ***Hbb-b1*** | hemoglobin, beta adult major chain | 0.40 | –1.34 | 0.0289 | 1.0000 |
| ***Tubb3*** | tubulin, beta 3 class III | 0.38 | -1.40 | 0.02132 | 1.0000 |
| ***Slc39a8*** | solute carrier family 39 (metal ion transporter), member 8 | 0.31 | –1.71 | 1.94E-05 | 0.137 |
| ***Cbfa2t3*** | core-binding factor, runt domain, $\alpha 2$ subunit, translocated to, 3 (*human*) | 0.04 | -4.55 | 0.00699 | 1.0000 |

**GD16.5 LIVER** ***P* = 0.6762**

| Gene symbol | Official gene name | Fold-Change | $\log_2$ Fold-Change | *P*val | $P_{adj}$ |
|---|---|---|---|---|---|
| ***Epor*** | erythropoietin receptor | 3.66 | +1.87 | 0.03593 | 1.0000 |
| ***Grina*** | glutamate receptor, ionotropic, N-methyl D-aspartate-associated protein 1 (glutamate binding) | 2.62 | 1.39 | 0.0421 | 1.0000 |

**GD16.5 KIDNEY** ***P* = 0.5224**

| Gene symbol | Official gene name | Fold-Change | $\log_2$ Fold-Change | *P*val | $P_{adj}$ |
|---|---|---|---|---|---|
| ***Asns*** | asparagine synthetase | 0.39 | –1.37 | 0.01991 | 1.0000 |
| ***Grina*** | glutamate receptor, ionotropic, *N*-methyl D-aspartate-associated protein 1 (Glx-binding) | 0.31 | -1.68 | 0.03533 | 1.0000 |
| ***Tmem56*** | transmembrane protein 56 | 0.30 | -1.73 | 0.03222 | 1.0000 |
| ***Paqr9*** | progestin and adipoQ receptor family member IX | 0.25 | -2.02 | 0.02769 | 1.0000 |
| ***Tal1*** | T-cell acute lymphocytic leukemia 1 | 0.20 | -2.30 | 0.01011 | 1.0000 |
| ***Rpp25*** | ribonuclease P/MRP 25 subunit | 0.12 | -3.01 | 0.03291 | 1.0000 |
| ***Slc30a10*** | solute carrier family 30, member 10 | 0.06 | –4.06 | 0.01406 | 1.0000 |

**GD16.5 LUNG** ***P* = 0.003366**

| Gene symbol | Official gene name | Fold-Change | $\log_2$ Fold-Change | *P*val | $P_{adj}$ |
|---|---|---|---|---|---|
| ***Lpcat1*** | lysophosphatidylcholine acyltransferase 1 | 2.00 | +1.00 | 0.0121 | 1.0000 |
| ***Capn5*** | calpain 5 | 0.39 | –1.35 | 0.04983 | 1.0000 |
| ***Slc4a1*** | solute carrier family 4 (anion exchanger), member 1 | 0.38 | –1.41 | 0.03483 | 1.0000 |
| ***Ermap*** | erythroblast membrane-associated protein | 0.36 | –1.48 | 0.02399 | 1.0000 |
| ***Tmem56*** | transmembrane protein 56 | 0.27 | -1.88 | 7.98E-05 | 0.109 |
| ***Hemgn*** | Hemogen | 0.25 | –2.02 | 0.00841 | 1.0000 |
| ***Pklr*** | pyruvate kinase liver and red blood cell | 0.21 | -2.24 | 0.02733 | 1.0000 |
| ***Slc14a1*** | solute carrier family 14 (urea transporter), member 1 | 0.19 | –2.39 | 0.01236 | 1.0000 |
| ***Slc30a10*** | solute carrier family 30, member 10 | 0.17 | –2.52 | 0.02308 | 1.0000 |
| ***Ctse*** | cathepsin E | 0.06 | -4.03 | 0.00489 | 1.0000 |

**GD16.5 HEART** ***P* = 0.6724**

| Gene symbol | Official gene name | Fold-Change | $\log_2$ Fold-Change | *P*val | $P_{adj}$ |
|---|---|---|---|---|---|
| ***Zfpm1*** | zinc-finger protein, multitype 1 | 2.80 | +1.49 | 0.03744 | 1.0000 |
| ***Fam46c*** | family with sequence similarity 46, member C | 0.45 | –1.16 | 0.02237 | 1.0000 |

**GD16.5 CEREBELLUM** *P* = 0.3652

| Gene symbol | Official gene name | Fold-Change | $\log_2$ Fold-Change | *P*val | $P_{adj}$ |
|---|---|---|---|---|---|
| ***Vamp5*** | vesicle-associated membrane protein 5 | 0.10 | –3.37 | 0.01757 | 1.0000 |

[a] This file contains the Fisher's exact test *P*-values in each tissue, testing for enrichment of GATA1-downstream targets in differentially-expressed genes.

[b] Genes in ***bolded red font*** denote all hematopoiesis-related genes and genes in other blood cell types and functions. Genes in ***bolded blue font*** denote members of the solute carrier (*Slc*) superfamily.

**TABLE S6.** Known HIF-downstream targets genes found in the present study — comparing *Slc39a8(neo/neo)* with *Slc39a8(+/+)* wild-type. $P$-value of <0.05 and absolute fold-change >2 were used as the cut-off values.

**GD13.5 YOLK SAC** ***P* = 4.206e–15**[a]

| Gene symbol[b] | Official gene name | Fold-Change | $\log_2$ Fold-Change | $P$val | $P_{adj}$ |
|---|---|---|---|---|---|
| ***Igfbp1*** | insulin-like growth factor binding protein 1 | 7.48 | +2.90 | 2.08E-14 | 4.08E-10 |
| ***Egln3*** | EGL nine homolog 3 (*C. elegans*) | 4.22 | 2.08 | 4.61E-09 | 1.51E-05 |
| ***Krt19*** | keratin 19 | 2.87 | 1.52 | 0.000943 | 0.600143 |
| ***Igfbp3*** | insulin-like growth factor binding protein 3 | 2.67 | 1.41 | 0.00298 | 1.00000 |
| ***Slc2a1*** | solute carrier family 2 (facilitated glucose transporter), member 1 | 2.55 | +1.35 | 0.000473 | 0.403399 |
| ***Bhlhe41*** | basic helix-loop-helix family, member e41 | 2.37 | 1.25 | 0.010568 | 1.00000 |
| ***Aldoa*** | aldolase A, fructose-bisphosphate | 2.35 | 1.24 | 0.031794 | 1.00000 |
| ***Hk1*** | hexokinase 1 | 2.25 | 1.17 | 0.024595 | 1.00000 |
| ***Tgfb3*** | transforming growth factor, β3 | 2.22 | 1.15 | 0.008699 | 1.00000 |
| ***Bhlhe40*** | basic helix-loop-helix family, member e40 | 2.21 | 1.14 | 0.006853 | 1.00000 |
| ***Gm5506*** | predicted gene 5506 | 2.17 | 1.12 | 0.024416 | 1.00000 |
| ***Pdgfa*** | platelet-derived growth factor, α | 2.07 | 1.05 | 0.007183 | 1.00000 |
| ***Pkm*** | pyruvate kinase, muscle | 2.06 | 1.05 | 0.003951 | 1.00000 |
| ***Cited2*** | Cbp/p300-interacting transactivator, with Glu/Asp-rich COOH-terminal domain, 2 | 2.06 | 1.04 | 0.000622 | 0.488022 |
| ***Trf*** | transferrin | 2.05 | 1.04 | 0.013549 | 1.00000 |

**GD13.5 PLACENTA** ***P* = 1.0000**

| Gene symbol | Official gene name | Fold-Change | $\log_2$ Fold-Change | $P$val | $P_{adj}$ |
|---|---|---|---|---|---|
|  | NO SIGNIFICANT TARGET GENES FOUND |  |  |  |  |

**GD16.5 LIVER** ***P* = 1.0000**

| Gene symbol | Official gene name | Fold-Change | $\log_2$ Fold-Change | $P$val | $P_{adj}$ |
|---|---|---|---|---|---|
|  | NO SIGNIFICANT TARGET GENES FOUND |  |  |  |  |

**GD16.5 KIDNEY** ***P* = 0.62707**

| Gene symbol | Official gene name | Fold-Change | $\log_2$ Fold-Change | $P$val | $P_{adj}$ |
|---|---|---|---|---|---|
| ***Met*** | met proto-oncogene | 2.30 | +1.20 | 0.022918 | 1 |

**GD16.5 LUNG** ***P* = 0.02360**

| Gene symbol | Official gene name | Fold-Change | $\log_2$ Fold-Change | $P$val | $P_{adj}$ |
|---|---|---|---|---|---|

| | | | | | |
|---|---|---|---|---|---|
| ***Abcb1a*** | ATP-binding cassette, sub-family B (MDR/TAP), member 1A | 2.24 | +1.16 | 0.018031 | 1.00000 |
| ***Cyp2s1*** | **cytochrome P450, family 2, subfamily s, polypeptide 1** | 0.46 | –1.11 | 0.026306 | 1.00000 |
| ***Trf*** | transferrin | 0.29 | –1.78 | 0.001129 | 0.831377 |
| | | | | | |
| **GD16.5 HEART *P* = 1.0000** | | | | | |
| **Gene symbol** | **Official gene name** | **Fold-Change** | **log$_2$ Fold-Change** | **$P$val** | **$P_{adj}$** |
| | NO SIGNIFICANT TARGET GENES FOUND | | | | |
| | | | | | |
| **GD16.5 CEREBELLUM *P* = 1.0000** | | | | | |
| **Gene symbol** | **Official gene name** | **Fold-Change** | **log$_2$ Fold-Change** | **$P$val** | **$P_{adj}$** |
| | NO SIGNIFICANT TARGET GENES FOUND | | | | |
| | | | | | |

[a]This file also contains the Fisher's exact test *P*-values in each tissue, testing for enrichment of HIF-downstream targets in differentially-expressed genes. [b]Genes in ***bolded red font*** denote hematopoiesis-related genes and genes in all derived blood cell types and functions. Genes in ***bolded blue font*** denote members of the solute carrier (*Slc*) superfamily. Gene in ***bolded green font*** denotes a member of the cytochrome P450 (*Cyp*) gene family.

**TABLE S7.** Significant “top five” categories that surfaced from Ingenuity Pathway Analysis (IPA)

**Top Canonical Pathways**

No significant pathways found

**Top Upstream Regulators**

| Upstream regulator | Molecule type | Predicted activation state | Activation *z*-score[a] | *P*-value of overlap[b] | Target molecules in dataset (alphabetical order) |
|---|---|---|---|---|---|
| **HIF1A** | Transcription regulator | Activated | 3.699 | 5.27e–13 | ALDOA, APLN, ASNS, BHLHE40, CITED2, EGLN3, ENO1, FSCN1, HIF3A, HMGCL, IGFBP3, KRT19, MIF, PDGFA, PKM, SLC16A3, SLC2A1, SLC2A3, STC2, TGFB3 |
| **Deferoxamine** | Chemical; drug | Activated | 2.907 | 2.59e–10 | ALDOA, APLN, BHLHE40, CITED2, EGLN3, ENO1, IGFBP3, ISG20, PKM, SLC2A1, SLC2A3, SPRY4, SULF2 |
| **LINC01139** | Long intergenic non-protein-coding RNA | Activated | 2.236 | 1.91e–09 | ALDOA, BHLHE40, IGFBP3, PKM, SLC16A3 |
| **CD38** | Enzyme | Activated | 2.47 | 3.09e–09 | ALDOA, ASNS, CITED2, EGLN3, LGALS3, MYADM, PKM, SDC1, SLC16A3, SLC2A1, TUBB2B |
| **β-estradiol** | Chemical – endogenous mammalian | - - - | 1.761 | 2.32e–08 | ALDOA, ANO2, BHLHE40, CCDC170, CITED2, CYP1B1, ENO1, GCH1, GHRH, GPRC5A, HDAC11, HLA-A, HUNK, IGFBP1, IGFBP3, KRT19, LGALS3, MAGEA3 (includes others), MAPT, MGARP, PDGFA, PITPNM2, PKM, PPP1R9B, SDC1, SLC2A1, SLC2A3, STC1, STC2, STK32B, TF, TGFB3 |

**Top Diseases and Biological Functions**

| Categories | Diseases or functions annotation | FDR adjusted *P*-value | Predicted activation state | Activation *z*-score | Molecules (alphabetical order) | Number of molecules |
|---|---|---|---|---|---|---|
| **Molecular transport** | Transport of molecule | 3.05e–05 | Increased | 3.156 | ADRA2B, ANK1, ANO2, AP2A1, APLN, APOC3, ATP5D, BHLHE40, BMP6, CFH, CITED2, CLEC5A, DIO2, GABRA1, GHRH, GRM7, HK1, HLA-A, KCNA4, LSS, MAP1B, MAPT, MIF, MT2, PKM, RELN, RHAG, SLC16A3, SLC1A4, SLC2A1, SLC2A3, SLC38A1, SNAP91, STC1, TF, TGFB3, THOC6, VLDLR | 38 |
| **Organismal development** | Morphology of head | 3.19e–04 | - - - | - - - | ADH7, ADRA2B, CFH, CYP1B1, EGLN3, FSCN1, GHRH, IGFBP1, MAP1B, MAPT, MIF, MT2, PDGFA, PPP1R9B, RELN, SEMA7A, SLC1A4, SLC2A1, SP6, SPRY4, STAMBP, STC1, SULF2, TGFB3, THOC6, TLR7, VLDLR | 27 |
| **Carbohydrate metabolism** | Glycolysis of cells | 3.19e–04 | - - - | 1.407 | ALDOA, CITED2, ENO1, ESRRB, HK1, MIF, PKM, SLC16A3, SLC2A1 | 9 |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Nervous system – development and function** | Morphology of nervous system | 9.78e–04 | **- - -** | **- - -** | AADAT, ADH7, CFH, CITED2, COL25A1, EGLN3, FSCN1, GABRA1, IGFBP1, MAP1B, MAPT, MIF, MT2, PPP1R9B, RELN, SEMA7A, SLC1A4, SLC2A1, SNAP91, STAMBP, STC1, SULF2, TGFB3, TLR7, VLDLR | 25 |
| **Cardiovascular disease;**<br>**Cell death and survival;**<br>**Connective tissue disorders;**<br>**Hematological disease;**<br>**Hereditary disorder;**<br>**Organismal injury and abnormalities** | Familial hemolytic anemia | 1.29e–03 | **- - -** | **- - -** | ALDOA, ANK1, CFH, HK1, RHAG | 5 |

[a] The “activation z-score” is used to infer likely activation-states of upstream regulators — based on comparison with a model that assigns random regulation directions.

[b] The *P*-value of overlap calls likely upstream-regulators, based on significant overlap between dataset genes, and known targets that are controlled by a transcription regulator.

**Figure S1. Heat map showing $\log_2$ fold-changes of each gene in each tissue.** With FDR <0.1 in all tissues, 29 genes were identified. Lung and kidney showed remarkably similar expression changes in these genes (correlation coefficient $R^2 = 0.93$).

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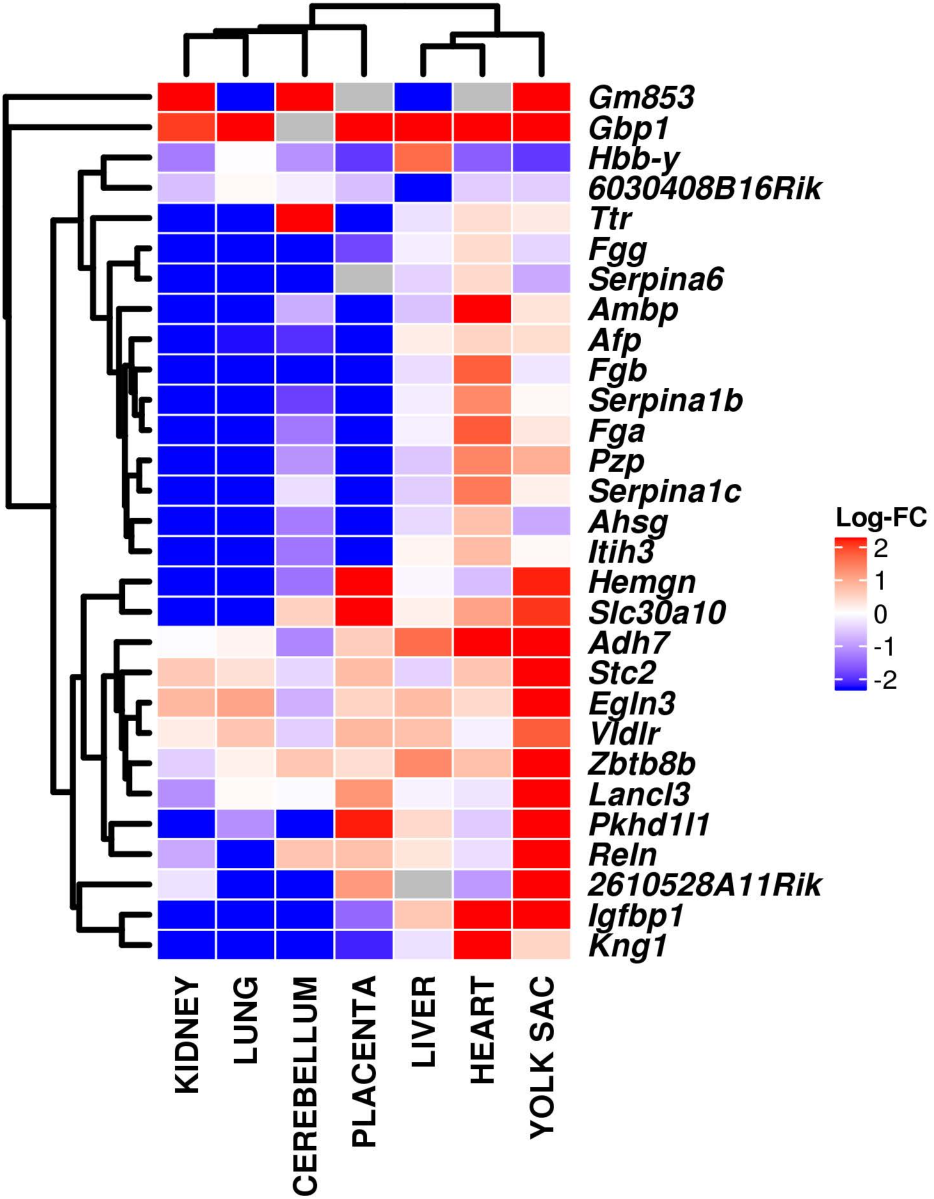
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