### Top 10 Genes Ranked by Potency of Perturbation (Sorted by BMD Median)

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| **Gene Symbol** | Entrez Gene IDs | Probe IDs | BMD1Std (BMDL1std-BMDU1std) in mg/kg | Maximum Fold Change | Direction of Expression Change |
| **Sds** | 25044 | 1369864\_a\_at | <22.0 (NR) | 2.6 | DOWN |
| **G6pc** | 25634 | 1370725\_a\_at,1386944\_a\_at | <22.0 (NR) | 3.4 | DOWN |
| **Cidea** | 291541 | 1389179\_at | <22.0 (NR) | 3.0 | UP |
| **C6** | 24237 | 1384580\_at | <22.0 (NR) | 2.5 | DOWN |
| **Ugt2b1** | 286954 | 1370698\_at | <22.0 (NR) | 2.5 | UP |
| **Cyp3a23/3a1** | 25642 | 1387118\_at | <22.0 (NR) | 2.6 | UP |
| **Cryl1** | 290277 | 1376051\_at | <22.0 (NR) | 3.5 | UP |
| **Abcc3** | 140668 | 1369698\_at | <22.0 (NR) | 10.7 | UP |
| **Akr7a3** | 26760 | 1368121\_at | <22.0 (NR) | 3.8 | UP |
| **Slc6a6** | 29464 | 1368778\_at,1374531\_at | <22.0 (NR) | 14.5 | DOWN |

Descriptions of orthologous human genes are shown due to the increased detail that is available in public resources such as UniprotKB (https://www.uniprot.org/uniprot/) and Entrez Gene (https://www.ncbi.nlm.nih.gov/gene/). Human UniprotKB was used as primary resource due to the greater breadth of annotation and depth of functional detail that is provided. Rat UniprotKB was used as the second resource if the primary source did not provide a detailed description of function. Human Entrez gene summary was used as third resource. Rat Entrez gene summary was used as the fourth resource.

<22.0 = A best-fit model as identified calculated a BMD that was less than 1/3 of the lowest tested dose in this study.

NR = The BMDL-BMDU range is not reportable because the BMD median is below the lower limit of extrapolation (less than 1/3 of the lowest tested dose in this study).

**Gene definition version:** https://cebs.niehs.nih.gov/cebs/study/002-00600-0002-000-0 V05282021

**Sds:** *Human Entrez Gene Summary (Human SDS):* This gene encodes one of three enzymes that are involved in metabolizing serine and glycine. L-serine dehydratase converts L-serine to pyruvate and ammonia and requires pyridoxal phosphate as a cofactor. The encoded protein can also metabolize threonine to NH4+ and 2-ketobutyrate. The encoded protein is found predominantly in the liver. [provided by RefSeq, Jul 2008]

**G6pc:** *Human Uniprot function (Human G6PC1):* Hydrolyzes glucose-6-phosphate to glucose in the endoplasmic reticulum. Forms with the glucose-6-phosphate transporter (SLC37A4/G6PT) the complex responsible for glucose production through glycogenolysis and gluconeogenesis. Hence, it is the key enzyme in homeostatic regulation of blood glucose levels.

**Cidea:** *Human Uniprot function (Human CIDEA):* Acts as a CEBPB coactivator in mammary epithelial cells to control the expression of a subset of CEBPB downstream target genes, including ID2, IGF1, PRLR, SOCS1, SOCS3, XDH, but not casein. By interacting with CEBPB, strengthens the association of CEBPB with the XDH promoter, increases histone acetylation and dissociates HDAC1 from the promoter (By similarity). Binds to lipid droplets and regulates their enlargement, thereby restricting lipolysis and favoring storage. At focal contact sites between lipid droplets, promotes directional net neutral lipid transfer from the smaller to larger lipid droplets. The transfer direction may be driven by the internal pressure difference between the contacting lipid droplet pair and occurs at a lower rate than that promoted by CIDEC. When overexpressed, induces apoptosis. The physiological significance of its role in apoptosis is unclear. {ECO0000250, ECO0000269|PubMed19843876}.

**C6:** *Human Uniprot function (Human C6):* Constituent of the membrane attack complex (MAC) that plays a key role in the innate and adaptive immune response by forming pores in the plasma membrane of target cells.

**Ugt2b1:** *Human Uniprot function (Human UGT2B17):* UDP-glucuronosyltransferase (UGT) that catalyzes phase II biotransformation reactions in which lipophilic substrates are conjugated with glucuronic acid to increase the metabolite's water solubility, thereby facilitating excretion into either the urine or bile (PubMed8798464, PubMed16595710, PubMed18719240, PubMed19022937, PubMed23288867). Catalyzes the glucuronidation of endogenous steroid hormones such as androgens (epitestosterone, androsterone) and estrogens (estradiol, epiestradiol) (PubMed8798464, PubMed16595710, PubMed18719240, PubMed19022937, PubMed23288867). {ECO0000269|PubMed16595710, ECO0000269|PubMed18719240, ECO0000269|PubMed19022937, ECO0000269|PubMed23288867, ECO0000269|PubMed8798464}.

**Cyp3a23/3a1:** *Human Uniprot function (Human CYP3A4):* A cytochrome P450 monooxygenase involved in the metabolism of sterols, steroid hormones, retinoids and fatty acids (PubMed:10681376, PubMed:11093772, PubMed:11555828, PubMed:14559847, PubMed:12865317, PubMed:15373842, PubMed:15764715, PubMed:20702771, PubMed:19965576, PubMed:21490593, PubMed:21576599). Mechanistically, uses molecular oxygen inserting one oxygen atom into a substrate, and reducing the second into a water molecule, with two electrons provided by NADPH via cytochrome P450 reductase (NADPH--hemoprotein reductase). Catalyzes the hydroxylation of carbon-hydrogen bonds (PubMed:2732228, PubMed:14559847, PubMed:12865317, PubMed:15373842, PubMed:15764715, PubMed:21576599, PubMed:21490593). Exhibits high catalytic activity for the formation of hydroxyestrogens from estrone (E1) and 17beta-estradiol (E2), namely 2-hydroxy E1 and E2, as well as D-ring hydroxylated E1 and E2 at the C-16 position (PubMed:11555828, PubMed:14559847, PubMed:12865317). Plays a role in the metabolism of androgens, particularly in oxidative deactivation of testosterone (PubMed:2732228, PubMed:15373842, PubMed:15764715, PubMed:22773874). Metabolizes testosterone to less biologically active 2beta- and 6beta-hydroxytestosterones (PubMed:2732228, PubMed:15373842, PubMed:15764715). Contributes to the formation of hydroxycholesterols (oxysterols), particularly A-ring hydroxylated cholesterol at the C-4beta position, and side chain hydroxylated cholesterol at the C-25 position, likely contributing to cholesterol degradation and bile acid biosynthesis (PubMed:21576599). Catalyzes bisallylic hydroxylation of polyunsaturated fatty acids (PUFA) (PubMed:9435160). Catalyzes the epoxidation of double bonds of PUFA with a preference for the last double bond (PubMed:19965576). Metabolizes endocannabinoid arachidonoylethanolamide (anandamide) to 8,9-, 11,12-, and 14,15-epoxyeicosatrienoic acid ethanolamides (EpETrE-EAs), potentially modulating endocannabinoid system signaling (PubMed:20702771). Plays a role in the metabolism of retinoids. Displays high catalytic activity for oxidation of all-trans-retinol to all-trans-retinal, a rate-limiting step for the biosynthesis of all-trans-retinoic acid (atRA) (PubMed:10681376). Further metabolizes atRA toward 4-hydroxyretinoate and may play a role in hepatic atRA clearance (PubMed:11093772). Responsible for oxidative metabolism of xenobiotics. Acts as a 2-exo-monooxygenase for plant lipid 1,8-cineole (eucalyptol) (PubMed:11159812). Metabolizes the majority of the administered drugs. Catalyzes sulfoxidation of the anthelmintics albendazole and fenbendazole (PubMed:10759686). Hydroxylates antimalarial drug quinine (PubMed:8968357). Acts as a 1,4-cineole 2-exo-monooxygenase (PubMed:11695850). {ECO:0000269|PubMed:10681376, ECO:0000269|PubMed:10759686, ECO:0000269|PubMed:11093772, ECO:0000269|PubMed:11159812, ECO:0000269|PubMed:11555828, ECO:0000269|PubMed:11695850, ECO:0000269|PubMed:12865317, ECO:0000269|PubMed:14559847, ECO:0000269|PubMed:15373842, ECO:0000269|PubMed:15764715, ECO:0000269|PubMed:19965576, ECO:0000269|PubMed:20702771, ECO:0000269|PubMed:21490593, ECO:0000269|PubMed:21576599, ECO:0000269|PubMed:22773874, ECO:0000269|PubMed:2732228, ECO:0000269|PubMed:8968357, ECO:0000269|PubMed:9435160}.

**Cryl1:** *Human Entrez Gene Summary (Human CRYL1):* The uronate cycle functions as an alternative glucose metabolic pathway, accounting for about 5% of daily glucose catabolism. The product of this gene catalyzes the dehydrogenation of L-gulonate into dehydro-L-gulonate in the uronate cycle. The enzyme requires NAD(H) as a coenzyme, and is inhibited by inorganic phosphate. A similar gene in the rabbit is thought to serve a structural role in the lens of the eye. [provided by RefSeq, Jul 2008]

**Abcc3:** *Human Uniprot function (Human ABCC3):* May act as an inducible transporter in the biliary and intestinal excretion of organic anions. Acts as an alternative route for the export of bile acids and glucuronides from cholestatic hepatocytes (By similarity). {ECO0000250}.

**Akr7a3:** *Human Uniprot function (Human AKR7A3):* Can reduce the dialdehyde protein-binding form of aflatoxin B1 (AFB1) to the non-binding AFB1 dialcohol. May be involved in protection of liver against the toxic and carcinogenic effects of AFB1, a potent hepatocarcinogen. {ECO0000269|PubMed18416522}.

**Slc6a6:** *Human Uniprot function (Human SLC6A6):* Sodium-dependent taurine and beta-alanine transporter. Chloride ions are necessary for optimal uptake. {ECO0000269|PubMed31345061, ECO0000269|PubMed31903486, ECO0000269|PubMed8382624}.