### Male Liver Top 10 GO Biological Process Gene Sets Ranked by Potency of Perturbation (Sorted by BMD Median)

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| --- | --- | --- | --- | --- | --- | --- | --- |
| **Category Name** | Input Genes/Platform Genes in Gene Set | % Gene Set Coverage | Active Genes | BMD1std Median of Gene Set Transcripts (mg/kg) | Median BMDL1Std-BMDU1Std (mg/kg) | Genes with Changed Direction Up | Genes with Changed Direction Down |
| **GO:0045638**negative regulation of myeloid cell differentiation | 3/31 | 10% | zfp36; pik3r1; nfkbia | 0.520 | 0.160-2.885 | 0 | 3 |
| **GO:0042035**regulation of cytokine biosynthetic process | 3/43 | 7% | zfp36; hspb1; egr1 | 0.750 | 0.186-4.702 | 0 | 3 |
| **GO:0007611**learning or memory | 4/79 | 5% | jun; hmgcr; fos; egr1 | 1.190 | 0.425-6.165 | 0 | 4 |
| **GO:0030178**negative regulation of Wnt signaling pathway | 3/31 | 10% | tsku; foxo3; egr1 | 1.384 | 0.541-4.702 | 0 | 3 |
| **GO:0007612**learning | 3/43 | 7% | jun; hmgcr; fos | 1.631 | 0.663-7.629 | 0 | 3 |
| **GO:0006695**cholesterol biosynthetic process | 3/21 | 14% | tm7sf2; hsd17b7; hmgcr | 1.631 | 0.663-7.629 | 0 | 3 |
| **GO:0043409**negative regulation of MAPK cascade | 3/51 | 6% | sirt3; hmgcr; dusp6 | 2.380 | 0.663-8.829 | 1 | 2 |
| **GO:0014072**response to isoquinoline alkaloid | 3/19 | 16% | fga; egr1; abcg2 | 5.217 | 2.734-11.386 | 1 | 2 |
| **GO:0008203**cholesterol metabolic process | 5/49 | 10% | tm7sf2; hsd17b7; hmgcr; fgl1; cyp7a1 | 5.721 | 0.985-22.363 | 0 | 5 |
| **GO:0051412**response to corticosterone | 3/27 | 11% | foxo3; fos; cdkn1a | 6.250 | 2.440-19.061 | 0 | 3 |

Official gene symbols from the Rat Genome Database are shown in the “Active Genes” column. Definitions of Gene Ontology terms were provided by the Gene Ontology Resource (http://geneontology.org/).

**GO process description version:** https://cebs.niehs.nih.gov/cebs/study/002-00600-0002-000-0 V04132020

**GO:0045638 negative regulation of myeloid cell differentiation:** Any process that stops, prevents, or reduces the frequency, rate or extent of myeloid cell differentiation.

**GO:0042035 regulation of cytokine biosynthetic process:** Any process that modulates the frequency, rate or extent of the chemical reactions and pathways resulting in the formation of cytokines.

**GO:0007611 learning or memory:** The acquisition and processing of information and/or the storage and retrieval of this information over time.

**GO:0030178 negative regulation of Wnt signaling pathway:** Any process that stops, prevents, or reduces the frequency, rate or extent of the Wnt signaling pathway.

**GO:0007612 learning:** Any process in an organism in which a relatively long-lasting adaptive behavioral change occurs as the result of experience.

**GO:0006695 cholesterol biosynthetic process:** The chemical reactions and pathways resulting in the formation of cholesterol, cholest-5-en-3 beta-ol, the principal sterol of vertebrates and the precursor of many steroids, including bile acids and steroid hormones.

**GO:0043409 negative regulation of MAPK cascade:** Any process that stops, prevents, or reduces the frequency, rate or extent of signal transduction mediated by the MAPKKK cascade.

**GO:0014072 response to isoquinoline alkaloid:** Any process that results in a change in state or activity of a cell or an organism (in terms of movement, secretion, enzyme production, gene expression, etc.) as a result of an isoquinoline alkaloid stimulus. An isoquinoline alkaloid is any member of a group of compounds with the heterocyclic ring structure of benzo(c)pyridine which is a structure characteristic of the group of opium alkaloids.

**GO:0008203 cholesterol metabolic process:** The chemical reactions and pathways involving cholesterol, cholest-5-en-3 beta-ol, the principal sterol of vertebrates and the precursor of many steroids, including bile acids and steroid hormones. It is a component of the plasma membrane lipid bilayer and of plasma lipoproteins and can be found in all animal tissues.

**GO:0051412 response to corticosterone:** Any process that results in a change in state or activity of a cell or an organism (in terms of movement, secretion, enzyme production, gene expression, etc.) as a result of a corticosterone stimulus. Corticosterone is a 21 carbon steroid hormone of the corticosteroid type, produced in the cortex of the adrenal glands. In many species, corticosterone is the principal glucocorticoid, involved in regulation of fuel metabolism, immune reactions, and stress responses.

### Female Liver Top 10 GO Biological Process Gene Sets Ranked by Potency of Perturbation (Sorted by BMD Median)

| **Category Name** | Input Genes/Platform Genes in Gene Set | % Gene Set Coverage | Active Genes | BMD1std Median of Gene Set Transcripts (mg/kg) | Median BMDL1Std-BMDU1Std (mg/kg) | Genes with Changed Direction Up | Genes with Changed Direction Down |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **GO:0018958**phenol-containing compound metabolic process | 4/31 | 13% | sult1b1; srd5a1; dao; cyp2e1 | 11.677 | 5.931-25.645 | 3 | 1 |
| **GO:0046395**carboxylic acid catabolic process | 13/87 | 15% | gcdh; ehhadh; eci2; eci1; ech1; decr1; dao; crat; cpt2; acox1; acot4; acot2; acaa2 | 12.316 | 8.410-24.399 | 12 | 1 |
| **GO:0044242**cellular lipid catabolic process | 13/64 | 20% | gcdh; ehhadh; eci2; eci1; ech1; decr1; crat; cpt2; apoa2; angptl3; acox1; acot2; acaa2 | 13.636 | 10.423-28.083 | 12 | 1 |
| **GO:0009062**fatty acid catabolic process | 11/42 | 26% | gcdh; ehhadh; eci2; eci1; ech1; decr1; crat; cpt2; acox1; acot2; acaa2 | 13.636 | 10.423-28.083 | 10 | 1 |
| **GO:0044282**small molecule catabolic process | 15/120 | 13% | sult1e1; sult1b1; gcdh; ehhadh; eci2; eci1; ech1; decr1; dao; crat; cpt2; acox1; acot4; acot2; acaa2 | 13.636 | 8.410-28.083 | 14 | 1 |
| **GO:0006635**fatty acid beta-oxidation | 10/33 | 30% | gcdh; ehhadh; eci2; eci1; ech1; decr1; crat; cpt2; acox1; acaa2 | 13.834 | 9.416-29.682 | 9 | 1 |
| **GO:0030258**lipid modification | 14/70 | 20% | pparg; gcdh; ephx2; ehhadh; eci2; eci1; ech1; decr1; cyp4a1; cyp2e1; crat; cpt2; acox1; acaa2 | 13.834 | 9.416-29.034 | 13 | 1 |
| **GO:0017001**antibiotic catabolic process | 3/22 | 14% | ugt2b1; sult1e1; sult1b1 | 15.463 | 7.694-35.088 | 3 | 0 |
| **GO:0006805**xenobiotic metabolic process | 9/62 | 15% | ugt2b1; sult1b1; cyp2j4; cyp2e1; cyp2d3; cyp2c24; cyp2c13; cyp2c11; cyp2a1 | 15.463 | 8.238-35.088 | 9 | 0 |
| **GO:1901361**organic cyclic compound catabolic process | 6/89 | 7% | ugt2b1; sult1e1; srd5a1; ephx2; dao; akr7a3 | 15.682 | 9.448-32.741 | 5 | 1 |

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**GO process description version:** https://cebs.niehs.nih.gov/cebs/study/002-00600-0002-000-0 V04132020

**GO:0018958 phenol-containing compound metabolic process:** The chemical reactions and pathways involving a phenol, any compound containing one or more hydroxyl groups directly attached to an aromatic carbon ring.

**GO:0046395 carboxylic acid catabolic process:** The chemical reactions and pathways resulting in the breakdown of carboxylic acids, any organic acid containing one or more carboxyl (-COOH) groups.

**GO:0044242 cellular lipid catabolic process:** The chemical reactions and pathways resulting in the breakdown of lipids, as carried out by individual cells.

**GO:0009062 fatty acid catabolic process:** The chemical reactions and pathways resulting in the breakdown of a fatty acid, any of the aliphatic monocarboxylic acids that can be liberated by hydrolysis from naturally occurring fats and oils. Fatty acids are predominantly straight-chain acids of 4 to 24 carbon atoms, which may be saturated or unsaturated; branched fatty acids and hydroxy fatty acids also occur, and very long chain acids of over 30 carbons are found in waxes.

**GO:0044282 small molecule catabolic process:** The chemical reactions and pathways resulting in the breakdown of small molecules, any low molecular weight, monomeric, non-encoded molecule.

**GO:0006635 fatty acid beta-oxidation:** A fatty acid oxidation process that results in the complete oxidation of a long-chain fatty acid. Fatty acid beta-oxidation begins with the addition of coenzyme A to a fatty acid, and occurs by successive cycles of reactions during each of which the fatty acid is shortened by a two-carbon fragment removed as acetyl coenzyme A; the cycle continues until only two or three carbons remain (as acetyl-CoA or propionyl-CoA respectively).

**GO:0030258 lipid modification:** The covalent alteration of one or more fatty acids in a lipid, resulting in a change in the properties of the lipid.

**GO:0017001 antibiotic catabolic process:** The chemical reactions and pathways resulting in the breakdown of antibiotic, a substance produced by or derived from certain fungi, bacteria, and other organisms, that can destroy or inhibit the growth of other microorganisms.

**GO:0006805 xenobiotic metabolic process:** The chemical reactions and pathways involving a xenobiotic compound, a compound foreign to living organisms. Used of chemical compounds, e.g. a xenobiotic chemical, such as a pesticide.

**GO:1901361 organic cyclic compound catabolic process:** The chemical reactions and pathways resulting in the breakdown of organic cyclic compound.