### Male Kidney 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:0048143**  astrocyte activation | 3/11 | 27% | il1b; grn; c1qa | <0.050 | NR | 1 | 2 |
| **GO:0002832**  negative regulation of response to biotic stimulus | 3/27 | 11% | parp14; grn; tkfc | <0.050 | NR | 0 | 3 |
| **GO:0006084**  acetyl-CoA metabolic process | 3/16 | 19% | hmgcs2; acot12; acaa2 | 1.346 | 0.541-4.058 | 2 | 1 |
| **GO:0006637**  acyl-CoA metabolic process | 6/31 | 19% | hmgcs2; acot4; acot2; acot12; acot1; acaa2 | 1.928 | 1.305-4.031 | 5 | 1 |
| **GO:0010883**  regulation of lipid storage | 3/22 | 14% | srebf1; nfkbia; c3 | 2.189 | 0.888-5.495 | 2 | 1 |
| **GO:0030522**  intracellular receptor signaling pathway | 3/42 | 7% | srebf1; nr1d2; nfkbia | 2.189 | 0.888-5.495 | 2 | 1 |
| **GO:0006721**  terpenoid metabolic process | 3/34 | 9% | pecr; hmgcs2; cyp2e1 | 2.994 | 0.682-13.980 | 2 | 1 |
| **GO:0002698**  negative regulation of immune effector process | 4/43 | 9% | lgals3; grn; enpp3; tkfc | 3.710 | 1.436-9.709 | 1 | 3 |
| **GO:0009062**  fatty acid catabolic process | 12/42 | 29% | hadh; etfdh; ehhadh; eci2; ech1; decr1; cpt2; adipoq; acox1; acot2; acadm; acaa2 | 3.895 | 1.678-6.474 | 12 | 0 |
| **GO:0000038**  very long-chain fatty acid metabolic process | 4/12 | 33% | acox1; acot4; acot2; acot1 | 4.235 | 2.759-6.872 | 4 | 0 |

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/).

<0.050 = 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).

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

**GO:0048143 astrocyte activation:** A change in morphology and behavior of an astrocyte resulting from exposure to a cytokine, chemokine, cellular ligand, or soluble factor.

**GO:0002832 negative regulation of response to biotic stimulus:** Any process that stops, prevents, or reduces the frequency, rate, or extent of a response to biotic stimulus.

**GO:0006084 acetyl-CoA metabolic process:** The chemical reactions and pathways involving acetyl-CoA, a derivative of coenzyme A in which the sulfhydryl group is acetylated; it is a metabolite derived from several pathways (e.g. glycolysis, fatty acid oxidation, amino-acid catabolism) and is further metabolized by the tricarboxylic acid cycle. It is a key intermediate in lipid and terpenoid biosynthesis.

**GO:0006637 acyl-CoA metabolic process:** The chemical reactions and pathways involving acyl-CoA, any derivative of coenzyme A in which the sulfhydryl group is in thiolester linkage with an acyl group.

**GO:0010883 regulation of lipid storage:** Any process that modulates the rate, frequency or extent of lipid storage. Lipid storage is the accumulation and maintenance in cells or tissues of lipids, compounds soluble in organic solvents but insoluble or sparingly soluble in aqueous solvents. Lipid reserves can be accumulated during early developmental stages for mobilization and utilization at later stages of development.

**GO:0030522 intracellular receptor signaling pathway:** Any series of molecular signals initiated by a ligand binding to an receptor located within a cell.

**GO:0006721 terpenoid metabolic process:** The chemical reactions and pathways involving terpenoids, any member of a class of compounds characterized by an isoprenoid chemical structure and including derivatives with various functional groups.

**GO:0002698 negative regulation of immune effector process:** Any process that stops, prevents, or reduces the frequency, rate, or extent of an immune effector process.

**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:0000038 very long-chain fatty acid metabolic process:** The chemical reactions and pathways involving a fatty acid which has a chain length greater than C22.

### Female Kidney 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:0006635**  fatty acid beta-oxidation | 8/33 | 24% | ppard; ehhadh; eci2; eci1; ech1; acadm; acadl; acaa2 | 21.079 | 13.312-34.031 | 7 | 1 |
| **GO:0019395**  fatty acid oxidation | 10/43 | 23% | ppard; hao2; ehhadh; eci2; eci1; ech1; cd36; acadm; acadl; acaa2 | 27.058 | 13.877-61.247 | 8 | 2 |
| **GO:0009062**  fatty acid catabolic process | 12/42 | 29% | ppard; pck2; pck1; ehhadh; eci2; eci1; ech1; ces1d; acot2; acadm; acadl; acaa2 | 27.540 | 15.179-63.270 | 10 | 2 |
| **GO:0006637**  acyl-CoA metabolic process | 7/31 | 23% | hmgcs2; acss2; acot4; acot2; acot12; acot1; acaa2 | 38.393 | 23.116-70.139 | 5 | 2 |
| **GO:0000038**  very long-chain fatty acid metabolic process | 3/12 | 25% | acot4; acot2; acot1 | 38.393 | 23.116-70.139 | 3 | 0 |
| **GO:0033875**  ribonucleoside bisphosphate metabolic process | 8/41 | 20% | pank1; hmgcs2; acss2; acot4; acot2; acot12; acot1; acaa2 | 44.906 | 31.624-70.563 | 6 | 2 |
| **GO:0030258**  lipid modification | 13/70 | 19% | ppard; hao2; ephx2; ehhadh; eci2; eci1; ech1; cyp2e1; cyp1a1; cd36; acadm; acadl; acaa2 | 49.703 | 38.943-83.829 | 10 | 3 |
| **GO:0009409**  response to cold | 3/27 | 11% | cxcl10; acadm; acadl | 61.062 | 46.535-88.000 | 2 | 1 |
| **GO:0009150**  purine ribonucleotide metabolic process | 10/80 | 13% | pank1; pde4c; hmgcs2; aldoc; acss2; acot4; acot2; acot12; acot1; acaa2 | 67.924 | 50.324-104.308 | 7 | 3 |
| **GO:0006732**  coenzyme metabolic process | 12/67 | 18% | vnn1; rgn; pank1; mthfd2; hmgcs2; gclc; acss2; acot4; acot2; acot12; acot1; acaa2 | 67.924 | 50.324-104.308 | 8 | 4 |

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

**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:0019395 fatty acid oxidation:** The removal of one or more electrons from a fatty acid, with or without the concomitant removal of a proton or protons, by reaction with an electron-accepting substance, by addition of oxygen or by removal of hydrogen.

**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:0006637 acyl-CoA metabolic process:** The chemical reactions and pathways involving acyl-CoA, any derivative of coenzyme A in which the sulfhydryl group is in thiolester linkage with an acyl group.

**GO:0000038 very long-chain fatty acid metabolic process:** The chemical reactions and pathways involving a fatty acid which has a chain length greater than C22.

**GO:0033875 ribonucleoside bisphosphate metabolic process:** The chemical reactions and pathways involving a ribonucleoside bisphosphate, a compound consisting of a nucleobase linked to a ribose sugar esterified with one phosphate group attached to each of two different hydroxyl groups on the sugar.

**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:0009409 response to cold:** 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 cold stimulus, a temperature stimulus below the optimal temperature for that organism.

**GO:0009150 purine ribonucleotide metabolic process:** The chemical reactions and pathways involving a purine ribonucleotide, a compound consisting of ribonucleoside (a purine base linked to a ribose sugar) esterified with a phosphate group at either the 3' or 5'-hydroxyl group of the sugar.

**GO:0006732 coenzyme metabolic process:** The chemical reactions and pathways involving coenzymes, any of various nonprotein organic cofactors that are required, in addition to an enzyme and a substrate, for an enzymatic reaction to proceed.