Top 10 Gene Ontology Biological Process Gene Sets Ranked by Potency of Perturbation, Sorted by Benchmark Dose Mediana

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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:0043153** entrainment of circadian clock by photoperiod | 3/27 | 11 | *Per3*; *Cry2*; *Bhlhe40* | <21.7b | NR | 3 | 0 |
| **GO:0097067** cellular response to thyroid hormone stimulus | 3/24 | 13 | *Gclc*; *Klf9*; *Gclm* | <21.7 | NR | 3 | 0 |
| **GO:0015804** neutral amino acid transport | 3/35 | 9 | *Slc3a2*; *Nfe2l1*; *Slc6a6* | 23.8 | 15.2–73.8 | 2 | 1 |
| **GO:0032966** negative regulation of collagen biosynthetic process | 3/17 | 18 | *Cyp2j4*; *Errfi1*; *Pparg* | 29.4 | 18.8–53.5 | 3 | 0 |
| **GO:0009404** toxin metabolic process | 4/18 | 22 | *Gsta3*; *Cyp1a1*; *Akr7a3*; *Ddc* | 29.7 | 14.9–66.7 | 4 | 0 |
| **GO:0120163** negative regulation of cold-induced thermogenesis | 3/42 | 7 | *Tle3*; *Id1*; *Aldh1a1* | 33.1 | 22.1–57.0 | 2 | 1 |
| **GO:0006825** copper ion transport | 3/15 | 20 | *Fkbp4*; *Steap4*; *Mmgt1* | 33.7 | 15.1–95.6 | 1 | 2 |
| **GO:0045599** negative regulation of fat cell differentiation | 3/51 | 6 | *Zadh2*; *Id4*; *Trib3* | 36.9 | 19.3–87.8 | 2 | 1 |
| **GO:0006801** superoxide metabolic process | 3/29 | 10 | *Cbs*; *Cybb*; *Apoa4* | 37.8 | 23.8–70.0 | 0 | 3 |
| **GO:0033194** response to hydroperoxide | 3/20 | 15 | *Dapk1*; *Chuk*; *Apoa4* | 37.8 | 23.8–70.0 | 1 | 2 |

Benchmark response set at 1 standard deviation from the mean.

BMD = benchmark dose; BMDL = benchmark dose lower confidence limit; BMDU = benchmark dose upper confidence limit; GO = Gene Ontology; NR = the BMDL–BMDU range is not reportable because the BMD median is below the lower limit of extrapolation (<1/3 the lowest nonzero dose tested).

aDefinitions of GO terms were adapted from the Gene Ontology Resource.[21](#_ENREF_21) Official gene symbols from the Rat Genome Database[22](#_ENREF_22) are shown in the “Active Genes” column.

b<21.7 = a best-fit model was identified and a BMD was estimated that was <1/3 the lowest nonzero dose tested.

**GO process description version:** <https://doi.org/10.22427/NTP-DATA-002-00600-0002-000-0>.

**GO:0043153 entrainment of circadian clock by photoperiod:** The synchronization of a circadian rhythm to photoperiod, the intermittent cycle of light (day) and dark (night).

**GO:0097067 cellular response to thyroid hormone stimulus:** A change in state or activity of a cell (in terms of movement, secretion, enzyme production, gene expression, etc.) as a result of a thyroid hormone stimulus.

**GO:0015804 neutral amino acid transport:** The directed movement of neutral amino acids—amino acids with no net charge—into, out of, or within a cell, or between cells, by means of some agent such as a transporter or pore.

**GO:0032966 negative regulation of collagen biosynthetic process:** Any process that stops, prevents, or reduces the frequency, rate, or extent of the chemical reactions and pathways resulting in the formation of collagen, any of a group of fibrous proteins of very high tensile strength that form the main component of connective tissue in animals.

**GO:0009404 toxin metabolic process:** The chemical reactions and pathways involving a toxin, a poisonous compound (typically a protein) that is produced by cells or organisms and that can cause disease when introduced into the body or tissues of an organism.

**GO:0120163 negative regulation of cold-induced thermogenesis:** Any process that stops, prevents, or reduces the rate of cold-induced thermogenesis.

**GO:0006825 copper ion transport:** The directed movement of copper (Cu) ions into, out of, or within a cell, or between cells, by means of some agent such as a transporter or pore.

**GO:0045599 negative regulation of fat cell differentiation:** Any process that stops, prevents, or reduces the frequency, rate, or extent of adipocyte differentiation.

**GO:0006801 superoxide metabolic process:** The chemical reactions and pathways involving superoxide, the superoxide anion O2- (superoxide free radical), or any compound containing this species.

**GO:0033194 response to hydroperoxide:** 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 hydroperoxide stimulus. Hydroperoxides are monosubstitution products of hydrogen peroxide, HOOH.