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:0006693** prostaglandin metabolic process | 3/36 | 8 | *Gstm1*; *Hpgd*; *Akr1c14* | <20.3b | NR | 2 | 1 |
| **GO:0042178** xenobiotic catabolic process | 5/18 | 28 | *Gstm1*; *Gstm4*; *Ugt2b1*; *Cyp1a1*; *Abcc2* | <20.3 | NR | 5 | 0 |
| **GO:0042759** long-chain fatty acid biosynthetic process | 3/18 | 17 | *Elovl6*; *Gstm1*; *Gstm4* | 23.8 | 15.2–58.5 | 3 | 0 |
| **GO:0006749** glutathione metabolic process | 7/55 | 13 | *Gstm1*; *Gstm4*; *Gstt3*; *Gclc*; *Ggt1*; *Cth*; *Hbb* | 29.4 | 15.2–95.4 | 5 | 2 |
| **GO:0043470** regulation of carbohydrate catabolic process | 3/60 | 5 | *App*; *Avpr1a*; *Ddit4* | 29.7 | 20.1–65.4 | 2 | 1 |
| **GO:0010799** regulation of peptidyl-threonine phosphorylation | 3/43 | 7 | *App*; *Ddit4*; *S1pr2* | 33.1 | 20.1–65.4 | 2 | 1 |
| **GO:0010996** response to auditory stimulus | 3/31 | 10 | *Casp3*; *App*; *Gclc* | 33.7 | 20.1–95.4 | 3 | 0 |
| **GO:0009410** response to xenobiotic stimulus | 3/15 | 20 | *Nqo1*; *Gclc*; *Cyp1a1* | 36.9 | 23.5–105.1 | 3 | 0 |
| **GO:0071869** response to catecholamine | 3/42 | 7 | *Fcgr1a*; *App*; *Egr1* | 37.8 | 20.1–198.3 | 1 | 2 |
| **GO:0006090** pyruvate metabolic process | 4/53 | 8 | *Pdhx*; *Pck2*; *Ccbl1*; *Me1* | 37.8 | 14.8–99.6 | 4 | 0 |

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.

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<20.3 = 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:0006693 prostaglandin metabolic process:** The chemical reactions and pathways involving prostaglandins, any of a group of biologically active metabolites that contain a cyclopentane ring due to the formation of a bond between two carbons of a fatty acid. They have a wide range of biological activities.

**GO:0042178 xenobiotic catabolic process:** The chemical reactions and pathways resulting in the breakdown of a xenobiotic compound, a compound foreign to the organism exposed to it. It may be synthesized by another organism (like ampicillin) or it can be a synthetic chemical.

**GO:0042759 long-chain fatty acid biosynthetic process:** The chemical reactions and pathways resulting in the formation of long-chain fatty acids, any fatty acid with a chain length between C13 and C22.

**GO:0006749 glutathione metabolic process:** The chemical reactions and pathways involving glutathione, the tripeptide glutamylcysteinylglycine, which acts as a coenzyme for some enzymes and as an antioxidant in the protection of sulfhydryl groups in enzymes and other proteins; it has a specific role in the reduction of hydrogen peroxide (H2O2) and oxidized ascorbate, and it participates in the gamma-glutamyl cycle.

**GO:0043470 regulation of carbohydrate catabolic process:** Any process that modulates the frequency, rate, or extent of the chemical reactions and pathways resulting in the breakdown of carbohydrates.

**GO:0010799 regulation of peptidyl-threonine phosphorylation:** Any process that modulates the frequency, rate, or extent of peptidyl-threonine phosphorylation. Peptidyl-threonine phosphorylation is the phosphorylation of peptidyl-threonine to form peptidyl-O-phospho-L-threonine.

**GO:0010996 response to auditory stimulus:** 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 auditory stimulus.

**GO:0009410 response to xenobiotic stimulus:** 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 stimulus from a xenobiotic, a compound foreign to the organism exposed to it. It may be synthesized by another organism (like ampicillin), or it can be a synthetic chemical.

**GO:0071869 response to catecholamine:** 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 catecholamine stimulus. A catecholamine is any of a group of biogenic amines that includes 4-(2-aminoethyl)pyrocatechol [4-(2-aminoethyl)benzene-1,2-diol] and derivatives formed by substitution.

**GO:0006090 pyruvate metabolic process:** The chemical reactions and pathways involving pyruvate, 2-oxopropanoate.