### Male 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:0071364**cellular response to epidermal growth factor stimulus | 3/20 | 15% | zfp36; ncl; myc | 0.368 | 0.103-1.817 | 1 | 2 |
| **GO:0070849**response to epidermal growth factor | 4/26 | 15% | zfp36; ncl; myc; acot2 | 0.690 | 0.456-1.597 | 2 | 2 |
| **GO:0006635**fatty acid beta-oxidation | 10/33 | 30% | slc27a2; gcdh; etfdh; ehhadh; eci1; ech1; crot; cpt1b; acox1; acadsb | 2.017 | 1.401-3.184 | 9 | 1 |
| **GO:0009062**fatty acid catabolic process | 12/42 | 29% | slc27a2; hacl1; gcdh; etfdh; ehhadh; eci1; ech1; crot; cpt1b; acox1; acot2; acadsb | 2.017 | 1.288-3.184 | 11 | 1 |
| **GO:0072329**monocarboxylic acid catabolic process | 15/48 | 31% | slc27a2; hacl1; gcdh; etfdh; ehhadh; eci1; ech1; cyp26b1; crot; cpt1b; agxt2; acox1; acot2; acadsb; abat | 2.238 | 1.439-3.909 | 12 | 3 |
| **GO:0070371**ERK1 and ERK2 cascade | 3/14 | 21% | tf; myc; apoa1 | 2.377 | 1.208-5.187 | 0 | 3 |
| **GO:0000038**very long-chain fatty acid metabolic process | 5/12 | 42% | slc27a2; acox1; acot4; acot2; acot1 | 2.721 | 1.888-4.505 | 5 | 0 |
| **GO:0046395**carboxylic acid catabolic process | 21/87 | 24% | cemip2; slc27a2; kynu; kmo; hacl1; gcdh; etfdh; ehhadh; eci1; ech1; cyp26b1; crot; cpt1b; cdo1; blmh; agxt2; acox1; acot4; acot2; acadsb; abat | 3.806 | 1.610-6.038 | 15 | 6 |
| **GO:0006637**acyl-CoA metabolic process | 9/31 | 29% | mpc2; kynu; gcdh; acss2; acot4; acot2; acot12; acot1; acadsb | 4.030 | 2.953-10.491 | 7 | 2 |
| **GO:0044282**small molecule catabolic process | 23/120 | 19% | cemip2; sult1e1; slc27a2; kynu; kmo; inpp1; hacl1; gcdh; etfdh; ehhadh; eci1; ech1; cyp26b1; crot; cpt1b; cdo1; blmh; agxt2; acox1; acot4; acot2; acadsb; abat | 4.136 | 1.888-10.491 | 17 | 6 |

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:0071364 cellular response to epidermal growth factor stimulus:** Any process that results in a change in state or activity of a cell (in terms of movement, secretion, enzyme production, gene expression, etc.) as a result of an epidermal growth factor stimulus.

**GO:0070849 response to epidermal growth factor:** 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 epidermal growth factor stimulus.

**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: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:0072329 monocarboxylic acid catabolic process:** The chemical reactions and pathways resulting in the breakdown of monocarboxylic acids, any organic acid containing one carboxyl (-COOH) group.

**GO:0070371 ERK1 and ERK2 cascade:** An intracellular protein kinase cascade containing at least ERK1 or ERK2 (MAPKs), a MEK (a MAPKK) and a MAP3K. The cascade may involve 4 different kinases, as it can also contain an additional tier the upstream MAP4K. The kinases in each tier phosphorylate and activate the kinase in the downstream tier to transmit a signal within a cell.

**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: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: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: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.

### 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:0050766**positive regulation of phagocytosis | 4/35 | 11% | cd36; c3; apoa2; ahsg | 44.730 | 22.260-122.653 | 2 | 2 |
| **GO:0050764**regulation of phagocytosis | 5/51 | 10% | cd36; c3; apoa2; alox15; ahsg | 48.555 | 27.154-159.716 | 2 | 3 |
| **GO:0002718**regulation of cytokine production involved in immune response | 3/36 | 8% | ticam1; cd36; apoa2 | 48.555 | 17.366-159.716 | 3 | 0 |
| **GO:0034381**plasma lipoprotein particle clearance | 3/11 | 27% | cd36; apoc3; apoa2 | 48.555 | 17.366-159.716 | 2 | 1 |
| **GO:0016051**carbohydrate biosynthetic process | 3/32 | 9% | gpd1; g6pd; acadm | 48.822 | 39.627-63.173 | 3 | 0 |
| **GO:0006399**tRNA metabolic process | 3/20 | 15% | tsen2; iars2; hsd17b10 | 57.734 | 46.011-76.940 | 3 | 0 |
| **GO:0051181**cofactor transport | 3/10 | 30% | slc27a1; slc22a8; abcg2 | 60.649 | 31.055-121.705 | 1 | 2 |
| **GO:0044262**cellular carbohydrate metabolic process | 3/40 | 8% | inpp1; acadm; abcg2 | 60.649 | 39.560-121.705 | 2 | 1 |
| **GO:0045926**negative regulation of growth | 4/72 | 6% | gdf15; g6pd; cdkn1a; ahsg | 61.369 | 35.006-115.629 | 2 | 2 |
| **GO:0006635**fatty acid beta-oxidation | 18/33 | 55% | slc27a2; hadhb; hadh; gcdh; etfdh; ehhadh; eci1; ech1; decr1; crot; crat; cpt2; cpt1b; acox1; acadsb; acadm; acadl; acaa2 | 64.027 | 46.553-95.058 | 17 | 1 |

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:0050766 positive regulation of phagocytosis:** Any process that activates or increases the frequency, rate or extent of phagocytosis.

**GO:0050764 regulation of phagocytosis:** Any process that modulates the frequency, rate or extent of phagocytosis, the process in which phagocytes engulf external particulate material.

**GO:0002718 regulation of cytokine production involved in immune response:** Any process that modulates the frequency, rate, or extent of cytokine production that contributes to an immune response.

**GO:0034381 plasma lipoprotein particle clearance:** The process in which a lipoprotein particle is removed from the blood via receptor-mediated endocytosis and its constituent parts degraded.

**GO:0016051 carbohydrate biosynthetic process:** The chemical reactions and pathways resulting in the formation of carbohydrates, any of a group of organic compounds based of the general formula Cx(H2O)y.

**GO:0006399 tRNA metabolic process:** The chemical reactions and pathways involving tRNA, transfer RNA, a class of relatively small RNA molecules responsible for mediating the insertion of amino acids into the sequence of nascent polypeptide chains during protein synthesis. Transfer RNA is characterized by the presence of many unusual minor bases, the function of which has not been completely established.

**GO:0051181 cofactor transport:** The directed movement of a cofactor into, out of or within a cell, or between cells, by means of some agent such as a transporter or pore. A cofactor is a substance that is required for the activity of an enzyme or other protein.

**GO:0044262 cellular carbohydrate metabolic process:** The chemical reactions and pathways involving carbohydrates, any of a group of organic compounds based of the general formula Cx(H2O)y, as carried out by individual cells.

**GO:0045926 negative regulation of growth:** Any process that stops, prevents or reduces the rate or extent of growth, the increase in size or mass of all or part of an organism.

**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).