

## Systems biology approaches and pathway tools for investigating cardiovascular disease

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This supplementary information provides the complete list of KEGG biochemical pathways that were identified by KegArray as affected by the different cholesterol treatments. The KegArray parameters were set to display a 1.1-fold difference and non-affected pathways were excluded. The information in Table S1 is for the 60 different pathways affected by low cholesterol in the diet (0.25% w/w), Table S2 is for the 76 pathways affected by high cholesterol in the diet (1.0% w/w) and Table S3 is the 77 pathways that were differentially affected between low and high cholesterol in the diet. The pathway names as well as the KEGG map ids (i.e., mmu01040) are provided for each pathway.

The KegArray tool is freely available for download from the website:  
<http://www.genome.jp/download/>

**Table S1. Pathway Search Results for Low Cholesterol Treatment<sup>a</sup>**

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mmu01040 Biosynthesis of unsaturated fatty acids
mmu00564 Glycerophospholipid metabolism
mmu03320 PPAR signaling pathway
mmu00100 Biosynthesis of steroids
mmu00071 Fatty acid metabolism
mmu00061 Fatty acid biosynthesis
mmu00591 Linoleic acid metabolism
mmu04910 Insulin signaling pathway
mmu00590 Arachidonic acid metabolism
mmu00592 alpha-Linolenic acid metabolism
mmu00650 Butanoate metabolism
mmu04920 Adipocytokine signaling pathway
mmu00120 Bile acid biosynthesis
mmu00150 Androgen and estrogen metabolism
mmu00561 Glycerolipid metabolism
mmu00565 Ether lipid metabolism
mmu00632 Benzoate degradation via CoA ligation
mmu00903 Limonene and pinene degradation
mmu00960 Alkaloid biosynthesis II
mmu01031 Glycan structures - biosynthesis 2
mmu04664 Fc epsilon RI signaling pathway
mmu04730 Long-term depression
mmu04912 GnRH signaling pathway
mmu00020 Citrate cycle (TCA cycle)
mmu00062 Fatty acid elongation in mitochondria
mmu00260 Glycine, serine and threonine metabolism
mmu00280 Valine, leucine and isoleucine degradation
mmu00350 Tyrosine metabolism
mmu00440 Aminophosphonate metabolism
mmu00562 Inositol phosphate metabolism
mmu00563 Glycosylphosphatidylinositol(GPI)-anchor biosynthesis
mmu00620 Pyruvate metabolism
mmu00830 Retinol metabolism
mmu00900 Terpenoid biosynthesis
mmu00920 Sulfur metabolism
mmu04010 MAPK signaling pathway
mmu04070 Phosphatidylinositol signaling system
mmu04370 VEGF signaling pathway
mmu04810 Regulation of actin cytoskeleton
mmu00051 Fructose and mannose metabolism
mmu00140 C21-Steroid hormone metabolism
mmu00252 Alanine and aspartate metabolism
mmu00310 Lysine degradation
mmu00360 Phenylalanine metabolism
mmu00363 Bisphenol A degradation
mmu00380 Tryptophan metabolism

mmu00410 beta-Alanine metabolism  
mmu00510 N-Glycan biosynthesis  
mmu00600 Sphingolipid metabolism  
mmu00604 Glycosphingolipid biosynthesis - ganglioseries  
mmu00624 1- and 2-Methylnaphthalene degradation  
mmu00625 Tetrachloroethene degradation  
mmu00630 Glyoxylate and dicarboxylate metabolism  
mmu00640 Propanoate metabolism  
mmu00720 Reductive carboxylate cycle (CO<sub>2</sub> fixation)  
mmu00930 Caprolactam degradation  
mmu01030 Glycan structures - biosynthesis 1  
mmu02010 ABC transporters - General  
mmu05010 Alzheimer's disease  
mmu05215 Prostate cancer

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<sup>a</sup>Data are from a KegArray-based analysis of quantified lipid and transcriptomics data from Kleemann et al.<sup>69</sup>. Displayed data are for KEGG metabolic pathways affected by exposure to low cholesterol with a 1.1-fold threshold in KegArray.

**Table S2. Pathway Search Results for High Cholesterol<sup>a</sup>**

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mmu01040 Biosynthesis of unsaturated fatty acids
mmu00564 Glycerophospholipid metabolism
mmu03320 PPAR signaling pathway
mmu00071 Fatty acid metabolism
mmu04920 Adipocytokine signaling pathway
mmu00100 Biosynthesis of steroids
mmu00600 Sphingolipid metabolism
mmu00565 Ether lipid metabolism
mmu00590 Arachidonic acid metabolism
mmu00591 Linoleic acid metabolism
mmu00650 Butanoate metabolism
mmu00061 Fatty acid biosynthesis
mmu00120 Bile acid biosynthesis
mmu00561 Glycerolipid metabolism
mmu00592 alpha-Linolenic acid metabolism
mmu01031 Glycan structures - biosynthesis 2
mmu04664 Fc epsilon RI signaling pathway
mmu04730 Long-term depression
mmu04910 Insulin signaling pathway
mmu04912 GnRH signaling pathway
mmu00062 Fatty acid elongation in mitochondria
mmu00150 Androgen and estrogen metabolism
mmu00280 Valine, leucine and isoleucine degradation
mmu04070 Phosphatidylinositol signaling system
mmu04370 VEGF signaling pathway
mmu00020 Citrate cycle (TCA cycle)
mmu00310 Lysine degradation
mmu00380 Tryptophan metabolism
mmu00562 Inositol phosphate metabolism
mmu00620 Pyruvate metabolism
mmu00632 Benzoate degradation via CoA ligation
mmu00830 Retinol metabolism
mmu00903 Limonene and pinene degradation
mmu00930 Caprolactam degradation
mmu04010 MAPK signaling pathway
mmu00252 Alanine and aspartate metabolism
mmu00260 Glycine, serine and threonine metabolism
mmu00281 Geraniol degradation
mmu00350 Tyrosine metabolism
mmu00410 beta-Alanine metabolism
mmu00440 Aminophosphonate metabolism
mmu00510 N-Glycan biosynthesis
mmu00563 Glycosylphosphatidylinositol(GPI)-anchor biosynthesis
mmu00604 Glycosphingolipid biosynthesis - ganglioseries
mmu00640 Propionate metabolism
mmu00900 Terpenoid biosynthesis
mmu00920 Sulfur metabolism

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mmu00960 Alkaloid biosynthesis II  
mmu01030 Glycan structures - biosynthesis 1  
mmu04810 Regulation of actin cytoskeleton  
mmu05215 Prostate cancer  
mmu00051 Fructose and mannose metabolism  
mmu00140 C21-Steroid hormone metabolism  
mmu00360 Phenylalanine metabolism  
mmu00363 Bisphenol A degradation  
mmu00624 1- and 2-Methylnaphthalene degradation  
mmu00625 Tetrachloroethene degradation  
mmu00630 Glyoxylate and dicarboxylate metabolism  
mmu00720 Reductive carboxylate cycle (CO<sub>2</sub> fixation)  
mmu01032 Glycan structures - degradation  
mmu02010 ABC transporters - General  
mmu04012 ErbB signaling pathway  
mmu04020 Calcium signaling pathway  
mmu04060 Cytokine-cytokine receptor interaction  
mmu04080 Neuroactive ligand-receptor interaction  
mmu04310 Wnt signaling pathway  
mmu04350 TGF-beta signaling pathway  
mmu04530 Tight junction  
mmu04630 Jak-STAT signaling pathway  
mmu04650 Natural killer cell mediated cytotoxicity  
mmu04662 B cell receptor signaling pathway  
mmu04670 Leukocyte transendothelial migration  
mmu04930 Type II diabetes mellitus  
mmu05010 Alzheimer's disease  
mmu05214 Glioma  
mmu05223 Non-small cell lung cancer

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<sup>a</sup>Data are from a KegArray-based analysis of quantified lipid and transcriptomics data from Kleemann et al.<sup>69</sup>. Displayed data are for KEGG metabolic pathways affected by exposure to high cholesterol with a 1.1-fold threshold in KegArray.

**Table S3. Pathway Search Results for High Cholesterol vs. Low Cholesterol<sup>a</sup>**

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mmu01040 Biosynthesis of unsaturated fatty acids
mmu03320 PPAR signaling pathway
mmu00564 Glycerophospholipid metabolism
mmu00071 Fatty acid metabolism
mmu04920 Adipocytokine signaling pathway
mmu00565 Ether lipid metabolism
mmu00590 Arachidonic acid metabolism
mmu00100 Biosynthesis of steroids
mmu00120 Bile acid biosynthesis
mmu00561 Glycerolipid metabolism
mmu00600 Sphingolipid metabolism
mmu00591 Linoleic acid metabolism
mmu00592 alpha-Linolenic acid metabolism
mmu04664 Fc epsilon RI signaling pathway
mmu04912 GnRH signaling pathway
mmu00650 Butanoate metabolism
mmu04370 VEGF signaling pathway
mmu04730 Long-term depression
mmu00061 Fatty acid biosynthesis
mmu00062 Fatty acid elongation in mitochondria
mmu00632 Benzoate degradation via CoA ligation
mmu00830 Retinol metabolism
mmu00903 Limonene and pinene degradation
mmu01031 Glycan structures - biosynthesis 2
mmu04010 MAPK signaling pathway
mmu04070 Phosphatidylinositol signaling system
mmu00150 Androgen and estrogen metabolism
mmu00260 Glycine, serine and threonine metabolism
mmu00280 Valine, leucine and isoleucine degradation
mmu00310 Lysine degradation
mmu00350 Tyrosine metabolism
mmu00380 Tryptophan metabolism
mmu00410 beta-Alanine metabolism
mmu00510 N-Glycan biosynthesis
mmu00562 Inositol phosphate metabolism
mmu00620 Pyruvate metabolism
mmu00624 1- and 2-Methylnaphthalene degradation
mmu00640 Propanoate metabolism
mmu00930 Caprolactam degradation
mmu00960 Alkaloid biosynthesis II
mmu01030 Glycan structures - biosynthesis 1
mmu04662 B cell receptor signaling pathway
mmu04910 Insulin signaling pathway
mmu00010 Glycolysis / Gluconeogenesis
mmu00020 Citrate cycle (TCA cycle)
mmu00051 Fructose and mannose metabolism
mmu00140 C21-Steroid hormone metabolism

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mmu00252 Alanine and aspartate metabolism  
mmu00281 Geraniol degradation  
mmu00360 Phenylalanine metabolism  
mmu00363 Bisphenol A degradation  
mmu00440 Aminophosphonate metabolism  
mmu00563 Glycosylphosphatidylinositol(GPI)-anchor biosynthesis  
mmu00604 Glycosphingolipid biosynthesis - ganglioseries  
mmu00625 Tetrachloroethene degradation  
mmu00630 Glyoxylate and dicarboxylate metabolism  
mmu00641 3-Chloroacrylic acid degradation  
mmu00680 Methane metabolism  
mmu00900 Terpenoid biosynthesis  
mmu00920 Sulfur metabolism  
mmu00980 Metabolism of xenobiotics by cytochrome P450  
mmu00982 Drug metabolism - cytochrome P450  
mmu01032 Glycan structures - degradation  
mmu02010 ABC transporters - General  
mmu04012 ErbB signaling pathway  
mmu04020 Calcium signaling pathway  
mmu04060 Cytokine-cytokine receptor interaction  
mmu04080 Neuroactive ligand-receptor interaction  
mmu04630 Jak-STAT signaling pathway  
mmu04650 Natural killer cell mediated cytotoxicity  
mmu04670 Leukocyte transendothelial migration  
mmu04810 Regulation of actin cytoskeleton  
mmu04930 Type II diabetes mellitus  
mmu05010 Alzheimer's disease  
mmu05214 Glioma  
mmu05215 Prostate cancer  
mmu05223 Non-small cell lung cancer

<sup>a</sup>Data are from a KegArray-based analysis of quantified lipid and transcriptomics data from Kleemann et al.<sup>69</sup>. Displayed data are for KEGG metabolic pathways that differ between exposure to low and high cholesterol with a 1.1-fold threshold in KegArray.