TableS1: Predicted functions for the ileal microbiota in Japanese quail based on KEGG classification.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Level 1** | **[%]** | **Level 2** | **[%]** | **Pathway** | **[%]** |
| **Metabolism** | 75.082 | **Amino acid metabolism** | 4.395 | Arginine biosynthesis | 0.355 |
| Alanine, aspartate and glutamate metabolism | 0.712 |
| Glycine, serine and threonine metabolism | 0.707 |
| Cysteine and methionine metabolism | 0.629 |
| Valine, leucine and isoleucine degradation | 0.184 |
| Valine, leucine and isoleucine biosynthesis | 0.170 |
| Lysine biosynthesis | 0.320 |
| Lysine degradation | 0.105 |
| Arginine and proline metabolism | 0.316 |
| Histidine metabolism | 0.118 |
| Tyrosine metabolism | 0.182 |
| Phenylalanine metabolism | 0.238 |
| Tryptophan metabolism | 0.117 |
| Phenylalanine, tyrosine and tryptophan biosynthesis | 0.243 |
| **Biosynthesis of other secondary metabolites** | 0.970 | Puromycin biosynthesis | 0.000 |
| Caffeine metabolism | 0.000 |
| Monobactam biosynthesis | 0.093 |
| Penicillin and cephalosporin biosynthesis | 0.006 |
| Clavulanic acid biosynthesis | 0.001 |
| Carbapenem biosynthesis | 0.025 |
| Prodigiosin biosynthesis | 0.250 |
| Novobiocin biosynthesis | 0.045 |
| Staurosporine biosynthesis | 0.000 |
| Phenazine biosynthesis | 0.022 |
| Streptomycin biosynthesis | 0.255 |
| Neomycin, kanamycin and gentamicin biosynthesis | 0.062 |
| Acarbose and validamycin biosynthesis | 0.036 |
| Indole alkaloid biosynthesis | 0.000 |
| Phenylpropanoid biosynthesis | 0.038 |
| Flavonoid biosynthesis | 0.004 |
| Isoflavonoid biosynthesis | 0.000 |
| Flavone and flavonol biosynthesis | 0.035 |
| Stilbenoid, diarylheptanoid and gingerol biosynthesis | 0.004 |
| Isoquinoline alkaloid biosynthesis | 0.026 |
| Tropane, piperidine and pyridine alkaloid biosynthesis | 0.053 |
| Betalain biosynthesis | 0.007 |
| Glucosinolate biosynthesis | 0.010 |
| **Carbohydrate metabolism** | 11.665 | Glycolysis / Gluconeogenesis | 1.438 |
| Citrate cycle (TCA cycle) | 0.415 |
| Pentose phosphate pathway | 0.791 |
| Pentose and glucuronate interconversions | 0.508 |
| Fructose and mannose metabolism | 1.034 |
| Galactose metabolism | 0.953 |
| Ascorbate and aldarate metabolism | 0.183 |
| Starch and sucrose metabolism | 1.422 |
| Amino sugar and nucleotide sugar metabolism | 1.674 |
| Inositol phosphate metabolism | 0.257 |
| Pyruvate metabolism | 1.150 |
| Glyoxylate and dicarboxylate metabolism | 0.551 |
| Propanoate metabolism | 0.737 |
| Butanoate metabolism | 0.447 |
| C5-Branched dibasic acid metabolism | 0.103 |
| **Chemical structure transformation maps** | 0.002 | Biosynthesis of terpenoids and steroids | 0.002 |
| **Energy metabolism** | 3.644 | Oxidative phosphorylation | 0.756 |
| Photosynthesis | 0.300 |
| Methane metabolism | 0.788 |
| Carbon fixation in photosynthetic organisms | 0.495 |
| Carbon fixation pathways in prokaryotes | 0.715 |
| Nitrogen metabolism | 0.269 |
| Sulfur metabolism | 0.321 |
| **Global and overview maps** | 38.367 | Metabolic pathways | 16.129 |
| Biosynthesis of secondary metabolites | 6.002 |
| Microbial metabolism in diverse environments | 5.068 |
| Biosynthesis of antibiotics | 5.085 |
| Carbon metabolism | 2.458 |
| 2-Oxocarboxylic acid metabolism | 0.304 |
| Fatty acid metabolism | 0.737 |
| Degradation of aromatic compounds | 0.366 |
| Biosynthesis of amino acids | 2.219 |
| **Glycan biosynthesis and metabolism** | 1.672 | N-Glycan biosynthesis | 0.006 |
| Other glycan degradation | 0.134 |
| Various types of N-glycan biosynthesis | 0.035 |
| Other types of O-glycan biosynthesis | 0.001 |
| Mannose type O-glycan biosynthesis | 0.001 |
| Glycosaminoglycan degradation | 0.115 |
| Glycosaminoglycan biosynthesis - chondroitin sulfate / dermatan sulfate | 0.000 |
| Glycosaminoglycan biosynthesis - heparan sulfate / heparin | 0.000 |
| Lipopolysaccharide biosynthesis | 0.392 |
| Peptidoglycan biosynthesis | 0.856 |
| Glycosylphosphatidylinositol (GPI)-anchor biosynthesis | 0.000 |
| Lipoarabinomannan (LAM) biosynthesis | 0.014 |
| Glycosphingolipid biosynthesis - lacto and neolacto series | 0.000 |
| Glycosphingolipid biosynthesis - globo and isoglobo series | 0.082 |
| Glycosphingolipid biosynthesis - ganglio series | 0.035 |
| **Lipid metabolism** | 2.624 | Fatty acid biosynthesis | 0.700 |
| Fatty acid elongation | 0.000 |
| Fatty acid degradation | 0.199 |
| Synthesis and degradation of ketone bodies | 0.055 |
| Cutin, suberine and wax biosynthesis | 0.000 |
| Steroid biosynthesis | 0.000 |
| Primary bile acid biosynthesis | 0.088 |
| Secondary bile acid biosynthesis | 0.101 |
| Steroid hormone biosynthesis | 0.021 |
| Glycerolipid metabolism | 0.490 |
| Glycerophospholipid metabolism | 0.622 |
| Ether lipid metabolism | 0.013 |
| Arachidonic acid metabolism | 0.021 |
| Linoleic acid metabolism | 0.006 |
| alpha-Linolenic acid metabolism | 0.021 |
| Sphingolipid metabolism | 0.085 |
| Biosynthesis of unsaturated fatty acids | 0.204 |
| **Metabolism of cofactors and vitamins** | 3.486 | Ubiquinone and other terpenoid-quinone biosynthesis | 0.182 |
| One carbon pool by folate | 0.440 |
| Thiamine metabolism | 0.363 |
| Riboflavin metabolism | 0.316 |
| Vitamin B6 metabolism | 0.120 |
| Nicotinate and nicotinamide metabolism | 0.479 |
| Pantothenate and CoA biosynthesis | 0.359 |
| Biotin metabolism | 0.422 |
| Lipoic acid metabolism | 0.062 |
| Folate biosynthesis | 0.337 |
| Retinol metabolism | 0.070 |
| Porphyrin and chlorophyll metabolism | 0.337 |
| **Metabolism of other amino acids** | 1.511 | beta-Alanine metabolism | 0.144 |
| Taurine and hypotaurine metabolism | 0.203 |
| Phosphonate and phosphinate metabolism | 0.120 |
| Selenocompound metabolism | 0.298 |
| Cyanoamino acid metabolism | 0.067 |
| D-Glutamine and D-glutamate metabolism | 0.158 |
| D-Arginine and D-ornithine metabolism | 0.001 |
| D-Alanine metabolism | 0.156 |
| Glutathione metabolism | 0.364 |
| **Metabolism of terpenoids and polyketides** | 0.828 | Tetracycline biosynthesis | 0.002 |
| Geraniol degradation | 0.037 |
| Biosynthesis of 12-, 14- and 16-membered macrolides | 0.001 |
| Polyketide sugar unit biosynthesis | 0.123 |
| Terpenoid backbone biosynthesis | 0.396 |
| Monoterpenoid biosynthesis | 0.000 |
| Limonene and pinene degradation | 0.031 |
| Carotenoid biosynthesis | 0.007 |
| Zeatin biosynthesis | 0.039 |
| Sesquiterpenoid and triterpenoid biosynthesis | 0.000 |
| Insect hormone biosynthesis | 0.006 |
| Biosynthesis of ansamycins | 0.023 |
| Type I polyketide structures | 0.003 |
| Biosynthesis of siderophore group nonribosomal peptides | 0.082 |
| Nonribosomal peptide structures | 0.043 |
| Biosynthesis of vancomycin group antibiotics | 0.022 |
| Biosynthesis of type II polyketide backbone | 0.000 |
| Biosynthesis of type II polyketide products | 0.004 |
| Biosynthesis of enediyne antibiotics | 0.008 |
| **Nucleotide metabolism** | 4.354 | Purine metabolism | 2.551 |
| Pyrimidine metabolism | 1.803 |
| **Xenobiotics biodegradation and metabolism** | 1.564 | Chlorocyclohexane and chlorobenzene degradation | 0.064 |
| Benzoate degradation | 0.257 |
| Bisphenol degradation | 0.000 |
| Fluorobenzoate degradation | 0.025 |
| Furfural degradation | 0.000 |
| Dioxin degradation | 0.064 |
| Xylene degradation | 0.066 |
| Toluene degradation | 0.027 |
| Polycyclic aromatic hydrocarbon degradation | 0.002 |
| Chloroalkane and chloroalkene degradation | 0.131 |
| Naphthalene degradation | 0.091 |
| Aminobenzoate degradation | 0.114 |
| Nitrotoluene degradation | 0.074 |
| Ethylbenzene degradation | 0.014 |
| Styrene degradation | 0.022 |
| Atrazine degradation | 0.011 |
| Caprolactam degradation | 0.031 |
| Metabolism of xenobiotics by cytochrome P450 | 0.095 |
| Drug metabolism - cytochrome P450 | 0.096 |
| Drug metabolism - other enzymes | 0.376 |
| Steroid degradation | 0.004 |
| **Genetic Information Processing** | 7.801 | **Folding, sorting and degradation** | 1.371 | RNA degradation | 0.591 |
| Proteasome | 0.002 |
| Protein export | 0.482 |
| Ubiquitin mediated proteolysis | 0.000 |
| Sulfur relay system | 0.258 |
| Protein processing in endoplasmic reticulum | 0.038 |
| **Replication and repair** | 2.997 | DNA replication | 0.591 |
| Base excision repair | 0.456 |
| Nucleotide excision repair | 0.355 |
| Mismatch repair | 0.766 |
| Homologous recombination | 0.822 |
| Non-homologous end-joining | 0.006 |
| **Transcription** | 0.187 | RNA polymerase | 0.184 |
| Basal transcription factors | 0.003 |
| **Translation** | 3.246 | Aminoacyl-tRNA biosynthesis | 1.030 |
| Ribosome biogenesis in eukaryotes | 0.046 |
| Ribosome | 2.028 |
| RNA transport | 0.142 |
| mRNA surveillance pathway | 0.000 |
| **Environmental Information Processing** | 7.791 | **Membrane transport** | 4.577 | ABC transporters | 2.431 |
| Phosphotransferase system (PTS) | 1.481 |
| Bacterial secretion system | 0.665 |
| **Signal transduction** | 3.211 | Two-component system | 2.597 |
| MAPK signaling pathway - yeast | 0.010 |
| MAPK signaling pathway - fly | 0.018 |
| Ras signaling pathway | 0.000 |
| MAPK signaling pathway - plant | 0.122 |
| Calcium signaling pathway | 0.001 |
| cGMP-PKG signaling pathway | 0.000 |
| cAMP signaling pathway | 0.000 |
| NF-kappa B signaling pathway | 0.000 |
| HIF-1 signaling pathway | 0.285 |
| FoxO signaling pathway | 0.028 |
| Phosphatidylinositol signaling system | 0.090 |
| Sphingolipid signaling pathway | 0.000 |
| Phospholipase D signaling pathway | 0.007 |
| PI3K-Akt signaling pathway | 0.008 |
| AMPK signaling pathway | 0.044 |
| Wnt signaling pathway | 0.000 |
| Notch signaling pathway | 0.000 |
| VEGF signaling pathway | 0.000 |
| Apelin signaling pathway | 0.000 |
| Hippo signaling pathway - fly | 0.000 |
| Hippo signaling pathway - multiple species | 0.000 |
| TNF signaling pathway | 0.000 |
| **Signaling molecules and interaction** | 0.002 | Cytokine-cytokine receptor interaction | 0.000 |
| Neuroactive ligand-receptor interaction | 0.002 |
| ECM-receptor interaction | 0.000 |
| **Cellular Processes** | 4.376 | **Cell growth and death** | 0.649 | Cell cycle - Caulobacter | 0.473 |
| Meiosis - yeast | 0.033 |
| p53 signaling pathway | 0.000 |
| Apoptosis | 0.001 |
| Apoptosis - fly | 0.039 |
| Apoptosis - multiple species | 0.000 |
| Ferroptosis | 0.025 |
| Necroptosis | 0.077 |
| **Cell motility** | 0.457 | Bacterial chemotaxis | 0.192 |
| Flagellar assembly | 0.265 |
| **Cellular community - eukaryotes** | 3.075 | Focal adhesion | 0.000 |
| Quorum sensing | 1.638 |
| Biofilm formation - Pseudomonas aeruginosa | 0.261 |
| Biofilm formation - Escherichia coli | 0.729 |
| Biofilm formation - Vibrio cholerae | 0.447 |
| **Transport and catabolism** | 0.196 | Mitophagy - animal | 0.000 |
| Autophagy - yeast | 0.004 |
| Lysosome | 0.085 |
| Endocytosis | 0.000 |
| Peroxisome | 0.107 |
| **Others** | 4.950 | **Others** | 4.950 | Others | 4.950 |

TableS2: Pearson correlation being significant (P < 0.05) for the predicted functions at the third level of KEGG classification.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Level1 | Level2 | Level3 | PUa | CaUa | BWGa | FIa | F:Ga |
| Metabolism | Carbohydrate metabolism | Citrate cycle (TCA cycle) |  |  |  | 0.122 |  |
| Metabolism | Carbohydrate metabolism | Pentose and glucuronate interconversions |  |  | 0.096 | 0.111 |  |
| Metabolism | Lipid metabolism | Steroid biosynthesis | 0.082 | 0.113 | 0.080 | 0.174 | 0.090 |
| Metabolism | Carbohydrate metabolism | Ascorbate and aldarate metabolism |  |  |  | 0.113 |  |
| Metabolism | Lipid metabolism | Fatty acid elongation |  |  |  | 0.074 |  |
| Metabolism | Lipid metabolism | Fatty acid degradation |  |  |  | 0.156 | 0.091 |
| Metabolism | Metabolism of terpenoids and polyketides | Geraniol degradation |  |  | 0.089 | 0.131 |  |
| Metabolism | Metabolism of cofactors and vitamins | Ubiquinone and other terpenoid-quinone biosynthesis |  |  |  | 0.115 |  |
| Metabolism | Energy metabolism | Oxidative phosphorylation |  |  |  | 0.082 |  |
| Metabolism | Amino acid metabolism | Arginine biosynthesis |  |  |  | 0.146 | 0.081 |
| Metabolism | Biosynthesis of other secondary metabolites | Caffeine metabolism | 0.073 |  |  | 0.093 |  |
| Metabolism | Metabolism of terpenoids and polyketides | Tetracycline biosynthesis |  | 0.085 |  | 0.121 | 0.126 |
| Metabolism | Amino acid metabolism | Glycine, serine and threonine metabolism |  | 0.102 |  | 0.169 | 0.126 |
| Metabolism | Biosynthesis of other secondary metabolites | Monobactam biosynthesis |  |  |  | 0.133 | 0.089 |
| Metabolism | Amino acid metabolism | Cysteine and methionine metabolism |  | 0.081 |  | 0.127 | 0.158 |
| Metabolism | Amino acid metabolism | Valine, leucine and isoleucine degradation |  | 0.107 |  | 0.164 | 0.136 |
| Metabolism | Amino acid metabolism | Lysine degradation |  |  | 0.075 | 0.157 |  |
| Metabolism | Amino acid metabolism | Valine, leucine and isoleucine biosynthesis |  |  |  | 0.139 | 0.089 |
| Metabolism | Amino acid metabolism | Lysine biosynthesis |  | 0.091 |  | 0.101 | 0.180 |
| Metabolism | Xenobiotics biodegradation and metabolism | Fluorobenzoate degradation |  |  | 0.092 | 0.091 |  |
| Metabolism | Biosynthesis of other secondary metabolites | Penicillin and cephalosporin biosynthesis |  |  |  | 0.126 | 0.183 |
| Metabolism | Amino acid metabolism | Arginine and proline metabolism |  |  |  | 0.136 | 0.054 |
| Metabolism | Biosynthesis of other secondary metabolites | Carbapenem biosynthesis |  |  |  | 0.093 | 0.148 |
| Metabolism | Amino acid metabolism | Histidine metabolism |  | 0.078 |  | 0.102 | 0.154 |
| Metabolism | Amino acid metabolism | Tyrosine metabolism |  |  |  | 0.149 | 0.110 |
| Metabolism | Amino acid metabolism | Phenylalanine metabolism |  |  |  | 0.115 |  |
| Metabolism | Xenobiotics biodegradation and metabolism | Benzoate degradation |  |  |  | 0.085 |  |
| Metabolism | Xenobiotics biodegradation and metabolism | Furfural degradation | 0.090 |  | 0.138 | 0.194 |  |
| Metabolism | Biosynthesis of other secondary metabolites | Staurosporine biosynthesis | 0.084 |  | 0.097 | 0.164 |  |
| Metabolism | Amino acid metabolism | Tryptophan metabolism |  | 0.078 |  | 0.142 | 0.107 |
| Metabolism | Amino acid metabolism | Phenylalanine, tyrosine and tryptophan biosynthesis |  | 0.070 |  | 0.125 | 0.164 |
| Metabolism | Biosynthesis of other secondary metabolites | Novobiocin biosynthesis |  | 0.073 |  | 0.133 | 0.156 |
| Metabolism | Metabolism of other amino acids | beta-Alanine metabolism |  |  | 0.106 | 0.149 |  |
| Metabolism | Biosynthesis of other secondary metabolites | Phenazine biosynthesis | 0.002 | 0.074 |  | 0.140 | 0.156 |
| Metabolism | Metabolism of other amino acids | Selenocompound metabolism |  |  | 0.155 | 0.167 |  |
| Metabolism | Glycan biosynthesis and metabolism | Other types of O-glycan biosynthesis |  | 0.076 |  | 0.111 | 0.100 |
| Metabolism | Metabolism of other amino acids | Cyano amino acid metabolism |  |  |  | 0.115 | 0.113 |
| Metabolism | Metabolism of other amino acids | D-Arginine and D-ornithine metabolism |  |  |  | 0.093 | 0.100 |
| Metabolism | Metabolism of terpenoids and polyketides | Biosynthesis of 12-, 14- and 16-membered macrolides | 0.101 | 0.069 | 0.103 | 0.165 |  |
| Metabolism | Lipid metabolism | Ether lipid metabolism |  |  | 0.090 | 0.090 |  |
| Metabolism | Lipid metabolism | Arachidonic acid metabolism |  |  | 0.084 | 0.116 |  |
| Metabolism | Glycan biosynthesis and metabolism | Mannose type O-glycan biosynthesis |  |  |  | 0.099 | 0.104 |
| Metabolism | Lipid metabolism | Linoleic acid metabolism |  |  | 0.095 | 0.091 |  |
| Metabolism | Lipid metabolism | alpha-Linolenic acid metabolism |  |  | 0.088 | 0.115 |  |
| Metabolism | Xenobiotics biodegradation and metabolism | Polycyclic aromatic hydrocarbon degradation | 0.083 | 0.072 |  | 0.125 |  |
| Metabolism | Xenobiotics biodegradation and metabolism | Toluene degradation |  |  | 0.091 | 0.103 |  |
| Metabolism | Xenobiotics biodegradation and metabolism | Naphthalene degradation |  |  | 0.070 | 0.139 |  |
| Metabolism | Biosynthesis of other secondary metabolites | Acarbose and validamycin biosynthesis |  |  |  | 0.071 | 0.125 |
| Metabolism | Carbohydrate metabolism | Glyoxylate and dicarboxylate metabolism |  |  | 0.070 | 0.137 |  |
| Metabolism | Xenobiotics biodegradation and metabolism | Ethylbenzene degradation |  |  | 0.081 | 0.124 |  |
| Metabolism | Glycan biosynthesis and metabolism | Lipoarabinomannan (LAM) biosynthesis |  |  |  | 0.073 |  |
| Metabolism | Metabolism of cofactors and vitamins | Folate biosynthesis |  |  | 0.072 | 0.142 |  |
| Metabolism | Metabolism of cofactors and vitamins | Porphyrin and chlorophyll metabolism |  |  | 0.092 | 0.125 |  |
| Metabolism | Metabolism of terpenoids and polyketides | Sesquiterpenoid and triterpenoid biosynthesis |  | 0.092 | 0.070 | 0.181 | 0.102 |
| Metabolism | Energy metabolism | Nitrogen metabolism |  |  | 0.077 | 0.118 |  |
| Metabolism | Energy metabolism | Sulfur metabolism |  |  | 0.078 | 0.118 |  |
| Metabolism | Xenobiotics biodegradation and metabolism | Caprolactam degradation |  |  | 0.084 | 0.140 |  |
| Metabolism | Xenobiotics biodegradation and metabolism | Chloroalkane and chloroalkene degradation |  |  |  | 0.174 | 0.112 |
| Metabolism | Biosynthesis of other secondary metabolites | Betalain biosynthesis |  |  | 0.096 | 0.101 |  |
| Metabolism | Metabolism of terpenoids and polyketides | Biosynthesis of siderophore group nonribosomal peptides |  |  | 0.085 | 0.092 |  |
| Metabolism | Global and overview maps | Microbial metabolism in diverse environments |  |  | 0.099 | 0.128 |  |
| Metabolism | Global and overview maps | Degradation of aromatic compounds |  |  | 0.086 | 0.138 |  |
| Environmental Information Processing | Signal transduction | NF-kappa B signaling pathway | 0.094 | 0.072 | 0.098 | 0.125 |  |
| Metabolism | Xenobiotics biodegradation and metabolism | Atrazine degradation |  | 0.079 |  | 0.131 |  |
| Metabolism | Carbohydrate metabolism | Butanoate metabolism |  |  |  | 0.133 |  |
| Metabolism | Carbohydrate metabolism | C5-Branched dibasic acid metabolism |  |  |  | 0.146 | 0.095 |
| Cellular Processes | Cellular community - prokaryotes | Biofilm formation - Escherichia coli |  |  | 0.083 | 0.068 |  |
| Cellular Processes | Cell motility | Flagellar assembly |  |  | 0.090 | 0.083 |  |
| Metabolism | Metabolism of cofactors and vitamins | Vitamin B6 metabolism |  |  |  | 0.115 |  |
| Metabolism | Metabolism of cofactors and vitamins | Pantothenate and CoA biosynthesis |  |  |  | 0.131 |  |
| Environmental Information Processing | Signal transduction | Hippo signaling pathway - fly | 0.100 | 0.072 | 0.133 | 0.195 |  |
| Metabolism | Biosynthesis of other secondary metabolites | Indole alkaloid biosynthesis | 0.079 | 0.072 |  | 0.104 |  |
| Metabolism | Metabolism of cofactors and vitamins | Retinol metabolism |  |  |  | 0.139 | 0.082 |
| Metabolism | Metabolism of terpenoids and polyketides | Limonene and pinene degradation |  | 0.080 |  | 0.153 | 0.120 |
| Metabolism | Metabolism of terpenoids and polyketides | Carotenoid biosynthesis |  | 0.086 |  | 0.099 | 0.155 |
| Genetic Information Processing | Replication and repair | Non-homologous end-joining |  |  | 0.115 | 0.119 |  |
| Metabolism | Metabolism of terpenoids and polyketides | Insect hormone biosynthesis |  | 0.103 |  | 0.157 | 0.150 |
| Environmental Information Processing | Signal transduction | Hippo signaling pathway - multiple species | 0.100 | 0.072 | 0.133 | 0.195 |  |
| Environmental Information Processing | Signal transduction | Phospholipase D signaling pathway |  |  | 0.074 | 0.085 |  |
| Metabolism | Biosynthesis of other secondary metabolites | Phenylpropanoid biosynthesis |  |  |  | 0.099 | 0.109 |
| Genetic Information Processing | Folding, sorting and degradation | Ubiquitin mediated proteolysis |  |  | 0.158 | 0.177 |  |
| Metabolism | Biosynthesis of other secondary metabolites | Isoflavonoid biosynthesis |  |  |  | 0.107 |  |
| Metabolism | Metabolism of terpenoids and polyketides | Type I polyketide structures | 0.080 | 0.088 |  | 0.116 | 0.098 |
| Metabolism | Biosynthesis of other secondary metabolites | Isoquinoline alkaloid biosynthesis |  |  |  | 0.128 |  |
| Metabolism | Biosynthesis of other secondary metabolites | Tropane, piperidine and pyridine alkaloid biosynthesis |  |  |  | 0.135 | 0.087 |
| Environmental Information Processing | Signal transduction | VEGF signaling pathway | 0.112 |  | 0.133 | 0.170 |  |
| Metabolism | Biosynthesis of other secondary metabolites | Glucosinolate biosynthesis |  |  |  | 0.159 | 0.094 |
| Metabolism | Xenobiotics biodegradation and metabolism | Metabolism of xenobiotics by cytochrome P450 |  |  |  | 0.124 |  |
| Metabolism | Metabolism of terpenoids and polyketides | Biosynthesis of type II polyketide products | 0.076 | 0.090 |  | 0.137 | 0.112 |
| Metabolism | Xenobiotics biodegradation and metabolism | Drug metabolism - cytochrome P450 |  |  |  | 0.125 |  |
| Metabolism | Global and overview maps | Biosynthesis of secondary metabolites |  | 0.090 |  | 0.119 | 0.165 |
| Metabolism | Metabolism of terpenoids and polyketides | Biosynthesis of ansamycins |  |  |  | 0.105 | 0.112 |
| Metabolism | Global and overview maps | Biosynthesis of amino acids |  | 0.084 |  | 0.118 | 0.178 |
| Environmental Information Processing | Signal transduction | Apelin signaling pathway | 0.101 |  | 0.127 | 0.162 |  |
| Metabolism | Metabolism of terpenoids and polyketides | Biosynthesis of vancomycin group antibiotics |  |  |  | 0.088 | 0.097 |
| Genetic Information Processing | Folding, sorting and degradation | Proteasome |  | 0.083 |  | 0.133 | 0.135 |
| Metabolism | Metabolism of terpenoids and polyketides | Biosynthesis of enediyne antibiotics |  |  |  | 0.088 |  |
| Environmental Information Processing | Signal transduction | cAMP signaling pathway |  | 0.069 |  | 0.104 |  |
| Cellular Processes | Cellular community - eukaryotes | Focal adhesion | 0.095 |  | 0.144 | 0.182 |  |
| Environmental Information Processing | Signaling molecules and interaction | ECM-receptor interaction | 0.095 |  | 0.144 | 0.182 |  |
| Metabolism | Global and overview maps | 2-Oxocarboxylic acid metabolism |  |  |  | 0.139 | 0.100 |
| Environmental Information Processing | Membrane transport | ABC transporters |  |  |  | 0.148 | 0.105 |
| Environmental Information Processing | Signal transduction | MAPK signaling pathway - yeast |  |  |  | 0.080 | 0.148 |
| Environmental Information Processing | Signal transduction | MAPK signaling pathway - fly |  |  |  | 0.089 |  |
| Environmental Information Processing | Signal transduction | cGMP-PKG signaling pathway |  |  |  | 0.071 |  |
| Environmental Information Processing | Signal transduction | FoxO signaling pathway |  |  |  | 0.094 | 0.116 |
| Environmental Information Processing | Signaling molecules and interaction | Neuroactive ligand-receptor interaction |  |  |  | 0.071 | 0.090 |
| Cellular Processes | Transport and catabolism | Mitophagy - animal |  |  |  | 0.161 | 0.080 |
| Cellular Processes | Transport and catabolism | Peroxisome |  |  |  | 0.143 | 0.127 |
| Cellular Processes | Cell growth and death | Ferroptosis |  |  |  | 0.139 | 0.141 |
| Cellular Processes | Cell growth and death | Necroptosis |  |  |  | 0.100 | 0.101 |
| Environmental Information Processing | Signal transduction | TNF signaling pathway |  |  |  | 0.161 | 0.080 |
| Metabolism | Carbohydrate metabolism | Glycolysis / Gluconeogenesis |  |  |  | -0.093 |  |
| Metabolism | Lipid metabolism | Fatty acid biosynthesis |  |  |  | -0.127 | -0.074 |
| Metabolism | Lipid metabolism | Primary bile acid biosynthesis |  |  |  | -0.124 | -0.075 |
| Metabolism | Lipid metabolism | Secondary bile acid biosynthesis |  |  |  | -0.126 | -0.089 |
| Metabolism | Energy metabolism | Photosynthesis |  |  |  | -0.110 | -0.090 |
| Metabolism | Nucleotide metabolism | Purine metabolism |  |  |  | -0.134 | -0.078 |
| Metabolism | Nucleotide metabolism | Pyrimidine metabolism |  |  |  | -0.134 | -0.076 |
| Metabolism | Biosynthesis of other secondary metabolites | Prodigiosin biosynthesis |  |  |  | -0.101 |  |
| Metabolism | Metabolism of other amino acids | Taurine and hypotaurine metabolism |  |  |  | -0.122 | -0.118 |
| Metabolism | Metabolism of other amino acids | D-Glutamine and D-glutamate metabolism |  |  |  | -0.120 | -0.095 |
| Metabolism | Metabolism of other amino acids | D-Alanine metabolism |  |  |  | -0.111 |  |
| Metabolism | Glycan biosynthesis and metabolism | Peptidoglycan biosynthesis |  |  |  | -0.115 |  |
| Metabolism | Lipid metabolism | Glycerolipid metabolism |  |  |  | -0.088 |  |
| Metabolism | Carbohydrate metabolism | Inositol phosphate metabolism |  |  |  | -0.110 |  |
| Metabolism | Lipid metabolism | Glycerophospholipid metabolism |  |  |  | -0.099 | -0.152 |
| Metabolism | Glycan biosynthesis and metabolism | Glycosphingolipid biosynthesis - globo and isoglobo series |  |  |  | -0.100 |  |
| Metabolism | Carbohydrate metabolism | Pyruvate metabolism |  |  |  | -0.118 | -0.085 |
| Metabolism | Energy metabolism | Methane metabolism |  |  |  | -0.116 | -0.083 |
| Metabolism | Energy metabolism | Carbon fixation in photosynthetic organisms |  |  |  | -0.123 | -0.118 |
| Metabolism | Energy metabolism | Carbon fixation pathways in prokaryotes |  |  |  | -0.106 | -0.110 |
| Metabolism | Metabolism of cofactors and vitamins | Nicotinate and nicotinamide metabolism |  |  |  | -0.096 | -0.076 |
| Metabolism | Metabolism of cofactors and vitamins | Biotin metabolism |  |  |  | -0.129 | -0.135 |
| Metabolism | Metabolism of terpenoids and polyketides | Terpenoid backbone biosynthesis |  |  |  | -0.111 |  |
| Metabolism | Metabolism of terpenoids and polyketides | Zeatin biosynthesis |  |  |  | -0.133 |  |
| Genetic Information Processing | Translation | Aminoacyl-tRNA biosynthesis |  |  |  | -0.126 |  |
| Metabolism | Global and overview maps | Metabolic pathways |  |  |  | -0.125 | -0.075 |
| Metabolism | Global and overview maps | Carbon metabolism |  |  |  | -0.080 |  |
| Metabolism | Global and overview maps | Fatty acid metabolism |  |  |  | -0.112 | -0.077 |
| Metabolism | Carbohydrate metabolism | Galactose metabolism |  |  | -0.097 | -0.148 |  |
| Metabolism | Carbohydrate metabolism | Starch and sucrose metabolism |  |  | -0.112 | -0.088 | 0.089 |
| Metabolism | Glycan biosynthesis and metabolism | Various types of N-glycan biosynthesis |  |  | -0.073 | -0.115 |  |
| Genetic Information Processing | Translation | Ribosome |  |  |  | -0.129 |  |
| Genetic Information Processing | Translation | RNA transport |  |  |  | -0.148 | -0.083 |
| Genetic Information Processing | Folding, sorting and degradation | RNA degradation |  |  |  | -0.128 |  |
| Genetic Information Processing | Transcription | RNA polymerase |  |  |  | -0.123 |  |
| Genetic Information Processing | Replication and repair | DNA replication |  |  |  | -0.119 |  |
| Metabolism | Carbohydrate metabolism | Amino sugar and nucleotide sugar metabolism |  |  | -0.080 | -0.125 |  |
| Genetic Information Processing | Folding, sorting and degradation | Protein export |  |  |  | -0.126 |  |
| Metabolism | Biosynthesis of other secondary metabolites | Streptomycin biosynthesis |  |  | -0.123 | -0.089 | 0.099 |
| Genetic Information Processing | Replication and repair | Base excision repair |  |  |  | -0.134 |  |
| Genetic Information Processing | Replication and repair | Nucleotide excision repair |  |  |  | -0.115 |  |
| Genetic Information Processing | Replication and repair | Mismatch repair |  |  |  | -0.133 |  |
| Genetic Information Processing | Replication and repair | Homologous recombination |  |  |  | -0.117 |  |
| Environmental Information Processing | Signal transduction | MAPK signaling pathway - plant |  |  |  | -0.123 |  |
| Metabolism | Glycan biosynthesis and metabolism | Glycosaminoglycan degradation |  |  | -0.070 | -0.131 |  |
| Metabolism | Biosynthesis of other secondary metabolites | Flavone and flavonol biosynthesis |  | -0.078 |  | -0.156 | -0.131 |
| Environmental Information Processing | Signal transduction | HIF-1 signaling pathway |  |  |  | -0.127 | -0.092 |
| Environmental Information Processing | Signal transduction | Phosphatidylinositol signaling system |  |  |  | -0.125 | -0.125 |
| Metabolism | Glycan biosynthesis and metabolism | Glycosaminoglycan biosynthesis - heparan sulfate / heparin |  |  | -0.097 | -0.070 | 0.101 |
| Cellular Processes | Cell growth and death | Cell cycle - Caulobacter |  |  |  | -0.148 | -0.096 |
| Cellular Processes | Cell growth and death | Meiosis - yeast |  |  |  | -0.125 |  |
| Metabolism | Glycan biosynthesis and metabolism | Glycosphingolipid biosynthesis - ganglio series |  |  | -0.071 | -0.114 |  |
| Metabolism | Metabolism of cofactors and vitamins | One carbon pool by folate |  |  | -0.084 | -0.142 |  |
| Genetic Information Processing | Folding, sorting and degradation | Protein processing in endoplasmic reticulum |  |  |  | -0.109 | -0.092 |
| Metabolism | Metabolism of cofactors and vitamins | Riboflavin metabolism |  |  | -0.108 | -0.114 |  |
| Metabolism | Xenobiotics biodegradation and metabolism | Drug metabolism - other enzymes |  | -0.071 |  | -0.136 | -0.129 |
| Cellular Processes | Cell growth and death | Apoptosis - fly |  |  |  | -0.101 | -0.069 |
| Environmental Information Processing | Signal transduction | AMPK signaling pathway |  | -0.078 |  | -0.169 | -0.142 |
| Metabolism | Global and overview maps | Biosynthesis of antibiotics |  |  | -0.083 | -0.070 |  |
| Cellular Processes | Transport and catabolism | Lysosome |  |  | -0.077 | -0.112 |  |

a For trait abbreviations see Table 1