Intragenic microRNAs autoregulate their host genes in both direct and indirect ways – a cross-species analysis

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SUPPLEMENTARY INFORMATION
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SUPPLEMENTARY FIGURE AND TABLE LEGENDS

**Supplementary Figure S1**: Flow chart of data acquisition and processing. Validation databases used: *starBase, miRTarBase, TarBase* (yellow hexagons).

**Supplementary Figure S2**: StringDB protein-protein Markov chain cluster analysis of HSA intragenic miRNA host genes. 35 cluster were defined with a number of connected nodes > 5.

**Supplementary Figure S3**: All HSA network-cluster were subject to a g:Profiler enrichment analysis for GO: Biological Process (A), GO:Cellulare Components (B), GO:Molecular Function (C) and KEGG (D). Significant enriched pathways were illustrated by the -log10(p-value).

**Supplementary Figure S4**: StringDB protein-protein Markov chain cluster analysis of MMU intragenic miRNA host genes. 19 cluster were defined with a number of connected nodes > 5.

**Supplementary Figure S5**: All MMU network-cluster were subject to a g:Profiler enrichment analysis for GO: Biological Process (A), GO:Cellulare Components (B), GO:Molecular Function (C) and KEGG (D). Significant enriched pathways were illustrated by the -log10(p-value).

**Supplementary Figure S6**: StringDB protein-protein Markov-chain cluster analysis on DME intragenic miRNA host genes. Two cluster were defined with a number of connected nodes > 5.

**Supplementary Figure S7**: All DME network-cluster were subject to a g:Profiler enrichment analysis for GO: Biological Process (A) and GO:Cellulare Components (B). Significant enriched pathways were illustrated by the -log10(p-value).

**Supplementary Table S1**: List of species miRNA groups and classifications from Ensembl genome catalog.
**Supplementary Tables S2.** Network statistics for protein-protein interaction enrichments.

**Supplementary Tables S3.** Essential vs. non-essential genes for the different miRNA types and species.

**Supplementary Tables S4.** Indirect autoregulation of host gene related protein-protein networks by HSA intragenic miRNAs.

**Supplementary Tables S5.** Indirect autoregulation of host gene related protein-protein networks by MMU intragenic miRNAs.

**Supplementary Tables S6.** Enrichment Table for each separate community in HSA, ranked by the p-value.

**Supplementary Tables S7.** Enrichment Table for each separate community in MMU, ranked by the p-value.

**Supplementary Table S8.** In- and out-degree for each community in the HSA network.

**Supplementary Table S9.** In- and out-degree for each community in the MMU network.
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**LOCATION / DIRECT AUTOREGULATION**

- *Ensembl* metadata
- *miRNAs* / genes
  - miRNA::gene location analysis
  - 189 species
  - HSA, MMU, DME
  - target prediction and IRM modelling
  - host genes
  - HSA, MMU
  - intragenic miRNA::host-gene validation

**FUNCTIONALITY**

- *miRNA host genes*
  - PPI confidence score ≥ 0.4
  - HSA, MMU, DME, DRE
  - *StringDB PPI host gene MCL*
  - cluster::intragenic miRNA prediction and validation
  - HSA, MMU
  - g:Profiler pathway enrichment

**INDIRECT AUTOREGULATION**

- *StringDB metadata*
  - PPI confidence score ≥ 0.9
  - HSA, MMU
  - community detection
  - communities containing > 5 intragenic miRNA host genes
  - intragenic miRNA::community gene validation
Supplementary Figure S3C
Supplementary Figure S3D
| Species Name | # genes | # mirnas | # intragenic | # antisense | # overlapping | Kingdom | Phylum | Class | Order | Family | Genus | Ensembl classification |
|-------------|---------|----------|--------------|-------------|--------------|---------|--------|-------|-------|--------|-------|------------------------|
| E. telfairi | Lesser hedgehog tenrec | 25,609 | 470 | 72 | 28 | 2 | Animalia | Chordata | Mammalia | Afrotheria | Echinops | Fish |
| P. capensis | Hyrax | 18,273 | 624 | 88 | 27 | 0 | Animalia | Chordata | Mammalia | Afrotheria | Procavia | Fish |
| L. africana | Elephant | 22,488 | 757 | 151 | 72 | 2 | Animalia | Chordata | Mammalia | Eutheria | Loxodonta | Mammalia |
| X. tropicalis | Xenopus | 19,588 | 333 | 56 | 14 | 0 | Animalia | Chordata | Amphibia | Anura | Pipidae | Amphibians |
| A. platyrynchos | Duck | 25,832 | 120 | 44 | 11 | 0 | Animalia | Chordata | Aves | Anseriformes | Anseridae | Anser |
| A. brachyrhynchos | Pink-footed goose | 22,530 | 111 | 37 | 10 | 1 | Animalia | Chordata | Aves | Anseriformes | Anseridae | Anser |
| A. haastii | Great spotted kiwi | 19,162 | 99 | 24 | 0 | 0 | Animalia | Chordata | Aves | Apertegyptiformes | Aphelodytidae | Aves |
| A. oweni | Little spotted kiwi | 18,792 | 102 | 33 | 10 | 0 | Animalia | Chordata | Aves | Apertegyptiformes | Aphelodytidae | Aves |
| A. rowi | Okarito brown kiwi | 18,830 | 104 | 34 | 14 | 1 | Animalia | Chordata | Aves | Apertegyptiformes | Aphelodytidae | Aves |
| D. novamundi | Emu | 19,140 | 102 | 40 | 14 | 2 | Animalia | Chordata | Aves | Carpodactyliformes | Scincidae | Aves |
| C. pugnax | Ruff | 19,928 | 124 | 49 | 9 | 0 | Animalia | Chordata | Aves | Apertegyptiformes | Aphelodytidae | Aves |
| C. pygmea | Spoon-billed sandpiper | 18,299 | 123 | 42 | 7 | 1 | Animalia | Chordata | Aves | Carpodactyliformes | Scincidae | Aves |
| N. meleagris | Helmed guineafowl | 23,108 | 149 | 58 | 17 | 1 | Animalia | Chordata | Aves | Galliformes | Numididae | Numida |
| C. japonica | Japanese quail | 21,413 | 148 | 57 | 15 | 0 | Animalia | Chordata | Aves | Galliformes | Phasianidae | Coturnix |
| G. gallus | Chicken | 23,216 | 1,140 | 569 | 155 | 8 | Animalia | Chordata | Aves | Galliformes | Phasianidae | Gallus |
| M. gallopavo | Turkey | 14,572 | 430 | 130 | 49 | 0 | Animalia | Chordata | Aves | Galliformes | Phasianidae | Meleagris |
| L. striata | Bengalese finch | 18,090 | 165 | 56 | 14 | 0 | Animalia | Chordata | Aves | Passeriformes | Estrildidae | Lonchura |
| T. guttata | Zebra finch | 18,316 | 302 | 68 | 37 | 1 | Animalia | Chordata | Aves | Passeriformes | Estrildidae | Taeniopygia |
| S. canaria | Common canary | 17,248 | 132 | 47 | 8 | 2 | Animalia | Chordata | Aves | Passeriformes | Fringillidae | Serinus |
| F. albicollis | Flycatcher | 21,398 | 510 | 146 | 42 | 2 | Animalia | Chordata | Aves | Passeriformes | Muscipulidae | Ficedula |
| C. caeruleus | Blue tit | 24,384 | 125 | 48 | 10 | 3 | Animalia | Chordata | Aves | Passeriformes | Paridae | Cyanister |
| P. major | Great tit | 19,874 | 132 | 63 | 13 | 1 | Animalia | Chordata | Aves | Passeriformes | Paridae | Parus |
| J. hyemalis | Dark-eyed junco | 17,351 | 126 | 47 | 16 | 1 | Animalia | Chordata | Aves | Passeriformes | Passerellidae | Junco |
| Z. albicollis | White-throated sparrow | 18,128 | 124 | 51 | 10 | 1 | Animalia | Chordata | Aves | Passeriformes | Passerellidae | Zonotrichia |
| L. corythaix | Blue-crowned manakin | 16,410 | 126 | 33 | 11 | 0 | Animalia | Chordata | Aves | Passeriformes | Pipridae | Lepidosittix |
| M. vitellinus | Golden-collared manakin | 18,507 | 114 | 48 | 15 | 1 | Animalia | Chordata | Aves | Passeriformes | Pipridae | Manacus |
| M. undulatus | Budgerigar | 16,849 | 96 | 27 | 10 | 0 | Animalia | Chordata | Aves | Passeriformes | Ptilastrachidae | Melopsittica |
| N. perdicaria | Chilean tinamou | 16,175 | 87 | 23 | 5 | 0 | Animalia | Chordata | Aves | Tinamiformes | Tinamidae | Tinamidae |
| C. pororus | Australian saltwater crocodile | 19,909 | 114 | 43 | 10 | 2 | Animalia | Chordata | Aves | Reptilia | Crocodylia | Crocodylus |
| S. punctatus | Tuatara | 23,086 | 123 | 24 | 5 | 1 | Animalia | Chordata | Aves | Reptilia | Teiidae | Sphenodon |
| P. viticeps | Central bearded dragon | 25,967 | 45 | 22 | 6 | 0 | Animalia | Chordata | Aves | Reptilia | Squamata | Agamidae |
| A. carolinensis | Anole lizard | 25,497 | 423 | 101 | 57 | 0 | Animalia | Chordata | Aves | Reptilia | Squamata | Anguidae |
| N. scutatus | Mainland tiger snake | 20,505 | 134 | 30 | 2 | 1 | Animalia | Chordata | Aves | Reptilia | Squamata | Elapidae |
| S. merianae | Argentine black and white tegu | 23,653 | 40 | 18 | 2 | 1 | Animalia | Chordata | Aves | Reptilia | Squamata | Teiidae |
| C. picta | Painted turtle | 26,547 | 270 | 109 | 26 | 2 | Animalia | Chordata | Aves | Reptilia | Testudines | Emydidae |
| C. albidus | Abingdon island giant tortoise | 23,086 | 123 | 24 | 5 | 1 | Animalia | Chordata | Aves | Reptilia | Testudines | Cheloniidae |
| G. agassizii | Agassiz’s desert tortoise | 24,134 | 115 | 13 | 4 | 0 | Animalia | Chordata | Aves | Reptilia | Therapsidae | Gopherus |
| P. sinensis | Chinese softshell turtle | 18,812 | 516 | 109 | 83 | 5 | Animalia | Chordata | Aves | Reptilia | Testudines | Trionychidae |
| A. testudineus | Climbing perch | 25,067 | 97 | 28 | 7 | 0 | Animalia | Chordata | Aves | Actinopterygii | Anabantiformes | Anabantoidei |
| O. latipes | Sailfin molly | 22,543 | 128 | 37 | 10 | 0 | Animalia | Chordata | Aves | Actinopterygii | Anabantiformes | Anabantoidei |
| O. latipes | Sailfin molly | 23,189 | 127 | 28 | 12 | 0 | Animalia | Chordata | Aves | Actinopterygii | Anabantiformes | Anabantoidei |
| O. latipes | Sailfin molly | 24,130 | 130 | 42 | 14 | 1 | Animalia | Chordata | Aves | Actinopterygii | Anabantiformes | Anabantoidei |
| O. latipes | Sailfin molly | 26,920 | 196 | 101 | 51 | 1 | Animalia | Chordata | Aves | Actinopterygii | Anabantiformes | Anabantoidei |
| D. retio | Zebrafish | 36,807 | 434 | 137 | 82 | 5 | Animalia | Chordata | Aves | Actinopterygii | Cyprinodontiformes | Cyprinidae |
| K. marmoratus | Mangrove rivulus | 22,236 | 78 | 22 | 4 | 0 | Animalia | Chordata | Aves | Actinopterygii | Cyprinodontiformes | Acheilognathidae |
-supplementary_table_s_1__list_of_species_miRNA_groups_and_classifications_from_Ensembl_genome_catalog
| Common Name                     | Scientific Name                        | Kingdom       | Phylum        | Class          | Order          | Family       | Subclass     | Superorder   | Order           | Class          | Subclass | Kingdom       |
|--------------------------------|----------------------------------------|---------------|---------------|----------------|----------------|--------------|--------------|--------------|----------------|----------------|-----------|---------------|
| C. vanegatus                   | Sheephead minnow                       | Animalia      | Chordata      | Mammalia       | Chiroptera     | Vespertilionidae | Laurasiatheria |             |                |                |           |               |
| M. lucifugus                   | Bat                                    | Animalia      | Chordata      | Mammalia       | Chiroptera     | Vespertilionidae | Laurasiatheria |             |                |                |           |               |
| P. vampyrus                    | Flying fox                             | Animalia      | Chordata      | Mammalia       | Chiroptera     | Pteropodidae   | Laurasiatheria |             |                |                |           |               |
| U. americanus                  | American black bear                    | Animalia      | Chordata      | Mammalia       | Carnivora     | Ursidae       | Laurasiatheria |             |                |                |           |               |
| A. melanoleuca                 | Giant panda                            | Animalia      | Chordata      | Mammalia       | Carnivora     | Ursidae       | Laurasiatheria |             |                |                |           |               |
| N. vison                       | American mink                          | Animalia      | Chordata      | Mammalia       | Carnivora     | Mustelidae    | Laurasiatheria |             |                |                |           |               |
| J. doméstica                   | Domestic cat                            | Animalia      | Chordata      | Mammalia       | Carnivora     | Felidae       | Laurasiatheria |             |                |                |           |               |
| V. vulpes                      | Red fox                                | Animalia      | Chordata      | Mammalia       | Carnivora     | Canidae       | Laurasiatheria |             |                |                |           |               |
| B. taurus                      | Brown bear                             | Animalia      | Chordata      | Mammalia       | Carnivora     | Ursidae       | Laurasiatheria |             |                |                |           |               |
| B. bison                       | American bison                         | Animalia      | Chordata      | Mammalia       | Carnivora     | Bovidae       | Laurasiatheria |             |                |                |           |               |
| B. mutus                       | Wild yak                               | Animalia      | Chordata      | Mammalia       | Carnivora     | Bovidae       | Laurasiatheria |             |                |                |           |               |
| B. taurus                      | Domestic horse                         | Animalia      | Chordata      | Mammalia       | Carnivora     | Equidae       | Laurasiatheria |             |                |                |           |               |
| F. heterofuscus                | Mammal man                              | Animalia      | Chordata      | Mammalia       | Primata       | Primates      | Laurasiatheria |             |                |                |           |               |
| T. rubripes                    | Fugu                                   | Animalia      | Chordata      | Actinopterygii | Siluriformes   | Cyprinodontidae | Laurasiatheria |             |                |                |           |               |
| T.igneris                      | Silver dollar                          | Animalia      | Chordata      | Actinopterygii | Siluriformes   | Cyprinodontidae | Laurasiatheria |             |                |                |           |               |
| X. couchanus                   | Mediterranean platyfish                | Animalia      | Chordata      | Actinopterygii | Pisciformes    | Cyprinodontidae | Laurasiatheria |             |                |                |           |               |
| X. vagus                       | Atlantic salmon trout                  | Animalia      | Chordata      | Actinopterygii | Perciformes    | Cyprinodontidae | Laurasiatheria |             |                |                |           |               |
| X. couchanus                   | Rainbow trout                          | Animalia      | Chordata      | Actinopterygii | Perciformes    | Cyprinodontidae | Laurasiatheria |             |                |                |           |               |
| X. couchanus                   | Channel catfish                        | Animalia      | Chordata      | Actinopterygii | Perciformes    | Cyprinodontidae | Laurasiatheria |             |                |                |           |               |
| X. couchanus                   | Yestrum]{channel catfish}              | Animalia      | Chordata      | Actinopterygii | Perciformes    | Cyprinodontidae | Laurasiatheria |             |                |                |           |               |
| S. maximus                     | Turbot                                 | Animalia      | Chordata      | Actinopterygii | Siluriformes   | Cyprinodontidae | Laurasiatheria |             |                |                |           |               |
| D. electricus                  | Electric eel                           | Animalia      | Chordata      | Actinopterygii | Siluriformes   | Cyprinodontidae | Laurasiatheria |             |                |                |           |               |
| F. heteroclitus                | Perch                                  | Animalia      | Chordata      | Actinopterygii | Siluriformes   | Cyprinodontidae | Laurasiatheria |             |                |                |           |               |
| C. variegatus                  | Sheepshead minnow                      | Animalia      | Chordata      | Actinopterygii | Siluriformes   | Cyprinodontidae | Laurasiatheria |             |                |                |           |               |
| P. reticulata                  | Sailfin Molly                          | Animalia      | Chordata      | Actinopterygii | Siluriformes   | Cyprinodontidae | Laurasiatheria |             |                |                |           |               |
| X. couchanus                   | Channel catfish                        | Animalia      | Chordata      | Actinopterygii | Siluriformes   | Cyprinodontidae | Laurasiatheria |             |                |                |           |               |
| X. couchanus                   | Rainbow trout                          | Animalia      | Chordata      | Actinopterygii | Perciformes    | Cyprinodontidae | Laurasiatheria |             |                |                |           |               |
| X. couchanus                   | Yestrum}{channel catfish}              | Animalia      | Chordata      | Actinopterygii | Perciformes    | Cyprinodontidae | Laurasiatheria |             |                |                |           |               |
| P. reticulata                  | Sailfin Molly                          | Animalia      | Chordata      | Actinopterygii | Siluriformes   | Cyprinodontidae | Laurasiatheria |             |                |                |           |               |
| X. couchanus                   | Channel catfish                        | Animalia      | Chordata      | Actinopterygii | Perciformes    | Cyprinodontidae | Laurasiatheria |             |                |                |           |               |
| X. couchanus                   | Rainbow trout                          | Animalia      | Chordata      | Actinopterygii | Perciformes    | Cyprinodontidae | Laurasiatheria |             |                |                |           |               |
| X. couchanus                   | Yestrum}{channel catfish}              | Animalia      | Chordata      | Actinopterygii | Perciformes    | Cyprinodontidae | Laurasiatheria |             |                |                |           |               |
| P. reticulata                  | Sailfin Molly                          | Animalia      | Chordata      | Actinopterygii | Siluriformes   | Cyprinodontidae | Laurasiatheria |             |                |                |           |               |
| X. couchanus                   | Channel catfish                        | Animalia      | Chordata      | Actinopterygii | Perciformes    | Cyprinodontidae | Laurasiatheria |             |                |                |           |               |
| X. couchanus                   | Rainbow trout                          | Animalia      | Chordata      | Actinopterygii | Perciformes    | Cyprinodontidae | Laurasiatheria |             |                |                |           |               |
| X. couchanus                   | Yestrum}{channel catfish}              | Animalia      | Chordata      | Actinopterygii | Perciformes    | Cyprinodontidae | Laurasiatheria |             |                |                |           |               |
| P. reticulata                  | Sailfin Molly                          | Animalia      | Chordata      | Actinopterygii | Siluriformes   | Cyprinodontidae | Laurasiatheria |             |                |                |           |               |
| X. couchanus                   | Channel catfish                        | Animalia      | Chordata      | Actinopterygii | Perciformes    | Cyprinodontidae | Laurasiatheria |             |                |                |           |               |
| X. couchanus                   | Rainbow trout                          | Animalia      | Chordata      | Actinopterygii | Perciformes    | Cyprinodontidae | Laurasiatheria |             |                |                |           |               |
| X. couchanus                   | Yestrum}{channel catfish}              | Animalia      | Chordata      | Actinopterygii | Perciformes    | Cyprinodontidae | Laurasiatheria |             |                |                |           |               |
| P. reticulata                  | Sailfin Molly                          | Animalia      | Chordata      | Actinopterygii | Siluriformes   | Cyprinodontidae | Laurasiatheria |             |                |                |           |               |
| X. couchanus                   | Channel catfish                        | Animalia      | Chordata      | Actinopterygii | Perciformes    | Cyprinodontidae | Laurasiatheria |             |                |                |           |               |
| X. couchanus                   | Rainbow trout                          | Animalia      | Chordata      | Actinopterygii | Perciformes    | Cyprinodontidae | Laurasiatheria |             |                |                |           |               |
| X. couchanus                   | Yestrum}{channel catfish}              | Animalia      | Chordata      | Actinopterygii | Perciformes    | Cyprinodontidae | Laurasiatheria |             |                |                |           |               |
| P. reticulata                  | Sailfin Molly                          | Animalia      | Chordata      | Actinopterygii | Siluriformes   | Cyprinodontidae | Laurasiatheria |             |                |                |           |               |
| X. couchanus                   | Channel catfish                        | Animalia      | Chordata      | Actinopterygii | Perciformes    | Cyprinodontidae | Laurasiatheria |             |                |                |           |               |
| X. couchanus                   | Rainbow trout                          | Animalia      | Chordata      | Actinopterygii | Perciformes    | Cyprinodontidae | Laurasiatheria |             |                |                |           |               |
| X. couchanus                   | Yestrum}{channel catfish}              | Animalia      | Chordata      | Actinopterygii | Perciformes    | Cyprinodontidae | Laurasiatheria |             |                |                |           |               |
| Species | Common Name | Common English Name | Genus | Family | Order | Class | Phylum | Kingdom | Other Information |
|---------|-------------|---------------------|-------|--------|-------|-------|-------|---------|------------------|
| E. europeae | Hedgehog | Erinaceus europaeus | Erinaceus | Erinaceidae | Eutheria | Chordata | Chordata | Animalia |  |
| S. araneus | Shrew | Sorex araneus | Sorex | Soricidae | Eutheria | Chordata | Chordata | Animalia |  |
| E. africanus | Donkey | Equus asinus | Equus | Equidae | Eutheria | Chordata | Chordata | Animalia |  |
| E. forus caballus | Horse | Equus africanus | Equus | Equidae | Eutheria | Chordata | Chordata | Animalia |  |
| C. intestinalis | Cintestinals | Ctenocephalides canis | Ctenocephalides | Ctenocephalidae | Eutheria | Chordata | Chordata | Animalia |  |
| C. tingitanus | Tingitanus | Ctenocephalides canis | Ctenocephalides | Ctenocephalidae | Eutheria | Chordata | Chordata | Animalia |  |
| E. ferus caballus | Donkey | Equus asinus | Equus | Equidae | Eutheria | Chordata | Chordata | Animalia |  |
| E. forus caballus | Horse | Equus africanus | Equus | Equidae | Eutheria | Chordata | Chordata | Animalia |  |
| C. intestinalis | Cintestinals | Ctenocephalides canis | Ctenocephalides | Ctenocephalidae | Eutheria | Chordata | Chordata | Animalia |  |
| C. tingitanus | Tingitanus | Ctenocephalides canis | Ctenocephalides | Ctenocephalidae | Eutheria | Chordata | Chordata | Animalia |  |
| E. ferus caballus | Donkey | Equus asinus | Equus | Equidae | Eutheria | Chordata | Chordata | Animalia |  |
| E. forus caballus | Horse | Equus africanus | Equus | Equidae | Eutheria | Chordata | Chordata | Animalia |  |
| C. intestinalis | Cintestinals | Ctenocephalides canis | Ctenocephalides | Ctenocephalidae | Eutheria | Chordata | Chordata | Animalia |  |
| C. tingitanus | Tingitanus | Ctenocephalides canis | Ctenocephalides | Ctenocephalidae | Eutheria | Chordata | Chordata | Animalia |  |
| Species                      | Common Name                  | Scientific Name                        | Size   | Mass  | Tail | Ear | Body | Genus | Family | Order | Subclass | Class | Phylum |
|-----------------------------|------------------------------|----------------------------------------|--------|-------|------|-----|------|-------|--------|--------|----------|-------|---------|
| P. maniculatus              | Northern American deer mouse| Peromyscus maniculatus                | 25,220 | 174   | 54   | 15  | 0    | Animalia | Chordata | Mammalia | Rodentia | Cricetidae | Rodents |
| J. jaculus                  | Lesser Egyptian jerboa      | Jaculus jaculus                       | 24,124 | 309   | 80   | 37  | 6    | Animalia | Chordata | Mammalia | Rodentia | Dipodidae | Jaculus Rodents |
| H. glaber female            | Naked mole-rat female       | Heterocephalus glaber                | 31,322 | 484   | 169  | 62  | 7    | Animalia | Chordata | Mammalia | Rodentia | Heterocephalidae | Heterocephalus Rodents |
| H. glaber male              | Naked mole-rat male         | Heterocephalus glaber                | 32,295 | 452   | 145  | 41  | 5    | Animalia | Chordata | Mammalia | Rodentia | Heterocephalidae | Heterocephalus Rodents |
| D. ordi                     | Kangaroo rat                | Dipodomys ordii                      | 20,140 | 402   | 113  | 34  | 5    | Animalia | Chordata | Mammalia | Rodentia | Heteromyidae | Dipodomyd Rodents |
| M. unguiculatus             | Mongolian gerbil             | Meriones unguiculatus                | 25,576 | 169   | 42   | 9   | 1    | Animalia | Chordata | Mammalia | Rodentia | Meriones | Rodents |
| M. caroli                   | Ryukyu mouse                | Mus caroli                           | 35,291 | 1,491 | 855  | 313 | 47   | Animalia | Chordata | Mammalia | Rodentia | Muridae | Mus Rodents |
| M. musculus                 | Mouse                        | Mus musculus                         | 54,128 | 2,265 | 1204 | 447 | 67   | Animalia | Chordata | Mammalia | Rodentia | Muridae | Mus Rodents |
| M. pahari                   | Shrew mouse                 | Spermophilus pahari                  | 33,703 | 1,385 | 817  | 259 | 47   | Animalia | Chordata | Mammalia | Rodentia | Muridae | Mus Rodents |
| M. spicilegus               | Steppe mouse                | Spermophilus spicilegus               | 30,274 | 598   | 292  | 57  | 14   | Animalia | Chordata | Mammalia | Rodentia | Muridae | Mus Rodents |
| M. spretus                  | Algerian mouse              | Meriones spretus                      | 36,943 | 1,614 | 885  | 288 | 47   | Animalia | Chordata | Mammalia | Rodentia | Muridae | Mus Rodents |
| R. norvegicus               | Rat                          | Rattus norvegicus                    | 31,295 | 1,388 | 489  | 216 | 44   | Animalia | Chordata | Mammalia | Rodentia | Muridae | Rattus Rodents |
| O. degus                    | Degu                         | Octodon degus                        | 25,438 | 405   | 123  | 42  | 5    | Animalia | Chordata | Mammalia | Rodentia | Octodontidae | Octodon Rodents |
| I. tridcemlineatus          | Squirrel                     | Ictidomys tridcemlineatus            | 24,742 | 459   | 161  | 53  | 4    | Animalia | Chordata | Mammalia | Rodentia | Sciuridae | Ictidomyd Rodents |
| M. marmota                  | Alpine marmot               | Marmota marmota                      | 23,856 | 168   | 46   | 11  | 0    | Animalia | Chordata | Mammalia | Rodentia | Sciuridae | Marmota Rodents |
| S. balearicus               | Daurian ground squirrel     | Spermophilus balearicus              | 24,820 | 175   | 47   | 8   | 0    | Animalia | Chordata | Mammalia | Rodentia | Sciuridae | Spermophilus Rodents |
| U. paryyi                   | Arctic ground squirrel      | Uroctellus paryyi                    | 25,340 | 175   | 69   | 13  | 1    | Animalia | Chordata | Mammalia | Rodentia | Sciuridae | Uroctellus Rodents |
| S. galii                    | Upper Galilee mountains blind mole rat | | 24,054 | 582   | 130  | 40  | 10   | Animalia | Chordata | Mammalia | Rodentia | Spalacidae | Spalax Rodents |
| T. belangeri                | Tree Shrew                  | Tupaiidae belangeri                 | 20,217 | 640   | 74   | 45  | 0    | Animalia | Chordata | Mammalia | Scandentia | Tupaiidae | Tupai Rodents |
| D. novemcinctus             | Armadillo                   | Dasypodidae novemcinctus             | 32,533 | 841   | 203  | 108 | 2    | Animalia | Chordata | Mammalia | Rodentia | Dasypodidae | Dasypus Xenarthra |
| C. hoffmanii                | Sloth                        | Choloepodidae hoffmanii             | 15,510 | 550   | 47   | 14  | 5    | Animalia | Chordata | Mammalia | Rodentia | Choloepodidae | Choloepus Xenarthra |
### Supplementary Table S2. Network statistics for protein-protein interaction enrichments

|                                | HSA  | MMU  | DME  |
|--------------------------------|------|------|------|
| number of nodes                | 909  | 595  | 126  |
| number of edges                | 4078 | 1456 | 71   |
| expected number of edges       | 3647 | 1307 | 46   |
| average node degree            | 8.97 | 4.89 | 1.13 |
| average local clustering coeff | 0.3  | 0.333| 0.318|
| p-value                        | 1.23E-12 | 2.68E-05 | 4.26E-04 |
Supplementary Table S3. Essential vs. non-essential genes for the different miRNA types and species

| species | intragenic | essential | non-essential |
|---------|-----------|-----------|---------------|
| HSA     | 444       | 493       |               |
| MMU     | 283       | 391       |               |
| DME     | 8         | 119       |               |
| antisense |         |           |               |
| HSA     | 81        | 133       |               |
| MMU     | 30        | 91        |               |
| DME     | 2         | 20        |               |
| overlapping |   |           |               |
| HSA     | 3         | 3         |               |
| MMU     | 1         | 3         |               |
| DME     | 0         | 3         |               |
Supplementary Table S4. Indirect autoregulation of host gene related protein-protein networks by HSA intragenic miRNAs

| community | # validated miRNAs | gene number | mRNA number | ratio genes | ratio miRNAs | interaction ratio |
|-----------|--------------------|-------------|-------------|-------------|--------------|------------------|
| 28        | 34                 | 60          | 18          | 0.57        | 1.89         | 3.15             |
| 11        | 216                | 264         | 36          | 0.82        | 6.00         | 2.27             |
| 35        | 56                 | 318         | 9           | 0.18        | 6.22         | 1.96             |
| 8         | 5745               | 1172        | 264         | 4.90        | 21.76        | 1.86             |
| 4         | 2585               | 994         | 141         | 2.60        | 18.33        | 1.84             |
| 7         | 192                | 209         | 51          | 0.92        | 3.76         | 1.80             |
| 13        | 573                | 398         | 81          | 1.44        | 7.07         | 1.78             |
| 6         | 1857               | 779         | 150         | 2.38        | 12.38        | 1.59             |
| 12        | 567                | 484         | 78          | 1.17        | 7.27         | 1.50             |
| 16        | 482                | 395         | 99          | 1.22        | 4.87         | 1.23             |
| 3         | 532                | 531         | 93          | 1.00        | 5.72         | 1.08             |
| 0         | 879                | 575         | 150         | 1.53        | 5.86         | 1.02             |
| 5         | 3939               | 1334        | 300         | 2.95        | 13.13        | 0.98             |
| 19        | 190                | 340         | 57          | 0.56        | 3.33         | 0.98             |
| 15        | 78                 | 182         | 45          | 0.43        | 1.73         | 0.95             |
| 30        | 3                  | 53          | 6           | 0.06        | 0.50         | 0.94             |
| 10        | 757                | 644         | 126         | 1.18        | 6.01         | 0.93             |
| 23        | 32                 | 124         | 30          | 0.26        | 1.07         | 0.86             |
| 14        | 483                | 542         | 105         | 0.89        | 4.60         | 0.85             |
| 18        | 76                 | 345         | 30          | 0.22        | 2.53         | 0.73             |
| 9         | 367                | 560         | 96          | 0.66        | 3.82         | 0.68             |
| 1         | 28                 | 146         | 30          | 0.19        | 0.93         | 0.64             |
| 2         | 22                 | 185         | 27          | 0.12        | 0.81         | 0.44             |
| 20        | 11                 | 108         | 27          | 0.10        | 0.41         | 0.38             |
| 22        | 0                  | 72          | 6           | 0.00        | 0.00         | 0.00             |
| 33        | 0                  | 49          | 6           | 0.00        | 0.00         | 0.00             |
## Supplementary Table S5. Indirect autoregulation of host gene related protein-protein networks by MMU intragenic miRNAs

| community | # validated miRNAs | gene number | miRNA number | ratio genes | ratio miRNAs | interaction ratio |
|-----------|--------------------|-------------|--------------|-------------|--------------|-------------------|
| 66        | 8                  | 20          | 12           | 0.40        | 0.67         | 3.33              |
| 1         | 11                 | 79          | 6            | 0.14        | 1.83         | 2.32              |
| 33        | 2                  | 10          | 9            | 0.20        | 0.22         | 2.22              |
| 28        | 35                 | 98          | 18           | 0.36        | 1.94         | 1.98              |
| 5         | 298                | 327         | 51           | 0.91        | 5.84         | 1.79              |
| 6         | 1540               | 868         | 117          | 1.77        | 13.16        | 1.52              |
| 3         | 275                | 381         | 51           | 0.72        | 5.39         | 1.42              |
| 13        | 830                | 746         | 93           | 1.11        | 8.92         | 1.20              |
| 12        | 191                | 427         | 39           | 0.45        | 4.90         | 1.15              |
| 7         | 269                | 464         | 54           | 0.58        | 4.98         | 1.07              |
| 0         | 163                | 356         | 51           | 0.46        | 3.20         | 0.90              |
| 8         | 1513               | 1064        | 186          | 1.42        | 8.13         | 0.76              |
| 23        | 13                 | 121         | 18           | 0.11        | 0.72         | 0.60              |
| 27        | 3                  | 91          | 6            | 0.03        | 0.50         | 0.55              |
| 10        | 137                | 522         | 48           | 0.26        | 2.85         | 0.55              |
| 17        | 7                  | 86          | 15           | 0.08        | 0.47         | 0.54              |
| 22        | 20                 | 218         | 18           | 0.09        | 1.11         | 0.51              |
| 20        | 14                 | 161         | 21           | 0.09        | 0.67         | 0.41              |
| 16        | 138                | 453         | 75           | 0.30        | 1.84         | 0.41              |
| 15        | 27                 | 229         | 30           | 0.12        | 0.90         | 0.39              |
| 30        | 13                 | 149         | 24           | 0.09        | 0.54         | 0.36              |
| 11        | 15                 | 254         | 21           | 0.06        | 0.71         | 0.28              |
| 9         | 6                  | 182         | 12           | 0.03        | 0.50         | 0.27              |
| 14        | 85                 | 495         | 63           | 0.17        | 1.35         | 0.27              |
| 4         | 62                 | 487         | 51           | 0.13        | 1.22         | 0.25              |
| 19        | 15                 | 444         | 21           | 0.03        | 0.71         | 0.16              |
| 21        | 0                  | 60          | 6            | 0.00        | 0.00         | 0.00              |
| 29        | 0                  | 51          | 6            | 0.00        | 0.00         | 0.00              |
| GO-Terms | description                        | source | p-value        | community |
|----------|------------------------------------|--------|---------------|-----------|
| KEGG:00564 | Glycerophospholipid metabolism    | KEGG   | 8.75376E-50   | 0         |
| GO:0008076 | voltage-gated potassium channel complex | GO:CC  | 1.8449E-37    | 0         |
| KEGG:04140 | Autophagy - animal                | KEGG   | 9.57788E-35   | 0         |
| KEGG:00600 | Sphingolipid metabolism           | KEGG   | 2.43173E-34   | 0         |
| GO:0005251 | delayed rectifier potassium channel activity | GO:MF  | 4.00956E-31   | 0         |
| KEGG:04150 | mTOR signaling pathway            | KEGG   | 1.51866E-27   | 0         |
| KEGG:04136 | Autophagy - other                | KEGG   | 4.92177E-27   | 0         |
| GO:000421 | autophagosome membrane            | GO:CC  | 1.38055E-19   | 0         |
| GO:0046513 | ceramide biosynthetic process     | GO:BP  | 2.44482E-19   | 0         |
| GO:0005789 | endoplasmic reticulum membrane    | GO:CC  | 1.19851E-18   | 0         |
| GO:000422 | autophagy of mitochondrion        | GO:BP  | 7.58406E-18   | 0         |
| GO:0005765 | lysosomal membrane                | GO:CC  | 5.02655E-17   | 0         |
| GO:0061952 | midbody abscission                | GO:BP  | 6.32525E-16   | 0         |
| GO:0051260 | protein homooligomerization       | GO:BP  | 3.525E-14     | 0         |
| GO:0034045 | phagophore assembly site membrane | GO:CC  | 1.2706E-13    | 0         |
| KEGG:0031932 | TORC2 complex                     | GO:CC  | 1.61458E-13   | 0         |
| KEGG:04211 | Longevity regulating pathway      | KEGG   | 2.35839E-13   | 0         |
| KEGG:04152 | AMPK signaling pathway            | KEGG   | 1.90445E-12   | 0         |
| KEGG:00565 | Ether lipid metabolism            | KEGG   | 3.88153E-12   | 0         |
| GO:0008813 | ESCRT I complex                  | GO:CC  | 6.42762E-12   | 0         |
| GO:0016024 | CDP-diacylglycerol biosynthetic process | GO:BP  | 6.60146E-12   | 0         |
| GO:1902188 | positive regulation of viral release from host cell | GO:BP  | 2.80176E-11   | 0         |
| KEGG:04810 | Regulation of actin cytoskeleton  | KEGG   | 3.14796E-89   | 1         |
| KEGG:04360 | Axon guidance                     | KEGG   | 8.15413E-82   | 1         |
| KEGG:04015 | Rap1 signaling pathway            | KEGG   | 6.94719E-70   | 1         |
| KEGG:04014 | Ras signaling pathway             | KEGG   | 1.37513E-67   | 1         |
| KEGG:04510 | Focal adhesion                    | KEGG   | 4.31344E-65   | 1         |
| KEGG:04151 | PI3K-Akt signaling pathway        | KEGG   | 6.36676E-61   | 1         |
| KEGG:04630 | JAK-STAT signaling pathway        | KEGG   | 1.60698E-52   | 1         |
| KEGG:04010 | MAPK signaling pathway            | KEGG   | 2.7643E-52    | 1         |
| GO:0008360 | regulation of cell shape          | GO:BP  | 2.99581E-49   | 1         |
| GO:0005925 | focal adhesion                    | GO:CC  | 6.52815E-49   | 1         |
| KEGG:00562 | inositol phosphate metabolism     | KEGG   | 6.95334E-44   | 1         |
| KEGG:04012 | ErbB signaling pathway            | KEGG   | 2.82346E-40   | 1         |
| GO:0005096 | GTPase activator activity         | GO:MF  | 1.18424E-37   | 1         |
| KEGG:01521 | EGFR tyrosine kinase inhibitor resistance | KEGG   | 1.82731E-37   | 1         |
| GO:0098978 | glutamatergic synapse             | GO:CC  | 6.37348E-36   | 1         |
| GO:0005829 | cytosol                           | GO:CC  | 7.02894E-36   | 1         |
| KEGG:005200 | Pathways in cancer                | KEGG   | 7.55941E-36   | 1         |
| KEGG:04070 | Phosphatidylinositol signaling system | KEGG   | 1.28306E-35   | 1         |
| GO:0007229 | integrin-mediated signaling pathway | GO:BP  | 4.37133E-34   | 1         |
| KEGG:04722 | Neurotrophin signaling pathway    | KEGG   | 5.08711E-33   | 1         |
| GO:0048013 | ephrin receptor signaling pathway | GO:BP  | 1.3818E-32    | 1         |
| GO:0051015 | actin filament binding            | GO:MF  | 4.27817E-32   | 1         |
| KEGG:05205 | Proteoglycans in cancer           | KEGG   | 8.82683E-30   | 1         |
| GO:0017124 | SH3 domain binding               | GO:MF  | 1.32455E-29   | 1         |
| KEGG:04664 | Fc epsilon RI signaling pathway   | KEGG   | 2.49902E-28   | 1         |
| KEGG:04666 | Fc gamma R-mediated phagocytosis   | KEGG   | 8.06999E-28   | 1         |
| GO:0005524 | ATP binding                       | GO:MF  | 2.08157E-27   | 1         |
| GO:0005516 | calmodulin binding               | GO:MF  | 1.25433E-26   | 1         |
| KEGG:05135 | Yersinia infection               | KEGG   | 1.07849E-25   | 1         |
| KEGG:05218 | Melanoma                         | KEGG   | 1.33566E-25   | 1         |
| GO:0008083 | growth factor activity            | GO:MF  | 2.04396E-24   | 1         |
| KEGG:04660 | T cell receptor signaling pathway | KEGG   | 3.09459E-24   | 1         |
GO:0008285 negative regulation of cell population proliferation
GO:BP 3.50155E-13 1
KEGG:04640 Hematopoietic cell lineage
KEGG 3.61431E-13 1
KEGG:04210 Apoptosis
KEGG 9.73427E-13 1
KEGG:04659 Th17 cell differentiation
KEGG 1.28413E-12 1
KEGG:05226 Gastric cancer
KEGG 1.30842E-12 1
GO:0030018 Z disc
GO:CC 1.5357E-12 1
GO:0030165 PDZ domain binding
GO:MF 2.04083E-12 1
KEGG:05215 Prostate cancer
KEGG 4.27916E-12 1
KEGG:05221 Acute myeloid leukemia
KEGG 3.3752E-12 1
GO:0000187 activation of MAPK activity
GO:BP 3.67304E-12 1
KEGG:05220 Gastric cancer
KEGG 5.79016E-12 1
KEGG:04659 Th17 cell differentiation
KEGG 1.28413E-12 1
KEGG:04625 C-type lectin receptor signaling pathway
KEGG 5.79701E-12 1
KEGG:04625 C-type lectin receptor signaling pathway
KEGG 5.79701E-12 1
GO:0032982 myosin filament
GO:CC 7.16826E-12 1
KEGG:04520 Adherens junction
KEGG 1.23243E-11 1
KEGG:05321 Inflammatory bowel disease (IBD)
KEGG 1.29151E-11 1
GO:1902287 semaphorin-plexin signaling pathway involved in axon guidance
GO:BP 1.99814E-11 1
GO:0016601 Rac protein signal transduction
GO:BP 2.01013E-11 1
GO:0030336 negative regulation of cell migration
GO:BP 2.49148E-11 1
GO:0090630 activation of GTPase activity
GO:BP 3.50886E-11 1
GO:0017154 sarcomere organization
GO:BP 4.0984E-11 1
GO:0043525 negative regulation of neuron apoptotic process
GO:BP 4.73207E-11 1
GO:0044331 cell-cell adhesion mediated by cadherin
GO:BP 5.65967E-11 1
GO:0045214 sarcomere organization
GO:BP 6.18626E-11 1
GO:0043524 negative regulation of neuron apoptotic process
GO:BP 7.77016E-11 1
KEGG:04658 Th1 and Th2 cell differentiation
KEGG 8.27435E-11 1
KEGG:04080 Neuroactive ligand-receptor interaction
KEGG 8.33437E-11 1
GO:0007218 chemokine-mediated signaling pathway
GO:BP 8.62748E-47 2
KEGG:04658 Th1 and Th2 cell differentiation
KEGG 8.27435E-11 1
KEGG:04080 Neuroactive ligand-receptor interaction
KEGG 8.33437E-11 1
KEGG:04080 Neuroactive ligand-receptor interaction
KEGG 8.33437E-11 1
GO:0005834 heterotrimeric G-protein complex
GO:CC 1.66751E-36 2
GO:0070098 chemokine-mediated signaling pathway
GO:BP 1.99814E-11 1
GO:0042923 neuropeptide binding
GO:MF 3.68767E-27 2
KEGG:04723 Retrograde endocannabinoid signaling
KEGG 5.51902E-26 2
KEGG:04723 Retrograde endocannabinoid signaling
KEGG 5.51902E-26 2
GO:0042923 neuropeptide binding
GO:MF 3.68767E-27 2
GO:0043950 positive regulation of cAMP-mediated signaling
GO:BP 3.85012E-23 2
GO:0043950 positive regulation of cAMP-mediated signaling
GO:BP 3.85012E-23 2
GO:0043950 positive regulation of cAMP-mediated signaling
GO:BP 3.85012E-23 2
GO:0043950 positive regulation of cAMP-mediated signaling
GO:BP 3.85012E-23 2
GO:0042923 neuropeptide binding
GO:MF 3.68767E-27 2
KEGG:04727 GABAergic synapse
KEGG 5.89491E-21 2
GO:004270 Vascular smooth muscle contraction
KEGG 5.89491E-21 2
| KEGG:00640 | Propanoate metabolism | KEGG | 2.47094E-29 | 3 |
| KEGG:00250 | Alanine, aspartate and glutamate metabolism | KEGG | 4.49917E-29 | 3 |
| KEGG:00280 | Valine, leucine and isoleucine degradation | KEGG | 6.68623E-28 | 3 |
| GO:0005758 | mitochondrial intermembrane space | GO:CC | 1.50603E-27 | 3 |
| GO:0016597 | amino acid binding | GO:MF | 9.70016E-27 | 3 |
| GO:0008137 | NADH dehydrogenase (ubiquinone) activity | GO:MF | 1.59559E-26 | 3 |
| GO:0006099 | tricarboxylic acid cycle | GO:BP | 2.53899E-26 | 3 |
| KEGG:00410 | beta-Alanine metabolism | KEGG | 3.41825E-25 | 3 |
| KEGG:00630 | Glyoxylate and dicarboxylate metabolism | KEGG | 3.27741E-24 | 3 |
| KEGG:00270 | Cysteine and methionine metabolism | KEGG | 1.71802E-23 | 3 |
| GO:0042803 | protein homodimerization activity | GO:MF | 5.31102E-23 | 3 |
| KEGG:00260 | Glycine, serine and threonine metabolism | KEGG | 1.93497E-21 | 3 |
| GO:0004129 | cytochrome-c oxidase activity | GO:MF | 5.36417E-19 | 3 |
| GO:0006541 | glutamine metabolic process | GO:BP | 1.02509E-17 | 3 |
| GO:0005782 | peroxisomal matrix | GO:CC | 1.47879E-17 | 3 |
| GO:00071 | Fatty acid degradation | KEGG | 3.94388E-17 | 3 |
| KEGG:00330 | Arginine and proline metabolism | KEGG | 4.4514E-17 | 3 |
| GO:00030 | Pentose phosphate pathway | GO:BP | 1.84319E-20 | 3 |
| GO:0046961 | proton-transporting ATPase activity, rotational mechanism | GO:MF | 5.65534E-16 | 3 |
| KEGG:00670 | One carbon pool by folate | KEGG | 1.90214E-15 | 3 |
| GO:0004550 | nucleoside diphosphate kinase activity | GO:MF | 2.24654E-15 | 3 |
| GO:0016471 | vacuolar proton-transporting V-type ATPase complex | GO:CC | 4.07885E-15 | 3 |
| KEGG:00760 | Nicotinate and nicotinamide metabolism | KEGG | 1.38377E-14 | 3 |
| KEGG:000350 | Tyrosine metabolism | KEGG | 1.47125E-14 | 3 |
| KEGG:00650 | Butanoate metabolism | KEGG | 1.73252E-14 | 3 |
| GO:0008483 | transaminase activity | GO:MF | 3.15081E-14 | 3 |
| KEGG:00340 | Histidine metabolism | KEGG | 6.51216E-14 | 3 |
| KEGG:00480 | Glutathione metabolism | KEGG | 1.84117E-13 | 3 |
| GO:0016831 | carboxy-lyase activity | GO:MF | 2.46622E-13 | 3 |
| KEGG:00770 | Pantothenate and CoA biosynthesis | KEGG | 1.42295E-12 | 3 |
| GO:003150 | protein import into mitochondrial matrix | GO:BP | 2.84517E-12 | 3 |
| KEGG:04966 | Collecting duct acid secretion | KEGG | 3.60288E-12 | 3 |
| KEGG:00051 | Fructose and mannose metabolism | KEGG | 4.25888E-12 | 3 |
| GO:0035999 | tetrahydrofolate interconversion | GO:BP | 5.83642E-12 | 3 |
| KEGG:01210 | 2-Oxocarboxylic acid metabolism | KEGG | 8.17373E-12 | 3 |
| KEGG:00220 | Arginine biosynthesis | KEGG | 8.17373E-12 | 3 |
| GO:0017101 | aminocycl-tRNA synthetase multienzyme complex | GO:CC | 2.15649E-11 | 3 |
| GO:0015986 | ATP synthesis coupled proton transport | GO:BP | 1.84231E-11 | 3 |
| GO:0046835 | carbohydrate phosphorylation | GO:BP | 2.70599E-11 | 3 |
| KEGG:00052 | Galactose metabolism | KEGG | 3.08099E-11 | 3 |
| KEGG:00500 | Starch and sucrose metabolism | KEGG | 3.08099E-11 | 3 |
| GO:0006002 | fructose 6-phosphate metabolic process | GO:BP | 3.90138E-11 | 3 |
| GO:0006103 | 2-oxoglutarate metabolic process | GO:BP | 4.53948E-11 | 3 |
| GO:0032482 | Rab protein signal transduction | GO:BP | 1.69599E-55 | 4 |
| GO:0005525 | GTP binding | GO:MF | 5.44405E-49 | 4 |
| GO:000139 | Golgi membrane | GO:CC | 8.0849E-45 | 4 |
| GO:003924 | GTase activity | GO:MF | 2.7619E-44 | 4 |
| GO:005814 | centriole | GO:CC | 2.67798E-40 | 4 |
| GO:0036064 | ciliary basal body | GO:CC | 2.13912E-38 | 4 |
GO:0032590  dendrite membrane  GO:CC  2.68165E-14  5
GO:0016934  extracellularly glycine-gated chloride channel activity  GO:MF  1.67442E-12  5
GO:0071420  cellular response to histamine  GO:BP  3.08593E-11  5
GO:0001228  DNA-binding transcription activator activity, RNA polymerase II-specific  GO:MF  7.08221E-85  6
GO:003714  transcription corepressor activity  GO:MF  1.37665E-57  6
GO:0003714  extracellularly glycine-gated chloride channel activity  GO:MF  1.23462E-42  6
GO:0042826  histone deacetylase binding  GO:MF  4.8588E-23  6
GO:0016592  mediator complex  GO:CC  1.20263E-39  6
GO:0046982  protein heterodimerization activity  GO:MF  7.45883E-38  6
GO:0000980  RNA polymerase II distal enhancer sequence-specific DNA binding  GO:MF  1.20039E-34  6
GO:0001227  DNA-binding transcription repressor activity, RNA polymerase II-specific  GO:MF  2.17259E-34  6
KEGG:04330  Notch signaling pathway  KEGG  2.62849E-34  6
GO:0004879  nuclear receptor activity  GO:MF  1.40043E-32  6
KEGG:05202  Transcriptional misregulation in cancer  KEGG  9.9941E-30  6
GO:0003714  extracellularly glycine-gated chloride channel activity  GO:MF  1.23462E-42  6
GO:0008270  zinc ion binding  GO:MF  2.66899E-29  6
GO:0004879  nuclear receptor activity  GO:MF  1.40043E-32  6
KEGG:04919  Thyroid hormone signaling pathway  KEGG  1.41937E-20  6
GO:0001102  RNA polymerase II activating transcription factor binding  GO:MF  1.19092E-18  6
GO:0035064  methylated histone binding  GO:MF  1.33837E-18  6
GO:0005719  nuclear euchromatin  GO:CC  3.03416E-18  6
GO:0035102  PRC1 complex  GO:CC  1.2979E-17  6
KEGG:05203  Viral carcinogenesis  KEGG  2.43868E-17  6
GO:0016605  PML body  GO:CC  1.1324E-16  6
GO:0016581  NuRD complex  GO:CC  1.97934E-16  6
GO:0071565  nBaf complex  GO:CC  2.59458E-16  6
GO:0016514  SWI/SNF complex  GO:CC  5.44055E-16  6
GO:0032922  circadian regulation of gene expression  GO:BP  9.3099E-16  6
GO:0043981  histone H4-K5 acetylation  GO:BP  1.17254E-15  6
GO:0043982  histone H4-K8 acetylation  GO:BP  1.17254E-15  6
GO:0016607  nuclear speck  GO:CC  2.26472E-15  6
GO:0071339  MLL1 complex  GO:CC  2.5824E-15  6
GO:0035019  somatic stem cell population maintenance  GO:BP  4.844E-15  6
GO:0035098  ESC/E(Z) complex  GO:CC  2.82958E-14  6
GO:0031011  Ino80 complex  GO:CC  6.91762E-14  6
KEGG:05322  Systemic lupus erythematosus  KEGG  1.08037E-13  6
KEGG:05225  Hepatocellular carcinoma  KEGG  1.41484E-13  6
GO:0043984  histone H4-K16 acetylation  GO:BP  2.14329E-13  6
GO:0046965  retinoid X receptor binding  GO:MF  2.29609E-13  6
GO:0070932  histone H3 deacetylation  GO:BP  2.4608E-13  6
GO:0043968  histone H2A acetylation  GO:BP  9.08479E-13  6
GO:0043065  positive regulation of apoptotic process  GO:BP  1.24527E-12  6
GO:0016580  Sin3 complex  GO:CC  1.28212E-12  6
GO:0071564  npBAF complex  GO:CC  2.06165E-12  6
GO:0000788  nuclear nucleosome  GO:CC  3.82489E-12  6
GO:0006335  DNA replication-dependent nucleosome assembly  GO:BP  4.77521E-12  6
KEGG:04110  Cell cycle  KEGG  7.67608E-12  6
KEGG:04550  Signaling pathways regulating pluripotency of stem cells  KEGG  8.85724E-12  6
GO:0006336  DNA replication-independent nucleosome assembly  GO:BP  1.22241E-11  6
GO:0006337  nucleosome disassembly  GO:BP  1.49965E-11  6
| ID     | Name                                          | KEGG      | GO:CC        |
|--------|-----------------------------------------------|-----------|-------------|
| KEGG:05222 | Small cell lung cancer                       |           |             |
| KEGG:03040 | Spliceosome                                   |           |             |
| GO:0016607 | nuclear speck                                 | GO:CC     | 5.90546E-78 |
| GO:0071005 | U2-type precatalytic spliceosome              | GO:CC     | 2.64265E-59 |
| KEGG:03013 | RNA transport                                 | KEGG      | 2.43202E-49 |
| KEGG:03022 | Basal transcription factors                   | KEGG      | 4.27996E-43 |
| GO:0071007 | U2-type catalytic step 2 spliceosome          | GO:CC     | 2.1861E-38  |
| GO:0005689 | U12-type spliceosomal complex                 | GO:CC     | 1.02773E-35 |
| GO:0005669 | transcription factor TFIIID complex           | GO:CC     | 1.91584E-33 |
| KEGG:03015 | mRNA surveillance pathway                     | KEGG      | 1.27804E-32 |
| KEGG:03020 | RNA polymerase                                | KEGG      | 1.49046E-23 |
| GO:0034719 | SMN-Sm protein complex                         | GO:CC     | 3.61691E-23 |
| GO:0005685 | U1 snRNP                                      | GO:CC     | 3.61691E-23 |
| GO:0017056 | structural constituent of nuclear pore        | GO:MF     | 4.63923E-22 |
| GO:0005666 | RNA polymerase III complex                    | GO:CC     | 5.25436E-21 |
| GO:0015030 | Cajal body                                    | GO:CC     | 6.33796E-20 |
| GO:0045292 | mRNA cis splicing, via spliceosome            | GO:BP     | 5.94796E-19 |
| GO:0005682 | US snRNP                                      | GO:CC     | 7.12039E-19 |
| GO:0032968 | positive regulation of transcription elongation from RNA polymerase II promoter | GO:BP     | 9.65264E-19 |
| GO:0001056 | RNA polymerase III activity                   | GO:MF     | 7.31256E-18 |
| GO:0071004 | U2-type prespliceosome                        | GO:CC     | 6.5158E-17  |
| GO:0008353 | RNA polymerase II CTD heptapeptide repeat kinase activity | GO:MF     | 1.7732E-16  |
| GO:0000974 | Prp19 complex                                 | GO:CC     | 1.77838E-16 |
| GO:0005665 | RNA polymerase II, core complex               | GO:CC     | 8.25658E-16 |
| GO:0016251 | RNA polymerase II general transcription initiation factor activity | GO:MF     | 1.14039E-15 |
| GO:0006606 | protein import into nucleus                   | GO:BP     | 4.3141E-14  |
| GO:0048025 | negative regulation of mRNA splicing, via spliceosome | GO:BP     | 7.88583E-14 |
| GO:0005687 | U4 snRNP                                      | GO:CC     | 8.65804E-14 |
| GO:0071006 | U2-type catalytic step 1 spliceosome          | GO:CC     | 1.76218E-13 |
| GO:006376  | mRNA splice site selection                    | GO:BP     | 4.43206E-13 |
| GO:0005847 | mRNA cleavage and polyadenylation specificity factor complex | GO:CC     | 1.03751E-12 |
| GO:1990446 | U1 snRNP binding                              | GO:MF     | 4.66826E-12 |
| GO:0001055 | RNA polymerase II activity                    | GO:MF     | 4.66826E-12 |
| GO:0000993 | RNA polymerase II complex binding             | GO:MF     | 9.17382E-12 |
| GO:0032797 | SMN complex                                   | GO:CC     | 3.07025E-11 |
| GO:0032039 | integrator complex                            | GO:CC     | 6.33115E-11 |
| KEGG:03460 | Fanconi anemia pathway                        | KEGG      | 6.74678E-72 |
| KEGG:03020 | DNA replication                               | KEGG      | 7.16352E-55 |
| KEGG:03440 | Homologous recombination                      | KEGG      | 1.95684E-44 |
| KEGG:03420 | Nucleotide excision repair                    | KEGG      | 4.62863E-41 |
| GO:0003697 | single-stranded DNA binding                   | GO:MF     | 1.68344E-38 |
| GO:0036297 | interstrand cross-link repair                  | GO:BP     | 3.46204E-33 |
| KEGG:03410 | Base excision repair                          | KEGG      | 7.75773E-33 |
| GO:0017116 | single-stranded DNA helicase activity          | GO:MF     | 2.60819E-29 |
| KEGG:03430 | Mismatch repair                               | KEGG      | 1.53377E-27 |
| GO:0003688 | DNA replication origin binding                 | GO:MF     | 3.64721E-26 |
| GO:0003887 | DNA-directed DNA polymerase activity          | GO:MF     | 1.44805E-24 |
| GO:0031297 | replication fork processing                   | GO:BP     | 2.11693E-23 |
| GO:0006298 | mismatch repair                               | GO:BP     | 4.60123E-19 |
| GO:0007277 | double-strand break repair via break-induced replication | GO:BP     | 3.00535E-18 |
| GO:0043138 | 3'-5' DNA helicase activity                   | GO:MF     | 3.39847E-17 |
| KEGG:04915 | Estrogen signaling pathway | KEGG | 8.92592E-47 | 30 |
|------------|---------------------------|------|-------------|---|
| GO:0045095 | keratin filament          | GO:CC| 1.22979E-44 | 30 |
| GO:0045109 | intermediate filament organization | GO:BP | 2.59E-14 | 30 |
| GO:0005890 | sodium:potassium-exchanging ATPase complex | GO:CC | 3.274E-28 | 31 |
| GO:0005391 | sodium:potassium-exchanging ATPase activity | GO:MF | 1.54917E-21 | 31 |
| GO:0010248 | establishment or maintenance of transmembrane electrochemical gradient | GO:BP | 4.88603E-19 | 31 |
| GO:0030007 | cellular potassium ion homeostasis | GO:BP | 4.88603E-19 | 31 |
| GO:0006883 | cellular sodium ion homeostasis | GO:BP | 7.78185E-18 | 31 |
| KEGG:04974 | Protein digestion and absorption | KEGG | 3.76008E-16 | 31 |
| KEGG:04964 | Proximal tubule bicarbonate reclamation | KEGG | 1.80345E-15 | 31 |
| KEGG:04960 | Aldosterone-regulated sodium reabsorption | KEGG | 2.49235E-15 | 31 |
| KEGG:04976 | Bile secretion | KEGG | 7.29832E-14 | 31 |
| KEGG:04973 | Carbohydrate digestion and absorption | KEGG | 3.03212E-12 | 31 |
| KEGG:04971 | Gastric acid secretion | KEGG | 4.81598E-12 | 31 |
| KEGG:04978 | Mineral absorption | KEGG | 8.4653E-12 | 31 |
| KEGG:04961 | Endocrine and other factor-regulated calcium reabsorption | KEGG | 4.15037E-11 | 31 |
| KEGG:05168 | Herpes simplex virus 1 infection | KEGG | 1.22744E-35 | 33 |
| GO:0046872 | metal ion binding | GO:MF | 2.23717E-33 | 33 |
| GO:0005634 | nucleus | GO:CC | 1.04894E-19 | 33 |
| GO:0003700 | DNA-binding transcription factor activity | GO:MF | 1.85789E-13 | 33 |
Supplementary Table S7. Enrichment Table for each separate community in MMU, ranked by the p-value

| GO-Terms                     | description                                                                 | source   | p-value       | community |
|------------------------------|------------------------------------------------------------------------------|----------|---------------|-----------|
| KEGG:04080                   | Neuroactive ligand-receptor interaction                                       | KEGG     | 1.1694E-15    | 0         |
| KEGG:0007218                 | neuropeptide signaling pathway                                               | GO:BP    | 1.51E-77      | 0         |
| KEGG:0070098                 | chemokine-mediated signaling pathway                                         | GO:BP    | 6.47311E-64   | 0         |
| KEGG:04062                   | Chemokine signaling pathway                                                 | KEGG     | 5.04813E-57   | 0         |
| KEGG:04742                   | Taste transduction                                                           | KEGG     | 4.36407E-41   | 0         |
| GO:0008009                   | chemokine activity                                                           | GO:MF    | 9.48515E-41   | 0         |
| KEGG:04061                   | Viral protein interaction with cytokine and cytokine receptor                 | KEGG     | 2.32747E-40   | 0         |
| GO:0001580                   | detection of chemical stimulus involved in sensory perception of bitter taste| GO:BP    | 1.45288E-37   | 0         |
| GO:0005834                   | heterotrimeric G-protein complex                                              | GO:CC    | 7.21798E-36   | 0         |
| GO:0016493                   | C-C chemokine receptor activity                                              | GO:MF    | 1.02348E-33   | 0         |
| KEGG:0019722                 | calcium-mediated signaling                                                   | GO:BP    | 1.26978E-33   | 0         |
| KEGG:0070374                 | positive regulation of ERK1 and ERK2 cascade                                  | GO:BP    | 1.09651E-31   | 0         |
| KEGG:04725                   | Cholinergic synapse                                                           | KEGG     | 4.76009E-30   | 0         |
| GO:0033038                   | bitter taste receptor activity                                               | GO:MF    | 6.23685E-29   | 0         |
| GO:0051482                   | positive regulation of cytosolic calcium ion concentration involved in phospholipase C-activating G protein-coupled signaling pathway | GO:BP | 6.97399E-28 | 0 |
| KEGG:04020                   | Calcium signaling pathway                                                    | KEGG     | 2.12107E-27   | 0         |
| KEGG:04724                   | Glutamatergic synapse                                                        | KEGG     | 4.41027E-26   | 0         |
| KEGG:04726                   | Serotonergic synapse                                                         | KEGG     | 3.16824E-24   | 0         |
| GO:0042923                   | neuropeptide binding                                                         | GO:MF    | 4.04353E-21   | 0         |
| GO:0031681                   | G-protein beta-subunit binding                                               | GO:MF    | 9.2994E-20    | 0         |
| GO:0031683                   | G-protein beta/gamma-subunit complex binding                                 | GO:MF    | 4.13755E-19   | 0         |
| KEGG:04060                   | Cytokine-cytokine receptor interaction                                       | KEGG     | 8.95659E-19   | 0         |
| KEGG:0045777                 | positive regulation of blood pressure                                       | GO:BP    | 1.03941E-18   | 0         |
| KEGG:04713                   | Circadian entrainment                                                       | KEGG     | 1.17819E-18   | 0         |
| GO:0061844                   | antimicrobial humoral immune response mediated by antimicrobial peptide      | GO:BP    | 1.63283E-17   | 0         |
| KEGG:04072                   | Phospholipase D signaling pathway                                            | KEGG     | 3.82586E-17   | 0         |
| GO:0099056                   | integral component of presynaptic membrane                                   | GO:CC    | 4.68531E-17   | 0         |
| KEGG:05163                   | Human cytomegalovirus infection                                              | KEGG     | 6.31757E-17   | 0         |
| GO:0048245                   | eosinophil chemotaxis                                                        | GO:BP    | 7.14071E-17   | 0         |
| KEGG:04723                   | Retrograde endocannabinoid signaling                                         | KEGG     | 1.50852E-16   | 0         |
| KEGG:04728                   | D损amnergic synapse                                                          | KEGG     | 1.75829E-16   | 0         |
| KEGG:0045907                 | positive regulation of vasconstriction                                       | GO:BP    | 4.43058E-16   | 0         |
| GO:0004993                   | G protein-coupled serotonin receptor activity                               | GO:MF    | 4.4572E-16    | 0         |
| KEGG:04926                   | Relaxin signaling pathway                                                     | KEGG     | 1.55076E-15   | 0         |
| KEGG:04371                   | Apelin signaling pathway                                                     | KEGG     | 9.00417E-15   | 0         |
| KEGG:05032                   | Morphine addiction                                                           | KEGG     | 1.50177E-14   | 0         |
| GO:0031680                   | G-protein beta/gamma-subunit complex                                          | GO:CC    | 3.69072E-14   | 0         |
| GO:0005184                   | neuropeptide hormone activity                                                | GO:MF    | 1.54817E-13   | 0         |
| GO:0071347                   | cellular response to interleukin-1                                           | GO:BP    | 7.80919E-13   | 0         |
| KEGG:04929                   | GnRH secretion                                                               | KEGG     | 8.93822E-13   | 0         |
| GO:0035815                   | positive regulation of renal sodium excretion                               | GO:BP    | 9.75909E-13   | 0         |
| GO:0043547                   | positive regulation of GTPase activity                                       | GO:BP    | 1.27572E-12   | 0         |
| GO:0001965                   | G-protein alpha-subunit binding                                              | GO:MF    | 1.48792E-12   | 0         |
| KEGG:04024                   | cAMP signaling pathway                                                       | KEGG     | 1.77136E-12   | 0         |
| GO:0042756                   | drinking behavior                                                            | GO:BP    | 8.51634E-12   | 0         |
| GO:0007626                   | locomotory behavior                                                          | GO:BP    | 8.95956E-12   | 0         |
| GO:0002430                   | complement receptor mediated signaling pathway                               | GO:BP    | 1.06672E-11   | 0         |
| GO:0007189                   | adenylyl cyclase-activating G protein-coupled receptor signaling pathway      | GO:BP    | 1.02392E-11   | 0         |
| GO:0051281                   | positive regulation of release of sequestered calcium ion into cytosol       | GO:BP    | 1.22295E-11   | 0         |
| KEGG:04924                   | Renin secretion                                                              | KEGG     | 2.18964E-11   | 0         |
| KEGG:04022                   | cGMP-PKG signaling pathway                                                   | KEGG     | 5.23951E-11   | 0         |
| GO:0007197                   | adenylyl cyclase-inhibiting G protein-coupled acetylcholine receptor signaling pathway | GO:BP | 8.63023E-11 | 0 |
| GO:0051378                   | serotonin binding                                                           | GO:MF    | 8.80097E-11   | 0         |
| KEGG:04080                   | Neuroactive ligand-receptor interaction                                       | KEGG     | 1.04608E-65   | 0         |
| GO:0043950                   | positive regulation of cAMP-mediated signaling                               | GO:BP    | 1.48659E-32   | 0         |
| KEGG:04024                   | cAMP signaling pathway                                                       | KEGG     | 1.15311E-28   | 0         |
| GO:0007190                   | activation of adenylyl cyclase activity                                       | GO:BP    | 1.13871E-24   | 0         |
| KEGG:04911                   | Insulin secretion                                                            | KEGG     | 3.36954E-21   | 0         |
| GO:0006171                   | cAMP biosynthetic process                                                     | GO:BP    | 2.18758E-19   | 0         |
| KEGG:04923                   | Regulation of lipolysis in adipocytes                                        | KEGG     | 6.08557E-17   | 0         |
| KEGG:04270 | Vascular smooth muscle contraction | KEGG:04096 | Ovarian steroidogenesis |
| KEGG:001594 | trace-amine receptor activity | GO:0001594 | trace-amine receptor activity |
| KEGG:04918 | Thyroid hormone synthesis | GO:0004298 | threonine-type endopeptidase activity |
| KEGG:0097647 | amylase receptor signaling pathway | GO:0031297 | four-way junction DNA binding |
| KEGG:04020 | Calcium signaling pathway | KEGG:0006303 | double-strand break repair via nonhomologous end joining |
| KEGG:04927 | Cortisol synthesis and secretion | KEGG:0006303 | double-strand break repair via nonhomologous end joining |
| KEGG:03460 | Fanconi anemia pathway | KEGG:0006303 | double-strand break repair via nonhomologous end joining |
| KEGG:03420 | Nucleotide excision repair | KEGG:0006303 | double-strand break repair via nonhomologous end joining |
| KEGG:03440 | Homologous recombination | KEGG:0006303 | double-strand break repair via nonhomologous end joining |
| GO:0003697 | single-stranded DNA binding | GO:0003689 | GO:0003689 |
| KEGG:03030 | DNA replication | GO:0003697 | single-stranded DNA helicase activity |
| KEGG:0036297 | interstrand cross-link repair | GO:0003697 | single-stranded DNA helicase activity |
| KEGG:03410 | Base excision repair | GO:0003697 | single-stranded DNA helicase activity |
| KEGG:03430 | Mismatch repair | GO:0003697 | single-stranded DNA helicase activity |
| GO:0003887 | DNA-directed DNA polymerase activity | GO:0003697 | single-stranded DNA helicase activity |
| KEGG:0006303 | double-strand break repair via nonhomologous end joining | GO:0006303 | double-strand break repair via nonhomologous end joining |
| GO:0003688 | DNA replication origin binding | GO:0003688 | DNA replication origin binding |
| GO:005524 | ATP binding | GO:005524 | ATP binding |
| GO:0017116 | single-stranded DNA helicase activity | GO:0017116 | single-stranded DNA helicase activity |
| GO:0004843 | thiol-dependent ubiquitin-specific protease activity | GO:0004843 | thiol-dependent ubiquitin-specific protease activity |
| GO:0035861 | site of double-strand break | GO:0035861 | site of double-strand break |
| KEGG:006298 | mismatch repair | KEGG:006298 | mismatch repair |
| GO:0000784 | nuclear chromosome, telomeric region | GO:0000784 | nuclear chromosome, telomeric region |
| GO:0043138 | 3'-5' DNA helicase activity | GO:0043138 | 3'-5' DNA helicase activity |
| GO:0043240 | Fanconi anemia nuclear complex | GO:0043240 | Fanconi anemia nuclear complex |
| GO:0030433 | ubiquitin-dependent ERAD pathway | GO:0030433 | ubiquitin-dependent ERAD pathway |
| GO:0000727 | double-strand break repair via break-induced replication | GO:0000727 | double-strand break repair via break-induced replication |
| KEGG:03450 | Non-homologous end-joining | KEGG:03450 | Non-homologous end-joining |
| GO:0036882 | chromatin binding | GO:0036882 | chromatin binding |
| GO:0031297 | replication fork processing | GO:0031297 | replication fork processing |
| GO:0006268 | DNA unwinding involved in DNA replication | GO:0006268 | DNA unwinding involved in DNA replication |
| GO:0042555 | MCM complex | GO:0042555 | MCM complex |
| GO:0031573 | intra-S DNA damage checkpoint | GO:0031573 | intra-S DNA damage checkpoint |
| GO:0010165 | response to X-ray | GO:0010165 | response to X-ray |
| GO:0000400 | four-way junction DNA binding | GO:0000400 | four-way junction DNA binding |
| GO:0000712 | resolution of meiotic recombination intermediates | GO:0000712 | resolution of meiotic recombination intermediates |
| GO:0031625 | ubiquitin protein ligase binding | GO:0031625 | ubiquitin protein ligase binding |
| GO:0008821 | crossover junction endodeoxyribonuclease activity | GO:0008821 | crossover junction endodeoxyribonuclease activity |
| KEGG:04110 | Cell cycle | KEGG:04110 | Cell cycle |
| GO:0003689 | DNA clamp loader activity | GO:0003689 | DNA clamp loader activity |
| GO:0031011 | Ino80 complex | GO:0031011 | Ino80 complex |
| GO:0043123 | positive regulation of I-kappaB kinase/NF-kappaB signaling | GO:0043123 | positive regulation of I-kappaB kinase/NF-kappaB signaling |
| KEGG:03050 | Proteasome | KEGG:03050 | Proteasome |
| KEGG:05169 | Epstein-Barr virus infection | KEGG:05169 | Epstein-Barr virus infection |
| KEGG:05217 | Basal cell carcinoma | KEGG:05217 | Basal cell carcinoma |
| KEGG:04064 | NF-kappa B signaling pathway | KEGG:04064 | NF-kappa B signaling pathway |
| KEGG:04310 | Wnt signaling pathway | KEGG:04310 | Wnt signaling pathway |
| GO:0051092 | positive regulation of NF-kappaB transcription factor activity | GO:0051092 | positive regulation of NF-kappaB transcription factor activity |
| KEGG:05200 | Pathways in cancer | KEGG:05200 | Pathways in cancer |
| KEGG:05226 | Gastric cancer | KEGG:05226 | Gastric cancer |
| KEGG:05165 | Human papillomavirus infection | KEGG:05165 | Human papillomavirus infection |
| KEGG:004298 | threonine-type endopeptidase activity | KEGG:004298 | threonine-type endopeptidase activity |
| GO:0005109 | frizzled binding | GO:0005109 | frizzled binding |
| KEGG:05224 | Breast cancer | KEGG:05224 | Breast cancer |
| KEGG:04622 | RIG-I-like receptor signaling pathway | KEGG:04622 | RIG-I-like receptor signaling pathway |
| GO:0010499 | proteasomal ubiquitin-independent protein catabolic process | GO:0010499 | proteasomal ubiquitin-independent protein catabolic process |
| KEGG:04934 | Cushing syndrome | KEGG:04934 | Cushing syndrome |
| KEGG:04668 | TNF signaling pathway | KEGG:04668 | TNF signaling pathway |
| KEGG:04620 | Toll-like receptor signaling pathway | KEGG:04620 | Toll-like receptor signaling pathway |
| KEGG:05162 | Measles | KEGG:05162 | Measles |
| KEGG:05161 | Hepatitis B | KEGG:05161 | Hepatitis B |
| KEGG:05225 | Hepatocellular carcinoma | KEGG:05225 | Hepatocellular carcinoma |
| KEGG:04110 | Cell cycle | KEGG:04110 | Cell cycle |
| KEGG:04390 | Hippo signaling pathway | KEGG:04390 | Hippo signaling pathway |
| GO:0004843 | thiol-dependent ubiquitin-specific protease activity | GO:MF | 9.47013E-20 | 4 |
| KE GG:05160 | Hepatitis C | KE GG | 1.75642E-19 | 4 |
| KE GG:04621 | NOD-like receptor signaling pathway | KE GG | 2.61605E-18 | 4 |
| GO:0009090 | negative regulation of canonical Wnt signaling pathway | GO:BP | 1.37457E-17 | 4 |
| KE GG:05164 | Influenza A | KE GG | 4.07995E-17 | 4 |
| GO:0019901 | protein kinase binding | GO:MF | 6.66198E-17 | 4 |
| GO:0005164 | tumor necrosis factor receptor binding | GO:MF | 1.27155E-16 | 4 |
| KE GG:05222 | Small cell lung cancer | KE GG | 1.25518E-15 | 4 |
| KE GG:04340 | Hedgehog signaling pathway | KE GG | 4.86201E-15 | 4 |
| GO:0019774 | proteasome core complex, beta-subunit complex | GO:CC | 9.42032E-15 | 4 |
| GO:0031625 | ubiquitin protein ligase binding | GO:MF | 5.69662E-14 | 4 |
| KE GG:04150 | mTOR signaling pathway | KE GG | 1.59083E-13 | 4 |
| KE GG:04218 | Cellular senescence | KE GG | 3.63199E-13 | 4 |
| KE GG:05145 | Toxoplasmosis | KE GG | 3.66742E-13 | 4 |
| GO:0035631 | CD40 receptor complex | GO:CC | 4.29271E-13 | 4 |
| GO:0005149 | interleukin-1 receptor binding | GO:MF | 4.30255E-13 | 4 |
| KE GG:04210 | Apoptosis | KE GG | 6.11191E-13 | 4 |
| KE GG:04550 | Signaling pathways regulating pluripotency of stem cells | KE GG | 7.61297E-13 | 4 |
| KE GG:05205 | Proteoglycans in cancer | KE GG | 1.05491E-12 | 4 |
| KE GG:04657 | IL-17 signaling pathway | KE GG | 1.44007E-12 | 4 |
| KE GG:04916 | Melanogenesis | KE GG | 1.49266E-12 | 4 |
| GO:0042802 | identical protein binding | GO:MF | 2.33116E-12 | 4 |
| GO:0008540 | proteasome regulatory particle, base subcomplex | GO:CC | 2.5365E-12 | 4 |
| GO:0043507 | positive regulation of JUN kinase activity | GO:BP | 3.5958E-12 | 4 |
| KE GG:05166 | Human T-cell leukemia virus 1 infection | KE GG | 1.36641E-11 | 4 |
| GO:0071260 | cellular response to mechanical stimulus | GO:BP | 1.85583E-11 | 4 |
| GO:0019773 | proteasome core complex, alpha-subunit complex | GO:CC | 1.95204E-11 | 4 |
| GO:0005654 | nucleoplasm | GO:CC | 2.92073E-11 | 4 |
| KE GG:04120 | Ubiquitin mediated proteolysis | KE GG | 3.094E-154 | 5 |
| GO:0031146 | SCF-dependent proteasomal ubiquitin-dependent protein catabolic process | GO:BP | 1.89964E-44 | 5 |
| GO:0061631 | ubiquitin conjugating enzyme activity | GO:MF | 2.54194E-39 | 5 |
| GO:0070936 | protein K48-linked ubiquitination | GO:BP | 8.62247E-34 | 5 |
| GO:0005680 | anaphase-promoting complex | GO:CC | 6.74193E-32 | 5 |
| GO:0070979 | protein K11-linked ubiquitination | GO:BP | 1.29906E-29 | 5 |
| GO:0051865 | protein autoubiquitination | GO:BP | 6.724E-22 | 5 |
| GO:0031463 | Cul3-RING ubiquitin ligase complex | GO:CC | 7.39775E-22 | 5 |
| GO:0080008 | Cul4-RING E3 ubiquitin ligase complex | GO:CC | 2.71905E-20 | 5 |
| GO:0006513 | protein monoubiquitination | GO:BP | 1.56735E-19 | 5 |
| GO:0031624 | ubiquitin conjugating enzyme binding | GO:MF | 1.49994E-17 | 5 |
| GO:0045116 | protein neddylation | GO:BP | 1.34997E-16 | 5 |
| GO:0031145 | anaphase-promoting complex-dependent catabolic process | GO:BP | 2.85332E-16 | 5 |
| GO:0070534 | protein K63-linked ubiquitination | GO:BP | 4.72498E-16 | 5 |
| GO:0097602 | cullin family protein binding | GO:MF | 1.555E-15 | 5 |
| GO:0000338 | protein deneddylation | GO:BP | 1.60197E-15 | 5 |
| GO:0031625 | ubiquitin protein ligase binding | GO:MF | 1.65891E-15 | 5 |
| GO:0005829 | cytosol | GO:CC | 8.44774E-15 | 5 |
| KE GG:04114 | Oocyte meiosis | KE GG | 4.12366E-13 | 5 |
| GO:0032436 | positive regulation of proteasomal ubiquitin-dependent protein catabolic process | GO:BP | 1.16154E-12 | 5 |

| KE GG:04110 | Cell cycle | KE GG | 2.15523E-11 | 5 |
| GO:0031462 | Cul2-RING ubiquitin ligase complex | GO:CC | 9.22853E-11 | 5 |
| GO:0005814 | centriole | GO:CC | 3.62278E-39 | 6 |
| GO:0000139 | Golgi membrane | GO:CC | 4.65282E-30 | 6 |
| KE GG:04145 | Phagosome | KE GG | 5.84038E-29 | 6 |
| GO:005829 | cytosol | GO:CC | 1.08326E-27 | 6 |
| GO:036064 | ciliary basal body | GO:CC | 8.43303E-27 | 6 |
| GO:0030992 | intracellular transport particle B | GO:CC | 5.84696E-25 | 6 |
| GO:0006890 | retrograde vesicle-mediated transport, Golgi to endoplasmic reticulum | GO:BP | 3.50009E-24 | 6 |
| KE GG:05323 | Rheumatoid arthritis | KE GG | 3.65796E-22 | 6 |
| GO:0006891 | intra-Golgi vesicle-mediated transport | GO:BP | 1.69766E-21 | 6 |
| GO:0005868 | cytoplasmic dynen complex | GO:CC | 5.30724E-21 | 6 |
| KE GG:04966 | Collecting duct acid secretion | KE GG | 3.26507E-19 | 6 |
| GO:0006606 | protein import into nucleus | GO:BP | 1.07736E-18 | 6 |
| GO:1905515 | non-motile cilium assembly | GO:BP | 1.79831E-18 | 6 |
| GO:0008574 | ATP-dependent microtubule motor activity, plus-end-directed | GO:MF | 1.26522E-17 | 6 |
KEGG:04114  Oocyte meiosis       KEGG:  2.7429E-17  6
GO:0017056  structural constituent of nuclear pore GO:MF:  2.78962E-17  6
GO:0005484  SNAP receptor activity       GO:MF:  3.32593E-17  6
KEGG:03013  RNA transport            KEGG:  5.14086E-17  6
GO:0048471  perinuclear region of cytoplasm KEGG:  9.37772E-17  6
GO:0031201  SNARE complex            GO:CC:  1.71428E-15  6
KEGG:04141  Protein processing in endoplasmic reticulum KEGG:  1.85744E-15  6
KEGG:04130  SNARE interactions in vesicular transport  KEGG:  1.98208E-15  6
GO:0036038  MKS complex                GO:CC:  5.26944E-16  6
GO:0016471  vacuolar proton-transporting V-type ATPase complex GO:CC:  1.38007E-14  6
GO:0051082  unfolded protein binding       GO:MF:  1.54638E-14  6
GO:0030127  COP II vesicle coat           GO:CC:  2.01788E-14  6
GO:0051085  chaperone cofactor-dependent protein refolding GO:BP:  4.47429E-14  6
GO:0046961  proton-transporting ATPase activity, rotational mechanism GO:MF:  5.68398E-14  6
GO:0005801  cis-Golgi network                   GO:CC:  1.68174E-13  6
GO:0008536  Ran GTPase binding              GO:MF:  4.07657E-13  6
GO:0030126  COP I vesicle coat                GO:CC:  4.45379E-13  6
GO:0097431  mitotic spindle pole                   GO:CC:  5.19437E-13  6
GO:0000132  establishment of mitotic spindle orientation   GO:BP:  3.88382E-12  6
GO:0005524  ATP binding                          GO:MF:  1.10408E-11  6
GO:0005200  structural constituent of cytoskeleton       GO:MF:  1.41733E-11  6
KEGG:04721  Synaptic vesicle cycle            KEGG:  2.05419E-11  6
GO:0030008  TRAPP complex                      GO:CC:  3.60976E-11  6
GO:0042613  MHC class II protein complex         GO:CC:  3.60976E-11  6
GO:0051087  chaperone binding                   GO:MF:  5.27637E-11  6
KEGG:04962  Vasopressin-regulated water reabsorption KEGG:  5.93328E-11  6
KEGG:04610  Complement and coagulation cascades       KEGG:  3.16091E-03  6
GO:0004252  serine-type endopeptidase activity          GO:MF:  6.74752E-36  7
KEGG:00532  Glycosaminoglycan biosynthesis - chondroitin sulfate / dermatan sulfate KEGG:  1.01942E-27  7
KEGG:04512  ECM-receptor interaction             KEGG:  1.69734E-27  7
KEGG:00534  Glycosaminoglycan biosynthesis - heparan sulfate / heparin KEGG:  6.39525E-26  7
KEGG:04510  Focal adhesion                       KEGG:  1.78391E-20  7
GO:0000998  cell surface                           GO:CC:  3.07314E-19  7
GO:0005509  calcium ion binding                  GO:MF:  1.00717E-18  7
KEGG:04151  PI3K-Akt signaling pathway             KEGG:  1.83507E-17  7
GO:0008083  growth factor activity                  GO:MF:  2.22395E-16  7
GO:005178  integrin binding                        GO:MF:  3.79414E-16  7
GO:0000139  Golgi membrane                           GO:CC:  6.59283E-16  7
GO:0008201  heparin binding                        GO:CC:  6.2338E-14  7
GO:0005796  Golgi lumen                            GO:CC:  1.79033E-13  7
GO:0032026  chondroitin sulfate biosynthetic process GO:BP:  1.88968E-13  7
GO:004867  serine-type endopeptidase inhibitor activity GO:MF:  2.09105E-13  7
GO:0010951  negative regulation of endopeptidase activity GO:BP:  2.95883E-13  7
GO:0034361  very-low-density lipoprotein particle   GO:CC:  3.68281E-13  7
GO:042157  lipoprotein metabolic process            GO:BP:  3.65467E-12  7
KEGG:04630  JAK-STAT signaling pathway             KEGG:  1.07998E-06  8
KEGG:04360  Axon guidance                         KEGG:  1.41949E-02  8
KEGG:04810  Regulation of actin cytoskeleton         KEGG:  2.67054E-01  8
KEGG:04014  Ras signaling pathway                  KEGG:  6.04292E-01  8
GO:0005096  GTPase activator activity              GO:MF:  3.69843E-49  8
GO:0035023  regulation of Rho protein signal transduction GO:BP:  1.01309E-45  8
GO:0098797  glutamatergic synapse                  GO:CC:  2.40537E-44  8
KEGG:04015  Rap1 signaling pathway                 KEGG:  2.53734E-42  8
GO:0017124  SH3 domain binding                     GO:MF:  1.52213E-39  8
KEGG:04144  Endocytosis                            KEGG:  4.72336E-37  8
GO:0008360  regulation of cell shape                GO:BP:  5.16487E-36  8
KEGG:04151  PI3K-Akt signaling pathway              KEGG:  1.50869E-35  8
KEGG:05200  Pathways in cancer                     KEGG:  3.54436E-35  8
GO:0048013  ephrin receptor signaling pathway       GO:BP:  2.46191E-34  8
KEGG:04010  MAPK signaling pathway                 KEGG:  9.69731E-34  8
KEGG:04060  Cytokine-cytokine receptor interaction  KEGG:  3.77155E-33  8
KEGG:04850  Natural killer cell mediated cytotoxicity KEGG:  4.42502E-33  8
KEGG:04666  Fc gamma R-mediated phagocytosis        KEGG:  7.75614E-33  8
KEGG:04012  ErbB signaling pathway                  KEGG:  3.18239E-32  8
GO:0005829  cytosol                                 GO:CC:  1.54484E-31  8
| KEGG:05100 | Bacterial invasion of epithelial cells | KEGG | 1.12971E-30 | 8 |
| GO:0005925 | focal adhesion | GO:CC | 2.62279E-28 | 8 |
| GO:0008083 | growth factor activity | GO:MF | 2.93484E-24 | 8 |
| GO:0046875 | ephrin receptor binding | GO:MF | 2.45273E-23 | 8 |
| GO:0005125 | cytokine activity | GO:MF | 7.57716E-23 | 8 |
| KEGG:05205 | Proteoglycans in cancer | KEGG | 1.0735E-22 | 8 |
| GO:0042531 | positive regulation of tyrosine phosphorylation of STAT protein | GO:BP | 1.85443E-22 | 8 |
| KEGG:01521 | EGFR tyrosine kinase inhibitor resistance | KEGG | 5.23909E-22 | 8 |
| KEGG:04722 | Neurotrophin signaling pathway | KEGG | 6.88264E-21 | 8 |
| GO:0008543 | fibroblast growth factor receptor signaling pathway | GO:BP | 9.8939E-21 | 8 |
| KEGG:04510 | Focal adhesion | KEGG | 6.27243E-20 | 8 |
| KEGG:05135 | Yersinia infection | KEGG | 8.64606E-20 | 8 |
| GO:0001784 | phosphotyrosine residue binding | GO:MF | 7.00116E-19 | 8 |
| KEGG:04664 | Fc epsilon RI signaling pathway | KEGG | 1.27916E-18 | 8 |
| GO:0004715 | non-membrane spanning protein tyrosine kinase activity | GO:MF | 1.5423E-18 | 8 |
| GO:0045499 | chemorepellent activity | GO:MF | 2.14618E-17 | 8 |
| KEGG:05218 | Melanoma | KEGG | 5.64028E-17 | 8 |
| KEGG:04662 | B cell receptor signaling pathway | KEGG | 1.63237E-16 | 8 |
| GO:0031901 | early endosome membrane | GO:CC | 2.51299E-16 | 8 |
| GO:0004198 | calcium-dependent cysteine-type endopeptidase activity | GO:MF | 3.64711E-16 | 8 |
| GO:0044871 | perinuclear region of cytoplasm | GO:CC | 7.35179E-16 | 8 |
| GO:0005070 | SH3/SH2 adaptor activity | GO:MF | 1.08702E-15 | 8 |
| KEGG:04660 | T cell receptor signaling pathway | KEGG | 1.88453E-15 | 8 |
| GO:0050772 | positive regulation of axonogenesis | GO:BP | 4.55974E-15 | 8 |
| GO:0001755 | neural crest cell migration | GO:BP | 5.84543E-15 | 8 |
| GO:0038083 | peptidyl-tyrosine autophosphorylation | GO:BP | 5.85316E-15 | 8 |
| GO:0030426 | growth cone | GO:CC | 9.65822E-15 | 8 |
| KEGG:04072 | Phospholipase D signaling pathway | KEGG | 6.82377E-14 | 8 |
| GO:0009897 | external side of plasma membrane | GO:CC | 8.84506E-14 | 8 |
| GO:0098685 | Schaffer collateral - CA1 synapse | GO:CC | 1.4311E-13 | 8 |
| KEGG:04062 | Chemokine signaling pathway | KEGG | 3.091E-13 | 8 |
| GO:0048490 | antigenerode SAPC nic vesicle transport | GO:BP | 3.99487E-13 | 8 |
| GO:0005884 | actin filament | GO:CC | 4.37015E-13 | 8 |
| GO:0042802 | identical protein binding | GO:MF | 5.01235E-13 | 8 |
| KEGG:04659 | Th17 cell differentiation | KEGG | 8.92994E-13 | 8 |
| GO:0042169 | SH2 domain binding | GO:MF | 1.18104E-12 | 8 |
| KEGG:05226 | Gastric cancer | KEGG | 1.3373E-12 | 8 |
| GO:0048268 | clathrin coat assembly | GO:BP | 1.43866E-12 | 8 |
| KEGG:04640 | Hematopoietic cell lineage | KEGG | 2.72132E-12 | 8 |
| GO:0016601 | Rac protein signal transduction | GO:BP | 3.1671E-12 | 8 |
| GO:0048843 | negative regulation of axon extension involved in axon guidance | GO:BP | 3.18201E-12 | 8 |
| KEGG:05224 | Breast cancer | KEGG | 4.97352E-12 | 8 |
| GO:0005911 | cell-cell junction | GO:CC | 5.36643E-12 | 8 |
| KEGG:04721 | Synaptic vesicle cycle | KEGG | 1.41714E-11 | 8 |
| KEGG:05206 | MicroRNAs in cancer | KEGG | 1.58377E-11 | 8 |
| KEGG:04520 | Adherens junction | KEGG | 1.86798E-11 | 8 |
| GO:0005885 | Arp2/3 protein complex | GO:CC | 4.14516E-11 | 8 |
| GO:0030336 | negative regulation of cell migration | GO:BP | 4.49191E-11 | 8 |
| GO:0043524 | negative regulation of neuron apoptotic process | GO:BP | 5.02693E-11 | 8 |
| KEGG:05321 | Inflammatory bowel disease (IBD) | KEGG | 5.93308E-11 | 8 |
| GO:0005005 | transmembrane-ephrin receptor activity | GO:MF | 6.73878E-11 | 8 |
| GO:0014068 | positive regulation of phosphatidylinositol 3-kinase signaling | GO:BP | 7.11338E-11 | 8 |
| KEGG:00190 | Oxidative phosphorylation | KEGG | 1.0733E-15 | 9 |
| KEGG:04714 | Thermogenesis | KEGG | 1.2758E-14 | 9 |
| KEGG:05012 | Parkinson disease | KEGG | 1.4315E-14 | 9 |
| KEGG:05010 | Alzheimer disease | KEGG | 5.8955E-13 | 9 |
| KEGG:05016 | Huntington disease | KEGG | 3.7753E-10 | 9 |
| KEGG:04932 | Non-alcoholic fatty liver disease (NAFLD) | KEGG | 1.07598E-92 | 9 |
| GO:0005747 | mitochondrial respiratory chain complex I | GO:CC | 6.81037E-83 | 9 |
| GO:0032981 | mitochondrial respiratory chain complex I assembly | GO:BP | 5.6372E-67 | 9 |
| KEGG:01100 | Metabolic pathways | KEGG | 2.93588E-54 | 9 |
| GO:0008137 | NADH dehydrogenase (ubiquinone) activity | GO:MF | 8.89785E-50 | 9 |
| KEGG:04723 | Retrograde endocannabinoid signaling | KEGG | 5.36584E-46 | 9 |
| GO:004129 | cytochrome-c oxidase activity | GO:MF | 1.03103E-37 | 9 |
| KEGG:04260 | Cardiac muscle contraction | KEGG | 1.03193E-29 | 9 |
| GO:0006120 | mitochondrial electron transport, NADH to ubiquinone | GO:BP | 3.65312E-22 | 9 |
| GO:000276 | mitochondrial proton-transporting ATP synthase complex, coupling factor F(o) | GO:BP | 3.79348E-20 | 9 |
| GO:0046933 | proton-transporting ATP synthase activity, rotational mechanism | GO:MF | 5.55023E-19 | 9 |
| GO:0005751 | mitochondrial respiratory chain complex IV | GO:CC | 1.13322E-16 | 9 |
| GO:0051537 | 2 iron, 2 sulfur cluster binding | GO:MF | 4.88689E-16 | 9 |
| KEGG:00860 | Porphyrin and chlorophyll metabolism | KEGG | 2.93099E-14 | 9 |
| GO:0051539 | 4 iron, 4 sulfur cluster binding | GO:MF | 1.43684E-13 | 9 |
| GO:0097428 | protein maturation by iron-sulfur cluster transfer | GO:BP | 6.2627E-13 | 9 |
| GO:0005750 | mitochondrial respiratory chain complex III | GO:CC | 1.03863E-12 | 9 |
| GO:006123 | mitochondrial electron transport, cytochrome c to oxygen | GO:BP | 1.94527E-11 | 9 |
| KEGG:01100 | Metabolic pathways | KEGG | 2.1031E-127 | 10 |
| KEGG:01200 | Carbon metabolism | KEGG | 2.32431E-74 | 10 |
| KEGG:01230 | Biosynthesis of amino acids | KEGG | 7.12848E-62 | 10 |
| KEGG:00520 | Amino sugar and nucleotide sugar metabolism | KEGG | 1.03717E-43 | 10 |
| KEGG:00010 | Glycolysis / Gluconeogenesis | KEGG | 3.45294E-41 | 10 |
| KEGG:00020 | Citrate cycle (TCA cycle) | KEGG | 1.91365E-31 | 10 |
| KEGG:00030 | Pentose phosphate pathway | KEGG | 3.69414E-30 | 10 |
| GO:0006099 | tricarboxylic acid cycle | GO:BP | 2.35814E-29 | 10 |
| KEGG:00052 | Galactose metabolism | KEGG | 4.19773E-28 | 10 |
| KEGG:00051 | Fructose and mannose metabolism | KEGG | 3.41084E-27 | 10 |
| KEGG:01210 | 2-Oxocarboxylic acid metabolism | KEGG | 7.20378E-24 | 10 |
| KEGG:00250 | Alanine, aspartate and glutamate metabolism | KEGG | 7.34121E-23 | 10 |
| KEGG:00220 | Arginine biosynthesis | KEGG | 2.82275E-21 | 10 |
| GO:0004364 | glutathione transferase activity | GO:MF | 2.22827E-18 | 10 |
| GO:0051287 | NAD binding | GO:MF | 5.70857E-18 | 10 |
| GO:0046835 | carbohydrate phosphorylation | GO:BP | 1.26235E-17 | 10 |
| KEGG:00531 | Glycosaminoglycan degradation | KEGG | 1.67224E-17 | 10 |
| KEGG:00500 | Starch and sucrose metabolism | KEGG | 1.72077E-17 | 10 |
| GO:0006002 | fructose 6-phosphate metabolic process | GO:BP | 6.70684E-17 | 10 |
| KEGG:00620 | Pyruvate metabolism | KEGG | 2.06076E-16 | 10 |
| KEGG:00520 | Central carbon metabolism in cancer | KEGG | 8.52358E-16 | 10 |
| GO:0006749 | glutathione metabolic process | GO:BP | 1.4964E-15 | 10 |
| GO:0006103 | 2-oxoglutarate metabolic process | GO:BP | 1.06258E-14 | 10 |
| GO:0042803 | protein homodimerization activity | GO:MF | 4.02538E-14 | 10 |
| KEGG:00380 | Tryptophan metabolism | KEGG | 5.99802E-14 | 10 |
| GO:0005615 | extracellular space | GO:CC | 1.82512E-13 | 10 |
| KEGG:00270 | Cysteine and methionine metabolism | KEGG | 2.81159E-13 | 10 |
| KEGG:00480 | Glutathione metabolism | KEGG | 3.36252E-13 | 10 |
| KEGG:04066 | HIF-1 signaling pathway | KEGG | 1.84032E-12 | 10 |
| KEGG:00350 | Tyrosine metabolism | KEGG | 2.12536E-12 | 10 |
| GO:0043209 | myelin sheath | GO:CC | 3.41447E-12 | 10 |
| KEGG:04142 | Lyosome | KEGG | 6.39275E-12 | 10 |
| GO:0030388 | fructose 1,6-bisphosphate metabolic process | GO:BP | 1.95471E-11 | 10 |
| GO:0006000 | fructose metabolic process | GO:BP | 8.27683E-11 | 10 |
| KEGG:00562 | Inositol phosphate metabolism | KEGG | 6.20871E-11 | 11 |
| KEGG:04070 | Phosphatidylinositol signaling system | KEGG | 2.37421E-53 | 11 |
| GO:098978 | glutamatergic synapse | GO:CC | 6.28843E-38 | 11 |
| KEGG:003281 | AMPA glutamate receptor complex | GO:CC | 2.74506E-32 | 11 |
| GO:0005516 | calmodulin binding | GO:MF | 5.0898E-24 | 11 |
| GO:0030054 | cell junction | GO:CC | 4.07266E-23 | 11 |
| GO:0046854 | phosphatidylinositol phosphorylation | GO:BP | 4.28697E-22 | 11 |
| KEGG:04020 | Calcium signaling pathway | KEGG | 2.18695E-21 | 11 |
| GO:0001518 | voltage-gated sodium channel complex | GO:CC | 1.48734E-16 | 11 |
| GO:099061 | integral component of postsynaptic density membrane | GO:CC | 2.21343E-20 | 11 |
| GO:0035235 | ionotropic glutamate receptor signaling pathway | GO:BP | 3.92992E-19 | 11 |
| GO:006182 | cGMP biosynthetic process | GO:BP | 1.50152E-18 | 11 |
| KEGG:04921 | Oxytocin signaling pathway | KEGG | 1.50356E-18 | 11 |
| GO:017146 | NMDA selective glutamate receptor complex | GO:CC | 2.47556E-18 | 11 |
| GO:0008331 | high voltage-gated calcium channel activity | GO:MF | 2.33057E-17 | 11 |
| GO:0007168 | receptor guanylyl cyclase signaling pathway | GO:BP | 8.05375E-15 | 11 |
| GO:004438 | phosphatidylinositol-3-phosphatase activity | GO:MF | 1.9632E-14 | 11 |
| GO:004383 | guanylate cyclase activity | GO:MF | 1.06835E-13 | 11 |
| GO:0046855 | inositol phosphate dephosphorylation | GO:BP | 1.19575E-13 | 11 |
| KEGG:04260 | Cardiac muscle contraction | KEGG | 1.29619E-13 | 11 |
| KEGG:04261 | Adrenergic signaling in cardiomyocytes | KEGG | 1.65764E-13 | 11 |
KEGG:04713  Circadian entrainment  KEGG  2.63648E-13  11
KEGG:04724  Glutamatergic synapse  KEGG  6.15453E-13  11
GO:0060076  excitatory synapse GO:CC  1.13133E-12  11
GO:0019228  neuronal action potential GO:BP  3.64131E-12  11
GO:0098919  structural constituent of postsynaptic density GO:MF  7.41366E-12  11
GO:0016941  natriuretic peptide receptor activity GO:MF  1.42116E-11  11
GO:0016308  1-phosphatidylinositol-4-phosphate 5-kinase activity GO:MF  1.42116E-11  11
KEGG:04911  Insulin secretion KEGG  3.28673E-11  11
KEGG:04022  cGMP-PKG signaling pathway KEGG  4.87749E-11  11
KEGG:05412  Arrhythmogenic right ventricular cardiomyopathy (ARVC) KEGG  5.75525E-11  11
KEGG:05031  Amphetamine addiction KEGG  6.66078E-11  11
GO:0030314  junctional membrane complex GO:CC  9.09328E-11  11
GO:0033017  sarcoplasmic reticulum membrane GO:CC  9.61372E-11  11
KEGG:04140  Autophagy - animal KEGG  5.13947E-11  12
GO:0005829  cytosol GO:CC  1.47135E-11  12
KEGG:04150  mTOR signaling pathway KEGG  7.40498E-11  12
KEGG:04136  Autophagy - other KEGG  3.44823E-11  12
KEGG:04350  TGF-beta signaling pathway KEGG  1.33271E-11  12
KEGG:04390  Hippo signaling pathway KEGG  2.54739E-11  12
KEGG:04211  Longevity regulating pathway KEGG  1.04566E-10  12
GO:0010862  positive regulation of pathway-restricted SMAD protein phosphorylation GO:BP  3.74101E-10  12
KEGG:04392  Hippo signaling pathway - multiple species KEGG  4.85039E-19  19
GO:0035329  hippo signaling GO:BP  4.24632E-18  12
KEGG:04137  Mitophagy - animal KEGG  5.42541E-18  12
GO:0000421  autophagosome membrane GO:CC  1.61897E-17  12
GO:0030057  desmosome GO:CC  4.63355E-17  12
GO:0031932  TORC2 complex GO:CC  5.38975E-17  12
GO:0061952  midbody abscission GO:BP  7.94381E-17  12
KEGG:0194262  negative regulation of TORC1 signaling GO:BP  4.36696E-14  12
KEGG:04152  AMPK signaling pathway KEGG  4.69541E-13  12
GO:0005923  bicellular tight junction GO:CC  8.82915E-14  12
KEGG:04530  Tight junction KEGG  1.19238E-13  12
GO:0042149  cellular response to glucose starvation GO:BP  2.12413E-12  12
GO:0043162  ubiquitin-dependent protein catabolic process via the multivesicular body sorting pathway GO:BP  3.42986E-12  12
KEGG:04068  FoxO signaling pathway KEGG  9.90497E-13  12
GO:0008285  negative regulation of cell population proliferation GO:BP  1.02372E-12  12
GO:0048185  activin binding GO:MF  1.17848E-12  12
GO:0034045  phagophore assembly site membrane GO:CC  1.51418E-12  12
GO:0042803  protein homodimerization activity GO:MF  1.99144E-12  12
GO:0045324  late endosome to vacuole transport GO:BP  1.11511E-11  12
KEGG:04213  Longevity regulating pathway - multiple species KEGG  2.20269E-11  12
GO:0000815  ESCRT III complex GO:CC  6.57491E-11  12
GO:000122  negative regulation of transcription by RNA polymerase II GO:BP  1.8457E-11  13
GO:0001228  DNA-binding transcription activator activity, RNA polymerase II-specific GO:MF  5.20895E-58  58
GO:0037314  transcription corepressor activity GO:MF  1.81157E-43  43
GO:0016592  mediator complex GO:CC  2.45735E-43  43
GO:0042826  histone deacetylase binding GO:MF  1.47418E-32  32
KEGG:04330  Notch signaling pathway KEGG  3.60533E-30  30
GO:0008270  zinc ion binding GO:MF  1.37803E-29  29
GO:0003707  steroid hormone receptor activity GO:MF  6.9789E-29  29
GO:0046982  protein heterodimerization activity GO:MF  3.07951E-24  24
GO:0005719  nuclear euchromatin GO:CC  6.16523E-24  24
KEGG:05034  Alcoholism KEGG  8.90915E-24  24
GO:0035267  Nup41 histone acetyltransferase complex GO:CC  1.46728E-22  22
KEGG:05202  Transcriptional misregulation in cancer KEGG  3.52188E-22  22
GO:0035064  methylated histone binding GO:MF  1.36316E-20  20
GO:0035102  PRC1 complex GO:CC  2.32359E-20  20
GO:0000980  RNA polymerase II distal enhancer sequence-specific DNA binding GO:MF  3.75161E-20  20
GO:0016581  NuRD complex GO:CC  3.60314E-19  19
KEGG:04919  Thyroid hormone signaling pathway KEGG  5.90232E-19  19
GO:0016514  SWI/SNF complex GO:CC  6.73773E-19  19
GO:0071565  nBAF complex GO:CC  7.05718E-19  19
GO:1990841  promoter-specific chromatin binding GO:MF  6.87351E-18  18
GO:0035914  skeletal muscle cell differentiation GO:BP  1.35963E-17  17
| GO:0001227 | DNA-binding transcription repressor activity, RNA polymerase II-specific | GO:MF | 1.77034E-17 | 13 |
| GO:0043968 | histone H2A acetylation | GO:BP | 2.00242E-17 | 13 |
| GO:0042800 | histone methyltransferase activity (H3-K4 specific) | GO:MF | 2.70255E-17 | 13 |
| GO:0004879 | nuclear receptor activity | GO:MF | 5.28162E-17 | 13 |
| GO:0035098 | ESC/E(Z) complex | GO:CC | 7.95616E-17 | 13 |
| GO:0035019 | somatic stem cell population maintenance | GO:BP | 2.2987E-16 | 13 |
| GO:0001102 | RNA polymerase II activating transcription factor binding | GO:MF | 2.50908E-16 | 13 |
| GO:0006337 | nucleosome disassembly | GO:BP | 5.37332E-16 | 13 |
| GO:0043982 | histone H4-K8 acetylation | GO:BP | 5.37332E-16 | 13 |
| GO:0043981 | histone H4-K5 acetylation | GO:BP | 5.37332E-16 | 13 |
| GO:0008285 | negative regulation of cell population proliferation | GO:BP | 9.13407E-16 | 13 |
| KEGG:05322 | Systemic lupus erythematosus | KEGG | 4.03273E-15 | 13 |
| GO:0016580 | Sin3 complex | GO:CC | 8.17106E-15 | 13 |
| GO:0071564 | npiBAF complex | GO:CC | 1.96088E-14 | 13 |
| GO:0043984 | histone H4-K16 acetylation | GO:BP | 2.14766E-14 | 13 |
| GO:0016342 | catenin complex | GO:CC | 1.27236E-13 | 13 |
| GO:0071339 | MLL1 complex | GO:CC | 2.25411E-12 | 13 |
| KEGG:05203 | Viral carcinogenesis | KEGG | 4.47553E-12 | 13 |
| GO:0003151 | outflow tract morphogenesis | GO:BP | 6.0726E-12 | 13 |
| GO:1990907 | beta-catenin-TCF complex | GO:CC | 6.319E-12 | 13 |
| GO:0016607 | nuclear speck | GO:CC | 1.45691E-11 | 13 |
| KEGG:00310 | Lysine degradation | KEGG | 2.21301E-11 | 13 |
| GO:0001085 | RNA polymerase II transcription factor binding | GO:MF | 3.3572E-11 | 13 |
| GO:0008584 | male gonad development | GO:BP | 4.07055E-11 | 13 |
| GO:0032482 | Rab protein signal transduction | GO:BP | 2.6366E-04 | 14 |
| GO:0008076 | voltage-gated potassium channel complex | GO:CC | 4.07326E-04 | 14 |
| KEGG:04514 | Cell adhesion molecules (CAMs) | KEGG | 1.76891E-40 | 14 |
| GO:0005251 | delayed rectifier potassium channel activity | GO:MF | 3.5572E-40 | 14 |
| KEGG:04145 | Phagosome | KEGG | 1.07118E-33 | 14 |
| GO:0009897 | external side of plasma membrane | GO:CC | 3.32473E-32 | 14 |
| GO:0003924 | GTPase activity | GO:MF | 2.43234E-27 | 14 |
| GO:0030670 | phagocytic vesicle membrane | GO:CC | 3.47362E-24 | 14 |
| GO:0005525 | GTP binding | GO:MF | 1.62971E-23 | 14 |
| GO:0042605 | peptide antigen binding | GO:MF | 2.80517E-22 | 14 |
| GO:0005892 | acetylcholine-gated channel complex | GO:CC | 4.04069E-22 | 14 |
| KEGG:04612 | Antigen processing and presentation | KEGG | 1.11323E-21 | 14 |
| KEGG:0022848 | acetylcholine-gated cation-selective channel activity | GO:MF | 5.69632E-21 | 14 |
| GO:0002476 | antigen processing and presentation of endogenous peptide antigen via MHC class I | GO:BP | 1.08901E-20 | 14 |
| GO:0001916 | positive regulation of T cell mediated cytotoxicity | GO:BP | 5.02223E-20 | 14 |
| GO:0002486 | antigen processing and presentation of endogenous peptide antigen via MHC class I via ER pathway, TAP-independent | GO:BP | 2.70969E-19 | 14 |
| KEGG:05332 | Graft-versus-host disease | KEGG | 6.06442E-19 | 14 |
| GO:0006886 | intracellular protein transport | GO:BP | 1.8273E-18 | 14 |
| GO:0045121 | membrane raft | GO:CC | 4.07633E-18 | 14 |
| GO:0019003 | GDP binding | GO:MF | 1.09991E-17 | 14 |
| GO:0070229 | integrin-mediated signaling pathway | GO:BP | 2.72593E-17 | 14 |
| GO:0042166 | acetylcholine binding | GO:MF | 6.19982E-17 | 14 |
| GO:0008305 | integrin complex | GO:CC | 1.00803E-16 | 14 |
| GO:0051260 | protein homooligomerization | GO:BP | 2.04054E-16 | 14 |
| KEGG:05416 | Viral myocarditis | KEGG | 7.71099E-15 | 14 |
| GO:0007160 | cell-matrix adhesion | GO:BP | 1.43136E-14 | 14 |
| KEGG:05330 | Allograft rejection | KEGG | 3.86825E-14 | 14 |
| GO:0098993 | anchored component of synaptic vesicle membrane | GO:CC | 4.17035E-14 | 14 |
| GO:0015464 | acetylcholine receptor activity | GO:MF | 1.0478E-13 | 14 |
| GO:0017112 | Rab guanyl-nucleotide exchange factor activity | GO:MF | 1.8263E-13 | 14 |
| KEGG:04940 | Type I diabetes mellitus | KEGG | 6.0253E-13 | 14 |
| GO:0062061 | TAP complex binding | GO:MF | 1.73885E-12 | 14 |
| GO:0060079 | excitatory postsynaptic potential | GO:BP | 3.69826E-12 | 14 |
| KEGG:05320 | Autoimmune thyroid disease | KEGG | 6.36752E-12 | 14 |
| KEGG:05170 | Human immunodeficiency virus 1 infection | KEGG | 2.06182E-11 | 14 |
| GO:007271 | synaptic transmission, cholinergic | GO:BP | 5.30237E-11 | 14 |
| GO:0042612 | MHC class I protein complex | GO:CC | 8.0623E-11 | 14 |
| GO:0030881 | beta-2-microglobulin binding | GO:MF | 9.14682E-11 | 14 |
| GO:0042610 | CD8 receptor binding | GO:MF | 9.14682E-11 | 14 |
| GO:0003735 | structural constituent of ribosome | GO:MF | 1.3222E-12 | 15 |
| KEGG:03010 | Ribosome | KEGG | 1.12355E-10 | 15 |
| GO:0022625 | cytosolic large ribosomal subunit | GO:CC | 1.66148E-89 | 15 |
| GO:0033743 | translation initiation factor activity | GO:MF | 1.16138E-77 | 15 |
| GO:0022627 | cytosolic small ribosomal subunit | GO:CC | 2.40863E-66 | 15 |
| GO:0042788 | polysomal ribosome | GO:CC | 2.77354E-39 | 15 |
| KEGG:03013 | RNA transport | KEGG | 5.70043E-37 | 15 |
| GO:0001732 | formation of cytoplasmic translation initiation complex | GO:BP | 7.31361E-29 | 15 |
| GO:0016282 | eukaryotic 43S preinitiation complex | GO:CC | 1.81134E-28 | 15 |
| GO:0033290 | eukaryotic 48S preinitiation complex | GO:CC | 1.04767E-27 | 15 |
| GO:0000184 | nuclear-transcribed mRNA catabolic process, nonsense-mediated decay | GO:BP | 9.99736E-21 | 15 |
| GO:0043022 | ribosome binding | GO:MF | 2.68754E-17 | 15 |
| GO:0001731 | formation of translation preinitiation complex | GO:BP | 5.04274E-17 | 15 |
| GO:0000028 | ribosomal small subunit assembly | GO:BP | 6.32705E-15 | 15 |
| GO:0071541 | eukaryotic translation initiation factor 3 complex, elf3m | GO:CC | 7.67282E-14 | 15 |
| KEGG:03015 | mRNA surveillance pathway | KEGG | 6.40058E-13 | 15 |
| GO:0031369 | translation initiation factor binding | GO:MF | 1.33208E-12 | 15 |
| GO:008250 | oligosaccharyltransferase complex | GO:CC | 1.23058E-11 | 15 |
| GO:0000027 | ribosomal large subunit assembly | GO:BP | 1.57132E-11 | 15 |
| GO:0006446 | regulation of translational initiation | GO:BP | 9.80757E-11 | 15 |
| KEGG:03040 | Spliceosome | KEGG | 5.2859E-17 | 16 |
| GO:0016607 | nuclear speck | GO:CC | 8.76266E-91 | 16 |
| GO:0071005 | U2-type precatalytic spliceosome | GO:CC | 1.96066E-68 | 16 |
| GO:0071007 | U2-type catalytic step 2 spliceosome | GO:CC | 1.64065E-42 | 16 |
| KEGG:03015 | mRNA surveillance pathway | KEGG | 2.05276E-42 | 16 |
| GO:0005689 | U12-type spliceosomal complex | GO:CC | 3.03779E-39 | 16 |
| GO:0046540 | U4/U6 x US tri-snRNP complex | GO:CC | 4.08891E-36 | 16 |
| KEGG:03022 | Basal transcription factors | KEGG | 7.56268E-34 | 16 |
| GO:0005669 | transcription factor TFIID complex | GO:CC | 2.4552E-31 | 16 |
| GO:0005686 | U2 snRNPs | GO:CC | 1.16496E-27 | 16 |
| GO:0003811 | regulation of alternative mRNA splicing, via spliceosome | GO:BP | 6.66685E-27 | 16 |
| GO:0005666 | RNA polymerase III complex | GO:CC | 5.72796E-26 | 16 |
| GO:0005685 | U1 snRNPs | GO:CC | 1.67814E-25 | 16 |
| GO:0034719 | SMN-Sm protein complex | GO:CC | 1.67814E-25 | 16 |
| KEGG:03020 | RNA polymerase | KEGG | 1.91397E-25 | 16 |
| KEGG:03013 | RNA transport | KEGG | 1.64902E-24 | 16 |
| GO:0001056 | RNA polymerase III activity | GO:MF | 1.19241E-22 | 16 |
| GO:0005682 | U5 snRNPs | GO:CC | 6.57842E-21 | 16 |
| GO:015030 | Cajal body | GO:CC | 4.78117E-20 | 16 |
| GO:0045292 | mRNA cis splicing, via spliceosome | GO:BP | 1.45324E-19 | 16 |
| GO:0071004 | U2-type prespliceosome | GO:CC | 1.17755E-18 | 16 |
| GO:0005847 | mRNA cleavage and polyadenylation specificity factor complex | GO:CC | 1.79593E-16 | 16 |
| GO:0009974 | Prp19 complex | GO:CC | 5.07374E-16 | 16 |
| GO:0048025 | negative regulation of mRNA splicing, via spliceosome | GO:BP | 8.01165E-16 | 16 |
| GO:0005687 | U4 snRNPs | GO:CC | 3.07526E-15 | 16 |
| GO:0005665 | RNA polymerase II, core complex | GO:CC | 4.53247E-15 | 16 |
| GO:0032968 | positive regulation of transcription elongation from RNA polymerase II promoter | GO:BP | 1.02276E-14 | 16 |
| GO:0000993 | RNA polymerase II complex binding | GO:MF | 4.81741E-14 | 16 |
| GO:0033276 | transcription factor TFFC complex | GO:CC | 7.65021E-14 | 16 |
| GO:1990446 | U1 snRNPs binding | GO:MF | 1.70251E-13 | 16 |
| GO:0000124 | SAGA complex | GO:CC | 8.33367E-13 | 16 |
| GO:0071006 | U2-type catalytic step 1 spliceosome | GO:CC | 8.33367E-13 | 16 |
| GO:0016251 | RNA polymerase II general transcription initiation factor activity | GO:MF | 8.75725E-13 | 16 |
| GO:0032797 | SMN complex | GO:CC | 1.53834E-12 | 16 |
| GO:0032039 | integrator complex | GO:CC | 1.68947E-12 | 16 |
| GO:0036396 | RNA N6-methyladenosine methyltransferase complex | GO:CC | 7.95599E-12 | 16 |
| GO:0004402 | histone acetyltransferase activity | GO:MF | 2.26079E-11 | 16 |
| GO:0098789 | pre-mRNA cleavage required for polyadenylation | GO:BP | 5.5435E-11 | 16 |
| GO:0001055 | RNA polymerase II activity | GO:MF | 7.93302E-11 | 16 |
| KEGG:00601 | Glycosphingolipid biosynthesis - lacto and neolacto series | KEGG | 1.92445E-48 | 17 |
| KEGG:00512 | Mucin type O-glycan biosynthesis | KEGG | 1.78461E-47 | 17 |
| KEGG:01100 | Metabolic pathways | KEGG | 4.22535E-42 | 17 |
| GO:0032580 | Golgi cisterna membrane | GO:CC | 1.1987E-30 | 17 |
GO:0004653 polypeptide N-acetylgalactosaminyltransferase activity
GO:0016021 integral component of membrane
KEGG:00063 Glycosphingolipid biosynthesis - globo and isogloblo series
KEGG:00033 Glycosaminoglycan biosynthesis - keratan sulfate
KEGG:00064 Glycosphingolipid biosynthesis - ganglio series
GO:0030311 poly-N-acetyllactosamine biosynthetic process
GO:0008532 N-acetyllactosaminide beta-1,3-N-acetylgalcosaminyltransferase activity
GO:0009312 oligosaccharide biosynthetic process
GO:0030259 lipid glycosylation
KEGG:000510 N-Glycan biosynthesis
KEGG:01100 Metabolic pathways
KEGG:00830 Retinol metabolism
GO:0007006 iron ion binding
KEGG:00140 Steroid hormone biosynthesis
GO:0020037 heme binding
KEGG:04146 Peroxisome
KEGG:000590 Arachidonic acid metabolism
KEGG:00071 Fatty acid degradation
KEGG:01212 Fatty acid metabolism
KEGG:005204 Chemical carcinogenesis
GO:0070330 aromatase activity
KEGG:000280 Valine, leucine and isoleucine degradation
GO:0042738 exogenous drug catabolic process
KEGG:00410 beta-Alanine metabolism
GO:0008392 arachidonic acid epoxygenase activity
KEGG:00650 Butanoate metabolism
KEGG:00980 Metabolism of xenobiotics by cytochrome P450
GO:0019373 epoxidegenase P450 pathway
KEGG:00260 Glycine, serine and threonine metabolism
GO:0042572 retinol metabolic process
KEGG:0004745 retinol dehydrogenase activity
KEGG:000661 Fatty acid biosynthesis
KEGG:000982 Drug metabolism - cytochrome P450
KEGG:00340 Histidine metabolism
KEGG:00062 Fatty acid elongation
KEGG:000591 Linoleic acid metabolism
GO:0005782 peroxisomal matrix
KEGG:00320 PPAR signaling pathway
KEGG:00120 Primary bile acid biosynthesis
KEGG:00053 Ascorbate and aldarate metabolism
KEGG:000670 One carbon pool by folate
KEGG:001040 Biosynthesis of unsaturated fatty acids
KEGG:001949 FAD binding
KEGG:00640 Propanoate metabolism
KEGG:0008401 retinoic acid 4-hydroxylase activity
KEGG:0003996 acyl-CoA ligase activity
GO:0051287 NAD binding
KEGG:0006695 cholesterol biosynthetic process
GO:0035999 tetrahydrofolate interconversion
KEGG:00900 Terpenoid backbone biosynthesis
KEGG:003359 fatty acid beta-oxidation using acyl-CoA dehydrogenase
KEGG:00630 Glyoxylate and dicarboxylate metabolism
KEGG:00380 Tryptophan metabolism
KEGG:0101020 estrogen 16-alpha-hydroxylase activity
KEGG:0051289 protein homotetramerization
KEGG:003170 pyridoxal phosphate binding
GO:0000662 fatty-acyl-CoA binding
KEGG:0035338 long-chain fatty-acyl-CoA biosynthetic process
GO:0015020 glucuronosyltransferase activity
KEGG:01200 Carbon metabolism
KEGG:00480 Glutathione metabolism
GO:0042803 protein homodimerization activity
KEGG:00350 Tyrosine metabolism
KEGG:00072 Synthesis and degradation of ketone bodies
KEGG:00100 Steroid biosynthesis
| KEGG:04913 | Ovarian steroidogenesis | KEGG | 3.67174E-12 | 19 |
| GO:0102391 | decanoate-CoA ligase activity | GO:MF | 6.57334E-12 | 19 |
| KEGG:04726 | Serotoninergic synapse | KEGG | 2.21604E-11 | 19 |
| GO:0003857 | 3-hydroxyacyl-CoA dehydrogenase activity | GO:MF | 2.99463E-11 | 19 |
| KEGG:00230 | Purine metabolism | KEGG | 2.7605E-100 | 20 |
| KEGG:00240 | Pyrimidine metabolism | KEGG | 8.85226E-73 | 20 |
| KEGG:01100 | Metabolic pathways | KEGG | 4.38655E-69 | 20 |
| KEGG:00760 | Nicotinate and nicotinamide metabolism | KEGG | 2.91517E-35 | 20 |
| GO:0004550 | nucleoside diphosphate kinase activity | GO:MF | 1.01148E-28 | 20 |
| KEGG:00083 | Drug metabolism - other enzymes | KEGG | 3.06396E-20 | 20 |
| GO:0005524 | ATP binding | GO:MF | 1.95226E-19 | 20 |
| GO:0046940 | nucleoside monophosphate phosphorylation | GO:BP | 3.40244E-19 | 20 |
| GO:0006165 | nucleoside diphosphate phosphorylation | GO:BP | 5.40929E-15 | 20 |
| GO:0004115 | 3',5'-cyclic-AMP phosphodiesterase activity | GO:MF | 2.17394E-14 | 20 |
| GO:0008253 | 5'-nucleotidase activity | GO:MF | 2.17394E-14 | 20 |
| KEGG:00730 | Thiamine metabolism | KEGG | 3.18128E-13 | 20 |
| KEGG:00740 | Riboflavin metabolism | KEGG | 4.54761E-13 | 20 |
| GO:0006183 | GTP biosynthetic process | GO:BP | 2.14529E-12 | 20 |
| KEGG:00770 | Pantothenate and CoA biosynthesis | KEGG | 4.44066E-12 | 20 |
| GO:0004017 | adenylate kinase activity | GO:MF | 5.01205E-12 | 20 |
| GO:0006198 | cAMP catabolic process | GO:BP | 6.70203E-11 | 20 |
| GO:0030150 | protein import into mitochondrial matrix | GO:BP | 4.41987E-24 | 21 |
| GO:0005742 | mitochondrial outer membrane translocase complex | GO:CC | 1.98684E-21 | 21 |
| KEGG:03008 | Ribosome biogenesis in eukaryotes | KEGG | 3.78769E-98 | 22 |
| GO:0032040 | small-subunit processome | GO:CC | 2.52144E-52 | 22 |
| GO:0030687 | preribosome, large subunit precursor | GO:CC | 7.01799E-35 | 22 |
| GO:0000176 | nuclear exosome (RNase complex) | GO:CC | 1.59014E-22 | 22 |
| KEGG:03018 | RNA degradation | KEGG | 9.84716E-22 | 22 |
| GO:0001682 | tRNA 5'-leader removal | GO:BP | 9.63304E-19 | 22 |
| GO:0033204 | ribonuclease P RNA binding | GO:MF | 1.40756E-18 | 22 |
| GO:0003724 | RNA helicase activity | GO:MF | 1.83553E-18 | 22 |
| GO:0004526 | ribonuclease P activity | GO:MF | 1.53658E-17 | 22 |
| GO:0034427 | nuclear-transcribed mRNA catabolic process, exonucleolytic, 3'-5' | GO:BP | 9.83391E-15 | 22 |
| GO:0000027 | ribosomal large subunit assembly | GO:BP | 3.27084E-14 | 22 |
| GO:0000177 | cytoplasmic exosome (RNase complex) | GO:CC | 4.20105E-13 | 22 |
| GO:0001650 | fibrillar center | GO:CC | 6.65056E-11 | 22 |
| GO:0034475 | U4 snRNA 3'-end processing | GO:BP | 9.44435E-11 | 22 |
| GO:0030020 | extracellular matrix structural constituent conferring tensile strength | GO:MF | 5.23144E-70 | 23 |
| KEGG:04974 | Protein digestion and absorption | KEGG | 1.13188E-51 | 23 |
| GO:0005615 | extracellular space | GO:CC | 3.12784E-36 | 23 |
| GO:0003109 | collagen fibril organization | GO:BP | 1.29255E-33 | 23 |
| GO:004222 | metalloendopeptidase activity | GO:MF | 2.42731E-25 | 23 |
| KEGG:04512 | ECM-receptor interaction | KEGG | 1.36643E-20 | 23 |
| KEGG:04510 | Focal adhesion | KEGG | 4.46554E-14 | 23 |
| GO:0008201 | heparin binding | GO:MF | 1.87255E-12 | 23 |
| GO:0048407 | platelet-derived growth factor binding | GO:MF | 1.98065E-11 | 23 |
| GO:0005587 | collagen type IV trimer | GO:CC | 5.05564E-11 | 23 |
| GO:0005762 | mitochondrial large ribosomal subunit | GO:CC | 8.8535E-116 | 27 |
| GO:0003735 | structural constituent of ribosome | GO:MF | 5.2581E-115 | 27 |
| KEGG:03010 | Ribosome | KEGG | 5.50745E-75 | 27 |
| GO:0005763 | mitochondrial small ribosomal subunit | GO:CC | 1.36717E-59 | 27 |
| GO:0019843 | rRNA binding | GO:MF | 9.54753E-13 | 27 |
| KEGG:05414 | Dilated cardiomyopathy (DCM) | KEGG | 1.73736E-14 | 28 |
| KEGG:05410 | Hypertrophic cardiomyopathy (HCM) | KEGG | 5.90324E-33 | 28 |
| GO:0051015 | actin filament binding | GO:MF | 1.86116E-25 | 28 |
| GO:0008307 | structural constituent of muscle | GO:MF | 3.74042E-16 | 28 |
| GO:0042383 | sarcosome | GO:CC | 4.3611E-16 | 28 |
| KEGG:04260 | Cardiac muscle contraction | KEGG | 8.71502E-16 | 28 |
| KEGG:04261 | Adrenergic signaling in cardiomyocytes | KEGG | 1.02887E-14 | 28 |
| GO:0030018 | Z disc | GO:CC | 1.57283E-14 | 28 |
| GO:0005523 | tropomyosin binding | GO:MF | 8.1264E-14 | 28 |
| GO:0005516 | calmodulin binding | GO:MF | 8.18777E-14 | 28 |
| KEGG:05412 | Arrhythmogenic right ventricular cardiomyopathy (ARVC) | KEGG | 2.81566E-13 | 28 |
| GO:0016012 | sargocyan complex | GO:CC | 2.14984E-12 | 28 |
| GO:0002026 | regulation of the force of heart contraction | GO:BP | 4.31058E-12 | 28 |
GO:0045214 sarcomere organization
GO:0055010 ventricular cardiac muscle tissue morphogenesis
GO:0001725 stress fiber
GO:0055003 cardiac myofibril assembly
KEGG:00970 Aminoacyl-tRNA biosynthesis
GO:0005524 ATP binding
GO:0000049 tRNA binding
GO:0017101 aminoacyl-tRNA synthetase multienzyme complex
GO:0002161 aminoacyl-tRNA editing activity
GO:0106074 aminoacyl-tRNA metabolism involved in translational fidelity
GO:004826 phenylalanine-tRNA ligase activity
KEGG:00564 Glycerophospholipid metabolism
GO:0004826 phenylalanine-tRNA ligase activity
KEGG:00565 Ether lipid metabolism
KEGG:00600 Sphingolipid metabolism
KEGG:01100 Metabolic pathways
KEGG:00561 Glycerolipid metabolism
KEGG:04975 Fat digestion and absorption
KEGG:04071 Sphingolipid signaling pathway
GO:0046512 sphingosine biosynthetic process
GO:0004622 lysophospholipase activity
GO:0102567 phospholipase A2 activity (consuming 1,2-dipalmitoylphosphatidylcholine)
GO:0102568 phospholipase A2 activity consuming 1,2-dioleoylphosphatidylethanolamine
KEGG:04972 Pancreatic secretion
KEGG:0006657 CDP-choline pathway
GO:0018024 CDP-diacylglycerol biosynthetic process
GO:0050482 arachidonic acid secretion
GO:0003841 1-acylglycerol-3-phosphate O-acyltransferase activity
GO:0009952 anterior/posterior pattern specification
GO:0009980 RNA polymerase II distal enhancer sequence-specific DNA binding
GO:0048704 embryonic skeletal system morphogenesis
KEGG:03018 RNA degradation
GO:0017148 negative regulation of translation
GO:0004535 poly(A)-specific ribonuclease activity
GO:0030015 CCR4-NOT core complex
GO:0031047 gene silencing by RNA
GO:0090503 RNA phosphodiester bond hydrolysis, exonucleolytic
GO:0000932 P-body
Supplementary Table S8. In- and out-degree for each community in the HSA network

| Community | In-degree | Out-degree | Community | In-degree | Out-degree |
|-----------|-----------|------------|-----------|-----------|------------|
| 0         | 29.93     | 24.40      | 13        | 39.43     | 33.94      |
| 1         | 24.82     | 19.78      | 14        | 33.29     | 18.48      |
| 2         | 24.09     | 13.56      | 15        | 23.84     | 30.17      |
| 3         | 15.06     | 51.87      | 16        | 34.40     | 25.24      |
| 4         | 23.61     | 57.90      | 18        | 23.94     | 14.85      |
| 5         | 30.05     | 23.79      | 19        | 23.88     | 32.37      |
| 6         | 34.06     | 35.12      | 20        | 34.89     | 8.25       |
| 7         | 39.86     | 32.54      | 22        | 15.81     | 6.03       |
| 8         | 39.89     | 34.23      | 23        | 19.94     | 31.11      |
| 9         | 36.12     | 13.91      | 28        | 24.34     | 63.13      |
| 10        | 39.80     | 17.21      | 30        | 25.79     | 10.52      |
| 11        | 31.00     | 55.16      | 33        | 4.35      | 4.20       |
| 12        | 25.94     | 39.87      | 35        | 34.37     | 34.87      |
Supplementary Table S9. In- and out-degree for each community in the MMU network

| community | in-degree | out-degree | community | in-degree | out-degree |
|-----------|-----------|------------|-----------|-----------|------------|
| 0         | 19.35     | 31.81      | 15        | 19.30     | 14.18      |
| 1         | 20.05     | 73.43      | 16        | 26.80     | 9.26       |
| 3         | 26.44     | 32.89      | 17        | 26.09     | 11.18      |
| 4         | 28.42     | 5.44       | 19        | 16.47     | 8.35       |
| 5         | 36.00     | 35.95      | 20        | 19.46     | 16.83      |
| 6         | 30.18     | 33.94      | 21        | 18.08     | 0.00       |
| 7         | 22.11     | 27.98      | 22        | 15.99     | 20.18      |
| 8         | 33.55     | 14.68      | 23        | 20.31     | 23.46      |
| 9         | 11.36     | 13.93      | 27        | 8.54      | 32.01      |
| 10        | 20.70     | 21.58      | 28        | 21.66     | 55.51      |
| 11        | 29.72     | 11.38      | 29        | 15.69     | 0.00       |
| 12        | 36.73     | 23.10      | 30        | 27.91     | 5.19       |
| 13        | 35.63     | 24.51      | 33        | 4.89      | 43.32      |
| 14        | 26.94     | 8.49       | 66        | 44.01     | 63.83      |