**Supplementary Information**

Table S1: Significant UP\_TISSUE enrichments and depletions.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Enriched** | | | | **Depleted** | | | |
| **Tissue** | **FE** | **p-value** | **Benjamini** | **Tissue** | **FE** | **p-value** | **Benjamini** |
| Plasma | 1.56 | 1.40E-06 | 1.64E-04 | Hair root | 1.30 | 1.22E-05 | 3.95E-03 |
| Fetal kidney | 1.55 | 1.58E-04 | 8.14E-03 | Umbilical cord blood | 1.17 | 6.56E-09 | 4.24E-06 |
| Hepatoma | 1.50 | 8.76E-05 | 5.83E-03 | Cajal-Retzius cell | 1.16 | 1.69E-05 | 3.63E-03 |
| Epithelium | 1.44 | 1.50E-37 | 7.01E-35 |  |  |  |  |
| Amygdala | 1.32 | 3.39E-05 | 2.63E-03 |  |  |  |  |
| Teratocarcinoma | 1.31 | 1.62E-04 | 7.55E-03 |  |  |  |  |
| Spleen | 1.26 | 3.12E-05 | 2.91E-03 |  |  |  |  |
| Testis | 1.21 | 1.22E-17 | 1.90E-15 |  |  |  |  |
| Brain | 1.18 | 1.80E-30 | 4.21E-28 |  |  |  |  |

Table S2: Significant UNIGENE\_EST\_QUARTILE enrichments and depletions.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Enriched** | | | | **Depleted** | | | |
| **Tissue** | **FE** | **p-value** | **Benjamini** | **Tissue** | **FE** | **p-value** | **Benjamini** |
| larynx\_normal\_3rd | 1.35 | 1.50E-26 | 1.14E-24 | salivary gland\_normal\_3rd | 1.05 | 2.77E-06 | 2.10E-04 |
| oral tumor\_disease\_3rd | 1.35 | 8.45E-24 | 1.60E-22 | neonate (< 4 weeks old)\_development\_3rd | 1.03 | 7.94E-04 | 1.50E-02 |
| pharynx\_normal\_3rd | 1.33 | 2.62E-14 | 1.99E-13 | non-glioma\_disease\_3rd | 1.03 | 1.49E-04 | 5.65E-03 |
| laryngeal cancer\_disease\_3rd | 1.33 | 2.42E-24 | 6.14E-23 | bone marrow\_normal\_3rd | 1.03 | 5.42E-04 | 1.36E-02 |
| tongue\_normal\_3rd | 1.31 | 6.07E-26 | 2.31E-24 | heart\_normal\_3rd | 1.02 | 9.88E-04 | 1.49E-02 |
| thyroid\_normal\_3rd | 1.26 | 3.36E-19 | 5.11E-18 | skin\_normal\_3rd | 1.02 | 1.59E-03 | 1.99E-02 |
| trachea\_normal\_3rd | 1.26 | 3.56E-16 | 3.66E-15 |  |  |  |  |
| pharyngeal tumor\_disease\_3rd | 1.25 | 1.93E-09 | 1.22E-08 |  |  |  |  |
| thyroid tumor\_disease\_3rd | 1.23 | 1.11E-14 | 9.37E-14 |  |  |  |  |
| mammary gland\_normal\_3rd | 1.22 | 8.77E-18 | 1.11E-16 |  |  |  |  |
| colorectal tumor\_disease\_3rd | 1.22 | 1.07E-14 | 1.01E-13 |  |  |  |  |
| breast (mammary gland) cancer\_disease\_3rd | 1.19 | 3.06E-11 | 2.11E-10 |  |  |  |  |
| adipose tissue\_normal\_3rd | 1.16 | 4.51E-07 | 2.28E-06 |  |  |  |  |
| colon\_normal\_3rd | 1.15 | 2.51E-09 | 1.47E-08 |  |  |  |  |
| uterine tumor\_disease\_3rd | 1.13 | 5.07E-07 | 2.41E-06 |  |  |  |  |
| eye\_normal\_3rd | 1.13 | 2.10E-08 | 1.14E-07 |  |  |  |  |
| muscle\_normal\_3rd | 1.12 | 7.95E-06 | 3.36E-05 |  |  |  |  |
| lymph node\_normal\_3rd | 1.12 | 4.02E-06 | 1.80E-05 |  |  |  |  |
| thymus\_normal\_3rd | 1.11 | 2.26E-04 | 9.02E-04 |  |  |  |  |
| ear\_normal\_3rd | 1.09 | 6.52E-03 | 2.05E-02 |  |  |  |  |
| pituitary gland\_normal\_3rd | 1.09 | 4.07E-03 | 1.34E-02 |  |  |  |  |
| connective tissue\_normal\_3rd | 1.08 | 8.06E-03 | 2.43E-02 |  |  |  |  |
| chondrosarcoma\_disease\_3rd | 1.08 | 1.63E-03 | 5.90E-03 |  |  |  |  |
| testis\_normal\_3rd | 1.07 | 6.92E-04 | 2.63E-03 |  |  |  |  |

Table S3: Significant InterPro enrichments and depletions.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Enriched** | | | | **Depleted** | | | |
| **Pfam** | **FE** | **p-value** | **Benjamini** | **Pfam** | **FE** | **p-value** | **Benjamini** |
| Dynein heavy chain | 4.50 | 1.95E-09 | 6.57E-07 | High sulphur keratin-associated protein | 1.29 | 1.64E-05 | 1.81E-02 |
| Dynein heavy chain domain | 4.50 | 1.95E-09 | 6.57E-07 | Small GTP-binding protein domain | 1.21 | 1.20E-07 | 2.35E-04 |
| Dynein heavy chain, coiled coil stalk | 4.50 | 1.95E-09 | 6.57E-07 | Thioredoxin-like fold | 1.20 | 5.50E-06 | 7.13E-03 |
| Dynein heavy chain, domain-2 | 4.50 | 1.95E-09 | 6.57E-07 | Olfactory receptor | 1.20 | 1.35E-17 | 3.51E-14 |
| Dynein heavy chain, P-loop containing D4 domain | 4.50 | 8.26E-09 | 2.35E-06 | GPCR, rhodopsin-like, 7TM | 1.18 | 1.72E-22 | 1.35E-18 |
| ATPase, dynein-related, AAA domain | 4.50 | 3.48E-08 | 7.60E-06 | G protein-coupled receptor, rhodopsin-like | 1.17 | 8.42E-22 | 3.29E-18 |
| Peptidase A2A, retrovirus RVP subgroup | 4.50 | 1.04E-05 | 9.89E-04 | Krueppel-associated box | 1.13 | 6.74E-07 | 1.05E-03 |
| Dynein heavy chain, domain-1 | 4.50 | 4.24E-05 | 3.41E-03 |  |  |  |  |
| Retroviral nucleocapsid protein Gag | 4.50 | 4.24E-05 | 3.41E-03 |  |  |  |  |
| Beta-retroviral matrix, N-terminal | 4.50 | 4.24E-05 | 3.41E-03 |  |  |  |  |
| PH-BEACH domain | 4.50 | 1.71E-04 | 1.08E-02 |  |  |  |  |
| Na/K/Cl co-transporter superfamily | 4.50 | 6.77E-04 | 3.62E-02 |  |  |  |  |
| Peptidase A2A, retrovirus, catalytic | 4.09 | 4.59E-05 | 3.54E-03 |  |  |  |  |
| Retrovirus capsid, N-terminal core | 4.05 | 1.70E-04 | 1.10E-02 |  |  |  |  |
| Myosin-like IQ motif-containing domain | 4.03 | 1.64E-08 | 4.33E-06 |  |  |  |  |
| BEACH domain | 4.00 | 6.20E-04 | 3.37E-02 |  |  |  |  |
| Retroviral envelope protein | 4.00 | 6.20E-04 | 3.37E-02 |  |  |  |  |
| MyTH4 domain | 4.00 | 6.20E-04 | 3.37E-02 |  |  |  |  |
| Myosin, N-terminal, SH3-like | 3.90 | 3.24E-06 | 3.54E-04 |  |  |  |  |
| Myosin tail | 3.79 | 2.35E-07 | 3.63E-05 |  |  |  |  |
| Spectrin/alpha-actinin | 3.57 | 1.18E-09 | 4.38E-07 |  |  |  |  |
| Spectrin repeat | 3.42 | 1.55E-07 | 2.61E-05 |  |  |  |  |
| Laminin, N-terminal | 3.38 | 9.01E-05 | 6.53E-03 |  |  |  |  |
| Myosin head, motor domain | 3.04 | 7.82E-09 | 2.42E-06 |  |  |  |  |
| Mitochondrial carrier protein | 3.00 | 6.15E-06 | 6.16E-04 |  |  |  |  |
| Peptidase aspartic, active site | 3.00 | 1.02E-04 | 6.99E-03 |  |  |  |  |
| G-patch domain | 2.96 | 1.09E-06 | 1.39E-04 |  |  |  |  |
| SNF2-related | 2.96 | 1.09E-06 | 1.39E-04 |  |  |  |  |
| Actinin-type, actin-binding, conserved site | 2.94 | 7.14E-05 | 5.28E-03 |  |  |  |  |
| Cadherin, N-terminal | 2.91 | 1.63E-12 | 6.71E-10 |  |  |  |  |
| Arf GTPase activating protein | 2.85 | 8.68E-06 | 8.46E-04 |  |  |  |  |
| IQ motif, EF-hand binding site | 2.85 | 1.34E-15 | 9.88E-13 |  |  |  |  |
| Mitochondrial carrier domain | 2.63 | 5.71E-08 | 1.11E-05 |  |  |  |  |
| Mitochondrial substrate/solute carrier | 2.63 | 5.71E-08 | 1.11E-05 |  |  |  |  |
| Bromodomain, conserved site | 2.60 | 4.26E-04 | 2.40E-02 |  |  |  |  |
| Cadherin conserved site | 2.59 | 1.97E-15 | 1.23E-12 |  |  |  |  |
| HECT | 2.57 | 2.86E-04 | 1.67E-02 |  |  |  |  |
| Cadherin | 2.52 | 7.39E-15 | 3.45E-12 |  |  |  |  |
| Cadherin-like | 2.51 | 5.04E-15 | 2.65E-12 |  |  |  |  |
| Aspartic peptidase | 2.50 | 7.04E-04 | 3.66E-02 |  |  |  |  |
| Laminin G domain | 2.48 | 1.38E-07 | 2.44E-05 |  |  |  |  |
| Forkhead-associated (FHA) domain | 2.43 | 9.60E-05 | 6.69E-03 |  |  |  |  |
| Kinesin, motor region, conserved site | 2.42 | 4.36E-05 | 3.43E-03 |  |  |  |  |
| Dbl homology (DH) domain | 2.41 | 3.34E-08 | 7.75E-06 |  |  |  |  |
| Bromodomain | 2.41 | 2.94E-05 | 2.48E-03 |  |  |  |  |
| Kinesin, motor domain | 2.40 | 1.99E-05 | 1.71E-03 |  |  |  |  |
| Armadillo-like helical | 2.38 | 1.70E-23 | 3.15E-20 |  |  |  |  |
| Calponin homology domain | 2.31 | 9.23E-08 | 1.71E-05 |  |  |  |  |
| Ubiquitin-associated/translation elongation factor EF1B, N-terminal, eukaryote | 2.25 | 1.62E-04 | 1.07E-02 |  |  |  |  |
| GPS domain | 2.25 | 7.84E-04 | 3.90E-02 |  |  |  |  |
| Rho GTPase activation protein | 2.23 | 3.32E-08 | 8.21E-06 |  |  |  |  |
| EGF-like, laminin | 2.19 | 7.78E-04 | 3.93E-02 |  |  |  |  |
| Zinc finger, PHD-finger | 2.17 | 1.09E-06 | 1.44E-04 |  |  |  |  |
| Rho GTPase-activating protein domain | 2.15 | 1.08E-05 | 1.00E-03 |  |  |  |  |
| Band 4.1 domain | 2.12 | 2.33E-04 | 1.45E-02 |  |  |  |  |
| FERM domain | 2.12 | 2.33E-04 | 1.45E-02 |  |  |  |  |
| FERM central domain | 2.12 | 2.33E-04 | 1.45E-02 |  |  |  |  |
| Armadillo-type fold | 2.09 | 7.25E-24 | 2.69E-20 |  |  |  |  |
| Pleckstrin homology domain | 2.04 | 2.71E-17 | 2.51E-14 |  |  |  |  |
| WW domain | 2.04 | 4.62E-04 | 2.56E-02 |  |  |  |  |
| Zinc finger, PHD-type | 2.02 | 4.39E-06 | 4.65E-04 |  |  |  |  |
| Zinc finger, PHD-type, conserved site | 2.02 | 9.39E-05 | 6.67E-03 |  |  |  |  |
| Zinc finger, FYVE/PHD-type | 1.95 | 4.92E-08 | 1.01E-05 |  |  |  |  |
| Helicase, superfamily 1/2, ATP-binding domain | 1.92 | 3.08E-06 | 3.45E-04 |  |  |  |  |
| Collagen triple helix repeat | 1.92 | 7.03E-05 | 5.31E-03 |  |  |  |  |
| Pleckstrin homology-like domain | 1.92 | 2.16E-21 | 2.67E-18 |  |  |  |  |
| Intermediate filament protein, conserved site | 1.90 | 7.00E-04 | 3.69E-02 |  |  |  |  |
| Helicase, C-terminal | 1.88 | 1.12E-05 | 1.01E-03 |  |  |  |  |
| Peptidase C19, ubiquitin carboxyl-terminal hydrolase 2 | 1.86 | 2.52E-04 | 1.54E-02 |  |  |  |  |
| AAA+ ATPase domain | 1.85 | 1.25E-06 | 1.55E-04 |  |  |  |  |
| PDZ domain | 1.83 | 4.30E-07 | 6.14E-05 |  |  |  |  |
| Immunoglobulin I-set | 1.82 | 1.99E-06 | 2.38E-04 |  |  |  |  |
| Galactose-binding domain-like | 1.81 | 4.25E-04 | 2.43E-02 |  |  |  |  |
| Intermediate filament protein | 1.79 | 8.40E-04 | 4.12E-02 |  |  |  |  |
| von Willebrand factor, type A | 1.76 | 2.70E-04 | 1.60E-02 |  |  |  |  |
| Immunoglobulin E-set | 1.73 | 2.56E-04 | 1.54E-02 |  |  |  |  |
| Src homology-3 domain | 1.71 | 1.58E-07 | 2.55E-05 |  |  |  |  |
| Fibronectin, type III | 1.63 | 5.57E-06 | 5.73E-04 |  |  |  |  |
| Ankyrin repeat-containing domain | 1.60 | 9.58E-07 | 1.32E-04 |  |  |  |  |
| Ankyrin repeat | 1.59 | 2.11E-06 | 2.44E-04 |  |  |  |  |
| Epidermal growth factor-like domain | 1.56 | 1.78E-05 | 1.57E-03 |  |  |  |  |
| Immunoglobulin subtype 2 | 1.51 | 3.77E-05 | 3.10E-03 |  |  |  |  |
| EGF-like, conserved site | 1.47 | 7.18E-04 | 3.68E-02 |  |  |  |  |
| P-loop containing nucleoside triphosphate hydrolase | 1.33 | 2.45E-07 | 3.64E-05 |  |  |  |  |
| Immunoglobulin subtype | 1.32 | 1.42E-04 | 9.53E-03 |  |  |  |  |

Table S4: Significant GO CC enrichments and depletions.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Enriched** | | | | **Depleted** | | | |
| **CC** | **FE** | **p-value** | **Benjamini** | **CC** | **FE** | **p-value** | **Benjamini** |
| spectrin | 4.55 | 3.94E-05 | 3.16E-03 | ribosome | 1.17 | 2.45E-05 | 1.76E-03 |
| axonemal dynein complex | 4.09 | 1.58E-04 | 7.50E-03 | mitochondrion | 1.05 | 8.74E-05 | 4.13E-02 |
| spectrin-associated cytoskeleton | 3.98 | 2.08E-03 | 4.83E-02 | integral component of membrane | 1.03 | 3.75E-08 | 5.43E-05 |
| nuclear pore nuclear basket | 3.79 | 1.36E-04 | 7.44E-03 |  |  |  |  |
| microtubule plus-end | 3.74 | 2.65E-06 | 4.62E-04 |  |  |  |  |
| myosin filament | 3.13 | 5.56E-04 | 1.98E-02 |  |  |  |  |
| costamere | 3.11 | 1.31E-04 | 7.60E-03 |  |  |  |  |
| dynein complex | 3.10 | 3.13E-05 | 2.97E-03 |  |  |  |  |
| viral capsid | 3.03 | 1.61E-03 | 3.93E-02 |  |  |  |  |
| apicolateral plasma membrane | 2.94 | 1.08E-03 | 3.38E-02 |  |  |  |  |
| nuclear periphery | 2.81 | 4.91E-04 | 1.88E-02 |  |  |  |  |
| viral envelope | 2.73 | 1.30E-03 | 3.52E-02 |  |  |  |  |
| desmosome | 2.65 | 5.75E-04 | 1.98E-02 |  |  |  |  |
| myosin complex | 2.46 | 3.16E-06 | 4.72E-04 |  |  |  |  |
| cell leading edge | 2.22 | 6.89E-04 | 2.30E-02 |  |  |  |  |
| adherens junction | 2.09 | 4.20E-04 | 1.67E-02 |  |  |  |  |
| kinesin complex | 2.06 | 4.00E-04 | 1.73E-02 |  |  |  |  |
| nuclear pore | 1.96 | 1.38E-04 | 7.17E-03 |  |  |  |  |
| basement membrane | 1.90 | 1.58E-04 | 7.85E-03 |  |  |  |  |
| microtubule | 1.89 | 1.55E-14 | 8.12E-12 |  |  |  |  |
| spindle pole | 1.88 | 1.14E-05 | 1.49E-03 |  |  |  |  |
| growth cone | 1.84 | 1.27E-05 | 1.47E-03 |  |  |  |  |
| centriole | 1.77 | 7.59E-05 | 4.95E-03 |  |  |  |  |
| recycling endosome | 1.69 | 4.03E-04 | 1.67E-02 |  |  |  |  |
| cytoskeleton | 1.69 | 2.80E-11 | 9.74E-09 |  |  |  |  |
| PML body | 1.67 | 1.30E-03 | 3.60E-02 |  |  |  |  |
| chromosome | 1.65 | 1.27E-03 | 3.63E-02 |  |  |  |  |
| cell-cell junction | 1.64 | 3.45E-05 | 3.00E-03 |  |  |  |  |
| dendritic spine | 1.64 | 1.94E-03 | 4.60E-02 |  |  |  |  |
| midbody | 1.62 | 5.24E-04 | 1.94E-02 |  |  |  |  |
| synapse | 1.61 | 4.95E-05 | 3.69E-03 |  |  |  |  |
| centrosome | 1.59 | 7.32E-10 | 1.91E-07 |  |  |  |  |
| axon | 1.52 | 1.09E-04 | 6.70E-03 |  |  |  |  |
| microtubule organizing center | 1.52 | 1.43E-03 | 3.75E-02 |  |  |  |  |
| actin cytoskeleton | 1.50 | 1.87E-04 | 8.45E-03 |  |  |  |  |
| cytoplasmic vesicle | 1.41 | 1.20E-03 | 3.61E-02 |  |  |  |  |
| apical plasma membrane | 1.36 | 1.45E-03 | 3.73E-02 |  |  |  |  |
| cell-cell adherens junction | 1.34 | 1.54E-03 | 3.84E-02 |  |  |  |  |
| protein complex | 1.30 | 1.20E-03 | 3.52E-02 |  |  |  |  |
| cytoplasm | 1.18 | 1.67E-15 | 1.74E-12 |  |  |  |  |
| nucleoplasm | 1.17 | 2.69E-07 | 5.62E-05 |  |  |  |  |
| membrane | 1.16 | 2.10E-05 | 2.19E-03 |  |  |  |  |
| cytosol | 1.12 | 6.14E-05 | 4.27E-03 |  |  |  |  |
| nucleus | 1.07 | 8.52E-04 | 2.74E-02 |  |  |  |  |

Table S5: Significant GO BP enrichments and depletions.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Enriched** | | | | **Depleted** | | | |
| **BP** | **FE** | **p-value** | **Benjamini** | **BP** | **FE** | **p-value** | **Benjamini** |
| tRNA export from nucleus | 2.63 | 3.69E-05 | 2.72E-02 | detection of chemical stimulus involved in sensory perception of smell | 1.20 | 6.97E-18 | 3.61E-14 |
| microtubule-based movement | 2.46 | 4.95E-10 | 1.11E-06 | detection of chemical stimulus involved in sensory perception | 1.25 | 1.37E-06 | 4.73E-03 |
| homophilic cell adhesion via plasma membrane adhesion molecules | 2.25 | 3.10E-14 | 2.09E-10 | sensory perception of smell | 1.18 | 1.24E-05 | 3.15E-02 |
| regulation of Rho protein signal transduction | 2.25 | 1.02E-07 | 1.38E-04 | G-protein coupled receptor signaling pathway | 1.15 | 8.98E-19 | 9.31E-15 |
| single organismal cell-cell adhesion | 1.98 | 2.05E-06 | 1.97E-03 |  |  |  |  |
| cytoskeleton organization | 1.76 | 1.48E-06 | 1.66E-03 |  |  |  |  |
| regulation of small GTPase mediated signal transduction | 1.72 | 3.44E-05 | 2.86E-02 |  |  |  |  |
| positive regulation of GTPase activity | 1.56 | 4.00E-12 | 1.35E-08 |  |  |  |  |
| cell adhesion | 1.52 | 8.97E-09 | 1.51E-05 |  |  |  |  |

Table S6: Significant GO MF enrichments and depletions.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Enriched** | | | | **Depleted** | | | |
| **MF** | **FE** | **p-value** | **Benjamini** | **MF** | **FE** | **p-value** | **Benjamini** |
| microfilament motor activity | 3.57 | 8.54E-07 | 1.58E-04 | odorant binding | 1.24 | 6.66E-06 | 8.48E-03 |
| structural constituent of nuclear pore | 2.97 | 1.14E-04 | 1.53E-02 | olfactory receptor activity | 1.20 | 7.19E-18 | 2.76E-14 |
| nuclear localization sequence binding | 2.71 | 7.24E-05 | 1.13E-02 | G-protein coupled receptor activity | 1.15 | 8.55E-15 | 1.64E-11 |
| microtubule motor activity | 2.68 | 2.40E-12 | 2.44E-09 |  |  |  |  |
| motor activity | 2.63 | 6.78E-10 | 3.46E-07 |  |  |  |  |
| spectrin binding | 2.57 | 4.74E-04 | 4.96E-02 |  |  |  |  |
| Rho guanyl-nucleotide exchange factor activity | 2.43 | 3.59E-09 | 1.05E-06 |  |  |  |  |
| calmodulin binding | 2.03 | 4.30E-12 | 2.92E-09 |  |  |  |  |
| ATPase activity | 1.85 | 1.25E-08 | 2.55E-06 |  |  |  |  |
| microtubule binding | 1.84 | 1.62E-09 | 5.52E-07 |  |  |  |  |
| structural constituent of cytoskeleton | 1.74 | 1.32E-04 | 1.67E-02 |  |  |  |  |
| guanyl-nucleotide exchange factor activity | 1.74 | 8.04E-05 | 1.16E-02 |  |  |  |  |
| actin binding | 1.68 | 8.75E-09 | 2.23E-06 |  |  |  |  |
| GTPase activator activity | 1.68 | 1.09E-08 | 2.47E-06 |  |  |  |  |
| protein kinase binding | 1.36 | 2.03E-04 | 2.41E-02 |  |  |  |  |
| chromatin binding | 1.35 | 3.00E-04 | 3.35E-02 |  |  |  |  |
| ATP binding | 1.34 | 1.15E-12 | 2.34E-09 |  |  |  |  |
| calcium ion binding | 1.32 | 4.90E-06 | 8.32E-04 |  |  |  |  |
| protein binding | 1.08 | 1.08E-09 | 4.42E-07 |  |  |  |  |

Table S7: Significant Reactome pathway enrichments and depletions.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Enriched** | | | | **Depleted** | | | |
| **Pathway** | **FE** | **p-value** | **Benjamini** | **Pathway** | **FE** | **p-value** | **Benjamini** |
| [Cation-coupled Chloride cotransporters](http://www.reactome.org/content/detail/R-HSA-426117) | 4.68 | 5.39E-04 | 2.80E-02 | [Peptide chain elongation](http://www.reactome.org/content/detail/R-HSA-156902) | 1.20 | 1.05E-04 | 3.80E-02 |
| [Anchoring fibril formation](http://www.reactome.org/content/detail/R-HSA-2214320) | 4.06 | 2.07E-06 | 7.64E-04 | [Viral mRNA Translation](http://www.reactome.org/content/detail/R-HSA-192823) | 1.20 | 1.05E-04 | 3.80E-02 |
| [Extracellular matrix organization](http://www.reactome.org/content/detail/R-HSA-1474244) | 3.43 | 2.00E-04 | 1.29E-02 | [Formation of a pool of free 40S subunits](http://www.reactome.org/content/detail/R-HSA-72689) | 1.20 | 4.62E-05 | 2.24E-02 |
| [Non-integrin membrane-ECM interactions](http://www.reactome.org/content/detail/R-HSA-3000171) | 3.04 | 2.05E-08 | 2.27E-05 | [G alpha (i) signalling events](http://www.reactome.org/content/detail/R-HSA-418594) | 1.19 | 3.90E-10 | 2.88E-07 |
| [Laminin interactions](http://www.reactome.org/content/detail/R-HSA-3000157) | 2.81 | 2.51E-05 | 3.08E-03 | [Olfactory Signaling Pathway](http://www.reactome.org/content/detail/R-HSA-381753) | 1.19 | 1.05E-16 | 1.64E-13 |
| [Pre-NOTCH Transcription and Translation](http://www.reactome.org/content/detail/R-HSA-1912408) | 2.74 | 6.79E-05 | 7.49E-03 |  |  |  |  |
| [NS1 Mediated Effects on Host Pathways](http://www.reactome.org/content/detail/R-HSA-168276) | 2.66 | 1.27E-05 | 3.50E-03 |  |  |  |  |
| [Regulation of Glucokinase by Glucokinase Regulatory Protein](http://www.reactome.org/content/detail/R-HSA-170822) | 2.57 | 1.94E-04 | 1.42E-02 |  |  |  |  |
| [Nuclear import of Rev protein](http://www.reactome.org/content/detail/R-HSA-180746) | 2.55 | 1.26E-04 | 1.07E-02 |  |  |  |  |
| [Rev-mediated nuclear export of HIV RNA](http://www.reactome.org/content/detail/R-HSA-165054) | 2.48 | 2.03E-04 | 1.24E-02 |  |  |  |  |
| [Vpr-mediated nuclear import of PICs](http://www.reactome.org/content/detail/R-HSA-180910) | 2.41 | 4.86E-04 | 2.65E-02 |  |  |  |  |
| [Nuclear Pore Complex (NPC) Disassembly](http://www.reactome.org/content/detail/R-HSA-3301854) | 2.41 | 3.16E-04 | 1.82E-02 |  |  |  |  |
| [Assembly of collagen fibrils and other multimeric structures](http://www.reactome.org/content/detail/R-HSA-2022090) | 2.24 | 1.95E-04 | 1.34E-02 |  |  |  |  |
| [Collagen biosynthesis and modifying enzymes](http://www.reactome.org/content/detail/R-HSA-1650814) | 2.17 | 1.43E-05 | 2.63E-03 |  |  |  |  |
| [Loss of Nlp from mitotic centrosomes](http://www.reactome.org/content/detail/R-HSA-380259) | 2.14 | 1.36E-05 | 3.00E-03 |  |  |  |  |
| [SUMOylation of RNA binding proteins](http://www.reactome.org/content/detail/R-HSA-4570464) | 2.09 | 8.45E-04 | 3.98E-02 |  |  |  |  |
| [Anchoring of the basal body to the plasma membrane](http://www.reactome.org/content/detail/R-HSA-5620912) | 2.05 | 1.24E-06 | 6.85E-04 |  |  |  |  |
| [Recruitment of mitotic centrosome proteins and complexes](http://www.reactome.org/content/detail/R-HSA-380270) | 2.04 | 2.32E-05 | 3.66E-03 |  |  |  |  |
| [Regulation of PLK1 Activity at G2/M Transition](http://www.reactome.org/content/detail/R-HSA-2565942) | 1.97 | 2.44E-05 | 3.37E-03 |  |  |  |  |
| [SUMOylation of DNA damage response and repair proteins](http://www.reactome.org/content/detail/R-HSA-3108214) | 1.95 | 1.26E-04 | 1.15E-02 |  |  |  |  |
| [ECM proteoglycans](http://www.reactome.org/content/detail/R-HSA-3000178) | 1.93 | 1.84E-04 | 1.44E-02 |  |  |  |  |
| [Regulation of HSF1-mediated heat shock response](http://www.reactome.org/content/detail/R-HSA-3371453) | 1.87 | 7.48E-04 | 3.69E-02 |  |  |  |  |
| [Rho GTPase cycle](http://www.reactome.org/content/detail/R-HSA-194840) | 1.74 | 8.86E-05 | 8.87E-03 |  |  |  |  |

Table S8: Significant sequence feature enrichments and depletions.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Enriched** | | | | **Depleted** | | | |
| **Seq Feature** | **FE** | **p-value** | **Benjamini** | **Seq Feature** | **FE** | **p-value** | **Benjamini** |
| region of interest:AAA 4 | 4.67 | 2.17E-08 | 1.07E-05 | disulfide bond | 1.06 | 6.61E-11 | 1.42E-06 |
| repeat:Spectrin 5 | 4.67 | 2.17E-08 | 1.07E-05 | transmembrane region | 1.03 | 3.45E-06 | 3.64E-02 |
| region of interest:AAA 3 | 4.67 | 2.17E-08 | 1.07E-05 |  |  |  |  |
| region of interest:Stem | 4.67 | 2.17E-08 | 1.07E-05 |  |  |  |  |
| region of interest:Stalk | 4.67 | 2.17E-08 | 1.07E-05 |  |  |  |  |
| region of interest:AAA 2 | 4.67 | 2.17E-08 | 1.07E-05 |  |  |  |  |
| region of interest:AAA 1 | 4.67 | 2.17E-08 | 1.07E-05 |  |  |  |  |
| region of interest:AAA 5 | 4.67 | 2.17E-08 | 1.07E-05 |  |  |  |  |
| repeat:Spectrin 7 | 4.67 | 9.45E-08 | 3.41E-05 |  |  |  |  |
| region of interest:AAA 6 | 4.67 | 9.45E-08 | 3.41E-05 |  |  |  |  |
| repeat:Spectrin 8 | 4.67 | 9.45E-08 | 3.41E-05 |  |  |  |  |
| repeat:Spectrin 6 | 4.67 | 9.45E-08 | 3.41E-05 |  |  |  |  |
| repeat:Spectrin 9 | 4.67 | 9.45E-08 | 3.41E-05 |  |  |  |  |
| repeat:Spectrin 17 | 4.67 | 4.09E-07 | 1.32E-04 |  |  |  |  |
| repeat:Spectrin 13 | 4.67 | 4.09E-07 | 1.32E-04 |  |  |  |  |
| repeat:Spectrin 16 | 4.67 | 4.09E-07 | 1.32E-04 |  |  |  |  |
| repeat:Spectrin 15 | 4.67 | 4.09E-07 | 1.32E-04 |  |  |  |  |
| repeat:Spectrin 11 | 4.67 | 4.09E-07 | 1.32E-04 |  |  |  |  |
| repeat:Spectrin 10 | 4.67 | 4.09E-07 | 1.32E-04 |  |  |  |  |
| repeat:Spectrin 14 | 4.67 | 4.09E-07 | 1.32E-04 |  |  |  |  |
| repeat:Spectrin 12 | 4.67 | 4.09E-07 | 1.32E-04 |  |  |  |  |
| region of interest:5 X 4 AA repeats of P-X-X-P | 4.67 | 3.18E-05 | 4.80E-03 |  |  |  |  |
| domain:Chromo 2 | 4.67 | 3.18E-05 | 4.80E-03 |  |  |  |  |
| repeat:Spectrin 18 | 4.67 | 3.18E-05 | 4.80E-03 |  |  |  |  |
| repeat:Spectrin 20 | 4.67 | 1.33E-04 | 1.39E-02 |  |  |  |  |
| domain:BEACH | 4.67 | 1.33E-04 | 1.39E-02 |  |  |  |  |
| repeat:Spectrin 19 | 4.67 | 1.33E-04 | 1.39E-02 |  |  |  |  |
| repeat:Spectrin 21 | 4.67 | 5.46E-04 | 4.36E-02 |  |  |  |  |
| domain:Laminin EGF-like 10 | 4.25 | 3.34E-05 | 4.96E-03 |  |  |  |  |
| domain:Laminin EGF-like 8 | 4.25 | 3.34E-05 | 4.96E-03 |  |  |  |  |
| domain:Laminin EGF-like 9 | 4.21 | 1.29E-04 | 1.36E-02 |  |  |  |  |
| domain:Laminin G-like 5 | 4.16 | 4.86E-04 | 4.03E-02 |  |  |  |  |
| domain:Laminin EGF-like 11 | 4.16 | 4.86E-04 | 4.03E-02 |  |  |  |  |
| repeat:PXXP 4 | 4.05 | 2.13E-06 | 5.14E-04 |  |  |  |  |
| repeat:PXXP 3 | 4.05 | 2.13E-06 | 5.14E-04 |  |  |  |  |
| repeat:PXXP 2 | 4.05 | 2.13E-06 | 5.14E-04 |  |  |  |  |
| repeat:PXXP 5 | 4.05 | 2.13E-06 | 5.14E-04 |  |  |  |  |
| repeat:PXXP 1 | 4.05 | 2.13E-06 | 5.14E-04 |  |  |  |  |
| repeat:Spectrin 4 | 4.01 | 9.75E-09 | 5.08E-06 |  |  |  |  |
| domain:Cadherin 9 | 3.96 | 2.98E-05 | 4.65E-03 |  |  |  |  |
| domain:Cadherin 8 | 3.96 | 2.98E-05 | 4.65E-03 |  |  |  |  |
| domain:Laminin EGF-like 6 | 3.96 | 2.98E-05 | 4.65E-03 |  |  |  |  |
| repeat:ANK 16 | 3.96 | 2.98E-05 | 4.65E-03 |  |  |  |  |
| repeat:ANK 18 | 3.90 | 1.08E-04 | 1.19E-02 |  |  |  |  |
| domain:Laminin EGF-like 7 | 3.90 | 1.08E-04 | 1.19E-02 |  |  |  |  |
| repeat:ANK 19 | 3.90 | 1.08E-04 | 1.19E-02 |  |  |  |  |
| repeat:ANK 17 | 3.90 | 1.08E-04 | 1.19E-02 |  |  |  |  |
| repeat:Spectrin 3 | 3.82 | 3.43E-08 | 1.53E-05 |  |  |  |  |
| repeat:ANK 20 | 3.82 | 3.83E-04 | 3.27E-02 |  |  |  |  |
| repeat:ANK 21 | 3.82 | 3.83E-04 | 3.27E-02 |  |  |  |  |
| domain:IPT/TIG 1 | 3.82 | 3.83E-04 | 3.27E-02 |  |  |  |  |
| repeat:Spectrin 1 | 3.78 | 2.29E-09 | 1.34E-06 |  |  |  |  |
| repeat:Spectrin 2 | 3.78 | 2.29E-09 | 1.34E-06 |  |  |  |  |
| domain:Cadherin 7 | 3.69 | 1.58E-06 | 3.91E-04 |  |  |  |  |
| domain:IPT/TIG 2 | 3.60 | 2.84E-04 | 2.56E-02 |  |  |  |  |
| domain:Laminin EGF-like 4 | 3.60 | 2.84E-04 | 2.56E-02 |  |  |  |  |
| domain:IPT/TIG 3 | 3.60 | 2.84E-04 | 2.56E-02 |  |  |  |  |
| domain:Actin-binding | 3.51 | 4.23E-06 | 8.83E-04 |  |  |  |  |
| domain:Laminin N-terminal | 3.51 | 6.26E-05 | 7.70E-03 |  |  |  |  |
| repeat:ANK 14 | 3.43 | 2.04E-04 | 1.93E-02 |  |  |  |  |
| repeat:ANK 13 | 3.43 | 2.04E-04 | 1.93E-02 |  |  |  |  |
| repeat:ANK 15 | 3.43 | 2.04E-04 | 1.93E-02 |  |  |  |  |
| domain:Laminin G-like 4 | 3.43 | 2.04E-04 | 1.93E-02 |  |  |  |  |
| region of interest:Actin-binding | 3.38 | 5.06E-08 | 1.98E-05 |  |  |  |  |
| domain:Importin N-terminal | 3.34 | 6.44E-04 | 4.92E-02 |  |  |  |  |
| domain:IQ 3 | 3.19 | 2.25E-05 | 3.63E-03 |  |  |  |  |
| short sequence motif:LXXLL motif 2 | 3.12 | 6.78E-05 | 8.12E-03 |  |  |  |  |
| short sequence motif:LXXLL motif 1 | 3.12 | 6.78E-05 | 8.12E-03 |  |  |  |  |
| region of interest:Triple-helical region | 3.05 | 4.61E-05 | 6.35E-03 |  |  |  |  |
| domain:Cadherin 6 | 3.04 | 6.71E-17 | 1.30E-13 |  |  |  |  |
| domain:Laminin G-like 3 | 3.04 | 1.99E-04 | 1.93E-02 |  |  |  |  |
| domain:IQ 1 | 2.97 | 1.18E-06 | 3.07E-04 |  |  |  |  |
| domain:IQ 2 | 2.97 | 1.18E-06 | 3.07E-04 |  |  |  |  |
| domain:Laminin G-like 2 | 2.96 | 4.98E-06 | 1.02E-03 |  |  |  |  |
| domain:Laminin G-like 1 | 2.96 | 4.98E-06 | 1.02E-03 |  |  |  |  |
| domain:Arf-GAP | 2.96 | 4.98E-06 | 1.02E-03 |  |  |  |  |
| domain:Myosin head-like | 2.91 | 5.47E-07 | 1.66E-04 |  |  |  |  |
| repeat:Solcar 3 | 2.84 | 6.81E-09 | 3.76E-06 |  |  |  |  |
| zinc finger region:PHD-type 2 | 2.80 | 2.62E-05 | 4.15E-03 |  |  |  |  |
| domain:CH 2 | 2.77 | 1.07E-04 | 1.19E-02 |  |  |  |  |
| domain:CH 1 | 2.77 | 1.07E-04 | 1.19E-02 |  |  |  |  |
| short sequence motif:DEAH box | 2.72 | 8.44E-07 | 2.40E-04 |  |  |  |  |
| domain:Cadherin 4 | 2.71 | 1.29E-16 | 1.16E-13 |  |  |  |  |
| domain:Cadherin 3 | 2.71 | 1.29E-16 | 1.16E-13 |  |  |  |  |
| zinc finger region:PHD-type 1 | 2.69 | 3.06E-05 | 4.69E-03 |  |  |  |  |
| repeat:Solcar 1 | 2.68 | 4.20E-08 | 1.71E-05 |  |  |  |  |
| repeat:Solcar 2 | 2.68 | 4.20E-08 | 1.71E-05 |  |  |  |  |
| domain:ABC transporter 2 | 2.67 | 2.02E-05 | 3.44E-03 |  |  |  |  |
| domain:ABC transporter 1 | 2.67 | 2.02E-05 | 3.44E-03 |  |  |  |  |
| domain:HECT | 2.67 | 1.85E-04 | 1.83E-02 |  |  |  |  |
| domain:Cadherin 1 | 2.64 | 9.71E-16 | 8.53E-13 |  |  |  |  |
| domain:Cadherin 2 | 2.64 | 9.71E-16 | 8.53E-13 |  |  |  |  |
| domain:Cadherin 5 | 2.63 | 3.25E-14 | 2.54E-11 |  |  |  |  |
| domain:Laminin EGF-like 2 | 2.60 | 4.72E-04 | 3.95E-02 |  |  |  |  |
| domain:PH 1 | 2.58 | 2.24E-05 | 3.69E-03 |  |  |  |  |
| domain:Bromo | 2.58 | 3.07E-04 | 2.71E-02 |  |  |  |  |
| domain:SH3 2 | 2.57 | 1.48E-05 | 2.61E-03 |  |  |  |  |
| compositionally biased region:Gln-rich | 2.55 | 9.21E-19 | 1.44E-15 |  |  |  |  |
| domain:Kinesin-motor | 2.55 | 6.40E-06 | 1.25E-03 |  |  |  |  |
| domain:FHA | 2.54 | 8.57E-05 | 1.00E-02 |  |  |  |  |
| domain:PH 2 | 2.53 | 5.62E-05 | 7.20E-03 |  |  |  |  |
| domain:SH3 1 | 2.52 | 3.68E-05 | 5.30E-03 |  |  |  |  |
| nucleotide phosphate-binding region:ATP 2 | 2.46 | 8.99E-05 | 1.02E-02 |  |  |  |  |
| nucleotide phosphate-binding region:ATP 1 | 2.46 | 8.99E-05 | 1.02E-02 |  |  |  |  |
| domain:DH | 2.41 | 1.71E-07 | 5.94E-05 |  |  |  |  |
| repeat:ANK 9 | 2.39 | 9.20E-05 | 1.03E-02 |  |  |  |  |
| domain:CH | 2.34 | 1.40E-04 | 1.44E-02 |  |  |  |  |
| domain:GPS | 2.34 | 4.98E-04 | 4.05E-02 |  |  |  |  |
| domain:IQ | 2.30 | 4.99E-06 | 9.96E-04 |  |  |  |  |
| repeat:ANK 8 | 2.24 | 2.04E-04 | 1.95E-02 |  |  |  |  |
| domain:Fibronectin type-III 4 | 2.23 | 1.10E-05 | 1.99E-03 |  |  |  |  |
| domain:Rho-GAP | 2.20 | 7.10E-06 | 1.36E-03 |  |  |  |  |
| repeat:HEAT 1 | 2.18 | 5.46E-05 | 7.09E-03 |  |  |  |  |
| repeat:HEAT 2 | 2.18 | 5.46E-05 | 7.09E-03 |  |  |  |  |
| domain:Fibronectin type-III 3 | 2.17 | 8.68E-07 | 2.40E-04 |  |  |  |  |
| compositionally biased region:Poly-Lys | 2.16 | 7.38E-16 | 7.29E-13 |  |  |  |  |
| domain:Fibronectin type-III 5 | 2.13 | 6.29E-04 | 4.92E-02 |  |  |  |  |
| compositionally biased region:Poly-Ser | 2.12 | 3.65E-34 | 1.14E-30 |  |  |  |  |
| compositionally biased region:Thr-rich | 2.11 | 3.92E-04 | 3.32E-02 |  |  |  |  |
| domain:FERM | 2.10 | 5.87E-04 | 4.64E-02 |  |  |  |  |
| compositionally biased region:Ser-rich | 2.09 | 3.83E-28 | 8.98E-25 |  |  |  |  |
| region of interest:Tail | 2.01 | 3.44E-05 | 5.03E-03 |  |  |  |  |
| repeat:ANK 7 | 2.00 | 2.85E-04 | 2.54E-02 |  |  |  |  |
| repeat:LRR 11 | 1.99 | 3.60E-06 | 7.85E-04 |  |  |  |  |
| domain:PDZ | 1.94 | 2.56E-06 | 5.72E-04 |  |  |  |  |
| region of interest:Head | 1.94 | 1.34E-04 | 1.39E-02 |  |  |  |  |
| compositionally biased region:His-rich | 1.94 | 3.16E-04 | 2.76E-02 |  |  |  |  |
| repeat:LRR 10 | 1.93 | 2.34E-06 | 5.36E-04 |  |  |  |  |
| domain:Fibronectin type-III 2 | 1.93 | 3.96E-07 | 1.33E-04 |  |  |  |  |
| repeat:LRR 13 | 1.93 | 1.96E-04 | 1.92E-02 |  |  |  |  |
| domain:Fibronectin type-III 1 | 1.92 | 5.27E-07 | 1.65E-04 |  |  |  |  |
| domain:PH | 1.91 | 1.00E-11 | 6.71E-09 |  |  |  |  |
| compositionally biased region:Poly-Leu | 1.90 | 6.97E-07 | 2.04E-04 |  |  |  |  |
| region of interest:Rod | 1.87 | 4.88E-04 | 4.01E-02 |  |  |  |  |
| domain:Ig-like C2-type 4 | 1.85 | 6.30E-04 | 4.89E-02 |  |  |  |  |
| repeat:ANK 6 | 1.84 | 8.53E-05 | 1.01E-02 |  |  |  |  |
| domain:EGF-like 2 | 1.84 | 2.19E-04 | 2.03E-02 |  |  |  |  |
| domain:Helicase C-terminal | 1.82 | 6.14E-05 | 7.66E-03 |  |  |  |  |
| short sequence motif:Cell attachment site | 1.80 | 3.56E-04 | 3.08E-02 |  |  |  |  |
| compositionally biased region:Poly-Asp | 1.79 | 5.06E-04 | 4.08E-02 |  |  |  |  |
| repeat:LRR 9 | 1.78 | 1.76E-05 | 3.06E-03 |  |  |  |  |
| repeat:LRR 12 | 1.77 | 6.37E-04 | 4.90E-02 |  |  |  |  |
| domain:Helicase ATP-binding | 1.76 | 1.12E-04 | 1.21E-02 |  |  |  |  |
| domain:Ig-like C2-type 3 | 1.75 | 4.96E-05 | 6.63E-03 |  |  |  |  |
| domain:EGF-like 1 | 1.75 | 8.83E-05 | 1.02E-02 |  |  |  |  |
| repeat:ANK 5 | 1.74 | 2.21E-05 | 3.70E-03 |  |  |  |  |
| compositionally biased region:Poly-Glu | 1.74 | 2.09E-17 | 2.81E-14 |  |  |  |  |
| repeat:ANK 1 | 1.72 | 4.13E-08 | 1.76E-05 |  |  |  |  |
| repeat:ANK 2 | 1.72 | 5.14E-08 | 1.93E-05 |  |  |  |  |
| repeat:LRR 8 | 1.71 | 3.77E-05 | 5.35E-03 |  |  |  |  |
| repeat:ANK 4 | 1.70 | 9.53E-06 | 1.75E-03 |  |  |  |  |
| repeat:LRR 6 | 1.70 | 9.62E-07 | 2.58E-04 |  |  |  |  |
| repeat:LRR 7 | 1.70 | 7.51E-06 | 1.41E-03 |  |  |  |  |
| repeat:ANK 3 | 1.69 | 1.34E-06 | 3.39E-04 |  |  |  |  |
| compositionally biased region:Glu-rich | 1.66 | 2.78E-08 | 1.30E-05 |  |  |  |  |
| repeat:TPR 3 | 1.65 | 1.17E-04 | 1.26E-02 |  |  |  |  |
| repeat:LRR 5 | 1.64 | 2.15E-06 | 5.05E-04 |  |  |  |  |
| domain:SH3 | 1.63 | 5.30E-05 | 6.99E-03 |  |  |  |  |
| compositionally biased region:Poly-Gln | 1.62 | 1.83E-04 | 1.83E-02 |  |  |  |  |
| compositionally biased region:Pro-rich | 1.62 | 1.41E-22 | 2.64E-19 |  |  |  |  |
| compositionally biased region:Poly-Arg | 1.59 | 5.91E-05 | 7.47E-03 |  |  |  |  |
| compositionally biased region:Poly-Pro | 1.59 | 2.28E-09 | 1.42E-06 |  |  |  |  |
| domain:Ig-like C2-type 1 | 1.53 | 2.23E-04 | 2.05E-02 |  |  |  |  |
| domain:Ig-like C2-type 2 | 1.52 | 2.60E-04 | 2.37E-02 |  |  |  |  |
| repeat:LRR 4 | 1.50 | 6.72E-05 | 8.16E-03 |  |  |  |  |
| compositionally biased region:Poly-Ala | 1.46 | 3.77E-06 | 8.04E-04 |  |  |  |  |
| nucleotide phosphate-binding region:ATP | 1.46 | 1.51E-13 | 1.09E-10 |  |  |  |  |
| repeat:LRR 1 | 1.46 | 4.23E-05 | 5.90E-03 |  |  |  |  |
| repeat:LRR 2 | 1.45 | 4.84E-05 | 6.56E-03 |  |  |  |  |
| compositionally biased region:Poly-Gly | 1.44 | 1.58E-04 | 1.60E-02 |  |  |  |  |
| repeat:LRR 3 | 1.42 | 2.09E-04 | 1.96E-02 |  |  |  |  |
| splice variant | 1.30 | 1.82E-68 | 1.71E-64 |  |  |  |  |
| sequence variant | 1.18 | 2.22E-68 | 1.04E-64 |  |  |  |  |

Table S9: Significant keyword enrichments and depletions.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Enriched** | | | | **Depleted** | | | |
| **Keyword** | **FE** | **p-value** | **Benjamini** | **Keyword** | **FE** | **p-value** | **Benjamini** |
| Ribosomal frameshifting | 3.61 | 5.90E-06 | 1.19E-04 | Redox-active center | 1.26 | 5.44E-04 | 2.96E-02 |
| Thick filament | 3.55 | 2.00E-05 | 3.39E-04 | Antibiotic | 1.20 | 6.55E-04 | 3.30E-02 |
| Dynein | 3.10 | 2.15E-07 | 4.98E-06 | Olfaction | 1.19 | 3.87E-17 | 9.25E-15 |
| Aspartyl protease | 3.10 | 7.24E-05 | 1.08E-03 | Ribosomal protein | 1.19 | 1.68E-07 | 1.72E-05 |
| Viral envelope protein | 2.93 | 6.00E-04 | 6.46E-03 | G-protein coupled receptor | 1.14 | 1.37E-17 | 4.92E-15 |
| Laminin EGF-like domain | 2.70 | 5.03E-05 | 8.07E-04 | Transducer | 1.14 | 2.56E-18 | 1.84E-15 |
| Bromodomain | 2.62 | 9.69E-06 | 1.89E-04 | Sensory transduction | 1.13 | 5.84E-11 | 1.05E-08 |
| Autism | 2.60 | 7.71E-04 | 7.88E-03 | Palmitate | 1.12 | 2.64E-05 | 1.72E-03 |
| Motor protein | 2.58 | 1.93E-17 | 1.72E-15 | Ribonucleoprotein | 1.10 | 5.39E-04 | 3.17E-02 |
| Transposable element | 2.56 | 3.29E-04 | 3.81E-03 | Lipoprotein | 1.10 | 3.30E-09 | 4.73E-07 |
| Basement membrane | 2.56 | 1.63E-05 | 2.83E-04 | Receptor | 1.06 | 2.31E-06 | 1.65E-04 |
| ERV | 2.49 | 8.08E-04 | 8.13E-03 | Mitochondrion | 1.05 | 7.81E-04 | 3.67E-02 |
| Myosin | 2.46 | 3.35E-06 | 6.99E-05 | Disulfide bond | 1.04 | 2.70E-07 | 2.15E-05 |
| Calmodulin-binding | 2.26 | 3.48E-13 | 1.67E-11 | Transmembrane | 1.03 | 9.41E-08 | 1.12E-05 |
| Triplet repeat expansion | 2.17 | 6.00E-03 | 4.77E-02 | Transmembrane helix | 1.03 | 1.93E-07 | 1.73E-05 |
| Autism spectrum disorder | 2.09 | 2.28E-03 | 1.89E-02 |  |  |  |  |
| Guanine-nucleotide releasing factor | 2.09 | 3.82E-10 | 1.50E-08 |  |  |  |  |
| Nuclear pore complex | 2.04 | 8.79E-04 | 8.70E-03 |  |  |  |  |
| Autocatalytic cleavage | 2.04 | 3.70E-04 | 4.21E-03 |  |  |  |  |
| Microtubule | 2.01 | 6.19E-16 | 4.63E-14 |  |  |  |  |
| Intermediate filament | 1.93 | 1.51E-04 | 2.09E-03 |  |  |  |  |
| Actin-binding | 1.90 | 7.05E-13 | 3.15E-11 |  |  |  |  |
| GTPase activation | 1.86 | 6.04E-09 | 1.99E-07 |  |  |  |  |
| Hydroxylation | 1.81 | 1.98E-04 | 2.58E-03 |  |  |  |  |
| Collagen | 1.80 | 1.78E-04 | 2.42E-03 |  |  |  |  |
| SH3 domain | 1.79 | 1.88E-08 | 5.35E-07 |  |  |  |  |
| Cell adhesion | 1.78 | 4.28E-17 | 3.35E-15 |  |  |  |  |
| Tight junction | 1.73 | 1.40E-03 | 1.27E-02 |  |  |  |  |
| Helicase | 1.72 | 3.28E-05 | 5.40E-04 |  |  |  |  |
| ANK repeat | 1.67 | 8.97E-08 | 2.25E-06 |  |  |  |  |
| mRNA transport | 1.67 | 1.03E-03 | 9.84E-03 |  |  |  |  |
| Coiled coil | 1.67 | 5.05E-87 | 1.58E-84 |  |  |  |  |
| Calcium transport | 1.66 | 1.80E-03 | 1.56E-02 |  |  |  |  |
| Cytoskeleton | 1.66 | 1.22E-29 | 1.53E-27 |  |  |  |  |
| Nucleotidyltransferase | 1.65 | 6.37E-03 | 4.88E-02 |  |  |  |  |
| Chromosomal rearrangement | 1.63 | 1.49E-08 | 4.44E-07 |  |  |  |  |
| Chromatin regulator | 1.62 | 2.39E-07 | 5.33E-06 |  |  |  |  |
| TPR repeat | 1.61 | 1.10E-04 | 1.56E-03 |  |  |  |  |
| Extracellular matrix | 1.60 | 1.85E-06 | 4.00E-05 |  |  |  |  |
| Cell projection | 1.60 | 6.71E-16 | 4.17E-14 |  |  |  |  |
| Ciliopathy | 1.59 | 1.40E-03 | 1.28E-02 |  |  |  |  |
| Cilium biogenesis/degradation | 1.57 | 7.04E-04 | 7.45E-03 |  |  |  |  |
| Biological rhythms | 1.56 | 2.23E-03 | 1.87E-02 |  |  |  |  |
| Cilium | 1.55 | 9.77E-05 | 1.42E-03 |  |  |  |  |
| Endocytosis | 1.54 | 3.96E-03 | 3.22E-02 |  |  |  |  |
| Mental retardation | 1.51 | 1.20E-05 | 2.28E-04 |  |  |  |  |
| Cell junction | 1.47 | 7.52E-10 | 2.62E-08 |  |  |  |  |
| EGF-like domain | 1.44 | 5.73E-04 | 6.39E-03 |  |  |  |  |
| Proto-oncogene | 1.44 | 7.35E-04 | 7.64E-03 |  |  |  |  |
| Calcium | 1.40 | 7.26E-10 | 2.67E-08 |  |  |  |  |
| ATP-binding | 1.40 | 7.04E-15 | 3.65E-13 |  |  |  |  |
| DNA repair | 1.40 | 5.87E-04 | 6.43E-03 |  |  |  |  |
| DNA damage | 1.39 | 2.25E-04 | 2.75E-03 |  |  |  |  |
| Deafness | 1.38 | 6.01E-03 | 4.73E-02 |  |  |  |  |
| Mitosis | 1.38 | 1.60E-03 | 1.42E-02 |  |  |  |  |
| Activator | 1.33 | 1.20E-05 | 2.21E-04 |  |  |  |  |
| Phosphoprotein | 1.33 | 1.13E-88 | 7.06E-86 |  |  |  |  |
| Isopeptide bond | 1.33 | 9.52E-09 | 2.98E-07 |  |  |  |  |
| Ubl conjugation | 1.32 | 2.48E-12 | 1.04E-10 |  |  |  |  |
| Repressor | 1.32 | 5.82E-05 | 9.11E-04 |  |  |  |  |
| Methylation | 1.32 | 1.42E-07 | 3.43E-06 |  |  |  |  |
| Protein transport | 1.31 | 6.82E-05 | 1.04E-03 |  |  |  |  |
| Cell division | 1.31 | 1.77E-03 | 1.55E-02 |  |  |  |  |
| Disease mutation | 1.29 | 2.84E-15 | 1.64E-13 |  |  |  |  |
| Cell cycle | 1.28 | 1.87E-04 | 2.49E-03 |  |  |  |  |
| Immunoglobulin domain | 1.26 | 1.38E-03 | 1.28E-02 |  |  |  |  |
| Nucleotide-binding | 1.24 | 4.55E-08 | 1.19E-06 |  |  |  |  |
| Cytoplasm | 1.24 | 4.82E-23 | 5.03E-21 |  |  |  |  |
| Differentiation | 1.23 | 1.83E-03 | 1.56E-02 |  |  |  |  |
| Alternative splicing | 1.22 | 7.27E-68 | 1.14E-65 |  |  |  |  |
| Polymorphism | 1.20 | 1.83E-76 | 3.83E-74 |  |  |  |  |
| Developmental protein | 1.20 | 9.18E-04 | 8.95E-03 |  |  |  |  |
| Zinc-finger | 1.19 | 1.58E-05 | 2.82E-04 |  |  |  |  |
| Transport | 1.15 | 2.25E-04 | 2.81E-03 |  |  |  |  |
| Transcription regulation | 1.13 | 2.64E-04 | 3.18E-03 |  |  |  |  |
| Transcription | 1.13 | 2.22E-04 | 2.83E-03 |  |  |  |  |
| Nucleus | 1.12 | 4.01E-08 | 1.09E-06 |  |  |  |  |
| Zinc | 1.12 | 1.07E-03 | 1.01E-02 |  |  |  |  |
| Metal-binding | 1.10 | 3.11E-04 | 3.67E-03 |  |  |  |  |
| Acetylation | 1.08 | 6.24E-03 | 4.84E-02 |  |  |  |  |