

**Supplementary Table VII. KEGG pathway enrichment on rich-club accessions performed through DAVID.**

| Category     | Term   | Count | %   | PValue   | Fold Enrichment | Bonferroni | Benjamini | FDR       |
|--------------|--|-------|-----|----------|-----------------|------------|-----------|-----------|
| KEGG_PATHWAY | hsa05200:Pathways in cancer                      | 83    | 20  | 1.09E-28 | 3.806961683     | 1.43E-26   | 1.43E-26  | 1.27E-25  |
| KEGG_PATHWAY | hsa04060:Cytokine-cytokine receptor interaction  | 65    | 16  | 1.18E-21 | 3.732384028     | 1.54E-19   | 7.71E-20  | 1.37E-18  |
| KEGG_PATHWAY | hsa04620:Toll-like receptor signaling pathway    | 38    | 9.1 | 3.75E-19 | 5.660261292     | 4.91E-17   | 1.64E-17  | 4.37E-16  |
| KEGG_PATHWAY | hsa04080:Neuroactive ligand-receptor interaction | 59    | 14  | 5.89E-18 | 3.467259153     | 7.71E-16   | 1.93E-16  | 6.86E-15  |
| KEGG_PATHWAY | hsa04210:Apoptosis                               | 33    | 7.9 | 9.33E-17 | 5.706488472     | 1.45E-14   | 2.44E-15  | 1.33E-13  |
| KEGG_PATHWAY | hsa04062:Chemokine signaling pathway             | 46    | 11  | 5.19E-15 | 3.700756257     | 6.84E-13   | 8.55E-14  | 6.08E-12  |
| KEGG_PATHWAY | hsa04722:Neurotrophin signaling pathway          | 37    | 8.9 | 6.61E-15 | 4.489048483     | 8.73E-13   | 9.69E-14  | 7.77E-12  |
| KEGG_PATHWAY | hsa04510:Focal adhesion                          | 43    | 10  | 7.59E-12 | 3.218449174     | 9.95E-10   | 8.29E-11  | 8.85E-09  |
| KEGG_PATHWAY | hsa04020:Calcium signaling pathway               | 39    | 9.3 | 2.93E-11 | 3.333697552     | 3.84E-09   | 2.95E-10  | 3.42E-08  |
| KEGG_PATHWAY | hsa04610:Complement and coagulation cascades     | 23    | 5.5 | 2.00E-10 | 5.014792899     | 2.62E-08   | 1.38E-09  | 2.33E-07  |
| KEGG_PATHWAY | hsa04630:Jak-STAT signaling pathway              | 34    | 8.1 | 9.52E-10 | 3.300057263     | 1.25E-07   | 5.94E-09  | 1.11E-06  |
| KEGG_PATHWAY | hsa04621:NOD-like receptor signaling pathway     | 21    | 5   | 1.09E-09 | 5.095676656     | 1.42E-07   | 6.46E-09  | 1.27E-06  |
| KEGG_PATHWAY | hsa04660:T cell receptor signaling pathway       | 27    | 6.5 | 4.08E-09 | 3.761094675     | 5.35E-07   | 2.32E-08  | 4.76E-06  |
| KEGG_PATHWAY | hsa04920:Adipocytokine signaling pathway         | 21    | 5   | 5.02E-09 | 4.715402279     | 6.58E-07   | 2.74E-08  | 5.86E-06  |
| KEGG_PATHWAY | hsa04540:Gap junction                            | 22    | 5.3 | 1.94E-07 | 3.718835184     | 2.55E-05   | 8.78E-07  | 2.27E-04  |
| KEGG_PATHWAY | hsa04010:MAPK signaling pathway                  | 42    | 10  | 2.03E-07 | 2.366531481     | 2.65E-05   | 8.85E-07  | 2.36E-04  |
| KEGG_PATHWAY | hsa04664:Fc epsilon RI signaling pathway         | 20    | 4.8 | 4.43E-07 | 3.857533        | 5.81E-05   | 1.87E-06  | 5.17E-04  |
| KEGG_PATHWAY | hsa04370:VEGF signaling pathway                  | 19    | 4.5 | 1.14E-06 | 3.811242604     | 1.49E-04   | 4.51E-06  | 0.0013244 |
| KEGG_PATHWAY | hsa05020:Prion diseases                          | 13    | 3.1 | 1.23E-06 | 5.587912088     | 1.61E-04   | 4.74E-06  | 0.0014336 |
| KEGG_PATHWAY | hsa04670:Leukocyte transendothelial migration    | 24    | 5.7 | 1.94E-06 | 3.059873634     | 2.54E-04   | 7.25E-06  | 0.0022596 |
| KEGG_PATHWAY | hsa04914:Progesterone-mediated oocyte maturation | 20    | 4.8 | 2.21E-06 | 3.498692721     | 2.89E-04   | 8.03E-06  | 0.0025717 |
| KEGG_PATHWAY | hsa04622:RIG-I-like receptor signaling pathway   | 18    | 4.3 | 2.35E-06 | 3.814067839     | 3.08E-04   | 8.32E-06  | 0.0027395 |
| KEGG_PATHWAY | hsa05211:Renal cell carcinoma                    | 17    | 4.1 | 8.92E-06 | 3.653634827     | 0.0011682  | 3.08E-05  | 0.0104043 |
| KEGG_PATHWAY | hsa04910:Insulin signaling pathway               | 24    | 5.7 | 2.04E-05 | 2.674556213     | 0.0026752  | 6.87E-05  | 0.0238429 |

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|--------------|---|----|-----|----------|-------------|-----------|-----------|-----------|
| KEGG_PATHWAY | hsa04810:Regulation of actin cytoskeleton             | 32 | 7.7 | 2.54E-05 | 2.239163341 | 0.0033265 | 8.33E-05  | 0.0296571 |
| KEGG_PATHWAY | hsa04623:Cytosolic DNA-sensing pathway                | 14 | 3.3 | 4.29E-05 | 3.829478214 | 0.0056092 | 1.37E-04  | 0.05006   |
| KEGG_PATHWAY | hsa05216:Thyroid cancer                               | 10 | 2.4 | 6.78E-05 | 5.187716792 | 0.0088389 | 2.11E-04  | 0.079001  |
| KEGG_PATHWAY | hsa04115:p53 signaling pathway                        | 15 | 3.6 | 1.11E-04 | 3.318612948 | 0.0144778 | 3.39E-04  | 0.1297362 |
| KEGG_PATHWAY | hsa04650:Natural killer cell mediated cytotoxicity    | 22 | 5.3 | 1.47E-04 | 2.488543845 | 0.0190732 | 4.38E-04  | 0.1712794 |
| KEGG_PATHWAY | hsa04930:Type II diabetes mellitus                    | 12 | 2.9 | 1.84E-04 | 3.841117966 | 0.0238267 | 5.36E-04  | 0.2144381 |
| KEGG_PATHWAY | hsa04912:GnRH signaling pathway                       | 18 | 4.3 | 1.99E-04 | 2.76325323  | 0.0256834 | 5.65E-04  | 0.2313482 |
| KEGG_PATHWAY | hsa04662:B cell receptor signaling pathway            | 15 | 3.6 | 3.31E-04 | 3.00887574  | 0.0424667 | 9.23E-04  | 0.3855468 |
| KEGG_PATHWAY | hsa04110:Cell cycle                                   | 20 | 4.8 | 4.99E-04 | 2.407100592 | 0.0632329 | 0.0013599 | 0.5797848 |
| KEGG_PATHWAY | hsa04940:Type I diabetes mellitus                     | 10 | 2.4 | 0.0014   | 3.581994928 | 0.1676889 | 0.0037389 | 1.6206431 |
| KEGG_PATHWAY | hsa04720:Long-term potentiation                       | 13 | 3.1 | 0.00147  | 2.876131222 | 0.1748946 | 0.0038375 | 1.6967613 |
| KEGG_PATHWAY | hsa04150:mTOR signaling pathway                       | 11 | 2.6 | 0.00185  | 3.182464725 | 0.215084  | 0.0047373 | 2.1327565 |
| KEGG_PATHWAY | hsa04916:Melanogenesis                                | 16 | 3.8 | 0.00198  | 2.431414739 | 0.228992  | 0.0049886 | 2.2883846 |
| KEGG_PATHWAY | hsa05330:Allograft rejection                          | 9  | 2.2 | 0.00201  | 3.761094675 | 0.2315336 | 0.0049567 | 2.3171006 |
| KEGG_PATHWAY | hsa05416:Viral myocarditis                            | 13 | 3.1 | 0.00215  | 2.75460455  | 0.2461126 | 0.005218  | 2.4835126 |
| KEGG_PATHWAY | hsa04144:Endocytosis                                  | 24 | 5.7 | 0.00217  | 1.962310265 | 0.2473718 | 0.0051537 | 2.4980222 |
| KEGG_PATHWAY | hsa04514:Cell adhesion molecules (CAMs)               | 19 | 4.5 | 0.00249  | 2.165478752 | 0.2787889 | 0.0058191 | 2.8674079 |
| KEGG_PATHWAY | hsa04672:Intestinal immune network for IgA production | 10 | 2.4 | 0.00428  | 3.070281367 | 0.4297956 | 0.009807  | 4.8777111 |
| KEGG_PATHWAY | hsa04520:Adherens junction                            | 13 | 3.1 | 0.00432  | 2.53996004  | 0.4329024 | 0.0097321 | 4.9239622 |
| KEGG_PATHWAY | hsa04114:Oocyte meiosis                               | 16 | 3.8 | 0.00557  | 2.188273265 | 0.5189714 | 0.0123273 | 6.306935  |
| KEGG_PATHWAY | hsa05010:Alzheimer's disease                          | 20 | 4.8 | 0.01079  | 1.845936037 | 0.7587075 | 0.0234172 | 11.887971 |
| KEGG_PATHWAY | hsa04350:TGF-beta signaling pathway                   | 13 | 3.1 | 0.0115   | 2.24801061  | 0.7802668 | 0.0245356 | 12.619045 |
| KEGG_PATHWAY | hsa05130:Pathogenic Escherichia coli infection        | 10 | 2.4 | 0.01175  | 2.639364684 | 0.7875014 | 0.0246715 | 12.879072 |
| KEGG_PATHWAY | hsa04730:Long-term depression                         | 11 | 2.6 | 0.0146   | 2.398379213 | 0.854311  | 0.0301132 | 15.75778  |
| KEGG_PATHWAY | hsa04666:Fc gamma R-mediated phagocytosis             | 13 | 3.1 | 0.02207  | 2.058704453 | 0.9462656 | 0.0446551 | 22.915083 |
| KEGG_PATHWAY | hsa04614:Renin-angiotensin system                     | 5  | 1.2 | 0.02264  | 4.424817264 | 0.9501988 | 0.0451008 | 23.43492  |
| KEGG_PATHWAY | hsa05332:Graft-versus-host disease                    | 7  | 1.7 | 0.04133  | 2.7002731   | 0.9960294 | 0.0803576 | 38.869988 |
| KEGG_PATHWAY | hsa04360:Axon guidance                                | 15 | 3.6 | 0.04512  | 1.74934636  | 0.9976375 | 0.086315  | 41.631052 |
| KEGG_PATHWAY | hsa04512:ECM-receptor interaction                     | 11 | 2.6 | 0.04956  | 1.97009721  | 0.9987169 | 0.0932779 | 44.7183   |

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|--------------|--|----|-----|---------|-------------|-----------|-----------|-----------|
| KEGG_PATHWAY | hsa04960:Aldosterone-regulated sodium reabsorption | 7  | 1.7 | 0.05104 | 2.568552461 | 0.9989536 | 0.0946688 | 45.712379 |
| KEGG_PATHWAY | hsa04270:Vascular smooth muscle contraction        | 13 | 3.1 | 0.06573 | 1.746222527 | 0.9998646 | 0.1194835 | 54.747302 |
| KEGG_PATHWAY | hsa05414:Dilated cardiomyopathy                    | 11 | 2.6 | 0.08169 | 1.79878441  | 0.9999858 | 0.1454964 | 62.982081 |