**Supplementary Table 4. Information of the pathways based on KEGG enrichment analysis**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Term | Count | % | *P*-Value | FDR |
| hsa05417:Lipid and atherosclerosis | 27 | 27.84  | 5.18E-21 | 5.23E-19 |
| hsa05162:Measles | 21 | 21.65  | 8.25E-18 | 4.17E-16 |
| hsa04933:AGE-RAGE signaling pathway in diabetic complications | 18 | 18.56  | 1.88E-16 | 4.20E-15 |
| hsa05161:Hepatitis B | 21 | 21.65  | 2.08E-16 | 4.20E-15 |
| hsa04625:C-type lectin receptor signaling pathway | 18 | 18.56  | 3.75E-16 | 6.32E-15 |
| hsa05169:Epstein-Barr virus infection | 22 | 22.68  | 1.28E-15 | 1.62E-14 |
| hsa05145:Toxoplasmosis | 18 | 18.56  | 1.28E-15 | 1.62E-14 |
| hsa04668:TNF signaling pathway | 18 | 18.56  | 1.97E-15 | 2.21E-14 |
| hsa05142:Chagas disease | 17 | 17.53  | 6.22E-15 | 6.28E-14 |
| hsa05167:Kaposi sarcoma-associated herpesvirus infection | 21 | 21.65  | 7.73E-15 | 7.10E-14 |
| hsa05152:Tuberculosis | 20 | 20.62  | 2.56E-14 | 2.16E-13 |
| hsa05163:Human cytomegalovirus infection | 21 | 21.65  | 1.34E-13 | 1.01E-12 |
| hsa05164:Influenza A | 19 | 19.59  | 1.40E-13 | 1.01E-12 |
| hsa04066:HIF-1 signaling pathway | 16 | 16.49  | 3.44E-13 | 2.32E-12 |
| hsa05166:Human T-cell leukemia virus 1 infection | 20 | 20.62  | 1.18E-12 | 7.47E-12 |
| hsa04722:Neurotrophin signaling pathway | 16 | 16.49  | 1.29E-12 | 7.67E-12 |
| hsa05205:Proteoglycans in cancer | 19 | 19.59  | 3.24E-12 | 1.82E-11 |
| hsa04620:Toll-like receptor signaling pathway | 15 | 15.46  | 5.22E-12 | 2.78E-11 |
| hsa05160:Hepatitis C | 17 | 17.53  | 6.68E-12 | 3.37E-11 |
| hsa05418:Fluid shear stress and atherosclerosis | 16 | 16.49  | 1.29E-11 | 6.18E-11 |
| hsa04370:VEGF signaling pathway | 12 | 12.37  | 1.94E-11 | 8.90E-11 |
| hsa04071:Sphingolipid signaling pathway | 15 | 15.46  | 2.53E-11 | 1.11E-10 |
| hsa04932:Non-alcoholic fatty liver disease | 16 | 16.49  | 6.25E-11 | 2.63E-10 |
| hsa04210:Apoptosis | 15 | 15.46  | 1.25E-10 | 5.05E-10 |
| hsa05135:Yersinia infection | 15 | 15.46  | 1.38E-10 | 5.37E-10 |
| hsa04936:Alcoholic liver disease | 15 | 15.46  | 2.24E-10 | 8.39E-10 |
| hsa05134:Legionellosis | 11 | 11.34  | 2.64E-10 | 9.54E-10 |
| hsa05212:Pancreatic cancer | 12 | 12.37  | 3.43E-10 | 1.19E-09 |
| hsa01522:Endocrine resistance | 13 | 13.40  | 3.81E-10 | 1.27E-09 |
| hsa04072:Phospholipase D signaling pathway | 15 | 15.46  | 3.91E-10 | 1.27E-09 |
| hsa05170:Human immunodeficiency virus 1 infection | 17 | 17.53  | 5.75E-10 | 1.81E-09 |
| hsa05208:Chemical carcinogenesis - reactive oxygen species | 17 | 17.53  | 1.21E-09 | 3.69E-09 |
| hsa05165:Human papillomavirus infection | 20 | 20.62  | 1.24E-09 | 3.69E-09 |
| hsa04062:Chemokine signaling pathway | 16 | 16.49  | 1.30E-09 | 3.76E-09 |
| hsa05235:PD-L1 expression and PD-1 checkpoint pathway in cancer | 12 | 12.37  | 1.95E-09 | 5.48E-09 |
| hsa05171:Coronavirus disease - COVID-19 | 17 | 17.53  | 2.30E-09 | 6.28E-09 |
| hsa05222:Small cell lung cancer | 12 | 12.37  | 2.80E-09 | 7.44E-09 |
| hsa04657:IL-17 signaling pathway | 12 | 12.37  | 3.53E-09 | 9.15E-09 |
| hsa01524:Platinum drug resistance | 11 | 11.34  | 3.98E-09 | 1.01E-08 |
| hsa05207:Chemical carcinogenesis - receptor activation | 16 | 16.49  | 5.13E-09 | 1.26E-08 |
| hsa05131:Shigellosis | 17 | 17.53  | 5.36E-09 | 1.29E-08 |
| hsa05133:Pertussis | 11 | 11.34  | 5.96E-09 | 1.38E-08 |
| hsa05132:Salmonella infection | 17 | 17.53  | 6.02E-09 | 1.38E-08 |
| hsa04621:NOD-like receptor signaling pathway | 15 | 15.46  | 7.91E-09 | 1.78E-08 |
| hsa05146:Amoebiasis | 12 | 12.37  | 8.51E-09 | 1.83E-08 |
| hsa01521:EGFR tyrosine kinase inhibitor resistance | 11 | 11.34  | 8.77E-09 | 1.84E-08 |
| hsa04926:Relaxin signaling pathway | 13 | 13.40  | 9.39E-09 | 1.93E-08 |
| hsa04931:Insulin resistance | 12 | 12.37  | 1.56E-08 | 3.16E-08 |
| hsa05210:Colorectal cancer | 11 | 11.34  | 2.03E-08 | 4.02E-08 |
| hsa04151:PI3K-Akt signaling pathway | 19 | 19.59  | 3.01E-08 | 5.86E-08 |
| hsa04917:Prolactin signaling pathway | 10 | 10.31  | 4.42E-08 | 8.42E-08 |
| hsa05215:Prostate cancer | 11 | 11.34  | 6.55E-08 | 1.22E-07 |
| hsa04218:Cellular senescence | 13 | 13.40  | 7.99E-08 | 1.47E-07 |
| hsa05220:Chronic myeloid leukemia | 10 | 10.31  | 9.19E-08 | 1.66E-07 |
| hsa05140:Leishmaniasis | 10 | 10.31  | 1.03E-07 | 1.83E-07 |
| hsa04068:FoxO signaling pathway | 12 | 12.37  | 1.18E-07 | 2.05E-07 |
| hsa04630:JAK-STAT signaling pathway | 13 | 13.40  | 1.59E-07 | 2.72E-07 |
| hsa05203:Viral carcinogenesis | 14 | 14.43  | 2.04E-07 | 3.37E-07 |
| hsa04012:ErbB signaling pathway | 10 | 10.31  | 2.46E-07 | 4.00E-07 |
| hsa05321:Inflammatory bowel disease | 9 | 9.28  | 3.66E-07 | 5.87E-07 |
| hsa05010:Alzheimer disease | 18 | 18.56  | 4.60E-07 | 7.19E-07 |
| hsa04930:Type II diabetes mellitus | 8 | 8.25  | 4.63E-07 | 7.19E-07 |
| hsa04660:T cell receptor signaling pathway | 11 | 11.34  | 5.35E-07 | 8.18E-07 |
| hsa05230:Central carbon metabolism in cancer | 9 | 9.28  | 6.55E-07 | 9.88E-07 |
| hsa04613:Neutrophil extracellular trap formation | 13 | 13.40  | 7.26E-07 | 1.08E-06 |
| hsa05206:microRNAs in cancer | 16 | 16.49  | 7.81E-07 | 1.14E-06 |
| hsa05223:Non-small cell lung cancer | 9 | 9.28  | 8.17E-07 | 1.18E-06 |
| hsa05144:Malaria | 8 | 8.25  | 8.34E-07 | 1.19E-06 |
| hsa05130:Pathogenic Escherichia coli infection | 13 | 13.40  | 1.07E-06 | 1.50E-06 |
| hsa05214:Glioma | 9 | 9.28  | 1.12E-06 | 1.55E-06 |
| hsa04510:Focal adhesion | 13 | 13.40  | 1.39E-06 | 1.87E-06 |
| hsa05415:Diabetic cardiomyopathy | 13 | 13.40  | 1.39E-06 | 1.87E-06 |
| hsa04380:Osteoclast differentiation | 11 | 11.34  | 1.47E-06 | 1.96E-06 |
| hsa04915:Estrogen signaling pathway | 11 | 11.34  | 1.69E-06 | 2.21E-06 |
| hsa04010:MAPK signaling pathway | 15 | 15.46  | 3.03E-06 | 3.92E-06 |
| hsa05226:Gastric cancer | 11 | 11.34  | 3.62E-06 | 4.57E-06 |
| hsa05020:Prion disease | 14 | 14.43  | 5.26E-06 | 6.56E-06 |
| hsa05221:Acute myeloid leukemia | 8 | 8.25  | 6.27E-06 | 7.73E-06 |
| hsa04014:Ras signaling pathway | 13 | 13.40  | 6.67E-06 | 8.12E-06 |
| hsa04664:Fc epsilon RI signaling pathway | 8 | 8.25  | 6.93E-06 | 8.24E-06 |
| hsa05211:Renal cell carcinoma | 8 | 8.25  | 7.65E-06 | 8.98E-06 |
| hsa05218:Melanoma | 8 | 8.25  | 1.02E-05 | 1.15E-05 |
| hsa05213:Endometrial cancer | 7 | 7.22  | 3.16E-05 | 3.55E-05 |
| hsa04935:Growth hormone synthesis, secretion and action | 9 | 9.28  | 3.78E-05 | 4.20E-05 |
| hsa04611:Platelet activation | 9 | 9.28  | 4.79E-05 | 5.26E-05 |
| hsa05323:Rheumatoid arthritis | 8 | 8.25  | 5.46E-05 | 5.93E-05 |
| hsa04650:Natural killer cell mediated cytotoxicity | 9 | 9.28  | 5.68E-05 | 6.11E-05 |
| hsa04140:Autophagy - animal | 10 | 10.31  | 5.96E-05 | 6.34E-05 |
| hsa05225:Hepatocellular carcinoma | 10 | 10.31  | 6.86E-05 | 7.21E-05 |
| hsa04666:Fc gamma R-mediated phagocytosis | 8 | 8.25  | 7.16E-05 | 7.44E-05 |
| hsa04015:Rap1 signaling pathway | 11 | 11.34  | 7.21E-05 | 7.44E-05 |
| hsa05231:Choline metabolism in cancer | 8 | 8.25  | 7.64E-05 | 7.80E-05 |
| hsa05168:Herpes simplex virus 1 infection | 17 | 17.53  | 8.42E-05 | 8.50E-05 |
| hsa04920:Adipocytokine signaling pathway | 7 | 7.22  | 9.25E-05 | 9.25E-05 |
| hsa04622:RIG-I-like receptor signaling pathway | 7 | 7.22  | 1.00E-04 | 1.00E-04 |
| hsa04024:cAMP signaling pathway | 11 | 11.34  | 1.28E-04 | 1.28E-04 |
| hsa04810:Regulation of actin cytoskeleton | 11 | 11.34  | 1.48E-04 | 1.48E-04 |
| hsa04725:Cholinergic synapse | 8 | 8.25  | 1.88E-04 | 1.88E-04 |
| hsa04623:Cytosolic DNA-sensing pathway | 7 | 7.22  | 2.38E-04 | 2.38E-04 |
| hsa04662:B cell receptor signaling pathway | 7 | 7.22  | 2.55E-04 | 2.55E-04 |
| hsa04211:Longevity regulating pathway | 7 | 7.22  | 3.49E-04 | 3.49E-04 |
| hsa04923:Regulation of lipolysis in adipocytes | 6 | 6.19  | 3.56E-04 | 3.56E-04 |
| hsa04750:Inflammatory mediator regulation of TRP channels | 7 | 7.22  | 5.85E-04 | 5.85E-04 |
| hsa04360:Axon guidance | 9 | 9.28  | 6.73E-04 | 6.73E-04 |
| hsa04914:Progesterone-mediated oocyte maturation | 7 | 7.22  | 7.24E-04 | 7.24E-04 |
| hsa04550:Signaling pathways regulating pluripotency of stem cells | 8 | 8.25  | 7.85E-04 | 7.85E-04 |
| hsa05017:Spinocerebellar ataxia | 8 | 8.25  | 7.85E-04 | 7.85E-04 |
| hsa05224:Breast cancer | 8 | 8.25  | 9.24E-04 | 9.24E-04 |
| hsa04672:Intestinal immune network for IgA production | 5 | 5.15  | 0.001752732 | 0.001752732 |
| hsa04919:Thyroid hormone signaling pathway | 7 | 7.22  | 0.001759262 | 0.001759262 |
| hsa04213:Longevity regulating pathway-multiple species | 5 | 5.15  | 0.003919271 | 0.003919271 |
| hsa04929:GnRH secretion | 5 | 5.15  | 0.004658163 | 0.004658163 |
| hsa04960:Aldosterone-regulated sodium reabsorption | 4 | 4.12  | 0.006939827 | 0.006939827 |
| hsa05100:Bacterial invasion of epithelial cells | 5 | 5.15  | 0.008939267 | 0.008939267 |
| hsa04152:AMPK signaling pathway | 6 | 6.19  | 0.009163537 | 0.009163537 |
| hsa05332:Graft-versus-host disease | 4 | 4.12  | 0.009870424 | 0.009870424 |
| hsa04973:Carbohydrate digestion and absorption | 4 | 4.12  | 0.013421984 | 0.013421984 |
| hsa04910:Insulin signaling pathway | 6 | 6.19  | 0.015096324 | 0.015096324 |
| hsa04261:Adrenergic signaling in cardiomyocytes | 6 | 6.19  | 0.023764982 | 0.023764982 |
| hsa04150:mTOR signaling pathway | 6 | 6.19  | 0.024958745 | 0.024958745 |
| hsa00562:Inositol phosphate metabolism | 4 | 4.12  | 0.042320235 | 0.042320235 |

AGE-RAGE, advanced glycosylation end product-receptor; AMPK, AMP-activated protein kinase; cAMP, cyclic adenosine monophosphate; EGFR, epidermal growth factor receptor; FDR, false discovery rate; FoxO, recombinant forkhead box protein O1; IL, interleukin; JAK-STAT, janus kinase-signal transducer and activator of transcription; KEGG, kyoto encyclopedia of genes and genomes; MAPK, mitogen-activated protein kinase; mTOR, mammalian target of rapamycin; NOD, nucleotide-binding, oligomerization domain; PD-1, programmed cell death protein 1; PD-L1, programmed cell death-ligand 1; PI3K-Akt, phosphatidylinositol 3-kinase-protein kinase B; RIG, retinoic acid induced gene; TNF, tumor necrosis factor; TRP, tryptophan; VEGF, vascular endothelial growth factors.