

Table S6 Pathway enrichment results based on the identified causal genes from the estimated CTS expression profiles of all cell types in the target tissue

### Depression

| pathway name                                                               | candidates |           | p-value | q-value | pathway source      |
|----------------------------------------------------------------------------|------------|-----------|---------|---------|---------------------|
|                                                                            | set size   | contained |         |         |                     |
| spliceosomal assembly                                                      | 9          | 1 (11.1%) | 0.00735 | 0.179   | <b>BioCarta</b>     |
| Unwinding of DNA                                                           | 12         | 1 (8.3%)  | 0.00979 | 0.179   | <b>Reactome</b>     |
| cdk regulation of dna replication                                          | 18         | 1 (5.6%)  | 0.0146  | 0.179   | <b>BioCarta</b>     |
| Assembly of the pre-replicative complex                                    | 20         | 1 (5.0%)  | 0.0163  | 0.179   | <b>Reactome</b>     |
| Orc1 removal from chromatin                                                | 26         | 1 (3.8%)  | 0.0211  | 0.179   | <b>Reactome</b>     |
| Phototransduction - Homo sapiens (human)                                   | 29         | 1 (3.6%)  | 0.0227  | 0.179   | <b>KEGG</b>         |
| DNA strand elongation                                                      | 32         | 1 (3.1%)  | 0.0259  | 0.179   | <b>Reactome</b>     |
| Activation of the pre-replicative complex                                  | 33         | 1 (3.0%)  | 0.0267  | 0.179   | <b>Reactome</b>     |
| Mammary gland development pathway - Pregnancy and lactation (Stage 3 of 4) | 33         | 1 (3.0%)  | 0.0267  | 0.179   | <b>Wikipathways</b> |
| DNA replication - Homo sapiens (human)                                     | 36         | 1 (2.8%)  | 0.0291  | 0.179   | <b>KEGG</b>         |
| Activation of ATR in response to replication stress                        | 37         | 1 (2.7%)  | 0.0299  | 0.179   | <b>Reactome</b>     |
| DNA Replication Pre-Initiation                                             | 37         | 1 (2.7%)  | 0.0299  | 0.179   | <b>Reactome</b>     |
| O-glycosylation of TSR domain-containing proteins                          | 39         | 1 (2.6%)  | 0.0315  | 0.179   | <b>Reactome</b>     |
| DNA Replication                                                            | 42         | 1 (2.4%)  | 0.0339  | 0.179   | <b>Wikipathways</b> |
| Renin-angiotensin-aldosterone system (RAAS)                                | 44         | 1 (2.3%)  | 0.0355  | 0.179   | <b>Wikipathways</b> |
| Switching of origins to a post-replicative state                           | 47         | 1 (2.1%)  | 0.0378  | 0.179   | <b>Reactome</b>     |
| Ion transport by P-type ATPases                                            | 47         | 1 (2.1%)  | 0.0378  | 0.179   | <b>Reactome</b>     |
| Formation of the ternary complex, and subsequently, the 43S complex        | 59         | 1 (1.7%)  | 0.0473  | 0.179   | <b>Reactome</b>     |

## Anxiety

| pathway name                                                     | candidates |           | p-value | q-value | pathway source               |
|------------------------------------------------------------------|------------|-----------|---------|---------|------------------------------|
|                                                                  | set size   | contained |         |         |                              |
| Extrinsic Pathway of Fibrin Clot Formation                       | 5          | 1 (20.0%) | 0.00297 | 0.0308  | <a href="#">Reactome</a>     |
| Macrophage markers                                               | 9          | 1 (11.1%) | 0.00535 | 0.0308  | <a href="#">Wikipathways</a> |
| Establishment of Sister Chromatid Cohesion                       | 11         | 1 (9.1%)  | 0.00653 | 0.0308  | <a href="#">Reactome</a>     |
| extrinsic prothrombin activation pathway                         | 13         | 1 (7.7%)  | 0.00772 | 0.0308  | <a href="#">BioCarta</a>     |
| Synthesis of bile acids and bile salts via 24-hydroxycholesterol | 14         | 1 (7.1%)  | 0.00831 | 0.0308  | <a href="#">Reactome</a>     |
| Oxysterols derived from cholesterol                              | 15         | 1 (6.7%)  | 0.0089  | 0.0308  | <a href="#">Wikipathways</a> |
| Bile Acid Biosynthesis                                           | 17         | 1 (5.9%)  | 0.0101  | 0.0308  | <a href="#">SMPDB</a>        |
| 27-Hydroxylase Deficiency                                        | 17         | 1 (5.9%)  | 0.0101  | 0.0308  | <a href="#">SMPDB</a>        |
| Congenital Bile Acid Synthesis Defect Type II                    | 17         | 1 (5.9%)  | 0.0101  | 0.0308  | <a href="#">SMPDB</a>        |
| Cerebrotendinous Xanthomatosis (CTX)                             | 17         | 1 (5.9%)  | 0.0101  | 0.0308  | <a href="#">SMPDB</a>        |
| Zellweger Syndrome                                               | 17         | 1 (5.9%)  | 0.0101  | 0.0308  | <a href="#">SMPDB</a>        |
| Familial Hypercholanemia (FHCA)                                  | 17         | 1 (5.9%)  | 0.0101  | 0.0308  | <a href="#">SMPDB</a>        |
| Congenital Bile Acid Synthesis Defect Type III                   | 17         | 1 (5.9%)  | 0.0101  | 0.0308  | <a href="#">SMPDB</a>        |
| Primary bile acid biosynthesis - Homo sapiens (human)            | 17         | 1 (5.9%)  | 0.0101  | 0.0308  | <a href="#">KEGG</a>         |
| Endogenous sterols                                               | 18         | 1 (5.6%)  | 0.0107  | 0.0308  | <a href="#">Reactome</a>     |
| Bivalirudin Action Pathway                                       | 20         | 1 (5.0%)  | 0.0119  | 0.0308  | <a href="#">SMPDB</a>        |
| Argatroban Action Pathway                                        | 20         | 1 (5.0%)  | 0.0119  | 0.0308  | <a href="#">SMPDB</a>        |
| Ximelagatran Action Pathway                                      | 20         | 1 (5.0%)  | 0.0119  | 0.0308  | <a href="#">SMPDB</a>        |
| Lepirudin Action Pathway                                         | 20         | 1 (5.0%)  | 0.0119  | 0.0308  | <a href="#">SMPDB</a>        |
| Coagulation                                                      | 20         | 1 (5.0%)  | 0.0119  | 0.0308  | <a href="#">SMPDB</a>        |
| Aminocaproic Acid Action Pathway                                 | 20         | 1 (5.0%)  | 0.0119  | 0.0308  | <a href="#">SMPDB</a>        |
| Tranexamic Acid Action Pathway                                   | 20         | 1 (5.0%)  | 0.0119  | 0.0308  | <a href="#">SMPDB</a>        |
| Urokinase Action Pathway                                         | 20         | 1 (5.0%)  | 0.0119  | 0.0308  | <a href="#">SMPDB</a>        |
| Retepase Action Pathway                                          | 20         | 1 (5.0%)  | 0.0119  | 0.0308  | <a href="#">SMPDB</a>        |
| Streptokinase Action Pathway                                     | 20         | 1 (5.0%)  | 0.0119  | 0.0308  | <a href="#">SMPDB</a>        |
| Tenecteplase Action Pathway                                      | 20         | 1 (5.0%)  | 0.0119  | 0.0308  | <a href="#">SMPDB</a>        |
| Alteplase Action Pathway                                         | 20         | 1 (5.0%)  | 0.0119  | 0.0308  | <a href="#">SMPDB</a>        |
| Anistreplase Action Pathway                                      | 20         | 1 (5.0%)  | 0.0119  | 0.0308  | <a href="#">SMPDB</a>        |
| Aprotinin Action Pathway                                         | 20         | 1 (5.0%)  | 0.0119  | 0.0308  | <a href="#">SMPDB</a>        |
| Phenindione Action Pathway                                       | 20         | 1 (5.0%)  | 0.0119  | 0.0308  | <a href="#">SMPDB</a>        |
| Dicoumarol Action Pathway                                        | 20         | 1 (5.0%)  | 0.0119  | 0.0308  | <a href="#">SMPDB</a>        |
| Warfarin Action Pathway                                          | 20         | 1 (5.0%)  | 0.0119  | 0.0308  | <a href="#">SMPDB</a>        |
| Acenocoumarol Action Pathway                                     | 20         | 1 (5.0%)  | 0.0119  | 0.0308  | <a href="#">SMPDB</a>        |
| Phenprocoumon Action Pathway                                     | 20         | 1 (5.0%)  | 0.0119  | 0.0308  | <a href="#">SMPDB</a>        |
| Dicumarol Action Pathway                                         | 20         | 1 (5.0%)  | 0.0119  | 0.0308  | <a href="#">SMPDB</a>        |
| Ardeparin Action Pathway                                         | 21         | 1 (4.8%)  | 0.0124  | 0.0308  | <a href="#">SMPDB</a>        |
| Heparin Action Pathway                                           | 21         | 1 (4.8%)  | 0.0124  | 0.0308  | <a href="#">SMPDB</a>        |
| Fondaparinux Action Pathway                                      | 21         | 1 (4.8%)  | 0.0124  | 0.0308  | <a href="#">SMPDB</a>        |
| Enoxaparin Action Pathway                                        | 21         | 1 (4.8%)  | 0.0124  | 0.0308  | <a href="#">SMPDB</a>        |
| STING pathway in Kawasaki-like disease and COVID-19              | 21         | 1 (4.8%)  | 0.0124  | 0.0308  | <a href="#">Wikipathways</a> |
| Citric acid cycle (TCA cycle)                                    | 22         | 1 (4.5%)  | 0.013   | 0.0315  | <a href="#">Reactome</a>     |
| Blood Clotting Cascade                                           | 23         | 1 (4.3%)  | 0.0136  | 0.0321  | <a href="#">Wikipathways</a> |
| Vitamin digestion and absorption - Homo sapiens (human)          | 24         | 1 (4.2%)  | 0.0142  | 0.0327  | <a href="#">KEGG</a>         |
| alpha-Linolenic acid metabolism - Homo sapiens (human)           | 25         | 1 (4.0%)  | 0.0148  | 0.0333  | <a href="#">KEGG</a>         |
| Acyl chain remodelling of PC                                     | 27         | 1 (3.7%)  | 0.016   | 0.0351  | <a href="#">Reactome</a>     |

|                                                             |    |          |        |        |                              |
|-------------------------------------------------------------|----|----------|--------|--------|------------------------------|
| Linoleic acid metabolism - Homo sapiens (human)             | 29 | 1 (3.4%) | 0.0171 | 0.0369 | <a href="#">KEGG</a>         |
| Synthesis of bile acids and bile salts                      | 30 | 1 (3.3%) | 0.0177 | 0.0373 | <a href="#">Reactome</a>     |
| Tyrosine metabolism - Homo sapiens (human)                  | 36 | 1 (2.8%) | 0.0212 | 0.0438 | <a href="#">KEGG</a>         |
| Formation of Fibrin Clot (Clotting Cascade)                 | 37 | 1 (2.7%) | 0.0218 | 0.0441 | <a href="#">Reactome</a>     |
| NGF-stimulated transcription                                | 40 | 1 (2.5%) | 0.0236 | 0.0467 | <a href="#">Reactome</a>     |
| phospholipases                                              | 41 | 1 (2.4%) | 0.0242 | 0.0469 | <a href="#">HumanCyc</a>     |
| Bile acid and bile salt metabolism                          | 43 | 1 (2.3%) | 0.0253 | 0.0482 | <a href="#">Reactome</a>     |
| Retinoid metabolism and transport                           | 45 | 1 (2.2%) | 0.0265 | 0.0495 | <a href="#">Reactome</a>     |
| Metabolism of fat-soluble vitamins                          | 49 | 1 (2.0%) | 0.0288 | 0.0519 | <a href="#">Reactome</a>     |
| Ether lipid metabolism - Homo sapiens (human)               | 49 | 1 (2.0%) | 0.0288 | 0.0519 | <a href="#">KEGG</a>         |
| Pyruvate metabolism and Citric Acid (TCA) cycle             | 53 | 1 (1.9%) | 0.0311 | 0.055  | <a href="#">Reactome</a>     |
| Cytochrome P450 - arranged by substrate type                | 57 | 1 (1.8%) | 0.0335 | 0.0581 | <a href="#">Reactome</a>     |
| Complement and Coagulation Cascades                         | 59 | 1 (1.7%) | 0.0346 | 0.059  | <a href="#">Wikipathways</a> |
| Nuclear Events (kinase and transcription factor activation) | 61 | 1 (1.6%) | 0.0358 | 0.059  | <a href="#">Reactome</a>     |
| Arachidonic acid metabolism - Homo sapiens (human)          | 61 | 1 (1.6%) | 0.0358 | 0.059  | <a href="#">KEGG</a>         |
| Oxidation by Cytochrome P450                                | 62 | 1 (1.6%) | 0.0363 | 0.059  | <a href="#">Wikipathways</a> |
| Complement and coagulation cascades - Homo sapiens (human)  | 85 | 1 (1.2%) | 0.0495 | 0.0791 | <a href="#">KEGG</a>         |

## Bipolar

| pathway name                                                           | candidates |           | p-value | q-value | pathway source      |
|------------------------------------------------------------------------|------------|-----------|---------|---------|---------------------|
|                                                                        | set size   | contained |         |         |                     |
| pyrimidine ribonucleosides salvage I                                   | 4          | 1 (25.0%) | 0.00119 | 0.031   | <b>HumanCyc</b>     |
| Acetylcholine Synthesis                                                | 7          | 1 (14.3%) | 0.00208 | 0.031   | <b>Wikipathways</b> |
| Betaine Metabolism                                                     | 8          | 1 (12.5%) | 0.00238 | 0.031   | <b>SMPDB</b>        |
| Reduction of cytosolic Ca++ levels                                     | 10         | 1 (10.0%) | 0.00297 | 0.031   | <b>Reactome</b>     |
| Pyrimidine salvage                                                     | 11         | 1 (9.1%)  | 0.00327 | 0.031   | <b>Reactome</b>     |
| Kennedy pathway from sphingolipids                                     | 14         | 1 (7.1%)  | 0.00416 | 0.031   | <b>Wikipathways</b> |
| Glycerolipids and Glycerophospholipids                                 | 22         | 1 (4.5%)  | 0.00654 | 0.031   | <b>Wikipathways</b> |
| Nucleotide salvage                                                     | 23         | 1 (4.3%)  | 0.00683 | 0.031   | <b>Reactome</b>     |
| Pyrimidine Metabolism                                                  | 23         | 1 (4.3%)  | 0.00683 | 0.031   | <b>SMPDB</b>        |
| UMP Synthase Deiciency (Orotic Aciduria)                               | 23         | 1 (4.3%)  | 0.00683 | 0.031   | <b>SMPDB</b>        |
| MNGIE (Mitochondrial Neurogastrointestinal Encephalopathy)             | 23         | 1 (4.3%)  | 0.00683 | 0.031   | <b>SMPDB</b>        |
| Beta Ureidopropionase Deficiency                                       | 23         | 1 (4.3%)  | 0.00683 | 0.031   | <b>SMPDB</b>        |
| Dihydropyrimidinase Deficiency                                         | 23         | 1 (4.3%)  | 0.00683 | 0.031   | <b>SMPDB</b>        |
| Platelet calcium homeostasis                                           | 26         | 1 (3.8%)  | 0.00772 | 0.0317  | <b>Reactome</b>     |
| Phospholipid Biosynthesis                                              | 28         | 1 (3.6%)  | 0.00831 | 0.0317  | <b>SMPDB</b>        |
| Synthesis of PC                                                        | 29         | 1 (3.4%)  | 0.00861 | 0.0317  | <b>Reactome</b>     |
| Glycine Serine metabolism                                              | 40         | 1 (2.5%)  | 0.0119  | 0.0405  | <b>INOH</b>         |
| Ion homeostasis                                                        | 44         | 1 (2.3%)  | 0.013   | 0.0405  | <b>Reactome</b>     |
| nfat and hypertrophy of the heart                                      | 44         | 1 (2.3%)  | 0.013   | 0.0405  | <b>BioCarta</b>     |
| Ion transport by P-type ATPases                                        | 47         | 1 (2.1%)  | 0.0139  | 0.0411  | <b>Reactome</b>     |
| One-carbon metabolism and related pathways                             | 52         | 1 (1.9%)  | 0.0154  | 0.0433  | <b>Wikipathways</b> |
| Pyrimidine metabolism - Homo sapiens (human)                           | 57         | 1 (1.8%)  | 0.0169  | 0.0452  | <b>KEGG</b>         |
| Arrhythmogenic right ventricular cardiomyopathy - Homo sapiens (human) | 77         | 1 (1.3%)  | 0.0227  | 0.0553  | <b>KEGG</b>         |
| Drug metabolism - other enzymes - Homo sapiens (human)                 | 80         | 1 (1.2%)  | 0.0236  | 0.0553  | <b>KEGG</b>         |
| Pyrimidine metabolism                                                  | 84         | 1 (1.2%)  | 0.0248  | 0.0553  | <b>Wikipathways</b> |
| Platelet homeostasis                                                   | 85         | 1 (1.2%)  | 0.0251  | 0.0553  | <b>Reactome</b>     |
| Cardiac muscle contraction - Homo sapiens (human)                      | 87         | 1 (1.1%)  | 0.0257  | 0.0553  | <b>KEGG</b>         |
| Hypertrophic cardiomyopathy - Homo sapiens (human)                     | 90         | 1 (1.1%)  | 0.0265  | 0.0553  | <b>KEGG</b>         |
| Dilated cardiomyopathy - Homo sapiens (human)                          | 96         | 1 (1.1%)  | 0.028   | 0.0553  | <b>KEGG</b>         |
| Glycerophospholipid metabolism - Homo sapiens (human)                  | 98         | 1 (1.0%)  | 0.0289  | 0.0553  | <b>KEGG</b>         |
| Pancreatic secretion - Homo sapiens (human)                            | 102        | 1 (1.0%)  | 0.03    | 0.0553  | <b>KEGG</b>         |
| Metabolism of nucleotides                                              | 102        | 1 (1.0%)  | 0.03    | 0.0553  | <b>Reactome</b>     |
| Cardiac conduction                                                     | 105        | 1 (1.0%)  | 0.0309  | 0.0553  | <b>Reactome</b>     |
| Thyroid hormone signaling pathway - Homo sapiens (human)               | 121        | 1 (0.8%)  | 0.0355  | 0.0617  | <b>KEGG</b>         |
| Glycerophospholipid biosynthesis                                       | 130        | 1 (0.8%)  | 0.0382  | 0.0636  | <b>Reactome</b>     |
| Glycerophospholipid metabolism                                         | 136        | 1 (0.7%)  | 0.0399  | 0.0636  | <b>EHMN</b>         |
| Spinocerebellar ataxia - Homo sapiens (human)                          | 143        | 1 (0.7%)  | 0.0419  | 0.0636  | <b>KEGG</b>         |
| Alzheimer,s disease                                                    | 144        | 1 (0.7%)  | 0.0422  | 0.0636  | <b>Wikipathways</b> |
| Male infertility                                                       | 145        | 1 (0.7%)  | 0.0425  | 0.0636  | <b>Wikipathways</b> |
| Adrenergic signaling in cardiomyocytes - Homo sapiens (human)          | 150        | 1 (0.7%)  | 0.0439  | 0.0636  | <b>KEGG</b>         |
| Calcium Regulation in the Cardiac Cell                                 | 151        | 1 (0.7%)  | 0.0442  | 0.0636  | <b>Wikipathways</b> |
| Myometrial relaxation and contraction pathways                         | 155        | 1 (0.6%)  | 0.0454  | 0.0637  | <b>Wikipathways</b> |
| Ion channel transport                                                  | 165        | 1 (0.6%)  | 0.0482  | 0.0655  | <b>Reactome</b>     |
| cGMP-PKG signaling pathway - Homo sapiens (human)                      | 167        | 1 (0.6%)  | 0.0488  | 0.0655  | <b>KEGG</b>         |

## Psychosis

| pathway name                                                     | candidates |           | p-value | q-value | pathway source               |
|------------------------------------------------------------------|------------|-----------|---------|---------|------------------------------|
|                                                                  | set size   | contained |         |         |                              |
| Synthesis of bile acids and bile salts via 24-hydroxycholesterol | 14         | 1 (7.1%)  | 0.00416 | 0.0199  | <a href="#">Reactome</a>     |
| Oxysterols derived from cholesterol                              | 15         | 1 (6.7%)  | 0.00446 | 0.0199  | <a href="#">Wikipathways</a> |
| Bile Acid Biosynthesis                                           | 17         | 1 (5.9%)  | 0.00505 | 0.0199  | <a href="#">SMPDB</a>        |
| 27-Hydroxylase Deficiency                                        | 17         | 1 (5.9%)  | 0.00505 | 0.0199  | <a href="#">SMPDB</a>        |
| Congenital Bile Acid Synthesis Defect Type II                    | 17         | 1 (5.9%)  | 0.00505 | 0.0199  | <a href="#">SMPDB</a>        |
| Cerebrotendinous Xanthomatosis (CTX)                             | 17         | 1 (5.9%)  | 0.00505 | 0.0199  | <a href="#">SMPDB</a>        |
| Zellweger Syndrome                                               | 17         | 1 (5.9%)  | 0.00505 | 0.0199  | <a href="#">SMPDB</a>        |
| Familial Hypercholanemia (FHCA)                                  | 17         | 1 (5.9%)  | 0.00505 | 0.0199  | <a href="#">SMPDB</a>        |
| Congenital Bile Acid Synthesis Defect Type III                   | 17         | 1 (5.9%)  | 0.00505 | 0.0199  | <a href="#">SMPDB</a>        |
| Primary bile acid biosynthesis - Homo sapiens (human)            | 17         | 1 (5.9%)  | 0.00505 | 0.0199  | <a href="#">KEGG</a>         |
| Endogenous sterols                                               | 18         | 1 (5.6%)  | 0.00535 | 0.0199  | <a href="#">Reactome</a>     |
| Vitamin digestion and absorption - Homo sapiens (human)          | 24         | 1 (4.2%)  | 0.00713 | 0.0228  | <a href="#">KEGG</a>         |
| alpha-Linolenic acid metabolism - Homo sapiens (human)           | 25         | 1 (4.0%)  | 0.00742 | 0.0228  | <a href="#">KEGG</a>         |
| Acyl chain remodelling of PC                                     | 27         | 1 (3.7%)  | 0.00802 | 0.0228  | <a href="#">Reactome</a>     |
| Linoleic acid metabolism - Homo sapiens (human)                  | 29         | 1 (3.4%)  | 0.00861 | 0.0228  | <a href="#">KEGG</a>         |
| Synthesis of bile acids and bile salts                           | 30         | 1 (3.3%)  | 0.0089  | 0.0228  | <a href="#">Reactome</a>     |
| Sensory Perception                                               | 585        | 2 (0.3%)  | 0.0107  | 0.0248  | <a href="#">Reactome</a>     |
| phospholipases                                                   | 41         | 1 (2.4%)  | 0.0122  | 0.0248  | <a href="#">HumanCyc</a>     |
| Bile acid and bile salt metabolism                               | 43         | 1 (2.3%)  | 0.0127  | 0.0248  | <a href="#">Reactome</a>     |
| Metabolism of lipids                                             | 646        | 2 (0.3%)  | 0.0129  | 0.0248  | <a href="#">Reactome</a>     |
| Retinoid metabolism and transport                                | 45         | 1 (2.2%)  | 0.0133  | 0.0248  | <a href="#">Reactome</a>     |
| Ion transport by P-type ATPases                                  | 47         | 1 (2.1%)  | 0.0139  | 0.0248  | <a href="#">Reactome</a>     |
| Metabolism of fat-soluble vitamins                               | 49         | 1 (2.0%)  | 0.0145  | 0.0248  | <a href="#">Reactome</a>     |
| Ether lipid metabolism - Homo sapiens (human)                    | 49         | 1 (2.0%)  | 0.0145  | 0.0248  | <a href="#">KEGG</a>         |
| Cytochrome P450 - arranged by substrate type                     | 57         | 1 (1.8%)  | 0.0169  | 0.0277  | <a href="#">Reactome</a>     |
| Arachidonic acid metabolism - Homo sapiens (human)               | 61         | 1 (1.6%)  | 0.018   | 0.0278  | <a href="#">KEGG</a>         |
| Oxidation by Cytochrome P450                                     | 62         | 1 (1.6%)  | 0.0183  | 0.0278  | <a href="#">Wikipathways</a> |
| Glycerophospholipid metabolism - Homo sapiens (human)            | 98         | 1 (1.0%)  | 0.0289  | 0.0414  | <a href="#">KEGG</a>         |
| Phase I - Functionalization of compounds                         | 101        | 1 (1.0%)  | 0.0297  | 0.0414  | <a href="#">Reactome</a>     |
| Visual phototransduction                                         | 103        | 1 (1.0%)  | 0.0303  | 0.0414  | <a href="#">Reactome</a>     |
| Metabolism of steroids                                           | 124        | 1 (0.8%)  | 0.0364  | 0.0482  | <a href="#">Reactome</a>     |
| Glycerophospholipid biosynthesis                                 | 130        | 1 (0.8%)  | 0.0382  | 0.0489  | <a href="#">Reactome</a>     |
| Ion channel transport                                            | 165        | 1 (0.6%)  | 0.0482  | 0.0599  | <a href="#">Reactome</a>     |

## T2DM\_Pancreas

| pathway name                                                                                                          | candidates |            |         |         | pathway source |
|-----------------------------------------------------------------------------------------------------------------------|------------|------------|---------|---------|----------------|
|                                                                                                                       | set size   | contained  | p-value | q-value |                |
| Endocytosis - Homo sapiens (human)                                                                                    | 252        | 9 (3.6%)   | 0.0019  | 0.609   | KEGG           |
| Autophagy - other - Homo sapiens (human)                                                                              | 32         | 3 (9.4%)   | 0.00514 | 0.609   | KEGG           |
| Senescence and Autophagy in Cancer                                                                                    | 106        | 5 (4.7%)   | 0.00631 | 0.609   | Wikipathways   |
| Aspartate and asparagine metabolism                                                                                   | 12         | 2 (16.7%)  | 0.0074  | 0.609   | Reactome       |
| Regulation of signaling by NODAL                                                                                      | 12         | 2 (16.7%)  | 0.0074  | 0.609   | Reactome       |
| Internalization of ErbB1                                                                                              | 39         | 3 (7.7%)   | 0.00896 | 0.609   | PID            |
| Biosynthesis of the N-glycan precursor (dolichol lipid-linked oligosaccharide, LLO) and transfer to a nascent protein | 77         | 4 (5.2%)   | 0.0103  | 0.609   | Reactome       |
| Biosynthesis of DPAn-3-derived 13-series resolvins                                                                    | 1          | 1 (100.0%) | 0.011   | 0.609   | Reactome       |
| Mtb iron assimilation by chelation                                                                                    | 1          | 1 (100.0%) | 0.011   | 0.609   | Reactome       |
| Latent infection - Other responses of Mtb to phagocytosis                                                             | 1          | 1 (100.0%) | 0.011   | 0.609   | Reactome       |
| Neurodegeneration with brain iron accumulation (NBIA) subtypes pathway                                                | 44         | 3 (6.8%)   | 0.0125  | 0.609   | Wikipathways   |
| Translesion synthesis by REV1                                                                                         | 16         | 2 (12.5%)  | 0.0131  | 0.609   | Reactome       |
| il 4 signaling pathway                                                                                                | 16         | 2 (12.5%)  | 0.0131  | 0.609   | BioCarta       |
| Translesion synthesis by POLK                                                                                         | 17         | 2 (11.8%)  | 0.0147  | 0.609   | Reactome       |
| Translesion synthesis by POLI                                                                                         | 17         | 2 (11.8%)  | 0.0147  | 0.609   | Reactome       |
| Autophagy - animal - Homo sapiens (human)                                                                             | 137        | 5 (3.6%)   | 0.0178  | 0.609   | KEGG           |
| TGF-beta signaling pathway - Homo sapiens (human)                                                                     | 94         | 4 (4.3%)   | 0.0201  | 0.609   | KEGG           |
| lissencephaly gene (lis1) in neuronal migration and development                                                       | 20         | 2 (10.0%)  | 0.0201  | 0.609   | BioCarta       |
| Signaling by NODAL                                                                                                    | 20         | 2 (10.0%)  | 0.0201  | 0.609   | Reactome       |
| Biosynthesis of DPAn-3-derived maresins                                                                               | 2          | 1 (50.0%)  | 0.0219  | 0.609   | Reactome       |
| Biosynthesis of electrophilic ?-3 PUFA oxo-derivatives                                                                | 2          | 1 (50.0%)  | 0.0219  | 0.609   | Reactome       |
| aspirin triggered resovlin E biosynthesis                                                                             | 2          | 1 (50.0%)  | 0.0219  | 0.609   | HumanCyc       |
| aspirin triggered resovlin D biosynthesis                                                                             | 2          | 1 (50.0%)  | 0.0219  | 0.609   | HumanCyc       |
| aspirin-triggered lipoxin biosynthesis                                                                                | 2          | 1 (50.0%)  | 0.0219  | 0.609   | HumanCyc       |
| Biosynthesis of DPAn-3-derived protectins and resolvins                                                               | 2          | 1 (50.0%)  | 0.0219  | 0.609   | Reactome       |
| resovlin D biosynthesis                                                                                               | 2          | 1 (50.0%)  | 0.0219  | 0.609   | HumanCyc       |
| estradiol biosynthesis II                                                                                             | 2          | 1 (50.0%)  | 0.0219  | 0.609   | HumanCyc       |
| NAD phosphorylation and dephosphorylation                                                                             | 2          | 1 (50.0%)  | 0.0219  | 0.609   | HumanCyc       |
| PAOs oxidise polyamines to amines                                                                                     | 2          | 1 (50.0%)  | 0.0219  | 0.609   | Reactome       |
| Negative regulation of MET activity                                                                                   | 21         | 2 (9.5%)   | 0.0221  | 0.609   | Reactome       |
| Sphingosine 1-phosphate (S1P) pathway                                                                                 | 21         | 2 (9.5%)   | 0.0221  | 0.609   | PID            |
| Arachidonic acid metabolism                                                                                           | 98         | 4 (4.1%)   | 0.023   | 0.609   | EHMN           |
| Nanoparticle triggered autophagic cell death                                                                          | 22         | 2 (9.1%)   | 0.0241  | 0.609   | Wikipathways   |
| Inositol Metabolism                                                                                                   | 22         | 2 (9.1%)   | 0.0241  | 0.609   | SMPDB          |
| ctcf: first multivalent nuclear factor                                                                                | 23         | 2 (8.7%)   | 0.0262  | 0.609   | BioCarta       |
| GPCRs, Class B Secretin-like                                                                                          | 23         | 2 (8.7%)   | 0.0262  | 0.609   | Wikipathways   |
| Phosphatidylinositol Phosphate Metabolism                                                                             | 23         | 2 (8.7%)   | 0.0262  | 0.609   | SMPDB          |
| Joubert syndrome                                                                                                      | 23         | 2 (8.7%)   | 0.0262  | 0.609   | SMPDB          |
| mTOR signaling pathway - Homo sapiens (human)                                                                         | 155        | 5 (3.2%)   | 0.0278  | 0.609   | KEGG           |
| G-protein activation                                                                                                  | 24         | 2 (8.3%)   | 0.0284  | 0.609   | Reactome       |
| ADP signalling through P2Y purinoceptor 1                                                                             | 24         | 2 (8.3%)   | 0.0284  | 0.609   | Reactome       |
| Thromboxane signalling through TP receptor                                                                            | 24         | 2 (8.3%)   | 0.0284  | 0.609   | Reactome       |
| Relationship between inflammation, COX-2 and EGFR                                                                     | 25         | 2 (8.0%)   | 0.0306  | 0.609   | Wikipathways   |
| skeletal muscle hypertrophy is regulated via akt-mtor pathway                                                         | 25         | 2 (8.0%)   | 0.0306  | 0.609   | BioCarta       |
| regulation of eif-4e and p70s6 kinase                                                                                 | 25         | 2 (8.0%)   | 0.0306  | 0.609   | BioCarta       |
| mtor signaling pathway                                                                                                | 25         | 2 (8.0%)   | 0.0306  | 0.609   | BioCarta       |
| Ribosome biogenesis in eukaryotes - Homo sapiens (human)                                                              | 110        | 4 (3.7%)   | 0.0314  | 0.609   | KEGG           |
| Synthesis of substrates in N-glycan biosynthesis                                                                      | 63         | 3 (4.8%)   | 0.0322  | 0.609   | Reactome       |
| Biosynthesis of aspirin-triggered D-series resolvins                                                                  | 3          | 1 (33.3%)  | 0.0327  | 0.609   | Reactome       |
| lipoxin biosynthesis                                                                                                  | 3          | 1 (33.3%)  | 0.0327  | 0.609   | HumanCyc       |
| Integration of viral DNA into host genomic DNA                                                                        | 3          | 1 (33.3%)  | 0.0327  | 0.609   | Reactome       |
| Autointegration results in viral DNA circles                                                                          | 3          | 1 (33.3%)  | 0.0327  | 0.609   | Reactome       |
| dolichol and dolichyl phosphate biosynthesis                                                                          | 3          | 1 (33.3%)  | 0.0327  | 0.609   | HumanCyc       |
| Inositol transporters                                                                                                 | 3          | 1 (33.3%)  | 0.0327  | 0.609   | Reactome       |
| Interconversion of polyamines                                                                                         | 3          | 1 (33.3%)  | 0.0327  | 0.609   | Reactome       |
| Follicle Stimulating Hormone (FSH) signaling pathway                                                                  | 27         | 2 (7.4%)   | 0.0353  | 0.609   | Wikipathways   |
| Regulation of insulin secretion                                                                                       | 67         | 3 (4.5%)   | 0.0376  | 0.609   | Reactome       |
| mucin core 1 and core 2 O -glycosylation                                                                              | 29         | 2 (6.9%)   | 0.0403  | 0.609   | HumanCyc       |
| Molecules associated with elastic fibres                                                                              | 30         | 2 (6.7%)   | 0.0429  | 0.609   | Reactome       |
| Autophagy                                                                                                             | 30         | 2 (6.7%)   | 0.0429  | 0.609   | Wikipathways   |
| Biosynthesis of E-series 18(R)-resolvins                                                                              | 4          | 1 (25.0%)  | 0.0433  | 0.609   | Reactome       |
| Biosynthesis of DPAn-3 SPMs                                                                                           | 4          | 1 (25.0%)  | 0.0433  | 0.609   | Reactome       |
| Biosynthesis of DPA-derived SPMs                                                                                      | 4          | 1 (25.0%)  | 0.0433  | 0.609   | Reactome       |
| Biosynthesis of D-series resolvins                                                                                    | 4          | 1 (25.0%)  | 0.0433  | 0.609   | Reactome       |
| ATP sensitive Potassium channels                                                                                      | 4          | 1 (25.0%)  | 0.0433  | 0.609   | Reactome       |
| Amine Oxidase reactions                                                                                               | 4          | 1 (25.0%)  | 0.0433  | 0.609   | Reactome       |
| Metabolism of steroid hormones                                                                                        | 31         | 2 (6.5%)   | 0.0455  | 0.609   | Reactome       |

|                                                                   |    |          |        |       |                              |
|-------------------------------------------------------------------|----|----------|--------|-------|------------------------------|
| Thrombin signalling through proteinase activated receptors (PARs) | 32 | 2 (6.2%) | 0.0482 | 0.609 | <a href="#">Reactome</a>     |
| Signal amplification                                              | 32 | 2 (6.2%) | 0.0482 | 0.609 | <a href="#">Reactome</a>     |
| 16p11.2 distal deletion syndrome                                  | 32 | 2 (6.2%) | 0.0482 | 0.609 | <a href="#">Wikipathways</a> |

## Prediabetes

| pathway name                                                           | candidates |            | p-value  | q-value | pathway source |
|------------------------------------------------------------------------|------------|------------|----------|---------|----------------|
|                                                                        | set size   | contained  |          |         |                |
| G beta:gamma signalling through PLC beta                               | 20         | 2 (10.0%)  | 0.000723 | 0.143   | Reactome       |
| Presynaptic function of Kainate receptors                              | 21         | 2 (9.5%)   | 0.000798 | 0.143   | Reactome       |
| Beta-catenin independent WNT signaling                                 | 94         | 3 (3.2%)   | 0.000859 | 0.143   | Reactome       |
| Serotonergic synapse - Homo sapiens (human)                            | 115        | 3 (2.7%)   | 0.00146  | 0.143   | KEGG           |
| Wnt signaling                                                          | 114        | 3 (2.6%)   | 0.0015   | 0.143   | Wikipathways   |
| Deactivation of the beta-catenin transactivating complex               | 30         | 2 (6.7%)   | 0.00163  | 0.143   | Reactome       |
| G-protein beta:gamma signalling                                        | 32         | 2 (6.2%)   | 0.00186  | 0.143   | Reactome       |
| Activation of kainate receptors upon glutamate binding                 | 32         | 2 (6.2%)   | 0.00186  | 0.143   | Reactome       |
| Biosynthesis of DPAn-3-derived 13-series resolvins                     | 1          | 1 (100.0%) | 0.00201  | 0.143   | Reactome       |
| Signaling by WNT                                                       | 282        | 4 (1.4%)   | 0.00225  | 0.143   | Reactome       |
| Degradation of beta-catenin by the destruction complex                 | 38         | 2 (5.3%)   | 0.00262  | 0.143   | Reactome       |
| Inositol phosphate metabolism                                          | 41         | 2 (4.9%)   | 0.00304  | 0.143   | INOH           |
| Metabolism                                                             | 1954       | 10 (0.5%)  | 0.00325  | 0.143   | Reactome       |
| Biosynthesis of DPAn-3-derived maresins                                | 2          | 1 (50.0%)  | 0.00402  | 0.143   | Reactome       |
| Biosynthesis of electrophilic ?-3 PUFA oxo-derivatives                 | 2          | 1 (50.0%)  | 0.00402  | 0.143   | Reactome       |
| aspirin triggered resolvin E biosynthesis                              | 2          | 1 (50.0%)  | 0.00402  | 0.143   | HumanCyc       |
| aspirin triggered resolvin D biosynthesis                              | 2          | 1 (50.0%)  | 0.00402  | 0.143   | HumanCyc       |
| aspirin-triggered lipoxin biosynthesis                                 | 2          | 1 (50.0%)  | 0.00402  | 0.143   | HumanCyc       |
| Biosynthesis of DPAn-3-derived protectins and resolvins                | 2          | 1 (50.0%)  | 0.00402  | 0.143   | Reactome       |
| resolvin D biosynthesis                                                | 2          | 1 (50.0%)  | 0.00402  | 0.143   | HumanCyc       |
| NOTCH1 Intracellular Domain Regulates Transcription                    | 48         | 2 (4.2%)   | 0.00414  | 0.143   | Reactome       |
| Wnt signaling pathway - Homo sapiens (human)                           | 166        | 3 (1.8%)   | 0.00436  | 0.143   | KEGG           |
| Inositol phosphate metabolism                                          | 51         | 2 (3.9%)   | 0.00467  | 0.143   | Reactome       |
| Ca2+ pathway                                                           | 55         | 2 (3.6%)   | 0.00541  | 0.143   | Reactome       |
| Biosynthesis of aspirin-triggered D-series resolvins                   | 3          | 1 (33.3%)  | 0.00602  | 0.143   | Reactome       |
| lipoxin biosynthesis                                                   | 3          | 1 (33.3%)  | 0.00602  | 0.143   | HumanCyc       |
| Toxicity of botulinum toxin type E (botE)                              | 3          | 1 (33.3%)  | 0.00602  | 0.143   | Reactome       |
| Kaposi sarcoma-associated herpesvirus infection - Homo sapiens (human) | 193        | 3 (1.6%)   | 0.00662  | 0.143   | KEGG           |
| Cytoprotection by HMOX1                                                | 65         | 2 (3.1%)   | 0.00748  | 0.143   | Reactome       |
| Regulation of insulin secretion                                        | 67         | 2 (3.0%)   | 0.00794  | 0.143   | Reactome       |
| Biosynthesis of E-series 18(R)-resolvins                               | 4          | 1 (25.0%)  | 0.00802  | 0.143   | Reactome       |
| Biosynthesis of DPAn-3 SPMs                                            | 4          | 1 (25.0%)  | 0.00802  | 0.143   | Reactome       |
| Biosynthesis of DPA-derived SPMs                                       | 4          | 1 (25.0%)  | 0.00802  | 0.143   | Reactome       |
| Biosynthesis of D-series resolvins                                     | 4          | 1 (25.0%)  | 0.00802  | 0.143   | Reactome       |
| Toxicity of botulinum toxin type A (botA)                              | 4          | 1 (25.0%)  | 0.00802  | 0.143   | Reactome       |
| Inositol phosphate metabolism - Homo sapiens (human)                   | 73         | 2 (2.7%)   | 0.00936  | 0.143   | KEGG           |
| Signaling by NOTCH1                                                    | 74         | 2 (2.7%)   | 0.00961  | 0.143   | Reactome       |
| Biosynthesis of E-series 18(S)-resolvins                               | 5          | 1 (20.0%)  | 0.01     | 0.143   | Reactome       |
| creatine-phosphate biosynthesis                                        | 5          | 1 (20.0%)  | 0.01     | 0.143   | HumanCyc       |
| lactate fermentation (reoxidation of cytosolic NADH)                   | 5          | 1 (20.0%)  | 0.01     | 0.143   | HumanCyc       |
| Toxicity of botulinum toxin type D (botD)                              | 5          | 1 (20.0%)  | 0.01     | 0.143   | Reactome       |
| Toxicity of botulinum toxin type F (botF)                              | 5          | 1 (20.0%)  | 0.01     | 0.143   | Reactome       |
| Human cytomegalovirus infection - Homo sapiens (human)                 | 225        | 3 (1.3%)   | 0.0101   | 0.143   | KEGG           |
| Notch                                                                  | 78         | 2 (2.6%)   | 0.0106   | 0.143   | INOH           |
| Synthesis of Lipoxins (LX)                                             | 6          | 1 (16.7%)  | 0.012    | 0.143   | Reactome       |
| Biosynthesis of EPA-derived SPMs                                       | 6          | 1 (16.7%)  | 0.012    | 0.143   | Reactome       |
| leukotriene biosynthesis                                               | 6          | 1 (16.7%)  | 0.012    | 0.143   | HumanCyc       |
| platelet amyloid precursor protein pathway                             | 6          | 1 (16.7%)  | 0.012    | 0.143   | BioCarta       |
| Ubiquitin-dependent degradation of Cyclin D                            | 7          | 1 (14.3%)  | 0.014    | 0.143   | Reactome       |
| Autodegradation of the E3 ubiquitin ligase COP1                        | 7          | 1 (14.3%)  | 0.014    | 0.143   | Reactome       |
| Vpu mediated degradation of CD4                                        | 7          | 1 (14.3%)  | 0.014    | 0.143   | Reactome       |

|                                                                              |              |        |       |                              |
|------------------------------------------------------------------------------|--------------|--------|-------|------------------------------|
| Modulation by Mtb of host immune system                                      | 7 1 (14.3%)  | 0.014  | 0.143 | <a href="#">Reactome</a>     |
| Ubiquitin Mediated Degradation of Phosphorylated Cdc25A                      | 7 1 (14.3%)  | 0.014  | 0.143 | <a href="#">Reactome</a>     |
| p53-Independent DNA Damage Response                                          | 7 1 (14.3%)  | 0.014  | 0.143 | <a href="#">Reactome</a>     |
| p53-Independent G1/S DNA damage checkpoint                                   | 7 1 (14.3%)  | 0.014  | 0.143 | <a href="#">Reactome</a>     |
| Opioid Signalling                                                            | 91 2 (2.2%)  | 0.0143 | 0.143 | <a href="#">Reactome</a>     |
| Integration of energy metabolism                                             | 91 2 (2.2%)  | 0.0143 | 0.143 | <a href="#">Reactome</a>     |
| Class B/2 (Secretin family receptors)                                        | 91 2 (2.2%)  | 0.0143 | 0.143 | <a href="#">Reactome</a>     |
| Regulation of TP53 Activity through Phosphorylation                          | 93 2 (2.2%)  | 0.0149 | 0.143 | <a href="#">Reactome</a>     |
| Biosynthesis of maresins                                                     | 8 1 (12.5%)  | 0.016  | 0.143 | <a href="#">Reactome</a>     |
| Fatty Acids bound to GPR40 (FFAR1) regulate insulin secretion                | 8 1 (12.5%)  | 0.016  | 0.143 | <a href="#">Reactome</a>     |
| Regulation of PTEN localization                                              | 8 1 (12.5%)  | 0.016  | 0.143 | <a href="#">Reactome</a>     |
| InlA-mediated entry of Listeria monocytogenes into host cells                | 8 1 (12.5%)  | 0.016  | 0.143 | <a href="#">Reactome</a>     |
| Circadian entrainment - Homo sapiens (human)                                 | 97 2 (2.1%)  | 0.0161 | 0.143 | <a href="#">KEGG</a>         |
| Cellular response to chemical stress                                         | 99 2 (2.0%)  | 0.0167 | 0.143 | <a href="#">Reactome</a>     |
| UCH proteinases                                                              | 102 2 (2.0%) | 0.0177 | 0.143 | <a href="#">Reactome</a>     |
| Synthesis of 5-ecosatetraenoic acids                                         | 9 1 (11.1%)  | 0.0179 | 0.143 | <a href="#">Reactome</a>     |
| PTK6 Regulates RTKs and Their Effectors AKT1 and DOK1                        | 9 1 (11.1%)  | 0.0179 | 0.143 | <a href="#">Reactome</a>     |
| Downregulation of ERBB4 signaling                                            | 9 1 (11.1%)  | 0.0179 | 0.143 | <a href="#">Reactome</a>     |
| Prevention of phagosomal-lysosomal fusion                                    | 9 1 (11.1%)  | 0.0179 | 0.143 | <a href="#">Reactome</a>     |
| ROS sensing by NFE2L2                                                        | 9 1 (11.1%)  | 0.0179 | 0.143 | <a href="#">Reactome</a>     |
| MicroRNAs in cardiomyocyte hypertrophy                                       | 104 2 (1.9%) | 0.0184 | 0.143 | <a href="#">Wikipathways</a> |
| Glucagon signaling pathway - Homo sapiens (human)                            | 107 2 (1.9%) | 0.0194 | 0.143 | <a href="#">KEGG</a>         |
| Calcitonin-like ligand receptors                                             | 10 1 (10.0%) | 0.0199 | 0.143 | <a href="#">Reactome</a>     |
| Acetylcholine regulates insulin secretion                                    | 10 1 (10.0%) | 0.0199 | 0.143 | <a href="#">Reactome</a>     |
| Stabilization of p53                                                         | 10 1 (10.0%) | 0.0199 | 0.143 | <a href="#">Reactome</a>     |
| SCF-beta-TrCP mediated degradation of Emi1                                   | 10 1 (10.0%) | 0.0199 | 0.143 | <a href="#">Reactome</a>     |
| Vif-mediated degradation of APOBEC3G                                         | 10 1 (10.0%) | 0.0199 | 0.143 | <a href="#">Reactome</a>     |
| FBXL7 down-regulates AURKA during mitotic entry and in early mitosis         | 10 1 (10.0%) | 0.0199 | 0.143 | <a href="#">Reactome</a>     |
| Pexophagy                                                                    | 10 1 (10.0%) | 0.0199 | 0.143 | <a href="#">Reactome</a>     |
| Regulation of RUNX3 expression and activity                                  | 10 1 (10.0%) | 0.0199 | 0.143 | <a href="#">Reactome</a>     |
| Degradation of AXIN                                                          | 10 1 (10.0%) | 0.0199 | 0.143 | <a href="#">Reactome</a>     |
| Neurotoxicity of clostridium toxins                                          | 10 1 (10.0%) | 0.0199 | 0.143 | <a href="#">Reactome</a>     |
| Negative regulation of activity of TFAP2 (AP-2) family transcription factors | 10 1 (10.0%) | 0.0199 | 0.143 | <a href="#">Reactome</a>     |
| Cholinergic synapse - Homo sapiens (human)                                   | 113 2 (1.8%) | 0.0215 | 0.143 | <a href="#">KEGG</a>         |
| Glutamatergic synapse - Homo sapiens (human)                                 | 114 2 (1.8%) | 0.0218 | 0.143 | <a href="#">KEGG</a>         |
| Creatine metabolism                                                          | 11 1 (9.1%)  | 0.0219 | 0.143 | <a href="#">Reactome</a>     |
| Dissolution of Fibrin Clot                                                   | 11 1 (9.1%)  | 0.0219 | 0.143 | <a href="#">Reactome</a>     |
| Free fatty acids regulate insulin secretion                                  | 11 1 (9.1%)  | 0.0219 | 0.143 | <a href="#">Reactome</a>     |
| Hh mutants are degraded by ERAD                                              | 11 1 (9.1%)  | 0.0219 | 0.143 | <a href="#">Reactome</a>     |
| Hh mutants abrogate ligand secretion                                         | 11 1 (9.1%)  | 0.0219 | 0.143 | <a href="#">Reactome</a>     |
| Regulation of BACH1 activity                                                 | 11 1 (9.1%)  | 0.0219 | 0.143 | <a href="#">Reactome</a>     |
| TGF-beta super family signaling pathway canonical                            | 115 2 (1.7%) | 0.0222 | 0.143 | <a href="#">INOH</a>         |
| Josephin domain DUBs                                                         | 12 1 (8.3%)  | 0.0239 | 0.143 | <a href="#">Reactome</a>     |
| Negative regulation of NOTCH4 signaling                                      | 12 1 (8.3%)  | 0.0239 | 0.143 | <a href="#">Reactome</a>     |
| Degradation of DVL                                                           | 12 1 (8.3%)  | 0.0239 | 0.143 | <a href="#">Reactome</a>     |
| Aspartate and asparagine metabolism                                          | 12 1 (8.3%)  | 0.0239 | 0.143 | <a href="#">Reactome</a>     |
| Wnt Mammals                                                                  | 120 2 (1.7%) | 0.024  | 0.143 | <a href="#">INOH</a>         |
| Wnt Canonical                                                                | 120 2 (1.7%) | 0.024  | 0.143 | <a href="#">INOH</a>         |
| Osteopontin Signaling                                                        | 13 1 (7.7%)  | 0.0258 | 0.143 | <a href="#">Wikipathways</a> |
| Downregulation of ERBB2:ERBB3 signaling                                      | 13 1 (7.7%)  | 0.0258 | 0.143 | <a href="#">Reactome</a>     |
| NF-kB is activated and signals survival                                      | 13 1 (7.7%)  | 0.0258 | 0.143 | <a href="#">Reactome</a>     |
| Suppression of phagosomal maturation                                         | 13 1 (7.7%)  | 0.0258 | 0.143 | <a href="#">Reactome</a>     |
| Relaxin signaling pathway - Homo sapiens (human)                             | 129 2 (1.6%) | 0.0275 | 0.143 | <a href="#">KEGG</a>         |
| fibrinolysis pathway                                                         | 14 1 (7.1%)  | 0.0278 | 0.143 | <a href="#">BioCarta</a>     |

|                                                                           |              |        |       |                              |
|---------------------------------------------------------------------------|--------------|--------|-------|------------------------------|
| Repression of WNT target genes                                            | 14 1 (7.1%)  | 0.0278 | 0.143 | <a href="#">Reactome</a>     |
| Membrane binding and targeting of GAG proteins                            | 14 1 (7.1%)  | 0.0278 | 0.143 | <a href="#">Reactome</a>     |
| Synthesis And Processing Of GAG, GAGPOL Polyproteins                      | 14 1 (7.1%)  | 0.0278 | 0.143 | <a href="#">Reactome</a>     |
| CDT1 association with the CDC6:ORC:origin complex                         | 14 1 (7.1%)  | 0.0278 | 0.143 | <a href="#">Reactome</a>     |
| Synthesis of IP2, IP, and Ins in the cytosol                              | 14 1 (7.1%)  | 0.0278 | 0.143 | <a href="#">Reactome</a>     |
| ADORA2B mediated anti-inflammatory cytokines production                   | 132 2 (1.5%) | 0.0287 | 0.143 | <a href="#">Reactome</a>     |
| Dopaminergic synapse - Homo sapiens (human)                               | 132 2 (1.5%) | 0.0287 | 0.143 | <a href="#">KEGG</a>         |
| Vascular smooth muscle contraction - Homo sapiens (human)                 | 133 2 (1.5%) | 0.0291 | 0.143 | <a href="#">KEGG</a>         |
| PAR4-mediated thrombin signaling events                                   | 15 1 (6.7%)  | 0.0297 | 0.143 | <a href="#">PID</a>          |
| GPR40 Pathway                                                             | 15 1 (6.7%)  | 0.0297 | 0.143 | <a href="#">Wikipathways</a> |
| Degradation of GLI2 by the proteasome                                     | 15 1 (6.7%)  | 0.0297 | 0.143 | <a href="#">Reactome</a>     |
| GLI3 is processed to GLI3R by the proteasome                              | 15 1 (6.7%)  | 0.0297 | 0.143 | <a href="#">Reactome</a>     |
| Constitutive Signaling by NOTCH1 HD Domain Mutants                        | 15 1 (6.7%)  | 0.0297 | 0.143 | <a href="#">Reactome</a>     |
| Signaling by NOTCH1 HD Domain Mutants in Cancer                           | 15 1 (6.7%)  | 0.0297 | 0.143 | <a href="#">Reactome</a>     |
| Spry regulation of FGF signaling                                          | 15 1 (6.7%)  | 0.0297 | 0.143 | <a href="#">Reactome</a>     |
| InlB-mediated entry of Listeria monocytogenes into host cell              | 15 1 (6.7%)  | 0.0297 | 0.143 | <a href="#">Reactome</a>     |
| Degradation of GLI1 by the proteasome                                     | 15 1 (6.7%)  | 0.0297 | 0.143 | <a href="#">Reactome</a>     |
| Regulation of innate immune responses to cytosolic DNA                    | 15 1 (6.7%)  | 0.0297 | 0.143 | <a href="#">Reactome</a>     |
| EPHA-mediated growth cone collapse                                        | 15 1 (6.7%)  | 0.0297 | 0.143 | <a href="#">Reactome</a>     |
| Metabolism of amino acids and derivatives                                 | 339 3 (0.9%) | 0.0298 | 0.143 | <a href="#">Reactome</a>     |
| Apelin signaling pathway - Homo sapiens (human)                           | 137 2 (1.5%) | 0.0307 | 0.143 | <a href="#">KEGG</a>         |
| Late endosomal microautophagy                                             | 16 1 (6.2%)  | 0.0317 | 0.143 | <a href="#">Reactome</a>     |
| p75NTR signals via NF-kB                                                  | 16 1 (6.2%)  | 0.0317 | 0.143 | <a href="#">Reactome</a>     |
| Translesion synthesis by REV1                                             | 16 1 (6.2%)  | 0.0317 | 0.143 | <a href="#">Reactome</a>     |
| MAP3K8 (TPL2)-dependent MAPK1/3 activation                                | 16 1 (6.2%)  | 0.0317 | 0.143 | <a href="#">Reactome</a>     |
| NRIF signals cell death from the nucleus                                  | 16 1 (6.2%)  | 0.0317 | 0.143 | <a href="#">Reactome</a>     |
| Defective CFTR causes cystic fibrosis                                     | 16 1 (6.2%)  | 0.0317 | 0.143 | <a href="#">Reactome</a>     |
| RHO GTPases activate CIT                                                  | 16 1 (6.2%)  | 0.0317 | 0.143 | <a href="#">Reactome</a>     |
| G alpha (s) signalling events                                             | 143 2 (1.4%) | 0.0332 | 0.143 | <a href="#">Reactome</a>     |
| Biosynthesis of DHA-derived SPMs                                          | 17 1 (5.9%)  | 0.0336 | 0.143 | <a href="#">Reactome</a>     |
| Beta5 beta6 beta7 and beta8 integrin cell surface interactions            | 17 1 (5.9%)  | 0.0336 | 0.143 | <a href="#">PID</a>          |
| TGF-beta receptor signaling in EMT (epithelial to mesenchymal transition) | 17 1 (5.9%)  | 0.0336 | 0.143 | <a href="#">Reactome</a>     |
| Translesion synthesis by POLK                                             | 17 1 (5.9%)  | 0.0336 | 0.143 | <a href="#">Reactome</a>     |
| Translesion synthesis by POLI                                             | 17 1 (5.9%)  | 0.0336 | 0.143 | <a href="#">Reactome</a>     |
| Regulation of HMOX1 expression and activity                               | 17 1 (5.9%)  | 0.0336 | 0.143 | <a href="#">Reactome</a>     |
| ABC transporter disorders                                                 | 17 1 (5.9%)  | 0.0336 | 0.143 | <a href="#">Reactome</a>     |
| Disorders of transmembrane transporters                                   | 17 1 (5.9%)  | 0.0336 | 0.143 | <a href="#">Reactome</a>     |
| Assembly Of The HIV Virion                                                | 17 1 (5.9%)  | 0.0336 | 0.143 | <a href="#">Reactome</a>     |
| Retrograde endocannabinoid signaling - Homo sapiens (human)               | 148 2 (1.4%) | 0.0353 | 0.143 | <a href="#">KEGG</a>         |
| G beta:gamma signalling through BTK                                       | 18 1 (5.6%)  | 0.0356 | 0.143 | <a href="#">Reactome</a>     |
| SCF(Skp2)-mediated degradation of p27/p21                                 | 18 1 (5.6%)  | 0.0356 | 0.143 | <a href="#">Reactome</a>     |
| RHO GTPases Activate ROCKs                                                | 18 1 (5.6%)  | 0.0356 | 0.143 | <a href="#">Reactome</a>     |
| Biosynthesis of specialized proresolving mediators (SPMs)                 | 19 1 (5.3%)  | 0.0375 | 0.143 | <a href="#">Reactome</a>     |
| Prostacyclin signalling through prostacyclin receptor                     | 19 1 (5.3%)  | 0.0375 | 0.143 | <a href="#">Reactome</a>     |
| Listeria monocytogenes entry into host cells                              | 19 1 (5.3%)  | 0.0375 | 0.143 | <a href="#">Reactome</a>     |
| p53-Dependent G1 DNA Damage Response                                      | 19 1 (5.3%)  | 0.0375 | 0.143 | <a href="#">Reactome</a>     |
| p53-Dependent G1/S DNA damage checkpoint                                  | 19 1 (5.3%)  | 0.0375 | 0.143 | <a href="#">Reactome</a>     |
| Translesion Synthesis by POLH                                             | 19 1 (5.3%)  | 0.0375 | 0.143 | <a href="#">Reactome</a>     |
| ER Quality Control Compartment (ERQC)                                     | 19 1 (5.3%)  | 0.0375 | 0.143 | <a href="#">Reactome</a>     |
| Asymmetric localization of PCP proteins                                   | 19 1 (5.3%)  | 0.0375 | 0.143 | <a href="#">Reactome</a>     |
| Oxytocin signaling pathway - Homo sapiens (human)                         | 154 2 (1.3%) | 0.038  | 0.143 | <a href="#">KEGG</a>         |
| Hyperornithinemia with gyrate atrophy (HOGA)                              | 20 1 (5.0%)  | 0.0395 | 0.143 | <a href="#">SMPDB</a>        |
| Creatine deficiency, guanidinoacetate methyltransferase deficiency        | 20 1 (5.0%)  | 0.0395 | 0.143 | <a href="#">SMPDB</a>        |
| L-arginine:glycine amidinotransferase deficiency                          | 20 1 (5.0%)  | 0.0395 | 0.143 | <a href="#">SMPDB</a>        |

|                                                                          |              |        |       |              |
|--------------------------------------------------------------------------|--------------|--------|-------|--------------|
| Hyperornithinemia-hyperammonemia-homocitrullinuria [HHH-syndrome]        | 20 1 (5.0%)  | 0.0395 | 0.143 | SMPDB        |
| Guanidinoacetate Methyltransferase Deficiency (GAMT Deficiency)          | 20 1 (5.0%)  | 0.0395 | 0.143 | SMPDB        |
| Prolinemia Type II                                                       | 20 1 (5.0%)  | 0.0395 | 0.143 | SMPDB        |
| Prolidase Deficiency (PD)                                                | 20 1 (5.0%)  | 0.0395 | 0.143 | SMPDB        |
| Arginine and Proline Metabolism                                          | 20 1 (5.0%)  | 0.0395 | 0.143 | SMPDB        |
| Hyperprolinemia Type I                                                   | 20 1 (5.0%)  | 0.0395 | 0.143 | SMPDB        |
| Hyperprolinemia Type II                                                  | 20 1 (5.0%)  | 0.0395 | 0.143 | SMPDB        |
| Ornithine Aminotransferase Deficiency (OAT Deficiency)                   | 20 1 (5.0%)  | 0.0395 | 0.143 | SMPDB        |
| Arginine: Glycine Amidinotransferase Deficiency (AGAT Deficiency)        | 20 1 (5.0%)  | 0.0395 | 0.143 | SMPDB        |
| G beta:gamma signalling through CDC42                                    | 20 1 (5.0%)  | 0.0395 | 0.143 | Reactome     |
| S1P1 pathway                                                             | 20 1 (5.0%)  | 0.0395 | 0.143 | PID          |
| D- <i>myo</i> -inositol-5-phosphate metabolism                           | 20 1 (5.0%)  | 0.0395 | 0.143 | HumanCyc     |
| Hedgehog ligand biogenesis                                               | 20 1 (5.0%)  | 0.0395 | 0.143 | Reactome     |
| TICAM1, RIP1-mediated IKK complex recruitment                            | 20 1 (5.0%)  | 0.0395 | 0.143 | Reactome     |
| Regulation of expression of SLITs and ROBOs                              | 20 1 (5.0%)  | 0.0395 | 0.143 | Reactome     |
| Regulation of TP53 Activity through Methylation                          | 20 1 (5.0%)  | 0.0395 | 0.143 | Reactome     |
| Assembly of the pre-replicative complex                                  | 20 1 (5.0%)  | 0.0395 | 0.143 | Reactome     |
| Regulation of lipid metabolism by PPARalpha                              | 20 1 (5.0%)  | 0.0395 | 0.143 | Reactome     |
| Sema4D induced cell migration and growth-cone collapse                   | 20 1 (5.0%)  | 0.0395 | 0.143 | Reactome     |
| Ribosome - Homo sapiens (human)                                          | 158 2 (1.3%) | 0.0398 | 0.143 | KEGG         |
| Synthesis of Leukotrienes (LT) and Eoxins (EX)                           | 21 1 (4.8%)  | 0.0414 | 0.143 | Reactome     |
| G1/S DNA Damage Checkpoints                                              | 21 1 (4.8%)  | 0.0414 | 0.143 | Reactome     |
| Negative regulation of MET activity                                      | 21 1 (4.8%)  | 0.0414 | 0.143 | Reactome     |
| Oxygen-dependent proline hydroxylation of Hypoxia-inducible Factor Alpha | 21 1 (4.8%)  | 0.0414 | 0.143 | Reactome     |
| Downregulation of SMAD2/3:SMAD4 transcriptional activity                 | 21 1 (4.8%)  | 0.0414 | 0.143 | Reactome     |
| Regulation of FZD by ubiquitination                                      | 21 1 (4.8%)  | 0.0414 | 0.143 | Reactome     |
| Regulation of TP53 Activity                                              | 163 2 (1.2%) | 0.0421 | 0.143 | Reactome     |
| Chemokine signaling pathway                                              | 165 2 (1.2%) | 0.0431 | 0.143 | Wikipathways |
| Protein localization                                                     | 165 2 (1.2%) | 0.0431 | 0.143 | Reactome     |
| ADP signalling through P2Y purinoceptor 12                               | 22 1 (4.5%)  | 0.0433 | 0.143 | Reactome     |
| PKC-gamma calcium signaling pathway in ataxia                            | 22 1 (4.5%)  | 0.0433 | 0.143 | Wikipathways |
| Chaperone Mediated Autophagy                                             | 22 1 (4.5%)  | 0.0433 | 0.143 | Reactome     |
| NOTCH2 Activation and Transmission of Signal to the Nucleus              | 22 1 (4.5%)  | 0.0433 | 0.143 | Reactome     |
| PINK1-PRKN Mediated Mitophagy                                            | 22 1 (4.5%)  | 0.0433 | 0.143 | Reactome     |
| Inositol Metabolism                                                      | 22 1 (4.5%)  | 0.0433 | 0.143 | SMPDB        |
| cGMP-PKG signaling pathway - Homo sapiens (human)                        | 167 2 (1.2%) | 0.044  | 0.143 | KEGG         |
| eicosanoid metabolism                                                    | 23 1 (4.3%)  | 0.0453 | 0.143 | BioCarta     |
| Prostaglandin Leukotriene metabolism                                     | 23 1 (4.3%)  | 0.0453 | 0.143 | INOH         |
| Eicosanoid Synthesis                                                     | 23 1 (4.3%)  | 0.0453 | 0.143 | Wikipathways |
| Adrenaline,noradrenaline inhibits insulin secretion                      | 23 1 (4.3%)  | 0.0453 | 0.143 | Reactome     |
| Blood Clotting Cascade                                                   | 23 1 (4.3%)  | 0.0453 | 0.143 | Wikipathways |
| Response of Mtb to phagocytosis                                          | 23 1 (4.3%)  | 0.0453 | 0.143 | Reactome     |
| IKK complex recruitment mediated by RIP1                                 | 23 1 (4.3%)  | 0.0453 | 0.143 | Reactome     |
| Cellular response to hypoxia                                             | 23 1 (4.3%)  | 0.0453 | 0.143 | Reactome     |
| Regulation of RAS by GAPs                                                | 23 1 (4.3%)  | 0.0453 | 0.143 | Reactome     |
| Autodegradation of Cdh1 by Cdh1:APC/C                                    | 23 1 (4.3%)  | 0.0453 | 0.143 | Reactome     |
| Uptake and actions of bacterial toxins                                   | 23 1 (4.3%)  | 0.0453 | 0.143 | Reactome     |
| RHO GTPases activate PAKs                                                | 23 1 (4.3%)  | 0.0453 | 0.143 | Reactome     |
| G-protein activation                                                     | 24 1 (4.2%)  | 0.0472 | 0.143 | Reactome     |
| ADP signalling through P2Y purinoceptor 1                                | 24 1 (4.2%)  | 0.0472 | 0.143 | Reactome     |
| Thromboxane signalling through TP receptor                               | 24 1 (4.2%)  | 0.0472 | 0.143 | Reactome     |
| Methionine Cysteine metabolism                                           | 24 1 (4.2%)  | 0.0472 | 0.143 | INOH         |
| Physiological and pathological hypertrophy of the heart                  | 24 1 (4.2%)  | 0.0472 | 0.143 | Wikipathways |
| DNA Damage Recognition in GG-NER                                         | 24 1 (4.2%)  | 0.0472 | 0.143 | Reactome     |

|                                                             |    |          |        |       |                              |
|-------------------------------------------------------------|----|----------|--------|-------|------------------------------|
| Calnexin/calreticulin cycle                                 | 24 | 1 (4.2%) | 0.0472 | 0.143 | <a href="#">Reactome</a>     |
| APC/C:Cdc20 mediated degradation of Securin                 | 24 | 1 (4.2%) | 0.0472 | 0.143 | <a href="#">Reactome</a>     |
| Sema4D in semaphorin signaling                              | 24 | 1 (4.2%) | 0.0472 | 0.143 | <a href="#">Reactome</a>     |
| G beta:gamma signalling through PI3Kgamma                   | 25 | 1 (4.0%) | 0.0491 | 0.143 | <a href="#">Reactome</a>     |
| Propanoate metabolism                                       | 25 | 1 (4.0%) | 0.0491 | 0.143 | <a href="#">INOH</a>         |
| Cancer immunotherapy by PD-1 blockade                       | 25 | 1 (4.0%) | 0.0491 | 0.143 | <a href="#">Wikipathways</a> |
| Signal Transduction of S1P Receptor                         | 25 | 1 (4.0%) | 0.0491 | 0.143 | <a href="#">Wikipathways</a> |
| SMAD2/SMAD3:SMAD4 heterotrimer regulates transcription      | 25 | 1 (4.0%) | 0.0491 | 0.143 | <a href="#">Reactome</a>     |
| NOTCH3 Activation and Transmission of Signal to the Nucleus | 25 | 1 (4.0%) | 0.0491 | 0.143 | <a href="#">Reactome</a>     |
| Regulation of PTEN stability and activity                   | 25 | 1 (4.0%) | 0.0491 | 0.143 | <a href="#">Reactome</a>     |
| APC/C:Cdc20 mediated degradation of Cyclin B                | 25 | 1 (4.0%) | 0.0491 | 0.143 | <a href="#">Reactome</a>     |
| Gap-filling DNA repair synthesis and ligation in GG-NER     | 25 | 1 (4.0%) | 0.0491 | 0.143 | <a href="#">Reactome</a>     |

# T1DM

| pathway name                                                                                                        | candidates |            | p-value  | q-value | pathway source |
|---------------------------------------------------------------------------------------------------------------------|------------|------------|----------|---------|----------------|
|                                                                                                                     | set size   | contained  |          |         |                |
| Oxidative phosphorylation - Homo sapiens (human)                                                                    | 133        | 4 (3.0%)   | 0.000471 | 0.127   | KEGG           |
| Translesion synthesis by REV1                                                                                       | 16         | 2 (12.5%)  | 0.000864 | 0.127   | Reactome       |
| Translesion synthesis by POLK                                                                                       | 17         | 2 (11.8%)  | 0.000978 | 0.127   | Reactome       |
| Translesion synthesis by POLI                                                                                       | 17         | 2 (11.8%)  | 0.000978 | 0.127   | Reactome       |
| Biosynthesis of DPAn-3-derived 13-series resolvins                                                                  | 1          | 1 (100.0%) | 0.00275  | 0.178   | Reactome       |
| ATR signaling pathway                                                                                               | 37         | 2 (5.4%)   | 0.00463  | 0.178   | PID            |
| Translesion synthesis by Y family DNA polymerases bypasses lesions on DNA template                                  | 38         | 2 (5.3%)   | 0.00488  | 0.178   | Reactome       |
| Biosynthesis of DPAn-3-derived maresins                                                                             | 2          | 1 (50.0%)  | 0.0055   | 0.178   | Reactome       |
| Biosynthesis of electrophilic ?-3 PUFA oxo-derivatives                                                              | 2          | 1 (50.0%)  | 0.0055   | 0.178   | Reactome       |
| aspirin triggered resolvins biosynthesis                                                                            | 2          | 1 (50.0%)  | 0.0055   | 0.178   | HumanCyc       |
| aspirin triggered resolvins biosynthesis                                                                            | 2          | 1 (50.0%)  | 0.0055   | 0.178   | HumanCyc       |
| aspirin-triggered lipoxin biosynthesis                                                                              | 2          | 1 (50.0%)  | 0.0055   | 0.178   | HumanCyc       |
| Biosynthesis of DPAn-3-derived protectins and resolvins                                                             | 2          | 1 (50.0%)  | 0.0055   | 0.178   | Reactome       |
| resolvins biosynthesis                                                                                              | 2          | 1 (50.0%)  | 0.0055   | 0.178   | HumanCyc       |
| NAD phosphorylation and dephosphorylation                                                                           | 2          | 1 (50.0%)  | 0.0055   | 0.178   | HumanCyc       |
| PAOs oxidise polyamines to amines                                                                                   | 2          | 1 (50.0%)  | 0.0055   | 0.178   | Reactome       |
| DNA Damage Bypass                                                                                                   | 47         | 2 (4.3%)   | 0.00738  | 0.183   | Reactome       |
| Biosynthesis of aspirin-triggered D-series resolvins                                                                | 3          | 1 (33.3%)  | 0.00824  | 0.183   | Reactome       |
| lipoxin biosynthesis                                                                                                | 3          | 1 (33.3%)  | 0.00824  | 0.183   | HumanCyc       |
| Integration of viral DNA into host genomic DNA                                                                      | 3          | 1 (33.3%)  | 0.00824  | 0.183   | Reactome       |
| Autointegration results in viral DNA circles                                                                        | 3          | 1 (33.3%)  | 0.00824  | 0.183   | Reactome       |
| Interconversion of polyamines                                                                                       | 3          | 1 (33.3%)  | 0.00824  | 0.183   | Reactome       |
| Ovarian steroidogenesis - Homo sapiens (human)                                                                      | 51         | 2 (3.9%)   | 0.00865  | 0.183   | KEGG           |
| The citric acid (TCA) cycle and respiratory electron transport                                                      | 162        | 3 (1.9%)   | 0.00991  | 0.183   | Reactome       |
| Legionellosis - Homo sapiens (human)                                                                                | 57         | 2 (3.5%)   | 0.0107   | 0.183   | KEGG           |
| Biosynthesis of E-series 18(R)-resolvins                                                                            | 4          | 1 (25.0%)  | 0.011    | 0.183   | Reactome       |
| Biosynthesis of DPAn-3 SPMs                                                                                         | 4          | 1 (25.0%)  | 0.011    | 0.183   | Reactome       |
| Biosynthesis of DPA-derived SPMs                                                                                    | 4          | 1 (25.0%)  | 0.011    | 0.183   | Reactome       |
| Biosynthesis of D-series resolvins                                                                                  | 4          | 1 (25.0%)  | 0.011    | 0.183   | Reactome       |
| Interleukin-18 signaling                                                                                            | 4          | 1 (25.0%)  | 0.011    | 0.183   | Reactome       |
| Amine Oxidase reactions                                                                                             | 4          | 1 (25.0%)  | 0.011    | 0.183   | Reactome       |
| Longevity regulating pathway - multiple species - Homo sapiens (human)                                              | 62         | 2 (3.2%)   | 0.0126   | 0.203   | KEGG           |
| Biosynthesis of E-series 18(S)-resolvins                                                                            | 5          | 1 (20.0%)  | 0.0137   | 0.203   | Reactome       |
| Interleukin-1 processing                                                                                            | 5          | 1 (20.0%)  | 0.0137   | 0.203   | Reactome       |
| spermine and spermidine degradation I                                                                               | 5          | 1 (20.0%)  | 0.0137   | 0.203   | HumanCyc       |
| Synthesis of Lipoxins (LX)                                                                                          | 6          | 1 (16.7%)  | 0.0164   | 0.224   | Reactome       |
| Biosynthesis of EPA-derived SPMs                                                                                    | 6          | 1 (16.7%)  | 0.0164   | 0.224   | Reactome       |
| leukotriene biosynthesis                                                                                            | 6          | 1 (16.7%)  | 0.0164   | 0.224   | HumanCyc       |
| p53 signaling pathway - Homo sapiens (human)                                                                        | 73         | 2 (2.7%)   | 0.0172   | 0.228   | KEGG           |
| 2-LTR circle formation                                                                                              | 7          | 1 (14.3%)  | 0.0191   | 0.234   | Reactome       |
| APOBEC3G mediated resistance to HIV-1 infection                                                                     | 7          | 1 (14.3%)  | 0.0191   | 0.234   | Reactome       |
| Biosynthesis of maresins                                                                                            | 8          | 1 (12.5%)  | 0.0218   | 0.234   | Reactome       |
| Axonal growth inhibition (RHOA activation)                                                                          | 8          | 1 (12.5%)  | 0.0218   | 0.234   | Reactome       |
| Glial Cell Differentiation                                                                                          | 8          | 1 (12.5%)  | 0.0218   | 0.234   | Wikipathways   |
| Synthesis of 5-ecosatetraenoic acids                                                                                | 9          | 1 (11.1%)  | 0.0245   | 0.234   | Reactome       |
| Integration of provirus                                                                                             | 9          | 1 (11.1%)  | 0.0245   | 0.234   | Reactome       |
| p75NTR regulates axonogenesis                                                                                       | 9          | 1 (11.1%)  | 0.0245   | 0.234   | Reactome       |
| Respiratory electron transport                                                                                      | 89         | 2 (2.2%)   | 0.0249   | 0.234   | Reactome       |
| Thermogenesis - Homo sapiens (human)                                                                                | 232        | 3 (1.3%)   | 0.0257   | 0.234   | KEGG           |
| Adenylate cyclase activating pathway                                                                                | 10         | 1 (10.0%)  | 0.0272   | 0.234   | Reactome       |
| dolichyl-diphosphooligosaccharide biosynthesis                                                                      | 10         | 1 (10.0%)  | 0.0272   | 0.234   | HumanCyc       |
| Establishment of Sister Chromatid Cohesion                                                                          | 11         | 1 (9.1%)   | 0.0299   | 0.234   | Reactome       |
| Early Phase of HIV Life Cycle                                                                                       | 12         | 1 (8.3%)   | 0.0326   | 0.234   | Reactome       |
| Formation of Senescence-Associated Heterochromatin Foci (SAHF)                                                      | 12         | 1 (8.3%)   | 0.0326   | 0.234   | Reactome       |
| Purine ribonucleoside monophosphate biosynthesis                                                                    | 12         | 1 (8.3%)   | 0.0326   | 0.234   | Reactome       |
| Electron Transport Chain (OXPHOS system in mitochondria)                                                            | 103        | 2 (1.9%)   | 0.0326   | 0.234   | Wikipathways   |
| S Phase                                                                                                             | 104        | 2 (1.9%)   | 0.0332   | 0.234   | Reactome       |
| Metabolism of polyamines                                                                                            | 13         | 1 (7.7%)   | 0.0352   | 0.234   | Reactome       |
| Adenylate cyclase inhibitory pathway                                                                                | 14         | 1 (7.1%)   | 0.0379   | 0.234   | Reactome       |
| Polymerase switching                                                                                                | 14         | 1 (7.1%)   | 0.0379   | 0.234   | Reactome       |
| Leading Strand Synthesis                                                                                            | 14         | 1 (7.1%)   | 0.0379   | 0.234   | Reactome       |
| Repression of WNT target genes                                                                                      | 14         | 1 (7.1%)   | 0.0379   | 0.234   | Reactome       |
| Nicotinate and Nicotinamide Metabolism                                                                              | 14         | 1 (7.1%)   | 0.0379   | 0.234   | SMPDB          |
| Toxoplasmosis - Homo sapiens (human)                                                                                | 112        | 2 (1.8%)   | 0.038    | 0.234   | KEGG           |
| Respiratory electron transport, ATP synthesis by chemiosmotic coupling, and heat production by uncoupling proteins. | 113        | 2 (1.8%)   | 0.0386   | 0.234   | Reactome       |
| Prion disease - Homo sapiens (human)                                                                                | 273        | 3 (1.1%)   | 0.0388   | 0.234   | KEGG           |
| InlB-mediated entry of Listeria monocytogenes into host cell                                                        | 15         | 1 (6.7%)   | 0.0405   | 0.234   | Reactome       |

|                                                                                             |     |          |        |       |                              |
|---------------------------------------------------------------------------------------------|-----|----------|--------|-------|------------------------------|
| Nucleobase biosynthesis                                                                     | 15  | 1 (6.7%) | 0.0405 | 0.234 | <a href="#">Reactome</a>     |
| Spinal Cord Injury                                                                          | 117 | 2 (1.7%) | 0.0411 | 0.234 | <a href="#">Wikipathways</a> |
| Nonsense Mediated Decay (NMD) enhanced by the Exon Junction Complex (EJC)                   | 117 | 2 (1.7%) | 0.0411 | 0.234 | <a href="#">Reactome</a>     |
| Nonsense-Mediated Decay (NMD)                                                               | 117 | 2 (1.7%) | 0.0411 | 0.234 | <a href="#">Reactome</a>     |
| DNA Repair Pathways Full Network                                                            | 119 | 2 (1.7%) | 0.0424 | 0.234 | <a href="#">Wikipathways</a> |
| LPA4-mediated signaling events                                                              | 16  | 1 (6.2%) | 0.0432 | 0.234 | <b>PID</b>                   |
| il 4 signaling pathway                                                                      | 16  | 1 (6.2%) | 0.0432 | 0.234 | <b>BioCarta</b>              |
| Mitochondrial complex III assembly                                                          | 16  | 1 (6.2%) | 0.0432 | 0.234 | <a href="#">Wikipathways</a> |
| PKA activation in glucagon signalling                                                       | 17  | 1 (5.9%) | 0.0458 | 0.234 | <a href="#">Reactome</a>     |
| PKA activation                                                                              | 17  | 1 (5.9%) | 0.0458 | 0.234 | <a href="#">Reactome</a>     |
| Biosynthesis of DHA-derived SPMs                                                            | 17  | 1 (5.9%) | 0.0458 | 0.234 | <a href="#">Reactome</a>     |
| endocytotic role of ndk phosphins and dynamin                                               | 17  | 1 (5.9%) | 0.0458 | 0.234 | <b>BioCarta</b>              |
| Deregulated CDK5 triggers multiple neurodegenerative pathways in Alzheimer,s disease models | 18  | 1 (5.6%) | 0.0485 | 0.234 | <a href="#">Reactome</a>     |
| Neurodegenerative Diseases                                                                  | 18  | 1 (5.6%) | 0.0485 | 0.234 | <a href="#">Reactome</a>     |

## T2DM\_related\_admission

| pathway name                                                   | candidates |            | p-value  | q-value | pathway source |
|----------------------------------------------------------------|------------|------------|----------|---------|----------------|
|                                                                | set size   | contained  |          |         |                |
| Biosynthesis of DPAn-3-derived maresins                        | 2          | 2 (100.0%) | 7.26E-05 | 0.0808  | Reactome       |
| lipoxin biosynthesis                                           | 3          | 2 (66.7%)  | 0.000217 | 0.12    | HumanCyc       |
| Biosynthesis of DPAn-3 SPMs                                    | 4          | 2 (50.0%)  | 0.000431 | 0.12    | Reactome       |
| Biosynthesis of DPA-derived SPMs                               | 4          | 2 (50.0%)  | 0.000431 | 0.12    | Reactome       |
| Synthesis of Lipoxins (LX)                                     | 6          | 2 (33.3%)  | 0.00107  | 0.237   | Reactome       |
| Arachidonic acid metabolism                                    | 98         | 5 (5.1%)   | 0.00152  | 0.282   | EHMN           |
| Aspartate and asparagine metabolism                            | 12         | 2 (16.7%)  | 0.00453  | 0.341   | Reactome       |
| Mitochondrial complex III assembly                             | 16         | 2 (12.5%)  | 0.00806  | 0.341   | Wikipathways   |
| Synthesis of Hepoxilins (HX) and Trioxilins (TrX)              | 1          | 1 (100.0%) | 0.00856  | 0.341   | Reactome       |
| Biosynthesis of DPAn-3-derived 13-series resolvins             | 1          | 1 (100.0%) | 0.00856  | 0.341   | Reactome       |
| Mtb iron assimilation by chelation                             | 1          | 1 (100.0%) | 0.00856  | 0.341   | Reactome       |
| Latent infection - Other responses of Mtb to phagocytosis      | 1          | 1 (100.0%) | 0.00856  | 0.341   | Reactome       |
| Biosynthesis of DHA-derived SPMs                               | 17         | 2 (11.8%)  | 0.00908  | 0.341   | Reactome       |
| Pyruvate metabolism and Citric Acid (TCA) cycle                | 53         | 3 (5.7%)   | 0.0105   | 0.341   | Reactome       |
| Biosynthesis of specialized proresolving mediators (SPMs)      | 19         | 2 (10.5%)  | 0.0113   | 0.341   | Reactome       |
| The citric acid (TCA) cycle and respiratory electron transport | 162        | 5 (3.1%)   | 0.0127   | 0.341   | Reactome       |
| Metabolism                                                     | 1954       | 26 (1.3%)  | 0.013    | 0.341   | Reactome       |
| Sphingosine 1-phosphate (S1P) pathway                          | 21         | 2 (9.5%)   | 0.0137   | 0.341   | PID            |
| Citric acid cycle (TCA cycle)                                  | 22         | 2 (9.1%)   | 0.015    | 0.341   | Reactome       |
| Inositol Metabolism                                            | 22         | 2 (9.1%)   | 0.015    | 0.341   | SMPDB          |
| Arachidonic acid metabolism - Homo sapiens (human)             | 61         | 3 (4.9%)   | 0.0153   | 0.341   | KEGG           |
| Eicosanoid Synthesis                                           | 23         | 2 (8.7%)   | 0.0163   | 0.341   | Wikipathways   |
| Prostaglandin Leukotriene metabolism                           | 23         | 2 (8.7%)   | 0.0163   | 0.341   | INOH           |
| ctcf: first multivalent nuclear factor                         | 23         | 2 (8.7%)   | 0.0163   | 0.341   | BioCarta       |
| GPCRs, Class B Secretin-like                                   | 23         | 2 (8.7%)   | 0.0163   | 0.341   | Wikipathways   |
| Phosphatidylinositol Phosphate Metabolism                      | 23         | 2 (8.7%)   | 0.0163   | 0.341   | SMPDB          |
| Joubert syndrome                                               | 23         | 2 (8.7%)   | 0.0163   | 0.341   | SMPDB          |
| Pathways affected in adenoid cystic carcinoma                  | 63         | 3 (4.8%)   | 0.0167   | 0.341   | Wikipathways   |
| Biosynthesis of DPAn-6 SPMs                                    | 2          | 1 (50.0%)  | 0.017    | 0.341   | Reactome       |
| Biosynthesis of electrophilic ?-3 PUFA oxo-derivatives         | 2          | 1 (50.0%)  | 0.017    | 0.341   | Reactome       |
| aspirin triggered resolvins E biosynthesis                     | 2          | 1 (50.0%)  | 0.017    | 0.341   | HumanCyc       |
| aspirin triggered resolvins D biosynthesis                     | 2          | 1 (50.0%)  | 0.017    | 0.341   | HumanCyc       |
| aspirin-triggered lipoxin biosynthesis                         | 2          | 1 (50.0%)  | 0.017    | 0.341   | HumanCyc       |
| Biosynthesis of DPAn-3-derived protectins and resolvins        | 2          | 1 (50.0%)  | 0.017    | 0.341   | Reactome       |
| resolvins D biosynthesis                                       | 2          | 1 (50.0%)  | 0.017    | 0.341   | HumanCyc       |
| estradiol biosynthesis II                                      | 2          | 1 (50.0%)  | 0.017    | 0.341   | HumanCyc       |
| NAD phosphorylation and dephosphorylation                      | 2          | 1 (50.0%)  | 0.017    | 0.341   | HumanCyc       |
| PAOs oxidise polyamines to amines                              | 2          | 1 (50.0%)  | 0.017    | 0.341   | Reactome       |
| Relationship between inflammation, COX-2 and EGFR              | 25         | 2 (8.0%)   | 0.0192   | 0.341   | Wikipathways   |
| skeletal muscle hypertrophy is regulated via akt-mTOR pathway  | 25         | 2 (8.0%)   | 0.0192   | 0.341   | BioCarta       |
| regulation of eIF-4e and p70S6 kinase                          | 25         | 2 (8.0%)   | 0.0192   | 0.341   | BioCarta       |
| mTOR signaling pathway                                         | 25         | 2 (8.0%)   | 0.0192   | 0.341   | BioCarta       |
| Follicle Stimulating Hormone (FSH) signaling pathway           | 27         | 2 (7.4%)   | 0.0222   | 0.341   | Wikipathways   |
| p53 signaling pathway - Homo sapiens (human)                   | 73         | 3 (4.1%)   | 0.0246   | 0.341   | KEGG           |
| Eicosanoid metabolism via lipoxygenases (LOX)                  | 29         | 2 (6.9%)   | 0.0254   | 0.341   | Wikipathways   |
| Biosynthesis of aspirin-triggered D-series resolvins           | 3          | 1 (33.3%)  | 0.0255   | 0.341   | Reactome       |
| dolichol and dolichyl phosphate biosynthesis                   | 3          | 1 (33.3%)  | 0.0255   | 0.341   | HumanCyc       |
| Inositol transporters                                          | 3          | 1 (33.3%)  | 0.0255   | 0.341   | Reactome       |
| Interconversion of polyamines                                  | 3          | 1 (33.3%)  | 0.0255   | 0.341   | Reactome       |
| Metabolism of amino acids and derivatives                      | 339        | 7 (2.1%)   | 0.0264   | 0.341   | Reactome       |
| Ketoprofen Action Pathway                                      | 30         | 2 (6.7%)   | 0.027    | 0.341   | SMPDB          |
| Acetylsalicylic Acid Action Pathway                            | 30         | 2 (6.7%)   | 0.027    | 0.341   | SMPDB          |
| Diflunisal Action Pathway                                      | 30         | 2 (6.7%)   | 0.027    | 0.341   | SMPDB          |
| Acetaminophen Action Pathway                                   | 30         | 2 (6.7%)   | 0.027    | 0.341   | SMPDB          |
| Sulindac Action Pathway                                        | 30         | 2 (6.7%)   | 0.027    | 0.341   | SMPDB          |
| Ketorolac Action Pathway                                       | 30         | 2 (6.7%)   | 0.027    | 0.341   | SMPDB          |
| Naproxen Action Pathway                                        | 30         | 2 (6.7%)   | 0.027    | 0.341   | SMPDB          |
| Flurbiprofen Action Pathway                                    | 30         | 2 (6.7%)   | 0.027    | 0.341   | SMPDB          |
| Antrafenine Action Pathway                                     | 30         | 2 (6.7%)   | 0.027    | 0.341   | SMPDB          |
| Trisalicylate-choline Action Pathway                           | 30         | 2 (6.7%)   | 0.027    | 0.341   | SMPDB          |
| Nepafenac Action Pathway                                       | 30         | 2 (6.7%)   | 0.027    | 0.341   | SMPDB          |
| Phenylbutazone Action Pathway                                  | 30         | 2 (6.7%)   | 0.027    | 0.341   | SMPDB          |
| Lornoxicam Action Pathway                                      | 30         | 2 (6.7%)   | 0.027    | 0.341   | SMPDB          |
| Salsalate Action Pathway                                       | 30         | 2 (6.7%)   | 0.027    | 0.341   | SMPDB          |
| Salicylic Acid Action Pathway                                  | 30         | 2 (6.7%)   | 0.027    | 0.341   | SMPDB          |
| Salicylate-sodium Action Pathway                               | 30         | 2 (6.7%)   | 0.027    | 0.341   | SMPDB          |
| Oxaprozin Action Pathway                                       | 30         | 2 (6.7%)   | 0.027    | 0.341   | SMPDB          |

|                                                                                                                       |              |        |       |              |
|-----------------------------------------------------------------------------------------------------------------------|--------------|--------|-------|--------------|
| Nabumetone Action Pathway                                                                                             | 30 2 (6.7%)  | 0.027  | 0.341 | SMPDB        |
| Bromfenac Action Pathway                                                                                              | 30 2 (6.7%)  | 0.027  | 0.341 | SMPDB        |
| Mefenamic Acid Action Pathway                                                                                         | 30 2 (6.7%)  | 0.027  | 0.341 | SMPDB        |
| Piroxicam Action Pathway                                                                                              | 30 2 (6.7%)  | 0.027  | 0.341 | SMPDB        |
| Carprofen Action Pathway                                                                                              | 30 2 (6.7%)  | 0.027  | 0.341 | SMPDB        |
| Fenoprofen Action Pathway                                                                                             | 30 2 (6.7%)  | 0.027  | 0.341 | SMPDB        |
| Antipyrine Action Pathway                                                                                             | 30 2 (6.7%)  | 0.027  | 0.341 | SMPDB        |
| Magnesium salicylate Action Pathway                                                                                   | 30 2 (6.7%)  | 0.027  | 0.341 | SMPDB        |
| Tenoxicam Action Pathway                                                                                              | 30 2 (6.7%)  | 0.027  | 0.341 | SMPDB        |
| Tiaprofenic Acid Action Pathway                                                                                       | 30 2 (6.7%)  | 0.027  | 0.341 | SMPDB        |
| Tolmetin Action Pathway                                                                                               | 30 2 (6.7%)  | 0.027  | 0.341 | SMPDB        |
| Suprofen Action Pathway                                                                                               | 30 2 (6.7%)  | 0.027  | 0.341 | SMPDB        |
| Etodolac Action Pathway                                                                                               | 30 2 (6.7%)  | 0.027  | 0.341 | SMPDB        |
| Rofecoxib Action Pathway                                                                                              | 30 2 (6.7%)  | 0.027  | 0.341 | SMPDB        |
| Diclofenac Action Pathway                                                                                             | 30 2 (6.7%)  | 0.027  | 0.341 | SMPDB        |
| Etoricoxib Action Pathway                                                                                             | 30 2 (6.7%)  | 0.027  | 0.341 | SMPDB        |
| Lumiracoxib Action Pathway                                                                                            | 30 2 (6.7%)  | 0.027  | 0.341 | SMPDB        |
| Valdecoxib Action Pathway                                                                                             | 30 2 (6.7%)  | 0.027  | 0.341 | SMPDB        |
| Meloxicam Action Pathway                                                                                              | 30 2 (6.7%)  | 0.027  | 0.341 | SMPDB        |
| Leukotriene C4 Synthesis Deficiency                                                                                   | 30 2 (6.7%)  | 0.027  | 0.341 | SMPDB        |
| Arachidonic Acid Metabolism                                                                                           | 30 2 (6.7%)  | 0.027  | 0.341 | SMPDB        |
| Oxidative phosphorylation - Homo sapiens (human)                                                                      | 133 4 (3.0%) | 0.0273 | 0.341 | KEGG         |
| Biosynthesis of the N-glycan precursor (dolichol lipid-linked oligosaccharide, LLO) and transfer to a nascent protein | 77 3 (3.9%)  | 0.0283 | 0.347 | Reactome     |
| Indomethacin Action Pathway                                                                                           | 31 2 (6.5%)  | 0.0287 | 0.347 | SMPDB        |
| Metabolism of steroid hormones                                                                                        | 31 2 (6.5%)  | 0.0287 | 0.347 | Reactome     |
| Autophagy - animal - Homo sapiens (human)                                                                             | 137 4 (2.9%) | 0.03   | 0.357 | KEGG         |
| IL-18 signaling pathway                                                                                               | 274 6 (2.2%) | 0.0303 | 0.357 | Wikipathways |
| Autophagy - other - Homo sapiens (human)                                                                              | 32 2 (6.2%)  | 0.0305 | 0.357 | KEGG         |
| Prostaglandin formation from arachidonate                                                                             | 33 2 (6.1%)  | 0.0323 | 0.372 | EHMN         |
| Biosynthesis of E-series 18(R)-resolvins                                                                              | 4 1 (25.0%)  | 0.0338 | 0.372 | Reactome     |
| Biosynthesis of D-series resolvins                                                                                    | 4 1 (25.0%)  | 0.0338 | 0.372 | Reactome     |
| 2-oxoisovalerate decarboxylation to isobutanoyl-CoA                                                                   | 4 1 (25.0%)  | 0.0338 | 0.372 | HumanCyc     |
| Interleukin-18 signaling                                                                                              | 4 1 (25.0%)  | 0.0338 | 0.372 | Reactome     |
| Amine Oxidase reactions                                                                                               | 4 1 (25.0%)  | 0.0338 | 0.372 | Reactome     |
| Nicotinate and nicotinamide metabolism - Homo sapiens (human)                                                         | 35 2 (5.7%)  | 0.036  | 0.388 | KEGG         |
| Overview of leukocyte-intrinsic Hippo pathway functions                                                               | 35 2 (5.7%)  | 0.036  | 0.388 | Wikipathways |
| Celecoxib Action Pathway                                                                                              | 36 2 (5.6%)  | 0.0379 | 0.4   | SMPDB        |
| Factors and pathways affecting insulin-like growth factor (IGF1)-Akt signaling                                        | 36 2 (5.6%)  | 0.0379 | 0.4   | Wikipathways |
| Androgen and estrogen biosynthesis and metabolism                                                                     | 87 3 (3.4%)  | 0.0386 | 0.4   | EHMN         |
| Mitochondrial translation termination                                                                                 | 88 3 (3.4%)  | 0.0397 | 0.4   | Reactome     |
| Androgen receptor signaling pathway                                                                                   | 89 3 (3.4%)  | 0.0408 | 0.4   | Wikipathways |
| TBC/RABGAPs                                                                                                           | 38 2 (5.3%)  | 0.0418 | 0.4   | Reactome     |
| Biosynthesis of E-series 18(S)-resolvins                                                                              | 5 1 (20.0%)  | 0.0421 | 0.4   | Reactome     |
| creatine-phosphate biosynthesis                                                                                       | 5 1 (20.0%)  | 0.0421 | 0.4   | HumanCyc     |
| Estrogen biosynthesis                                                                                                 | 5 1 (20.0%)  | 0.0421 | 0.4   | Reactome     |
| Tyrosine catabolism                                                                                                   | 5 1 (20.0%)  | 0.0421 | 0.4   | Reactome     |
| tyrosine degradation                                                                                                  | 5 1 (20.0%)  | 0.0421 | 0.4   | HumanCyc     |
| Interleukin-1 processing                                                                                              | 5 1 (20.0%)  | 0.0421 | 0.4   | Reactome     |
| spermine and spermidine degradation I                                                                                 | 5 1 (20.0%)  | 0.0421 | 0.4   | HumanCyc     |
| Galactose catabolism                                                                                                  | 5 1 (20.0%)  | 0.0421 | 0.4   | Reactome     |
| mTOR signaling pathway - Homo sapiens (human)                                                                         | 155 4 (2.6%) | 0.0432 | 0.407 | KEGG         |
| Internalization of ErbB1                                                                                              | 39 2 (5.1%)  | 0.0438 | 0.407 | PID          |
| Rheumatoid arthritis - Homo sapiens (human)                                                                           | 93 3 (3.3%)  | 0.0443 | 0.407 | KEGG         |
| Glucose metabolism                                                                                                    | 93 3 (3.3%)  | 0.0443 | 0.407 | Reactome     |
| ErbB2/ErbB3 signaling events                                                                                          | 40 2 (5.0%)  | 0.0459 | 0.418 | PID          |
| TGF-beta signaling pathway - Homo sapiens (human)                                                                     | 94 3 (3.2%)  | 0.0467 | 0.418 | KEGG         |
| Mitochondrial translation                                                                                             | 94 3 (3.2%)  | 0.0467 | 0.418 | Reactome     |
| Inositol phosphate metabolism                                                                                         | 41 2 (4.9%)  | 0.048  | 0.418 | INOH         |

## T2DM\_requiring\_insulin

| pathway name                                                          | candidates |            | p-value | q-value | pathway source               |
|-----------------------------------------------------------------------|------------|------------|---------|---------|------------------------------|
|                                                                       | set size   | contained  |         |         |                              |
| Aspartate and asparagine metabolism                                   | 12         | 2 (16.7%)  | 0.0011  | 0.405   | <a href="#">Reactome</a>     |
| Oleoyl-phe metabolism                                                 | 1          | 1 (100.0%) | 0.00417 | 0.405   | <a href="#">Reactome</a>     |
| Relationship between inflammation, COX-2 and EGFR                     | 25         | 2 (8.0%)   | 0.00481 | 0.405   | <a href="#">Wikipathways</a> |
| estradiol biosynthesis II                                             | 2          | 1 (50.0%)  | 0.00832 | 0.405   | <a href="#">HumanCyc</a>     |
| Validated transcriptional targets of AP1 family members Fra1 and Fra2 | 37         | 2 (5.4%)   | 0.0104  | 0.405   | <a href="#">PID</a>          |
| TGF-beta super family signaling pathway canonical                     | 115        | 3 (2.6%)   | 0.0122  | 0.405   | <a href="#">INOH</a>         |
| Heart Development                                                     | 47         | 2 (4.3%)   | 0.0164  | 0.405   | <a href="#">Wikipathways</a> |
| Estrogen biosynthesis                                                 | 5          | 1 (20.0%)  | 0.0207  | 0.405   | <a href="#">Reactome</a>     |
| Galactose catabolism                                                  | 5          | 1 (20.0%)  | 0.0207  | 0.405   | <a href="#">Reactome</a>     |
| Ectoderm Differentiation                                              | 142        | 3 (2.1%)   | 0.0213  | 0.405   | <a href="#">Wikipathways</a> |
| mRNA 3,-end processing                                                | 58         | 2 (3.4%)   | 0.0243  | 0.405   | <a href="#">Reactome</a>     |
| estradiol biosynthesis I                                              | 6          | 1 (16.7%)  | 0.0248  | 0.405   | <a href="#">HumanCyc</a>     |
| p75NTR negatively regulates cell cycle via SC1                        | 6          | 1 (16.7%)  | 0.0248  | 0.405   | <a href="#">Reactome</a>     |
| Mitochondrial Uncoupling                                              | 6          | 1 (16.7%)  | 0.0248  | 0.405   | <a href="#">Reactome</a>     |
| Notch signaling pathway - Homo sapiens (human)                        | 59         | 2 (3.4%)   | 0.0251  | 0.405   | <a href="#">KEGG</a>         |
| SARS-CoV-2 innate immunity evasion and cell-specific immune response  | 60         | 2 (3.4%)   | 0.0251  | 0.405   | <a href="#">Wikipathways</a> |
| Mitochondrial protein import                                          | 65         | 2 (3.1%)   | 0.03    | 0.405   | <a href="#">Reactome</a>     |
| Protein localization                                                  | 165        | 3 (1.8%)   | 0.0314  | 0.405   | <a href="#">Reactome</a>     |
| RNA Polymerase II Transcription Termination                           | 67         | 2 (3.0%)   | 0.0317  | 0.405   | <a href="#">Reactome</a>     |
| Glial Cell Differentiation                                            | 8          | 1 (12.5%)  | 0.0329  | 0.405   | <a href="#">Wikipathways</a> |
| AP-1 transcription factor network                                     | 70         | 2 (2.9%)   | 0.0344  | 0.405   | <a href="#">PID</a>          |
| p75(NTR)-mediated signaling                                           | 70         | 2 (2.9%)   | 0.0344  | 0.405   | <a href="#">PID</a>          |
| Erythrocytes take up oxygen and release carbon dioxide                | 9          | 1 (11.1%)  | 0.0369  | 0.405   | <a href="#">Reactome</a>     |
| Activation of PUMA and translocation to mitochondria                  | 9          | 1 (11.1%)  | 0.0369  | 0.405   | <a href="#">Reactome</a>     |
| Transport of Mature mRNA derived from an Intron-Containing Transcript | 75         | 2 (2.7%)   | 0.039   | 0.405   | <a href="#">Reactome</a>     |
| EGFR Transactivation by Gastrin                                       | 10         | 1 (10.0%)  | 0.0409  | 0.405   | <a href="#">Reactome</a>     |
| Calcineurin activates NFAT                                            | 10         | 1 (10.0%)  | 0.0409  | 0.405   | <a href="#">Reactome</a>     |
| Notch                                                                 | 78         | 2 (2.6%)   | 0.0419  | 0.405   | <a href="#">INOH</a>         |
| Glucocorticoid receptor regulatory network                            | 80         | 2 (2.5%)   | 0.0438  | 0.405   | <a href="#">PID</a>          |
| Establishment of Sister Chromatid Cohesion                            | 11         | 1 (9.1%)   | 0.0449  | 0.405   | <a href="#">Reactome</a>     |
| Glycogen synthesis                                                    | 11         | 1 (9.1%)   | 0.0449  | 0.405   | <a href="#">Reactome</a>     |
| Transport of Mature Transcript to Cytoplasm                           | 84         | 2 (2.4%)   | 0.0479  | 0.405   | <a href="#">Reactome</a>     |
| Reversible hydration of carbon dioxide                                | 12         | 1 (8.3%)   | 0.0489  | 0.405   | <a href="#">Reactome</a>     |
| 17-Beta Hydroxysteroid Dehydrogenase III Deficiency                   | 12         | 1 (8.3%)   | 0.0489  | 0.405   | <a href="#">SMPDB</a>        |
| Androgen and Estrogen Metabolism                                      | 12         | 1 (8.3%)   | 0.0489  | 0.405   | <a href="#">SMPDB</a>        |
| Aromatase deficiency                                                  | 12         | 1 (8.3%)   | 0.0489  | 0.405   | <a href="#">SMPDB</a>        |
| CLEC7A (Dectin-1) induces NFAT activation                             | 12         | 1 (8.3%)   | 0.0489  | 0.405   | <a href="#">Reactome</a>     |
| TP53 Regulates Transcription of Death Receptors and Ligands           | 12         | 1 (8.3%)   | 0.0489  | 0.405   | <a href="#">Reactome</a>     |

## Obesity\_SAT

| pathway name                                                                         | candidates |            | p-value  | q-value | pathway source |
|--------------------------------------------------------------------------------------|------------|------------|----------|---------|----------------|
|                                                                                      | set size   | contained  |          |         |                |
| Eicosanoid metabolism via cyclooxygenases (COX)                                      | 30         | 4 (13.3%)  | 0.000721 | 0.414   | Wikipathways   |
| Initiation of transcription and translation elongation at the HIV-1 LTR              | 32         | 4 (12.5%)  | 0.000926 | 0.414   | Wikipathways   |
| bile acid biosynthesis, neutral pathway                                              | 15         | 3 (20.0%)  | 0.00103  | 0.414   | HumanCyc       |
| serine biosynthesis (phosphorylated route)                                           | 4          | 2 (50.0%)  | 0.00111  | 0.414   | HumanCyc       |
| The fatty acid cycling model                                                         | 5          | 2 (40.0%)  | 0.00184  | 0.421   | Reactome       |
| The proton buffering model                                                           | 5          | 2 (40.0%)  | 0.00184  | 0.421   | Reactome       |
| PPAR signaling pathway                                                               | 68         | 5 (7.4%)   | 0.00243  | 0.421   | Wikipathways   |
| Metabolic reprogramming in colon cancer                                              | 42         | 4 (9.5%)   | 0.00259  | 0.421   | Wikipathways   |
| Mitochondrial Uncoupling                                                             | 6          | 2 (33.3%)  | 0.00273  | 0.421   | Reactome       |
| overview of telomerase rna component gene hterc transcriptional regulation           | 7          | 2 (28.6%)  | 0.00378  | 0.421   | BioCarta       |
| serine and glycine biosynthesis                                                      | 7          | 2 (28.6%)  | 0.00378  | 0.421   | HumanCyc       |
| Amino sugar and nucleotide sugar metabolism - Homo sapiens (human)                   | 48         | 4 (8.3%)   | 0.00422  | 0.421   | KEGG           |
| alpha-Linolenic acid metabolism - Homo sapiens (human)                               | 25         | 3 (12.0%)  | 0.00473  | 0.421   | KEGG           |
| RUNX3 regulates p14-ARF                                                              | 8          | 2 (25.0%)  | 0.005    | 0.421   | Reactome       |
| Peroxisome - Homo sapiens (human)                                                    | 82         | 5 (6.1%)   | 0.00544  | 0.421   | KEGG           |
| mechanism of gene regulation by peroxisome proliferators via ppara                   | 52         | 4 (7.7%)   | 0.00563  | 0.421   | BioCarta       |
| TRIF-mediated programmed cell death                                                  | 9          | 2 (22.2%)  | 0.00637  | 0.421   | Reactome       |
| Omega-6 fatty acid metabolism                                                        | 28         | 3 (10.7%)  | 0.00653  | 0.421   | EHMN           |
| Eicosanoid metabolism via lipooxygenases (LOX)                                       | 29         | 3 (10.3%)  | 0.00722  | 0.421   | Wikipathways   |
| Cytochrome P450 - arranged by substrate type                                         | 57         | 4 (7.0%)   | 0.00779  | 0.421   | Reactome       |
| Protein localization                                                                 | 165        | 7 (4.2%)   | 0.00787  | 0.421   | Reactome       |
| Regulation of the apoptosome activity                                                | 10         | 2 (20.0%)  | 0.00789  | 0.421   | Reactome       |
| Formation of apoptosome                                                              | 10         | 2 (20.0%)  | 0.00789  | 0.421   | Reactome       |
| Citrate cycle (TCA cycle) - Homo sapiens (human)                                     | 30         | 3 (10.0%)  | 0.00794  | 0.421   | KEGG           |
| Regulation of TP53 Activity through Acetylation                                      | 30         | 3 (10.0%)  | 0.00794  | 0.421   | Reactome       |
| TCA cycle                                                                            | 30         | 3 (10.0%)  | 0.00794  | 0.421   | EHMN           |
| Peroxisomal lipid metabolism                                                         | 30         | 3 (10.0%)  | 0.00794  | 0.421   | Reactome       |
| Fructose Mannose metabolism                                                          | 30         | 3 (10.0%)  | 0.00794  | 0.421   | INOH           |
| Ethanol effects on histone modifications                                             | 31         | 3 (9.7%)   | 0.0087   | 0.421   | Wikipathways   |
| protein kinase a at the centrosome                                                   | 12         | 2 (16.7%)  | 0.0114   | 0.421   | BioCarta       |
| Trihydroxycoprostanoil-CoA beta-oxidation                                            | 12         | 2 (16.7%)  | 0.0114   | 0.421   | EHMN           |
| Beta-oxidation of very long chain fatty acids                                        | 12         | 2 (16.7%)  | 0.0114   | 0.421   | Reactome       |
| Cytochrome c-mediated apoptotic response                                             | 12         | 2 (16.7%)  | 0.0114   | 0.421   | Reactome       |
| Peroxisomal protein import                                                           | 64         | 4 (6.2%)   | 0.0116   | 0.421   | Reactome       |
| RNA Polymerase II Transcription                                                      | 1307       | 28 (2.1%)  | 0.012    | 0.421   | Reactome       |
| Phase I - Functionalization of compounds                                             | 101        | 5 (5.0%)   | 0.0128   | 0.421   | Reactome       |
| Estrogen Receptor Pathway                                                            | 13         | 2 (15.4%)  | 0.0133   | 0.421   | Wikipathways   |
| role of mitochondria in apoptotic signaling                                          | 13         | 2 (15.4%)  | 0.0133   | 0.421   | BioCarta       |
| 7-oxo-C and 7beta-HC pathways                                                        | 13         | 2 (15.4%)  | 0.0133   | 0.421   | Wikipathways   |
| Gene expression (Transcription)                                                      | 1439       | 30 (2.1%)  | 0.0134   | 0.421   | Reactome       |
| FLT3 mutants bind TKIs                                                               | 1          | 1 (100.0%) | 0.0138   | 0.421   | Reactome       |
| Intestinal lipid absorption                                                          | 1          | 1 (100.0%) | 0.0138   | 0.421   | Reactome       |
| ATR signaling pathway                                                                | 37         | 3 (8.1%)   | 0.0142   | 0.421   | PID            |
| Spinocerebellar ataxia - Homo sapiens (human)                                        | 143        | 6 (4.2%)   | 0.0142   | 0.421   | KEGG           |
| Sterol regulatory element-binding proteins (SREBP) signaling                         | 68         | 4 (5.9%)   | 0.0143   | 0.421   | Wikipathways   |
| Regulation of Telomerase                                                             | 68         | 4 (5.9%)   | 0.0143   | 0.421   | PID            |
| Omega-3-Omega-6 FA synthesis                                                         | 14         | 2 (14.3%)  | 0.0154   | 0.421   | Wikipathways   |
| transcription regulation by methyltransferase of carml                               | 14         | 2 (14.3%)  | 0.0154   | 0.421   | BioCarta       |
| Osteoblast Signaling                                                                 | 14         | 2 (14.3%)  | 0.0154   | 0.421   | Wikipathways   |
| Positive epigenetic regulation of rRNA expression                                    | 109        | 5 (4.6%)   | 0.0167   | 0.421   | Reactome       |
| the prc2 complex sets long-term gene silencing through modification of histone tails | 15         | 2 (13.3%)  | 0.0176   | 0.421   | BioCarta       |
| FOXO-mediated transcription of cell death genes                                      | 15         | 2 (13.3%)  | 0.0176   | 0.421   | Reactome       |
| Glutamate and glutamine metabolism                                                   | 15         | 2 (13.3%)  | 0.0176   | 0.421   | Reactome       |
| PPAR signaling pathway - Homo sapiens (human)                                        | 76         | 4 (5.4%)   | 0.019    | 0.421   | KEGG           |

|                                                                              |                |        |       |              |
|------------------------------------------------------------------------------|----------------|--------|-------|--------------|
| E2F transcription factor network                                             | 75 4 (5.3%)    | 0.0198 | 0.421 | PID          |
| Polo-like kinase mediated events                                             | 16 2 (12.5%)   | 0.0199 | 0.421 | Reactome     |
| Omega-3 fatty acid metabolism                                                | 16 2 (12.5%)   | 0.0199 | 0.421 | EHMN         |
| Phytanic acid peroxisomal oxidation                                          | 16 2 (12.5%)   | 0.0199 | 0.421 | EHMN         |
| Apoptotic factor-mediated response                                           | 16 2 (12.5%)   | 0.0199 | 0.421 | Reactome     |
| Caspase activation via Death Receptors in the presence of ligand             | 16 2 (12.5%)   | 0.0199 | 0.421 | Reactome     |
| Herpes simplex virus 1 infection - Homo sapiens (human)                      | 498 13 (2.6%)  | 0.0204 | 0.421 | KEGG         |
| Regulation of nuclear SMAD2/3 signaling                                      | 77 4 (5.2%)    | 0.0216 | 0.421 | PID          |
| TCA Cycle (aka Krebs or citric acid cycle)                                   | 17 2 (11.8%)   | 0.0224 | 0.421 | Wikipathways |
| Bile Acid Biosynthesis                                                       | 17 2 (11.8%)   | 0.0224 | 0.421 | SMPDB        |
| 27-Hydroxylase Deficiency                                                    | 17 2 (11.8%)   | 0.0224 | 0.421 | SMPDB        |
| Congenital Bile Acid Synthesis Defect Type II                                | 17 2 (11.8%)   | 0.0224 | 0.421 | SMPDB        |
| Cerebrotendinous Xanthomatosis (CTX)                                         | 17 2 (11.8%)   | 0.0224 | 0.421 | SMPDB        |
| Zellweger Syndrome                                                           | 17 2 (11.8%)   | 0.0224 | 0.421 | SMPDB        |
| Familial Hypercholanemia (FHCA)                                              | 17 2 (11.8%)   | 0.0224 | 0.421 | SMPDB        |
| Congenital Bile Acid Synthesis Defect Type III                               | 17 2 (11.8%)   | 0.0224 | 0.421 | SMPDB        |
| Primary bile acid biosynthesis - Homo sapiens (human)                        | 17 2 (11.8%)   | 0.0224 | 0.421 | KEGG         |
| The citric acid (TCA) cycle and respiratory electron transport               | 162 6 (3.7%)   | 0.0247 | 0.421 | Reactome     |
| Endogenous sterols                                                           | 18 2 (11.1%)   | 0.025  | 0.421 | Reactome     |
| Fructose intolerance, hereditary                                             | 18 2 (11.1%)   | 0.025  | 0.421 | SMPDB        |
| Fructose and Mannose Degradation                                             | 18 2 (11.1%)   | 0.025  | 0.421 | SMPDB        |
| Fructosuria                                                                  | 18 2 (11.1%)   | 0.025  | 0.421 | SMPDB        |
| Acyl chain remodelling of PG                                                 | 18 2 (11.1%)   | 0.025  | 0.421 | Reactome     |
| Fanconi anemia pathway                                                       | 46 3 (6.5%)    | 0.0253 | 0.421 | PID          |
| Regulation of TP53 Activity                                                  | 163 6 (3.7%)   | 0.0253 | 0.421 | Reactome     |
| Energy Metabolism                                                            | 47 3 (6.4%)    | 0.0268 | 0.421 | Wikipathways |
| Activation of Na-permeable kainate receptors                                 | 2 1 (50.0%)    | 0.0274 | 0.421 | Reactome     |
| Disorders of Folate Metabolism and Transport                                 | 2 1 (50.0%)    | 0.0274 | 0.421 | Wikipathways |
| GDP-L-fucose biosynthesis II (from L-fucose)                                 | 2 1 (50.0%)    | 0.0274 | 0.421 | HumanCyc     |
| PAOs oxidise polyamines to amines                                            | 2 1 (50.0%)    | 0.0274 | 0.421 | Reactome     |
| Apoptosis Modulation by HSP70                                                | 19 2 (10.5%)   | 0.0277 | 0.421 | Wikipathways |
| Hematopoietic Stem Cell Gene Regulation by GABP alpha-beta Complex           | 19 2 (10.5%)   | 0.0277 | 0.421 | Wikipathways |
| TCA cycle                                                                    | 19 2 (10.5%)   | 0.0277 | 0.421 | HumanCyc     |
| fatty acid $\beta$ -oxidation (peroxisome)                                   | 19 2 (10.5%)   | 0.0277 | 0.421 | HumanCyc     |
| NOTCH1 Intracellular Domain Regulates Transcription                          | 48 3 (6.2%)    | 0.0283 | 0.421 | Reactome     |
| Metabolism of steroids                                                       | 124 5 (4.0%)   | 0.0284 | 0.421 | Reactome     |
| Synthesis of bile acids and bile salts via 7 $\alpha$ -hydroxycholesterol    | 20 2 (10.0%)   | 0.0305 | 0.421 | Reactome     |
| Apoptosis                                                                    | 127 5 (3.9%)   | 0.0311 | 0.421 | Reactome     |
| Sensory processing of sound by outer hair cells of the cochlea               | 50 3 (6.0%)    | 0.0314 | 0.421 | Reactome     |
| Generic Transcription Pathway                                                | 1178 24 (2.0%) | 0.0333 | 0.421 | Reactome     |
| Pyruvate dehydrogenase deficiency (E3)                                       | 21 2 (9.5%)    | 0.0334 | 0.421 | SMPDB        |
| Pyruvate dehydrogenase deficiency (E2)                                       | 21 2 (9.5%)    | 0.0334 | 0.421 | SMPDB        |
| 2-ketoglutarate dehydrogenase complex deficiency                             | 21 2 (9.5%)    | 0.0334 | 0.421 | SMPDB        |
| Mitochondrial complex II deficiency                                          | 21 2 (9.5%)    | 0.0334 | 0.421 | SMPDB        |
| Fumarase deficiency                                                          | 21 2 (9.5%)    | 0.0334 | 0.421 | SMPDB        |
| Congenital lactic acidosis                                                   | 21 2 (9.5%)    | 0.0334 | 0.421 | SMPDB        |
| Citric Acid Cycle                                                            | 21 2 (9.5%)    | 0.0334 | 0.421 | SMPDB        |
| HS-GAG degradation                                                           | 21 2 (9.5%)    | 0.0334 | 0.421 | Reactome     |
| DNA Repair                                                                   | 323 9 (2.8%)   | 0.0343 | 0.421 | Reactome     |
| role of brca1 brca2 and atr in cancer susceptibility                         | 22 2 (9.1%)    | 0.0364 | 0.421 | BioCarta     |
| Effect of progerin on genes involved in Hutchinson-Gilford progeria syndrome | 22 2 (9.1%)    | 0.0364 | 0.421 | Wikipathways |
| PDGFR-alpha signaling pathway                                                | 22 2 (9.1%)    | 0.0364 | 0.421 | PID          |
| Citric acid cycle (TCA cycle)                                                | 22 2 (9.1%)    | 0.0364 | 0.421 | Reactome     |
| Acyl chain remodelling of PS                                                 | 22 2 (9.1%)    | 0.0364 | 0.421 | Reactome     |
| Inositol Metabolism                                                          | 22 2 (9.1%)    | 0.0364 | 0.421 | SMPDB        |
| Pyruvate metabolism and Citric Acid (TCA) cycle                              | 53 3 (5.7%)    | 0.0364 | 0.421 | Reactome     |
| Bile acid biosynthesis                                                       | 53 3 (5.7%)    | 0.0364 | 0.421 | EHMN         |

|                                                                      |                |        |       |              |
|----------------------------------------------------------------------|----------------|--------|-------|--------------|
| Apoptosis Modulation and Signaling                                   | 92 4 (4.3%)    | 0.0382 | 0.421 | Wikipathways |
| Constitutive Signaling by NOTCH1 HD+PEST Domain Mutants              | 54 3 (5.6%)    | 0.0382 | 0.421 | Reactome     |
| Constitutive Signaling by NOTCH1 PEST Domain Mutants                 | 54 3 (5.6%)    | 0.0382 | 0.421 | Reactome     |
| Signaling by NOTCH1 PEST Domain Mutants in Cancer                    | 54 3 (5.6%)    | 0.0382 | 0.421 | Reactome     |
| Signaling by NOTCH1 HD+PEST Domain Mutants in Cancer                 | 54 3 (5.6%)    | 0.0382 | 0.421 | Reactome     |
| Signaling by NOTCH1 in Cancer                                        | 54 3 (5.6%)    | 0.0382 | 0.421 | Reactome     |
| Heparan sulfate/heparin (HS-GAG) metabolism                          | 54 3 (5.6%)    | 0.0382 | 0.421 | Reactome     |
| Metabolism                                                           | 1954 36 (1.8%) | 0.0389 | 0.421 | Reactome     |
| IKK complex recruitment mediated by RIP1                             | 23 2 (8.7%)    | 0.0395 | 0.421 | Reactome     |
| Di-unsaturated fatty acid beta-oxidation                             | 23 2 (8.7%)    | 0.0395 | 0.421 | EHMN         |
| Phosphatidylinositol Phosphate Metabolism                            | 23 2 (8.7%)    | 0.0395 | 0.421 | SMPDB        |
| Joubert syndrome                                                     | 23 2 (8.7%)    | 0.0395 | 0.421 | SMPDB        |
| Validated transcriptional targets of TAp63 isoforms                  | 55 3 (5.5%)    | 0.04   | 0.421 | PID          |
| Electron transport from NADPH to Ferredoxin                          | 3 1 (33.3%)    | 0.0407 | 0.421 | Reactome     |
| glutamine degradation/glutamate biosynthesis                         | 3 1 (33.3%)    | 0.0407 | 0.421 | HumanCyc     |
| methylglyoxal degradation I                                          | 3 1 (33.3%)    | 0.0407 | 0.421 | HumanCyc     |
| Pyruvaldehyde Degradation                                            | 3 1 (33.3%)    | 0.0407 | 0.421 | SMPDB        |
| tetrahydrofolate salvage from 5,10-methenyltetrahydrofolate          | 3 1 (33.3%)    | 0.0407 | 0.421 | HumanCyc     |
| 1,25-dihydroxyvitamin D <sub>3</sub> biosynthesis                    | 3 1 (33.3%)    | 0.0407 | 0.421 | HumanCyc     |
| <i>N</i> -acetylglucosamine degradation I                            | 3 1 (33.3%)    | 0.0407 | 0.421 | HumanCyc     |
| Inositol transporters                                                | 3 1 (33.3%)    | 0.0407 | 0.421 | Reactome     |
| Interconversion of polyamines                                        | 3 1 (33.3%)    | 0.0407 | 0.421 | Reactome     |
| Signaling events mediated by HDAC Class I                            | 56 3 (5.4%)    | 0.0418 | 0.421 | PID          |
| Epigenetic regulation of gene expression                             | 140 5 (3.6%)   | 0.0432 | 0.421 | Reactome     |
| Iron uptake and transport                                            | 57 3 (5.3%)    | 0.0437 | 0.421 | Reactome     |
| Sensory processing of sound                                          | 58 3 (5.2%)    | 0.0457 | 0.421 | Reactome     |
| stathmin and breast cancer resistance to antimicrotubule agents      | 25 2 (8.0%)    | 0.046  | 0.421 | BioCarta     |
| Saturated fatty acids beta-oxidation                                 | 25 2 (8.0%)    | 0.046  | 0.421 | EHMN         |
| Programmed Cell Death                                                | 142 5 (3.5%)   | 0.0466 | 0.421 | Reactome     |
| Direct p53 effectors                                                 | 142 5 (3.5%)   | 0.0466 | 0.421 | PID          |
| SARS-CoV-2 innate immunity evasion and cell-specific immune response | 60 3 (5.1%)    | 0.0476 | 0.421 | Wikipathways |
| PPAR-alpha pathway                                                   | 26 2 (7.7%)    | 0.0494 | 0.421 | Wikipathways |
| Activation of gene expression by SREBF (SREBP)                       | 26 2 (7.7%)    | 0.0494 | 0.421 | Reactome     |
| Caspase activation via extrinsic apoptotic signalling pathway        | 26 2 (7.7%)    | 0.0494 | 0.421 | Reactome     |
| A tetrasaccharide linker sequence is required for GAG synthesis      | 26 2 (7.7%)    | 0.0494 | 0.421 | Reactome     |

# CAD\_SAT

| pathway name                                                                   | candidates |           | p-value | q-value | pathway source |
|--------------------------------------------------------------------------------|------------|-----------|---------|---------|----------------|
|                                                                                | set size   | contained |         |         |                |
| Leptin signaling pathway                                                       | 76         | 3 (3.9%)  | 0.00236 | 0.289   | Wikipathways   |
| Propanoate metabolism - Homo sapiens (human)                                   | 34         | 2 (5.9%)  | 0.00626 | 0.289   | KEGG           |
| Fatty acid beta-oxidation                                                      | 34         | 2 (5.9%)  | 0.00626 | 0.289   | Wikipathways   |
| Cysteine and methionine metabolism - Homo sapiens (human)                      | 50         | 2 (4.0%)  | 0.0132  | 0.289   | KEGG           |
| S-methyl-5-thio- $\alpha$ -D-ribose 1-phosphate degradation                    | 4          | 1 (25.0%) | 0.0139  | 0.289   | HumanCyc       |
| mechanism of gene regulation by peroxisome proliferators via ppara             | 52         | 2 (3.8%)  | 0.0142  | 0.289   | BioCarta       |
| Beta oxidation of hexanoyl-CoA to butanoyl-CoA                                 | 5          | 1 (20.0%) | 0.0174  | 0.289   | Reactome       |
| Beta oxidation of butanoyl-CoA to acetyl-CoA                                   | 5          | 1 (20.0%) | 0.0174  | 0.289   | Reactome       |
| Galactose catabolism                                                           | 5          | 1 (20.0%) | 0.0174  | 0.289   | Reactome       |
| lactate fermentation (reoxidation of cytosolic NADH)                           | 5          | 1 (20.0%) | 0.0174  | 0.289   | HumanCyc       |
| Leptin                                                                         | 62         | 2 (3.2%)  | 0.0198  | 0.289   | NetPath        |
| D-galactose degradation V (Leloir pathway)                                     | 6          | 1 (16.7%) | 0.0208  | 0.289   | HumanCyc       |
| Methionine salvage pathway                                                     | 6          | 1 (16.7%) | 0.0208  | 0.289   | Reactome       |
| HIF-1-alpha transcription factor network                                       | 66         | 2 (3.0%)  | 0.0223  | 0.289   | PID            |
| Integrated breast cancer pathway                                               | 67         | 2 (3.0%)  | 0.0229  | 0.289   | Wikipathways   |
| Sterol regulatory element-binding proteins (SREBP) signaling                   | 68         | 2 (2.9%)  | 0.0236  | 0.289   | Wikipathways   |
| Glycolysis in senescence                                                       | 7          | 1 (14.3%) | 0.0242  | 0.289   | Wikipathways   |
| overview of telomerase rna component gene hterc transcriptional regulation     | 7          | 1 (14.3%) | 0.0242  | 0.289   | BioCarta       |
| coenzyme A biosynthesis                                                        | 7          | 1 (14.3%) | 0.0242  | 0.289   | HumanCyc       |
| AP-1 transcription factor network                                              | 70         | 2 (2.9%)  | 0.0249  | 0.289   | PID            |
| Butyrate Metabolism                                                            | 8          | 1 (12.5%) | 0.0277  | 0.289   | SMPDB          |
| Mitochondrial Beta-Oxidation of Short Chain Saturated Fatty Acids              | 8          | 1 (12.5%) | 0.0277  | 0.289   | SMPDB          |
| Short-chain 3-hydroxyacyl-CoA dehydrogenase deficiency (SCHAD)                 | 8          | 1 (12.5%) | 0.0277  | 0.289   | SMPDB          |
| Galactosemia III                                                               | 8          | 1 (12.5%) | 0.0277  | 0.289   | SMPDB          |
| Galactosemia II (GALK)                                                         | 8          | 1 (12.5%) | 0.0277  | 0.289   | SMPDB          |
| Nucleotide Sugars Metabolism                                                   | 8          | 1 (12.5%) | 0.0277  | 0.289   | SMPDB          |
| HIF1A and PPARG regulation of glycolysis                                       | 8          | 1 (12.5%) | 0.0277  | 0.289   | Wikipathways   |
| Regulation of commissural axon pathfinding by SLIT and ROBO                    | 8          | 1 (12.5%) | 0.0277  | 0.289   | Reactome       |
| Coenzyme A biosynthesis                                                        | 8          | 1 (12.5%) | 0.0277  | 0.289   | Reactome       |
| Ethanol metabolism resulting in production of ROS by CYP2E1                    | 9          | 1 (11.1%) | 0.0311  | 0.289   | Wikipathways   |
| ROBO receptors bind AKAP5                                                      | 9          | 1 (11.1%) | 0.0311  | 0.289   | Reactome       |
| NS1 Mediated Effects on Host Pathways                                          | 10         | 1 (10.0%) | 0.0345  | 0.289   | Reactome       |
| SLBP independent Processing of Histone Pre-mRNAs                               | 10         | 1 (10.0%) | 0.0345  | 0.289   | Reactome       |
| overview of telomerase protein component gene htert transcriptional regulation | 10         | 1 (10.0%) | 0.0345  | 0.289   | BioCarta       |
| mitochondrial fatty acid beta-oxidation of saturated fatty acids               | 11         | 1 (9.1%)  | 0.0378  | 0.289   | Reactome       |
| CMP phosphorylation                                                            | 11         | 1 (9.1%)  | 0.0378  | 0.289   | HumanCyc       |
| SLBP Dependent Processing of Replication-Dependent Histone Pre-mRNAs           | 11         | 1 (9.1%)  | 0.0378  | 0.289   | Reactome       |
| Computational Model of Aerobic Glycolysis                                      | 12         | 1 (8.3%)  | 0.0412  | 0.289   | Wikipathways   |
| pyrimidine deoxyribonucleotide phosphorylation                                 | 12         | 1 (8.3%)  | 0.0412  | 0.289   | HumanCyc       |
| guanosine deoxyribonucleotides <i>de novo</i> biosynthesis                     | 12         | 1 (8.3%)  | 0.0412  | 0.289   | HumanCyc       |
| adenosine deoxyribonucleotides <i>de novo</i> biosynthesis                     | 12         | 1 (8.3%)  | 0.0412  | 0.289   | HumanCyc       |
| phospholipase c-epsilon pathway                                                | 12         | 1 (8.3%)  | 0.0412  | 0.289   | BioCarta       |
| Galactose Metabolism                                                           | 13         | 1 (7.7%)  | 0.0446  | 0.289   | SMPDB          |
| Galactosemia                                                                   | 13         | 1 (7.7%)  | 0.0446  | 0.289   | SMPDB          |
| Galactose metabolism                                                           | 13         | 1 (7.7%)  | 0.0446  | 0.289   | INOH           |
| Assembly of active LPL and LIPC lipase complexes                               | 13         | 1 (7.7%)  | 0.0446  | 0.289   | Reactome       |
| Familial lipoprotein lipase deficiency                                         | 13         | 1 (7.7%)  | 0.0446  | 0.289   | SMPDB          |
| Glycerolipid Metabolism                                                        | 13         | 1 (7.7%)  | 0.0446  | 0.289   | SMPDB          |
| Glycerol Kinase Deficiency                                                     | 13         | 1 (7.7%)  | 0.0446  | 0.289   | SMPDB          |
| D-glyceric acidura                                                             | 13         | 1 (7.7%)  | 0.0446  | 0.289   | SMPDB          |
| purine deoxyribonucleosides salvage                                            | 13         | 1 (7.7%)  | 0.0446  | 0.289   | HumanCyc       |

|                                                                   |    |          |        |       |                              |
|-------------------------------------------------------------------|----|----------|--------|-------|------------------------------|
| guanosine ribonucleotides <i>de novo</i> biosynthesis             | 13 | 1 (7.7%) | 0.0446 | 0.289 | <a href="#">HumanCyc</a>     |
| UTP and CTP <i>de novo</i> biosynthesis                           | 13 | 1 (7.7%) | 0.0446 | 0.289 | <a href="#">HumanCyc</a>     |
| attenuation of gpcr signaling                                     | 13 | 1 (7.7%) | 0.0446 | 0.289 | <a href="#">BioCarta</a>     |
| effects of calcineurin in keratinocyte differentiation            | 13 | 1 (7.7%) | 0.0446 | 0.289 | <a href="#">BioCarta</a>     |
| Estrogen Receptor Pathway                                         | 13 | 1 (7.7%) | 0.0446 | 0.289 | <a href="#">Wikipathways</a> |
| eNOS activation                                                   | 13 | 1 (7.7%) | 0.0446 | 0.289 | <a href="#">Reactome</a>     |
| Long chain acyl-CoA dehydrogenase deficiency (LCAD)               | 14 | 1 (7.1%) | 0.0479 | 0.289 | <a href="#">SMPDB</a>        |
| Trifunctional protein deficiency                                  | 14 | 1 (7.1%) | 0.0479 | 0.289 | <a href="#">SMPDB</a>        |
| Carnitine palmitoyl transferase deficiency (II)                   | 14 | 1 (7.1%) | 0.0479 | 0.289 | <a href="#">SMPDB</a>        |
| Very-long-chain acyl coa dehydrogenase deficiency (VLCAD)         | 14 | 1 (7.1%) | 0.0479 | 0.289 | <a href="#">SMPDB</a>        |
| Medium chain acyl-coa dehydrogenase deficiency (MCAD)             | 14 | 1 (7.1%) | 0.0479 | 0.289 | <a href="#">SMPDB</a>        |
| Short Chain Acyl CoA Dehydrogenase Deficiency (SCAD Deficiency)   | 14 | 1 (7.1%) | 0.0479 | 0.289 | <a href="#">SMPDB</a>        |
| Fatty acid Metabolism                                             | 14 | 1 (7.1%) | 0.0479 | 0.289 | <a href="#">SMPDB</a>        |
| Glutaric Aciduria Type I                                          | 14 | 1 (7.1%) | 0.0479 | 0.289 | <a href="#">SMPDB</a>        |
| Ethylmalonic Encephalopathy                                       | 14 | 1 (7.1%) | 0.0479 | 0.289 | <a href="#">SMPDB</a>        |
| Carnitine palmitoyl transferase deficiency (I)                    | 14 | 1 (7.1%) | 0.0479 | 0.289 | <a href="#">SMPDB</a>        |
| transcription regulation by methyltransferase of carm1            | 14 | 1 (7.1%) | 0.0479 | 0.289 | <a href="#">BioCarta</a>     |
| CREB1 phosphorylation through the activation of Adenylate Cyclase | 14 | 1 (7.1%) | 0.0479 | 0.289 | <a href="#">Reactome</a>     |
| Vitamin B5 (pantothenate) metabolism                              | 14 | 1 (7.1%) | 0.0479 | 0.289 | <a href="#">Reactome</a>     |

## T2DM\_SAT

| pathway name                                                                  | candidates |            | p-value | q-value | pathway source               |
|-------------------------------------------------------------------------------|------------|------------|---------|---------|------------------------------|
|                                                                               | set size   | contained  |         |         |                              |
| Cytokine Signaling in Immune system                                           | 471        | 6 (1.3%)   | 0.00251 | 0.11    | <a href="#">Reactome</a>     |
| Quinapril Metabolism Pathway                                                  | 1          | 1 (100.0%) | 0.00298 | 0.11    | <a href="#">SMPDB</a>        |
| Ramipril Metabolism Pathway                                                   | 1          | 1 (100.0%) | 0.00298 | 0.11    | <a href="#">SMPDB</a>        |
| Fosinopril Metabolism Pathway                                                 | 1          | 1 (100.0%) | 0.00298 | 0.11    | <a href="#">SMPDB</a>        |
| Moexipril Metabolism Pathway                                                  | 1          | 1 (100.0%) | 0.00298 | 0.11    | <a href="#">SMPDB</a>        |
| Cilazapril Metabolism Pathway                                                 | 1          | 1 (100.0%) | 0.00298 | 0.11    | <a href="#">SMPDB</a>        |
| Enalapril Metabolism Pathway                                                  | 1          | 1 (100.0%) | 0.00298 | 0.11    | <a href="#">SMPDB</a>        |
| Benazepril Metabolism Pathway                                                 | 1          | 1 (100.0%) | 0.00298 | 0.11    | <a href="#">SMPDB</a>        |
| Spirapril Metabolism Pathway                                                  | 1          | 1 (100.0%) | 0.00298 | 0.11    | <a href="#">SMPDB</a>        |
| Trandolapril Metabolism Pathway                                               | 1          | 1 (100.0%) | 0.00298 | 0.11    | <a href="#">SMPDB</a>        |
| Temocapril Metabolism Pathway                                                 | 1          | 1 (100.0%) | 0.00298 | 0.11    | <a href="#">SMPDB</a>        |
| Conversion of Angiotensinogen to Angiotensin II                               | 1          | 1 (100.0%) | 0.00298 | 0.11    | <a href="#">Wikipathways</a> |
| FLT3 mutants bind TKIs                                                        | 1          | 1 (100.0%) | 0.00298 | 0.11    | <a href="#">Reactome</a>     |
| TNFs bind their physiological receptors                                       | 29         | 2 (6.9%)   | 0.00334 | 0.115   | <a href="#">Reactome</a>     |
| African trypanosomiasis - Homo sapiens (human)                                | 37         | 2 (5.6%)   | 0.00511 | 0.133   | <a href="#">KEGG</a>         |
| Intra-Golgi traffic                                                           | 45         | 2 (4.4%)   | 0.00789 | 0.133   | <a href="#">Reactome</a>     |
| 1,25-dihydroxyvitamin D <sub>3</sub> biosynthesis                             | 3          | 1 (33.3%)  | 0.00891 | 0.133   | <a href="#">HumanCyc</a>     |
| TNFR2 non-canonical NF-kB pathway                                             | 50         | 2 (4.0%)   | 0.00968 | 0.133   | <a href="#">Reactome</a>     |
| RANKL-RANK signaling pathway                                                  | 55         | 2 (3.6%)   | 0.0116  | 0.133   | <a href="#">Wikipathways</a> |
| Olmesartan Action Pathway                                                     | 4          | 1 (25.0%)  | 0.0119  | 0.133   | <a href="#">SMPDB</a>        |
| Losartan Action Pathway                                                       | 4          | 1 (25.0%)  | 0.0119  | 0.133   | <a href="#">SMPDB</a>        |
| Irbesartan Action Pathway                                                     | 4          | 1 (25.0%)  | 0.0119  | 0.133   | <a href="#">SMPDB</a>        |
| Forasartan Action Pathway                                                     | 4          | 1 (25.0%)  | 0.0119  | 0.133   | <a href="#">SMPDB</a>        |
| Valsartan Action Pathway                                                      | 4          | 1 (25.0%)  | 0.0119  | 0.133   | <a href="#">SMPDB</a>        |
| Telmisartan Action Pathway                                                    | 4          | 1 (25.0%)  | 0.0119  | 0.133   | <a href="#">SMPDB</a>        |
| Candesartan Action Pathway                                                    | 4          | 1 (25.0%)  | 0.0119  | 0.133   | <a href="#">SMPDB</a>        |
| Eprosartan Action Pathway                                                     | 4          | 1 (25.0%)  | 0.0119  | 0.133   | <a href="#">SMPDB</a>        |
| Temocapril Action Pathway                                                     | 4          | 1 (25.0%)  | 0.0119  | 0.133   | <a href="#">SMPDB</a>        |
| Spirapril Action Pathway                                                      | 4          | 1 (25.0%)  | 0.0119  | 0.133   | <a href="#">SMPDB</a>        |
| Trandolapril Action Pathway                                                   | 4          | 1 (25.0%)  | 0.0119  | 0.133   | <a href="#">SMPDB</a>        |
| Ramipril Action Pathway                                                       | 4          | 1 (25.0%)  | 0.0119  | 0.133   | <a href="#">SMPDB</a>        |
| Rescinnamine Action Pathway                                                   | 4          | 1 (25.0%)  | 0.0119  | 0.133   | <a href="#">SMPDB</a>        |
| Perindopril Action Pathway                                                    | 4          | 1 (25.0%)  | 0.0119  | 0.133   | <a href="#">SMPDB</a>        |
| Quinapril Action Pathway                                                      | 4          | 1 (25.0%)  | 0.0119  | 0.133   | <a href="#">SMPDB</a>        |
| Lisinopril Action Pathway                                                     | 4          | 1 (25.0%)  | 0.0119  | 0.133   | <a href="#">SMPDB</a>        |
| Moexipril Action Pathway                                                      | 4          | 1 (25.0%)  | 0.0119  | 0.133   | <a href="#">SMPDB</a>        |
| Fosinopril Action Pathway                                                     | 4          | 1 (25.0%)  | 0.0119  | 0.133   | <a href="#">SMPDB</a>        |
| Enalapril Action Pathway                                                      | 4          | 1 (25.0%)  | 0.0119  | 0.133   | <a href="#">SMPDB</a>        |
| Benazepril Action Pathway                                                     | 4          | 1 (25.0%)  | 0.0119  | 0.133   | <a href="#">SMPDB</a>        |
| Cilazapril Action Pathway                                                     | 4          | 1 (25.0%)  | 0.0119  | 0.133   | <a href="#">SMPDB</a>        |
| Captopril Action Pathway                                                      | 4          | 1 (25.0%)  | 0.0119  | 0.133   | <a href="#">SMPDB</a>        |
| Angiotensin Metabolism                                                        | 4          | 1 (25.0%)  | 0.0119  | 0.133   | <a href="#">SMPDB</a>        |
| serine biosynthesis (phosphorylated route)                                    | 4          | 1 (25.0%)  | 0.0119  | 0.133   | <a href="#">HumanCyc</a>     |
| FLT3 signaling through SRC family kinases                                     | 5          | 1 (20.0%)  | 0.0148  | 0.155   | <a href="#">Reactome</a>     |
| Degradation pathway of sphingolipids, including diseases                      | 5          | 1 (20.0%)  | 0.0148  | 0.155   | <a href="#">Wikipathways</a> |
| Acetylcholine inhibits contraction of outer hair cells                        | 5          | 1 (20.0%)  | 0.0148  | 0.155   | <a href="#">Reactome</a>     |
| Beta1 integrin cell surface interactions                                      | 66         | 2 (3.0%)   | 0.0164  | 0.169   | <a href="#">PID</a>          |
| Intra-Golgi and retrograde Golgi-to-ER traffic                                | 186        | 3 (1.6%)   | 0.0177  | 0.178   | <a href="#">Reactome</a>     |
| SARS-CoV-2 and angiotensin-converting enzyme 2 receptor- molecular mechanisms | 7          | 1 (14.3%)  | 0.0207  | 0.195   | <a href="#">Wikipathways</a> |
| STAT5 Activation                                                              | 7          | 1 (14.3%)  | 0.0207  | 0.195   | <a href="#">Reactome</a>     |
| serine and glycine biosynthesis                                               | 7          | 1 (14.3%)  | 0.0207  | 0.195   | <a href="#">HumanCyc</a>     |
| ERCC6 (CSB) and EHMT2 (G9a) positively regulate rRNA expression               | 80         | 2 (2.5%)   | 0.0231  | 0.207   | <a href="#">Reactome</a>     |
| Mitochondrial CII Assembly                                                    | 8          | 1 (12.5%)  | 0.0236  | 0.207   | <a href="#">Wikipathways</a> |

|                                                                                      |              |        |       |                     |
|--------------------------------------------------------------------------------------|--------------|--------|-------|---------------------|
| a4b7 Integrin signaling                                                              | 8 1 (12.5%)  | 0.0236 | 0.207 | <b>PID</b>          |
| Sulfur relay system - Homo sapiens (human)                                           | 8 1 (12.5%)  | 0.0236 | 0.207 | <b>KEGG</b>         |
| STAT5 activation downstream of FLT3 ITD mutants                                      | 9 1 (11.1%)  | 0.0265 | 0.22  | <b>Reactome</b>     |
| Ca <sup>2+</sup> activated K <sup>+</sup> channels                                   | 9 1 (11.1%)  | 0.0265 | 0.22  | <b>Reactome</b>     |
| Serine biosynthesis                                                                  | 9 1 (11.1%)  | 0.0265 | 0.22  | <b>Reactome</b>     |
| Sphingolipid metabolism                                                              | 87 2 (2.3%)  | 0.0276 | 0.225 | <b>Reactome</b>     |
| regulation of spermatogenesis by crem                                                | 10 1 (10.0%) | 0.0294 | 0.225 | <b>BioCarta</b>     |
| NS1 Mediated Effects on Host Pathways                                                | 10 1 (10.0%) | 0.0294 | 0.225 | <b>Reactome</b>     |
| regulation of transcriptional activity by pml                                        | 10 1 (10.0%) | 0.0294 | 0.225 | <b>BioCarta</b>     |
| FGFR2b ligand binding and activation                                                 | 10 1 (10.0%) | 0.0294 | 0.225 | <b>Reactome</b>     |
| Negative regulation of FLT3                                                          | 11 1 (9.1%)  | 0.0323 | 0.235 | <b>Reactome</b>     |
| Interferon gamma signaling                                                           | 96 2 (2.1%)  | 0.0331 | 0.235 | <b>Reactome</b>     |
| Hematopoietic cell lineage - Homo sapiens (human)                                    | 99 2 (2.0%)  | 0.0343 | 0.235 | <b>KEGG</b>         |
| melatonin degradation I                                                              | 12 1 (8.3%)  | 0.0352 | 0.235 | <b>HumanCyc</b>     |
| Purine ribonucleoside monophosphate biosynthesis                                     | 12 1 (8.3%)  | 0.0352 | 0.235 | <b>Reactome</b>     |
| Pre-NOTCH Processing in Golgi                                                        | 12 1 (8.3%)  | 0.0352 | 0.235 | <b>Reactome</b>     |
| superpathway of melatonin degradation                                                | 13 1 (7.7%)  | 0.038  | 0.235 | <b>HumanCyc</b>     |
| guanosine ribonucleotides <i>de novo</i> biosynthesis                                | 13 1 (7.7%)  | 0.038  | 0.235 | <b>HumanCyc</b>     |
| Purine nucleotides nucleosides metabolism                                            | 107 2 (1.9%) | 0.0403 | 0.235 | <b>INOH</b>         |
| Osteoblast Signaling                                                                 | 14 1 (7.1%)  | 0.0409 | 0.235 | <b>Wikipathways</b> |
| Positive epigenetic regulation of rRNA expression                                    | 109 2 (1.9%) | 0.041  | 0.235 | <b>Reactome</b>     |
| repression of pain sensation by the transcriptional regulator dream                  | 15 1 (6.7%)  | 0.0438 | 0.235 | <b>BioCarta</b>     |
| Signaling by FLT3 ITD and TKD mutants                                                | 15 1 (6.7%)  | 0.0438 | 0.235 | <b>Reactome</b>     |
| IL-6-type cytokine receptor ligand interactions                                      | 15 1 (6.7%)  | 0.0438 | 0.235 | <b>Reactome</b>     |
| bile acid biosynthesis, neutral pathway                                              | 15 1 (6.7%)  | 0.0438 | 0.235 | <b>HumanCyc</b>     |
| the prc2 complex sets long-term gene silencing through modification of histone tails | 15 1 (6.7%)  | 0.0438 | 0.235 | <b>BioCarta</b>     |
| Mercaptopurine Metabolism Pathway                                                    | 15 1 (6.7%)  | 0.0438 | 0.235 | <b>SMPDB</b>        |
| Nucleobase biosynthesis                                                              | 15 1 (6.7%)  | 0.0438 | 0.235 | <b>Reactome</b>     |
| Osteoclast Signaling                                                                 | 16 1 (6.2%)  | 0.0466 | 0.235 | <b>Wikipathways</b> |
| Interactome of polycomb repressive complex 2 (PRC2)                                  | 16 1 (6.2%)  | 0.0466 | 0.235 | <b>Wikipathways</b> |
| Polo-like kinase mediated events                                                     | 16 1 (6.2%)  | 0.0466 | 0.235 | <b>Reactome</b>     |
| Transcription of E2F targets under negative control by DREAM complex                 | 16 1 (6.2%)  | 0.0466 | 0.235 | <b>Reactome</b>     |
| TCA Cycle and Deficiency of Pyruvate Dehydrogenase complex (PDHc)                    | 16 1 (6.2%)  | 0.0466 | 0.235 | <b>Wikipathways</b> |
| Amplification and Expansion of Oncogenic Pathways as Metastatic Traits               | 16 1 (6.2%)  | 0.0466 | 0.235 | <b>Wikipathways</b> |
| guanosine nucleotides <i>de novo</i> biosynthesis                                    | 16 1 (6.2%)  | 0.0466 | 0.235 | <b>HumanCyc</b>     |
| Glycosphingolipid biosynthesis - neolactoseries                                      | 16 1 (6.2%)  | 0.0466 | 0.235 | <b>EHMN</b>         |
| ACE Inhibitor Pathway                                                                | 17 1 (5.9%)  | 0.0495 | 0.235 | <b>Wikipathways</b> |
| Doxorubicin Metabolism Pathway                                                       | 17 1 (5.9%)  | 0.0495 | 0.235 | <b>SMPDB</b>        |
| TCA Cycle (aka Krebs or citric acid cycle)                                           | 17 1 (5.9%)  | 0.0495 | 0.235 | <b>Wikipathways</b> |
| Cells and molecules involved in local acute inflammatory response                    | 17 1 (5.9%)  | 0.0495 | 0.235 | <b>Wikipathways</b> |
| Beta5 beta6 beta7 and beta8 integrin cell surface interactions                       | 17 1 (5.9%)  | 0.0495 | 0.235 | <b>PID</b>          |

## Hypertension\_SAT

| pathway name                                                                  | candidates |            | p-value | q-value | pathway source |
|-------------------------------------------------------------------------------|------------|------------|---------|---------|----------------|
|                                                                               | set size   | contained  |         |         |                |
| Quinapril Metabolism Pathway                                                  | 1          | 1 (100.0%) | 0.00328 | 0.129   | SMPDB          |
| Ramipril Metabolism Pathway                                                   | 1          | 1 (100.0%) | 0.00328 | 0.129   | SMPDB          |
| Fosinopril Metabolism Pathway                                                 | 1          | 1 (100.0%) | 0.00328 | 0.129   | SMPDB          |
| Moexipril Metabolism Pathway                                                  | 1          | 1 (100.0%) | 0.00328 | 0.129   | SMPDB          |
| Cilazapril Metabolism Pathway                                                 | 1          | 1 (100.0%) | 0.00328 | 0.129   | SMPDB          |
| Enalapril Metabolism Pathway                                                  | 1          | 1 (100.0%) | 0.00328 | 0.129   | SMPDB          |
| Benazepril Metabolism Pathway                                                 | 1          | 1 (100.0%) | 0.00328 | 0.129   | SMPDB          |
| Spirapril Metabolism Pathway                                                  | 1          | 1 (100.0%) | 0.00328 | 0.129   | SMPDB          |
| Trandolapril Metabolism Pathway                                               | 1          | 1 (100.0%) | 0.00328 | 0.129   | SMPDB          |
| Temocapril Metabolism Pathway                                                 | 1          | 1 (100.0%) | 0.00328 | 0.129   | SMPDB          |
| Conversion of Angiotensinogen to Angiotensin II                               | 1          | 1 (100.0%) | 0.00328 | 0.129   | Wikipathways   |
| glutamate removal from folates                                                | 1          | 1 (100.0%) | 0.00328 | 0.129   | HumanCyc       |
| Cargo recognition for clathrin-mediated endocytosis                           | 105        | 3 (2.9%)   | 0.00487 | 0.146   | Reactome       |
| PAOs oxidise polyamines to amines                                             | 2          | 1 (50.0%)  | 0.00654 | 0.146   | Reactome       |
| Interconversion of polyamines                                                 | 3          | 1 (33.3%)  | 0.00979 | 0.146   | Reactome       |
| Intestinal immune network for IgA production - Homo sapiens (human)           | 49         | 2 (4.3%)   | 0.0103  | 0.146   | KEGG           |
| Antigen processing: Ubiquitination & Proteasome degradation                   | 265        | 4 (1.5%)   | 0.0108  | 0.146   | Reactome       |
| Clathrin-mediated endocytosis                                                 | 142        | 3 (2.1%)   | 0.0112  | 0.146   | Reactome       |
| Olmesartan Action Pathway                                                     | 4          | 1 (25.0%)  | 0.013   | 0.146   | SMPDB          |
| Losartan Action Pathway                                                       | 4          | 1 (25.0%)  | 0.013   | 0.146   | SMPDB          |
| Irbesartan Action Pathway                                                     | 4          | 1 (25.0%)  | 0.013   | 0.146   | SMPDB          |
| Forasartan Action Pathway                                                     | 4          | 1 (25.0%)  | 0.013   | 0.146   | SMPDB          |
| Valsartan Action Pathway                                                      | 4          | 1 (25.0%)  | 0.013   | 0.146   | SMPDB          |
| Telmisartan Action Pathway                                                    | 4          | 1 (25.0%)  | 0.013   | 0.146   | SMPDB          |
| Candesartan Action Pathway                                                    | 4          | 1 (25.0%)  | 0.013   | 0.146   | SMPDB          |
| Eprosartan Action Pathway                                                     | 4          | 1 (25.0%)  | 0.013   | 0.146   | SMPDB          |
| Temocapril Action Pathway                                                     | 4          | 1 (25.0%)  | 0.013   | 0.146   | SMPDB          |
| Spirapril Action Pathway                                                      | 4          | 1 (25.0%)  | 0.013   | 0.146   | SMPDB          |
| Trandolapril Action Pathway                                                   | 4          | 1 (25.0%)  | 0.013   | 0.146   | SMPDB          |
| Ramipril Action Pathway                                                       | 4          | 1 (25.0%)  | 0.013   | 0.146   | SMPDB          |
| Rescinnamine Action Pathway                                                   | 4          | 1 (25.0%)  | 0.013   | 0.146   | SMPDB          |
| Perindopril Action Pathway                                                    | 4          | 1 (25.0%)  | 0.013   | 0.146   | SMPDB          |
| Quinapril Action Pathway                                                      | 4          | 1 (25.0%)  | 0.013   | 0.146   | SMPDB          |
| Lisinopril Action Pathway                                                     | 4          | 1 (25.0%)  | 0.013   | 0.146   | SMPDB          |
| Moexipril Action Pathway                                                      | 4          | 1 (25.0%)  | 0.013   | 0.146   | SMPDB          |
| Fosinopril Action Pathway                                                     | 4          | 1 (25.0%)  | 0.013   | 0.146   | SMPDB          |
| Enalapril Action Pathway                                                      | 4          | 1 (25.0%)  | 0.013   | 0.146   | SMPDB          |
| Benazepril Action Pathway                                                     | 4          | 1 (25.0%)  | 0.013   | 0.146   | SMPDB          |
| Cilazapril Action Pathway                                                     | 4          | 1 (25.0%)  | 0.013   | 0.146   | SMPDB          |
| Captopril Action Pathway                                                      | 4          | 1 (25.0%)  | 0.013   | 0.146   | SMPDB          |
| Angiotensin Metabolism                                                        | 4          | 1 (25.0%)  | 0.013   | 0.146   | SMPDB          |
| Amine Oxidase reactions                                                       | 4          | 1 (25.0%)  | 0.013   | 0.146   | Reactome       |
| Binding and entry of HIV virion                                               | 5          | 1 (20.0%)  | 0.0163  | 0.17    | Reactome       |
| hiv-1 defeats host-mediated resistance by cem15                               | 5          | 1 (20.0%)  | 0.0163  | 0.17    | BioCarta       |
| spermine and spermidine degradation I                                         | 5          | 1 (20.0%)  | 0.0163  | 0.17    | HumanCyc       |
| Fc-epsilon receptor I signaling in mast cells                                 | 62         | 2 (3.2%)   | 0.0175  | 0.179   | PID            |
| Class I MHC mediated antigen processing & presentation                        | 316        | 4 (1.3%)   | 0.0195  | 0.195   | Reactome       |
| SARS-CoV-2 and angiotensin-converting enzyme 2 receptor- molecular mechanisms | 7          | 1 (14.3%)  | 0.0227  | 0.223   | Wikipathways   |
| Mitochondrial CII Assembly                                                    | 8          | 1 (12.5%)  | 0.0259  | 0.241   | Wikipathways   |
| Acute viral myocarditis                                                       | 78         | 2 (2.6%)   | 0.0269  | 0.241   | Wikipathways   |
| Prostanoid ligand receptors                                                   | 9          | 1 (11.1%)  | 0.0291  | 0.241   | Reactome       |
| ROS sensing by NFE2L2                                                         | 9          | 1 (11.1%)  | 0.0291  | 0.241   | Reactome       |
| Prevention of phagosomal-lysosomal fusion                                     | 9          | 1 (11.1%)  | 0.0291  | 0.241   | Reactome       |

|                                                                        |              |        |       |                     |
|------------------------------------------------------------------------|--------------|--------|-------|---------------------|
| CXCR4-mediated signaling events                                        | 86 2 (2.3%)  | 0.0322 | 0.241 | <b>PID</b>          |
| RHOBTB3 ATPase cycle                                                   | 10 1 (10.0%) | 0.0323 | 0.241 | <b>Reactome</b>     |
| Respiratory electron transport                                         | 89 2 (2.2%)  | 0.0343 | 0.241 | <b>Reactome</b>     |
| CMP phosphorylation                                                    | 11 1 (9.1%)  | 0.0355 | 0.241 | <b>HumanCyc</b>     |
| cxcr4 signaling pathway                                                | 11 1 (9.1%)  | 0.0355 | 0.241 | <b>BioCarta</b>     |
| pertussis toxin-insensitive ccr5 signaling in macrophage               | 11 1 (9.1%)  | 0.0355 | 0.241 | <b>BioCarta</b>     |
| Rheumatoid arthritis - Homo sapiens (human)                            | 93 2 (2.2%)  | 0.0364 | 0.241 | <b>KEGG</b>         |
| CD28 dependent Vav1 pathway                                            | 12 1 (8.3%)  | 0.0386 | 0.241 | <b>Reactome</b>     |
| pyrimidine deoxyribonucleotide phosphorylation                         | 12 1 (8.3%)  | 0.0386 | 0.241 | <b>HumanCyc</b>     |
| guanosine deoxyribonucleotides <i>de novo</i> biosynthesis             | 12 1 (8.3%)  | 0.0386 | 0.241 | <b>HumanCyc</b>     |
| adenosine deoxyribonucleotides <i>de novo</i> biosynthesis             | 12 1 (8.3%)  | 0.0386 | 0.241 | <b>HumanCyc</b>     |
| Early Phase of HIV Life Cycle                                          | 12 1 (8.3%)  | 0.0386 | 0.241 | <b>Reactome</b>     |
| Degradation of DVL                                                     | 12 1 (8.3%)  | 0.0386 | 0.241 | <b>Reactome</b>     |
| Pre-NOTCH Processing in Golgi                                          | 12 1 (8.3%)  | 0.0386 | 0.241 | <b>Reactome</b>     |
| Processing of DNA double-strand break ends                             | 99 2 (2.0%)  | 0.0409 | 0.241 | <b>Reactome</b>     |
| Control of immune tolerance by vasoactive intestinal peptide           | 13 1 (7.7%)  | 0.0418 | 0.241 | <b>Wikipathways</b> |
| purine deoxyribonucleosides salvage                                    | 13 1 (7.7%)  | 0.0418 | 0.241 | <b>HumanCyc</b>     |
| guanosine ribonucleotides <i>de novo</i> biosynthesis                  | 13 1 (7.7%)  | 0.0418 | 0.241 | <b>HumanCyc</b>     |
| UTP and CTP <i>de novo</i> biosynthesis                                | 13 1 (7.7%)  | 0.0418 | 0.241 | <b>HumanCyc</b>     |
| Methotrexate Action Pathway                                            | 13 1 (7.7%)  | 0.0418 | 0.241 | <b>SMPDB</b>        |
| Folate malabsorption, hereditary                                       | 13 1 (7.7%)  | 0.0418 | 0.241 | <b>SMPDB</b>        |
| Methylenetetrahydrofolate Reductase Deficiency (MTHFRD)                | 13 1 (7.7%)  | 0.0418 | 0.241 | <b>SMPDB</b>        |
| Folate Metabolism                                                      | 13 1 (7.7%)  | 0.0418 | 0.241 | <b>SMPDB</b>        |
| Suppression of phagosomal maturation                                   | 13 1 (7.7%)  | 0.0418 | 0.241 | <b>Reactome</b>     |
| Metabolism of polyamines                                               | 13 1 (7.7%)  | 0.0418 | 0.241 | <b>Reactome</b>     |
| GPCRs, Other                                                           | 101 2 (2.0%) | 0.0432 | 0.241 | <b>Wikipathways</b> |
| Genes related to primary cilium development (based on CRISPR)          | 103 2 (1.9%) | 0.0447 | 0.241 | <b>Wikipathways</b> |
| Shigellosis - Homo sapiens (human)                                     | 246 3 (1.2%) | 0.0464 | 0.241 | <b>KEGG</b>         |
| Macroautophagy                                                         | 106 2 (1.9%) | 0.0471 | 0.241 | <b>Reactome</b>     |
| Cancer immunotherapy by CTLA4 blockade                                 | 15 1 (6.7%)  | 0.048  | 0.241 | <b>Wikipathways</b> |
| superpathway of pyrimidine ribonucleotides <i>de novo</i> biosynthesis | 15 1 (6.7%)  | 0.048  | 0.241 | <b>HumanCyc</b>     |
| Eicosanoid ligand-binding receptors                                    | 15 1 (6.7%)  | 0.048  | 0.241 | <b>Reactome</b>     |
| InlB-mediated entry of Listeria monocytogenes into host cell           | 15 1 (6.7%)  | 0.048  | 0.241 | <b>Reactome</b>     |
| gamma-aminobutyric acid receptor life cycle pathway                    | 15 1 (6.7%)  | 0.048  | 0.241 | <b>BioCarta</b>     |
| Endocytosis - Homo sapiens (human)                                     | 252 3 (1.2%) | 0.0492 | 0.241 | <b>KEGG</b>         |

## Heart\_failure\_SAT

| pathway name                                                         | candidates |           | p-value | q-value | pathway source |
|----------------------------------------------------------------------|------------|-----------|---------|---------|----------------|
|                                                                      | set size   | contained |         |         |                |
| Overview of leukocyte-intrinsic Hippo pathway functions              | 35         | 2 (5.7%)  | 0.00393 | 0.214   | Wikipathways   |
| HSF1-dependent transactivation                                       | 37         | 2 (5.4%)  | 0.00438 | 0.214   | Reactome       |
| Endocytosis - Homo sapiens (human)                                   | 252        | 4 (1.6%)  | 0.00444 | 0.214   | KEGG           |
| GDP-L-fucose biosynthesis II (from L-fucose)                         | 2          | 1 (50.0%) | 0.00535 | 0.214   | HumanCyc       |
| Tight junction - Homo sapiens (human)                                | 169        | 3 (1.8%)  | 0.0103  | 0.214   | KEGG           |
| Composition of Lipid Particles                                       | 4          | 1 (25.0%) | 0.0107  | 0.214   | Wikipathways   |
| NAD salvage                                                          | 4          | 1 (25.0%) | 0.0107  | 0.214   | HumanCyc       |
| Axon guidance - Homo sapiens (human)                                 | 182        | 3 (1.6%)  | 0.0126  | 0.214   | KEGG           |
| lactate fermentation (reoxidation of cytosolic NADH)                 | 5          | 1 (20.0%) | 0.0133  | 0.214   | HumanCyc       |
| Binding and entry of HIV virion                                      | 5          | 1 (20.0%) | 0.0133  | 0.214   | Reactome       |
| hiv-1 defeats host-mediated resistance by cem15                      | 5          | 1 (20.0%) | 0.0133  | 0.214   | BioCarta       |
| NAD biosynthesis from 2-amino-3-carboxymuconate semialdehyde         | 5          | 1 (20.0%) | 0.0133  | 0.214   | HumanCyc       |
| HIF-1-alpha transcription factor network                             | 66         | 2 (3.0%)  | 0.0134  | 0.214   | PID            |
| Joubert Syndrome                                                     | 72         | 2 (2.8%)  | 0.0159  | 0.214   | Wikipathways   |
| mitochondrial L-carnitine shuttle                                    | 6          | 1 (16.7%) | 0.016   | 0.214   | HumanCyc       |
| Metabolic pathway of LDL, HDL and TG, including diseases             | 6          | 1 (16.7%) | 0.016   | 0.214   | Wikipathways   |
| GDP-fucose biosynthesis                                              | 6          | 1 (16.7%) | 0.016   | 0.214   | Reactome       |
| Bacterial invasion of epithelial cells - Homo sapiens (human)        | 77         | 2 (2.6%)  | 0.018   | 0.214   | KEGG           |
| Glycolysis in senescence                                             | 7          | 1 (14.3%) | 0.0186  | 0.214   | Wikipathways   |
| ca-calmodulin-dependent protein kinase activation                    | 8          | 1 (12.5%) | 0.0212  | 0.214   | BioCarta       |
| Excitatory Neural Signalling Through 5-HTR 7 and Serotonin           | 8          | 1 (12.5%) | 0.0212  | 0.214   | SMPDB          |
| HIF1A and PPARG regulation of glycolysis                             | 8          | 1 (12.5%) | 0.0212  | 0.214   | Wikipathways   |
| HDL remodeling                                                       | 9          | 1 (11.1%) | 0.0239  | 0.214   | Reactome       |
| Calcium signaling pathway - Homo sapiens (human)                     | 240        | 3 (1.3%)  | 0.0258  | 0.214   | KEGG           |
| Mitochondrial Beta-Oxidation of Long Chain Saturated Fatty Acids     | 10         | 1 (10.0%) | 0.0265  | 0.214   | SMPDB          |
| Beta Oxidation of Very Long Chain Fatty Acids                        | 10         | 1 (10.0%) | 0.0265  | 0.214   | SMPDB          |
| Adrenoleukodystrophy, X-linked                                       | 10         | 1 (10.0%) | 0.0265  | 0.214   | SMPDB          |
| Carnitine-acylcarnitine translocase deficiency                       | 10         | 1 (10.0%) | 0.0265  | 0.214   | SMPDB          |
| RHOBTB3 ATPase cycle                                                 | 10         | 1 (10.0%) | 0.0265  | 0.214   | Reactome       |
| FBXL7 down-regulates AURKA during mitotic entry and in early mitosis | 10         | 1 (10.0%) | 0.0265  | 0.214   | Reactome       |
| FGFR2b ligand binding and activation                                 | 10         | 1 (10.0%) | 0.0265  | 0.214   | Reactome       |
| AKT phosphorylates targets in the nucleus                            | 10         | 1 (10.0%) | 0.0265  | 0.214   | Reactome       |
| Cellular response to heat stress                                     | 97         | 2 (2.1%)  | 0.0277  | 0.214   | Reactome       |
| Shigellosis - Homo sapiens (human)                                   | 246        | 3 (1.2%)  | 0.0278  | 0.214   | KEGG           |
| B Cell Receptor Signaling Pathway                                    | 98         | 2 (2.0%)  | 0.0283  | 0.214   | Wikipathways   |
| Carnitine metabolism                                                 | 11         | 1 (9.1%)  | 0.0291  | 0.214   | Reactome       |
| CMP phosphorylation                                                  | 11         | 1 (9.1%)  | 0.0291  | 0.214   | HumanCyc       |
| cxcr4 signaling pathway                                              | 11         | 1 (9.1%)  | 0.0291  | 0.214   | BioCarta       |
| pertussis toxin-insensitive ccr5 signaling in macrophage             | 11         | 1 (9.1%)  | 0.0291  | 0.214   | BioCarta       |
| Signaling by Leptin                                                  | 11         | 1 (9.1%)  | 0.0291  | 0.214   | Reactome       |
| Genes related to primary cilium development (based on CRISPR)        | 103        | 2 (1.9%)  | 0.031   | 0.214   | Wikipathways   |
| CaMK IV-mediated phosphorylation of CREB                             | 12         | 1 (8.3%)  | 0.0317  | 0.214   | Reactome       |
| Oxidation of Branched Chain Fatty Acids                              | 12         | 1 (8.3%)  | 0.0317  | 0.214   | SMPDB          |
| Serotonin receptors                                                  | 12         | 1 (8.3%)  | 0.0317  | 0.214   | Reactome       |
| Computational Model of Aerobic Glycolysis                            | 12         | 1 (8.3%)  | 0.0317  | 0.214   | Wikipathways   |
| pyrimidine deoxyribonucleotide phosphorylation                       | 12         | 1 (8.3%)  | 0.0317  | 0.214   | HumanCyc       |
| guanosine deoxyribonucleotides <i>de novo</i> biosynthesis           | 12         | 1 (8.3%)  | 0.0317  | 0.214   | HumanCyc       |
| adenosine deoxyribonucleotides <i>de novo</i> biosynthesis           | 12         | 1 (8.3%)  | 0.0317  | 0.214   | HumanCyc       |
| Early Phase of HIV Life Cycle                                        | 12         | 1 (8.3%)  | 0.0317  | 0.214   | Reactome       |

|                                                                           |                |        |                                    |
|---------------------------------------------------------------------------|----------------|--------|------------------------------------|
| Beta-oxidation of very long chain fatty acids                             | 12 1 (8.3%)    | 0.0317 | 0.214 <a href="#">Reactome</a>     |
| NAD <i>de novo</i> biosynthesis                                           | 12 1 (8.3%)    | 0.0317 | 0.214 <a href="#">HumanCyc</a>     |
| Regulation of localization of FOXO transcription factors                  | 12 1 (8.3%)    | 0.0317 | 0.214 <a href="#">Reactome</a>     |
| EGFR1                                                                     | 455 4 (0.9%)   | 0.0323 | 0.214 <a href="#">NetPath</a>      |
| GPCRs, Class A Rhodopsin-like                                             | 261 3 (1.1%)   | 0.0323 | 0.214 <a href="#">Wikipathways</a> |
| Glucagon signaling pathway - Homo sapiens (human)                         | 107 2 (1.9%)   | 0.0332 | 0.214 <a href="#">KEGG</a>         |
| Purine nucleotides nucleosides metabolism                                 | 107 2 (1.9%)   | 0.0332 | 0.214 <a href="#">INOH</a>         |
| purine deoxyribonucleosides salvage                                       | 13 1 (7.7%)    | 0.0343 | 0.214 <a href="#">HumanCyc</a>     |
| guanosine ribonucleotides <i>de novo</i> biosynthesis                     | 13 1 (7.7%)    | 0.0343 | 0.214 <a href="#">HumanCyc</a>     |
| UTP and CTP <i>de novo</i> biosynthesis                                   | 13 1 (7.7%)    | 0.0343 | 0.214 <a href="#">HumanCyc</a>     |
| HIF-1 signaling pathway - Homo sapiens (human)                            | 109 2 (1.8%)   | 0.0344 | 0.214 <a href="#">KEGG</a>         |
| Long chain acyl-CoA dehydrogenase deficiency (LCAD)                       | 14 1 (7.1%)    | 0.0369 | 0.214 <a href="#">SMPDB</a>        |
| Trifunctional protein deficiency                                          | 14 1 (7.1%)    | 0.0369 | 0.214 <a href="#">SMPDB</a>        |
| Carnitine palmitoyl transferase deficiency (II)                           | 14 1 (7.1%)    | 0.0369 | 0.214 <a href="#">SMPDB</a>        |
| Very-long-chain acyl coa dehydrogenase deficiency (VLCAD)                 | 14 1 (7.1%)    | 0.0369 | 0.214 <a href="#">SMPDB</a>        |
| Medium chain acyl-coa dehydrogenase deficiency (MCAD)                     | 14 1 (7.1%)    | 0.0369 | 0.214 <a href="#">SMPDB</a>        |
| Short Chain Acyl CoA Dehydrogenase Deficiency (SCAD Deficiency)           | 14 1 (7.1%)    | 0.0369 | 0.214 <a href="#">SMPDB</a>        |
| Fatty acid Metabolism                                                     | 14 1 (7.1%)    | 0.0369 | 0.214 <a href="#">SMPDB</a>        |
| Glutaric Aciduria Type I                                                  | 14 1 (7.1%)    | 0.0369 | 0.214 <a href="#">SMPDB</a>        |
| Ethylmalonic Encephalopathy                                               | 14 1 (7.1%)    | 0.0369 | 0.214 <a href="#">SMPDB</a>        |
| Carnitine palmitoyl transferase deficiency (I)                            | 14 1 (7.1%)    | 0.0369 | 0.214 <a href="#">SMPDB</a>        |
| Prolactin receptor signaling                                              | 14 1 (7.1%)    | 0.0369 | 0.214 <a href="#">Reactome</a>     |
| superpathway of pyrimidine ribonucleotides <i>de novo</i> biosynthesis    | 15 1 (6.7%)    | 0.0395 | 0.214 <a href="#">HumanCyc</a>     |
| Neurotrophin signaling pathway - Homo sapiens (human)                     | 119 2 (1.7%)   | 0.0403 | 0.214 <a href="#">KEGG</a>         |
| Cori Cycle                                                                | 16 1 (6.2%)    | 0.042  | 0.214 <a href="#">Wikipathways</a> |
| hypoxia-inducible factor in the cardiovascular system                     | 16 1 (6.2%)    | 0.042  | 0.214 <a href="#">BioCarta</a>     |
| pyrimidine deoxyribonucleotides biosynthesis from CTP                     | 16 1 (6.2%)    | 0.042  | 0.214 <a href="#">HumanCyc</a>     |
| guanosine nucleotides <i>de novo</i> biosynthesis                         | 16 1 (6.2%)    | 0.042  | 0.214 <a href="#">HumanCyc</a>     |
| pyrimidine deoxyribonucleotides <i>de novo</i> biosynthesis               | 16 1 (6.2%)    | 0.042  | 0.214 <a href="#">HumanCyc</a>     |
| Amplification and Expansion of Oncogenic Pathways as Metastatic Traits    | 16 1 (6.2%)    | 0.042  | 0.214 <a href="#">Wikipathways</a> |
| NAD <sup>+</sup> metabolism                                               | 16 1 (6.2%)    | 0.042  | 0.214 <a href="#">Wikipathways</a> |
| Mitochondrial LC-Fatty Acid Beta-Oxidation                                | 17 1 (5.9%)    | 0.0446 | 0.214 <a href="#">Wikipathways</a> |
| superpathway of pyrimidine deoxyribonucleoside salvage                    | 17 1 (5.9%)    | 0.0446 | 0.214 <a href="#">HumanCyc</a>     |
| TGF-beta receptor signaling in EMT (epithelial to mesenchymal transition) | 17 1 (5.9%)    | 0.0446 | 0.214 <a href="#">Reactome</a>     |
| Purine metabolism - Homo sapiens (human)                                  | 130 2 (1.6%)   | 0.0466 | 0.214 <a href="#">KEGG</a>         |
| Fructose intolerance, hereditary                                          | 18 1 (5.6%)    | 0.0472 | 0.214 <a href="#">SMPDB</a>        |
| Fructose and Mannose Degradation                                          | 18 1 (5.6%)    | 0.0472 | 0.214 <a href="#">SMPDB</a>        |
| Fructosuria                                                               | 18 1 (5.6%)    | 0.0472 | 0.214 <a href="#">SMPDB</a>        |
| JAK-STAT-Ncore                                                            | 18 1 (5.6%)    | 0.0472 | 0.214 <a href="#">Signalink</a>    |
| Signal Transduction                                                       | 2432 11 (0.5%) | 0.0484 | 0.214 <a href="#">Reactome</a>     |
| Serotonin Receptor 4-6-7 and NR3C Signaling                               | 19 1 (5.3%)    | 0.0497 | 0.214 <a href="#">Wikipathways</a> |

## Stroke\_SAT

| pathway name                                                                         | candidates |           | p-value | q-value | pathway source |
|--------------------------------------------------------------------------------------|------------|-----------|---------|---------|----------------|
|                                                                                      | set size   | contained |         |         |                |
| Hippo signaling pathway - multiple species - Homo sapiens (human)                    | 29         | 2 (6.9%)  | 0.00142 | 0.163   | KEGG           |
| PAOs oxidise polyamines to amines                                                    | 2          | 1 (50.0%) | 0.00387 | 0.163   | Reactome       |
| Melanin biosynthesis                                                                 | 3          | 1 (33.3%) | 0.0058  | 0.163   | Reactome       |
| Interconversion of polyamines                                                        | 3          | 1 (33.3%) | 0.0058  | 0.163   | Reactome       |
| Peroxisomal protein import                                                           | 64         | 2 (3.1%)  | 0.00675 | 0.163   | Reactome       |
| eumelanin biosynthesis                                                               | 4          | 1 (25.0%) | 0.00772 | 0.163   | HumanCyc       |
| Amine Oxidase reactions                                                              | 4          | 1 (25.0%) | 0.00772 | 0.163   | Reactome       |
| Physiological factors                                                                | 5          | 1 (20.0%) | 0.00964 | 0.163   | Reactome       |
| spermine and spermidine degradation I                                                | 5          | 1 (20.0%) | 0.00964 | 0.163   | HumanCyc       |
| Peroxisome - Homo sapiens (human)                                                    | 82         | 2 (2.4%)  | 0.0109  | 0.163   | KEGG           |
| COPI-mediated anterograde transport                                                  | 83         | 2 (2.4%)  | 0.0111  | 0.163   | Reactome       |
| TYSND1 cleaves peroxisomal proteins                                                  | 7          | 1 (14.3%) | 0.0135  | 0.163   | Reactome       |
| chondroitin sulfate degradation (metazoa)                                            | 7          | 1 (14.3%) | 0.0135  | 0.163   | HumanCyc       |
| coenzyme A biosynthesis                                                              | 7          | 1 (14.3%) | 0.0135  | 0.163   | HumanCyc       |
| brca1 dependent ub ligase activity                                                   | 8          | 1 (12.5%) | 0.0154  | 0.163   | BioCarta       |
| Coenzyme A biosynthesis                                                              | 8          | 1 (12.5%) | 0.0154  | 0.163   | Reactome       |
| Visual phototransduction                                                             | 103        | 2 (1.9%)  | 0.0168  | 0.163   | Reactome       |
| Tyrosine metabolism                                                                  | 108        | 2 (1.9%)  | 0.0184  | 0.163   | EHMN           |
| Gamma-carboxylation of protein precursors                                            | 10         | 1 (10.0%) | 0.0192  | 0.163   | Reactome       |
| Removal of aminoterminal propeptides from gamma-carboxylated proteins                | 10         | 1 (10.0%) | 0.0192  | 0.163   | Reactome       |
| 3-oxo-10R-octadecatrienoate beta-oxidation                                           | 11         | 1 (9.1%)  | 0.0211  | 0.163   | EHMN           |
| Gamma-carboxylation, transport, and amino-terminal cleavage of proteins              | 11         | 1 (9.1%)  | 0.0211  | 0.163   | Reactome       |
| Trihydroxycoprostanoyl-CoA beta-oxidation                                            | 12         | 1 (8.3%)  | 0.023   | 0.163   | EHMN           |
| Beta-oxidation of very long chain fatty acids                                        | 12         | 1 (8.3%)  | 0.023   | 0.163   | Reactome       |
| Scavenging of heme from plasma                                                       | 12         | 1 (8.3%)  | 0.023   | 0.163   | Reactome       |
| how does salmonella hijack a cell                                                    | 12         | 1 (8.3%)  | 0.023   | 0.163   | BioCarta       |
| Estrogen Receptor Pathway                                                            | 13         | 1 (7.7%)  | 0.0249  | 0.163   | Wikipathways   |
| alpha-linolenic acid (ALA) metabolism                                                | 13         | 1 (7.7%)  | 0.0249  | 0.163   | Reactome       |
| alpha-linolenic (omega3) and linoleic (omega6) acid metabolism                       | 13         | 1 (7.7%)  | 0.0249  | 0.163   | Reactome       |
| Metabolism of polyamines                                                             | 13         | 1 (7.7%)  | 0.0249  | 0.163   | Reactome       |
| Lysosome - Homo sapiens (human)                                                      | 128        | 2 (1.6%)  | 0.0252  | 0.163   | KEGG           |
| Omega-3-Omega-6 FA synthesis                                                         | 14         | 1 (7.1%)  | 0.0268  | 0.163   | Wikipathways   |
| Vitamin B5 (pantothenate) metabolism                                                 | 14         | 1 (7.1%)  | 0.0268  | 0.163   | Reactome       |
| ER to Golgi Anterograde Transport                                                    | 136        | 2 (1.5%)  | 0.0282  | 0.163   | Reactome       |
| the pre2 complex sets long-term gene silencing through modification of histone tails | 15         | 1 (6.7%)  | 0.0287  | 0.163   | BioCarta       |
| Vesicle-mediated transport                                                           | 617        | 4 (0.6%)  | 0.0295  | 0.163   | Reactome       |
| Omega-3 fatty acid metabolism                                                        | 16         | 1 (6.2%)  | 0.0305  | 0.163   | EHMN           |
| Phytanic acid peroxisomal oxidation                                                  | 16         | 1 (6.2%)  | 0.0305  | 0.163   | EHMN           |
| SUMOylation of DNA methylation proteins                                              | 17         | 1 (5.9%)  | 0.0324  | 0.163   | Reactome       |
| Glycosaminoglycan degradation                                                        | 17         | 1 (5.9%)  | 0.0324  | 0.163   | Wikipathways   |
| role of pi3k subunit p85 in regulation of actin organization and cell migration      | 17         | 1 (5.9%)  | 0.0324  | 0.163   | BioCarta       |
| y branching of actin filaments                                                       | 17         | 1 (5.9%)  | 0.0324  | 0.163   | BioCarta       |
| role of nicotinic acetylcholine receptors in the regulation of apoptosis             | 17         | 1 (5.9%)  | 0.0324  | 0.163   | BioCarta       |
| Tyrosinemia, transient, of the newborn                                               | 18         | 1 (5.6%)  | 0.0343  | 0.163   | SMPDB          |
| Dopamine beta-hydroxylase deficiency                                                 | 18         | 1 (5.6%)  | 0.0343  | 0.163   | SMPDB          |
| Tyrosine Metabolism                                                                  | 18         | 1 (5.6%)  | 0.0343  | 0.163   | SMPDB          |
| Alkaptonuria                                                                         | 18         | 1 (5.6%)  | 0.0343  | 0.163   | SMPDB          |
| Monoamine oxidase-a deficiency (MAO-A)                                               | 18         | 1 (5.6%)  | 0.0343  | 0.163   | SMPDB          |
| Hawkinsinuria                                                                        | 18         | 1 (5.6%)  | 0.0343  | 0.163   | SMPDB          |
| Tyrosinemia Type I                                                                   | 18         | 1 (5.6%)  | 0.0343  | 0.163   | SMPDB          |
| fatty acid $\beta$ -oxidation (peroxisome)                                           | 19         | 1 (5.3%)  | 0.0362  | 0.163   | HumanCyc       |
| Glycosaminoglycan degradation - Homo sapiens (human)                                 | 19         | 1 (5.3%)  | 0.0362  | 0.163   | KEGG           |
| Signaling by Hippo                                                                   | 20         | 1 (5.0%)  | 0.038   | 0.163   | Reactome       |
| Mono-unsaturated fatty acid beta-oxidation                                           | 21         | 1 (4.8%)  | 0.0399  | 0.163   | EHMN           |
| Pantothenate and CoA biosynthesis - Homo sapiens (human)                             | 21         | 1 (4.8%)  | 0.0399  | 0.163   | KEGG           |
| HS-GAG degradation                                                                   | 21         | 1 (4.8%)  | 0.0399  | 0.163   | Reactome       |
| Protein localization                                                                 | 165        | 2 (1.2%)  | 0.0402  | 0.163   | Reactome       |
| Ion channel transport                                                                | 165        | 2 (1.2%)  | 0.0402  | 0.163   | Reactome       |

|                                                                 |     |          |        |       |                          |
|-----------------------------------------------------------------|-----|----------|--------|-------|--------------------------|
| Transport to the Golgi and subsequent modification              | 167 | 2 (1.2%) | 0.0411 | 0.163 | <a href="#">Reactome</a> |
| role of brca1 brca2 and atr in cancer susceptibility            | 22  | 1 (4.5%) | 0.0418 | 0.163 | <a href="#">BioCarta</a> |
| Tight junction - Homo sapiens (human)                           | 169 | 2 (1.2%) | 0.042  | 0.163 | <a href="#">KEGG</a>     |
| Di-unsaturated fatty acid beta-oxidation                        | 23  | 1 (4.3%) | 0.0436 | 0.166 | <a href="#">EHMN</a>     |
| Metabolism of vitamins and cofactors                            | 180 | 2 (1.1%) | 0.047  | 0.166 | <a href="#">Reactome</a> |
| Saturated fatty acids beta-oxidation                            | 25  | 1 (4.0%) | 0.0473 | 0.166 | <a href="#">EHMN</a>     |
| alpha-Linolenic acid metabolism - Homo sapiens (human)          | 25  | 1 (4.0%) | 0.0473 | 0.166 | <a href="#">KEGG</a>     |
| Disulfiram Action Pathway                                       | 25  | 1 (4.0%) | 0.0473 | 0.166 | <a href="#">SMPDB</a>    |
| Alpha9 beta1 integrin signaling events                          | 25  | 1 (4.0%) | 0.0473 | 0.166 | <a href="#">PID</a>      |
| Insulin receptor recycling                                      | 26  | 1 (3.8%) | 0.0492 | 0.166 | <a href="#">Reactome</a> |
| A tetrasaccharide linker sequence is required for GAG synthesis | 26  | 1 (3.8%) | 0.0492 | 0.166 | <a href="#">Reactome</a> |
| Intra-Golgi and retrograde Golgi-to-ER traffic                  | 186 | 2 (1.1%) | 0.0499 | 0.166 | <a href="#">Reactome</a> |

# Obesity\_VAT

| pathway name                                                                                                                | candidates |            | p-value  | q-value | pathway source               |
|-----------------------------------------------------------------------------------------------------------------------------|------------|------------|----------|---------|------------------------------|
|                                                                                                                             | set size   | contained  |          |         |                              |
| Cation-coupled Chloride cotransporters                                                                                      | 7          | 3 (42.9%)  | 3.68E-05 | 0.0393  | <a href="#">Reactome</a>     |
| Fatty Acid Omega Oxidation                                                                                                  | 15         | 3 (20.0%)  | 0.00045  | 0.24    | <a href="#">Wikipathways</a> |
| Neomycin, kanamycin and gentamicin biosynthesis - Homo sapiens (human)                                                      | 5          | 2 (40.0%)  | 0.00104  | 0.247   | <a href="#">KEGG</a>         |
| D- <i>myo</i> -inositol-5-phosphate metabolism                                                                              | 20         | 3 (15.0%)  | 0.00109  | 0.247   | <a href="#">HumanCyc</a>     |
| Switching of origins to a post-replicative state                                                                            | 47         | 4 (8.5%)   | 0.00139  | 0.247   | <a href="#">Reactome</a>     |
| Inositol Metabolism                                                                                                         | 22         | 3 (13.6%)  | 0.00145  | 0.247   | <a href="#">SMPDB</a>        |
| Retrograde transport at the Trans-Golgi-Network                                                                             | 49         | 4 (8.2%)   | 0.00162  | 0.247   | <a href="#">Reactome</a>     |
| Inositol phosphate metabolism                                                                                               | 51         | 4 (7.8%)   | 0.00188  | 0.251   | <a href="#">Reactome</a>     |
| CDK-mediated phosphorylation and removal of Cdc6                                                                            | 29         | 3 (10.3%)  | 0.00325  | 0.34    | <a href="#">Reactome</a>     |
| Phase I - Functionalization of compounds                                                                                    | 101        | 5 (5.0%)   | 0.00395  | 0.34    | <a href="#">Reactome</a>     |
| Metabolism                                                                                                                  | 1954       | 32 (1.6%)  | 0.00479  | 0.34    | <a href="#">Reactome</a>     |
| superpathway of inositol phosphate compounds                                                                                | 70         | 4 (5.7%)   | 0.00594  | 0.34    | <a href="#">HumanCyc</a>     |
| Celecoxib Action Pathway                                                                                                    | 36         | 3 (8.3%)   | 0.00603  | 0.34    | <a href="#">SMPDB</a>        |
| Miscellaneous substrates                                                                                                    | 12         | 2 (16.7%)  | 0.00655  | 0.34    | <a href="#">Reactome</a>     |
| Inositol phosphate metabolism - Homo sapiens (human)                                                                        | 73         | 4 (5.5%)   | 0.00688  | 0.34    | <a href="#">KEGG</a>         |
| D- <i>myo</i> -inositol (1,4,5)-trisphosphate degradation                                                                   | 13         | 2 (15.4%)  | 0.00769  | 0.34    | <a href="#">HumanCyc</a>     |
| Synthesis of DNA                                                                                                            | 76         | 4 (5.3%)   | 0.00792  | 0.34    | <a href="#">Reactome</a>     |
| Synaptic vesicle cycle - Homo sapiens (human)                                                                               | 78         | 4 (5.1%)   | 0.00867  | 0.34    | <a href="#">KEGG</a>         |
| Inositol phosphate metabolism                                                                                               | 41         | 3 (7.3%)   | 0.00867  | 0.34    | <a href="#">INOH</a>         |
| Synthesis of IP2, IP, and Ins in the cytosol                                                                                | 14         | 2 (14.3%)  | 0.00892  | 0.34    | <a href="#">Reactome</a>     |
| DNA Replication                                                                                                             | 81         | 4 (4.9%)   | 0.00988  | 0.34    | <a href="#">Reactome</a>     |
| Fatty acids                                                                                                                 | 15         | 2 (13.3%)  | 0.0102   | 0.34    | <a href="#">Reactome</a>     |
| geranylgeranyldiphosphate biosynthesis                                                                                      | 1          | 1 (100.0%) | 0.0103   | 0.34    | <a href="#">HumanCyc</a>     |
| L-serine degradation                                                                                                        | 1          | 1 (100.0%) | 0.0103   | 0.34    | <a href="#">HumanCyc</a>     |
| Beta5 beta6 beta7 and beta8 integrin cell surface interactions                                                              | 17         | 2 (11.8%)  | 0.0131   | 0.34    | <a href="#">PID</a>          |
| Huntington disease - Homo sapiens (human)                                                                                   | 306        | 8 (2.6%)   | 0.0142   | 0.34    | <a href="#">KEGG</a>         |
| cdk regulation of dna replication                                                                                           | 18         | 2 (11.1%)  | 0.0146   | 0.34    | <a href="#">BioCarta</a>     |
| GABA synthesis, release, reuptake and degradation                                                                           | 19         | 2 (10.5%)  | 0.0162   | 0.34    | <a href="#">Reactome</a>     |
| Na+/Cl- dependent neurotransmitter transporters                                                                             | 19         | 2 (10.5%)  | 0.0162   | 0.34    | <a href="#">Reactome</a>     |
| superpathway of D- <i>myo</i> -inositol (1,4,5)-trisphosphate metabolism                                                    | 20         | 2 (10.0%)  | 0.0179   | 0.34    | <a href="#">HumanCyc</a>     |
| Assembly of the pre-replicative complex                                                                                     | 20         | 2 (10.0%)  | 0.0179   | 0.34    | <a href="#">Reactome</a>     |
| Phosphatidylinositol signaling system - Homo sapiens (human)                                                                | 97         | 4 (4.1%)   | 0.0181   | 0.34    | <a href="#">KEGG</a>         |
| Conversion from APC/C:Cdc20 to APC/C:Cdh1 in late anaphase                                                                  | 21         | 2 (9.5%)   | 0.0196   | 0.34    | <a href="#">Reactome</a>     |
| Phosphorylation of the APC/C                                                                                                | 21         | 2 (9.5%)   | 0.0196   | 0.34    | <a href="#">Reactome</a>     |
| Aripiprazole Metabolic Pathway                                                                                              | 2          | 1 (50.0%)  | 0.0206   | 0.34    | <a href="#">Wikipathways</a> |
| Cytosolic iron-sulfur cluster assembly                                                                                      | 2          | 1 (50.0%)  | 0.0206   | 0.34    | <a href="#">Reactome</a>     |
| PAOs oxidise polyamines to amines                                                                                           | 2          | 1 (50.0%)  | 0.0206   | 0.34    | <a href="#">Reactome</a>     |
| Inactivation of APC/C via direct inhibition of the APC/C complex                                                            | 22         | 2 (9.1%)   | 0.0214   | 0.34    | <a href="#">Reactome</a>     |
| Inhibition of the proteolytic activity of APC/C required for the onset of anaphase by mitotic spindle checkpoint components | 22         | 2 (9.1%)   | 0.0214   | 0.34    | <a href="#">Reactome</a>     |
| Electron Transport Chain (OXPHOS system in mitochondria)                                                                    | 103        | 4 (3.9%)   | 0.0221   | 0.34    | <a href="#">Wikipathways</a> |
| S Phase                                                                                                                     | 104        | 4 (3.8%)   | 0.0228   | 0.34    | <a href="#">Reactome</a>     |
| Laminin interactions                                                                                                        | 23         | 2 (8.7%)   | 0.0233   | 0.34    | <a href="#">Reactome</a>     |
| Autodegradation of Cdh1 by Cdh1:APC/C                                                                                       | 23         | 2 (8.7%)   | 0.0233   | 0.34    | <a href="#">Reactome</a>     |
| Ciliary landscape                                                                                                           | 213        | 6 (2.8%)   | 0.0234   | 0.34    | <a href="#">Wikipathways</a> |
| Urea cycle and metabolism of arginine, proline, glutamate, aspartate and asparagine                                         | 105        | 4 (3.8%)   | 0.0235   | 0.34    | <a href="#">EHMN</a>         |
| APC/C:Cdc20 mediated degradation of Securin                                                                                 | 24         | 2 (8.3%)   | 0.0253   | 0.34    | <a href="#">Reactome</a>     |
| Biological oxidations                                                                                                       | 219        | 6 (2.7%)   | 0.0263   | 0.34    | <a href="#">Reactome</a>     |
| APC/C:Cdc20 mediated degradation of Cyclin B                                                                                | 25         | 2 (8.0%)   | 0.0273   | 0.34    | <a href="#">Reactome</a>     |
| Orc1 removal from chromatin                                                                                                 | 26         | 2 (7.7%)   | 0.0294   | 0.34    | <a href="#">Reactome</a>     |
| Activation of gene expression by SREBF (SREBP)                                                                              | 26         | 2 (7.7%)   | 0.0294   | 0.34    | <a href="#">Reactome</a>     |
| RAB geranylgeranylation                                                                                                     | 65         | 3 (4.6%)   | 0.0297   | 0.34    | <a href="#">Reactome</a>     |
| Constitutive Signaling by NOTCH1 t(7;9)(NOTCH1:M1580_K2555) Translocation Mutant                                            | 3          | 1 (33.3%)  | 0.0307   | 0.34    | <a href="#">Reactome</a>     |
| Signaling by NOTCH1 t(7;9)(NOTCH1:M1580_K2555) Translocation Mutant                                                         | 3          | 1 (33.3%)  | 0.0307   | 0.34    | <a href="#">Reactome</a>     |
| Adrenaline signalling through Alpha-2 adrenergic receptor                                                                   | 3          | 1 (33.3%)  | 0.0307   | 0.34    | <a href="#">Reactome</a>     |
| Desipramine Metabolism Pathway                                                                                              | 3          | 1 (33.3%)  | 0.0307   | 0.34    | <a href="#">SMPDB</a>        |
| Interleukin-38 signaling                                                                                                    | 3          | 1 (33.3%)  | 0.0307   | 0.34    | <a href="#">Reactome</a>     |
| UTP and CTP dephosphorylation I                                                                                             | 3          | 1 (33.3%)  | 0.0307   | 0.34    | <a href="#">HumanCyc</a>     |
| Interconversion of polyamines                                                                                               | 3          | 1 (33.3%)  | 0.0307   | 0.34    | <a href="#">Reactome</a>     |
| D- <i>myo</i> -inositol (1,4,5)-trisphosphate biosynthesis                                                                  | 27         | 2 (7.4%)   | 0.0315   | 0.34    | <a href="#">HumanCyc</a>     |
| APC-Cdc20 mediated degradation of Nek2A                                                                                     | 27         | 2 (7.4%)   | 0.0315   | 0.34    | <a href="#">Reactome</a>     |
| Glycolysis / Gluconeogenesis - Homo sapiens (human)                                                                         | 67         | 3 (4.5%)   | 0.0321   | 0.34    | <a href="#">KEGG</a>         |
| COPII-mediated vesicle transport                                                                                            | 68         | 3 (4.4%)   | 0.0334   | 0.34    | <a href="#">Reactome</a>     |
| NOTCH-Ncore                                                                                                                 | 28         | 2 (7.1%)   | 0.0337   | 0.34    | <a href="#">Signalink</a>    |
| Transport of small molecules                                                                                                | 641        | 12 (1.9%)  | 0.0339   | 0.34    | <a href="#">Reactome</a>     |
| Fragile X Syndrome                                                                                                          | 119        | 4 (3.4%)   | 0.035    | 0.34    | <a href="#">Wikipathways</a> |
| Cell cycle                                                                                                                  | 120        | 4 (3.3%)   | 0.0359   | 0.34    | <a href="#">Wikipathways</a> |
| Synthesis of IP3 and IP4 in the cytosol                                                                                     | 29         | 2 (6.9%)   | 0.036    | 0.34    | <a href="#">Reactome</a>     |
| Cdc20:Phospho-APC/C mediated degradation of Cyclin A                                                                        | 29         | 2 (6.9%)   | 0.036    | 0.34    | <a href="#">Reactome</a>     |

|                                                                                                          |              |        |       |                              |
|----------------------------------------------------------------------------------------------------------|--------------|--------|-------|------------------------------|
| Molecules associated with elastic fibres                                                                 | 30 2 (6.7%)  | 0.0383 | 0.34  | <a href="#">Reactome</a>     |
| Ketoprofen Action Pathway                                                                                | 30 2 (6.7%)  | 0.0383 | 0.34  | <a href="#">SMPDB</a>        |
| Acetylsalicylic Acid Action Pathway                                                                      | 30 2 (6.7%)  | 0.0383 | 0.34  | <a href="#">SMPDB</a>        |
| Diflunisal Action Pathway                                                                                | 30 2 (6.7%)  | 0.0383 | 0.34  | <a href="#">SMPDB</a>        |
| Acetaminophen Action Pathway                                                                             | 30 2 (6.7%)  | 0.0383 | 0.34  | <a href="#">SMPDB</a>        |
| Sulindac Action Pathway                                                                                  | 30 2 (6.7%)  | 0.0383 | 0.34  | <a href="#">SMPDB</a>        |
| Ketorolac Action Pathway                                                                                 | 30 2 (6.7%)  | 0.0383 | 0.34  | <a href="#">SMPDB</a>        |
| Naproxen Action Pathway                                                                                  | 30 2 (6.7%)  | 0.0383 | 0.34  | <a href="#">SMPDB</a>        |
| Flurbiprofen Action Pathway                                                                              | 30 2 (6.7%)  | 0.0383 | 0.34  | <a href="#">SMPDB</a>        |
| Antrafenine Action Pathway                                                                               | 30 2 (6.7%)  | 0.0383 | 0.34  | <a href="#">SMPDB</a>        |
| Trisalicylate-choline Action Pathway                                                                     | 30 2 (6.7%)  | 0.0383 | 0.34  | <a href="#">SMPDB</a>        |
| Nepafenac Action Pathway                                                                                 | 30 2 (6.7%)  | 0.0383 | 0.34  | <a href="#">SMPDB</a>        |
| Phenylbutazone Action Pathway                                                                            | 30 2 (6.7%)  | 0.0383 | 0.34  | <a href="#">SMPDB</a>        |
| Lornoxicam Action Pathway                                                                                | 30 2 (6.7%)  | 0.0383 | 0.34  | <a href="#">SMPDB</a>        |
| Salsalate Action Pathway                                                                                 | 30 2 (6.7%)  | 0.0383 | 0.34  | <a href="#">SMPDB</a>        |
| Salicylic Acid Action Pathway                                                                            | 30 2 (6.7%)  | 0.0383 | 0.34  | <a href="#">SMPDB</a>        |
| Salicylate-sodium Action Pathway                                                                         | 30 2 (6.7%)  | 0.0383 | 0.34  | <a href="#">SMPDB</a>        |
| Oxaprozin Action Pathway                                                                                 | 30 2 (6.7%)  | 0.0383 | 0.34  | <a href="#">SMPDB</a>        |
| Nabumetone Action Pathway                                                                                | 30 2 (6.7%)  | 0.0383 | 0.34  | <a href="#">SMPDB</a>        |
| Bromfenac Action Pathway                                                                                 | 30 2 (6.7%)  | 0.0383 | 0.34  | <a href="#">SMPDB</a>        |
| Mefenamic Acid Action Pathway                                                                            | 30 2 (6.7%)  | 0.0383 | 0.34  | <a href="#">SMPDB</a>        |
| Piroxicam Action Pathway                                                                                 | 30 2 (6.7%)  | 0.0383 | 0.34  | <a href="#">SMPDB</a>        |
| Carprofen Action Pathway                                                                                 | 30 2 (6.7%)  | 0.0383 | 0.34  | <a href="#">SMPDB</a>        |
| Fenoprofen Action Pathway                                                                                | 30 2 (6.7%)  | 0.0383 | 0.34  | <a href="#">SMPDB</a>        |
| Antipyrine Action Pathway                                                                                | 30 2 (6.7%)  | 0.0383 | 0.34  | <a href="#">SMPDB</a>        |
| Magnesium salicylate Action Pathway                                                                      | 30 2 (6.7%)  | 0.0383 | 0.34  | <a href="#">SMPDB</a>        |
| Tenoxicam Action Pathway                                                                                 | 30 2 (6.7%)  | 0.0383 | 0.34  | <a href="#">SMPDB</a>        |
| Tiaprofenic Acid Action Pathway                                                                          | 30 2 (6.7%)  | 0.0383 | 0.34  | <a href="#">SMPDB</a>        |
| Tolmetin Action Pathway                                                                                  | 30 2 (6.7%)  | 0.0383 | 0.34  | <a href="#">SMPDB</a>        |
| Suprofen Action Pathway                                                                                  | 30 2 (6.7%)  | 0.0383 | 0.34  | <a href="#">SMPDB</a>        |
| Etodolac Action Pathway                                                                                  | 30 2 (6.7%)  | 0.0383 | 0.34  | <a href="#">SMPDB</a>        |
| Rofecoxib Action Pathway                                                                                 | 30 2 (6.7%)  | 0.0383 | 0.34  | <a href="#">SMPDB</a>        |
| Diclofenac Action Pathway                                                                                | 30 2 (6.7%)  | 0.0383 | 0.34  | <a href="#">SMPDB</a>        |
| Etoricoxib Action Pathway                                                                                | 30 2 (6.7%)  | 0.0383 | 0.34  | <a href="#">SMPDB</a>        |
| Lumiracoxib Action Pathway                                                                               | 30 2 (6.7%)  | 0.0383 | 0.34  | <a href="#">SMPDB</a>        |
| Valdecoxib Action Pathway                                                                                | 30 2 (6.7%)  | 0.0383 | 0.34  | <a href="#">SMPDB</a>        |
| Meloxicam Action Pathway                                                                                 | 30 2 (6.7%)  | 0.0383 | 0.34  | <a href="#">SMPDB</a>        |
| Leukotriene C4 Synthesis Deficiency                                                                      | 30 2 (6.7%)  | 0.0383 | 0.34  | <a href="#">SMPDB</a>        |
| Arachidonic Acid Metabolism                                                                              | 30 2 (6.7%)  | 0.0383 | 0.34  | <a href="#">SMPDB</a>        |
| Eicosanoid metabolism via cyclooxygenases (COX)                                                          | 30 2 (6.7%)  | 0.0383 | 0.34  | <a href="#">Wikipathways</a> |
| Trafficking of AMPA receptors                                                                            | 30 2 (6.7%)  | 0.0383 | 0.34  | <a href="#">Reactome</a>     |
| Glutamate binding, activation of AMPA receptors and synaptic plasticity                                  | 30 2 (6.7%)  | 0.0383 | 0.34  | <a href="#">Reactome</a>     |
| APC:Cdc20 mediated degradation of cell cycle proteins prior to satisfaction of the cell cycle checkpoint | 30 2 (6.7%)  | 0.0383 | 0.34  | <a href="#">Reactome</a>     |
| APC/C:Cdh1 mediated degradation of Cdc20 and other APC/C:Cdh1 targeted proteins in late mitosis/early G1 | 30 2 (6.7%)  | 0.0383 | 0.34  | <a href="#">Reactome</a>     |
| Cell cycle - Homo sapiens (human)                                                                        | 124 4 (3.2%) | 0.0398 | 0.34  | <a href="#">KEGG</a>         |
| Activated NOTCH1 Transmits Signal to the Nucleus                                                         | 31 2 (6.5%)  | 0.0406 | 0.34  | <a href="#">Reactome</a>     |
| Galactose metabolism - Homo sapiens (human)                                                              | 31 2 (6.5%)  | 0.0406 | 0.34  | <a href="#">KEGG</a>         |
| Indomethacin Action Pathway                                                                              | 31 2 (6.5%)  | 0.0406 | 0.34  | <a href="#">SMPDB</a>        |
| Regulation of cholesterol biosynthesis by SREBP (SREBF)                                                  | 31 2 (6.5%)  | 0.0406 | 0.34  | <a href="#">Reactome</a>     |
| generation of amyloid b-peptide by ps1                                                                   | 4 1 (25.0%)  | 0.0408 | 0.34  | <a href="#">BioCarta</a>     |
| Clomipramine Metabolism Pathway                                                                          | 4 1 (25.0%)  | 0.0408 | 0.34  | <a href="#">SMPDB</a>        |
| Codeine Metabolism Pathway                                                                               | 4 1 (25.0%)  | 0.0408 | 0.34  | <a href="#">SMPDB</a>        |
| myo -inositol <i>de novo</i> biosynthesis                                                                | 4 1 (25.0%)  | 0.0408 | 0.34  | <a href="#">HumanCyc</a>     |
| Reuptake of GABA                                                                                         | 4 1 (25.0%)  | 0.0408 | 0.34  | <a href="#">Reactome</a>     |
| <i>trans, trans</i> -farnesyl diphosphate biosynthesis                                                   | 4 1 (25.0%)  | 0.0408 | 0.34  | <a href="#">HumanCyc</a>     |
| trehalose degradation                                                                                    | 4 1 (25.0%)  | 0.0408 | 0.34  | <a href="#">HumanCyc</a>     |
| NR1D1 (REV-ERBA) represses gene expression                                                               | 4 1 (25.0%)  | 0.0408 | 0.34  | <a href="#">Reactome</a>     |
| Thiamine Metabolism                                                                                      | 4 1 (25.0%)  | 0.0408 | 0.34  | <a href="#">SMPDB</a>        |
| Valine, leucine and isoleucine biosynthesis - Homo sapiens (human)                                       | 4 1 (25.0%)  | 0.0408 | 0.34  | <a href="#">KEGG</a>         |
| Amine Oxidase reactions                                                                                  | 4 1 (25.0%)  | 0.0408 | 0.34  | <a href="#">Reactome</a>     |
| E2F transcription factor network                                                                         | 75 3 (4.0%)  | 0.0427 | 0.351 | <a href="#">PID</a>          |
| Constitutive Androstane Receptor Pathway                                                                 | 32 2 (6.2%)  | 0.0431 | 0.351 | <a href="#">Wikipathways</a> |
| APC/C:Cdc20 mediated degradation of mitotic proteins                                                     | 32 2 (6.2%)  | 0.0431 | 0.351 | <a href="#">Reactome</a>     |
| Intra-Golgi and retrograde Golgi-to-ER traffic                                                           | 186 5 (2.7%) | 0.044  | 0.355 | <a href="#">Reactome</a>     |
| Fructose and mannose metabolism - Homo sapiens (human)                                                   | 33 2 (6.1%)  | 0.0455 | 0.355 | <a href="#">KEGG</a>         |
| Activation of the pre-replicative complex                                                                | 33 2 (6.1%)  | 0.0455 | 0.355 | <a href="#">Reactome</a>     |
| Tyrosine metabolism                                                                                      | 33 2 (6.1%)  | 0.0455 | 0.355 | <a href="#">INOH</a>         |
| Cargo concentration in the ER                                                                            | 33 2 (6.1%)  | 0.0455 | 0.355 | <a href="#">Reactome</a>     |
| Activation of APC/C and APC/C:Cdc20 mediated degradation of mitotic proteins                             | 33 2 (6.1%)  | 0.0455 | 0.355 | <a href="#">Reactome</a>     |
| Notch                                                                                                    | 78 3 (3.8%)  | 0.047  | 0.364 | <a href="#">INOH</a>         |
| Monoamine GPCRs                                                                                          | 34 2 (5.9%)  | 0.0481 | 0.365 | <a href="#">Wikipathways</a> |

|                                                  |     |          |        |       |              |
|--------------------------------------------------|-----|----------|--------|-------|--------------|
| Mitochondrial CIV Assembly                       | 34  | 2 (5.9%) | 0.0481 | 0.365 | Wikipathways |
| Oxidative phosphorylation - Homo sapiens (human) | 133 | 4 (3.0%) | 0.0493 | 0.365 | KEGG         |

# CAD\_VAT

| pathway name                                                                       | candidates |           | p-value  | q-value | pathway source |
|------------------------------------------------------------------------------------|------------|-----------|----------|---------|----------------|
|                                                                                    | set size   | contained |          |         |                |
| Arachidonic acid metabolism - Homo sapiens (human)                                 | 61         | 3 (4.9%)  | 0.000902 | 0.0343  | KEGG           |
| Acyl chain remodelling of PS                                                       | 22         | 2 (9.1%)  | 0.00212  | 0.0343  | Reactome       |
| Ketoprofen Action Pathway                                                          | 30         | 2 (6.7%)  | 0.00393  | 0.0343  | SMPDB          |
| Acetylsalicylic Acid Action Pathway                                                | 30         | 2 (6.7%)  | 0.00393  | 0.0343  | SMPDB          |
| Diflunisal Action Pathway                                                          | 30         | 2 (6.7%)  | 0.00393  | 0.0343  | SMPDB          |
| Acetaminophen Action Pathway                                                       | 30         | 2 (6.7%)  | 0.00393  | 0.0343  | SMPDB          |
| Sulindac Action Pathway                                                            | 30         | 2 (6.7%)  | 0.00393  | 0.0343  | SMPDB          |
| Ketorolac Action Pathway                                                           | 30         | 2 (6.7%)  | 0.00393  | 0.0343  | SMPDB          |
| Naproxen Action Pathway                                                            | 30         | 2 (6.7%)  | 0.00393  | 0.0343  | SMPDB          |
| Flurbiprofen Action Pathway                                                        | 30         | 2 (6.7%)  | 0.00393  | 0.0343  | SMPDB          |
| Antrafenine Action Pathway                                                         | 30         | 2 (6.7%)  | 0.00393  | 0.0343  | SMPDB          |
| Trisalicylate-choline Action Pathway                                               | 30         | 2 (6.7%)  | 0.00393  | 0.0343  | SMPDB          |
| Nepafenac Action Pathway                                                           | 30         | 2 (6.7%)  | 0.00393  | 0.0343  | SMPDB          |
| Phenylbutazone Action Pathway                                                      | 30         | 2 (6.7%)  | 0.00393  | 0.0343  | SMPDB          |
| Lornoxicam Action Pathway                                                          | 30         | 2 (6.7%)  | 0.00393  | 0.0343  | SMPDB          |
| Salsalate Action Pathway                                                           | 30         | 2 (6.7%)  | 0.00393  | 0.0343  | SMPDB          |
| Salicylic Acid Action Pathway                                                      | 30         | 2 (6.7%)  | 0.00393  | 0.0343  | SMPDB          |
| Salicylate-sodium Action Pathway                                                   | 30         | 2 (6.7%)  | 0.00393  | 0.0343  | SMPDB          |
| Oxaprozin Action Pathway                                                           | 30         | 2 (6.7%)  | 0.00393  | 0.0343  | SMPDB          |
| Nabumetone Action Pathway                                                          | 30         | 2 (6.7%)  | 0.00393  | 0.0343  | SMPDB          |
| Bromfenac Action Pathway                                                           | 30         | 2 (6.7%)  | 0.00393  | 0.0343  | SMPDB          |
| Mefenamic Acid Action Pathway                                                      | 30         | 2 (6.7%)  | 0.00393  | 0.0343  | SMPDB          |
| Piroxicam Action Pathway                                                           | 30         | 2 (6.7%)  | 0.00393  | 0.0343  | SMPDB          |
| Carprofen Action Pathway                                                           | 30         | 2 (6.7%)  | 0.00393  | 0.0343  | SMPDB          |
| Fenoprofen Action Pathway                                                          | 30         | 2 (6.7%)  | 0.00393  | 0.0343  | SMPDB          |
| Antipyrine Action Pathway                                                          | 30         | 2 (6.7%)  | 0.00393  | 0.0343  | SMPDB          |
| Magnesium salicylate Action Pathway                                                | 30         | 2 (6.7%)  | 0.00393  | 0.0343  | SMPDB          |
| Tenoxicam Action Pathway                                                           | 30         | 2 (6.7%)  | 0.00393  | 0.0343  | SMPDB          |
| Tiaprofenic Acid Action Pathway                                                    | 30         | 2 (6.7%)  | 0.00393  | 0.0343  | SMPDB          |
| Tolmetin Action Pathway                                                            | 30         | 2 (6.7%)  | 0.00393  | 0.0343  | SMPDB          |
| Suprofen Action Pathway                                                            | 30         | 2 (6.7%)  | 0.00393  | 0.0343  | SMPDB          |
| Etodolac Action Pathway                                                            | 30         | 2 (6.7%)  | 0.00393  | 0.0343  | SMPDB          |
| Rofecoxib Action Pathway                                                           | 30         | 2 (6.7%)  | 0.00393  | 0.0343  | SMPDB          |
| Diclofenac Action Pathway                                                          | 30         | 2 (6.7%)  | 0.00393  | 0.0343  | SMPDB          |
| Etoricoxib Action Pathway                                                          | 30         | 2 (6.7%)  | 0.00393  | 0.0343  | SMPDB          |
| Lumiracoxib Action Pathway                                                         | 30         | 2 (6.7%)  | 0.00393  | 0.0343  | SMPDB          |
| Valdecoxib Action Pathway                                                          | 30         | 2 (6.7%)  | 0.00393  | 0.0343  | SMPDB          |
| Meloxicam Action Pathway                                                           | 30         | 2 (6.7%)  | 0.00393  | 0.0343  | SMPDB          |
| Leukotriene C4 Synthesis Deficiency                                                | 30         | 2 (6.7%)  | 0.00393  | 0.0343  | SMPDB          |
| Arachidonic Acid Metabolism                                                        | 30         | 2 (6.7%)  | 0.00393  | 0.0343  | SMPDB          |
| Indomethacin Action Pathway                                                        | 31         | 2 (6.5%)  | 0.00419  | 0.0357  | SMPDB          |
| Celecoxib Action Pathway                                                           | 36         | 2 (5.6%)  | 0.00562  | 0.0467  | SMPDB          |
| TP53 Regulates Transcription of Cell Death Genes                                   | 44         | 2 (4.5%)  | 0.00831  | 0.0674  | Reactome       |
| Direct p53 effectors                                                               | 142        | 3 (2.1%)  | 0.00982  | 0.0779  | PID            |
| Ibuprofen Action Pathway                                                           | 50         | 2 (4.0%)  | 0.0106   | 0.0824  | SMPDB          |
| Arachidonic acid metabolism                                                        | 60         | 2 (3.3%)  | 0.0151   | 0.114   | Reactome       |
| SUMO is proteolytically processed                                                  | 6          | 1 (16.7%) | 0.0186   | 0.138   | Reactome       |
| Linoleate metabolism                                                               | 72         | 2 (2.8%)  | 0.0212   | 0.148   | EHMN           |
| Arachidonate Epoxigenase - Epoxide Hydrolase                                       | 7          | 1 (14.3%) | 0.0217   | 0.148   | Wikipathways   |
| Cation-coupled Chloride cotransporters                                             | 7          | 1 (14.3%) | 0.0217   | 0.148   | Reactome       |
| Phosphate bond hydrolysis by NUDT proteins                                         | 7          | 1 (14.3%) | 0.0217   | 0.148   | Reactome       |
| Synthesis of epoxy (EET) and dihydroxyeicosatrienoic acids (DHET)                  | 8          | 1 (12.5%) | 0.0247   | 0.154   | Reactome       |
| Biosynthesis of maresins                                                           | 8          | 1 (12.5%) | 0.0247   | 0.154   | Reactome       |
| Eicosanoid metabolism via cytochrome P450 monooxygenases (CYP) pathway             | 8          | 1 (12.5%) | 0.0247   | 0.154   | Wikipathways   |
| Regulation of cytoskeletal remodeling and cell spreading by IPP complex components | 8          | 1 (12.5%) | 0.0247   | 0.154   | Reactome       |
| Conjugation of salicylate with glycine                                             | 8          | 1 (12.5%) | 0.0247   | 0.154   | Reactome       |
| RNA degradation - Homo sapiens (human)                                             | 79         | 2 (2.5%)  | 0.0253   | 0.155   | KEGG           |
| Rap1 signaling pathway - Homo sapiens (human)                                      | 210        | 3 (1.4%)  | 0.0277   | 0.156   | KEGG           |
| C20 prostanoid biosynthesis                                                        | 9          | 1 (11.1%) | 0.0278   | 0.156   | HumanCyc       |
| Conjugation of carboxylic acids                                                    | 9          | 1 (11.1%) | 0.0278   | 0.156   | Reactome       |
| Amino Acid conjugation                                                             | 9          | 1 (11.1%) | 0.0278   | 0.156   | Reactome       |
| Processing and activation of SUMO                                                  | 9          | 1 (11.1%) | 0.0278   | 0.156   | Reactome       |
| Creatine metabolism                                                                | 11         | 1 (9.1%)  | 0.0339   | 0.188   | Reactome       |
| Ras signaling pathway - Homo sapiens (human)                                       | 232        | 3 (1.3%)  | 0.0356   | 0.191   | KEGG           |
| mRNA surveillance pathway - Homo sapiens (human)                                   | 98         | 2 (2.0%)  | 0.0375   | 0.191   | KEGG           |
| Arachidonic acid metabolism                                                        | 98         | 2 (2.0%)  | 0.0375   | 0.191   | EHMN           |
| Glycerophospholipid metabolism - Homo sapiens (human)                              | 98         | 2 (2.0%)  | 0.0375   | 0.191   | KEGG           |
| Assembly of active LPL and LIPC lipase complexes                                   | 13         | 1 (7.7%)  | 0.0399   | 0.191   | Reactome       |
| Familial lipoprotein lipase deficiency                                             | 13         | 1 (7.7%)  | 0.0399   | 0.191   | SMPDB          |
| Glycerolipid Metabolism                                                            | 13         | 1 (7.7%)  | 0.0399   | 0.191   | SMPDB          |
| Glycerol Kinase Deficiency                                                         | 13         | 1 (7.7%)  | 0.0399   | 0.191   | SMPDB          |
| D-glyceric aciduria                                                                | 13         | 1 (7.7%)  | 0.0399   | 0.191   | SMPDB          |

|                                                                                                                                      |     |          |        |       |                              |
|--------------------------------------------------------------------------------------------------------------------------------------|-----|----------|--------|-------|------------------------------|
| Transcriptional regulation of testis differentiation                                                                                 | 13  | 1 (7.7%) | 0.0399 | 0.191 | <a href="#">Reactome</a>     |
| Heme biosynthesis                                                                                                                    | 14  | 1 (7.1%) | 0.0429 | 0.193 | <a href="#">Reactome</a>     |
| Somatic sex determination                                                                                                            | 14  | 1 (7.1%) | 0.0429 | 0.193 | <a href="#">Wikipathways</a> |
| TP53 regulates transcription of several additional cell death genes whose specific roles in p53-dependent apoptosis remain uncertain | 14  | 1 (7.1%) | 0.0429 | 0.193 | <a href="#">Reactome</a>     |
| Hereditary Coproporphyria (HCP)                                                                                                      | 15  | 1 (6.7%) | 0.0459 | 0.193 | <a href="#">SMPDB</a>        |
| Porphyria Variegata (PV)                                                                                                             | 15  | 1 (6.7%) | 0.0459 | 0.193 | <a href="#">SMPDB</a>        |
| Congenital Erythropoietic Porphyria (CEP) or Gunther Disease                                                                         | 15  | 1 (6.7%) | 0.0459 | 0.193 | <a href="#">SMPDB</a>        |
| Acute Intermittent Porphyria                                                                                                         | 15  | 1 (6.7%) | 0.0459 | 0.193 | <a href="#">SMPDB</a>        |
| Porphyrin Metabolism                                                                                                                 | 15  | 1 (6.7%) | 0.0459 | 0.193 | <a href="#">SMPDB</a>        |
| triacylglycerol degradation                                                                                                          | 15  | 1 (6.7%) | 0.0459 | 0.193 | <a href="#">HumanCyc</a>     |
| Beta-catenin phosphorylation cascade                                                                                                 | 15  | 1 (6.7%) | 0.0459 | 0.193 | <a href="#">Reactome</a>     |
| Phase II - Conjugation of compounds                                                                                                  | 111 | 2 (1.8%) | 0.047  | 0.195 | <a href="#">Reactome</a>     |
| Synthesis of Prostaglandins (PG) and Thromboxanes (TX)                                                                               | 16  | 1 (6.2%) | 0.0489 | 0.196 | <a href="#">Reactome</a>     |
| Cell-extracellular matrix interactions                                                                                               | 16  | 1 (6.2%) | 0.0489 | 0.196 | <a href="#">Reactome</a>     |
| Acyl chain remodelling of PI                                                                                                         | 16  | 1 (6.2%) | 0.0489 | 0.196 | <a href="#">Reactome</a>     |

## T2DM\_VAT

| pathway name                                                                                                                | candidates |           |          |         | pathway source               |
|-----------------------------------------------------------------------------------------------------------------------------|------------|-----------|----------|---------|------------------------------|
|                                                                                                                             | set size   | contained | p-value  | q-value |                              |
| Cation-coupled Chloride cotransporters                                                                                      | 7          | 2 (28.6%) | 0.000341 | 0.117   | <a href="#">Reactome</a>     |
| Fatty Acid Omega Oxidation                                                                                                  | 15         | 2 (13.3%) | 0.00167  | 0.117   | <a href="#">Wikipathways</a> |
| Tyrosinemia, transient, of the newborn                                                                                      | 18         | 2 (11.1%) | 0.00241  | 0.117   | <a href="#">SMPDB</a>        |
| Dopamine beta-hydroxylase deficiency                                                                                        | 18         | 2 (11.1%) | 0.00241  | 0.117   | <a href="#">SMPDB</a>        |
| Tyrosine Metabolism                                                                                                         | 18         | 2 (11.1%) | 0.00241  | 0.117   | <a href="#">SMPDB</a>        |
| Alkaptonuria                                                                                                                | 18         | 2 (11.1%) | 0.00241  | 0.117   | <a href="#">SMPDB</a>        |
| Monoamine oxidase-a deficiency (MAO-A)                                                                                      | 18         | 2 (11.1%) | 0.00241  | 0.117   | <a href="#">SMPDB</a>        |
| Hawkinsinuria                                                                                                               | 18         | 2 (11.1%) | 0.00241  | 0.117   | <a href="#">SMPDB</a>        |
| Tyrosinemia Type I                                                                                                          | 18         | 2 (11.1%) | 0.00241  | 0.117   | <a href="#">SMPDB</a>        |
| Conversion from APC/C:Cdc20 to APC/C:Cdh1 in late anaphase                                                                  | 21         | 2 (9.5%)  | 0.00329  | 0.117   | <a href="#">Reactome</a>     |
| Phosphorylation of the APC/C                                                                                                | 21         | 2 (9.5%)  | 0.00329  | 0.117   | <a href="#">Reactome</a>     |
| Acyl chain remodelling of PS                                                                                                | 22         | 2 (9.1%)  | 0.00361  | 0.117   | <a href="#">Reactome</a>     |
| Inactivation of APC/C via direct inhibition of the APC/C complex                                                            | 22         | 2 (9.1%)  | 0.00361  | 0.117   | <a href="#">Reactome</a>     |
| Inhibition of the proteolytic activity of APC/C required for the onset of anaphase by mitotic spindle checkpoint components | 22         | 2 (9.1%)  | 0.00361  | 0.117   | <a href="#">Reactome</a>     |
| Autodegradation of Cdh1 by Cdh1:APC/C                                                                                       | 23         | 2 (8.7%)  | 0.00394  | 0.118   | <a href="#">Reactome</a>     |
| APC/C:Cdc20 mediated degradation of Securin                                                                                 | 24         | 2 (8.3%)  | 0.00429  | 0.118   | <a href="#">Reactome</a>     |
| Disulfiram Action Pathway                                                                                                   | 25         | 2 (8.0%)  | 0.00465  | 0.118   | <a href="#">SMPDB</a>        |
| APC/C:Cdc20 mediated degradation of Cyclin B                                                                                | 25         | 2 (8.0%)  | 0.00465  | 0.118   | <a href="#">Reactome</a>     |
| APC-Cdc20 mediated degradation of Nek2A                                                                                     | 27         | 2 (7.4%)  | 0.00541  | 0.13    | <a href="#">Reactome</a>     |
| Cdc20:Phospho-APC/C mediated degradation of Cyclin A                                                                        | 29         | 2 (6.9%)  | 0.00622  | 0.132   | <a href="#">Reactome</a>     |
| CDK-mediated phosphorylation and removal of Cdc6                                                                            | 29         | 2 (6.9%)  | 0.00622  | 0.132   | <a href="#">Reactome</a>     |
| APC:Cdc20 mediated degradation of cell cycle proteins prior to satisfaction of the cell cycle checkpoint                    | 30         | 2 (6.7%)  | 0.00665  | 0.132   | <a href="#">Reactome</a>     |
| APC/C:Cdh1 mediated degradation of Cdc20 and other APC/C:Cdh1 targeted proteins in late mitosis/early G1                    | 30         | 2 (6.7%)  | 0.00665  | 0.132   | <a href="#">Reactome</a>     |
| APC/C:Cdc20 mediated degradation of mitotic proteins                                                                        | 32         | 2 (6.2%)  | 0.00755  | 0.133   | <a href="#">Reactome</a>     |
| Type I collagen synthesis in the context of Osteogenesis imperfecta                                                         | 33         | 2 (6.1%)  | 0.00801  | 0.133   | <a href="#">Wikipathways</a> |
| Activation of APC/C and APC/C:Cdc20 mediated degradation of mitotic proteins                                                | 33         | 2 (6.1%)  | 0.00801  | 0.133   | <a href="#">Reactome</a>     |
| Phase I - Functionalization of compounds                                                                                    | 101        | 3 (3.0%)  | 0.00815  | 0.133   | <a href="#">Reactome</a>     |
| PAOs oxidise polyamines to amines                                                                                           | 2          | 1 (50.0%) | 0.00817  | 0.133   | <a href="#">Reactome</a>     |
| Tyrosine metabolism - Homo sapiens (human)                                                                                  | 36         | 2 (5.6%)  | 0.00948  | 0.149   | <a href="#">KEGG</a>         |
| Regulation of APC/C activators between G1/S and early anaphase                                                              | 37         | 2 (5.4%)  | 0.01     | 0.152   | <a href="#">Reactome</a>     |
| phospholipases                                                                                                              | 41         | 2 (4.9%)  | 0.0122   | 0.169   | <a href="#">HumanCyc</a>     |
| Melanin biosynthesis                                                                                                        | 3          | 1 (33.3%) | 0.0122   | 0.169   | <a href="#">Reactome</a>     |
| Interconversion of polyamines                                                                                               | 3          | 1 (33.3%) | 0.0122   | 0.169   | <a href="#">Reactome</a>     |
| APC/C-mediated degradation of cell cycle proteins                                                                           | 44         | 2 (4.5%)  | 0.0139   | 0.182   | <a href="#">Reactome</a>     |
| Regulation of mitotic cell cycle                                                                                            | 44         | 2 (4.5%)  | 0.0139   | 0.182   | <a href="#">Reactome</a>     |
| Switching of origins to a post-replicative state                                                                            | 47         | 2 (4.3%)  | 0.0158   | 0.195   | <a href="#">Reactome</a>     |
| eumelanin biosynthesis                                                                                                      | 4          | 1 (25.0%) | 0.0163   | 0.195   | <a href="#">HumanCyc</a>     |
| Amine Oxidase reactions                                                                                                     | 4          | 1 (25.0%) | 0.0163   | 0.195   | <a href="#">Reactome</a>     |
| Ubiquitin mediated proteolysis - Homo sapiens (human)                                                                       | 140        | 3 (2.1%)  | 0.0196   | 0.22    | <a href="#">KEGG</a>         |
| Dopamine receptors                                                                                                          | 5          | 1 (20.0%) | 0.0203   | 0.22    | <a href="#">Reactome</a>     |
| fatty acid $\alpha$ -oxidation                                                                                              | 5          | 1 (20.0%) | 0.0203   | 0.22    | <a href="#">HumanCyc</a>     |
| spermine and spermidine degradation I                                                                                       | 5          | 1 (20.0%) | 0.0203   | 0.22    | <a href="#">HumanCyc</a>     |
| Complex I biogenesis                                                                                                        | 57         | 2 (3.5%)  | 0.0227   | 0.236   | <a href="#">Reactome</a>     |
| Metabolism                                                                                                                  | 1954       | 14 (0.7%) | 0.023    | 0.236   | <a href="#">Reactome</a>     |
| Alpha-oxidation of phytanate                                                                                                | 6          | 1 (16.7%) | 0.0243   | 0.236   | <a href="#">Reactome</a>     |
| Refsum Disease                                                                                                              | 6          | 1 (16.7%) | 0.0243   | 0.236   | <a href="#">SMPDB</a>        |
| Phytanic Acid Peroxisomal Oxidation                                                                                         | 6          | 1 (16.7%) | 0.0243   | 0.236   | <a href="#">SMPDB</a>        |
| Oxidative phosphorylation                                                                                                   | 61         | 2 (3.3%)  | 0.0258   | 0.245   | <a href="#">Wikipathways</a> |
| Peroxisomal protein import                                                                                                  | 64         | 2 (3.1%)  | 0.0282   | 0.245   | <a href="#">Reactome</a>     |
| TYSND1 cleaves peroxisomal proteins                                                                                         | 7          | 1 (14.3%) | 0.0283   | 0.245   | <a href="#">Reactome</a>     |
| tryptophan degradation to 2-amino-3-carboxymuconate semialdehyde                                                            | 7          | 1 (14.3%) | 0.0283   | 0.245   | <a href="#">HumanCyc</a>     |
| DSCAM interactions                                                                                                          | 7          | 1 (14.3%) | 0.0283   | 0.245   | <a href="#">Reactome</a>     |
| The citric acid (TCA) cycle and respiratory electron transport                                                              | 162        | 3 (1.9%)  | 0.0286   | 0.245   | <a href="#">Reactome</a>     |
| RAB geranylgeranylation                                                                                                     | 65         | 2 (3.1%)  | 0.029    | 0.245   | <a href="#">Reactome</a>     |
| Protein localization                                                                                                        | 165        | 3 (1.8%)  | 0.03     | 0.248   | <a href="#">Reactome</a>     |
| Eicosanoid metabolism via cytochrome P450 monooxygenases (CYP) pathway                                                      | 8          | 1 (12.5%) | 0.0323   | 0.258   | <a href="#">Wikipathways</a> |
| NAD Biosynthesis II (from tryptophan)                                                                                       | 8          | 1 (12.5%) | 0.0323   | 0.258   | <a href="#">Wikipathways</a> |
| RHO GTPases Activate Rhotekin and RhoGins                                                                                   | 9          | 1 (11.1%) | 0.0363   | 0.259   | <a href="#">Reactome</a>     |
| Synthesis of (16-20)-hydroxyeicosatetraenoic acids (HETE)                                                                   | 9          | 1 (11.1%) | 0.0363   | 0.259   | <a href="#">Reactome</a>     |
| tryptophan degradation                                                                                                      | 9          | 1 (11.1%) | 0.0363   | 0.259   | <a href="#">HumanCyc</a>     |
| Uptake and function of anthrax toxins                                                                                       | 9          | 1 (11.1%) | 0.0363   | 0.259   | <a href="#">Reactome</a>     |
| Synthesis of DNA                                                                                                            | 76         | 2 (2.6%)  | 0.0387   | 0.259   | <a href="#">Reactome</a>     |
| Ras signaling                                                                                                               | 184        | 3 (1.6%)  | 0.0395   | 0.259   | <a href="#">Wikipathways</a> |
| DNA Replication                                                                                                             | 81         | 2 (2.5%)  | 0.0434   | 0.259   | <a href="#">Reactome</a>     |
| MET activates RAS signaling                                                                                                 | 11         | 1 (9.1%)  | 0.0441   | 0.259   | <a href="#">Reactome</a>     |
| Peroxisome - Homo sapiens (human)                                                                                           | 82         | 2 (2.4%)  | 0.0444   | 0.259   | <a href="#">KEGG</a>         |
| Ethanol oxidation                                                                                                           | 12         | 1 (8.3%)  | 0.0481   | 0.259   | <a href="#">Reactome</a>     |
| Eicosanoids                                                                                                                 | 12         | 1 (8.3%)  | 0.0481   | 0.259   | <a href="#">Reactome</a>     |

|                                         |    |          |        |       |                              |
|-----------------------------------------|----|----------|--------|-------|------------------------------|
| Miscellaneous substrates                | 12 | 1 (8.3%) | 0.0481 | 0.259 | <a href="#">Reactome</a>     |
| Oxidation of Branched Chain Fatty Acids | 12 | 1 (8.3%) | 0.0481 | 0.259 | <a href="#">SMPDB</a>        |
| Iron metabolism in placenta             | 12 | 1 (8.3%) | 0.0481 | 0.259 | <a href="#">Wikipathways</a> |
| NAD <i>de novo</i> biosynthesis         | 12 | 1 (8.3%) | 0.0481 | 0.259 | <a href="#">HumanCyc</a>     |

## Hypertension\_VAT

| pathway name                                                            | candidates |           | p-value | q-value | pathway source |
|-------------------------------------------------------------------------|------------|-----------|---------|---------|----------------|
|                                                                         | set size   | contained |         |         |                |
| Trafficking of AMPA receptors                                           | 30         | 2 (6.7%)  | 0.00393 | 0.269   | Reactome       |
| Glutamate binding, activation of AMPA receptors and synaptic plasticity | 30         | 2 (6.7%)  | 0.00393 | 0.269   | Reactome       |
| Nucleobase catabolism                                                   | 36         | 2 (5.6%)  | 0.00562 | 0.269   | Reactome       |
| Pyrimidine metabolism                                                   | 135        | 3 (2.2%)  | 0.00856 | 0.269   | EHMN           |
| SUMOylation of transcription cofactors                                  | 47         | 2 (4.3%)  | 0.00944 | 0.269   | Reactome       |
| SUMOylation of RNA binding proteins                                     | 48         | 2 (4.2%)  | 0.00983 | 0.269   | Reactome       |
| Adrenergic signaling in cardiomyocytes - Homo sapiens (human)           | 150        | 3 (2.0%)  | 0.0114  | 0.269   | KEGG           |
| NR1D1 (REV-ERBA) represses gene expression                              | 4          | 1 (25.0%) | 0.0124  | 0.269   | Reactome       |
| SUMO E3 ligases SUMOylate target proteins                               | 177        | 3 (1.7%)  | 0.0177  | 0.269   | Reactome       |
| Glycolysis and Gluconeogenesis                                          | 67         | 2 (3.0%)  | 0.018   | 0.269   | EHMN           |
| SUMOylation                                                             | 182        | 3 (1.6%)  | 0.0191  | 0.269   | Reactome       |
| Glycolysis                                                              | 73         | 2 (2.8%)  | 0.0212  | 0.269   | Reactome       |
| SUMOylation of chromatin organization proteins                          | 72         | 2 (2.8%)  | 0.0212  | 0.269   | Reactome       |
| Phosphate bond hydrolysis by NUDT proteins                              | 7          | 1 (14.3%) | 0.0217  | 0.269   | Reactome       |
| Thyroid hormone synthesis - Homo sapiens (human)                        | 75         | 2 (2.7%)  | 0.0229  | 0.269   | KEGG           |
| Peptide GPCRs                                                           | 75         | 2 (2.7%)  | 0.0229  | 0.269   | Wikipathways   |
| SUMOylation of DNA damage response and repair proteins                  | 78         | 2 (2.6%)  | 0.0247  | 0.269   | Reactome       |
| Linoleic acid (LA) metabolism                                           | 8          | 1 (12.5%) | 0.0247  | 0.269   | Reactome       |
| ROBO receptors bind AKAP5                                               | 9          | 1 (11.1%) | 0.0278  | 0.269   | Reactome       |
| Insulin secretion - Homo sapiens (human)                                | 86         | 2 (2.3%)  | 0.0296  | 0.269   | KEGG           |
| Cardiac muscle contraction - Homo sapiens (human)                       | 87         | 2 (2.3%)  | 0.0302  | 0.269   | KEGG           |
| Formyl peptide receptors bind formyl peptides and many other ligands    | 10         | 1 (10.0%) | 0.0308  | 0.269   | Reactome       |
| Non-homologous end joining                                              | 10         | 1 (10.0%) | 0.0308  | 0.269   | Wikipathways   |
| Purine metabolism                                                       | 222        | 3 (1.4%)  | 0.0319  | 0.269   | EHMN           |
| Glucose metabolism                                                      | 93         | 2 (2.2%)  | 0.0335  | 0.269   | Reactome       |
| Lactose Degradation                                                     | 11         | 1 (9.1%)  | 0.0339  | 0.269   | SMPDB          |
| Lactose Intolerance                                                     | 11         | 1 (9.1%)  | 0.0339  | 0.269   | SMPDB          |
| Dissolution of Fibrin Clot                                              | 11         | 1 (9.1%)  | 0.0339  | 0.269   | Reactome       |
| Synthesis of PIPs at the late endosome membrane                         | 11         | 1 (9.1%)  | 0.0339  | 0.269   | Reactome       |
| Trehalose Degradation                                                   | 12         | 1 (8.3%)  | 0.0369  | 0.269   | SMPDB          |
| Pyrimidine catabolism                                                   | 12         | 1 (8.3%)  | 0.0369  | 0.269   | Reactome       |
| Omega-9 FA synthesis                                                    | 12         | 1 (8.3%)  | 0.0369  | 0.269   | Wikipathways   |
| Hormone ligand-binding receptors                                        | 13         | 1 (7.7%)  | 0.0399  | 0.269   | Reactome       |
| Non-homologous end-joining - Homo sapiens (human)                       | 13         | 1 (7.7%)  | 0.0399  | 0.269   | KEGG           |
| DNA-PK pathway in nonhomologous end joining                             | 13         | 1 (7.7%)  | 0.0399  | 0.269   | PID            |
| alpha-linolenic acid (ALA) metabolism                                   | 13         | 1 (7.7%)  | 0.0399  | 0.269   | Reactome       |
| alpha-linolenic (omega3) and linoleic (omega6) acid metabolism          | 13         | 1 (7.7%)  | 0.0399  | 0.269   | Reactome       |
| Metabolism of nucleotides                                               | 102        | 2 (2.0%)  | 0.0404  | 0.269   | Reactome       |
| Cardiac conduction                                                      | 105        | 2 (1.9%)  | 0.0425  | 0.269   | Reactome       |
| LGI-ADAM interactions                                                   | 14         | 1 (7.1%)  | 0.0429  | 0.269   | Reactome       |
| Macroautophagy                                                          | 106        | 2 (1.9%)  | 0.0433  | 0.269   | Reactome       |
| Phase 2 - plateau phase                                                 | 15         | 1 (6.7%)  | 0.0459  | 0.269   | Reactome       |
| N-Glycan antennae elongation                                            | 15         | 1 (6.7%)  | 0.0459  | 0.269   | Reactome       |
| Autophagy                                                               | 113        | 2 (1.8%)  | 0.0485  | 0.269   | Reactome       |
| Late endosomal microautophagy                                           | 16         | 1 (6.2%)  | 0.0489  | 0.269   | Reactome       |
| Synthesis of PIPs at the early endosome membrane                        | 16         | 1 (6.2%)  | 0.0489  | 0.269   | Reactome       |

## Heart\_failure\_VAT

| pathway name                                                                        | candidates |           |         |         | pathway source               |
|-------------------------------------------------------------------------------------|------------|-----------|---------|---------|------------------------------|
|                                                                                     | set size   | contained | p-value | q-value |                              |
| Synthesis of PA                                                                     | 37         | 2 (5.4%)  | 0.00566 | 0.284   | <a href="#">Reactome</a>     |
| PAOs oxidise polyamines to amines                                                   | 2          | 1 (50.0%) | 0.00609 | 0.284   | <a href="#">Reactome</a>     |
| PTK6 Down-Regulation                                                                | 3          | 1 (33.3%) | 0.00913 | 0.284   | <a href="#">Reactome</a>     |
| Interconversion of polyamines                                                       | 3          | 1 (33.3%) | 0.00913 | 0.284   | <a href="#">Reactome</a>     |
| PTK6 Activates STAT3                                                                | 4          | 1 (25.0%) | 0.0122  | 0.284   | <a href="#">Reactome</a>     |
| NR1D1 (REV-ERBA) represses gene expression                                          | 4          | 1 (25.0%) | 0.0122  | 0.284   | <a href="#">Reactome</a>     |
| Amine Oxidase reactions                                                             | 4          | 1 (25.0%) | 0.0122  | 0.284   | <a href="#">Reactome</a>     |
| TGF-beta Receptor Signaling                                                         | 55         | 2 (3.6%)  | 0.0122  | 0.284   | <a href="#">Wikipathways</a> |
| TGF-beta receptor signaling in skeletal dysplasias                                  | 59         | 2 (3.4%)  | 0.0139  | 0.284   | <a href="#">Wikipathways</a> |
| PTK6 Expression                                                                     | 5          | 1 (20.0%) | 0.0152  | 0.284   | <a href="#">Reactome</a>     |
| PTK6 Regulates Proteins Involved in RNA Processing                                  | 5          | 1 (20.0%) | 0.0152  | 0.284   | <a href="#">Reactome</a>     |
| spermine and spermidine degradation I                                               | 5          | 1 (20.0%) | 0.0152  | 0.284   | <a href="#">HumanCyc</a>     |
| PTK6 Regulates Cell Cycle                                                           | 6          | 1 (16.7%) | 0.0182  | 0.284   | <a href="#">Reactome</a>     |
| PTK6 promotes HIF1A stabilization                                                   | 6          | 1 (16.7%) | 0.0182  | 0.284   | <a href="#">Reactome</a>     |
| Acyl chain remodeling of CL                                                         | 6          | 1 (16.7%) | 0.0182  | 0.284   | <a href="#">Reactome</a>     |
| Anchoring fibril formation                                                          | 7          | 1 (14.3%) | 0.0212  | 0.284   | <a href="#">Reactome</a>     |
| Cation-coupled Chloride cotransporters                                              | 7          | 1 (14.3%) | 0.0212  | 0.284   | <a href="#">Reactome</a>     |
| Focal Adhesion                                                                      | 198        | 3 (1.5%)  | 0.0223  | 0.284   | <a href="#">Wikipathways</a> |
| G1/S Transition                                                                     | 76         | 2 (2.6%)  | 0.0225  | 0.284   | <a href="#">Reactome</a>     |
| Synaptic vesicle cycle - Homo sapiens (human)                                       | 78         | 2 (2.6%)  | 0.0236  | 0.284   | <a href="#">KEGG</a>         |
| Regulation of cytoskeletal remodeling and cell spreading by IPP complex components  | 8          | 1 (12.5%) | 0.0242  | 0.284   | <a href="#">Reactome</a>     |
| Linoleic acid (LA) metabolism                                                       | 8          | 1 (12.5%) | 0.0242  | 0.284   | <a href="#">Reactome</a>     |
| regulation of map kinase pathways through dual specificity phosphatases             | 9          | 1 (11.1%) | 0.0271  | 0.284   | <a href="#">BioCarta</a>     |
| btg family proteins and cell cycle regulation                                       | 9          | 1 (11.1%) | 0.0271  | 0.284   | <a href="#">BioCarta</a>     |
| Type I hemidesmosome assembly                                                       | 9          | 1 (11.1%) | 0.0271  | 0.284   | <a href="#">Reactome</a>     |
| PTK6 Regulates RTKs and Their Effectors AKT1 and DOK1                               | 9          | 1 (11.1%) | 0.0271  | 0.284   | <a href="#">Reactome</a>     |
| ECM-receptor interaction - Homo sapiens (human)                                     | 88         | 2 (2.3%)  | 0.0295  | 0.284   | <a href="#">KEGG</a>         |
| Cell junction organization                                                          | 89         | 2 (2.2%)  | 0.0301  | 0.284   | <a href="#">Reactome</a>     |
| RUNX1 and FOXP3 control the development of regulatory T lymphocytes (Tregs)         | 10         | 1 (10.0%) | 0.0301  | 0.284   | <a href="#">Reactome</a>     |
| RHOBTB3 ATPase cycle                                                                | 10         | 1 (10.0%) | 0.0301  | 0.284   | <a href="#">Reactome</a>     |
| Non-homologous end joining                                                          | 10         | 1 (10.0%) | 0.0301  | 0.284   | <a href="#">Wikipathways</a> |
| Collagen formation                                                                  | 91         | 2 (2.2%)  | 0.0314  | 0.284   | <a href="#">Reactome</a>     |
| Alpha6 beta4 integrin-ligand interactions                                           | 11         | 1 (9.1%)  | 0.0331  | 0.284   | <a href="#">PID</a>          |
| ALK2 signaling events                                                               | 11         | 1 (9.1%)  | 0.0331  | 0.284   | <a href="#">PID</a>          |
| BMP2-WNT4-FOXO1 pathway in primary endometrial stromal cell differentiation         | 11         | 1 (9.1%)  | 0.0331  | 0.284   | <a href="#">Wikipathways</a> |
| Dissolution of Fibrin Clot                                                          | 11         | 1 (9.1%)  | 0.0331  | 0.284   | <a href="#">Reactome</a>     |
| Creatine metabolism                                                                 | 11         | 1 (9.1%)  | 0.0331  | 0.284   | <a href="#">Reactome</a>     |
| Stimuli-sensing channels                                                            | 94         | 2 (2.1%)  | 0.0333  | 0.284   | <a href="#">Reactome</a>     |
| Glycerophospholipid metabolism - Homo sapiens (human)                               | 98         | 2 (2.0%)  | 0.0359  | 0.284   | <a href="#">KEGG</a>         |
| Unwinding of DNA                                                                    | 12         | 1 (8.3%)  | 0.036   | 0.284   | <a href="#">Reactome</a>     |
| Pyrimidine catabolism                                                               | 12         | 1 (8.3%)  | 0.036   | 0.284   | <a href="#">Reactome</a>     |
| Omega-9 FA synthesis                                                                | 12         | 1 (8.3%)  | 0.036   | 0.284   | <a href="#">Wikipathways</a> |
| Pancreatic secretion - Homo sapiens (human)                                         | 102        | 2 (2.0%)  | 0.0386  | 0.284   | <a href="#">KEGG</a>         |
| Hormone ligand-binding receptors                                                    | 13         | 1 (7.7%)  | 0.039   | 0.284   | <a href="#">Reactome</a>     |
| ERBB2 Activates PTK6 Signaling                                                      | 13         | 1 (7.7%)  | 0.039   | 0.284   | <a href="#">Reactome</a>     |
| Non-homologous end-joining - Homo sapiens (human)                                   | 13         | 1 (7.7%)  | 0.039   | 0.284   | <a href="#">KEGG</a>         |
| DNA-PK pathway in nonhomologous end joining                                         | 13         | 1 (7.7%)  | 0.039   | 0.284   | <a href="#">PID</a>          |
| alpha-linolenic acid (ALA) metabolism                                               | 13         | 1 (7.7%)  | 0.039   | 0.284   | <a href="#">Reactome</a>     |
| alpha-linolenic (omega3) and linoleic (omega6) acid metabolism                      | 13         | 1 (7.7%)  | 0.039   | 0.284   | <a href="#">Reactome</a>     |
| Metabolism of polyamines                                                            | 13         | 1 (7.7%)  | 0.039   | 0.284   | <a href="#">Reactome</a>     |
| S Phase                                                                             | 104        | 2 (1.9%)  | 0.04    | 0.284   | <a href="#">Reactome</a>     |
| Mitotic G1 phase and G1/S transition                                                | 104        | 2 (1.9%)  | 0.04    | 0.284   | <a href="#">Reactome</a>     |
| Urea cycle and metabolism of arginine, proline, glutamate, aspartate and asparagine | 105        | 2 (1.9%)  | 0.0407  | 0.284   | <a href="#">EHMN</a>         |

|                                                                                      |    |          |        |       |                          |
|--------------------------------------------------------------------------------------|----|----------|--------|-------|--------------------------|
| PTK6 Regulates RHO GTPases, RAS GTPase and MAP kinases                               | 14 | 1 (7.1%) | 0.0419 | 0.285 | <a href="#">Reactome</a> |
| the prc2 complex sets long-term gene silencing through modification of histone tails | 15 | 1 (6.7%) | 0.0448 | 0.285 | <a href="#">BioCarta</a> |
| RAF-independent MAPK1/3 activation                                                   | 16 | 1 (6.2%) | 0.0478 | 0.285 | <a href="#">Reactome</a> |
| Cell-extracellular matrix interactions                                               | 16 | 1 (6.2%) | 0.0478 | 0.285 | <a href="#">Reactome</a> |
| TFAP2 (AP-2) family regulates transcription of growth factors and their receptors    | 16 | 1 (6.2%) | 0.0478 | 0.285 | <a href="#">Reactome</a> |
| Acyl chain remodelling of PI                                                         | 16 | 1 (6.2%) | 0.0478 | 0.285 | <a href="#">Reactome</a> |

## Stroke\_VAT

| pathway name                                                                      | candidates |            | p-value | q-value | pathway source |
|-----------------------------------------------------------------------------------|------------|------------|---------|---------|----------------|
|                                                                                   | set size   | contained  |         |         |                |
| BMP Signaling Pathway in Eyelid Development                                       | 20         | 2 (10.0%)  | 0.00201 | 0.277   | Wikipathways   |
| geranylgeranyldiphosphate biosynthesis                                            | 1          | 1 (100.0%) | 0.00335 | 0.277   | HumanCyc       |
| alk in cardiac myocytes                                                           | 27         | 2 (7.4%)   | 0.00365 | 0.277   | BioCarta       |
| D- <i>myo</i> -inositol (1,4,5)-trisphosphate biosynthesis                        | 27         | 2 (7.4%)   | 0.00365 | 0.277   | HumanCyc       |
| NOTCH-Ncore                                                                       | 28         | 2 (7.1%)   | 0.00392 | 0.277   | Signalink      |
| Activated NOTCH1 Transmits Signal to the Nucleus                                  | 31         | 2 (6.5%)   | 0.0048  | 0.277   | Reactome       |
| Cytosolic iron-sulfur cluster assembly                                            | 2          | 1 (50.0%)  | 0.00669 | 0.277   | Reactome       |
| PAOs oxidise polyamines to amines                                                 | 2          | 1 (50.0%)  | 0.00669 | 0.277   | Reactome       |
| phospholipases                                                                    | 41         | 2 (4.9%)   | 0.00828 | 0.277   | HumanCyc       |
| BMP receptor signaling                                                            | 41         | 2 (4.9%)   | 0.00828 | 0.277   | PID            |
| Dopaminergic synapse - Homo sapiens (human)                                       | 132        | 3 (2.3%)   | 0.00974 | 0.277   | KEGG           |
| Constitutive Signaling by NOTCH1 t(7;9)(NOTCH1:M1580_K2555) Translocation Mutant  | 3          | 1 (33.3%)  | 0.01    | 0.277   | Reactome       |
| Signaling by NOTCH1 t(7;9)(NOTCH1:M1580_K2555) Translocation Mutant               | 3          | 1 (33.3%)  | 0.01    | 0.277   | Reactome       |
| Interconversion of polyamines                                                     | 3          | 1 (33.3%)  | 0.01    | 0.277   | Reactome       |
| Presenilin action in Notch and Wnt signaling                                      | 46         | 2 (4.3%)   | 0.0103  | 0.277   | PID            |
| Autophagy - animal - Homo sapiens (human)                                         | 137        | 3 (2.2%)   | 0.0108  | 0.277   | KEGG           |
| Clathrin-mediated endocytosis                                                     | 142        | 3 (2.1%)   | 0.0119  | 0.277   | Reactome       |
| generation of amyloid b-peptide by ps1                                            | 4          | 1 (25.0%)  | 0.0133  | 0.277   | BioCarta       |
| <i>trans</i> , <i>trans</i> -farnesyl diphosphate biosynthesis                    | 4          | 1 (25.0%)  | 0.0133  | 0.277   | HumanCyc       |
| proline biosynthesis                                                              | 4          | 1 (25.0%)  | 0.0133  | 0.277   | HumanCyc       |
| Amine Oxidase reactions                                                           | 4          | 1 (25.0%)  | 0.0133  | 0.277   | Reactome       |
| TGF-beta Receptor Signaling                                                       | 55         | 2 (3.6%)   | 0.0146  | 0.277   | Wikipathways   |
| TGF-beta receptor signaling in skeletal dysplasias                                | 59         | 2 (3.4%)   | 0.0166  | 0.277   | Wikipathways   |
| Dopamine receptors                                                                | 5          | 1 (20.0%)  | 0.0166  | 0.277   | Reactome       |
| spermine and spermidine degradation I                                             | 5          | 1 (20.0%)  | 0.0166  | 0.277   | HumanCyc       |
| Novel intracellular components of RIG-I-like receptor (RLR) pathway               | 60         | 2 (3.3%)   | 0.0172  | 0.277   | Wikipathways   |
| Peroxisomal protein import                                                        | 64         | 2 (3.1%)   | 0.0194  | 0.277   | Reactome       |
| Glypican 3 network                                                                | 6          | 1 (16.7%)  | 0.0199  | 0.277   | PID            |
| Downstream signaling in naïve CD8+ T cells                                        | 68         | 2 (2.9%)   | 0.0217  | 0.277   | PID            |
| Epithelial cell signaling in Helicobacter pylori infection - Homo sapiens (human) | 70         | 2 (2.9%)   | 0.0229  | 0.277   | KEGG           |
| superpathway of inositol phosphate compounds                                      | 70         | 2 (2.9%)   | 0.0229  | 0.277   | HumanCyc       |
| RIG-I-like receptor signaling pathway - Homo sapiens (human)                      | 70         | 2 (2.9%)   | 0.0229  | 0.277   | KEGG           |
| Nef Mediated CD8 Down-regulation                                                  | 7          | 1 (14.3%)  | 0.0232  | 0.277   | Reactome       |
| DSCAM interactions                                                                | 7          | 1 (14.3%)  | 0.0232  | 0.277   | Reactome       |
| Vitamin B2 (riboflavin) metabolism                                                | 7          | 1 (14.3%)  | 0.0232  | 0.277   | Reactome       |
| Cellular Senescence                                                               | 187        | 3 (1.6%)   | 0.0242  | 0.277   | Reactome       |
| Inositol phosphate metabolism - Homo sapiens (human)                              | 73         | 2 (2.7%)   | 0.0248  | 0.277   | KEGG           |
| Signaling by NOTCH                                                                | 190        | 3 (1.6%)   | 0.0252  | 0.277   | Reactome       |
| Signaling by NOTCH1                                                               | 74         | 2 (2.7%)   | 0.0254  | 0.277   | Reactome       |
| Competing endogenous RNAs (ceRNAs) regulate PTEN translation                      | 8          | 1 (12.5%)  | 0.0265  | 0.277   | Reactome       |
| Regulation of PTEN mRNA translation                                               | 8          | 1 (12.5%)  | 0.0265  | 0.277   | Reactome       |
| Rapid glucocorticoid signaling                                                    | 8          | 1 (12.5%)  | 0.0265  | 0.277   | PID            |
| Conjugation of salicylate with glycine                                            | 8          | 1 (12.5%)  | 0.0265  | 0.277   | Reactome       |
| TP53 Regulates Metabolic Genes                                                    | 76         | 2 (2.6%)   | 0.0267  | 0.277   | Reactome       |
| Transcriptional regulation by RUNX1                                               | 196        | 3 (1.5%)   | 0.0274  | 0.277   | Reactome       |
| Notch                                                                             | 78         | 2 (2.6%)   | 0.028   | 0.277   | INOH           |
| Class A/1 (Rhodopsin-like receptors)                                              | 346        | 4 (1.2%)   | 0.0281  | 0.277   | Reactome       |
| Nef Mediated CD4 Down-regulation                                                  | 9          | 1 (11.1%)  | 0.0298  | 0.277   | Reactome       |
| Conjugation of carboxylic acids                                                   | 9          | 1 (11.1%)  | 0.0298  | 0.277   | Reactome       |
| Amino Acid conjugation                                                            | 9          | 1 (11.1%)  | 0.0298  | 0.277   | Reactome       |
| Peroxisome - Homo sapiens (human)                                                 | 82         | 2 (2.4%)   | 0.0308  | 0.277   | KEGG           |
| Axon guidance                                                                     | 356        | 4 (1.1%)   | 0.0308  | 0.277   | Reactome       |
| Peptide ligand-binding receptors                                                  | 207        | 3 (1.4%)   | 0.0319  | 0.277   | Reactome       |
| VLDLR internalisation and degradation                                             | 10         | 1 (10.0%)  | 0.033   | 0.277   | Reactome       |
| Activation of the AP-1 family of transcription factors                            | 10         | 1 (10.0%)  | 0.033   | 0.277   | Reactome       |
| RUNX1 and FOXP3 control the development of regulatory T lymphocytes (Tregs)       | 10         | 1 (10.0%)  | 0.033   | 0.277   | Reactome       |

|                                                                                |               |        |                       |
|--------------------------------------------------------------------------------|---------------|--------|-----------------------|
| ALK2 signaling events                                                          | 11 1 (9.1%)   | 0.0362 | 0.277 <b>PID</b>      |
| BMP2-WNT4-FOXO1 pathway in primary endometrial stromal cell differentiation    | 11 1 (9.1%)   | 0.0362 | 0.277 Wikipathways    |
| PIP3 activates AKT signaling                                                   | 218 3 (1.4%)  | 0.0363 | 0.277 <b>Reactome</b> |
| Biological oxidations                                                          | 219 3 (1.4%)  | 0.0367 | 0.277 <b>Reactome</b> |
| Nervous system development                                                     | 379 4 (1.1%)  | 0.0375 | 0.277 <b>Reactome</b> |
| PTEN Regulation                                                                | 93 2 (2.2%)   | 0.0387 | 0.277 <b>Reactome</b> |
| TGF-beta signaling pathway - Homo sapiens (human)                              | 94 2 (2.1%)   | 0.0395 | 0.277 <b>KEGG</b>     |
| superpathway of geranylgeranyldiphosphate biosynthesis I (via mevalonate)      | 12 1 (8.3%)   | 0.0395 | 0.277 <b>HumanCyc</b> |
| Generic Transcription Pathway                                                  | 1178 8 (0.7%) | 0.0397 | 0.277 <b>Reactome</b> |
| Inflammatory mediator regulation of TRP channels - Homo sapiens (human)        | 98 2 (2.0%)   | 0.0426 | 0.277 <b>KEGG</b>     |
| Metabolism of polyamines                                                       | 13 1 (7.7%)   | 0.0427 | 0.277 <b>Reactome</b> |
| Progesterone-mediated oocyte maturation - Homo sapiens (human)                 | 100 2 (2.0%)  | 0.0441 | 0.277 <b>KEGG</b>     |
| AGE-RAGE signaling pathway in diabetic complications - Homo sapiens (human)    | 100 2 (2.0%)  | 0.0441 | 0.277 <b>KEGG</b>     |
| Wnt signaling pathway and pluripotency                                         | 101 2 (2.0%)  | 0.0449 | 0.277 Wikipathways    |
| L1CAM interactions                                                             | 102 2 (2.0%)  | 0.0458 | 0.277 <b>Reactome</b> |
| Retrograde neurotrophin signalling                                             | 14 1 (7.1%)   | 0.0459 | 0.277 <b>Reactome</b> |
| Cargo recognition for clathrin-mediated endocytosis                            | 105 2 (1.9%)  | 0.0482 | 0.277 <b>Reactome</b> |
| Shigellosis - Homo sapiens (human)                                             | 246 3 (1.2%)  | 0.049  | 0.277 <b>KEGG</b>     |
| Constitutive Signaling by NOTCH1 HD Domain Mutants                             | 15 1 (6.7%)   | 0.0491 | 0.277 <b>Reactome</b> |
| Signaling by NOTCH1 HD Domain Mutants in Cancer                                | 15 1 (6.7%)   | 0.0491 | 0.277 <b>Reactome</b> |
| WNT5A-dependent internalization of FZD4                                        | 15 1 (6.7%)   | 0.0491 | 0.277 <b>Reactome</b> |
| Beta-catenin phosphorylation cascade                                           | 15 1 (6.7%)   | 0.0491 | 0.277 <b>Reactome</b> |
| EPHA-mediated growth cone collapse                                             | 15 1 (6.7%)   | 0.0491 | 0.277 <b>Reactome</b> |
| Glutamate and glutamine metabolism                                             | 15 1 (6.7%)   | 0.0491 | 0.277 <b>Reactome</b> |
| Regulation of sister chromatid separation at the metaphase-anaphase transition | 15 1 (6.7%)   | 0.0491 | 0.277 Wikipathways    |
| GPR40 Pathway                                                                  | 15 1 (6.7%)   | 0.0491 | 0.277 Wikipathways    |

## Depression\_TRD

| pathway name                                                                         | candidates |           |         |         | pathway source |
|--------------------------------------------------------------------------------------|------------|-----------|---------|---------|----------------|
|                                                                                      | set size   | contained | p-value | q-value |                |
| trehalose degradation                                                                | 4          | 1 (25.0%) | 0.00238 | 0.0759  | HumanCyc       |
| D-galactose degradation V (Leloir pathway)                                           | 6          | 1 (16.7%) | 0.00357 | 0.0759  | HumanCyc       |
| sucrose degradation                                                                  | 8          | 1 (12.5%) | 0.00476 | 0.0759  | HumanCyc       |
| spliceosomal assembly                                                                | 9          | 1 (11.1%) | 0.00535 | 0.0759  | BioCarta       |
| the prc2 complex sets long-term gene silencing through modification of histone tails | 15         | 1 (6.7%)  | 0.0089  | 0.0759  | BioCarta       |
| Glycolysis                                                                           | 15         | 1 (6.7%)  | 0.0089  | 0.0759  | SMPDB          |
| Glycogenosis, Type VII. Tarui disease                                                | 15         | 1 (6.7%)  | 0.0089  | 0.0759  | SMPDB          |
| Fanconi-bickel syndrome                                                              | 15         | 1 (6.7%)  | 0.0089  | 0.0759  | SMPDB          |
| SUMOylation of DNA methylation proteins                                              | 17         | 1 (5.9%)  | 0.0101  | 0.0759  | Reactome       |
| Gluconeogenesis                                                                      | 22         | 1 (4.5%)  | 0.013   | 0.0759  | SMPDB          |
| Glycogenosis, Type IA. Von gierke disease                                            | 22         | 1 (4.5%)  | 0.013   | 0.0759  | SMPDB          |
| Glycogenosis, Type IC                                                                | 22         | 1 (4.5%)  | 0.013   | 0.0759  | SMPDB          |
| Glycogen Storage Disease Type 1A (GSD1A) or Von Gierke Disease                       | 22         | 1 (4.5%)  | 0.013   | 0.0759  | SMPDB          |
| Triosephosphate isomerase                                                            | 22         | 1 (4.5%)  | 0.013   | 0.0759  | SMPDB          |
| Fructose-1,6-diphosphatase deficiency                                                | 22         | 1 (4.5%)  | 0.013   | 0.0759  | SMPDB          |
| Phosphoenolpyruvate carboxykinase deficiency 1 (PEPCK1)                              | 22         | 1 (4.5%)  | 0.013   | 0.0759  | SMPDB          |
| Glycogenosis, Type IB                                                                | 22         | 1 (4.5%)  | 0.013   | 0.0759  | SMPDB          |
| Vitamin digestion and absorption - Homo sapiens (human)                              | 24         | 1 (4.2%)  | 0.0142  | 0.0771  | KEGG           |
| alpha-Linolenic acid metabolism - Homo sapiens (human)                               | 25         | 1 (4.0%)  | 0.0148  | 0.0771  | KEGG           |
| Acyl chain remodelling of PC                                                         | 27         | 1 (3.7%)  | 0.016   | 0.0771  | Reactome       |
| NOTCH-Ncore                                                                          | 28         | 1 (3.6%)  | 0.0166  | 0.0771  | Signalink      |
| Linoleic acid metabolism - Homo sapiens (human)                                      | 29         | 1 (3.4%)  | 0.0171  | 0.0771  | KEGG           |
| Galactose metabolism - Homo sapiens (human)                                          | 31         | 1 (3.2%)  | 0.0183  | 0.0788  | KEGG           |
| Transcriptional Regulation by E2F6                                                   | 35         | 1 (2.9%)  | 0.0207  | 0.0852  | Reactome       |
| RUNX1 interacts with co-factors whose precise effect on RUNX1 targets is not known   | 39         | 1 (2.6%)  | 0.023   | 0.0865  | Reactome       |
| phospholipases                                                                       | 41         | 1 (2.4%)  | 0.0242  | 0.0865  | HumanCyc       |
| Deposition of new CENPA-containing nucleosomes at the centromere                     | 43         | 1 (2.3%)  | 0.0253  | 0.0865  | Reactome       |
| Nucleosome assembly                                                                  | 43         | 1 (2.3%)  | 0.0253  | 0.0865  | Reactome       |
| Retinoid metabolism and transport                                                    | 45         | 1 (2.2%)  | 0.0265  | 0.0865  | Reactome       |
| SUMOylation of transcription cofactors                                               | 47         | 1 (2.1%)  | 0.0277  | 0.0865  | Reactome       |
| SUMOylation of RNA binding proteins                                                  | 48         | 1 (2.1%)  | 0.0282  | 0.0865  | Reactome       |
| Metabolism of fat-soluble vitamins                                                   | 49         | 1 (2.0%)  | 0.0288  | 0.0865  | Reactome       |
| Ether lipid metabolism - Homo sapiens (human)                                        | 49         | 1 (2.0%)  | 0.0288  | 0.0865  | KEGG           |
| Regulation of PTEN gene transcription                                                | 60         | 1 (1.7%)  | 0.0352  | 0.101   | Reactome       |
| Arachidonic acid metabolism - Homo sapiens (human)                                   | 61         | 1 (1.6%)  | 0.0358  | 0.101   | KEGG           |
| Mitochondrial protein import                                                         | 65         | 1 (1.5%)  | 0.0381  | 0.105   | Reactome       |
| Glycolysis / Gluconeogenesis - Homo sapiens (human)                                  | 67         | 1 (1.5%)  | 0.0392  | 0.105   | KEGG           |
| SUMOylation of chromatin organization proteins                                       | 72         | 1 (1.4%)  | 0.0421  | 0.108   | Reactome       |
| MECP2 and Associated Rett Syndrome                                                   | 73         | 1 (1.4%)  | 0.0427  | 0.108   | Wikipathways   |
| SUMOylation of DNA damage response and repair proteins                               | 78         | 1 (1.3%)  | 0.0455  | 0.113   | Reactome       |

## Depression\_Admission

| pathway name                                                | candidates |           | p-value | q-value | pathway source |
|-------------------------------------------------------------|------------|-----------|---------|---------|----------------|
|                                                             | set size   | contained |         |         |                |
| Glial Cell Differentiation                                  | 8          | 1 (12.5%) | 0.00179 | 0.0214  | Wikipathways   |
| Regulation of Microtubule Cytoskeleton                      | 46         | 1 (2.2%)  | 0.0102  | 0.0325  | Wikipathways   |
| Notch-mediated HES/HEY network                              | 48         | 1 (2.1%)  | 0.0107  | 0.0325  | PID            |
| Notch                                                       | 58         | 1 (1.7%)  | 0.0129  | 0.0325  | NetPath        |
| Notch Signaling Pathway Netpath                             | 61         | 1 (1.6%)  | 0.0136  | 0.0325  | Wikipathways   |
| Interferon gamma signaling                                  | 96         | 1 (1.0%)  | 0.0213  | 0.0426  | Reactome       |
| Osteoblast differentiation                                  | 118        | 1 (0.8%)  | 0.0261  | 0.0448  | Wikipathways   |
| Sudden Infant Death Syndrome (SIDS) Susceptibility Pathways | 159        | 1 (0.6%)  | 0.0351  | 0.0477  | Wikipathways   |
| Interferon Signaling                                        | 162        | 1 (0.6%)  | 0.0357  | 0.0477  | Reactome       |

## T2DM\_mortality

| pathway name                                                           | candidates |           | p-value | q-value | pathway source |
|------------------------------------------------------------------------|------------|-----------|---------|---------|----------------|
|                                                                        | set size   | contained |         |         |                |
| Oxidative phosphorylation - Homo sapiens (human)                       | 133        | 2 (1.5%)  | 0.0107  | 0.204   | KEGG           |
| MASTL Facilitates Mitotic Progression                                  | 10         | 1 (10.0%) | 0.0119  | 0.204   | Reactome       |
| Zinc influx into cells by the SLC39 gene family                        | 10         | 1 (10.0%) | 0.0119  | 0.204   | Reactome       |
| Assembly of active LPL and LIPC lipase complexes                       | 13         | 1 (7.7%)  | 0.0154  | 0.204   | Reactome       |
| Familial lipoprotein lipase deficiency                                 | 13         | 1 (7.7%)  | 0.0154  | 0.204   | SMPDB          |
| Glycerolipid Metabolism                                                | 13         | 1 (7.7%)  | 0.0154  | 0.204   | SMPDB          |
| Glycerol Kinase Deficiency                                             | 13         | 1 (7.7%)  | 0.0154  | 0.204   | SMPDB          |
| D-glyceric aciduria                                                    | 13         | 1 (7.7%)  | 0.0154  | 0.204   | SMPDB          |
| triacylglycerol degradation                                            | 15         | 1 (6.7%)  | 0.0177  | 0.204   | HumanCyc       |
| Zinc transporters                                                      | 17         | 1 (5.9%)  | 0.0201  | 0.204   | Reactome       |
| retinol biosynthesis                                                   | 19         | 1 (5.3%)  | 0.0224  | 0.204   | HumanCyc       |
| TP53 Regulates Transcription of Genes Involved in Cytochrome C Release | 20         | 1 (5.0%)  | 0.0236  | 0.204   | Reactome       |
| Triacylglyceride synthesis                                             | 24         | 1 (4.2%)  | 0.0282  | 0.204   | Wikipathways   |
| Plasma lipoprotein remodeling                                          | 26         | 1 (3.8%)  | 0.0305  | 0.204   | Reactome       |
| Insulin receptor recycling                                             | 26         | 1 (3.8%)  | 0.0305  | 0.204   | Reactome       |
| Metal ion SLC transporters                                             | 26         | 1 (3.8%)  | 0.0305  | 0.204   | Reactome       |
| Collecting duct acid secretion - Homo sapiens (human)                  | 27         | 1 (3.7%)  | 0.0317  | 0.204   | KEGG           |
| Statin inhibition of cholesterol production                            | 31         | 1 (3.2%)  | 0.0363  | 0.204   | Wikipathways   |
| Ovarian infertility                                                    | 31         | 1 (3.2%)  | 0.0363  | 0.204   | Wikipathways   |
| Transferrin endocytosis and recycling                                  | 31         | 1 (3.2%)  | 0.0363  | 0.204   | Reactome       |
| Transport of small molecules                                           | 641        | 3 (0.5%)  | 0.0381  | 0.204   | Reactome       |
| Fatty acid beta-oxidation                                              | 34         | 1 (2.9%)  | 0.0398  | 0.204   | Wikipathways   |
| Amino acids regulate mTORC1                                            | 34         | 1 (2.9%)  | 0.0398  | 0.204   | Reactome       |
| ROS and RNS production in phagocytes                                   | 35         | 1 (2.9%)  | 0.0409  | 0.204   | Reactome       |
| Zinc homeostasis                                                       | 37         | 1 (2.7%)  | 0.0432  | 0.204   | Wikipathways   |
| adenosine ribonucleotides <i>de novo</i> biosynthesis                  | 38         | 1 (2.6%)  | 0.0443  | 0.204   | HumanCyc       |

## T2DM\_admission

| pathway name                                                                                | candidates |           |         |         | pathway source               |
|---------------------------------------------------------------------------------------------|------------|-----------|---------|---------|------------------------------|
|                                                                                             | set size   | contained | p-value | q-value |                              |
| Proximal tubule bicarbonate reclamation - Homo sapiens (human)                              | 23         | 2 (8.7%)  | 0.00135 | 0.198   | <a href="#">KEGG</a>         |
| PAOs oxidise polyamines to amines                                                           | 2          | 1 (50.0%) | 0.00476 | 0.198   | <a href="#">Reactome</a>     |
| Interconversion of polyamines                                                               | 3          | 1 (33.3%) | 0.00713 | 0.198   | <a href="#">Reactome</a>     |
| Proximal tubule transport                                                                   | 57         | 2 (3.5%)  | 0.00809 | 0.198   | <a href="#">Wikipathways</a> |
| Amine Oxidase reactions                                                                     | 4          | 1 (25.0%) | 0.0095  | 0.198   | <a href="#">Reactome</a>     |
| O-linked glycosylation of mucins                                                            | 66         | 2 (3.0%)  | 0.0107  | 0.198   | <a href="#">Reactome</a>     |
| hiv-1 defeats host-mediated resistance by cem15                                             | 5          | 1 (20.0%) | 0.0119  | 0.198   | <a href="#">BioCarta</a>     |
| spermine and spermidine degradation I                                                       | 5          | 1 (20.0%) | 0.0119  | 0.198   | <a href="#">HumanCyc</a>     |
| TP53 Regulates Metabolic Genes                                                              | 76         | 2 (2.6%)  | 0.014   | 0.198   | <a href="#">Reactome</a>     |
| Potential therapeutics for SARS                                                             | 80         | 2 (2.5%)  | 0.0155  | 0.198   | <a href="#">Reactome</a>     |
| NoRC negatively regulates rRNA expression                                                   | 81         | 2 (2.5%)  | 0.0155  | 0.198   | <a href="#">Reactome</a>     |
| Peroxisome - Homo sapiens (human)                                                           | 82         | 2 (2.4%)  | 0.0162  | 0.198   | <a href="#">KEGG</a>         |
| IL-2 signaling                                                                              | 7          | 1 (14.3%) | 0.0166  | 0.198   | <a href="#">INOH</a>         |
| APOBEC3G mediated resistance to HIV-1 infection                                             | 7          | 1 (14.3%) | 0.0166  | 0.198   | <a href="#">Reactome</a>     |
| Cardiac muscle contraction - Homo sapiens (human)                                           | 87         | 2 (2.3%)  | 0.0181  | 0.198   | <a href="#">KEGG</a>         |
| Negative epigenetic regulation of rRNA expression                                           | 89         | 2 (2.3%)  | 0.0185  | 0.198   | <a href="#">Reactome</a>     |
| Dual hijack model of Vif in HIV infection                                                   | 8          | 1 (12.5%) | 0.0189  | 0.198   | <a href="#">Wikipathways</a> |
| Erythrocytes take up oxygen and release carbon dioxide                                      | 9          | 1 (11.1%) | 0.0212  | 0.198   | <a href="#">Reactome</a>     |
| reversal of insulin resistance by leptin                                                    | 9          | 1 (11.1%) | 0.0212  | 0.198   | <a href="#">BioCarta</a>     |
| MTHFR deficiency                                                                            | 10         | 1 (10.0%) | 0.0236  | 0.198   | <a href="#">Wikipathways</a> |
| Trans-sulfuration pathway                                                                   | 10         | 1 (10.0%) | 0.0236  | 0.198   | <a href="#">Wikipathways</a> |
| NLR Proteins                                                                                | 10         | 1 (10.0%) | 0.0236  | 0.198   | <a href="#">Wikipathways</a> |
| RUNX1 and FOXP3 control the development of regulatory T lymphocytes (Tregs)                 | 10         | 1 (10.0%) | 0.0236  | 0.198   | <a href="#">Reactome</a>     |
| Leptin and adiponectin                                                                      | 10         | 1 (10.0%) | 0.0236  | 0.198   | <a href="#">Wikipathways</a> |
| Activation of PPARGC1A (PGC-1alpha) by phosphorylation                                      | 10         | 1 (10.0%) | 0.0236  | 0.198   | <a href="#">Reactome</a>     |
| Vif-mediated degradation of APOBEC3G                                                        | 10         | 1 (10.0%) | 0.0236  | 0.198   | <a href="#">Reactome</a>     |
| Pancreatic secretion - Homo sapiens (human)                                                 | 102        | 2 (2.0%)  | 0.0244  | 0.198   | <a href="#">KEGG</a>         |
| Urea cycle and metabolism of arginine, proline, glutamate, aspartate and asparagine         | 105        | 2 (1.9%)  | 0.0258  | 0.198   | <a href="#">EHMN</a>         |
| Lactose Degradation                                                                         | 11         | 1 (9.1%)  | 0.0259  | 0.198   | <a href="#">SMPDB</a>        |
| Lactose Intolerance                                                                         | 11         | 1 (9.1%)  | 0.0259  | 0.198   | <a href="#">SMPDB</a>        |
| Interaction With Cumulus Cells And The Zona Pellucida                                       | 11         | 1 (9.1%)  | 0.0259  | 0.198   | <a href="#">Reactome</a>     |
| MET activates RAS signaling                                                                 | 11         | 1 (9.1%)  | 0.0259  | 0.198   | <a href="#">Reactome</a>     |
| Trehalose Degradation                                                                       | 12         | 1 (8.3%)  | 0.0282  | 0.198   | <a href="#">SMPDB</a>        |
| Reversible hydration of carbon dioxide                                                      | 12         | 1 (8.3%)  | 0.0282  | 0.198   | <a href="#">Reactome</a>     |
| FOXP3 in COVID-19                                                                           | 12         | 1 (8.3%)  | 0.0282  | 0.198   | <a href="#">Wikipathways</a> |
| Interleukin-2 signaling                                                                     | 12         | 1 (8.3%)  | 0.0282  | 0.198   | <a href="#">Reactome</a>     |
| Activation of AMPK downstream of NMDARs                                                     | 12         | 1 (8.3%)  | 0.0282  | 0.198   | <a href="#">Reactome</a>     |
| Regulation of signaling by NODAL                                                            | 12         | 1 (8.3%)  | 0.0282  | 0.198   | <a href="#">Reactome</a>     |
| SARS-CoV Infections                                                                         | 111        | 2 (1.8%)  | 0.0286  | 0.198   | <a href="#">Reactome</a>     |
| O-linked glycosylation                                                                      | 115        | 2 (1.7%)  | 0.0305  | 0.198   | <a href="#">Reactome</a>     |
| Erythrocytes take up carbon dioxide and release oxygen                                      | 13         | 1 (7.7%)  | 0.0305  | 0.198   | <a href="#">Reactome</a>     |
| O2/CO2 exchange in erythrocytes                                                             | 13         | 1 (7.7%)  | 0.0305  | 0.198   | <a href="#">Reactome</a>     |
| FGFR3c ligand binding and activation                                                        | 13         | 1 (7.7%)  | 0.0305  | 0.198   | <a href="#">Reactome</a>     |
| FGFR3 ligand binding and activation                                                         | 13         | 1 (7.7%)  | 0.0305  | 0.198   | <a href="#">Reactome</a>     |
| Metabolism of polyamines                                                                    | 13         | 1 (7.7%)  | 0.0305  | 0.198   | <a href="#">Reactome</a>     |
| il 2 signaling pathway                                                                      | 14         | 1 (7.1%)  | 0.0329  | 0.198   | <a href="#">BioCarta</a>     |
| Repression of WNT target genes                                                              | 14         | 1 (7.1%)  | 0.0329  | 0.198   | <a href="#">Reactome</a>     |
| Phytochemical activity on NRF2 transcriptional activation                                   | 15         | 1 (6.7%)  | 0.0352  | 0.198   | <a href="#">Wikipathways</a> |
| COVID-19 adverse outcome pathway                                                            | 15         | 1 (6.7%)  | 0.0352  | 0.198   | <a href="#">Wikipathways</a> |
| Mitochondrial complex III assembly                                                          | 16         | 1 (6.2%)  | 0.0375  | 0.198   | <a href="#">Wikipathways</a> |
| Acyl chain remodelling of PI                                                                | 16         | 1 (6.2%)  | 0.0375  | 0.198   | <a href="#">Reactome</a>     |
| Nitrogen metabolism - Homo sapiens (human)                                                  | 17         | 1 (5.9%)  | 0.0398  | 0.198   | <a href="#">KEGG</a>         |
| SUMOylation of DNA methylation proteins                                                     | 17         | 1 (5.9%)  | 0.0398  | 0.198   | <a href="#">Reactome</a>     |
| Deregulated CDK5 triggers multiple neurodegenerative pathways in Alzheimer,s disease models | 18         | 1 (5.6%)  | 0.042   | 0.198   | <a href="#">Reactome</a>     |
| Neurodegenerative Diseases                                                                  | 18         | 1 (5.6%)  | 0.042   | 0.198   | <a href="#">Reactome</a>     |
| Acyl chain remodelling of PG                                                                | 18         | 1 (5.6%)  | 0.042   | 0.198   | <a href="#">Reactome</a>     |
| Signaling by FLT3 fusion proteins                                                           | 18         | 1 (5.6%)  | 0.042   | 0.198   | <a href="#">Reactome</a>     |
| Signaling by cytosolic FGFR1 fusion mutants                                                 | 18         | 1 (5.6%)  | 0.042   | 0.198   | <a href="#">Reactome</a>     |
| Epigenetic regulation of gene expression                                                    | 140        | 2 (1.4%)  | 0.0431  | 0.198   | <a href="#">Reactome</a>     |
| Hematopoietic Stem Cell Gene Regulation by GABP alpha-beta Complex                          | 19         | 1 (5.3%)  | 0.0443  | 0.198   | <a href="#">Wikipathways</a> |
| Ephrin signaling                                                                            | 19         | 1 (5.3%)  | 0.0443  | 0.198   | <a href="#">Reactome</a>     |

|                                                                                                      |      |          |        |       |                          |
|------------------------------------------------------------------------------------------------------|------|----------|--------|-------|--------------------------|
| S-Adenosylhomocysteine (SAH) Hydrolase Deficiency                                                    | 20   | 1 (5.0%) | 0.0466 | 0.198 | SMPDB                    |
| Methionine Metabolism                                                                                | 20   | 1 (5.0%) | 0.0466 | 0.198 | SMPDB                    |
| Methionine Adenosyltransferase Deficiency                                                            | 20   | 1 (5.0%) | 0.0466 | 0.198 | SMPDB                    |
| Glycine N-methyltransferase Deficiency                                                               | 20   | 1 (5.0%) | 0.0466 | 0.198 | SMPDB                    |
| Hypermethioninemia                                                                                   | 20   | 1 (5.0%) | 0.0466 | 0.198 | SMPDB                    |
| Methylenetetrahydrofolate Reductase Deficiency (MTHFRD)                                              | 20   | 1 (5.0%) | 0.0466 | 0.198 | SMPDB                    |
| Homocystinuria-megaloblastic anemia due to defect in cobalamin metabolism, cblG complementation type | 20   | 1 (5.0%) | 0.0466 | 0.198 | SMPDB                    |
| Cystathionine Beta-Synthase Deficiency                                                               | 20   | 1 (5.0%) | 0.0466 | 0.198 | SMPDB                    |
| Signaling by NODAL                                                                                   | 20   | 1 (5.0%) | 0.0466 | 0.198 | <a href="#">Reactome</a> |
| TP53 Regulates Transcription of Genes Involved in Cytochrome C Release                               | 20   | 1 (5.0%) | 0.0466 | 0.198 | <a href="#">Reactome</a> |
| Mitochondrial tRNA aminoacylation                                                                    | 21   | 1 (4.8%) | 0.0489 | 0.198 | <a href="#">Reactome</a> |
| FLT3 signaling in disease                                                                            | 21   | 1 (4.8%) | 0.0489 | 0.198 | <a href="#">Reactome</a> |
| Gene expression (Transcription)                                                                      | 1439 | 7 (0.5%) | 0.0489 | 0.198 | <a href="#">Reactome</a> |
| Non-alcoholic fatty liver disease - Homo sapiens (human)                                             | 150  | 2 (1.3%) | 0.0494 | 0.198 | <a href="#">KEGG</a>     |

## CAD\_mortality\_SAT

| pathway name                                                                                  | candidates |           | p-value | q-value | pathway source               |
|-----------------------------------------------------------------------------------------------|------------|-----------|---------|---------|------------------------------|
|                                                                                               | set size   | contained |         |         |                              |
| Laminin interactions                                                                          | 23         | 2 (8.7%)  | 0.00103 | 0.286   | <a href="#">Reactome</a>     |
| Non-integrin membrane-ECM interactions                                                        | 42         | 2 (4.8%)  | 0.00343 | 0.286   | <a href="#">Reactome</a>     |
| ECM proteoglycans                                                                             | 56         | 2 (3.6%)  | 0.00602 | 0.286   | <a href="#">Reactome</a>     |
| Integrin cell surface interactions                                                            | 66         | 2 (3.0%)  | 0.00828 | 0.286   | <a href="#">Reactome</a>     |
| Proteoglycans in cancer - Homo sapiens (human)                                                | 205        | 3 (1.5%)  | 0.00866 | 0.286   | <a href="#">KEGG</a>         |
| Arrhythmogenic Right Ventricular Cardiomyopathy                                               | 74         | 2 (2.7%)  | 0.0103  | 0.286   | <a href="#">Wikipathways</a> |
| Degradation pathway of sphingolipids, including diseases                                      | 5          | 1 (20.0%) | 0.0104  | 0.286   | <a href="#">Wikipathways</a> |
| Arrhythmogenic right ventricular cardiomyopathy - Homo sapiens (human)                        | 77         | 2 (2.6%)  | 0.0111  | 0.286   | <a href="#">KEGG</a>         |
| ECM-receptor interaction - Homo sapiens (human)                                               | 88         | 2 (2.3%)  | 0.0144  | 0.286   | <a href="#">KEGG</a>         |
| ca-calmodulin-dependent protein kinase activation                                             | 8          | 1 (12.5%) | 0.0166  | 0.286   | <a href="#">BioCarta</a>     |
| Cross-presentation of particulate exogenous antigens (phagosomes)                             | 8          | 1 (12.5%) | 0.0166  | 0.286   | <a href="#">Reactome</a>     |
| Bile acids synthesis and enterohepatic circulation                                            | 9          | 1 (11.1%) | 0.0186  | 0.286   | <a href="#">Wikipathways</a> |
| SLBP independent Processing of Histone Pre-mRNAs                                              | 10         | 1 (10.0%) | 0.0207  | 0.286   | <a href="#">Reactome</a>     |
| Gamma-carboxylation of protein precursors                                                     | 10         | 1 (10.0%) | 0.0207  | 0.286   | <a href="#">Reactome</a>     |
| Removal of aminoterminal propeptides from gamma-carboxylated proteins                         | 10         | 1 (10.0%) | 0.0207  | 0.286   | <a href="#">Reactome</a>     |
| Liver X receptor pathway                                                                      | 10         | 1 (10.0%) | 0.0207  | 0.286   | <a href="#">Wikipathways</a> |
| Apoptotic cleavage of cell adhesion proteins                                                  | 11         | 1 (9.1%)  | 0.0227  | 0.286   | <a href="#">Reactome</a>     |
| SLBP Dependent Processing of Replication-Dependent Histone Pre-mRNAs                          | 11         | 1 (9.1%)  | 0.0227  | 0.286   | <a href="#">Reactome</a>     |
| Gamma-carboxylation, transport, and amino-terminal cleavage of proteins                       | 11         | 1 (9.1%)  | 0.0227  | 0.286   | <a href="#">Reactome</a>     |
| CaMK IV-mediated phosphorylation of CREB                                                      | 12         | 1 (8.3%)  | 0.0247  | 0.286   | <a href="#">Reactome</a>     |
| PECAM1 interactions                                                                           | 12         | 1 (8.3%)  | 0.0247  | 0.286   | <a href="#">Reactome</a>     |
| Osteopontin Signaling                                                                         | 13         | 1 (7.7%)  | 0.0268  | 0.286   | <a href="#">Wikipathways</a> |
| MFAP5-mediated ovarian cancer cell motility and invasiveness                                  | 13         | 1 (7.7%)  | 0.0268  | 0.286   | <a href="#">Wikipathways</a> |
| Integrin                                                                                      | 124        | 2 (1.6%)  | 0.0273  | 0.286   | <a href="#">INOH</a>         |
| PDGFR-beta signaling pathway                                                                  | 127        | 2 (1.6%)  | 0.0286  | 0.286   | <a href="#">PID</a>          |
| Osteoblast Signaling                                                                          | 14         | 1 (7.1%)  | 0.0288  | 0.286   | <a href="#">Wikipathways</a> |
| Lysosome - Homo sapiens (human)                                                               | 128        | 2 (1.6%)  | 0.029   | 0.286   | <a href="#">KEGG</a>         |
| Late endosomal microautophagy                                                                 | 16         | 1 (6.2%)  | 0.0329  | 0.286   | <a href="#">Reactome</a>     |
| Beta5 beta6 beta7 and beta8 integrin cell surface interactions                                | 17         | 1 (5.9%)  | 0.0349  | 0.286   | <a href="#">PID</a>          |
| Clathrin-mediated endocytosis                                                                 | 142        | 2 (1.4%)  | 0.0351  | 0.286   | <a href="#">Reactome</a>     |
| MFAP5 effect on permeability and motility of endothelial cells via cytoskeleton rearrangement | 18         | 1 (5.6%)  | 0.0369  | 0.286   | <a href="#">Wikipathways</a> |
| ABC transporters in lipid homeostasis                                                         | 18         | 1 (5.6%)  | 0.0369  | 0.286   | <a href="#">Reactome</a>     |
| Unblocking of NMDA receptors, glutamate binding and activation                                | 20         | 1 (5.0%)  | 0.0409  | 0.286   | <a href="#">Reactome</a>     |
| Syndecan interactions                                                                         | 20         | 1 (5.0%)  | 0.0409  | 0.286   | <a href="#">Reactome</a>     |
| regulation of pgc-1a                                                                          | 21         | 1 (4.8%)  | 0.0429  | 0.286   | <a href="#">BioCarta</a>     |
| HS-GAG degradation                                                                            | 21         | 1 (4.8%)  | 0.0429  | 0.286   | <a href="#">Reactome</a>     |
| EGF-EGFR signaling pathway                                                                    | 162        | 2 (1.2%)  | 0.0445  | 0.286   | <a href="#">Wikipathways</a> |
| Ras activation upon Ca2+ influx through NMDA receptor                                         | 22         | 1 (4.5%)  | 0.0449  | 0.286   | <a href="#">Reactome</a>     |
| Signal transduction by L1                                                                     | 22         | 1 (4.5%)  | 0.0449  | 0.286   | <a href="#">Reactome</a>     |
| PDGFR-alpha signaling pathway                                                                 | 22         | 1 (4.5%)  | 0.0449  | 0.286   | <a href="#">PID</a>          |
| Chaperone Mediated Autophagy                                                                  | 22         | 1 (4.5%)  | 0.0449  | 0.286   | <a href="#">Reactome</a>     |
| Long-term potentiation                                                                        | 23         | 1 (4.3%)  | 0.0469  | 0.286   | <a href="#">Reactome</a>     |
| Negative regulation of NMDA receptor-mediated neuronal transmission                           | 23         | 1 (4.3%)  | 0.0469  | 0.286   | <a href="#">Reactome</a>     |
| Plexin-D1 Signaling                                                                           | 24         | 1 (4.2%)  | 0.0489  | 0.286   | <a href="#">PID</a>          |
| snRNP Assembly                                                                                | 24         | 1 (4.2%)  | 0.0489  | 0.286   | <a href="#">Reactome</a>     |
| Metabolism of non-coding RNA                                                                  | 24         | 1 (4.2%)  | 0.0489  | 0.286   | <a href="#">Reactome</a>     |

## CAD\_admission\_SAT

| pathway name                                                                     | candidates |            | p-value  | q-value | pathway source |
|----------------------------------------------------------------------------------|------------|------------|----------|---------|----------------|
|                                                                                  | set size   | contained  |          |         |                |
| TCA Cycle (aka Krebs or citric acid cycle)                                       | 17         | 2 (11.8%)  | 0.000875 | 0.0573  | Wikipathways   |
| TCA cycle                                                                        | 19         | 2 (10.5%)  | 0.0011   | 0.0573  | HumanCyc       |
| Pyruvate dehydrogenase deficiency (E3)                                           | 21         | 2 (9.5%)   | 0.00134  | 0.0573  | SMPDB          |
| Pyruvate dehydrogenase deficiency (E2)                                           | 21         | 2 (9.5%)   | 0.00134  | 0.0573  | SMPDB          |
| 2-ketoglutarate dehydrogenase complex deficiency                                 | 21         | 2 (9.5%)   | 0.00134  | 0.0573  | SMPDB          |
| Mitochondrial complex II deficiency                                              | 21         | 2 (9.5%)   | 0.00134  | 0.0573  | SMPDB          |
| Fumarase deficiency                                                              | 21         | 2 (9.5%)   | 0.00134  | 0.0573  | SMPDB          |
| Congenital lactic acidosis                                                       | 21         | 2 (9.5%)   | 0.00134  | 0.0573  | SMPDB          |
| Citric Acid Cycle                                                                | 21         | 2 (9.5%)   | 0.00134  | 0.0573  | SMPDB          |
| Citric acid cycle (TCA cycle)                                                    | 22         | 2 (9.1%)   | 0.00147  | 0.0573  | Reactome       |
| The oncogenic action of 2-hydroxyglutarate                                       | 27         | 2 (7.4%)   | 0.00222  | 0.0577  | SMPDB          |
| The oncogenic action of L-2-hydroxyglutarate in Hydroxyglutaricaciduria          | 29         | 2 (6.9%)   | 0.00256  | 0.0577  | SMPDB          |
| Metabolism of Tetrahydrocannabinol (THC)                                         | 1          | 1 (100.0%) | 0.00261  | 0.0577  | Wikipathways   |
| Citrate cycle (TCA cycle) - Homo sapiens (human)                                 | 30         | 2 (6.7%)   | 0.00274  | 0.0577  | KEGG           |
| The oncogenic action of D-2-hydroxyglutarate in Hydroxyglutaricaciduria          | 30         | 2 (6.7%)   | 0.00274  | 0.0577  | SMPDB          |
| TCA cycle                                                                        | 30         | 2 (6.7%)   | 0.00274  | 0.0577  | EHMN           |
| The oncogenic action of Succinate                                                | 31         | 2 (6.5%)   | 0.00292  | 0.0577  | SMPDB          |
| The oncogenic action of Fumarate                                                 | 31         | 2 (6.5%)   | 0.00292  | 0.0577  | SMPDB          |
| Transferrin endocytosis and recycling                                            | 31         | 2 (6.5%)   | 0.00292  | 0.0577  | Reactome       |
| Citrate cycle                                                                    | 32         | 2 (6.2%)   | 0.00311  | 0.0577  | INOH           |
| Constitutive Androstane Receptor Pathway                                         | 32         | 2 (6.2%)   | 0.00311  | 0.0577  | Wikipathways   |
| Type I collagen synthesis in the context of Osteogenesis imperfecta              | 33         | 2 (6.1%)   | 0.00331  | 0.0585  | Wikipathways   |
| Glutaminolysis and Cancer                                                        | 37         | 2 (5.4%)   | 0.00415  | 0.0701  | SMPDB          |
| Activation of Na-permeable kainate receptors                                     | 2          | 1 (50.0%)  | 0.0052   | 0.0843  | Reactome       |
| Transport of small molecules                                                     | 641        | 6 (0.9%)   | 0.00573  | 0.0891  | Reactome       |
| Warburg Effect                                                                   | 45         | 2 (4.4%)   | 0.00609  | 0.091   | SMPDB          |
| superpathway of conversion of glucose to acetyl CoA and entry into the TCA cycle | 48         | 2 (4.3%)   | 0.00662  | 0.0954  | HumanCyc       |
| Rosiglitazone Metabolism Pathway                                                 | 3          | 1 (33.3%)  | 0.0078   | 0.105   | SMPDB          |
| N-acetylglucosamine degradation I                                                | 3          | 1 (33.3%)  | 0.0078   | 0.105   | HumanCyc       |
| Pyruvate metabolism and Citric Acid (TCA) cycle                                  | 53         | 2 (3.8%)   | 0.00836  | 0.108   | Reactome       |
| Ion channel transport                                                            | 165        | 3 (1.8%)   | 0.00893  | 0.112   | Reactome       |
| C21-steroid hormone biosynthesis and metabolism                                  | 57         | 2 (3.5%)   | 0.00962  | 0.113   | EHMN           |
| Iron uptake and transport                                                        | 57         | 2 (3.5%)   | 0.00962  | 0.113   | Reactome       |
| Mineral absorption - Homo sapiens (human)                                        | 59         | 2 (3.4%)   | 0.0103   | 0.115   | KEGG           |
| N-acetylglucosamine degradation II                                               | 4          | 1 (25.0%)  | 0.0104   | 0.115   | HumanCyc       |
| HIF-1-alpha transcription factor network                                         | 66         | 2 (3.0%)   | 0.0127   | 0.131   | PID            |
| Doxepin Metabolism Pathway                                                       | 5          | 1 (20.0%)  | 0.013    | 0.131   | SMPDB          |
| Acetylcholine inhibits contraction of outer hair cells                           | 5          | 1 (20.0%)  | 0.013    | 0.131   | Reactome       |
| Integrated breast cancer pathway                                                 | 67         | 2 (3.0%)   | 0.0131   | 0.131   | Wikipathways   |
| Fluoroacetic acid toxicity                                                       | 6          | 1 (16.7%)  | 0.0155   | 0.142   | Wikipathways   |
| Biosynthesis of maresin-like SPMs                                                | 6          | 1 (16.7%)  | 0.0155   | 0.142   | Reactome       |
| Fluoxetine Metabolism Pathway                                                    | 6          | 1 (16.7%)  | 0.0155   | 0.142   | SMPDB          |
| Leptin signaling pathway                                                         | 76         | 2 (2.6%)   | 0.0167   | 0.142   | Wikipathways   |
| Caffeine Metabolism                                                              | 7          | 1 (14.3%)  | 0.0181   | 0.142   | SMPDB          |
| Arachidonate Epoxigenase - Epoxide Hydrolase                                     | 7          | 1 (14.3%)  | 0.0181   | 0.142   | Wikipathways   |
| overview of telomerase rna component gene hterc transcriptional regulation       | 7          | 1 (14.3%)  | 0.0181   | 0.142   | BioCarta       |
| Celecoxib Metabolism Pathway                                                     | 8          | 1 (12.5%)  | 0.0207   | 0.142   | SMPDB          |
| Synthesis of epoxy (EET) and dihydroxyeicosatrienoic acids (DHET)                | 8          | 1 (12.5%)  | 0.0207   | 0.142   | Reactome       |
| Ifosfamide Action Pathway                                                        | 8          | 1 (12.5%)  | 0.0207   | 0.142   | SMPDB          |
| Ifosfamide Metabolism Pathway                                                    | 8          | 1 (12.5%)  | 0.0207   | 0.142   | SMPDB          |
| Biosynthesis of maresins                                                         | 8          | 1 (12.5%)  | 0.0207   | 0.142   | Reactome       |
| Nevirapine Metabolism Pathway                                                    | 8          | 1 (12.5%)  | 0.0207   | 0.142   | SMPDB          |
| Mitochondrial CII Assembly                                                       | 8          | 1 (12.5%)  | 0.0207   | 0.142   | Wikipathways   |
| Bile secretion - Homo sapiens (human)                                            | 90         | 2 (2.2%)   | 0.0229   | 0.142   | KEGG           |
| Synthesis of (16-20)-hydroxyeicosatetraenoic acids (HETE)                        | 9          | 1 (11.1%)  | 0.0232   | 0.142   | Reactome       |
| Cyclophosphamide Action Pathway                                                  | 9          | 1 (11.1%)  | 0.0232   | 0.142   | SMPDB          |
| Cyclophosphamide Metabolism Pathway                                              | 9          | 1 (11.1%)  | 0.0232   | 0.142   | SMPDB          |
| Clopidogrel Metabolism Pathway                                                   | 9          | 1 (11.1%)  | 0.0232   | 0.142   | SMPDB          |
| Clopidogrel Action Pathway                                                       | 9          | 1 (11.1%)  | 0.0232   | 0.142   | SMPDB          |
| Ca2+ activated K+ channels                                                       | 9          | 1 (11.1%)  | 0.0232   | 0.142   | Reactome       |
| Ethanol metabolism resulting in production of ROS by CYP2E1                      | 9          | 1 (11.1%)  | 0.0232   | 0.142   | Wikipathways   |
| UDP-N-acetyl-D-galactosamine biosynthesis II                                     | 9          | 1 (11.1%)  | 0.0232   | 0.142   | HumanCyc       |
| Bile acids synthesis and enterohepatic circulation                               | 9          | 1 (11.1%)  | 0.0232   | 0.142   | Wikipathways   |
| Amino Acid metabolism                                                            | 91         | 2 (2.2%)   | 0.0234   | 0.142   | Wikipathways   |
| Apoptosis Modulation and Signaling                                               | 92         | 2 (2.2%)   | 0.0238   | 0.143   | Wikipathways   |
| NS1 Mediated Effects on Host Pathways                                            | 10         | 1 (10.0%)  | 0.0258   | 0.145   | Reactome       |
| SLBP independent Processing of Histone Pre-mRNAs                                 | 10         | 1 (10.0%)  | 0.0258   | 0.145   | Reactome       |
| overview of telomerase protein component gene htert transcriptional regulation   | 10         | 1 (10.0%)  | 0.0258   | 0.145   | BioCarta       |
| Liver X receptor pathway                                                         | 10         | 1 (10.0%)  | 0.0258   | 0.145   | Wikipathways   |
| Valproic Acid Metabolism Pathway                                                 | 11         | 1 (9.1%)   | 0.0283   | 0.153   | SMPDB          |
| CYP2E1 reactions                                                                 | 11         | 1 (9.1%)   | 0.0283   | 0.153   | Reactome       |
| SLBP Dependent Processing of Replication-Dependent Histone Pre-mRNAs             | 11         | 1 (9.1%)   | 0.0283   | 0.153   | Reactome       |
| Cargo recognition for clathrin-mediated endocytosis                              | 105        | 2 (1.9%)   | 0.0305   | 0.158   | Reactome       |
| Activation of Ca-permeable Kainate Receptor                                      | 12         | 1 (8.3%)   | 0.0308   | 0.158   | Reactome       |
| Ionotropic activity of kainate receptors                                         | 12         | 1 (8.3%)   | 0.0308   | 0.158   | Reactome       |
| Iron metabolism in placenta                                                      | 12         | 1 (8.3%)   | 0.0308   | 0.158   | Wikipathways   |

|                                                                                                                             |     |          |        |       |                          |
|-----------------------------------------------------------------------------------------------------------------------------|-----|----------|--------|-------|--------------------------|
| Post-translational protein phosphorylation                                                                                  | 107 | 2 (1.9%) | 0.0315 | 0.159 | <a href="#">Reactome</a> |
| role of mitochondria in apoptotic signaling                                                                                 | 13  | 1 (7.7%) | 0.0334 | 0.16  | <a href="#">BioCarta</a> |
| Valproic acid pathway                                                                                                       | 13  | 1 (7.7%) | 0.0334 | 0.16  | Wikipathways             |
| effects of calcineurin in keratinocyte differentiation                                                                      | 13  | 1 (7.7%) | 0.0334 | 0.16  | <a href="#">BioCarta</a> |
| Estrogen Receptor Pathway                                                                                                   | 13  | 1 (7.7%) | 0.0334 | 0.16  | Wikipathways             |
| IL-18 signaling pathway                                                                                                     | 274 | 3 (1.1%) | 0.034  | 0.161 | Wikipathways             |
| Serotonergic synapse - Homo sapiens (human)                                                                                 | 115 | 2 (1.8%) | 0.0348 | 0.163 | <a href="#">KEGG</a>     |
| Osteoblast Signaling                                                                                                        | 14  | 1 (7.1%) | 0.0359 | 0.166 | Wikipathways             |
| Sorafenib Metabolism Pathway                                                                                                | 15  | 1 (6.7%) | 0.0384 | 0.172 | SMPDB                    |
| IL-6-type cytokine receptor ligand interactions                                                                             | 15  | 1 (6.7%) | 0.0384 | 0.172 | <a href="#">Reactome</a> |
| Osteoclast Signaling                                                                                                        | 16  | 1 (6.2%) | 0.0409 | 0.172 | Wikipathways             |
| TCA Cycle and Deficiency of Pyruvate Dehydrogenase complex (PDHc)                                                           | 16  | 1 (6.2%) | 0.0409 | 0.172 | Wikipathways             |
| human cytomegalovirus and map kinase pathways                                                                               | 16  | 1 (6.2%) | 0.0409 | 0.172 | <a href="#">BioCarta</a> |
| mRNA decay by 3, to 5, exoribonuclease                                                                                      | 16  | 1 (6.2%) | 0.0409 | 0.172 | <a href="#">Reactome</a> |
| Regulation of Insulin-like Growth Factor (IGF) transport and uptake by Insulin-like Growth Factor Binding Proteins (IGFBPs) | 124 | 2 (1.6%) | 0.0412 | 0.172 | <a href="#">Reactome</a> |
| Biosynthesis of DHA-derived SPMs                                                                                            | 17  | 1 (5.9%) | 0.0434 | 0.172 | <a href="#">Reactome</a> |
| Sialuria or French Type Sialuria                                                                                            | 17  | 1 (5.9%) | 0.0434 | 0.172 | SMPDB                    |
| Sialuria or French Type Sialuria                                                                                            | 17  | 1 (5.9%) | 0.0434 | 0.172 | SMPDB                    |
| Amino Sugar Metabolism                                                                                                      | 17  | 1 (5.9%) | 0.0434 | 0.172 | SMPDB                    |
| G(M2)-Gangliosidosis: Variant B, Tay-sachs disease                                                                          | 17  | 1 (5.9%) | 0.0434 | 0.172 | SMPDB                    |
| Tay-Sachs Disease                                                                                                           | 17  | 1 (5.9%) | 0.0434 | 0.172 | SMPDB                    |
| Salla Disease/Infantile Sialic Acid Storage Disease                                                                         | 17  | 1 (5.9%) | 0.0434 | 0.172 | SMPDB                    |
| Lysosome - Homo sapiens (human)                                                                                             | 128 | 2 (1.6%) | 0.0437 | 0.172 | <a href="#">KEGG</a>     |
| ncRNAs involved in STAT3 signaling in hepatocellular carcinoma                                                              | 18  | 1 (5.6%) | 0.0459 | 0.177 | Wikipathways             |
| ABC transporters in lipid homeostasis                                                                                       | 18  | 1 (5.6%) | 0.0459 | 0.177 | <a href="#">Reactome</a> |
| Oxidative phosphorylation - Homo sapiens (human)                                                                            | 133 | 2 (1.5%) | 0.0468 | 0.178 | <a href="#">KEGG</a>     |
| Biosynthesis of specialized proresolving mediators (SPMs)                                                                   | 19  | 1 (5.3%) | 0.0484 | 0.179 | <a href="#">Reactome</a> |
| Mitochondrial Gene Expression                                                                                               | 19  | 1 (5.3%) | 0.0484 | 0.179 | Wikipathways             |
| Translesion Synthesis by POLH                                                                                               | 19  | 1 (5.3%) | 0.0484 | 0.179 | <a href="#">Reactome</a> |
| Nuclear Receptors Meta-Pathway                                                                                              | 317 | 3 (0.9%) | 0.0489 | 0.179 | Wikipathways             |

# CAD\_mortality\_VAT

| pathway name                                                                                                                         | candidates |           |          |         | pathway source |
|--------------------------------------------------------------------------------------------------------------------------------------|------------|-----------|----------|---------|----------------|
|                                                                                                                                      | set size   | contained | p-value  | q-value |                |
| Cytokine-cytokine receptor interaction - Homo sapiens (human)                                                                        | 295        | 6 (2.0%)  | 0.000328 | 0.143   | KEGG           |
| Osteoblast Signaling                                                                                                                 | 14         | 2 (14.3%) | 0.000889 | 0.18    | Wikipathways   |
| cdk regulation of dna replication                                                                                                    | 18         | 2 (11.1%) | 0.00148  | 0.18    | BioCarta       |
| Assembly of the pre-replicative complex                                                                                              | 20         | 2 (10.0%) | 0.00183  | 0.18    | Reactome       |
| Plexin-D1 Signaling                                                                                                                  | 24         | 2 (8.3%)  | 0.00264  | 0.18    | PID            |
| Orc1 removal from chromatin                                                                                                          | 26         | 2 (7.7%)  | 0.0031   | 0.18    | Reactome       |
| TNFs bind their physiological receptors                                                                                              | 29         | 2 (6.9%)  | 0.00385  | 0.18    | Reactome       |
| RNA Polymerase I Promoter Escape                                                                                                     | 30         | 2 (6.7%)  | 0.00411  | 0.18    | Reactome       |
| RNA Polymerase I Transcription Termination                                                                                           | 31         | 2 (6.5%)  | 0.00439  | 0.18    | Reactome       |
| RNA Polymerase I Transcription Initiation                                                                                            | 32         | 2 (6.2%)  | 0.00467  | 0.18    | Reactome       |
| Activation of the pre-replicative complex                                                                                            | 33         | 2 (6.1%)  | 0.00496  | 0.18    | Reactome       |
| RNA Polymerase I Promoter Clearance                                                                                                  | 33         | 2 (6.1%)  | 0.00496  | 0.18    | Reactome       |
| RNA Polymerase I Transcription                                                                                                       | 35         | 2 (5.7%)  | 0.00557  | 0.18    | Reactome       |
| Activation of ATR in response to replication stress                                                                                  | 37         | 2 (5.4%)  | 0.00621  | 0.18    | Reactome       |
| DNA Replication Pre-Initiation                                                                                                       | 37         | 2 (5.4%)  | 0.00621  | 0.18    | Reactome       |
| DNA Replication                                                                                                                      | 42         | 2 (4.8%)  | 0.00795  | 0.216   | Wikipathways   |
| Switching of origins to a post-replicative state                                                                                     | 47         | 2 (4.3%)  | 0.00987  | 0.253   | Reactome       |
| TNFR2 non-canonical NF-kB pathway                                                                                                    | 50         | 2 (4.0%)  | 0.0111   | 0.269   | Reactome       |
| NR1D1 (REV-ERBA) represses gene expression                                                                                           | 4          | 1 (25.0%) | 0.0127   | 0.278   | Reactome       |
| Developmental Biology                                                                                                                | 676        | 6 (0.9%)  | 0.0198   | 0.278   | Reactome       |
| ceramide <i>de novo</i> biosynthesis                                                                                                 | 7          | 1 (14.3%) | 0.0222   | 0.278   | HumanCyc       |
| Phosphate bond hydrolysis by NUDT proteins                                                                                           | 7          | 1 (14.3%) | 0.0222   | 0.278   | Reactome       |
| Chemokine signaling pathway - Homo sapiens (human)                                                                                   | 192        | 3 (1.6%)  | 0.0233   | 0.278   | KEGG           |
| Synthesis of DNA                                                                                                                     | 76         | 2 (2.6%)  | 0.0246   | 0.278   | Reactome       |
| G1/S Transition                                                                                                                      | 76         | 2 (2.6%)  | 0.0246   | 0.278   | Reactome       |
| CDC6 association with the ORC:origin complex                                                                                         | 8          | 1 (12.5%) | 0.0253   | 0.278   | Reactome       |
| IL-4 signaling                                                                                                                       | 8          | 1 (12.5%) | 0.0253   | 0.278   | INOH           |
| Cross-presentation of particulate exogenous antigens (phagosomes)                                                                    | 8          | 1 (12.5%) | 0.0253   | 0.278   | Reactome       |
| Linoleic acid (LA) metabolism                                                                                                        | 8          | 1 (12.5%) | 0.0253   | 0.278   | Reactome       |
| Axon guidance                                                                                                                        | 356        | 4 (1.1%)  | 0.0266   | 0.278   | Reactome       |
| DNA Replication                                                                                                                      | 81         | 2 (2.5%)  | 0.0276   | 0.278   | Reactome       |
| regulation of map kinase pathways through dual specificity phosphatases                                                              | 9          | 1 (11.1%) | 0.0284   | 0.278   | BioCarta       |
| btg family proteins and cell cycle regulation                                                                                        | 9          | 1 (11.1%) | 0.0284   | 0.278   | BioCarta       |
| IL-13 signaling                                                                                                                      | 10         | 1 (10.0%) | 0.0316   | 0.278   | INOH           |
| Formyl peptide receptors bind formyl peptides and many other ligands                                                                 | 10         | 1 (10.0%) | 0.0316   | 0.278   | Reactome       |
| RUNX1 and FOXP3 control the development of regulatory T lymphocytes (Tregs)                                                          | 10         | 1 (10.0%) | 0.0316   | 0.278   | Reactome       |
| Nervous system development                                                                                                           | 379        | 4 (1.1%)  | 0.0324   | 0.278   | Reactome       |
| B-WICH complex positively regulates rRNA expression                                                                                  | 94         | 2 (2.2%)  | 0.0356   | 0.278   | Reactome       |
| PECAM1 interactions                                                                                                                  | 12         | 1 (8.3%)  | 0.0378   | 0.278   | Reactome       |
| Unwinding of DNA                                                                                                                     | 12         | 1 (8.3%)  | 0.0378   | 0.278   | Reactome       |
| Regulation of signaling by NODAL                                                                                                     | 12         | 1 (8.3%)  | 0.0378   | 0.278   | Reactome       |
| Omega-9 FA synthesis                                                                                                                 | 12         | 1 (8.3%)  | 0.0378   | 0.278   | Wikipathways   |
| Hematopoietic cell lineage - Homo sapiens (human)                                                                                    | 99         | 2 (2.0%)  | 0.0392   | 0.278   | KEGG           |
| Viral protein interaction with cytokine and cytokine receptor - Homo sapiens (human)                                                 | 100        | 2 (2.0%)  | 0.0407   | 0.278   | KEGG           |
| Osteopontin Signaling                                                                                                                | 13         | 1 (7.7%)  | 0.0408   | 0.278   | Wikipathways   |
| MFAP5-mediated ovarian cancer cell motility and invasiveness                                                                         | 13         | 1 (7.7%)  | 0.0408   | 0.278   | Wikipathways   |
| alpha-linolenic acid (ALA) metabolism                                                                                                | 13         | 1 (7.7%)  | 0.0408   | 0.278   | Reactome       |
| alpha-linolenic (omega3) and linoleic (omega6) acid metabolism                                                                       | 13         | 1 (7.7%)  | 0.0408   | 0.278   | Reactome       |
| Pancreatic secretion - Homo sapiens (human)                                                                                          | 102        | 2 (2.0%)  | 0.0421   | 0.278   | KEGG           |
| JAK-STAT-Core                                                                                                                        | 104        | 2 (1.9%)  | 0.0436   | 0.278   | Signalink      |
| S Phase                                                                                                                              | 104        | 2 (1.9%)  | 0.0436   | 0.278   | Reactome       |
| Mitotic G1 phase and G1/S transition                                                                                                 | 104        | 2 (1.9%)  | 0.0436   | 0.278   | Reactome       |
| Nicotinate and Nicotinamide Metabolism                                                                                               | 14         | 1 (7.1%)  | 0.0439   | 0.278   | SMPDB          |
| CDT1 association with the CDC6:ORC:origin complex                                                                                    | 14         | 1 (7.1%)  | 0.0439   | 0.278   | Reactome       |
| TP53 regulates transcription of several additional cell death genes whose specific roles in p53-dependent apoptosis remain uncertain | 14         | 1 (7.1%)  | 0.0439   | 0.278   | Reactome       |
| Positive epigenetic regulation of rRNA expression                                                                                    | 109        | 2 (1.9%)  | 0.0467   | 0.278   | Reactome       |
| Interleukin-4 and Interleukin-13 signaling                                                                                           | 15         | 1 (6.7%)  | 0.047    | 0.278   | Reactome       |
| IL-6-type cytokine receptor ligand interactions                                                                                      | 15         | 1 (6.7%)  | 0.047    | 0.278   | Reactome       |
| Metabolism of water-soluble vitamins and cofactors                                                                                   | 111        | 2 (1.8%)  | 0.0491   | 0.278   | Reactome       |

## CAD\_admission\_VAT

| pathway name                                                                                                                         | candidates |           |          |         | pathway source           |
|--------------------------------------------------------------------------------------------------------------------------------------|------------|-----------|----------|---------|--------------------------|
|                                                                                                                                      | set size   | contained | p-value  | q-value |                          |
| Metabolism                                                                                                                           | 1954       | 14 (0.7%) | 0.000752 | 0.245   | <a href="#">Reactome</a> |
| Glutamate and glutamine metabolism                                                                                                   | 15         | 2 (13.3%) | 0.000842 | 0.245   | <a href="#">Reactome</a> |
| Trafficking of AMPA receptors                                                                                                        | 30         | 2 (6.7%)  | 0.00339  | 0.245   | <a href="#">Reactome</a> |
| Glutamate binding, activation of AMPA receptors and synaptic plasticity                                                              | 30         | 2 (6.7%)  | 0.00339  | 0.245   | <a href="#">Reactome</a> |
| Urea cycle and metabolism of arginine, proline, glutamate, aspartate and asparagine                                                  | 105        | 3 (2.9%)  | 0.00346  | 0.245   | <a href="#">EHMN</a>     |
| Gluconeogenesis                                                                                                                      | 35         | 2 (5.9%)  | 0.00434  | 0.245   | <a href="#">Reactome</a> |
| Fragile X Syndrome                                                                                                                   | 119        | 3 (2.5%)  | 0.00491  | 0.245   | Wikipathways             |
| Alanine, aspartate and glutamate metabolism - Homo sapiens (human)                                                                   | 37         | 2 (5.4%)  | 0.00513  | 0.245   | <a href="#">KEGG</a>     |
| Cytosolic iron-sulfur cluster assembly                                                                                               | 2          | 1 (50.0%) | 0.0058   | 0.245   | <a href="#">Reactome</a> |
| PAOs oxidise polyamines to amines                                                                                                    | 2          | 1 (50.0%) | 0.0058   | 0.245   | <a href="#">Reactome</a> |
| Glycine Serine metabolism                                                                                                            | 40         | 2 (5.0%)  | 0.00597  | 0.245   | <a href="#">INOH</a>     |
| Glycolysis and Gluconeogenesis                                                                                                       | 45         | 2 (4.4%)  | 0.00751  | 0.245   | Wikipathways             |
| Interconversion of polyamines                                                                                                        | 3          | 1 (33.3%) | 0.00868  | 0.245   | <a href="#">Reactome</a> |
| Role of Calcineurin-dependent NFAT signaling in lymphocytes                                                                          | 56         | 2 (3.6%)  | 0.0115   | 0.245   | <a href="#">PID</a>      |
| Malate-Aspartate Shuttle                                                                                                             | 4          | 1 (25.0%) | 0.0116   | 0.245   | SMPDB                    |
| 4-hydroxyproline degradation                                                                                                         | 4          | 1 (25.0%) | 0.0116   | 0.245   | <a href="#">HumanCyc</a> |
| Reuptake of GABA                                                                                                                     | 4          | 1 (25.0%) | 0.0116   | 0.245   | <a href="#">Reactome</a> |
| Amine Oxidase reactions                                                                                                              | 4          | 1 (25.0%) | 0.0116   | 0.245   | <a href="#">Reactome</a> |
| Developmental Biology                                                                                                                | 676        | 6 (0.9%)  | 0.0125   | 0.245   | <a href="#">Reactome</a> |
| malate-aspartate shuttle                                                                                                             | 5          | 1 (20.0%) | 0.0144   | 0.245   | <a href="#">HumanCyc</a> |
| tetrapyrrole biosynthesis                                                                                                            | 5          | 1 (20.0%) | 0.0144   | 0.245   | <a href="#">HumanCyc</a> |
| glycine betaine degradation                                                                                                          | 5          | 1 (20.0%) | 0.0144   | 0.245   | <a href="#">HumanCyc</a> |
| spermine and spermidine degradation I                                                                                                | 5          | 1 (20.0%) | 0.0144   | 0.245   | <a href="#">HumanCyc</a> |
| RAB geranylgeranylation                                                                                                              | 65         | 2 (3.1%)  | 0.0152   | 0.245   | <a href="#">Reactome</a> |
| Metabolism of amino acids and derivatives                                                                                            | 339        | 4 (1.2%)  | 0.0164   | 0.245   | <a href="#">Reactome</a> |
| Phenylalanine, tyrosine and tryptophan biosynthesis - Homo sapiens (human)                                                           | 6          | 1 (16.7%) | 0.0173   | 0.245   | <a href="#">KEGG</a>     |
| Glypican 3 network                                                                                                                   | 6          | 1 (16.7%) | 0.0173   | 0.245   | <a href="#">PID</a>      |
| Pantothenate and CoA Biosynthesis                                                                                                    | 6          | 1 (16.7%) | 0.0173   | 0.245   | SMPDB                    |
| Choline catabolism                                                                                                                   | 6          | 1 (16.7%) | 0.0173   | 0.245   | <a href="#">Reactome</a> |
| Nef Mediated CD8 Down-regulation                                                                                                     | 7          | 1 (14.3%) | 0.0201   | 0.245   | <a href="#">Reactome</a> |
| Porphyrin metabolism                                                                                                                 | 7          | 1 (14.3%) | 0.0201   | 0.245   | <a href="#">INOH</a>     |
| ceramide <i>de novo</i> biosynthesis                                                                                                 | 7          | 1 (14.3%) | 0.0201   | 0.245   | <a href="#">HumanCyc</a> |
| superpathway of choline degradation to L-serine                                                                                      | 7          | 1 (14.3%) | 0.0201   | 0.245   | <a href="#">HumanCyc</a> |
| Synaptic vesicle cycle - Homo sapiens (human)                                                                                        | 78         | 2 (2.6%)  | 0.0215   | 0.245   | <a href="#">KEGG</a>     |
| Rapid glucocorticoid signaling                                                                                                       | 8          | 1 (12.5%) | 0.023    | 0.245   | <a href="#">PID</a>      |
| Conjugation of salicylate with glycine                                                                                               | 8          | 1 (12.5%) | 0.023    | 0.245   | <a href="#">Reactome</a> |
| Biological oxidations                                                                                                                | 219        | 3 (1.4%)  | 0.0254   | 0.245   | <a href="#">Reactome</a> |
| Nef Mediated CD4 Down-regulation                                                                                                     | 9          | 1 (11.1%) | 0.0258   | 0.245   | <a href="#">Reactome</a> |
| C20 prostanoid biosynthesis                                                                                                          | 9          | 1 (11.1%) | 0.0258   | 0.245   | <a href="#">HumanCyc</a> |
| ATR Signaling                                                                                                                        | 9          | 1 (11.1%) | 0.0258   | 0.245   | Wikipathways             |
| heme biosynthesis                                                                                                                    | 9          | 1 (11.1%) | 0.0258   | 0.245   | <a href="#">HumanCyc</a> |
| Heme Biosynthesis                                                                                                                    | 9          | 1 (11.1%) | 0.0258   | 0.245   | Wikipathways             |
| ROBO receptors bind AKAP5                                                                                                            | 9          | 1 (11.1%) | 0.0258   | 0.245   | <a href="#">Reactome</a> |
| Bicarbonate transporters                                                                                                             | 9          | 1 (11.1%) | 0.0258   | 0.245   | <a href="#">Reactome</a> |
| Conjugation of carboxylic acids                                                                                                      | 9          | 1 (11.1%) | 0.0258   | 0.245   | <a href="#">Reactome</a> |
| Amino Acid conjugation                                                                                                               | 9          | 1 (11.1%) | 0.0258   | 0.245   | <a href="#">Reactome</a> |
| VLDLR internalisation and degradation                                                                                                | 10         | 1 (10.0%) | 0.0287   | 0.245   | <a href="#">Reactome</a> |
| Activation of the AP-1 family of transcription factors                                                                               | 10         | 1 (10.0%) | 0.0287   | 0.245   | <a href="#">Reactome</a> |
| Formyl peptide receptors bind formyl peptides and many other ligands                                                                 | 10         | 1 (10.0%) | 0.0287   | 0.245   | <a href="#">Reactome</a> |
| Glucose metabolism                                                                                                                   | 93         | 2 (2.2%)  | 0.0292   | 0.245   | <a href="#">Reactome</a> |
| Post-translational modification: synthesis of GPI-anchored proteins                                                                  | 94         | 2 (2.1%)  | 0.0304   | 0.245   | <a href="#">Reactome</a> |
| Alanine and aspartate metabolism                                                                                                     | 12         | 1 (8.3%)  | 0.0343   | 0.245   | Wikipathways             |
| Aspartate and asparagine metabolism                                                                                                  | 12         | 1 (8.3%)  | 0.0343   | 0.245   | <a href="#">Reactome</a> |
| Transmission across Chemical Synapses                                                                                                | 249        | 3 (1.2%)  | 0.0352   | 0.245   | <a href="#">Reactome</a> |
| Phenylalanine degradation                                                                                                            | 13         | 1 (7.7%)  | 0.0371   | 0.245   | <a href="#">INOH</a>     |
| Argininemia                                                                                                                          | 13         | 1 (7.7%)  | 0.0371   | 0.245   | SMPDB                    |
| Citrullinemia Type I                                                                                                                 | 13         | 1 (7.7%)  | 0.0371   | 0.245   | SMPDB                    |
| Carbamoyl Phosphate Synthetase Deficiency                                                                                            | 13         | 1 (7.7%)  | 0.0371   | 0.245   | SMPDB                    |
| Argininosuccinic Aciduria                                                                                                            | 13         | 1 (7.7%)  | 0.0371   | 0.245   | SMPDB                    |
| Urea Cycle                                                                                                                           | 13         | 1 (7.7%)  | 0.0371   | 0.245   | SMPDB                    |
| Ornithine Transcarbamylase Deficiency (OTC Deficiency)                                                                               | 13         | 1 (7.7%)  | 0.0371   | 0.245   | SMPDB                    |
| L-kynurenine degradation                                                                                                             | 13         | 1 (7.7%)  | 0.0371   | 0.245   | <a href="#">HumanCyc</a> |
| Degradation of cysteine and homocysteine                                                                                             | 13         | 1 (7.7%)  | 0.0371   | 0.245   | <a href="#">Reactome</a> |
| Transcriptional regulation of testis differentiation                                                                                 | 13         | 1 (7.7%)  | 0.0371   | 0.245   | <a href="#">Reactome</a> |
| Homologous recombination                                                                                                             | 13         | 1 (7.7%)  | 0.0371   | 0.245   | Wikipathways             |
| hemoglobins chaperone                                                                                                                | 13         | 1 (7.7%)  | 0.0371   | 0.245   | <a href="#">BioCarta</a> |
| sarcosine oncometabolite pathway                                                                                                     | 13         | 1 (7.7%)  | 0.0371   | 0.245   | SMPDB                    |
| Metabolism of polyamines                                                                                                             | 13         | 1 (7.7%)  | 0.0371   | 0.245   | <a href="#">Reactome</a> |
| Retrograde neurotrophin signalling                                                                                                   | 14         | 1 (7.1%)  | 0.0399   | 0.245   | <a href="#">Reactome</a> |
| Somatic sex determination                                                                                                            | 14         | 1 (7.1%)  | 0.0399   | 0.245   | Wikipathways             |
| Removal of the Flap Intermediate                                                                                                     | 14         | 1 (7.1%)  | 0.0399   | 0.245   | <a href="#">Reactome</a> |
| Mismatch repair (MMR) directed by MSH2:MSH3 (MutSbeta)                                                                               | 14         | 1 (7.1%)  | 0.0399   | 0.245   | <a href="#">Reactome</a> |
| Mismatch repair (MMR) directed by MSH2:MSH6 (MutSalpha)                                                                              | 14         | 1 (7.1%)  | 0.0399   | 0.245   | <a href="#">Reactome</a> |
| Heme biosynthesis                                                                                                                    | 14         | 1 (7.1%)  | 0.0399   | 0.245   | <a href="#">Reactome</a> |
| Vitamin B5 (pantothenate) metabolism                                                                                                 | 14         | 1 (7.1%)  | 0.0399   | 0.245   | <a href="#">Reactome</a> |
| TP53 regulates transcription of several additional cell death genes whose specific roles in p53-dependent apoptosis remain uncertain | 14         | 1 (7.1%)  | 0.0399   | 0.245   | <a href="#">Reactome</a> |
| Phase II - Conjugation of compounds                                                                                                  | 111        | 2 (1.8%)  | 0.0411   | 0.245   | <a href="#">Reactome</a> |
| WNT5A-dependent internalization of FZD4                                                                                              | 15         | 1 (6.7%)  | 0.0427   | 0.245   | <a href="#">Reactome</a> |
| Processive synthesis on the lagging strand                                                                                           | 15         | 1 (6.7%)  | 0.0427   | 0.245   | <a href="#">Reactome</a> |
| Mismatch Repair                                                                                                                      | 15         | 1 (6.7%)  | 0.0427   | 0.245   | <a href="#">Reactome</a> |

|                                                              |     |          |        |       |                          |
|--------------------------------------------------------------|-----|----------|--------|-------|--------------------------|
| Hereditary Coproporphyria (HCP)                              | 15  | 1 (6.7%) | 0.0427 | 0.245 | SMPDB                    |
| Porphyria Variegata (PV)                                     | 15  | 1 (6.7%) | 0.0427 | 0.245 | SMPDB                    |
| Congenital Erythropoietic Porphyria (CEP) or Gunther Disease | 15  | 1 (6.7%) | 0.0427 | 0.245 | SMPDB                    |
| Acute Intermittent Porphyria                                 | 15  | 1 (6.7%) | 0.0427 | 0.245 | SMPDB                    |
| Porphyrin Metabolism                                         | 15  | 1 (6.7%) | 0.0427 | 0.245 | SMPDB                    |
| Wnt signaling                                                | 114 | 2 (1.8%) | 0.0431 | 0.245 | Wikipathways             |
| Trafficking of GluR2-containing AMPA receptors               | 16  | 1 (6.2%) | 0.0455 | 0.245 | <a href="#">Reactome</a> |
| Synthesis of Prostaglandins (PG) and Thromboxanes (TX)       | 16  | 1 (6.2%) | 0.0455 | 0.245 | <a href="#">Reactome</a> |
| Removal of the Flap Intermediate from the C-strand           | 16  | 1 (6.2%) | 0.0455 | 0.245 | <a href="#">Reactome</a> |
| Translesion synthesis by REV1                                | 16  | 1 (6.2%) | 0.0455 | 0.245 | <a href="#">Reactome</a> |
| Sphingolipid signaling pathway - Homo sapiens (human)        | 119 | 2 (1.7%) | 0.0466 | 0.245 | <a href="#">KEGG</a>     |
| endocytotic role of ndk phosphins and dynamin                | 17  | 1 (5.9%) | 0.0483 | 0.245 | <a href="#">BioCarta</a> |
| Phenylalanine metabolism - Homo sapiens (human)              | 17  | 1 (5.9%) | 0.0483 | 0.245 | <a href="#">KEGG</a>     |
| Canonical and non-canonical TGF-B signaling                  | 17  | 1 (5.9%) | 0.0483 | 0.245 | Wikipathways             |
| Translesion synthesis by POLK                                | 17  | 1 (5.9%) | 0.0483 | 0.245 | <a href="#">Reactome</a> |
| Translesion synthesis by POLI                                | 17  | 1 (5.9%) | 0.0483 | 0.245 | <a href="#">Reactome</a> |
| Sulfation Biotransformation Reaction                         | 17  | 1 (5.9%) | 0.0483 | 0.245 | Wikipathways             |