Secretome Signature of Cardiopoietic Cells Echoed in Rescued Infarcted Heart Proteome

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**SUPPORTING TABLES**

**Table S1. Differential secretome network nodes and topological properties.** Using a 2-fold differential expression cutoff for upregulated (orange) or downregulated (blue) proteins, the measured secretome was submitted to Ingenuity Pathway Analysis (IPA) for network generation. Additional network-integrated (rose) nodes were derived from the IPA-based network neighborhood, obtained from direct and indirect relationships for derivation of pairwise interactions (edges). Network edges were undirected, unweighted, with multi-edge node pairs merged as a single interaction, yielding a 520 node network comprised of 8977 edges, with connectivity exhibiting a power law distribution ($y = 46.50x^{-0.73}$, $r = 0.77$) indicative of non-stochastic scale-free architecture [1,2]. Imported into Cytoscape v.3.8.2 [3], the embedded application NetworkAnalyzer [4] was used to interpret network node topology. The node topological values for degree, clustering coefficient, average shortest path length, and betweenness centrality are included [1,2]. Degree represents number of connections, or edges, between a node and other nodes in the network. Clustering coefficient identifies the ratio of nodes connected to it, i.e. first neighbors, that also connect to one another, relative to total number of possible edges between first neighbors of the node. Average shortest path length
represents the mean path length to all other nodes in the network, where the length of each node pair equals the minimum number of edges required to connect the nodes. Betweenness centrality measures the proportion of all shortest paths within the network that pass through that node.

Table S1 – Differential secretome network nodes and topological properties

| Node      | Network Inclusion Basis | Log2 FC | Degree | Clustering Coefficient | Average Shortest Path Length | Betweenness Centrality |
|-----------|-------------------------|---------|--------|-------------------------|------------------------------|------------------------|
| ACKR2     | Upregulated in Secretome| 1.196   | 15     | 0.476                   | 2.102                        | 2.76E-04               |
| ACVR1     | Upregulated in Secretome| 3.169   | 23     | 0.271                   | 2.262                        | 0.00137026             |
| ACVR1B    | Upregulated in Secretome| 1.539   | 8      | 0.357                   | 2.898                        | 1.14E-04               |
| ACVR2B    | Upregulated in Secretome| 1.063   | 18     | 0.248                   | 2.231                        | 0.00111215             |
| AGER      | Upregulated in Secretome| 1.431   | 51     | 0.441                   | 1.954                        | 0.00163980             |
| AGRP      | Upregulated in Secretome| 1.193   | 6      | 0.667                   | 2.422                        | 3.15E-06               |
| ALCAM     | Upregulated in Secretome| 10.46   | 25     | 0.451                   | 2.052                        | 1.08E-04               |
| ANGPT1    | Upregulated in Secretome| 1.107   | 33     | 0.639                   | 2.012                        | 1.17E-04               |
| AREG      | Upregulated in Secretome| 1.017   | 49     | 0.391                   | 1.979                        | 0.00110732             |
| BIK       | Upregulated in Secretome| 8.153   | 11     | 0.345                   | 2.222                        | 1.60E-04               |
| BMP5      | Upregulated in Secretome| 1.810   | 5      | 0.300                   | 2.505                        | 1.99E-04               |
| BPIFA1    | Upregulated in Secretome| 1.881   | 4      | 0.833                   | 2.370                        | 3.20E-07               |
| CCL16     | Upregulated in Secretome| 1.031   | 5      | 0                   | 2.676                        | 1.06E-05               |
| CCL20     | Upregulated in Secretome| 1.023   | 50     | 0.367                   | 1.958                        | 0.00125906             |
| CCL21     | Upregulated in Secretome| 1.380   | 19     | 0.456                   | 2.114                        | 2.10E-04               |
| CCL25     | Upregulated in Secretome| 1.450   | 13     | 0.385                   | 2.270                        | 7.32E-05               |
| CCL7      | Upregulated in Secretome| 1.567   | 30     | 0.460                   | 2.023                        | 4.50E-04               |
| CCN3      | Upregulated in Secretome| 1.011   | 22     | 0.416                   | 2.067                        | 4.00E-04               |
| CD14      | Upregulated in Secretome| 1.404   | 61     | 0.375                   | 1.944                        | 0.00188661             |
| CD163     | Upregulated in Secretome| 2.891   | 14     | 0.409                   | 2.175                        | 1.46E-04               |
| CD40      | Upregulated in Secretome| 1.213   | 113    | 0.239                   | 1.823                        | 0.01255221             |
| CD40LG    | Upregulated in Secretome| 1.157   | 102    | 0.255                   | 1.854                        | 0.007490950            |
| CD80      | Upregulated in Secretome| 3.153   | 54     | 0.416                   | 1.981                        | 0.00147156             |
| CER1      | Upregulated in Secretome| 1.179   | 3      | 0.333                   | 2.740                        | 2.23E-05               |
| CRIM1     | Upregulated in Secretome| 1.340   | 1      | 0                      | 2.805                        | 0                   |
| CSF2RA    | Upregulated in Secretome| 1.025   | 12     | 0.178                   | 2.331                        | 8.48E-05               |
| CTNNB1    | Upregulated in Secretome| 1.593   | 135    | 0.201                   | 1.761                        | 0.02373687             |
| CXCL13    | Upregulated in Secretome| 1.921   | 25     | 0.387                   | 2.060                        | 3.81E-04               |
| CXCL2     | Upregulated in Secretome| 1.837   | 64     | 0.269                   | 1.929                        | 0.00318728             |
| CXCR3     | Upregulated in Secretome| 1.060   | 34     | 0.426                   | 2.015                        | 4.45E-04               |
| DEF81     | Upregulated in Secretome| 10.82   | 12     | 0.106                   | 2.563                        | 1.79E-04               |
| DEF84A/DEF84B | Upregulated in Secretome | 7.654 | 32 | 0.485 | 2.054 | 4.66E-04 |
| DKK1      | Upregulated in Secretome| 2.001   | 25     | 0.310                   | 2.064                        | 0.00126210             |
| EDAR      | Upregulated in Secretome| 1.067   | 6      | 0.800                   | 2.222                        | 1.51E-06               |
| EGF       | Upregulated in Secretome| 1.040   | 160    | 0.184                   | 1.711                        | 0.02409543             |
| EGFR      | Upregulated in Secretome| 1.124   | 179    | 0.187                   | 1.672                        | 0.02768148             |
| Gene   | Condition                        | Value   | Expression | P-value  |
|--------|----------------------------------|---------|------------|----------|
| FADD   | Upregulated in Secretome         | 1.010   | 34         | 2.031    | 4.75E-04 |
| FG6    | Upregulated in Secretome         | 1.279   | 7          | 0.476    | 2.428    | 9.55E-06 |
| FLT3   | Upregulated in Secretome         | 1.067   | 26         | 0.475    | 2.067    | 2.19E-04 |
| FRZB   | Upregulated in Secretome         | 1.019   | 9          | 0.190    | 2.272    | 3.68E-04 |
| FSTL3  | Upregulated in Secretome         | 1.090   | 10         | 0.422    | 2.347    | 1.94E-04 |
| Fzd1   | Upregulated in Secretome         | 2.647   | 14         | 0.348    | 2.220    | 1.22E-04 |
| Fzd3   | Upregulated in Secretome         | 1.126   | 5          | 0.600    | 2.530    | 7.01E-06 |
| Fzd7   | Upregulated in Secretome         | 1.011   | 4          | 0.167    | 2.628    | 8.90E-06 |
| GDF1   | Upregulated in Secretome         | 1.059   | 1          | 0        | 3.104    | 0        |
| GDF10  | Upregulated in Secretome         | 1.402   | 3          | 0        | 2.728    | 9.75E-06 |
| GDF5   | Upregulated in Secretome         | 1.067   | 26         | 0.475    | 2.067    | 2.19E-04 |
| FRA3   | Upregulated in Secretome         | 1.019   | 9          | 0.190    | 2.272    | 3.68E-04 |
| Gf1    | Upregulated in Secretome         | 1.220   | 5          | 0.500    | 2.366    | 2.30E-05 |
| HGF    | Upregulated in Secretome         | 1.091   | 109        | 0.242    | 1.815    | 0.01051231 |
| HRG    | Upregulated in Secretome         | 2.321   | 7          | 0.286    | 2.276    | 5.78E-05 |
| IGF1R  | Upregulated in Secretome         | 1.050   | 57         | 0.358    | 1.933    | 0.00314263 |
| IGFBP3 | Upregulated in Secretome         | 1.134   | 14         | 0.374    | 2.135    | 3.91E-04 |
| IGFBP6 | Upregulated in Secretome         | 1.143   | 21         | 0.412    | 2.225    | 1.01E-04 |
| IL13RA1| Upregulated in Secretome         | 2.067   | 25         | 0.553    | 2.100    | 2.57E-04 |
| IL1B   | Upregulated in Secretome         | 1.095   | 249        | 0.142    | 1.536    | 0.05581781 |
| IL1R2  | Upregulated in Secretome         | 1.121   | 21         | 0.386    | 2.108    | 4.59E-04 |
| IL21R  | Upregulated in Secretome         | 1.708   | 19         | 0.412    | 2.225    | 1.01E-04 |
| IL2RA  | Upregulated in Secretome         | 2.572   | 58         | 0.411    | 1.950    | 0.00120549 |
| IL5RA  | Upregulated in Secretome         | 1.208   | 15         | 0.372    | 2.349    | 9.12E-05 |
| IL7R   | Upregulated in Secretome         | 1.805   | 32         | 0.419    | 2.033    | 0.00110582 |
| IL9    | Upregulated in Secretome         | 1.777   | 53         | 0.280    | 1.973    | 0.00259936 |
| INHBB  | Upregulated in Secretome         | 1.139   | 22         | 0.342    | 2.133    | 0.00146804 |
| ITAL   | Upregulated in Secretome         | 1.051   | 33         | 0.460    | 2.013    | 4.73E-04 |
| LCK    | Upregulated in Secretome         | 2.147   | 66         | 0.331    | 1.938    | 0.00298968 |
| LECT2  | Upregulated in Secretome         | 1.528   | 7          | 0.500    | 2.231    | 1.47E-04 |
| LEFTY2 | Upregulated in Secretome         | 2.370   | 4          | 0.333    | 2.495    | 1.98E-04 |
| LEP    | Upregulated in Secretome         | 2.369   | 105        | 0.249    | 1.829    | 0.00878198 |
| LTB1   | Upregulated in Secretome         | 2.009   | 14         | 0.505    | 2.135    | 6.08E-05 |
| MFPR   | Upregulated in Secretome         | 1.297   | 1          | 0        | 3.829    | 0        |
| Micos10-Nbl1/Nbl1 | Upregulated in Secretome | 1.801   | 5          | 0.100    | 2.705    | 4.90E-05 |
| MMP11  | Upregulated in Secretome         | 1.669   | 17         | 0.305    | 2.189    | 4.38E-04 |
| MMP24  | Upregulated in Secretome         | 1.248   | 4          | 0.167    | 2.807    | 2.36E-05 |
| MMP25  | Upregulated in Secretome         | 2.494   | 10         | 0.067    | 2.441    | 2.70E-04 |
| MMP9   | Upregulated in Secretome         | 1.346   | 151        | 0.220    | 1.728    | 0.02442419 |
| NGF    | Upregulated in Secretome         | 1.427   | 83         | 0.278    | 1.882    | 0.00551956 |
| NRG1   | Upregulated in Secretome         | 2.597   | 69         | 0.280    | 1.929    | 0.00746085 |
| NRG2   | Upregulated in Secretome         | 2.291   | 13         | 0.167    | 2.270    | 6.23E-04 |
| Ntf4   | Upregulated in Secretome         | 1.046   | 7          | 0.400    | 2.445    | 5.75E-06 |
| PDGFA  | Upregulated in Secretome         | 1.971   | 34         | 0.363    | 2.019    | 0.00102798 |
| Gene   | Expression | Significance | p-value       |
|--------|------------|--------------|---------------|
| PF4    | Upregulated in Secretome 2.252 | 39 | 0.402 | 2.015 | 0.00151662 |
| PGF    | Upregulated in Secretome 1.158 | 25 | 0.538 | 2.042 | 4.79E-04 |
| PRL    | Upregulated in Secretome 1.093 | 78 | 0.323 | 1.879 | 0.00622396 |
| SELE   | Upregulated in Secretome 1.797 | 65 | 0.331 | 1.919 | 0.00347760 |
| SFLP   | Upregulated in Secretome 1.292 | 42 | 0.354 | 2.029 | 8.63E-04 |
| SFRP4  | Upregulated in Secretome 1.480 | 6 | 0.200 | 2.611 | 1.14E-04 |
| SMAD1  | Upregulated in Secretome 3.058 | 41 | 0.248 | 1.990 | 0.00345672 |
| SMAD9  | Upregulated in Secretome 2.324 | 8 | 0.467 | 2.308 | 6.91E-05 |
| TFPI   | Upregulated in Secretome 1.073 | 14 | 0.485 | 2.160 | 3.85E-05 |
| TLR3   | Upregulated in Secretome 1.276 | 63 | 0.361 | 1.969 | 0.00276959 |
| TLR4   | Upregulated in Secretome 1.350 | 124 | 0.247 | 1.802 | 0.01053974 |
| TNFAIP6| Upregulated in Secretome 1.093 | 32 | 0.331 | 2.015 | 0.00622396 |
| TNFRSF10A| Upregulated in Secretome 1.719 | 26 | 0.496 | 2.040 | 5.31E-04 |
| TNFRSF12A| Upregulated in Secretome 2.470 | 20 | 0.301 | 2.150 | 2.65E-04 |
| TNFRSF17| Upregulated in Secretome 4.737 | 10 | 0.711 | 2.291 | 1.45E-05 |
| TNFRSF19| Upregulated in Secretome 1.331 | 6 | 0.500 | 2.434 | 1.19E-05 |
| TNFRSF25| Upregulated in Secretome 2.430 | 23 | 0.443 | 2.114 | 3.11E-04 |
| TNFRSF6B| Upregulated in Secretome 1.005 | 11 | 0.722 | 2.170 | 5.46E-06 |
| TNFRSF11| Upregulated in Secretome 1.724 | 82 | 0.360 | 1.869 | 0.00631266 |
| TNFRSF18| Upregulated in Secretome 1.055 | 10 | 0.489 | 2.318 | 4.12E-05 |
| TYMP   | Upregulated in Secretome 1.452 | 46 | 0.283 | 1.983 | 0.00402958 |
| 26s Proteasome | Network-integrated by IPA | 46 | 0.283 | 1.983 | 0.00402958 |
| 7S NGF | Network-integrated by IPA | 6 | 0.600 | 2.247 | 7.65E-06 |
| AChR   | Network-integrated by IPA | 13 | 0.345 | 2.143 | 4.73E-05 |
| Actin  | Network-integrated by IPA | 58 | 0.266 | 1.963 | 0.00254670 |
| Actinin| Network-integrated by IPA | 6 | 0.533 | 2.644 | 2.30E-05 |
| ADCY   | Network-integrated by IPA | 42 | 0.386 | 1.979 | 0.00112747 |
| adhesion molecule | Network-integrated by IPA | 15 | 0.686 | 2.114 | 6.40E-05 |
| ADRB   | Network-integrated by IPA | 25 | 0.415 | 2.100 | 2.02E-04 |
| Akt    | Network-integrated by IPA | 231 | 0.162 | 1.566 | 0.04584410 |
| ALDH   | Network-integrated by IPA | 4 | 0.833 | 2.254 | 1.21E-06 |
| Alp    | Network-integrated by IPA | 57 | 0.299 | 1.931 | 0.00868658 |
| Alpha 1 antitrypsin | Network-integrated by IPA | 5 | 0.500 | 2.445 | 3.15E-05 |
| Alpha Actinin | Network-integrated by IPA | 18 | 0.433 | 2.239 | 4.12E-05 |
| Alpha catenin | Network-integrated by IPA | 36 | 0.326 | 2.010 | 6.80E-04 |
| ALT    | Network-integrated by IPA | 12 | 0.439 | 2.175 | 1.41E-04 |
| Ampa Receptor | Network-integrated by IPA | 21 | 0.509 | 2.108 | 6.36E-05 |
| AMPK   | Network-integrated by IPA | 65 | 0.323 | 1.911 | 0.00615539 |
| amylase | Network-integrated by IPA | 4 | 0.333 | 2.568 | 1.64E-06 |
| Angiotensin II receptor type 1 | Network-integrated by IPA | 16 | 0.604 | 2.129 | 2.40E-05 |
| Ap1    | Network-integrated by IPA | 108 | 0.307 | 1.821 | 0.00578316 |
| Ap2    | Network-integrated by IPA | 8 | 0.679 | 2.202 | 5.68E-06 |
| Atrial Natriuretic Peptide | Network-integrated by IPA | 10 | 0.444 | 2.277 | 4.77E-05 |
| BCR (complex) | Network-integrated by IPA | 74 | 0.270 | 1.927 | 0.00305543 |
| BMP    | Network-integrated by IPA | 9 | 0.278 | 2.453 | 3.65E-04 |
| C/EBP  | Network-integrated by IPA | 25 | 0.628 | 2.046 | 7.26E-05 |
| C1q    | Network-integrated by IPA | 23 | 0.481 | 2.087 | 1.51E-04 |
| C1QTNFS | Network-integrated by IPA | 5 | 0 | 2.830 | 0.00385410 |
| C8     | Network-integrated by IPA | 4 | 0.500 | 2.474 | 2.12E-06 |
| Protein                      | Network-integrated by IPA | p-value 1 | p-value 2 | p-value 3 |
|-----------------------------|----------------------------|-----------|-----------|-----------|
| CALC                        |                            | 17        | 2.100     | 1.41E-04  |
| Calcineurin A               |                            | 17        | 2.083     | 5.44E-05  |
| Calcineurin protein(s)      |                            | 40        | 2.017     | 7.20E-04  |
| Calmodulin                  |                            | 52        | 1.971     | 0.00259892|
| calpain                     |                            | 44        | 1.996     | 8.70E-04  |
| CaMKII                      |                            | 42        | 2.029     | 6.09E-04  |
| cAMP-dependent protein kinase |                          | 14        | 2.224     | 1.23E-04  |
| Casein                      |                            | 10        | 2.173     | 8.47E-06  |
| caspase                     |                            | 61        | 1.944     | 0.00169845|
| Caspase 3/7                 |                            | 15        | 2.139     | 9.58E-05  |
| Cbp/p300                    |                            | 24        | 2.064     | 6.88E-04  |
| C-C chemokine receptor      |                            | 14        | 2.468     | 4.81E-05  |
| CCR6                        |                            | 24        | 2.104     | 5.55E-04  |
| CD3                         |                            | 91        | 1.882     | 0.00462799|
| CD3 group                   |                            | 18        | 2.098     | 3.47E-05  |
| CD4                         |                            | 44        | 2.002     | 7.49E-04  |
| CD80/CD86                   |                            | 5         | 2.291     | 1.10E-05  |
| CD81                        |                            | 34        | 2.054     | 3.84E-04  |
| CD9                         |                            | 27        | 2.054     | 1.41E-04  |
| Cebp                        |                            | 6         | 2.227     | 5.85E-05  |
| CG                          |                            | 43        | 1.967     | 0.00226555|
| chemokine                   |                            | 54        | 2.002     | 0.00269833|
| chemokine receptor          |                            | 13        | 2.453     | 4.47E-05  |
| Cip                         |                            | 12        | 2.141     | 3.19E-05  |
| Ck2                         |                            | 29        | 2.050     | 4.76E-04  |
| Cofilin                     |                            | 33        | 2.023     | 2.76E-04  |
| collagen                    |                            | 27        | 2.031     | 1.57E-04  |
| Collagen Alpha1             |                            | 30        | 2.044     | 3.67E-04  |
| Collagen type I (complex)   |                            | 46        | 1.960     | 0.00100575|
| Collagen type I (family)     |                            | 30        | 2.013     | 0.00124740|
| Collagen type II            |                            | 19        | 2.077     | 4.49E-04  |
| Collagen type III           |                            | 8         | 2.227     | 3.13E-06  |
| Collagen type IV            |                            | 31        | 2.052     | 3.87E-04  |
| Collagen(s)                 |                            | 64        | 1.921     | 0.00152763|
| Complement                  |                            | 20        | 2.137     | 6.34E-05  |
| Cpla2                       |                            | 22        | 2.062     | 4.63E-05  |
| CPT1                        |                            | 8         | 2.721     | 1.09E-05  |
| Cr3                         |                            | 21        | 2.100     | 6.11E-05  |
| Creb                        |                            | 92        | 1.846     | 0.00495748|
| c-Src                       |                            | 11        | 2.252     | 5.28E-06  |
| Cyclin A                    |                            | 38        | 1.979     | 3.46E-04  |
| Cyclin B                    |                            | 12        | 2.266     | 2.28E-05  |
| Cyclin D                    |                            | 33        | 2.021     | 7.60E-04  |
| Cyclin E                    |                            | 25        | 2.033     | 1.12E-04  |
| cyclooxgenase               |                            | 14        | 2.096     | 1.07E-04  |
| CYP19                       |                            | 10        | 2.141     | 6.22E-06  |
| cytochrome C                |                            | 30        | 2.050     | 2.98E-04  |
| Protein                      | Network-integrated by IPA | 138 | 0.223 | 1.765 | 0.01417424 |
|-----------------------------|---------------------------|-----|-------|-------|-------------|
| cytokine                    |                           | 27  | 0.170 | 2.277 | 4.36E-04    |
| cytokine receptor           |                           | 7   | 0.714 | 2.353 | 5.21E-06    |
| death receptor              |                           | 27  | 0.497 | 2.064 | 5.53E-04    |
| DEFB103A/DEFB103B           |                           | 7   | 0.500 | 2.337 | 4.11E-06    |
| DNA-PK                      |                           | 17  | 0.706 | 2.087 | 3.92E-05    |
| Dynamin                     |                           | 19  | 0.537 | 2.094 | 1.56E-04    |
| E2f                         |                           | 12  | 0.500 | 2.262 | 2.50E-05    |
| EF-1 alpha                  |                           | 11  | 0.509 | 2.287 | 1.62E-05    |
| EGFR ligand                 |                           | 9   | 0.639 | 2.356 | 3.59E-06    |
| EGFR/PDGFR/IGFR             |                           | 6   | 0.133 | 2.620 | 3.97E-05    |
| EGLN                        |                           | 17  | 0.706 | 2.087 | 3.92E-05    |
| elastase                    |                           | 16  | 0.383 | 2.314 | 9.68E-05    |
| Eotaxin                     |                           | 7   | 0.619 | 2.466 | 7.39E-06    |
| ERBB dimer                  |                           | 3   | 1.000 | 2.632 | 0           |
| ERBB1 dimer                 |                           | 8   | 0.429 | 2.516 | 7.43E-05    |
| ERBB4 ligand                |                           | 5   | 0.500 | 2.798 | 7.13E-06    |
| ERK                         |                           | 198 | 0.189 | 1.630 | 0.0225725   |
| ERK1/2                      |                           | 253 | 0.146 | 1.522 | 0.05730879  |
| Erm                         |                           | 23  | 0.443 | 2.114 | 1.61E-04    |
| estrogen receptor           |                           | 55  | 0.307 | 1.942 | 0.00687069  |
| ETS                         |                           | 11  | 0.618 | 2.112 | 6.78E-05    |
| EZR                         |                           | 53  | 0.392 | 1.956 | 9.22E-04    |
| F Actin                     | Network-integrated by IPA | 48  | 0.298 | 2.004 | 0.00112561  |
| farnesyl transferase        |                           | 9   | 0.833 | 2.152 | 2.27E-06    |
| Fascin                      |                           | 14  | 0.667 | 2.104 | 2.31E-05    |
| Fc gamma receptor           |                           | 35  | 0.469 | 2.012 | 3.63E-04    |
| Fcer1                       |                           | 41  | 0.454 | 1.992 | 5.89E-04    |
| Fcgr2                       |                           | 9   | 0.667 | 2.191 | 6.89E-06    |
| Fcgr3                       |                           | 22  | 0.498 | 2.066 | 1.66E-04    |
| Fgf                         |                           | 34  | 0.335 | 2.048 | 0.00129124  |
| Fgfr                        |                           | 28  | 0.474 | 2.091 | 6.50E-04    |
| Fibrin                      |                           | 15  | 0.448 | 2.204 | 1.13E-04    |
| Fibrinogen                  |                           | 38  | 0.381 | 2.002 | 0.00109532  |
| Filamin                     |                           | 13  | 0.410 | 2.224 | 3.10E-05    |
| FKHR                        |                           | 5   | 0.700 | 2.362 | 2.00E-06    |
| Focal adhesion kinase       |                           | 63  | 0.416 | 1.931 | 0.00124524  |
| Foxo                        |                           | 12  | 0.489 | 2.164 | 1.28E-04    |
| Frizzled                    |                           | 14  | 0.318 | 2.401 | 3.89E-04    |
| FSH                         |                           | 54  | 0.300 | 1.954 | 0.00446164  |
| G protein                   |                           | 45  | 0.280 | 2.035 | 0.00143373  |
| G protein alphai            |                           | 31  | 0.522 | 2.066 | 1.66E-04    |
| G protein beta gamma        |                           | 26  | 0.566 | 2.098 | 1.56E-04    |
| GABP                        |                           | 4   | 0     | 2.765 | 7.28E-06    |
| Gap                         |                           | 15  | 0.705 | 2.216 | 1.41E-05    |
| GC-GCR dimer                |                           | 8   | 0.214 | 2.337 | 4.04E-05    |
| Gcn5I                       |                           | 7   | 0.238 | 2.672 | 3.11E-05    |
| gelatinase                  |                           | 12  | 0.818 | 2.119 | 6.05E-06    |
| Gene               | Type                          | Value1 | Value2 | Value3     |
|--------------------|-------------------------------|--------|--------|------------|
| GLP2R              | Network-integrated by IPA     | 5      | 0.667  | 2.476      | 9.30E-07  |
| Glycogen synthase  | Network-integrated by IPA     | 19     | 0.544  | 2.125      | 5.94E-05  |
| GNRH               | Network-integrated by IPA     | 23     | 0.514  | 2.106      | 0.00391951|
| GOT                | Network-integrated by IPA     | 10     | 0.667  | 2.150      | 1.82E-05  |
| GPCR               | Network-integrated by IPA     | 57     | 0.298  | 1.996      | 0.00379348|
| G-protein beta     | Network-integrated by IPA     | 24     | 0.481  | 2.183      | 1.20E-04  |
| growth factor      | Network-integrated by IPA     | 32     | 0.587  | 2.002      | 2.42E-04  |
| growth factor      | Network-integrated by IPA     | 24     | 0.450  | 2.189      | 3.15E-04  |
| Growth hormone     | Network-integrated by IPA     | 60     | 0.289  | 1.934      | 0.00323770|
| Gsk3               | Network-integrated by IPA     | 57     | 0.389  | 1.925      | 0.00143901|
| HDac               | Network-integrated by IPA     | 35     | 0.242  | 2.029      | 0.00119344|
| HDL                | Network-integrated by IPA     | 41     | 0.503  | 1.988      | 4.65E-04  |
| hemoglobin         | Network-integrated by IPA     | 14     | 0.318  | 2.177      | 8.41E-04  |
| Hif1               | Network-integrated by IPA     | 28     | 0.329  | 2.094      | 2.31E-04  |
| HISTONE            | Network-integrated by IPA     | 25     | 0.372  | 2.062      | 5.55E-04  |
| histone deacetylase| Network-integrated by IPA     | 17     | 0.272  | 2.114      | 3.41E-04  |
| Histone h3         | Network-integrated by IPA     | 74     | 0.354  | 1.888      | 0.00298870|
| Histone h4         | Network-integrated by IPA     | 44     | 0.328  | 1.975      | 0.00156388|
| HLA-DR             | Network-integrated by IPA     | 24     | 0.551  | 2.079      | 1.23E-04  |
| HLA-DR group       | Network-integrated by IPA     | 13     | 0.718  | 2.106      | 2.02E-05  |
| HRAS               | Network-integrated by IPA     | 112    | 0.266  | 1.807      | 0.01224617|
| Hsp27              | Network-integrated by IPA     | 47     | 0.447  | 1.971      | 0.00122219|
| Hsp70              | Network-integrated by IPA     | 52     | 0.422  | 1.929      | 9.21E-04  |
| Hsp90              | Network-integrated by IPA     | 60     | 0.391  | 1.925      | 0.00102522|
| Hspg               | Network-integrated by IPA     | 12     | 0.424  | 2.262      | 7.96E-05  |
| Ikappa b kinase    | Network-integrated by IPA     | 20     | 0.579  | 2.067      | 1.71E-04  |
| Icam               | Network-integrated by IPA     | 7      | 0.333  | 2.274      | 4.68E-05  |
| Ifn                | Network-integrated by IPA     | 49     | 0.363  | 1.988      | 7.78E-04  |
| IFN alpha/beta     | Network-integrated by IPA     | 19     | 0.478  | 2.222      | 1.32E-04  |
| IFN Beta           | Network-integrated by IPA     | 61     | 0.418  | 1.934      | 0.00122841|
| Ifn gamma          | Network-integrated by IPA     | 32     | 0.502  | 2.021      | 2.15E-04  |
| IFN type 1         | Network-integrated by IPA     | 19     | 0.427  | 2.243      | 1.07E-04  |
| Ifnar              | Network-integrated by IPA     | 16     | 0.575  | 2.171      | 8.38E-05  |
| IgA                | Network-integrated by IPA     | 37     | 0.415  | 2.042      | 7.08E-04  |
| IgD                | Network-integrated by IPA     | 9      | 0.810  | 2.514      | 1.12E-06  |
| Ige                | Network-integrated by IPA     | 76     | 0.304  | 1.906      | 0.00343837|
| IGF                | Network-integrated by IPA     | 14     | 0.637  | 2.119      | 2.00E-04  |
| Igfbp              | Network-integrated by IPA     | 11     | 0.164  | 2.489      | 7.18E-05  |
| IgG                | Network-integrated by IPA     | 93     | 0.256  | 1.859      | 0.00720870|
| IgG1               | Network-integrated by IPA     | 35     | 0.368  | 2.050      | 8.41E-04  |
| IgG2a              | Network-integrated by IPA     | 29     | 0.426  | 2.066      | 4.20E-04  |
| IgG2b              | Network-integrated by IPA     | 13     | 0.538  | 2.204      | 3.78E-05  |
| IgG2c              | Network-integrated by IPA     | 3      | 0.333  | 2.784      | 2.03E-06  |
| IgG3               | Network-integrated by IPA     | 20     | 0.411  | 2.187      | 1.58E-04  |
| IgG4               | Network-integrated by IPA     | 7      | 0.571  | 2.341      | 2.39E-05  |
| Igm                | Network-integrated by IPA     | 64     | 0.355  | 1.950      | 0.00185718|
| Ikb                | Network-integrated by IPA     | 40     | 0.422  | 2.015      | 5.79E-04  |
| IKK (complex)      | Network-integrated by IPA     | 46     | 0.443  | 1.944      | 7.38E-04  |
| IkB (family)       | Network-integrated by IPA     | 28     | 0.538  | 2.058      | 2.44E-04  |
| IL1                | Network-integrated by IPA     | 139    | 0.233  | 1.751      | 0.01247602|
| Gene Name                  | Classification          | Network Integrated by IPA | P-Value 1 | P-Value 2 | P-Value 3 |
|---------------------------|-------------------------|---------------------------|-----------|-----------|-----------|
| IL12 (complex)            |                         | Network-integrated by IPA | 96        | 0.294     | 1.859     |
| IL12 (family)             |                         | Network-integrated by IPA | 79        | 0.310     | 1.911     |
| IL12RB2/IL23R             |                         | Network-integrated by IPA | 4         | 1.000     | 2.299     |
| IL17a dimer               |                         | Network-integrated by IPA | 12        | 0.470     | 2.195     |
| IL-17f dimer              |                         | Network-integrated by IPA | 8         | 0.250     | 2.447     |
| IL17R                     |                         | Network-integrated by IPA | 18        | 0.346     | 2.185     |
| IL-1R                     |                         | Network-integrated by IPA | 26        | 0.543     | 2.062     |
| IL-1R/TLR                 |                         | Network-integrated by IPA | 5         | 0.700     | 2.620     |
| IL23                      |                         | Network-integrated by IPA | 32        | 0.466     | 2.056     |
| IL-2R                     |                         | Network-integrated by IPA | 19        | 0.444     | 2.233     |
| IL31                      |                         | Network-integrated by IPA | 20        | 0.642     | 2.058     |
| IL8r                      |                         | Network-integrated by IPA | 17        | 0.596     | 2.083     |
| Immunoglobulin            |                         | Network-integrated by IPA | 134       | 0.220     | 1.775     |
| Interferon alpha          |                         | Network-integrated by IPA | 9         | 0.583     | 2.239     |
| Inhibin                   |                         | Network-integrated by IPA | 6         | 0.533     | 2.397     |
| Insulin                   |                         | Network-integrated by IPA | 118       | 0.231     | 1.798     |
| Integrin                  |                         | Network-integrated by IPA | 74        | 0.300     | 1.908     |
| Integrin alpha V beta 3   |                         | Network-integrated by IPA | 14        | 0.352     | 2.260     |
| Interleukin               |                         | Network-integrated by IPA | 87        | 0.308     | 1.873     |
| IRAK                      |                         | Network-integrated by IPA | 4         | 0.333     | 2.923     |
| IRF                       |                         | Network-integrated by IPA | 20        | 0.562     | 2.141     |
| JAK                       |                         | Network-integrated by IPA | 16        | 0.517     | 2.193     |
| JAK1/2                    |                         | Network-integrated by IPA | 36        | 0.351     | 2.067     |
| JNK1/2                    |                         | Network-integrated by IPA | 7         | 0.381     | 2.235     |
| Jnk                       |                         | Network-integrated by IPA | 32        | 0.402     | 2.019     |
| JUN/JUNB/JUND             |                         | Network-integrated by IPA | 196       | 0.180     | 1.634     |
| L1CAM                     |                         | Network-integrated by IPA | 21        | 0.398     | 2.100     |
| Laminin (complex)         |                         | Network-integrated by IPA | 27        | 0.457     | 2.050     |
| Laminin1                  |                         | Network-integrated by IPA | 45        | 0.405     | 1.960     |
| Ldh (complex)             |                         | Network-integrated by IPA | 16        | 0.633     | 2.094     |
| LDL                       |                         | Network-integrated by IPA | 21        | 0.462     | 2.092     |
| LDL-cholesterol           |                         | Network-integrated by IPA | 6         | 0.333     | 2.408     |
| Lfa-1                     |                         | Network-integrated by IPA | 15        | 0.295     | 2.397     |
| LGALS1                    |                         | Network-integrated by IPA | 41        | 0.328     | 1.998     |
| LGALS3                    |                         | Network-integrated by IPA | 45        | 0.385     | 1.963     |
| Lh                        |                         | Network-integrated by IPA | 51        | 0.410     | 1.948     |
| Lymphotoxin               |                         | Network-integrated by IPA | 10        | 0.556     | 2.204     |
| MAC                       |                         | Network-integrated by IPA | 18        | 0.542     | 2.089     |
| MAP2K1/2                  |                         | Network-integrated by IPA | 64        | 0.389     | 1.911     |
| Mapk                      |                         | Network-integrated by IPA | 157       | 0.209     | 1.715     |
| MEF2                      |                         | Network-integrated by IPA | 15        | 0.390     | 2.133     |
| Mek                       |                         | Network-integrated by IPA | 75        | 0.397     | 1.890     |
| Metalloprotease           |                         | Network-integrated by IPA | 28        | 0.413     | 2.025     |
| MHC Class I (complex)     |                         | Network-integrated by IPA | 17        | 0.404     | 2.177     |
| MHC CLASS I (family)      |                         | Network-integrated by IPA | 20        | 0.425     | 2.114     |
| MHC Class II (complex)    |                         | Network-integrated by IPA | 36        | 0.426     | 2.050     |
| MHC II                    |                         | Network-integrated by IPA | 22        | 0.558     | 2.069     |
| mir-34                    |                         | Network-integrated by IPA | 17        | 0.457     | 2.127     |
| Protein               | Network-integrated by IPA | Score | P-value |
|-----------------------|---------------------------|-------|---------|
| MITF                  |                           | 30    | 0.508   |
| MKK3/6                |                           | 16    | 0.558   |
| Mlc                   |                           | 35    | 0.360   |
| Mmp                   |                           | 63    | 0.352   |
| Mt-mmp                |                           | 5     | 0.100   |
| MTORC1                |                           | 35    | 0.413   |
| Mucin                 |                           | 14    | 0.253   |
| myosin-light-chain kinase |                     |       |         |
| Na+,K+ -ATPase         |                           | 17    | 0.500   |
| NADPH oxidase         |                           | 37    | 0.561   |
| N-Cadherin            |                           | 8     | 0.857   |
| Nck                   |                           | 22    | 0.505   |
| N-cor                 |                           | 24    | 0.322   |
| Neurotrophin          |                           | 20    | 0.563   |
| NFAT (complex)        |                           | 24    | 0.420   |
| Nfat (family)         |                           | 55    | 0.398   |
| NFkB (complex)        |                           | 222   | 0.163   |
| NFkB (family)         |                           | 24    | 0.571   |
| NfkB1-RelA            |                           | 18    | 0.575   |
| NfkB-RelA             |                           | 10    | 0.643   |
| Ngf                   |                           | 7     | 0.095   |
| NMT1                  |                           | 4     | 0.333   |
| NMT2                  |                           | 5     | 0.400   |
| Nos                   |                           | 37    | 0.492   |
| Notch                 |                           | 25    | 0.458   |
| Nr1h                  |                           | 26    | 0.351   |
| NRG (family)          |                           | 22    | 0.479   |
| P glycoprotein        |                           | 24    | 0.459   |
| P38 MAPK              |                           | 203   | 0.183   |
| p70 S6k               |                           | 49    | 0.499   |
| p85 (pik3r)           |                           | 51    | 0.455   |
| Pak                   |                           | 29    | 0.504   |
| PARP                  |                           | 21    | 0.476   |
| Pde4                  |                           | 11    | 0.673   |
| Pdgf (complex)        |                           | 65    | 0.320   |
| PDGF (family)         |                           | 9     | 0.444   |
| Pdgf Ab               |                           | 19    | 0.462   |
| PDGF BB               |                           | 71    | 0.310   |
| PDGF-AA               |                           | 18    | 0.680   |
| PDGF-DD               |                           | 8     | 0.267   |
| Pdgfr                 |                           | 46    | 0.426   |
| PEPCK                 |                           | 23    | 0.245   |
| peptidase             |                           | 5     | 0.900   |
| PFK                   |                           | 9     | 0.361   |
| PI3K (complex)        |                           | 201   | 0.187   |
| PI3K (family)         |                           | 44    | 0.414   |
| PI3K beta             |                           | 14    | 0.571   |
| PI3K p85              |                           | 37    | 0.392   |
| PIK3CA                |                           | 54    | 0.363   |
| Pka                   |                           | 109   | 0.251   |
| Protein/Phenotype | Description | FDR | q Value | p Value  |
|-------------------|-------------|------|---------|----------|
| Pka catalytic subunit | Network-integrated by IPA | 20 | 0.438 | 2.127 | 1.43E-04 |
| Pkc(s) | Network-integrated by IPA | 144 | 0.223 | 1.742 | 0.01402139 |
| PLA2 | Network-integrated by IPA | 23 | 0.565 | 2.044 | 9.65E-05 |
| PLC gamma | Network-integrated by IPA | 46 | 0.315 | 1.981 | 0.00135967 |
| Pld | Network-integrated by IPA | 53 | 0.302 | 1.987 | 0.00197737 |
| potassium channel | Network-integrated by IPA | 47 | 0.396 | 1.97 | 6.90E-04 |
| PP1 protein complex group | Network-integrated by IPA | 7 | 0.667 | 2.303 | 3.32E-06 |
| PP2A | Network-integrated by IPA | 36 | 0.385 | 2.054 | 6.63E-04 |
| Ppp2c | Network-integrated by IPA | 26 | 0.508 | 2.05 | 8.05E-04 |
| PROTEASE | Network-integrated by IPA | 50 | 0.419 | 1.967 | 6.97E-04 |
| Protein phosphatase | Network-integrated by IPA | 19 | 0.566 | 2.112 | 5.16E-05 |
| PTK | Network-integrated by IPA | 46 | 0.315 | 1.981 | 0.00135967 |
| Rac | Network-integrated by IPA | 53 | 0.302 | 1.987 | 9.65E-05 |
| Raf | Network-integrated by IPA | 44 | 0.425 | 2.027 | 4.25E-04 |
| Rap1 | Network-integrated by IPA | 50 | 0.449 | 1.971 | 8.78E-04 |
| Rar | Network-integrated by IPA | 23 | 0.486 | 2.079 | 1.46E-04 |
| Ras homolog | Network-integrated by IPA | 12 | 0.333 | 2.277 | 6.19E-05 |
| Rb | Network-integrated by IPA | 11 | 0.600 | 2.145 | 2.32E-05 |
| Rock | Network-integrated by IPA | 75 | 0.331 | 1.902 | 0.00221807 |
| Rho gdi | Network-integrated by IPA | 50 | 0.449 | 1.971 | 8.78E-04 |
| RNA polymerase II | Network-integrated by IPA | 36 | 0.276 | 2.029 | 6.80E-04 |
| Rnr | Network-integrated by IPA | 19 | 0.382 | 2.166 | 2.23E-04 |
| R-RSmad | Network-integrated by IPA | 46 | 0.320 | 1.975 | 0.00136026 |
| R-sk | Network-integrated by IPA | 4 | 0.500 | 2.262 | 3.09E-06 |
| R-Smad | Network-integrated by IPA | 27 | 0.293 | 2.118 | 7.91E-04 |
| Rock | Network-integrated by IPA | 39 | 0.411 | 1.998 | 4.30E-04 |
| RPS6KA | Network-integrated by IPA | 21 | 0.474 | 2.079 | 3.80E-04 |
| Sod | Network-integrated by IPA | 30 | 0.455 | 2.056 | 3.70E-04 |
| Secretase gamma | Network-integrated by IPA | 6 | 0.167 | 2.782 | 4.82E-06 |
| Secreted MMP | Network-integrated by IPA | 4 | 0.333 | 2.694 | 7.84E-06 |
| Selectin | Network-integrated by IPA | 5 | 0.500 | 2.478 | 2.64E-06 |
| Sfk | Network-integrated by IPA | 5 | 0.485 | 2.010 | 3.26E-04 |
| SFRP | Network-integrated by IPA | 5 | 0.400 | 2.809 | 3.63E-05 |
| Shc | Network-integrated by IPA | 46 | 0.364 | 1.992 | 7.46E-04 |
| Smad | Network-integrated by IPA | 19 | 0.419 | 2.112 | 3.25E-04 |
| SMAD1/5 | Network-integrated by IPA | 14 | 0.484 | 2.104 | 1.56E-04 |
| Smad1/5/8 | Network-integrated by IPA | 12 | 0.379 | 2.260 | 3.86E-04 |
| Smad2/3 | Network-integrated by IPA | 19 | 0.419 | 2.141 | 9.76E-04 |
| Sod | Network-integrated by IPA | 20 | 0.711 | 2.060 | 3.10E-05 |
| Protein                              | Network-integrated by IPA | 6   | 0.333 | 2.428 | 1.72E-05 |
|-------------------------------------|---------------------------|-----|-------|-------|--------|
| somatostatin receptor               |                           | 28  | 0.653 | 2.048 | 8.06E-05|
| Sos                                 |                           | 13  | 0.769 | 2.119 | 1.29E-05|
| sphingomyelinase                    |                           | 24  | 0.525 | 2.033 | 1.12E-04|
| Sphk                                |                           | 7   | 0.667 | 2.222 | 1.13E-05|
| SR (family)                         |                           | 74  | 0.332 | 1.898 | 0.00232033|
| STAT                                |                           | 46  | 0.318 | 1.987 | 9.92E-04|
| Stat3-Stat3                         |                           | 10  | 0.750 | 2.216 | 4.19E-06|
| STAT5a/b                            |                           | 64  | 0.333 | 1.933 | 0.00240339|
| SYK/ZAP                             |                           | 31  | 0.495 | 2.042 | 1.42E-04|
| TCF                                 |                           | 12  | 0.400 | 2.264 | 5.27E-05|
| SRC (family)                        |                           | 74  | 0.332 | 1.898 | 0.00232033|
| TCR                                 |                           | 93  | 0.258 | 1.879 | 0.00448837|
| TEC/BTK/ITK/IX/K/BM                 |                           | 24  | 0.482 | 2.087 | 9.20E-05|
| Tgf beta                            |                           | 101 | 0.271 | 1.832 | 0.00666028|
| TGFB1                               |                           | 230 | 0.148 | 1.568 | 0.05547221|
| TGFB1                               |                           | 20  | 0.374 | 2.075 | 0.00133989|
| TH1 Cytokine                        |                           | 10  | 0.422 | 2.239 | 2.45E-05|
| TH17 Cytokine                       |                           | 6   | 0.667 | 2.590 | 3.59E-06|
| TH2 Cytokine                        |                           | 14  | 0.363 | 2.250 | 6.59E-05|
| Thrombospondin                      |                           | 15  | 0.400 | 2.218 | 1.35E-04|
| thymidine kinase                    |                           | 14  | 0.143 | 2.482 | 1.87E-04|
| thyroid hormone receptor            |                           | 16  | 0.319 | 2.312 | 8.02E-05|
| Timp                                |                           | 12  | 0.742 | 2.123 | 8.87E-06|
| Tlr                                 |                           | 53  | 0.393 | 2.000 | 0.00127370|
| TLR2/3/4/9                          |                           | 7   | 0.667 | 2.595 | 5.65E-06|
| TLR2/TLR4                           |                           | 11  | 0.636 | 2.195 | 1.26E-05|
| TLR6                                |                           | 24  | 0.693 | 2.077 | 3.27E-04|
| TLR7/8                              |                           | 6   | 0.667 | 2.187 | 4.52E-06|
| Tnf (family)                        |                           | 70  | 0.326 | 1.913 | 0.00265730|
| Tnf receptor                        |                           | 29  | 0.476 | 2.058 | 1.79E-04|
| TRAF                                |                           | 11  | 0.800 | 2.152 | 7.63E-06|
| transglutaminase                    |                           | 13  | 0.667 | 2.098 | 4.25E-04|
| TSH                                 |                           | 34  | 0.425 | 2.027 | 5.63E-04|
| Type I BMP receptor                 |                           | 5   | 0.500 | 2.715 | 1.81E-05|
| Type I Receptor                     |                           | 4   | 0.667 | 2.904 | 1.84E-05|
| tyrosine kinase                     |                           | 26  | 0.385 | 2.087 | 4.64E-04|
| Ubiquitin                           |                           | 27  | 0.330 | 2.094 | 2.72E-04|
| VAV                                 |                           | 38  | 0.463 | 2.040 | 2.75E-04|
| Vegf                                |                           | 133 | 0.248 | 1.763 | 0.01109959|
| VitaminD3-VDR-RXR                    |                           | 6   | 0.200 | 2.676 | 1.60E-05|
| voltage-gated calcium channel       |                           | 18  | 0.294 | 2.297 | 2.25E-04|
| Wnt                                 |                           | 21  | 0.386 | 2.135 | 0.00129485|
| YAP1                                |                           | 44  | 0.310 | 1.985 | 0.00152682|
| ACVR2A                              | Downregulated in Secretome | -1.214 | 22 | 0.190 | 2.401 | 0.00126091|
| ANGPT2                              | Downregulated in Secretome | -1.421 | 59 | 0.412 | 1.927 | 0.00112465|
| ANGPTL1                             | Downregulated in Secretome | -1.577 | 2 | 1.000 | 2.453 | 0.00112465|
| ANGPTL2                             | Downregulated in Secretome | -1.133 | 8 | 0.533 | 2.241 | 6.78E-05|
| BMPRL1                              | Downregulated in Secretome | -1.172 | 15 | 0.295 | 2.617 | 3.52E-04|
| Gene    | Description               | Fold Change | q-value | p-value       |
|---------|---------------------------|-------------|---------|---------------|
| CCL22   | Downregulated in Secretome| -1.005      | 28      | 0.548         |
| CCL27   | Downregulated in Secretome| -1.770      | 9       | 0.750         |
| CCL28   | Downregulated in Secretome| -1.460      | 12      | 0.394         |
| CCL3    | Downregulated in Secretome| -2.345      | 67      | 0.384         |
| CCR7    | Downregulated in Secretome| -2.313      | 51      | 0.400         |
| CCR9    | Downregulated in Secretome| -1.284      | 15      | 0.514         |
| CHRD1   | Downregulated in Secretome| -1.613      | 4       | 0.667         |
| CNTF    | Downregulated in Secretome| -1.843      | 33      | 0.561         |
| CXCL11  | Downregulated in Secretome| -2.566      | 39      | 0.476         |
| CXCL14  | Downregulated in Secretome| -3.236      | 16      | 0.297         |
| CXCR2   | Downregulated in Secretome| -1.571      | 30      | 0.402         |
| DLK1    | Downregulated in Secretome| -1.638      | 25      | 0.372         |
| EREG    | Downregulated in Secretome| -1.144      | 34      | 0.433         |
| FGFR23  | Downregulated in Secretome| -2.425      | 11      | 0.582         |
| FGFR4   | Downregulated in Secretome| -1.351      | 25      | 0.443         |
| FGFRL1  | Downregulated in Secretome| -2.645      | 4       | 0.167         |
| FST1L1  | Downregulated in Secretome| -2.370      | 25      | 0.419         |
| GCG     | Downregulated in Secretome| -2.026      | 43      | 0.300         |
| GDF15   | Downregulated in Secretome| -1.142      | 32      | 0.441         |
| HBEGF   | Downregulated in Secretome| -3.074      | 56      | 0.357         |
| IL17C   | Downregulated in Secretome| -1.473      | 13      | 0.564         |
| IL17F   | Downregulated in Secretome| -1.571      | 30      | 0.402         |
| IL18RAP | Downregulated in Secretome| -1.220      | 21      | 0.532         |
| IL1RN   | Downregulated in Secretome| -2.123      | 69      | 0.297         |
| IL21    | Downregulated in Secretome| -1.148      | 66      | 0.336         |
| IL23A   | Downregulated in Secretome| -1.317      | 41      | 0.440         |
| IL25    | Downregulated in Secretome| -1.288      | 33      | 0.385         |
| LCN1    | Downregulated in Secretome| -1.429      | 1       | 0             |
| LEPR    | Downregulated in Secretome| -1.447      | 35      | 0.390         |
| OSM     | Downregulated in Secretome| -1.747      | 73      | 0.303         |
| PTGDR2  | Downregulated in Secretome| -1.044      | 8       | 0.286         |
| PTP3    | Downregulated in Secretome| -1.929      | 23      | 0.543         |
| SIGLEC9 | Downregulated in Secretome| -1.436      | 11      | 0.417         |
| SLC2A1  | Downregulated in Secretome| -1.526      | 36      | 0.414         |
| TGFB1   | Downregulated in Secretome| -1.791      | 53      | 0.282         |
| THBS2   | Downregulated in Secretome| -1.723      | 19      | 0.426         |
| TIMP2   | Downregulated in Secretome| -3.051      | 35      | 0.434         |
| TMEFF1  | Downregulated in Secretome| -2.251      | 1       | 0             |
| TNF     | Downregulated in Secretome| -1.314      | 336     | 0.105         |
| TNFRSF11B| Downregulated in Secretome| -1.682      | 33      | 0.568         |
| TNFRSF13| Downregulated in Secretome| -1.822      | 28      | 0.298         |
| TRADD   | Downregulated in Secretome| -2.960      | 29      | 0.538         |
| WIKKKN2 | Downregulated in Secretome| -2.062      | 1       | 0             |
Table S2. Enriched secretome network biological processes. The IPA-derived 520 node secretome network was queried through the Cytoscape [3] embedded application BiNGO (Bioinformatic Network Gene Ontology) [5] to extract enriched Gene Ontology (GO) biological processes (BP). Specifically, to identify overrepresented BP, a hypergeometric test with Benjamini & Hochberg false discovery rate (B-H FDR) correction with significance cutoff set at $p < 0.001$ and the full GO-BP annotation as background reference. Resulting enriched processes form a nested hierarchy of GO parent and child terms comprising 660 nodes (583 with $p < 0.001$) with 1129 edges. The most significant BP clustered into 8 categories, representing General Processes. Specifically, the top 100 BP are represented by ‘Regulation’ (56 processes), followed by ‘Development’ (14), ‘Signaling’ (8), ‘Motility’ (8), ‘Stimulus/Stress Response’ (6), ‘Immunity/Inflammation’ (5), ‘Cellular’ (2), and ‘Behavior’ (1).

Table S2 – Enriched secretome network biological processes

| -log (adj p-value) | Rank | BiNGO Biological Process                                      | General process |
|-------------------|------|---------------------------------------------------------------|-----------------|
| 47.152            | 1    | positive regulation of cellular process                      | Regulation      |
| 46.830            | 2    | positive regulation of biological process                     |                 |
| 45.904            | 3    | biological regulation                                         |                 |
| 44.747            | 4    | regulation of cellular process                                |                 |
| 43.320            | 5    | regulation of biological process                              |                 |
| 34.980            | 12   | regulation of multicellular organismal process                |                 |
| 31.662            | 15   | regulation of developmental process                           |                 |
| 27.254            | 20   | regulation of cell communication                               |                 |
| 26.728            | 21   | regulation of cell proliferation                              |                 |
| 25.547            | 25   | regulation of signaling pathway                               |                 |
| 24.455            | 27   | positive regulation of signal transduction                    |                 |
| 24.330            | 28   | positive regulation of signaling process                      |                 |
| 24.205            | 29   | positive regulation of cell communication                     |                 |
| 24.080            | 30   | negative regulation of biological process                     |                 |
| 23.903            | 31   | positive regulation of signaling pathway                      |                 |
| 22.977            | 34   | positive regulation of developmental process                  |                 |
| 22.028            | 38   | positive regulation of cell proliferation                     |                 |
| 21.234            | 41   | negative regulation of cellular process                       |                 |
| 19.923            | 44   | regulation of cell differentiation                            |                 |
| 18.637            | 47   | positive regulation of immune system process                  |                 |
| 18.437            | 49   | regulation of response to stimulus                            |                 |
| 17.909            | 50   | positive regulation of cell differentiation                   |                 |
| 17.754            | 51   | regulation of phosphorylation                                 |                 |
| 17.602 | 52  | regulation of protein amino acid phosphorylation |
| 17.352 | 53  | regulation of phosphorus metabolic process       |
| 17.352 | 54  | regulation of phosphate metabolic process        |
| 17.317 | 55  | regulation of signal transduction                |
| 17.246 | 56  | positive regulation of cellular metabolic process|
| 17.246 | 57  | positive regulation of intracellular protein kinase cascade |
| 17.206 | 58  | regulation of signaling process                  |
| 17.147 | 59  | positive regulation of metabolic process         |
| 17.045 | 60  | regulation of protein modification process       |
| 16.859 | 61  | regulation of intracellular protein kinase cascade|
| 16.518 | 62  | regulation of metabolic process                  |
| 15.841 | 63  | positive regulation of macromolecule metabolic process |
| 15.669 | 64  | regulation of MAPKKK cascade                     |
| 15.337 | 65  | regulation of biological quality                 |
| 15.238 | 66  | positive regulation of cell activation           |
| 14.893 | 67  | regulation of cell activation                    |
| 14.882 | 68  | regulation of cellular protein metabolic process |
| 14.620 | 69  | regulation of lymphocyte activation              |
| 14.545 | 70  | positive regulation of lymphocyte activation     |
| 14.133 | 71  | positive regulation of leukocyte activation      |
| 13.907 | 72  | regulation of cellular metabolic process         |
| 13.888 | 73  | regulation of leukocyte activation               |
| 13.738 | 74  | positive regulation of MAPKKK cascade            |
| 13.485 | 75  | regulation of macromolecule metabolic process    |
| 13.336 | 76  | regulation of protein metabolic process          |
| 13.309 | 77  | positive regulation of molecular function        |
| 13.143 | 78  | positive regulation of multicellular organismal process |
| 12.846 | 79  | regulation of primary metabolic process          |
| 12.648 | 80  | regulation of growth                             |
| 12.368 | 81  | regulation of apoptosis                          |
| 12.231 | 82  | regulation of programmed cell death              |
| 12.169 | 83  | regulation of immune response                    |
| 12.050 | 84  | regulation of cell death                         |
| 42.834 | 85  | developmental process                            |
| 42.436 | 86  | anatomical structure development                 |
| 42.436 | 87  | multicellular organismal development             |
| 40.405 | 88  | system development                               |
| 34.498 | 89  | organ development                                |
| 29.681 | 90  | cellular developmental process                   |
| 29.369 | 91  | cell differentiation                            |
| 25.686 | 92  | anatomical structure morphogenesis               |
| 18.527 | 93  | tissue development                               |
| 14.249 | 94  | nervous system development                       |
| 13.195 | 95  | organ morphogenesis                             |
| 12.490 | 96  | growth                                         |
| 12.986 | 97  | blood vessel development                         |
| 11.978 | 98  | skeletal system development                      |
| 34.511 | 99  | signaling                                       |
| 25.792 | 100 | signaling pathway                               |
| 25.731 | 101 | enzyme linked receptor protein signaling pathway  |
| Rank | Gene ID | Gene Name | Description |
|------|---------|-----------|-------------|
| 25.547 | 26 | cell surface receptor linked signaling pathway |
| 22.154 | 36 | signaling process |
| 22.154 | 37 | signal transmission |
| 18.834 | 46 | signal transduction |
| 16.518 | 63 | transmembrane receptor protein tyrosine kinase signaling pathway |
| 22.428 | 35 | locomotion |
| 15.916 | 65 | locomotory behavior |
| 15.150 | 71 | cellular component movement |
| 14.249 | 77 | taxis |
| 14.249 | 78 | chemotaxis |
| 13.117 | 89 | cell migration |
| 12.145 | 96 | localization of cell |
| 12.145 | 97 | cell motility |
| 35.321 | 11 | response to stimulus |
| 21.377 | 39 | response to wounding |
| 20.428 | 43 | defense response |
| 19.869 | 45 | response to chemical stimulus |
| 16.377 | 64 | response to external stimulus |
| 15.334 | 69 | response to stress |
| 36.202 | 10 | immune system process |
| 29.489 | 18 | immune response |
| 23.246 | 33 | inflammatory response |
| 21.321 | 40 | regulation of immune system process |
| 13.224 | 86 | cell activation |
| 31.617 | 16 | multicellular organismal process |
| 23.659 | 32 | cellular process |
| 20.706 | 42 | behavior |
Table S3. miR-146 dependent network nodes and topological properties. Upstream regulator analysis prioritized miR-146 and a miR-146 dependent regulatory cassette connecting downstream to 101 of the 155 differentially expressed secretome proteins. This 101 protein subset was submitted to IPA with a 2-fold differential expression cutoff for upregulated (orange) or downregulated (blue) proteins. Network-integrated (rose) nodes were derived from the IPA-based network neighborhood, obtained from direct and indirect relationships for derivation of pairwise interactions (edges). Network edges were undirected, unweighted, with multi-edge node pairs merged as a single interaction, resulting in a 430 node network with 6755 edges, with network connectivity demonstrating a power law distribution \(y = 40.08x^{-0.71}, r = 0.79\) consistent with non-random scale-free architecture [1,2]. Imported into Cytoscape [3], NetworkAnalyzer [4] was applied to interpret network node topology of the miR-146 dependent subset of the differentially expressed secretome. Listed topological parameters are identical to those listed in Table S1.

Table S3 – miR-146 dependent network nodes and topological properties

| Node      | Network Inclusion Basis | Log2 FC | Degree | Clustering Coefficient | Average Shortest Path Length | Betweenness Centrality |
|-----------|-------------------------|---------|--------|------------------------|-----------------------------|------------------------|
| ACKR2     | Upregulated in Secretome| 1.196   | 12     | 0.485                  | 2.191                       | 3.19E-04               |
| AGER      | Upregulated in Secretome| 1.431   | 42     | 0.422                  | 1.965                       | 0.00210857            |
| AGRP      | Upregulated in Secretome| 1.193   | 5      | 0.800                  | 2.524                       | 3.41E-05              |
| ALCAM     | Upregulated in Secretome| 10.46   | 26     | 0.257                  | 2.075                       | 0.00126733            |
| ANGPT1    | Upregulated in Secretome| 1.107   | 35     | 0.519                  | 1.995                       | 3.09E-04              |
| AREG      | Upregulated in Secretome| 1.017   | 49     | 0.365                  | 1.963                       | 0.00219055            |
| BIK       | Upregulated in Secretome| 8.153   | 10     | 0.267                  | 2.403                       | 6.55E-05              |
| BPIFA1    | Upregulated in Secretome| 1.881   | 5      | 0.800                  | 2.329                       | 2.67E-06              |
| CCL20     | Upregulated in Secretome| 1.023   | 38     | 0.344                  | 1.991                       | 0.00151276            |
| CCL7      | Upregulated in Secretome| 1.567   | 24     | 0.506                  | 2.049                       | 2.57E-04              |
| CCN3      | Upregulated in Secretome| 1.011   | 21     | 0.327                  | 2.126                       | 6.26E-04              |
| CD14      | Upregulated in Secretome| 1.404   | 42     | 0.394                  | 1.981                       | 9.14E-04              |
| CD163     | Upregulated in Secretome| 2.891   | 11     | 0.250                  | 2.394                       | 2.02E-04              |
| CD40      | Upregulated in Secretome| 1.213   | 85     | 0.255                  | 1.851                       | 0.01201139            |
| CD40LG    | Upregulated in Secretome| 1.157   | 83     | 0.263                  | 1.862                       | 0.00859056            |
| CD80      | Upregulated in Secretome| 3.153   | 48     | 0.392                  | 1.965                       | 0.00336553            |
| CRIM1     | Upregulated in Secretome| 1.340   | 14     | 0.385                  | 2.343                       | 3.53E-04              |
| CSF2RA    | Upregulated in Secretome| 1.025   | 12     | 0.178                  | 2.308                       | 1.87E-04              |
| Gene       | Functional Category | Fold Change | p-Value | q-Value |
|-----------|---------------------|-------------|---------|---------|
| CTNNB1    | Upregulated in Secretome | 1.593       | 0.02865061 |
| CXCL13    | Upregulated in Secretome | 1.921       | 5.6E-04  |
| CXCL2     | Upregulated in Secretome | 1.837       | 0.00383465 |
| CXCR3     | Upregulated in Secretome | 1.060       | 4.7E-04  |
| DEFB4A/ DEFB4B | Upregulated in Secretome | 7.654       | 5.7E-04  |
| DKK1      | Upregulated in Secretome | 2.001       | 0.003074 |
| EDAR      | Upregulated in Secretome | 1.067       | 9.90E-07 |
| EGF       | Upregulated in Secretome | 1.040       | 0.0388255 |
| EGFR      | Upregulated in Secretome | 1.124       | 0.00383465 |
| FADD      | Upregulated in Secretome | 1.010       | 0.00115867 |
| FRZB      | Upregulated in Secretome | 1.019       | 3.97E-04 |
| FZD1      | Upregulated in Secretome | 2.647       | 8.43E-05  |
| FZD7      | Upregulated in Secretome | 1.111       | 2.03E-05  |
| HGF       | Upregulated in Secretome | 1.091       | 0.02367151 |
| IGF1R     | Upregulated in Secretome | 1.249       | 0.01210658 |
| IGFBP3    | Upregulated in Secretome | 1.050       | 0.00423877 |
| IGFBP6    | Upregulated in Secretome | 1.134       | 2.84E-04  |
| IGFBP7    | Upregulated in Secretome | 1.701       | 2.06E-04  |
| IL17RA    | Upregulated in Secretome | 1.134       | 0.00266359 |
| IL17RB    | Upregulated in Secretome | 2.584       | 5.96E-04  |
| IL17RD    | Upregulated in Secretome | 1.071       | 1.40E-07  |
| IL18R1    | Upregulated in Secretome | 2.067       | 4.65E-04  |
| IL1B      | Upregulated in Secretome | 1.095       | 0.07097365 |
| IL1R2     | Upregulated in Secretome | 1.121       | 0.00104414 |
| IL21R     | Upregulated in Secretome | 1.708       | 1.88E-04  |
| IL2RA     | Upregulated in Secretome | 2.572       | 0.00174296 |
| IL5RA     | Upregulated in Secretome | 1.208       | 1.79E-04  |
| IL7R      | Upregulated in Secretome | 1.805       | 8.95E-04  |
| IL9       | Upregulated in Secretome | 1.777       | 0.00243335 |
| ITGAL     | Upregulated in Secretome | 1.051       | 9.88E-04  |
| LEP       | Upregulated in Secretome | 2.369       | 0.01260958 |
| MMP9      | Upregulated in Secretome | 1.346       | 0.02980729 |
| NGF       | Upregulated in Secretome | 1.427       | 0.00684951 |
| PDGFA     | Upregulated in Secretome | 1.971       | 5.24E-04  |
| PF4       | Upregulated in Secretome | 2.252       | 7.01E-04  |
| PRL       | Upregulated in Secretome | 1.093       | 0.00931091 |
| SELE      | Upregulated in Secretome | 1.797       | 0.00421343 |
| SELP      | Upregulated in Secretome | 1.292       | 5.61E-04  |
| SFRP4     | Upregulated in Secretome | 1.480       | 0.00116709 |
| SMAD1     | Upregulated in Secretome | 3.058       | 0.00560806 |
| SMAD9     | Upregulated in Secretome | 2.324       | 2.40E-05  |
| TFPI      | Upregulated in Secretome | 1.073       | 8.89E-06  |
| TLR3      | Upregulated in Secretome | 1.276       | 3.38E-04  |
| TLR4      | Upregulated in Secretome | 1.350       | 9.98E-04  |
| TNFAIP6   | Upregulated in Secretome | 1.049       | 3.08E-04  |
| TNFRSF10A | Upregulated in Secretome | 1.719       | 1.40E-04  |
| TNFRSF6B  | Upregulated in Secretome | 1.005       | 0.00330715 |
| TNFSF11   | Upregulated in Secretome | 1.724       | 6.63E-04  |
| TYMP      | Upregulated in Secretome | 1.452       | 4.54E-06  |
| 26s Proteasome | Network-integrated by IPA | 47          | 0.030715  |
| Gene                     | Network-integrated by IPA | P-value  |
|--------------------------|--------------------------|----------|
| 7S NGF                   |                          |          |
| Actin                    |                          |          |
| ADCY                     |                          |          |
| adhesion molecule        |                          |          |
| ADRB                     |                          |          |
| Akt                      |                          |          |
| ALDH                     |                          |          |
| Alp                      |                          |          |
| Alpha Actinin            |                          |          |
| Alpha catenin            |                          |          |
| ALT                      |                          |          |
| Ampa Receptor            |                          |          |
| AMPK                     |                          |          |
| amylase                  |                          |          |
| Angiotensin II receptor type 1 |                |          |
| Ap1                      |                          |          |
| Ap2                      |                          |          |
| Atrial Natriuretic Peptide |                        |          |
| ATXN7                    |                          |          |
| BCR (complex)            |                          |          |
| C/EBP                    |                          |          |
| C1q                      |                          |          |
| C8                       |                          |          |
| CACNA1A                  |                          |          |
| CALC                     |                          |          |
| Calcineurin A            |                          |          |
| Calcineurin protein(s)   |                          |          |
| Calmodulin               |                          |          |
| calpain                  |                          |          |
| CaMKII                   |                          |          |
| Casein                   |                          |          |
| caspase                  |                          |          |
| Caspase 3/7              |                          |          |
| Cbp/p300                 |                          |          |
| C-C chemokine receptor   |                          |          |
| CD3                      |                          |          |
| CD3 group                |                          |          |
| CD4                      |                          |          |
| CD80/CD86                |                          |          |
| CD9                      |                          |          |
| Cebp                     |                          |          |
| CG                       |                          |          |
| chemokine                |                          |          |
| chemokine receptor       |                          |          |
| Clap                     |                          |          |
| Ck2                      |                          |          |
| Cofilin                  |                          |          |
| collagen                 |                          |          |
| Protein/Complex       | Network-integrated by IPA | p-value 1 | p-value 2 | p-value 3 |
|----------------------|---------------------------|-----------|-----------|-----------|
| Collagen Alpha1      | Network-integrated by IPA | 21        | 0.503     | 2.093     | 2.99E-04  |
| Collagen type I      | Network-integrated by IPA | 38        | 0.476     | 1.979     | 0.00107657|
| Collagen type I (complex) | Network-integrated by IPA | 23        | 0.336     | 2.054     | 9.41E-04  |
| Collagen type II     | Network-integrated by IPA | 14        | 0.516     | 2.175     | 2.13E-04  |
| Collagen type III    | Network-integrated by IPA | 7         | 0.714     | 2.333     | 1.10E-05  |
| Collagen type IV     | Network-integrated by IPA | 24        | 0.290     | 2.193     | 4.66E-04  |
| Collagen type II (complex) | Network-integrated by IPA | 45        | 0.338     | 1.963     | 0.00177709|
| Complement           | Network-integrated by IPA | 13        | 0.455     | 2.319     | 4.49E-05  |
| CPIA2                | Network-integrated by IPA | 21        | 0.543     | 2.049     | 9.75E-05  |
| CPT1                 | Network-integrated by IPA | 8         | 0.267     | 2.723     | 2.58E-05  |
| Cr3                  | Network-integrated by IPA | 19        | 0.456     | 2.154     | 1.10E-04  |
| Creb                 | Network-integrated by IPA | 85        | 0.323     | 1.825     | 0.00560351|
| CREB1                | Network-integrated by IPA | 73        | 0.313     | 1.865     | 0.00782967|
| CREBBP               | Network-integrated by IPA | 72        | 0.331     | 1.855     | 0.00519244|
| c-Src                | Network-integrated by IPA | 11        | 0.556     | 2.207     | 1.19E-05  |
| Cyclin A             | Network-integrated by IPA | 34        | 0.401     | 1.979     | 5.75E-04  |
| Cyclin D             | Network-integrated by IPA | 25        | 0.514     | 2.124     | 4.87E-04  |
| Cyclin E             | Network-integrated by IPA | 24        | 0.511     | 2.044     | 2.16E-04  |
| Cyclooxygenase       | Network-integrated by IPA | 14        | 0.560     | 2.100     | 1.92E-04  |
| CYP19                | Network-integrated by IPA | 10        | 0.714     | 2.170     | 9.68E-06  |
| cytochrome C         | Network-integrated by IPA | 27        | 0.397     | 2.082     | 4.69E-04  |
| cytokine             | Network-integrated by IPA | 121       | 0.199     | 1.748     | 0.01927696|
| cytokine receptor    | Network-integrated by IPA | 20        | 0.176     | 2.357     | 4.20E-04  |
| DNA-PK               | Network-integrated by IPA | 8         | 0.600     | 2.287     | 9.16E-06  |
| Dynamin              | Network-integrated by IPA | 12        | 0.697     | 2.186     | 3.05E-05  |
| E2f                  | Network-integrated by IPA | 18        | 0.467     | 2.093     | 2.26E-04  |
| Ecm                  | Network-integrated by IPA | 9         | 0.333     | 2.436     | 3.52E-05  |
| EGFR ligand          | Network-integrated by IPA | 9         | 0.611     | 2.415     | 2.80E-05  |
| EGFR/EGFR/IGFR       | Network-integrated by IPA | 7         | 0.810     | 2.347     | 8.87E-06  |
| EGLN                 | Network-integrated by IPA | 6         | 0.200     | 2.578     | 9.08E-05  |
| elastase             | Network-integrated by IPA | 15        | 0.505     | 2.156     | 2.94E-04  |
| EOMES                | Network-integrated by IPA | 19        | 0.294     | 2.186     | 9.99E-04  |
| Eotaxin              | Network-integrated by IPA | 4         | 0.833     | 2.401     | 2.71E-06  |
| EP300                | Network-integrated by IPA | 82        | 0.226     | 1.834     | 0.01637025|
| ERBB                 | Network-integrated by IPA | 12        | 0.455     | 2.319     | 4.35E-05  |
| ErbB1 dimer          | Network-integrated by IPA | 5         | 0.600     | 2.541     | 5.56E-06  |
| ErbB1-ErbB4 dimer    | Network-integrated by IPA | 2         | 1.000     | 2.890     | 0         |
| ERK                  | Network-integrated by IPA | 142       | 0.202     | 1.702     | 0.02154021|
| ERK1/2               | Network-integrated by IPA | 169       | 0.176     | 1.615     | 0.03875768|
| Erm                  | Network-integrated by IPA | 16        | 0.538     | 2.191     | 4.09E-05  |
| ESR1                 | Network-integrated by IPA | 112       | 0.232     | 1.760     | 0.01689657|
| ESR2                 | Network-integrated by IPA | 63        | 0.286     | 1.895     | 0.00730406|
| estrogen receptor    | Network-integrated by IPA | 53        | 0.329     | 1.937     | 0.00303107|
| ETS                  | Network-integrated by IPA | 11        | 0.655     | 2.133     | 6.75E-05  |
| F Actin              | Network-integrated by IPA | 40        | 0.317     | 2.012     | 9.29E-04  |
| farnesyl transferase | Network-integrated by IPA | 7         | 0.619     | 2.438     | 6.86E-06  |
| Fascin               | Network-integrated by IPA | 12        | 0.644     | 2.152     | 1.72E-05  |
| Fc gamma receptor    | Network-integrated by IPA | 32        | 0.401     | 2.016     | 7.78E-04  |
| Fc gamma receptor    | Network-integrated by IPA | 38        | 0.400     | 1.995     | 0.00150239|
| Protein               | Category                  | Rank | Fold Change | p-Value   |
|-----------------------|---------------------------|------|-------------|-----------|
| Fcgr2                 | Network-integrated by IPA |      | 9           | 0.639     |
| Fcgr3                 | Network-integrated by IPA |      | 11          | 0.436     |
| Fgf                   | Network-integrated by IPA |      | 21          | 0.474     |
| Fibrin                | Network-integrated by IPA |      | 9           | 0.444     |
| Fibrinogen            | Network-integrated by IPA |      | 23          | 0.368     |
| FKHR                  | Network-integrated by IPA |      | 6           | 0.733     |
| Focal adhesion kinase | Network-integrated by IPA |      | 57          | 0.345     |
| Foxo                  | Network-integrated by IPA |      | 10          | 0.643     |
| Frizzled              | Network-integrated by IPA |      | 14          | 0.273     |
| FSH                   | Network-integrated by IPA |      | 47          | 0.383     |
| G protein             | Network-integrated by IPA |      | 46          | 0.257     |
| G protein alpha i     | Network-integrated by IPA |      | 31          | 0.485     |
| G protein beta gamma  | Network-integrated by IPA |      | 25          | 0.570     |
| Gap                   | Network-integrated by IPA |      | 13          | 0.800     |
| GC-GCR dimer          | Network-integrated by IPA |      | 10          | 0.267     |
| gelatinase            | Network-integrated by IPA |      | 8           | 0.679     |
| Glycogen synthase     | Network-integrated by IPA |      | 17          | 0.514     |
| GNRH                  | Network-integrated by IPA |      | 14          | 0.549     |
| GOT                   | Network-integrated by IPA |      | 6           | 0.800     |
| GPCR                  | Network-integrated by IPA |      | 51          | 0.357     |
| G-protein beta        | Network-integrated by IPA |      | 23          | 0.486     |
| growth factor         | Network-integrated by IPA |      | 29          | 0.537     |
| growth factor receptor| Network-integrated by IPA |      | 21          | 0.520     |
| Growth hormone        | Network-integrated by IPA |      | 48          | 0.289     |
| Gsk3                  | Network-integrated by IPA |      | 58          | 0.370     |
| Hdac                  | Network-integrated by IPA |      | 33          | 0.262     |
| HDL                   | Network-integrated by IPA |      | 27          | 0.427     |
| hemoglobin            | Network-integrated by IPA |      | 12          | 0.222     |
| Hif1                  | Network-integrated by IPA |      | 24          | 0.329     |
| HISTONE               | Network-integrated by IPA |      | 20          | 0.359     |
| histone deacetylase   | Network-integrated by IPA |      | 13          | 0.154     |
| Histone h3            | Network-integrated by IPA |      | 70          | 0.337     |
| Histone h4            | Network-integrated by IPA |      | 42          | 0.313     |
| HLA-DR                | Network-integrated by IPA |      | 19          | 0.585     |
| HLA-DR group          | Network-integrated by IPA |      | 8           | 0.607     |
| HRAS                  | Network-integrated by IPA |      | 100         | 0.282     |
| Hsp27                 | Network-integrated by IPA |      | 43          | 0.421     |
| Hsp70                 | Network-integrated by IPA |      | 48          | 0.371     |
| Hsp90                 | Network-integrated by IPA |      | 55          | 0.369     |
| Hspg                  | Network-integrated by IPA |      | 7           | 0.286     |
| I kappa b kinase      | Network-integrated by IPA |      | 16          | 0.558     |
| Icam                  | Network-integrated by IPA |      | 4           | 0.333     |
| Ifn                   | Network-integrated by IPA |      | 33          | 0.286     |
| IFN alpha/beta        | Network-integrated by IPA |      | 19          | 0.456     |
| IFN Beta              | Network-integrated by IPA |      | 55          | 0.342     |
| IFN gamma             | Network-integrated by IPA |      | 28          | 0.365     |
| IFN type 1            | Network-integrated by IPA |      | 19          | 0.357     |
| Ifnar                 | Network-integrated by IPA |      | 16          | 0.458     |
| Iga                   | Network-integrated by IPA |      | 28          | 0.458     |
| Gene          | Network-integrated by IPA | Fold Change | P Value   |
|--------------|---------------------------|-------------|-----------|
| IgD          |                           | 9           | 0.810     |
| IgE          |                           | 70          | 0.290     |
| IgF          |                           | 13          | 0.603     |
| Igfbp        |                           | 8           | 0.250     |
| IgG          |                           | 73          | 0.280     |
| IgG1         |                           | 27          | 0.453     |
| IgG2a        |                           | 23          | 0.455     |
| IgG2b        |                           | 12          | 0.591     |
| IgG3         |                           | 13          | 0.410     |
| Igm          |                           | 47          | 0.383     |
| Ikb          |                           | 31          | 0.414     |
| IKK (complex)|                           | 39          | 0.445     |
| IL1          |                           | 99          | 0.242     |
| IL12 (complex)|                         | 74          | 0.304     |
| IL12 (family)|                           | 59          | 0.311     |
| IL12RB2/IL23R|                          | 4           | 1.000     |
| IL17a dimer  |                           | 9           | 0.556     |
| IL-17f dimer |                           | 6           | 0.333     |
| IL17R        |                           | 15          | 0.343     |
| IL-1R        |                           | 24          | 0.511     |
| IL-1R/TLR    |                           | 4           | 0.333     |
| IL23         |                           | 26          | 0.412     |
| IIRr         |                           | 14          | 0.473     |
| Immunoglobulin|                          | 108         | 0.225     |
| Importin alpha|                         | 9           | 0.417     |
| Insulin      |                           | 113         | 0.217     |
| Integrin     |                           | 55          | 0.338     |
| Integrin alpha V beta 3 |                 | 12          | 0.288     |
| Interferon alpha |                       | 70          | 0.309     |
| INTERLEUKIN  |                           | 3           | 0.667     |
| IRAK         |                           | 15          | 0.449     |
| IRF          |                           | 14          | 0.385     |
| ITK          |                           | 35          | 0.330     |
| JAK          |                           | 36          | 0.307     |
| JAK1/2       |                           | 7           | 0.238     |
| JNK1/2       |                           | 20          | 0.392     |
| Jnk          |                           | 121         | 0.216     |
| L1CAM        |                           | 24          | 0.398     |
| Laminin (complex)|                        | 32          | 0.407     |
| Laminin1     |                           | 12          | 0.530     |
| Ldh (complex)|                           | 19          | 0.351     |
| LDL          |                           | 63          | 0.355     |
| Lfa-1        |                           | 11          | 0.278     |
| Lh           |                           | 41          | 0.472     |
| Lymphotoxin  |                           | 8           | 0.393     |
| MAC          |                           | 17          | 0.449     |
| MAFB         |                           | 12          | 0.356     |
| MAP2K1       |                           | 79          | 0.348     |
| MAP2K1/2     |                           | 50          | 0.384     |
| Gene                  | Sequence | Value 1 | Value 2 | Value 3    |
|----------------------|----------|---------|---------|------------|
| Mapk                 |          |         |         |            |
| MEF2                 |          |         |         |            |
| Mek                  |          |         |         |            |
| Metalloprotease      |          |         |         |            |
| MHC Class I (complex)|          |         |         |            |
| MHC CLASS I (family) |          |         |         |            |
| MHC Class II (complex)|        |         |         |            |
| MHC II               |          |         |         |            |
| mir-148              |          |         |         |            |
| mir-17-5p (and other miRNAs w/seed AAAGUGC) | |         |         |            |
| mir-192              |          |         |         |            |
| mir-214              |          |         |         |            |
| MKK3/6               |          |         |         |            |
| Mlc                  |          |         |         |            |
| Mmp                  |          |         |         |            |
| MTOC1                |          |         |         |            |
| Mucin                |          |         |         |            |
| MYCN                 |          |         |         |            |
| myosin-light-chain kinase | |         |         |            |
| NADPH oxidase        |          |         |         |            |
| N-Cadherin           |          |         |         |            |
| N-cor                |          |         |         |            |
| NFAT (complex)       |          |         |         |            |
| Nfat (family)        |          |         |         |            |
| NFkB (complex)       |          |         |         |            |
| NFkB (family)        |          |         |         |            |
| NfkB1-RelA           |          |         |         |            |
| NfkB-RelA            |          |         |         |            |
| Ngf                  |          |         |         |            |
| Nos                  |          |         |         |            |
| Notch                |          |         |         |            |
| Nr1h                 |          |         |         |            |
| P glycoprotein       |          |         |         |            |
| P38 MAPK             |          |         |         |            |
| p70 S6k              |          |         |         |            |
| p85 (pik3r)          |          |         |         |            |
| Pak                  |          |         |         |            |
| PARP                 |          |         |         |            |
| Pde4                 |          |         |         |            |
| Pdgf (complex)       |          |         |         |            |
| PDGF (family)        |          |         |         |            |
| Pdgf Ab              |          |         |         |            |
| PDGF-BB              |          |         |         |            |
| PDGF-AA              |          |         |         |            |
| Pdgfr                |          |         |         |            |
| PECK                 |          |         |         |            |
| peptidase            |          |         |         |            |
| Gene Family               | Network-integrated by IPA | Fold Change | Significance  |
|---------------------------|---------------------------|-------------|--------------|
| PI3K (complex)            | Network-integrated by IPA | 174         | 0.194 1.611 0.0369184 |
| PI3K (family)             | Network-integrated by IPA | 44          | 0.410 1.942 9.67E-04 |
| PI3K beta                 | Network-integrated by IPA | 14          | 0.484 2.168 1.68E-04 |
| PI3K p85                  | Network-integrated by IPA | 28          | 0.406 2.075 4.66E-04 |
| Pka                      | Network-integrated by IPA | 102         | 0.231 1.790 0.01403193 |
| Pka catalytic subunit     | Network-integrated by IPA | 19          | 0.434 2.152 2.01E-04 |
| Pkc(s)                    | Network-integrated by IPA | 132         | 0.224 1.706 0.0216697 |
| PL2A                     | Network-integrated by IPA | 15          | 0.533 2.198 7.65E-05 |
| PLC                      | Network-integrated by IPA | 44          | 0.410 1.942 9.67E-04 |
| PLC gamma                | Network-integrated by IPA | 42          | 0.355 1.986 0.00205206 |
| Pld                      | Network-integrated by IPA | 43          | 0.370 1.972 0.00119474 |
| potassium channel         | Network-integrated by IPA | 6           | 0.667 2.315 3.33E-06 |
| PP1 protein complex group | Network-integrated by IPA | 32          | 0.437 2.054 5.13E-04 |
| PP2A                     | Network-integrated by IPA | 47          | 0.399 1.958 0.00111421 |
| Ppp2c                    | Network-integrated by IPA | 16          | 0.615 2.152 4.23E-05 |
| PRKAA                    | Network-integrated by IPA | 18          | 0.510 2.154 4.61E-04 |
| Pro-inflammatory Cytokine | Network-integrated by IPA | 31          | 0.432 2.016 8.03E-04 |
| Proinsulin               | Network-integrated by IPA | 20          | 0.368 2.077 0.00340287 |
| PROTEASE                 | Network-integrated by IPA | 7           | 0.667 2.294 6.62E-06 |
| protein phosphatase      | Network-integrated by IPA | 9           | 0.556 2.336 2.91E-05 |
| PTK                      | Network-integrated by IPA | 23          | 0.433 2.089 2.35E-04 |
| Rab5                     | Network-integrated by IPA | 9           | 0.583 2.249 2.29E-05 |
| Rac                      | Network-integrated by IPA | 68          | 0.309 1.890 0.00422844 |
| Raf                      | Network-integrated by IPA | 39          | 0.443 2.028 5.80E-04 |
| Rap1                     | Network-integrated by IPA | 37          | 0.518 2.026 4.24E-04 |
| RAS                      | Network-integrated by IPA | 104         | 0.279 1.781 0.01098207 |
| Ras homolog              | Network-integrated by IPA | 53          | 0.374 1.935 0.00201869 |
| RNA polymerase II        | Network-integrated by IPA | 44          | 0.339 1.946 0.00190489 |
| Rock                     | Network-integrated by IPA | 31          | 0.374 2.030 4.29E-04 |
| RPS6KA                   | Network-integrated by IPA | 16          | 0.440 2.193 2.33E-04 |
| Rsk                      | Network-integrated by IPA | 30          | 0.478 2.014 3.07E-04 |
| R-Smad                   | Network-integrated by IPA | 6           | 0.167 2.762 9.22E-06 |
| RUNX3                    | Network-integrated by IPA | 32          | 0.232 2.037 0.0028904 |
| Rxr                      | Network-integrated by IPA | 18          | 0.375 2.226 2.80E-04 |
| S100A1                   | Network-integrated by IPA | 13          | 0.473 2.235 1.08E-04 |
| S100B                    | Network-integrated by IPA | 22          | 0.532 2.079 1.97E-04 |
| SAA                      | Network-integrated by IPA | 20          | 0.529 2.091 8.30E-04 |
| Sapk                     | Network-integrated by IPA | 16          | 0.542 2.152 7.26E-05 |
| SCAVENGER receptor CLASS A | Network-integrated by IPA | 5           | 0.700 2.473 1.20E-06 |
| Secretase gamma          | Network-integrated by IPA | 15          | 0.436 2.172 6.86E-05 |
| secreted MMP             | Network-integrated by IPA | 1           | 0 2.709 0 |
| Sfk                      | Network-integrated by IPA | 30          | 0.467 2.000 4.30E-04 |
| SFRP                     | Network-integrated by IPA | 4           | 0.500 3.196 2.45E-05 |
| Shc                      | Network-integrated by IPA | 42          | 0.385 1.991 0.00105954 |
| Smad                     | Network-integrated by IPA | 17          | 0.352 2.291 0.00100901 |
| SMAD1/5                  | Network-integrated by IPA | 9           | 0.278 2.312 1.22E-04 |
| Smad1/5/8                | Network-integrated by IPA | 9           | 0.472 2.361 4.90E-04 |
| Smad2/3                  | Network-integrated by IPA | 14          | 0.303 2.186 1.76E-04 |
| Gene                        | Status                              | Fold Change | p-value       |
|-----------------------------|-------------------------------------|-------------|---------------|
| SMARCD3                     | Network-integrated by IPA           | 11          | 0.444        |
| SMO                         | Network-integrated by IPA           | 15          | 0.282        |
| Sod                         | Network-integrated by IPA           | 15          | 0.543        |
| somatostatin receptor       | Network-integrated by IPA           | 5           | 0.200        |
| Sos                         | Network-integrated by IPA           | 22          | 0.641        |
| sphingomyelinase            | Network-integrated by IPA           | 13          | 0.628        |
| Spk                         | Network-integrated by IPA           | 21          | 0.410        |
| sPla2                       | Network-integrated by IPA           | 4           | 0.667        |
| SRC (family)                | Network-integrated by IPA           | 71          | 0.277        |
| STAT                        | Network-integrated by IPA           | 37          | 0.341        |
| Stat3-Stat3                 | Network-integrated by IPA           | 10          | 0.679        |
| STAT5a/b                    | Network-integrated by IPA           | 58          | 0.295        |
| SYK/ZAP                     | Network-integrated by IPA           | 26          | 0.460        |
| TEC/BTK/ITK/TXK/BA X        | Network-integrated by IPA           | 65          | 0.256        |
| TGF beta                    | Network-integrated by IPA           | 17          | 0.478        |
| TGFBR                       | Network-integrated by IPA           | 3           | 0.333        |
| TH1 Cytokine                | Network-integrated by IPA           | 4           | 0.667        |
| TH17 Cytokine               | Network-integrated by IPA           | 3           | 0.333        |
| TH2 Cytokine                | Network-integrated by IPA           | 5           | 0.400        |
| thymidine kinase            | Network-integrated by IPA           | 11          | 0.382        |
| Timp                        | Network-integrated by IPA           | 4           | 0.333        |
| Trl                          | Network-integrated by IPA           | 4           | 0.833        |
| Tnf (family)                | Network-integrated by IPA           | 17          | 0.404        |
| Tnf receptor                | Network-integrated by IPA           | 2           | 0            |
| TRAF                         | Network-integrated by IPA           | 3           | 1.000        |
| transglutaminase            | Network-integrated by IPA           | 6           | 0.933        |
| TRIM25                      | Network-integrated by IPA           | 4           | 0.500        |
| TSH                          | Network-integrated by IPA           | 5           | 0.500        |
| tyrosine kinase             | Network-integrated by IPA           | 8           | 0.179        |
| Ubiquitin                   | Network-integrated by IPA           | 6           | 0            |
| VAV                         | Network-integrated by IPA           | 19          | 0.345        |
| Vegf                         | Network-integrated by IPA           | 89          | 0.284        |
| VEGFA                       | Network-integrated by IPA           | 78          | 0.343        |
| VitaminD3-VDR-RXR            | Network-integrated by IPA           | 1           | 0            |
| voltage-gated calcium channel| Network-integrated by IPA           | 13          | 0.359        |
| Wnt                         | Network-integrated by IPA           | 10          | 0.244        |
| ACVR2A                      | Downregulated in Secretome          | -1.214      | 0.212        |
| ANGPT2                      | Downregulated in Secretome          | -1.421      | 0.355        |
| ANGPTL2                     | Downregulated in Secretome          | -1.133      | 0.619        |
| CCL22                       | Downregulated in Secretome          | -1.005      | 0.644        |
| CCL27                       | Downregulated in Secretome          | -1.770      | 0.800        |
| CCL28                       | Downregulated in Secretome          | -1.460      | 0.361        |
| CCL3                        | Downregulated in Secretome          | -2.345      | 0.365        |
| CCR7                        | Downregulated in Secretome          | -2.313      | 0.399        |
| CNTF                        | Downregulated in Secretome          | -1.843      | 0.437        |
| CXCL11                      | Downregulated in Secretome          | -2.566      | 0.526        |
| CXCL14                      | Downregulated in Secretome          | -3.236      | 0.311        |
| CXCR2                       | Downregulated in Secretome          | -1.157      | 0.342        |
| Gene   | Expression Status       | -log10(p-value) | FDR   | log2 Fold Change |
|--------|-------------------------|----------------|-------|-----------------|
| DLK1   | Downregulated in Secretome | -1.638       | 18    | 2.149           |
| EREG   | Downregulated in Secretome | -1.114       | 23    | 2.112           |
| FGFR4  | Downregulated in Secretome | -1.351       | 19    | 2.142           |
| FGFR1L | Downregulated in Secretome | -2.645       | 2     | 3.019           |
| GDF15  | Downregulated in Secretome | -1.142       | 26    | 2.093           |
| HBEGF  | Downregulated in Secretome | -3.074       | 52    | 1.928           |
| IL17C  | Downregulated in Secretome | -1.473       | 11    | 2.308           |
| IL17F  | Downregulated in Secretome | -1.571       | 26    | 2.086           |
| IL1RN  | Downregulated in Secretome | -2.123       | 41    | 2.026           |
| IL21   | Downregulated in Secretome | -1.148       | 62    | 1.935           |
| IL23A  | Downregulated in Secretome | -1.317       | 36    | 1.974           |
| IL25   | Downregulated in Secretome | -1.288       | 28    | 2.112           |
| LEPR   | Downregulated in Secretome | -1.447       | 31    | 2.091           |
| OSM    | Downregulated in Secretome | -1.747       | 69    | 1.883           |
| PTX3   | Downregulated in Secretome | -1.929       | 19    | 2.117           |
| SLC2A1 | Downregulated in Secretome | -1.526       | 24    | 2.077           |
| TGFBR1 | Downregulated in Secretome | -1.791       | 18    | 2.205           |
| THBS2  | Downregulated in Secretome | -1.723       | 8     | 2.340           |
| TIMP2  | Downregulated in Secretome | -3.051       | 17    | 2.156           |
| TNF    | Downregulated in Secretome | -1.314       | 139   | 1.690           |
| TNFRSF11B | Downregulated in Secretome | -1.682      | 15    | 2.149           |
| TRADD  | Downregulated in Secretome | -2.960       | 9     | 2.235           |
Table S4. Enriched miR-146 dependent network biological processes. In Cytoscape [3], BiNGO [5] was used to interpret enriched GO-BP of the IPA-derived 430 node miR-146 dependent network. Using a hypergeometric test with B-H FDR correction and significance cutoff at $p < 0.001$ with the full GO-BP annotation as background reference, the secretome network was surveyed for overrepresented BP. The resulting BiNGO network comprised 619 nodes (558 with $p < 0.001$) with 1077 edges connecting a GO parent and child term nested hierarchy. As in the full secretome BiNGO analysis, the 100 most significant BP of the miR-146 dependent network clustered into 8 general process categories, which are listed by categories appearing most frequently and BP within each category listed by -log $p$-value in descending order of significance. Specifically, the top 100 BP are represented by ‘Regulation’ (61 processes), followed by ‘Development’ (18), ‘Signaling’ (8), ‘Stimulus/Stress Response’ (5), ‘Immunity/Inflammation’ (4), ‘Cellular’ (2), ‘Motility’ (1), and ‘Behavior’ (1).

Table S4 – Enriched miR-146 dependent network biological processes

| -log (adj p-value) | Rank | BiNGO Biological Process                              | General process |
|--------------------|------|------------------------------------------------------|-----------------|
| 52.513             | 1    | positive regulation of biological process            |                 |
| 52.513             | 2    | positive regulation of cellular process               |                 |
| 40.051             | 5    | biological regulation                                 |                 |
| 39.383             | 6    | regulation of cellular process                        |                 |
| 38.560             | 9    | regulation of biological process                      |                 |
| 34.979             | 12   | regulation of multicellular organismal process        | Regulation      |
| 29.375             | 19   | regulation of cell communication                      |                 |
| 29.043             | 20   | regulation of developmental process                   |                 |
| 28.012             | 21   | regulation of cell proliferation                      |                 |
| 26.620             | 23   | negative regulation of biological process             |                 |
| 26.533             | 24   | positive regulation of metabolic process              |                 |
| 25.976             | 25   | regulation of metabolic process                        | Regulation      |
| 25.498             | 26   | positive regulation of cellular metabolic process     |                 |
| 24.851             | 28   | positive regulation of macromolecule metabolic process|                 |
| 23.935             | 29   | negative regulation of cellular process               |                 |
| 23.230             | 30   | positive regulation of cell communication             |                 |
| 23.096             | 31   | regulation of cellular metabolic process              | Regulation      |
| 22.886             | 32   | positive regulation of cell proliferation             |                 |
| 22.592             | 34   | positive regulation of signal transduction            |                 |
| 22.543             | 35   | positive regulation of developmental process          |                 |
| 22.493             | 36   | positive regulation of signaling process              |                 |
|   |   |   |
|---|---|---|
| 22.348 | 37 | regulation of macromolecule metabolic process |
| 22.127 | 38 | regulation of signaling pathway |
| 21.116 | 40 | positive regulation of signaling pathway |
| 20.719 | 41 | regulation of primary metabolic process |
| 18.413 | 46 | regulation of protein amino acid phosphorylation |
| 18.302 | 47 | regulation of signal transduction |
| 18.266 | 48 | regulation of phosphorylation |
| 18.192 | 49 | regulation of signaling process |
| 18.008 | 51 | positive regulation of biosynthetic process |
| 17.909 | 52 | regulation of phosphate metabolic process |
| 17.909 | 53 | regulation of phosphorus metabolic process |
| 17.888 | 54 | regulation of cell death |
| 17.888 | 55 | regulation of cell differentiation |
| 17.839 | 57 | positive regulation of macromolecule biosynthetic process |
| 17.224 | 59 | regulation of apoptosis |
| 17.190 | 60 | positive regulation of cellular biosynthetic process |
| 17.100 | 64 | regulation of programmed cell death |
| 17.043 | 65 | regulation of biological quality |
| 16.853 | 66 | positive regulation of nitrogen compound metabolic process |
| 16.745 | 67 | regulation of protein modification process |
| 16.387 | 70 | regulation of intracellular protein kinase cascade |
| 16.177 | 72 | positive regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolic process |
| 16.098 | 73 | positive regulation of intracellular protein kinase cascade |
| 16.055 | 74 | regulation of biosynthetic process |
| 15.420 | 76 | positive regulation of cell differentiation |
| 15.114 | 77 | regulation of cellular protein metabolic process |
| 14.861 | 79 | regulation of immune system process |
| 14.694 | 80 | regulation of response to stimulus |
| 14.693 | 81 | regulation of cellular biosynthetic process |
| 14.693 | 82 | regulation of MAPKKK cascade |
| 14.025 | 84 | positive regulation of multicellular organismal process |
| 13.858 | 85 | regulation of cellular localization |
| 13.679 | 87 | regulation of protein metabolic process |
| 13.655 | 89 | regulation of localization |
| 13.603 | 90 | positive regulation of MAPKKK cascade |
| 13.471 | 92 | positive regulation of immune system process |
| 13.247 | 95 | regulation of macromolecule biosynthetic process |
| 12.864 | 98 | regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolic process |
| 12.858 | 99 | positive regulation of transcription from RNA polymerase II promoter |
| 12.825 | 100 | positive regulation of RNA metabolic process |
| 42.566 | 3 | anatomical structure development |
| 40.853 | 4 | system development |
| 39.340 | 7 | developmental process |
| 38.350 | 10 | multicellular organismal development |
| 37.601 | 11 | organ development |
| 30.593 | 14 | anatomical structure morphogenesis |
| 30.178 | 15 | cellular developmental process |
| 29.715 | 17 | cell differentiation |
| 18.873 | 45 | nervous system development |

**Development**
| Value  | Count | Description                                      | Category               |
|--------|-------|--------------------------------------------------|------------------------|
| 18.180 | 50    | organ morphogenesis                              |                        |
| 17.121 | 62    | tissue development                               |                        |
| 16.367 | 71    | cell development                                 |                        |
| 14.999 | 78    | central nervous system development               |                        |
| 14.532 | 83    | cellular component organization                   |                        |
| 13.665 | 88    | neurogenesis                                     |                        |
| 13.528 | 91    | brain development                                |                        |
| 13.297 | 94    | generation of neurons                            |                        |
| 13.232 | 96    | gland development                                |                        |
| 27.193 | 22    | signaling                                        | Signaling              |
| 19.889 | 42    | signaling pathway                                |                        |
| 17.105 | 63    | enzyme linked receptor protein signaling pathway  |                        |
| 16.696 | 68    | signal transmission                              |                        |
| 16.696 | 69    | signaling process                                |                        |
| 15.820 | 75    | cell surface receptor linked signaling pathway    |                        |
| 13.733 | 86    | signal transduction                              |                        |
| 13.455 | 93    | transmembrane receptor protein tyrosine kinase signaling pathway |          |
| 38.634 | 8     | response to stimulus                             | Stimulus/Stress Response |
| 22.607 | 33    | response to chemical stimulus                    |                        |
| 19.602 | 43    | response to wounding                             |                        |
| 17.860 | 56    | defense response                                 |                        |
| 17.782 | 58    | response to stress                               |                        |
| 34.680 | 13    | immune system process                            | Immunity/Inflammation  |
| 29.435 | 18    | immune response                                  |                        |
| 19.097 | 44    | inflammatory response                            |                        |
| 12.916 | 97    | cell activation                                  |                        |
| 30.040 | 16    | multicellular organismal process                 | Cellular               |
| 25.381 | 27    | cellular process                                 |                        |
| 17.149 | 61    | locomotion                                       | Motility               |
| 21.874 | 39    | behavior                                         | Behavior               |
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