

## **Neuron-autonomous transcriptome changes upon ischemia/reperfusion injury**

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data. J.S., X.C. and Y.N. wrote the paper.

Data deposition: The microarray data reported in this paper have been deposited in the  
bioproject at NCBI (<https://www.ncbi.nlm.nih.gov/bioproject/?term=PRJNA376061>).

The authors declare no conflict of interest.

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### **Supplemental Figure 1. Optimization of siRNA transfection efficiency**

Representative images of primary hippocampal cultures transfected with siRNA1 to Itga5 at different concentrations. Left column: phase contrast image. Right column: Cy3 fluorescence.

### **Supplemental Figure 2. Flow diagram of transcriptome sequencing and bioinformatics analysis pipeline**

### **Supplemental Figures 3-6. Comparisons of co-expression network and identification of pathways**

OGD 45 min/R 0 h vs OGD 0 min/R 0 h (Supplemental Fig. 3) OGD 45 min/R 6 h vs OGD 45 min/R 0 h (Supplemental Fig. 4) OGD 45 min/R 12 h (Supplemental Fig. 5) vs OGD 45 min/R 0 h, OGD 45 min/R 18 h vs OGD 45 min/R 0 h (Supplemental Fig. 6). The red and green nodes represent consensus up-regulated or down-regulated terms in the particular pathways, respectively. The yellow nodes represent both up-regulated and down-regulated terms identified in the same particular pathway.

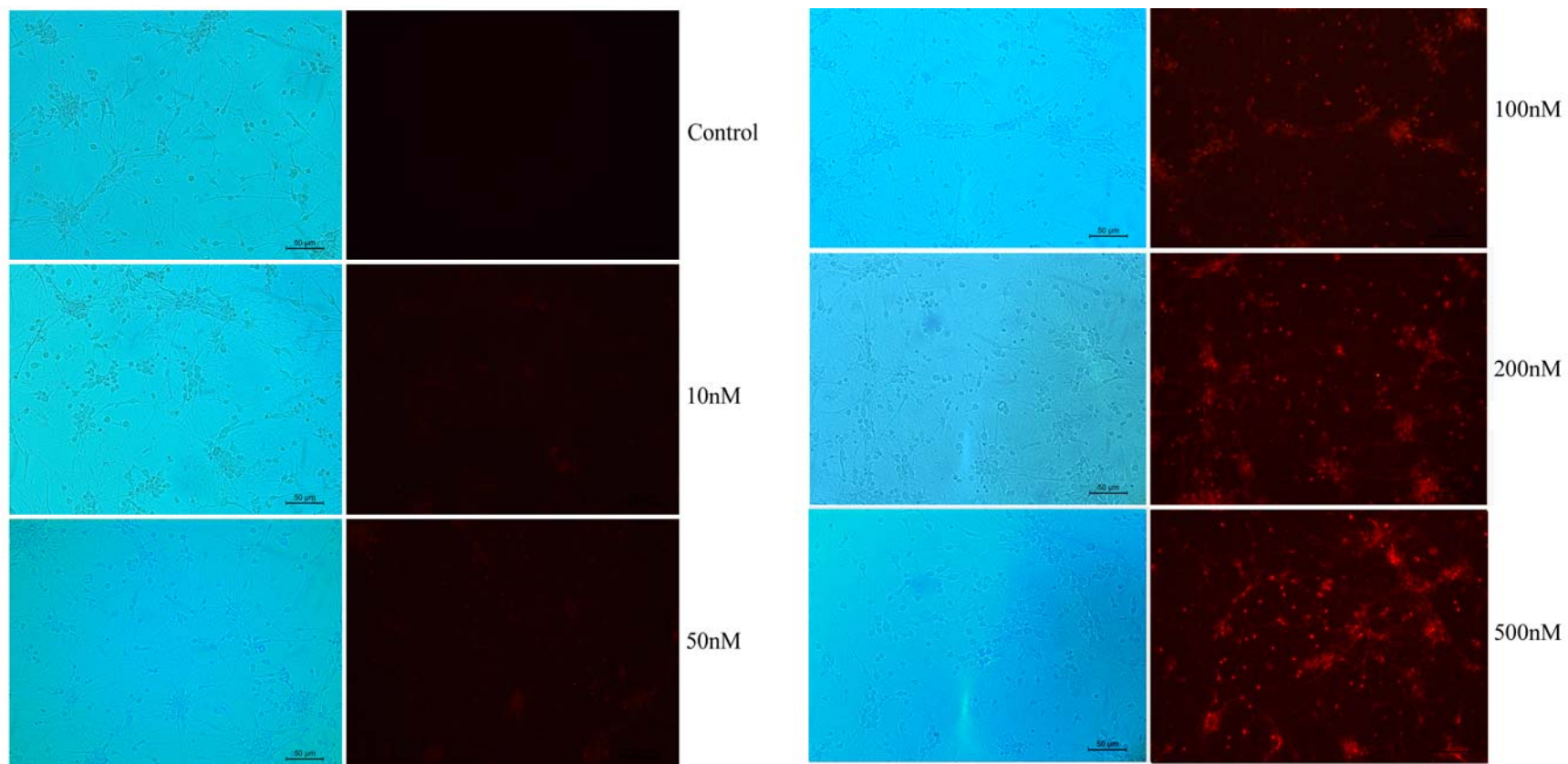
### **Supplemental Figures 7-10. Co-expression network analysis and identification of key regulatory genes upon oxygen glucose deprivation (OGD) and OGD with reperfusion.**

Co-expression network analysis of key regulatory genes for OGD 45 min/R 0 h vs OGD 0 min/R 0 h (Supplemental Fig. 7); OGD 45 min/R 6 h vs OGD 45 min/R 0 h (Supplemental Fig. 8); OGD 45 min/R 12 h vs (Supplemental Fig. 9) and OGD 45 min/R 18 h vs OGD 45 min/R 0 h (Supplemental Fig. 10). The red nodes represented up-regulated genes, and the green nodes represented down-regulated genes.

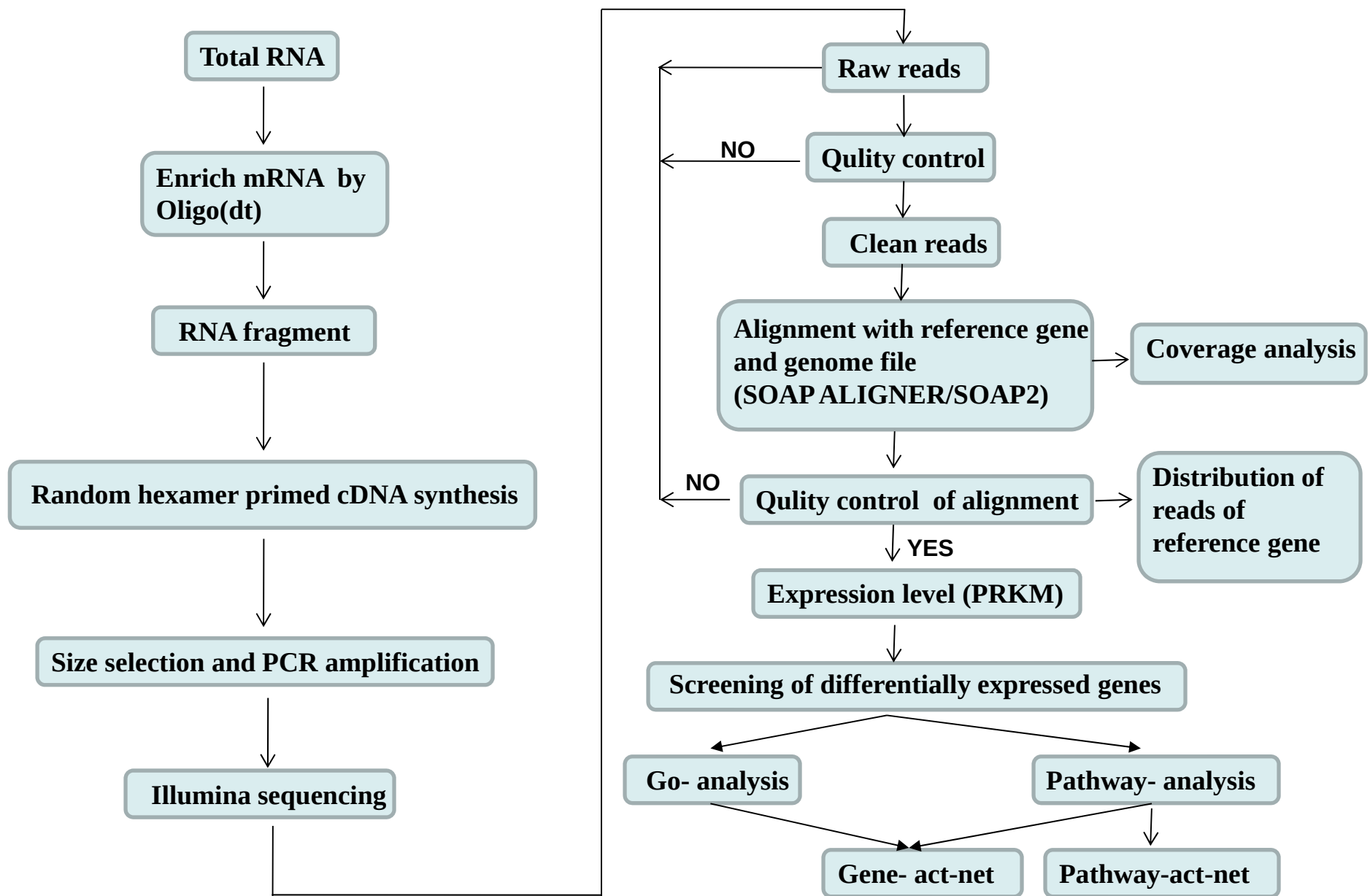
### **Supplemental Figure 11. Correlation between qPCR verification and RNA-Seq data**

**(A-D)** Linear regression between results of qPCR and RNA-Seq data for for OGD 45 min/R 0 h vs OGD 0 min/R 0 h (A); OGD 45 min/R 6 h vs OGD 45 min/R 0 h (B); OGD 45 min/R 12 h vs OGD 45 min/R 0 h (C); and OGD 45 min/R 18 h vs OGD 45 min/R 0 h (D).



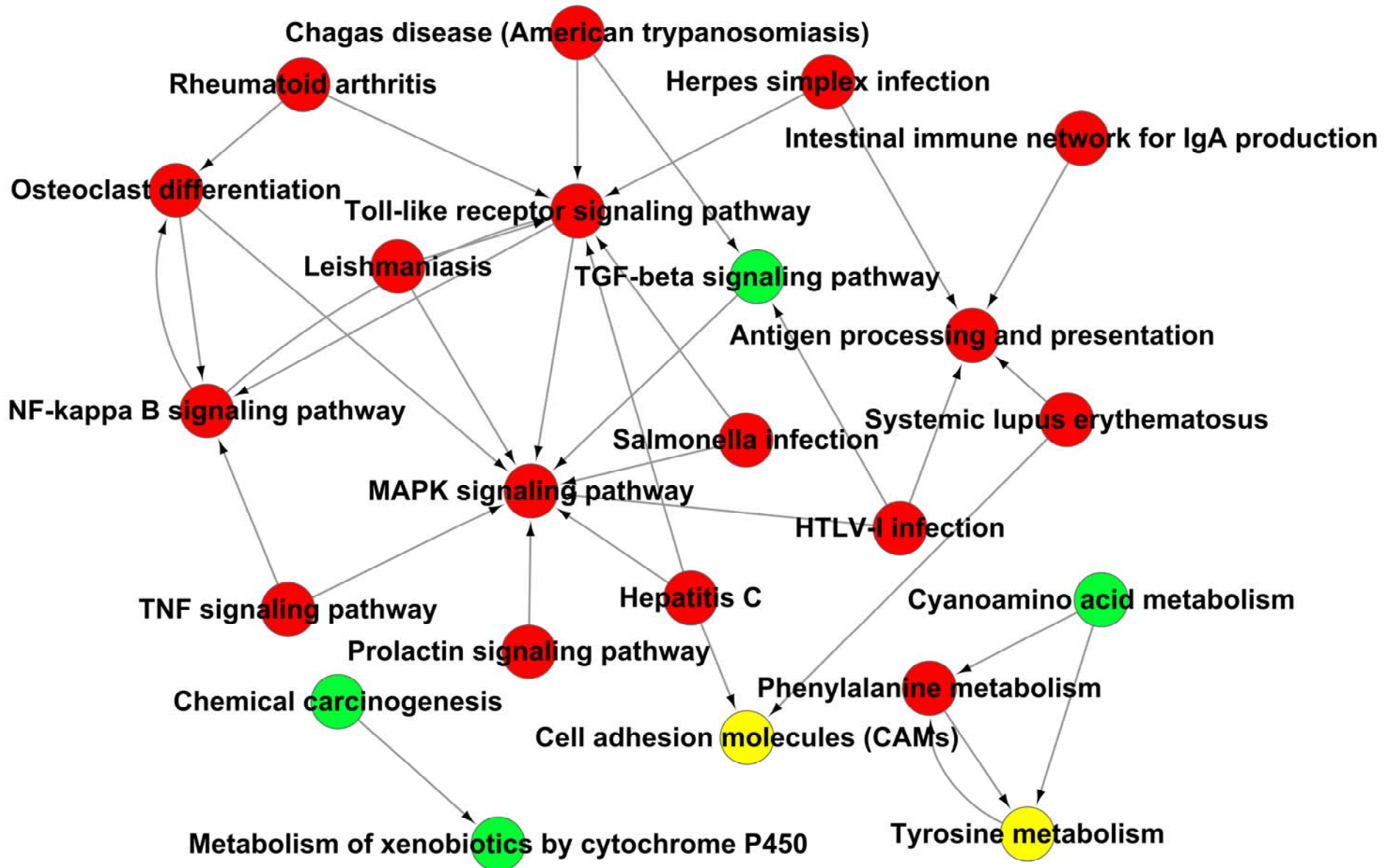


**Supplemental Fig. 1**



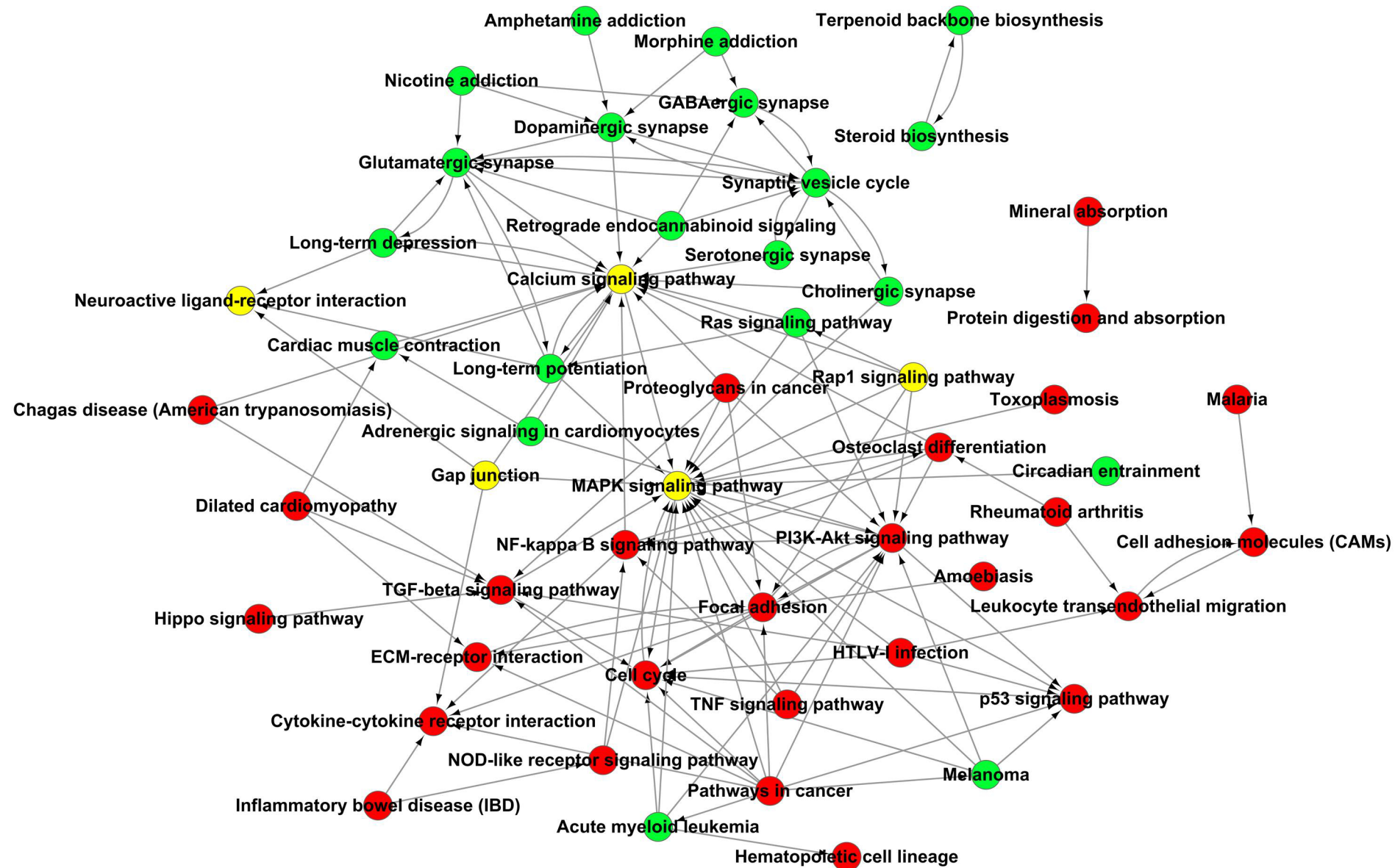
**Supplemental Fig. 2**

# OGD



Supplementary Fig. 3

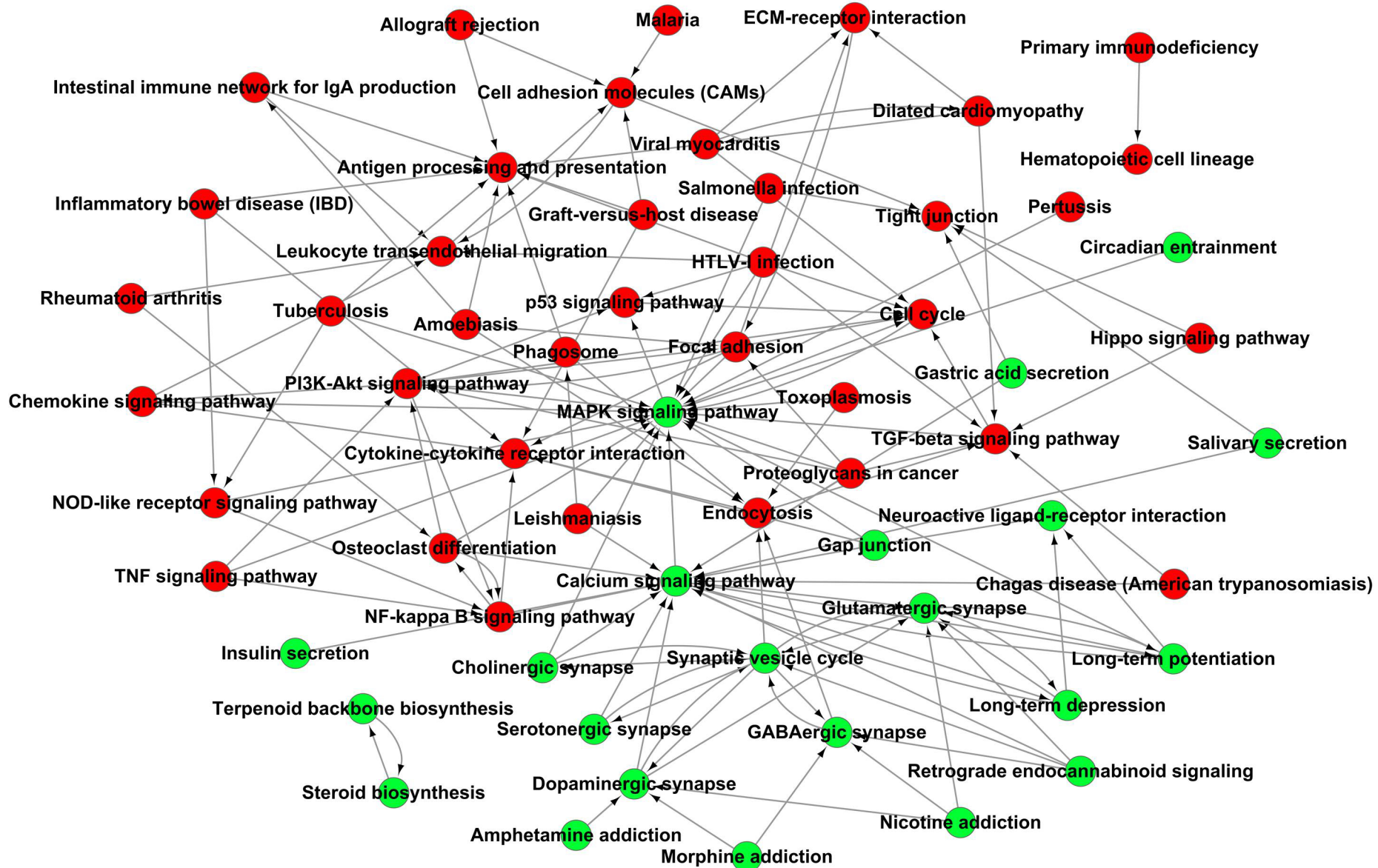
## OGD/R 6h



### Supplementary Fig. 4

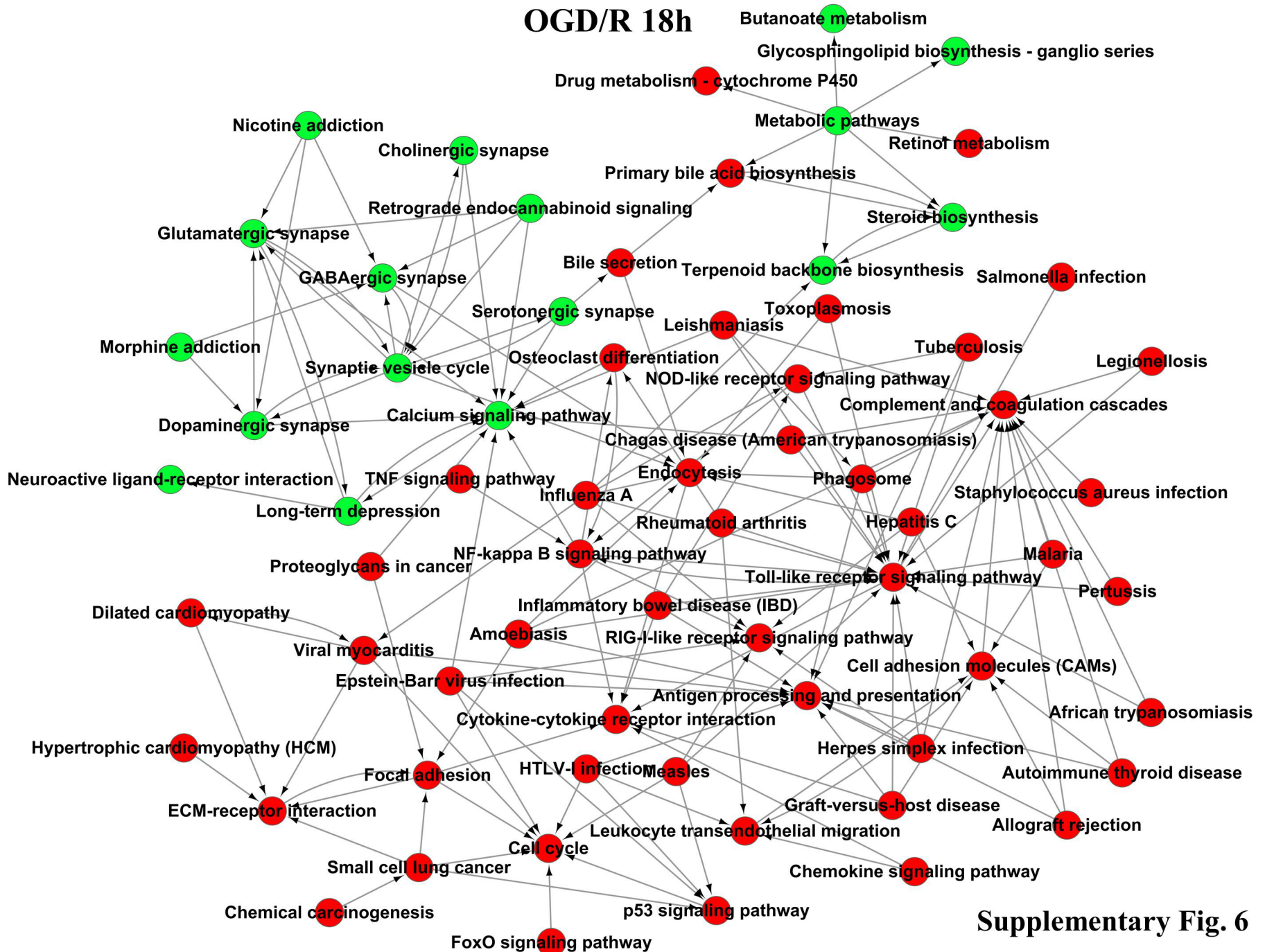


# OGD/R 12h



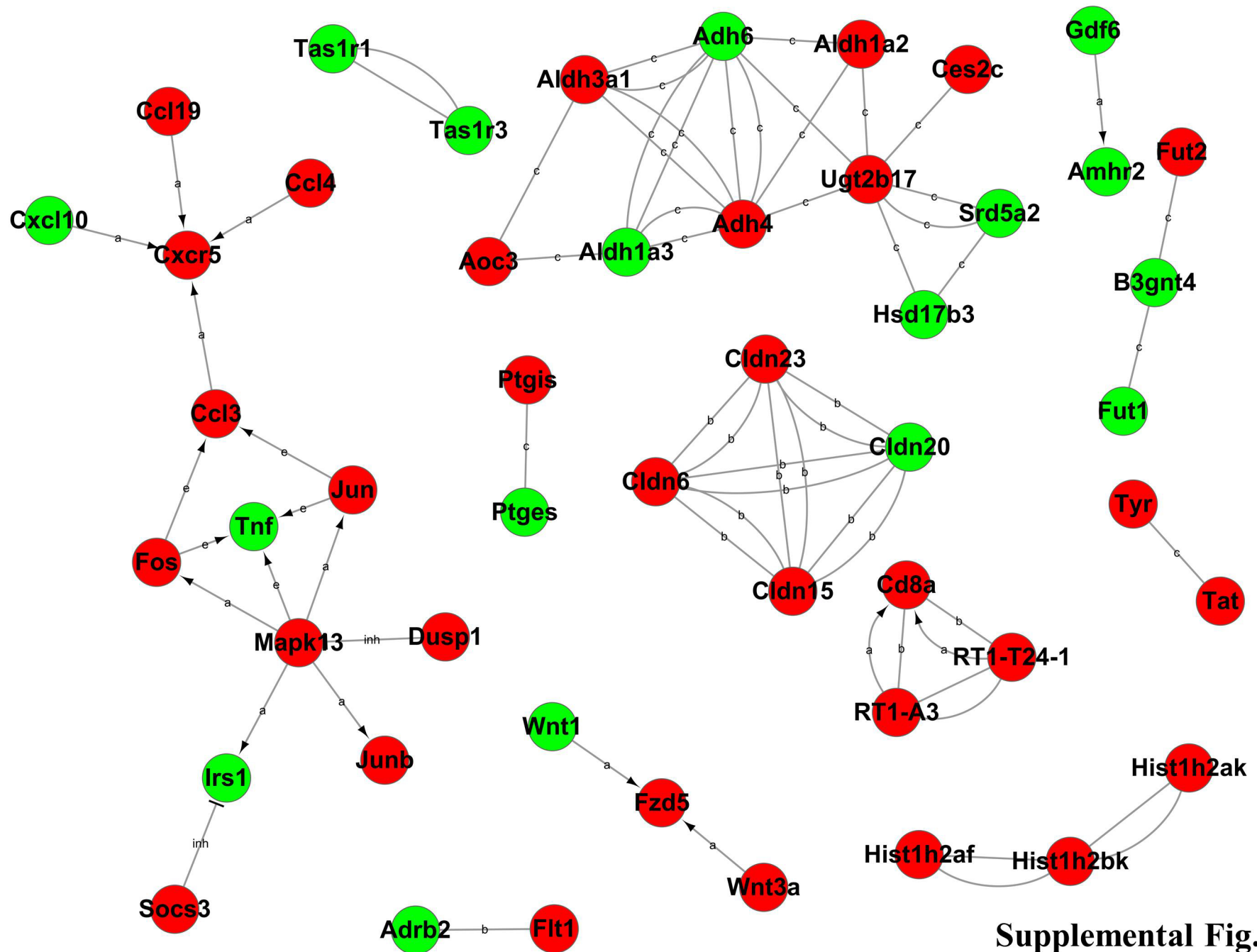
Supplementary Fig. 5

# OGD/R 18h



Supplementary Fig. 6

# OGD



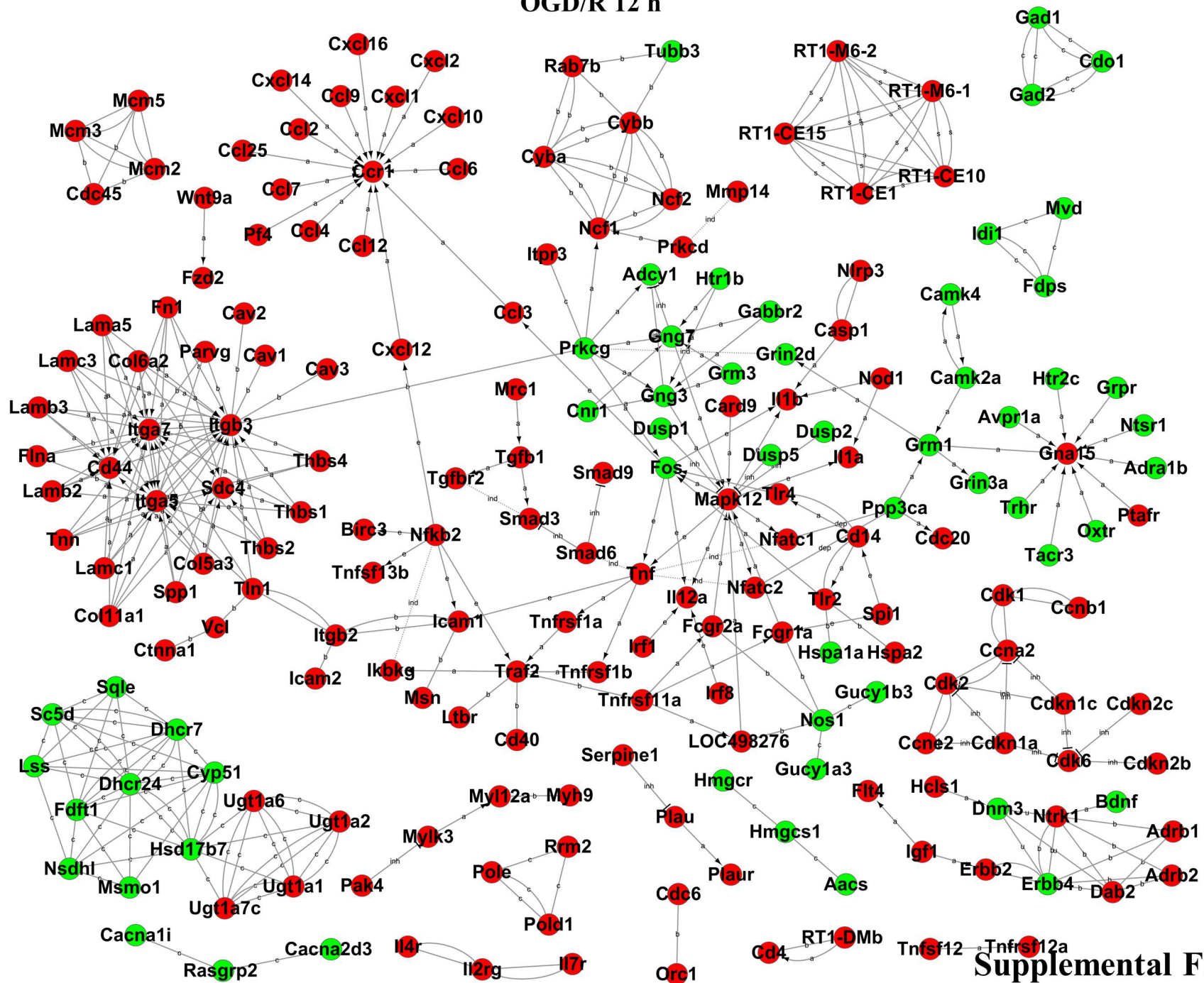
Supplemental Fig. 7





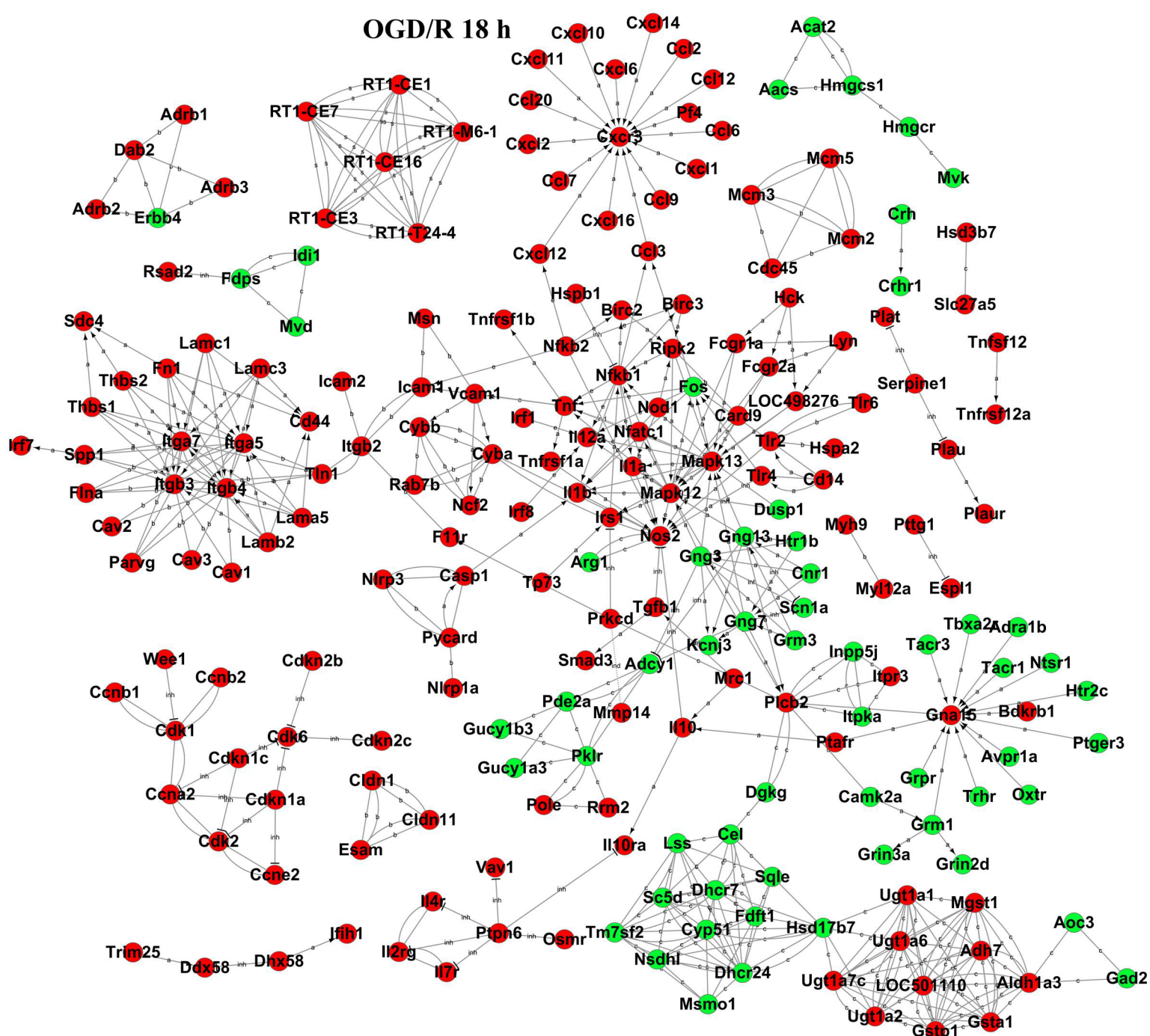


# OGD/R 12 h

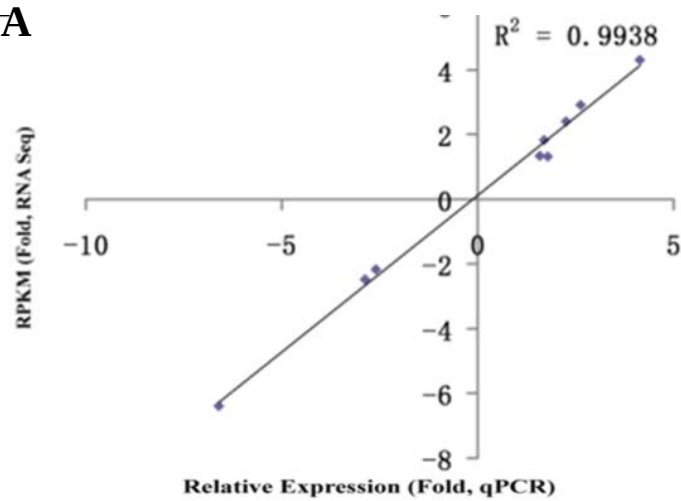
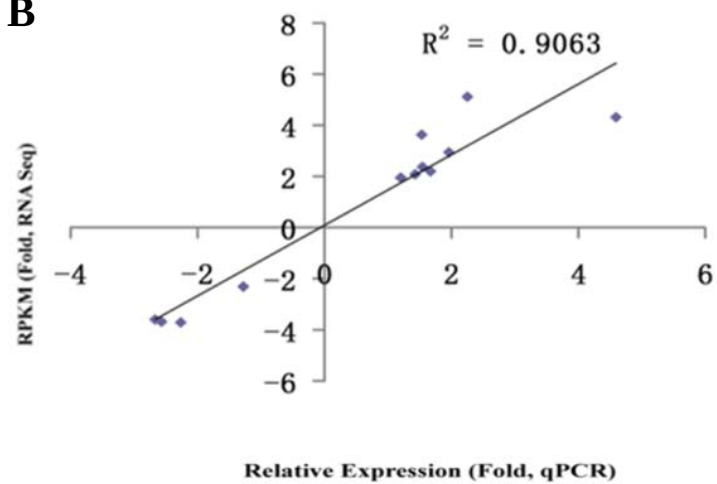
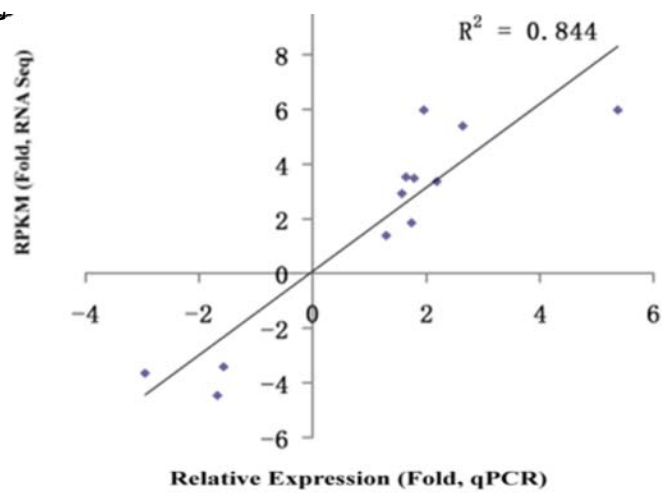
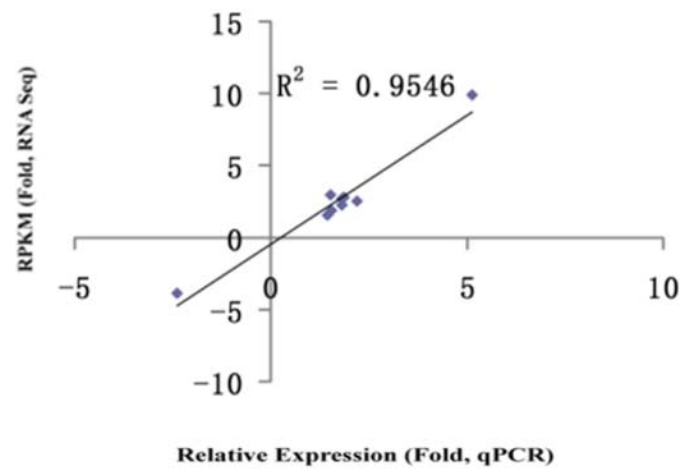


Supplemental Fig. 9

OGD/R 18 h



Supplemental Fig. 10

**A****B****C****D**

**Supplemental Fig. 11**

**Supplemental Table 2** Primers sequences for qRT-PCR.

| NO. | Primers | Sequences (5'-3')     |                       |
|-----|---------|-----------------------|-----------------------|
|     |         | Forward               | Reverse               |
| 1   | Adcy4   | ATCAAGGCTCATTGGGCTCC  | CCATAGGAAGTCCAGGCGAC  |
| 2   | Adh6    | ACTGTTGGAGCCCTAGCATC  | TGAACTGCCTCATTGGCCTC  |
| 3   | Camk2a  | AGATGTGCGACCCCTGAATG  | TGAGTGATGCGGATGTAGGC  |
| 4   | Ccl19   | AGCCTTGGCCTCTCAGATTG  | TCTTCGCAATCGTTAGCACC  |
| 5   | Ccl3    | TGCTGTTCTTCTCTGCACCAT | CTTGGACCCAGGTCTCTTTGG |
| 6   | Ccl4    | ATAGGCTCTGACCCCTCCAC  | GCACAGATTTCCTGCCTTTT  |
| 7   | Cd44    | CCCCTTCACAGCCTACTGG   | TGCTGTTGTGTGGGGCTAT   |
| 8   | Cdk1    | GGGAACAGAGAGGGTCCGTT  | ATTTCCTGGATTGCCGTACT  |
| 9   | Cldn15  | CTGGGAGTCTCCAATGCTG   | AGCAAGTATGTGAAGGCCCC  |
| 10  | ErbB4   | ACAGCACCCCAATCAAGCTCA | GCACTAGGTGTGGGTGATCC  |
| 11  | Esam    | AGGCCACAGCATCAAAACGA  | TTCAAAGATCCACGGACGGT  |
| 12  | Fn1     | TTTCCCATTACGCCGTTGGA  | TCATCCGCTGGCCATTTTCT  |
| 13  | Fos     | ACTACGAGGCGTCATCCTCC  | GTTGGCACTAGAGACGGACA  |
| 14  | Gdf6    | GGTGCCTCACGAGTACATGC  | TGAGAGCGTGGACACATCAA  |
| 15  | Grm1    | ACGGCCTGCAAAGAGAATGA  | ACAAACAGCGTCACGAGGAT  |
| 16  | Icam1   | TGAGCGACATTGGGGAAGAC  | CTACTGAGAGCTGTGTCCGC  |
| 17  | Il1a    | ATCAGCACCTCACAGCTTCC  | TCTCTCCCGATGAGTAGGC   |
| 18  | Il1b    | ACAAGCAACGACAAAATCCC  | GACAAACCGCTTTTCCATCT  |
| 19  | Itga5   | CAAGACGCTCCAGTGAGGATT | AGACGTGAGGTCCTGGTTGT  |
| 20  | Mapk12  | CCTTCCAGTCGGAGCTGTTT  | CCAGGTCAGTGCCCATGAAT  |
| 21  | Mapk13  | TGCCTTAGAGCGGGAGAAAC  | AGCTTCATCCCACTTCGTCG  |
| 22  | Pla2g5  | CTTGGGCTGCCAGCATAAAC  | GCAGCCGTAGAAGCCATAGT  |
| 23  | Spp1    | CCGAGGTGATAGCTTGGCTT  | CTCTTCATCGGGAGGTGAG   |
| 24  | Thbs1   | GTGACAAGATGGAGAGCGCA  | AGGACGTTGGTTGAAGTGAG  |
| 25  | Thbs2   | ACCAATGCCACCTACCACTG  | TGTCCTTCTCATCGCTCACG  |
| 26  | Tlr4    | ATCTGAGCTTCAACCCCTGA  | AGTACCAAGGTTGAGAGCTGG |
| 27  | Tnf     | CCCAACAAGGAGGAGAAGTT  | TTGCTACGACGTGGGCTA    |



**Supplemental Table 3 Selected differentially expressed genes between OGD45min/R0h and OGD0min/R0h cultured neurons**

| AccID  | Description                         | Degree | log2 Ratio   | gene<br>Up-Down | Pathway Term                         | P-Value     | FDR         | Enrichment  |
|--------|-------------------------------------|--------|--------------|-----------------|--------------------------------------|-------------|-------------|-------------|
| Cldn15 | Claudin-15                          | 6      | 1.582618974  | Up              | Cell adhesion molecules (CAMs)       | 0.003739565 | 0.08921534  | 3.81852552  |
| Mapk13 | Mitogen-activated protein kinase 13 | 6      | 1.688784531  | Up              | TNF signaling pathway                | 0.002442273 | 0.083401036 | 4.790513834 |
|        |                                     |        |              |                 | Toll-like receptor signaling pathway | 0.009937366 | 0.175787278 | 4.104022755 |
|        |                                     |        |              |                 | MAPK signaling pathway               | 0.026403246 | 0.272998397 | 2.381724392 |
| Ccl3   | C-C motif chemokine 3               | 3      | 1.785053369  | Up              | Toll-like receptor signaling pathway | 0.009937366 | 0.175787278 | 4.104022755 |
| Ccl4   | C-C motif chemokine 4               | 1      | 2.260690879  | Up              | Toll-like receptor signaling pathway | 0.009937366 | 0.175787278 | 4.104022755 |
| Ccl19  | C-C motif chemokine                 | 1      | 2.639202503  | Up              | NF-kappa B signaling pathway         | 0.02603463  | 0.272998397 | 3.777466106 |
| Fos    | Proto-oncogene c-Fos                | 3      | 4.132877251  | Up              | TNF signaling pathway                | 0.002442273 | 0.083401036 | 4.790513834 |
|        |                                     |        |              |                 | Toll-like receptor signaling pathway | 0.009937366 | 0.175787278 | 4.104022755 |
|        |                                     |        |              |                 | MAPK signaling pathway               | 0.026403246 | 0.272998397 | 2.381724392 |
| Tnf    | Tumor necrosis factor               | 3      | -1.868592138 | Down            | TGF-beta signaling pathway           | 0.015445311 | 0.290252201 | 6.189989785 |
| Adh6   | Alcohol dehydrogenase 6             | 8      | -6.600279954 | Down            | Tyrosine metabolism                  | 0.029676521 | 0.290252201 | 7.984189723 |
| Gdf6   | Growth/differentiation factor 6     | 1      | -6.612261242 | Down            | TGF-beta signaling pathway           | 0.015445311 | 0.290252201 | 6.189989785 |

**Supplemental Table 4 Selected differentially expressed genes between OGD45min/R6h and OGD45min/R0h cultured neurons.**

| AccID  | Description                        | Degree | log2 Ratio  | gene<br>Up-Down | Pathway Term                           | P-Value     | FDR         | Enrichment  |
|--------|------------------------------------|--------|-------------|-----------------|----------------------------------------|-------------|-------------|-------------|
| Thbs2  | Protein Thbs2                      | 4      | 1.208721250 | Up              | Focal adhesion                         | 1.25643E-07 | 1.60823E-05 | 2.77449289  |
| Mapk12 | Mapk12 protein                     | 11     | 1.427740485 | Up              | Rap1 signaling pathway                 | 0.002784001 | 0.032324643 | 1.878227373 |
|        |                                    |        |             |                 | MAPK signaling pathway                 | 0.004474485 | 0.042424751 | 1.718373397 |
|        |                                    |        |             |                 | TNF signaling pathway                  | 0.004793678 | 0.043827916 | 2.234358797 |
|        |                                    |        |             |                 | NOD-like receptor signaling pathway    | 0.015001981 | 0.103797491 | 2.400190114 |
| Thbs1  | Uncharacterized protein            | 4      | 1.529887873 | Up              | Focal adhesion                         | 1.25643E-07 | 1.60823E-05 | 2.77449289  |
|        |                                    |        |             |                 | PI3K-Akt signaling pathway             | 3.2287E-07  | 2.75516E-05 | 2.317055037 |
|        |                                    |        |             |                 | ECM-receptor interaction               | 9.27097E-07 | 4.93318E-05 | 3.719031419 |
|        |                                    |        |             |                 | TGF-beta signaling pathway             | 0.000719331 | 0.015345734 | 2.761567053 |
|        |                                    |        |             |                 | Rap1 signaling pathway                 | 0.002784001 | 0.032324643 | 1.878227373 |
| Adcy4  | Adenylate cyclase type 4           | 11     | 1.547891516 | Up              | p53 signaling pathway                  | 0.007680619 | 0.062333575 | 2.425455273 |
|        |                                    |        |             |                 | Rap1 signaling pathway                 | 0.002784001 | 0.032324643 | 1.878227373 |
|        |                                    |        |             |                 | Calcium signaling pathway              | 0.002904167 | 0.032324643 | 1.949392986 |
|        |                                    |        |             |                 | Gap junction                           | 0.029860507 | 0.144775866 | 1.961006391 |
| Pla2g5 | Calcium-dependent phospholipase A2 | 3      | 1.671483552 | Up              | MAPK signaling pathway                 | 0.004474485 | 0.042424751 | 1.718373397 |
|        |                                    |        |             |                 | Ras signaling pathway                  | 0.042069125 | 0.175418163 | 1.517157208 |
| Cd44   | CD44 antigen                       | 10     | 1.967606107 | Up              | ECM-receptor interaction               | 9.27097E-07 | 4.93318E-05 | 3.719031419 |
| Itga5  | Protein Itga5                      | 18     | 2.256309291 | Up              | Focal adhesion                         | 1.25643E-07 | 1.60823E-05 | 2.77449289  |
|        |                                    |        |             |                 | PI3K-Akt signaling pathway             | 3.2287E-07  | 2.75516E-05 | 2.317055037 |
|        |                                    |        |             |                 | ECM-receptor interaction               | 9.27097E-07 | 4.93318E-05 | 3.719031419 |
| Tnf    | Tumor necrosis factor              | 7      | 4.597665486 | Up              | Cytokine-cytokine receptor interaction | 3.98553E-11 | 1.02029E-08 | 3.220900282 |
|        |                                    |        |             |                 | NF-kappa B signaling pathway           | 0.000424993 | 0.012425797 | 2.807964349 |
|        |                                    |        |             |                 | TGF-beta signaling pathway             | 0.000719331 | 0.015345734 | 2.761567053 |
|        |                                    |        |             |                 | MAPK signaling pathway                 | 0.004474485 | 0.042424751 | 1.718373397 |
|        |                                    |        |             |                 | NOD-like receptor signaling pathway    | 0.015001981 | 0.103797491 | 2.400190114 |

|        |                                                                   |    |              |      |                                         |             |             |             |
|--------|-------------------------------------------------------------------|----|--------------|------|-----------------------------------------|-------------|-------------|-------------|
| Camk2a | Calcium/calmodulin-dependent protein kinase type II subunit alpha | 8  | -1.277260327 | Down | Ras signaling pathway                   | 0.015001981 | 0.042069125 | 0.175418163 |
|        |                                                                   | 8  |              |      | Calcium signaling pathway               | 2.36631E-10 | 2.6266E-08  | 4.866213542 |
|        |                                                                   | 8  |              |      | Dopaminergic synapse                    | 1.37943E-05 | 0.000382792 | 3.940982807 |
| ErbB4  | Receptor protein-tyrosine kinase                                  | 13 | -2.268959603 | Down | Long-term potentiation                  | 0.00066081  | 0.008149991 | 4.163994503 |
|        |                                                                   |    |              |      | Calcium signaling pathway               | 2.36631E-10 | 2.6266E-08  | 4.866213542 |
|        |                                                                   |    |              |      | MAPK signaling pathway                  | 7.98005E-05 | 0.001610519 | 2.669347889 |
|        |                                                                   |    |              |      | Ras signaling pathway                   | 0.000726164 | 0.008484658 | 2.536095417 |
|        |                                                                   |    |              |      | Gap junction                            | 0.000884579 | 0.009818822 | 3.642264695 |
|        |                                                                   |    |              |      | Rap1 signaling pathway                  | 0.002339552 | 0.022581765 | 2.392124935 |
| Grm1   | Metabotropic glutamate receptor 1                                 | 5  | -2.566792921 | Down | PI3K-Akt signaling pathway              | 0.014925041 | 0.099282651 | 1.817062778 |
|        |                                                                   |    |              |      | Neuroactive ligand-receptor interaction | 1.53187E-16 | 3.40076E-14 | 5.312682642 |
|        |                                                                   |    |              |      | Calcium signaling pathway               | 2.36631E-10 | 2.6266E-08  | 4.866213542 |
|        |                                                                   |    |              |      | Glutamatergic synapse                   | 3.28785E-08 | 1.82476E-06 | 5.110043005 |
|        |                                                                   |    |              |      | Long-term potentiation                  | 0.00066081  | 0.008149991 | 4.163994503 |
|        |                                                                   |    |              |      | Gap junction                            | 0.000884579 | 0.009818822 | 3.642264695 |
| Fos    | Proto-oncogene c-Fos                                              | 6  | -2.668593002 | Down | Long-term depression                    | 0.002526847 | 0.023373338 | 3.701328447 |
|        |                                                                   |    |              |      | Dopaminergic synapse                    | 1.37943E-05 | 0.000382792 | 3.940982807 |
|        |                                                                   |    |              |      | MAPK signaling pathway                  | 7.98005E-05 | 0.001610519 | 2.669347889 |

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**Supplemental Table 5 Selected differentially expressed genes between OGD45min/R12h and OGD45min/R0h cultured neurons**

| AccID  | Description                                                       | Degree | log2 Ratio   | gene Up-Down | PathwayTerm                             | P-Value     | FDR         | Enrichment  |
|--------|-------------------------------------------------------------------|--------|--------------|--------------|-----------------------------------------|-------------|-------------|-------------|
| Icam1  | Intercellular adhesion molecule 1                                 | 5      | 1.298448611  | Up           | NF-kappa B signaling pathway            | 3.07951E-06 | 0.000128313 | 3.445309603 |
|        |                                                                   |        |              |              | Cell adhesion molecules (CAMs)          | 3.81722E-05 | 0.000636203 | 2.50931677  |
|        |                                                                   |        |              |              | TNF signaling pathway                   | 0.000201274 | 0.002396115 | 2.659561129 |
| Fn1    | Fibronectin                                                       | 5      | 1.569976688  | Up           | ECM-receptor interaction                | 4.16222E-06 | 0.000132053 | 3.37277677  |
|        |                                                                   |        |              |              | Focal adhesion                          | 1.27199E-05 | 0.000289089 | 2.332067446 |
|        |                                                                   |        |              |              | PI3K-Akt signaling pathway              | 0.000830533 | 0.007415474 | 1.751107686 |
| Itga5  | Protein Itga5                                                     | 19     | 1.644490656  | Up           | Focal adhesion                          | 1.27199E-05 | 0.000289089 | 2.332067446 |
| Il1b   | Interleukin-1 beta                                                | 4      | 1.79216521   | Up           | Cytokine-cytokine receptor interaction  | 5.09337E-11 | 1.27334E-08 | 3.089543938 |
|        |                                                                   |        |              |              | NF-kappa B signaling pathway            | 3.07951E-06 | 0.000128313 | 3.445309603 |
|        |                                                                   |        |              |              | NOD-like receptor signaling pathway     | 7.80545E-06 | 0.000216818 | 3.918103448 |
| Ccl3   | C-C motif chemokine 3                                             | 2      | 1.951336752  | Up           | TNF signaling pathway                   | 0.000201274 | 0.002396115 | 2.659561129 |
|        |                                                                   |        |              |              | Cytokine-cytokine receptor interaction  | 5.09337E-11 | 1.27334E-08 | 3.089543938 |
|        |                                                                   |        |              |              | Chemokine signaling pathway             | 0.002375374 | 0.016966961 | 1.957875116 |
| Spp1   | Osteopontin                                                       | 3      | 2.179380881  | Up           | ECM-receptor interaction                | 4.16222E-06 | 0.000132053 | 3.37277677  |
|        |                                                                   |        |              |              | Focal adhesion                          | 1.27199E-05 | 0.000289089 | 2.332067446 |
|        |                                                                   |        |              |              | PI3K-Akt signaling pathway              | 0.000830533 | 0.007415474 | 1.751107686 |
| Il1a   | Interleukin-1 alpha                                               | 2      | 2.639382492  | Up           | Cytokine-cytokine receptor interaction  | 5.09337E-11 | 1.27334E-08 | 3.089543938 |
| Tnf    | Tumor necrosis factor                                             | 8      | 5.379609955  | Up           | Cytokine-cytokine receptor interaction  | 5.09337E-11 | 1.27334E-08 | 3.089543938 |
|        |                                                                   |        |              |              | NF-kappa B signaling pathway            | 3.07951E-06 | 0.000128313 | 3.445309603 |
|        |                                                                   |        |              |              | NOD-like receptor signaling pathway     | 7.80545E-06 | 0.000216818 | 3.918103448 |
|        |                                                                   |        |              |              | TGF-beta signaling pathway              | 0.000113583 | 0.001494513 | 2.974041069 |
|        |                                                                   |        |              |              | Calcium signaling pathway               | 4.97807E-09 | 5.60033E-07 | 4.30899287  |
| Camk2a | Calcium/calmodulin-dependent protein kinase type II subunit alpha | 3      | -1.566460051 | Down         | Cholinergic synapse                     | 6.64634E-05 | 0.001869282 | 3.79444519  |
|        |                                                                   |        |              |              | Dopaminergic synapse                    | 0.007819491 | 0.079972067 | 2.48803292  |
|        |                                                                   |        |              |              | Long-term potentiation                  | 0.013301852 | 0.11084877  | 2.974024608 |
|        |                                                                   |        |              |              | Neuroactive ligand-receptor interaction | 3.40182E-14 | 7.6541E-12  | 4.661746948 |
| Grm1   | Metabotropic glutamate receptor 1                                 | 5      | -1.681575724 | Down         | Calcium signaling pathway               | 4.97807E-09 | 5.60033E-07 | 4.30899287  |



|     |                      |   |              |      |                        |             |             |             |
|-----|----------------------|---|--------------|------|------------------------|-------------|-------------|-------------|
|     |                      |   |              |      | Glutamatergic synapse  | 2.40907E-05 | 0.001355102 | 3.753992683 |
|     |                      |   |              |      | Gap junction           | 0.001613508 | 0.02268996  | 3.344647736 |
|     |                      |   |              |      | Long-term depression   | 0.013301852 | 0.11084877  | 2.974024608 |
|     |                      |   |              |      | Long-term potentiation | 0.013301852 | 0.11084877  | 2.974024608 |
| Fos | Proto-oncogene c-Fos | 8 | -2.952729203 | Down | Cholinergic synapse    | 6.64634E-05 | 0.001869282 | 3.79444519  |
|     |                      |   |              |      | MAPK signaling pathway | 0.000567081 | 0.009113799 | 2.344654752 |
|     |                      |   |              |      | Dopaminergic synapse   | 0.007819491 | 0.079972067 | 2.48803292  |

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**Supplemental Table 6 Selected differentially expressed genes between OGD45min/R18h and OGD45min/R0h cultured neurons**

| AccID  | Description                                  | Degree | log2 Ratio   | gene Up-Down | PathwayTerm                            | P-Value     | FDR         | Enrichment  |
|--------|----------------------------------------------|--------|--------------|--------------|----------------------------------------|-------------|-------------|-------------|
| Cd44   | CD44 antigen                                 | 5      | 1.507596682  | Up           | ECM-receptor interaction               | 0.001537207 | 0.01106789  | 2.471614935 |
| Cdk1   | Cyclin-dependent kinase 1                    | 7      | 1.521599365  | Up           | Cell cycle                             | 1.26943E-05 | 0.00017772  | 2.872888889 |
|        |                                              |        |              |              | p53 signaling pathway                  | 0.00017122  | 0.001598054 | 3.089518668 |
| Mapk12 | Mapk12 protein                               | 20     | 1.550057886  | up           | NOD-like receptor signaling pathway    | 2.02192E-08 | 2.45663E-06 | 5.56716218  |
|        |                                              |        |              |              | TNF signaling pathway                  | 6.1728E-07  | 2.59258E-05 | 3.39020979  |
|        |                                              |        |              |              | Toll-like receptor signaling pathway   | 0.000392821 | 0.00341348  | 2.581675853 |
|        |                                              |        |              |              | Leukocyte transendothelial migration   | 0.000628128 | 0.00510607  | 2.355529053 |
|        |                                              |        |              |              | FoxO signaling pathway                 | 0.001472367 | 0.01091284  | 2.186066531 |
|        |                                              |        |              |              | RIG-I-like receptor signaling pathway  | 0.00646248  | 0.033928023 | 2.394074074 |
| Esam   | Endothelial cell-selective adhesion molecule | 4      | 1.808660045  | Up           | Cell adhesion molecules (CAMs)         | 0.000948451 | 0.007469053 | 2.144715188 |
| Spp1   | Osteopontin                                  | 5      | 1.813772968  | Up           | Toll-like receptor signaling pathway   | 0.000392821 | 0.00341348  | 2.581675853 |
|        |                                              |        |              |              | ECM-receptor interaction               | 0.001537207 | 0.01106789  | 2.471614935 |
|        |                                              |        |              |              | PI3K-Akt signaling pathway             | 0.001596964 | 0.011178747 | 1.697560044 |
|        |                                              |        |              |              | Focal adhesion                         | 0.001696697 | 0.011555883 | 1.886215595 |
| Icam1  | Intercellular adhesion molecule 1            | 5      | 1.861984172  | Up           | TNF signaling pathway                  | 6.1728E-07  | 2.59258E-05 | 3.39020979  |
|        |                                              |        |              |              | NF-kappa B signaling pathway           | 1.16862E-06 | 3.68115E-05 | 3.564378274 |
|        |                                              |        |              |              | Leukocyte transendothelial migration   | 0.000628128 | 0.00510607  | 2.355529053 |
|        |                                              |        |              |              | Cell adhesion molecules (CAMs)         | 0.000948451 | 0.007469053 | 2.144715188 |
| Il1a   | Interleukin-1 alpha                          | 5      | 2.198418136  | Up           | Cytokine-cytokine receptor interaction | 1.73319E-10 | 4.36765E-08 | 3.007444169 |
| Tnf    | Tumor necrosis factor                        | 9      | 5.119447582  | Up           | Cytokine-cytokine receptor interaction | 1.73319E-10 | 4.36765E-08 | 3.007444169 |
|        |                                              |        |              |              | NF-kappa B signaling pathway           | 1.16862E-06 | 3.68115E-05 | 3.564378274 |
|        |                                              |        |              |              | RIG-I-like receptor signaling pathway  | 0.00646248  | 0.033928023 | 2.394074074 |
|        |                                              |        |              |              | TGF-beta signaling pathway             | 0.010018741 | 0.048552358 | 2.172668779 |
| Fos    | Proto-oncogene c-Fos                         | 8      | -2.395136975 | Down         | Cholinergic synapse                    | 0.000508371 | 0.009659048 | 3.631312306 |

|                            |             |             |             |
|----------------------------|-------------|-------------|-------------|
| Dopaminergic synapse       | 0.001963335 | 0.024137468 | 3.03044768  |
| Estrogen signaling pathway | 0.007481381 | 0.071073122 | 3.033175355 |
| MAPK signaling pathway     | 0.016543222 | 0.137109791 | 1.947144349 |
| Oxytocin signaling pathway | 0.036372062 | 0.245218092 | 2.101491157 |

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