

# Scripting Pathway Analysis and Data Overlays in R

Workshop

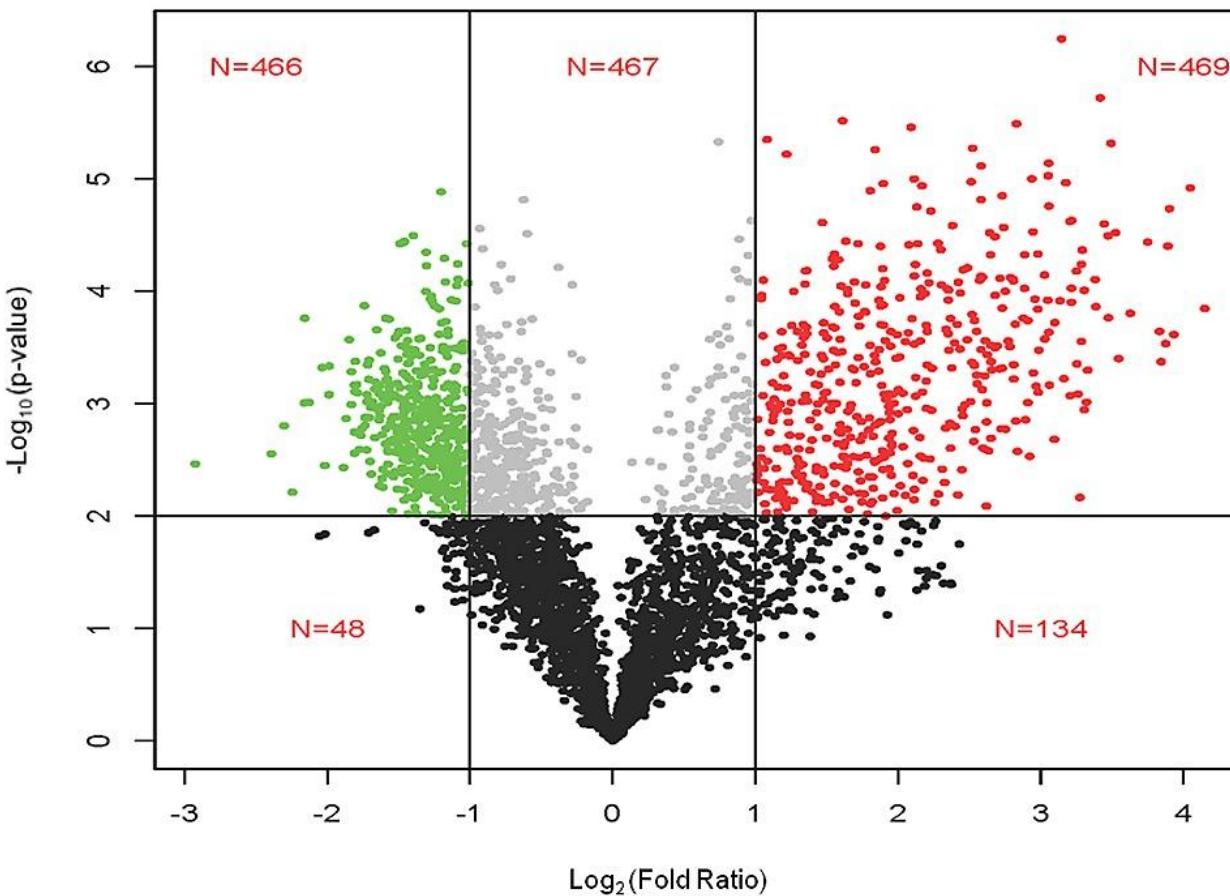
# Upcoming Workshops

- ◆ **10/26-27** - Introduction to RNA-Seq Analysis
- ◆ **11/9** - Single Cell Analysis
- ◆ **11/19** - Machine Learning

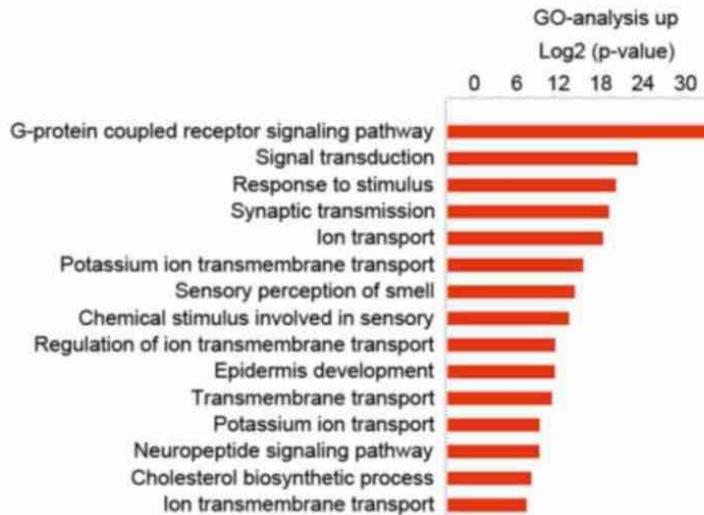
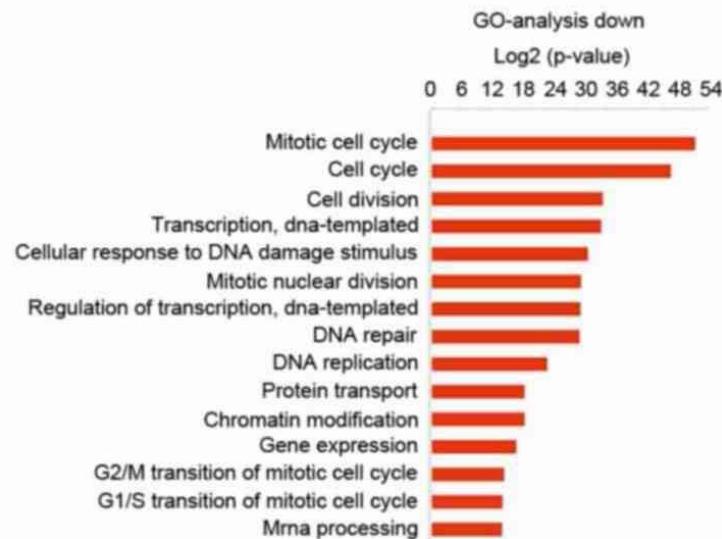
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|    | A           | B               | C           | D         | E          |
|----|-------------|-----------------|-------------|-----------|------------|
| 1  | hgnc_symbol | EnsemblID       | logFC       | Pvalue    | FDR        |
| 2  | FGFBP2      | ENSG00000137441 | 4.95372148  | 2.07E-11  | 2.52E-09   |
| 3  | IGKJ4       | ENSG00000211594 | 4.57014526  | 5.80E-13  | 1.02E-10   |
| 4  | GPR3        | ENSG00000181773 | 3.07384469  | 2.37E-06  | 6.68E-05   |
| 5  | RPS20P10    | ENSG00000233971 | 3.0736699   | 1.59E-05  | 0.00033744 |
| 6  | RPS23P1     | ENSG00000243504 | 2.87680167  | 0.0004883 | 0.00566507 |
| 7  | RPS3AP44    | ENSG00000234031 | 2.87189316  | 2.02E-05  | 0.00041197 |
| 8  | RPS21       | ENSG00000171858 | 1.78201017  | 5.40E-16  | 2.76E-13   |
| 9  | ERGIC3      | ENSG00000125991 | 1.04270392  | 4.08E-07  | 1.48E-05   |
| 10 | ATP5F1E     | ENSG00000124172 | 1.0419011   | 1.74E-07  | 6.97E-06   |
| 11 | OST4        | ENSG00000228474 | 1.04082316  | 8.61E-06  | 0.00020192 |
| 12 | MIR663AHG   | ENSG00000227195 | 1.03864596  | 1.16E-07  | 4.96E-06   |
| 13 | BCR         | ENSG00000186716 | 1.02217198  | 2.66E-08  | 1.37E-06   |
| 14 | HIST1H2AG   | ENSG00000196787 | 1.02057118  | 9.38E-05  | 0.00148878 |
| 15 | SSR2        | ENSG00000163479 | 1.01915311  | 4.30E-10  | 3.79E-08   |
| 16 | EEF1A1      | ENSG00000156508 | -1.01124735 | 1.08E-07  | 4.62E-06   |
| 17 | TMEM159     | ENSG00000011638 | -1.00983307 | 0.0017788 | 0.01498506 |
| 18 | C12orf57    | ENSG00000111678 | -1.00900966 | 0.0009472 | 0.00942208 |
| 19 | ELOB        | ENSG00000103363 | -1.9700433  | 1.64E-05  | 0.00034533 |
| 20 | B2M         | ENSG00000166710 | -1.96259859 | 3.78E-07  | 1.37E-05   |
| 21 | EIF3K       | ENSG00000178982 | -2.9604061  | 2.65E-06  | 7.30E-05   |
| 22 | FIBP        | ENSG00000172500 | -2.95401909 | 0.0005135 | 0.00591282 |
| 23 | SCARNA17    | ENSG00000251992 | -2.95163973 | 1.74E-06  | 5.18E-05   |
| 24 | HLA-B       | ENSG00000234745 | -2.94688319 | 6.68E-08  | 3.10E-06   |
| 25 | C7orf26     | ENSG00000146576 | -3.94240445 | 0.0001522 | 0.00222598 |
| 26 | JTB         | ENSG00000143543 | -3.94165989 | 1.89E-06  | 5.60E-05   |
| 27 | OBSN        | ENSG00000154358 | -3.93820271 | 0.0003276 | 0.00410635 |
| 28 | TMEM14C     | ENSG00000111843 | -3.93798301 | 0.0022893 | 0.01811524 |
| 29 | ATP5MG      | ENSG00000167283 | -3.93536083 | 0.0001484 | 0.00217798 |
| 30 | COX4I1      | ENSG00000131143 | -4.91954634 | 2.37E-06  | 6.68E-05   |
| 31 | CCT3        | ENSG00000163468 | -4.91242065 | 1.55E-05  | 0.00033124 |
| 32 | SSR4        | ENSG00000180879 | -4.9086354  | 0.0002098 | 0.00286687 |
| 33 | SNHG22      | ENSG00000267322 | -4.90693154 | 9.03E-05  | 0.00144651 |
| 34 | NDUFA4      | ENSG00000189043 | -5.879366   | 1.02E-06  | 3.31E-05   |
| 35 | NDUFS8      | ENSG00000110717 | -5.87563243 | 0.0022648 | 0.01795672 |
| 36 | ACTB        | ENSG00000075624 | -5.8670115  | 4.30E-06  | 0.00011161 |

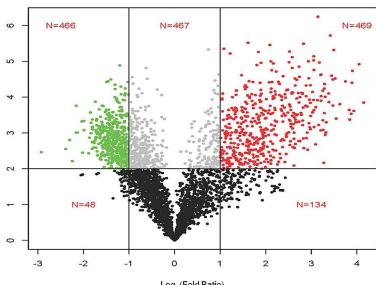
|    | A           | B               | C           | D         | E          |
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| 3  | IGKJ4       | ENSG00000211594 | 4.57014526  | 5.80E-13  | 1.02E-10   |
| 4  | GPR3        | ENSG00000181773 | 3.07384469  | 2.37E-06  | 6.68E-05   |
| 5  | RPS20P10    | ENSG00000233971 | 3.0736699   | 1.59E-05  | 0.00033744 |
| 6  | RPS23P1     | ENSG00000243504 | 2.87680167  | 0.0004883 | 0.00566507 |
| 7  | RPS3AP44    | ENSG00000234031 | 2.87189316  | 2.02E-05  | 0.00041197 |
| 8  | RPS21       | ENSG00000171858 | 1.78201017  | 5.40E-16  | 2.76E-13   |
| 9  | ERGIC3      | ENSG00000125991 | 1.04270392  | 4.08E-07  | 1.48E-05   |
| 10 | ATP5F1E     | ENSG00000124172 | 1.0419011   | 1.74E-07  | 6.97E-06   |
| 11 | OST4        | ENSG00000228474 | 1.04082316  | 8.61E-06  | 0.00020192 |
| 12 | MIR663AHG   | ENSG00000227195 | 1.03864596  | 1.16E-07  | 4.96E-06   |
| 13 | BCR         | ENSG00000186716 | 1.02217198  | 2.66E-08  | 1.37E-06   |
| 14 | HIST1H2AG   | ENSG00000196787 | 1.02057118  | 9.38E-05  | 0.00148878 |
| 15 | SSR2        | ENSG00000163479 | 1.01915311  | 4.30E-10  | 3.79E-08   |
| 16 | EEF1A1      | ENSG00000156508 | -1.01124735 | 1.08E-07  | 4.62E-06   |
| 17 | TMEM159     | ENSG00000011638 | -1.00983307 | 0.0017788 | 0.01498506 |
| 18 | C12orf57    | ENSG00000111678 | -1.00900966 | 0.0009472 | 0.00942208 |
| 19 | ELOB        | ENSG00000103363 | -1.9700433  | 1.64E-05  | 0.00034533 |
| 20 | B2M         | ENSG00000166710 | -1.96259859 | 3.78E-07  | 1.37E-05   |
| 21 | EIF3K       | ENSG00000178982 | -2.9604061  | 2.65E-06  | 7.30E-05   |
| 22 | FIBP        | ENSG00000172500 | -2.95401909 | 0.0005135 | 0.00591282 |
| 23 | SCARNA17    | ENSG00000251992 | -2.95163973 | 1.74E-06  | 5.18E-05   |
| 24 | HLA-B       | ENSG00000234745 | -2.94688319 | 6.68E-08  | 3.10E-06   |
| 25 | C7orf26     | ENSG00000146576 | -3.94240445 | 0.0001522 | 0.00222598 |
| 26 | JTB         | ENSG00000143543 | -3.94165989 | 1.89E-06  | 5.60E-05   |
| 27 | OBSCN       | ENSG00000154358 | -3.93820271 | 0.0003276 | 0.00410635 |
| 28 | TMEM14C     | ENSG00000111843 | -3.93798301 | 0.0022893 | 0.01811524 |
| 29 | ATP5MG      | ENSG00000167283 | -3.93536083 | 0.0001484 | 0.00217798 |
| 30 | COX4I1      | ENSG00000131143 | -4.91954634 | 2.37E-06  | 6.68E-05   |
| 31 | CCT3        | ENSG00000163468 | -4.91242065 | 1.55E-05  | 0.00033124 |
| 32 | SSR4        | ENSG00000180879 | -4.9086354  | 0.0002098 | 0.00286687 |
| 33 | SNHG22      | ENSG00000267322 | -4.90693154 | 9.03E-05  | 0.00144651 |
| 34 | NDUFA4      | ENSG00000189043 | -5.879366   | 1.02E-06  | 3.31E-05   |
| 35 | NDUFS8      | ENSG00000110717 | -5.87563243 | 0.0022648 | 0.01795672 |
| 36 | ACTB        | ENSG00000075624 | -5.8670115  | 4.30E-06  | 0.00011161 |



|    | Name     | Ensembl ID      | B          | C         | P-value    | OR |
|----|----------|-----------------|------------|-----------|------------|----|
| 1  | Hsp90aa1 | ENSG00000174648 | 4.93731448 | 2.075131  | 3.35E-09   |    |
| 2  | GAPDH    | ENSG00000125920 | 4.87311148 | 2.075131  | 3.35E-09   |    |
| 3  | GPR3     | ENSG00000127755 | 3.07374545 | 2.37126   | 6.84E-05   |    |
| 4  | GRIN2B   | ENSG00000127755 | 3.07374545 | 2.37126   | 6.84E-05   |    |
| 5  | HPK2IP1  | ENSG00000125944 | 2.97850587 | 0.020481  | 0.0566467  |    |
| 6  | HPK3IP4  | ENSG00000125944 | 2.97850587 | 0.020481  | 0.0566467  |    |
| 7  | HPK3IP4  | ENSG00000125944 | 2.97850587 | 0.020481  | 0.0566467  |    |
| 8  | IUBP     | ENSG00000125944 | 2.97850587 | 0.020481  | 0.0566467  |    |
| 9  | IRAK4    | ENSG00000125952 | 2.87385516 | 2.20245   | 0.00011397 |    |
| 10 | ITGB1BP1 | ENSG00000125952 | 2.87385516 | 2.20245   | 0.00011397 |    |
| 11 | ITGB1    | ENSG00000125952 | 1.04210392 | 4.02E-07  | 1.48E-06   |    |
| 12 | ITGB1BP1 | ENSG00000125952 | 1.04210392 | 4.02E-07  | 1.48E-06   |    |
| 13 | ICAM1    | ENSG00000125978 | 1.04983515 | 8.41E-06  | 0.00010369 |    |
| 14 | ICAM1    | ENSG00000125978 | 1.04983515 | 8.41E-06  | 0.00010369 |    |
| 15 | ITGB1    | ENSG00000125978 | 1.04983515 | 8.41E-06  | 0.00010369 |    |
| 16 | ITGB1BP1 | ENSG00000125978 | 1.04983515 | 8.41E-06  | 0.00010369 |    |
| 17 | ITGB1BP1 | ENSG00000125978 | 1.04983515 | 8.41E-06  | 0.00010369 |    |
| 18 | ITGB1BP1 | ENSG00000115878 | 1.02030295 | 0.0004972 | 0.00042126 |    |
| 19 | ITGB1BP1 | ENSG00000115878 | 1.02030295 | 0.0004972 | 0.00042126 |    |
| 20 | KDM5A    | ENSG00000125970 | 1.94265689 | 3.78E-07  | 1.37E-06   |    |
| 21 | KDM5A    | ENSG00000125970 | 1.94265689 | 3.78E-07  | 1.37E-06   |    |
| 22 | KIF5B    | ENSG00000125920 | 2.95010009 | 0.0205115 | 0.0591282  |    |
| 23 | SCAMP1   | ENSG00000125920 | 2.95010009 | 0.0205115 | 0.0591282  |    |
| 24 | SCAMP1   | ENSG00000125920 | 2.95010009 | 0.0205115 | 0.0591282  |    |
| 25 | Ctbp2    | ENSG00000125978 | 3.92426648 | 0.0001532 | 0.0222358  |    |
| 26 | Ctbp2    | ENSG00000125978 | 3.92426648 | 0.0001532 | 0.0222358  |    |
| 27 | CDKN1A   | ENSG00000125948 | 3.93822727 | 0.0002678 | 0.0404506  |    |
| 28 | APMPC    | ENSG00000125948 | 3.93910893 | 0.0001484 | 0.0217798  |    |
| 29 | APMPC    | ENSG00000125948 | 3.93910893 | 0.0001484 | 0.0217798  |    |
| 30 | CETP     | ENSG00000125948 | 4.02426651 | 1.52E-06  | 4.68E-06   |    |
| 31 | SMC3     | ENSG00000125978 | 4.20962554 | 0.0002039 | 0.03289487 |    |
| 32 | SMC3     | ENSG00000125978 | 4.20962554 | 0.0002039 | 0.03289487 |    |
| 33 | NDUFA22  | ENSG00000125941 | 4.871954   | 1.02E-04  | 3.81E-06   |    |
| 34 | NDUFA22  | ENSG00000125941 | 4.871954   | 1.02E-04  | 3.81E-06   |    |
| 35 | NDUFB8   | ENSG00000125941 | 4.88031513 | 4.02E-04  | 0.00011245 |    |
| 36 | ACTB     | ENSG00000125941 | 4.88031513 | 4.02E-04  | 0.00011245 |    |

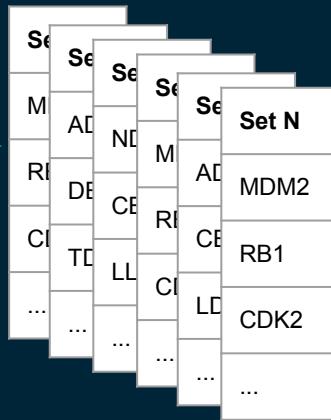


|    | Name    | Symbol | Ensembl         | B         | Input     | C         | PValue    | FCR | E |
|----|---------|--------|-----------------|-----------|-----------|-----------|-----------|-----|---|
| 1  | Npc1    |        | ENSG00000174648 | 4.9371448 | 2.07513   | 2.07513   | 0.536409  |     |   |
| 2  | Faf1    |        | ENSG00000172948 | 4.8770008 | 2.07513   | 2.07513   | 0.536409  |     |   |
| 3  | Grin1   |        | ENSG00000177573 | 3.7734545 | 2.37126   | 2.37126   | 0.648639  |     |   |
| 4  | Grin2b  |        | ENSG00000177573 | 3.7734545 | 2.37126   | 2.37126   | 0.648639  |     |   |
| 5  | Rps2lp1 |        | ENSG00000145944 | 2.8780587 | 0.0204881 | 0.0204881 | 0.0566469 |     |   |
| 6  | Rps2lp1 |        | ENSG00000145944 | 2.8780587 | 0.0204881 | 0.0204881 | 0.0566469 |     |   |
| 7  | Rps2lp1 |        | ENSG00000145944 | 2.8780587 | 0.0204881 | 0.0204881 | 0.0566469 |     |   |
| 8  | Grin2a  |        | ENSG00000145944 | 2.8780587 | 0.0204881 | 0.0204881 | 0.0566469 |     |   |
| 9  | Grin2a  |        | ENSG00000125913 | 1.0421092 | 4.084707  | 4.084707  | 1.486456  |     |   |
| 10 | Grin2a  |        | ENSG00000125913 | 1.0421092 | 4.084707  | 4.084707  | 1.486456  |     |   |
| 11 | Otx1    |        | ENSG00000125913 | 1.0421092 | 4.084707  | 4.084707  | 1.486456  |     |   |
| 12 | Otx1    |        | ENSG00000125913 | 1.0421092 | 4.084707  | 4.084707  | 1.486456  |     |   |
| 13 | Otx1    |        | ENSG00000125913 | 1.0421092 | 4.084707  | 4.084707  | 1.486456  |     |   |
| 14 | Grin2a  |        | ENSG00000125913 | 1.0421092 | 4.084707  | 4.084707  | 1.486456  |     |   |
| 15 | Hmox1   |        | ENSG00000125913 | 1.0421092 | 4.084707  | 4.084707  | 1.486456  |     |   |
| 16 | Grin2a  |        | ENSG00000125913 | 1.0421092 | 4.084707  | 4.084707  | 1.486456  |     |   |
| 17 | Grin2a  |        | ENSG00000125913 | 1.0421092 | 4.084707  | 4.084707  | 1.486456  |     |   |
| 18 | Grin2a  |        | ENSG00000115871 | 1.0203075 | 0.0004742 | 0.0004742 | 0.0562566 |     |   |
| 19 | Grin2a  |        | ENSG00000115871 | 1.0203075 | 0.0004742 | 0.0004742 | 0.0562566 |     |   |
| 20 | Kdm1    |        | ENSG00000115871 | 1.0203075 | 0.0004742 | 0.0004742 | 0.0562566 |     |   |
| 21 | Kdm1    |        | ENSG00000115871 | 1.0203075 | 0.0004742 | 0.0004742 | 0.0562566 |     |   |
| 22 | Hfp     |        | ENSG00000172920 | 2.0540100 | 0.0201155 | 0.0201155 | 0.0591382 |     |   |
| 23 | Scnai2  |        | ENSG00000115923 | 1.7406197 | 1.7406197 | 1.7406197 | 0.516105  |     |   |
| 24 | Ctbp1   |        | ENSG00000166704 | 3.8719564 | 0.0001532 | 0.0001532 | 0.0222538 |     |   |
| 25 | Ctbp1   |        | ENSG00000166704 | 3.8719564 | 0.0001532 | 0.0001532 | 0.0222538 |     |   |
| 26 | Ctbp1   |        | ENSG00000166704 | 3.8719564 | 0.0001532 | 0.0001532 | 0.0222538 |     |   |
| 27 | Orbp1   |        | ENSG00000145944 | 3.5380227 | 0.0002378 | 0.0002378 | 0.0240508 |     |   |
| 28 | Arpm1   |        | ENSG00000125913 | 0.9316103 | 0.0204881 | 0.0204881 | 0.0566469 |     |   |
| 29 | Arpm1   |        | ENSG00000125913 | 0.9316103 | 0.0204881 | 0.0204881 | 0.0566469 |     |   |
| 30 | Ctbp1   |        | ENSG00000145944 | 4.0242605 | 1.3274006 | 1.3274006 | 0.4867165 |     |   |
| 31 | Ctcb1   |        | ENSG00000125913 | 4.0242605 | 1.3274006 | 1.3274006 | 0.4867165 |     |   |
| 32 | Scm1    |        | ENSG00000125913 | 4.0242605 | 1.3274006 | 1.3274006 | 0.4867165 |     |   |
| 33 | Scm1    |        | ENSG00000125913 | 4.0242605 | 1.3274006 | 1.3274006 | 0.4867165 |     |   |
| 34 | Ndufa4  |        | ENSG00000115941 | 0.8719564 | 1.021464  | 1.021464  | 0.311050  |     |   |
| 35 | Ndufa4  |        | ENSG00000115941 | 0.8719564 | 1.021464  | 1.021464  | 0.311050  |     |   |
| 36 | Actb    |        | ENSG00000125913 | 0.8805133 | 0.405154  | 0.405154  | 0.0566469 |     |   |



# Functional Enrichment Analysis

| DE Genes |
|----------|
| ABL1     |
| TP53     |
| MDM2     |
| ...      |



= GO Analysis



= Pathway Analysis



| GO Term or Pathway | Ratio | P-Value | Z-Score | List of Genes          |
|--------------------|-------|---------|---------|------------------------|
| Cell Cycle         | 9/45  | 4.2E-12 | 2.5     | MDM2, ABL1, RB1, ...   |
| DNA Repair         | 9/52  | 2.6E-10 | 3.2     | MDM2, ABL1, RB1, ...   |
| TNF Signaling      | 8/40  | 1.1E-10 | 2.4     | CDK2, TNFA1, ABL1, ... |

# Functional Enrichment Analysis

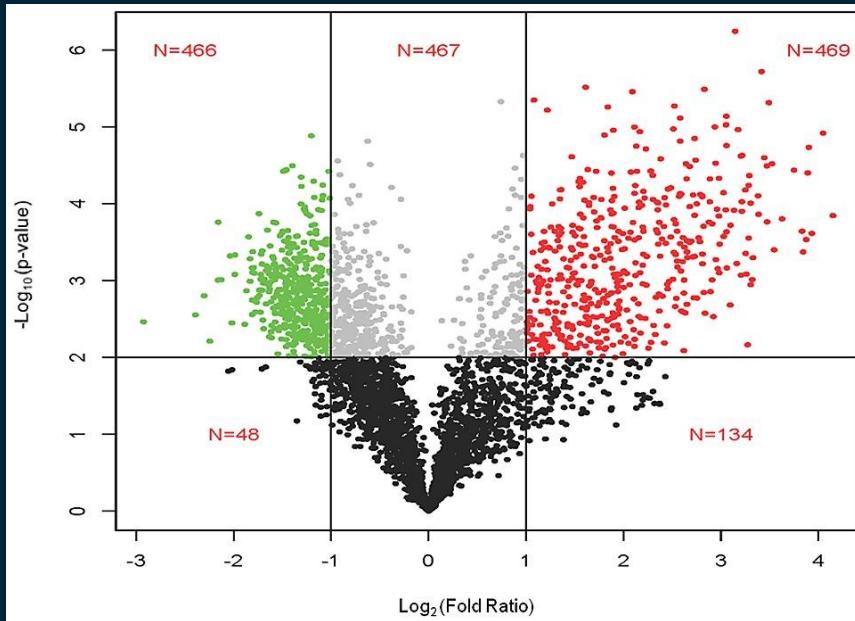
## 1. Overrepresentation Analysis (ORA)

- Pick cutoffs
- Apply Fisher's Exact Test or Hypergeometric Test

## 2. Gene Set Enrichment Analysis (GSEA)

- Rank all genes
- Apply GSEA method

# 1. Overrepresentation Analysis (ORA)



## Pick cutoffs

- Log2FC
- Adjusted p-value
- Upregulated
- Downregulated
- Significantly changed

# 1. Overrepresentation Analysis (ORA)

## Apply statistical test

- Fisher's exact test or Hypergeometric test
- See detailed descriptions and comparisons

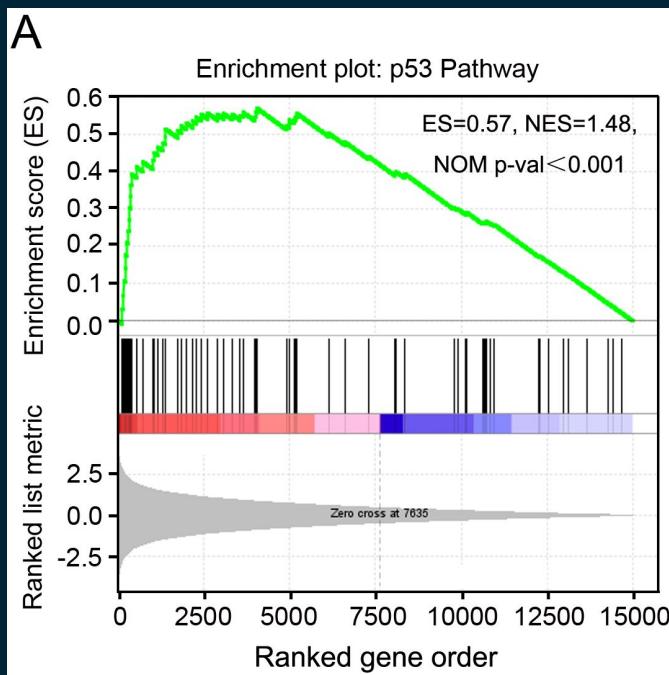
## Important factors

- Source of ontology and pathways sets
- Pre-filtering
- Post-filtering
- Use of background or reference set

## 2. Gene Set Enrichment Analysis (GSEA)

### Rank all genes

- $\text{sign}(\log_{2}\text{FC}) * -\log(\text{Pvalue})$



## 2. Gene Set Enrichment Analysis (GSEA)

### Appy statistical test

- Subramanian, et al. PNAS 2005

### Important factors

- Source of ontology and pathways sets
- Pre-filtering
- Post-filtering

### Advantages

- No arbitrary cutoffs
- Background is built into ranked gene set

*Which method should I use?*

Both!

# Survey of Tools

- **Enrichr** - simple test of 154 resources (ORA only)
  - Paste in human or mouse symbols
  - Browse and export results
  - Can't provide background set
  - See [documentation](#)
- **WebGestalt** - advanced test on select resources
  - Paste in symbols or identifiers ~15 species
  - Specify background set
  - Advanced options; advanced data visualizations
  - See [Wang, et al. NAR 2017](#)

# Survey of Tools

- ***clusterProfiler*** - R package
  - ORA and GSEA
  - Advanced input and configuration options
  - Built-in GO analysis; expansion options
  - Build-in data visualization; expansion options
  - See [documentation](#)

*Which tool should I use?*

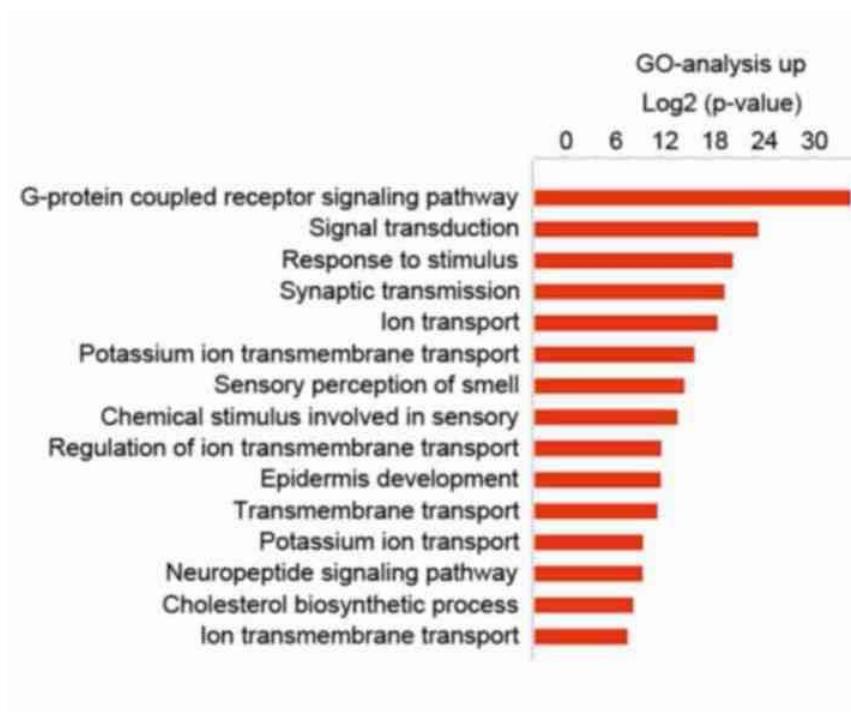
Multiple!

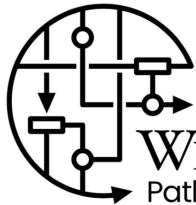
# Additional Reading

- Huang 2009
- Tipney & Hunter 2010
- Kelder, Pico, et al. 2010
- Nguyen, et al. 2019

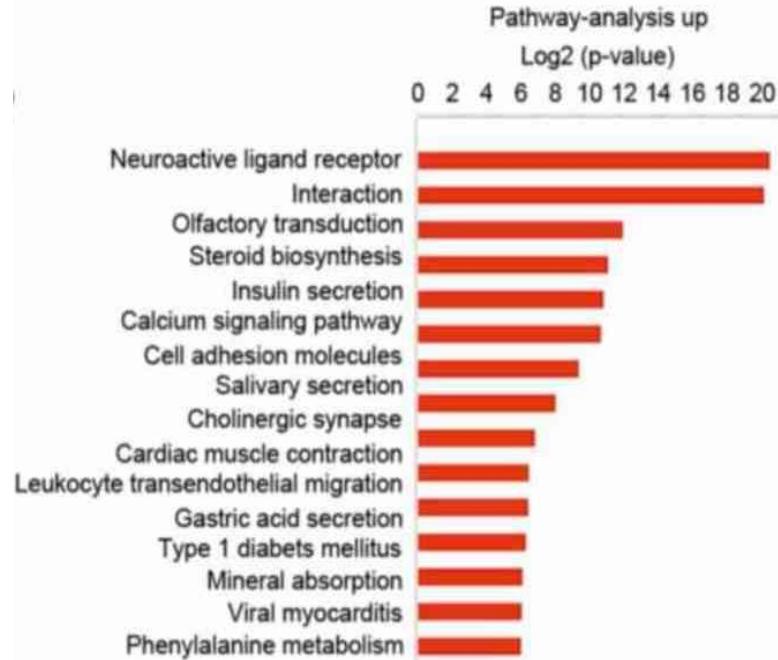


**GENEONTOLOGY**  
Unifying Biology

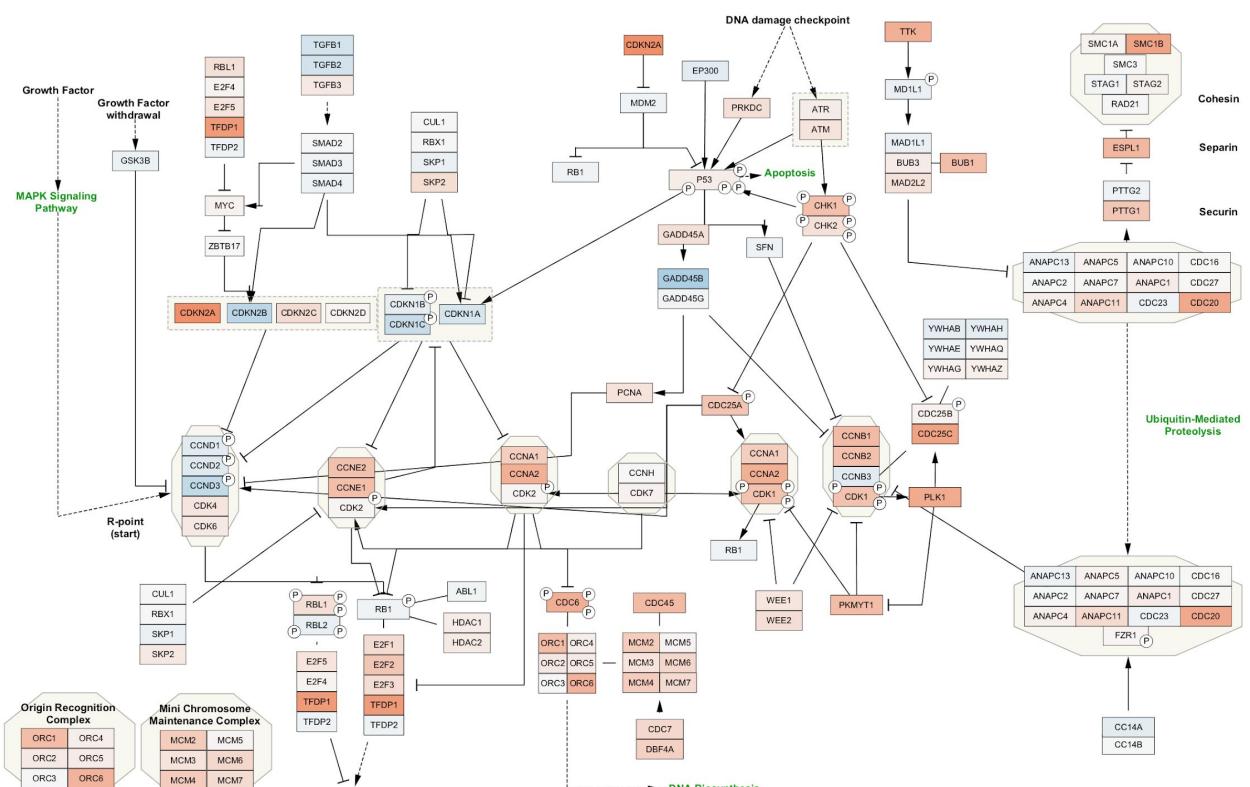
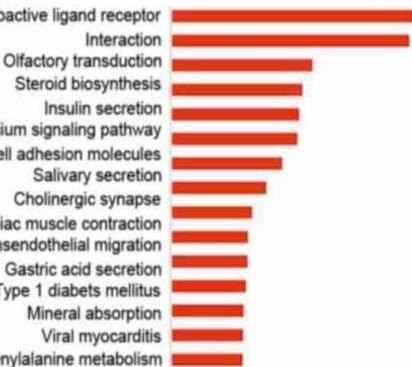




**WIKIPATHWAYS**  
Pathways for the People



| A           | B               | C            | D         | E         |
|-------------|-----------------|--------------|-----------|-----------|
| hgnc_symbol | EnsemblID       | logFC        | Pvalue    | FDR       |
| FGF19P2     | ENSG00000137441 | 4.93±7.2148  | 2.07E-11  | 2.52E-4   |
| IGKJ4       | ENSG00000211594 | 4.570±14526  | 5.80E-13  | 1.02E-3   |
| GPR3        | ENSG00000181773 | 3.073±84469  | 2.37E-06  | 6.68E-4   |
| RP52OPI0    | ENSG00000133971 | 3.073±66699  | 1.59E-05  | 0.0003374 |
| RP523P1     | ENSG00000234031 | 2.718±89316  | 2.02E-06  | 0.0004115 |
| RP523P4     | ENSG00000171858 | 1.782±21017  | 5.40E-16  | 2.78E-4   |
| ERGIC3      | ENSG00000125981 | 1.042±70398  | 4.08E-07  | 1.48E-4   |
| ATP5F1E     | ENSG00000124172 | 1.041±90101  | 1.74E-07  | 6.97E-4   |
| DS14        | ENSG00000127745 | 1.038±45956  | 8.43E-07  | 0.0003000 |
| MME63AHG    | ENSG00000227185 | 1.038±45956  | 1.16E-07  | 4.86E-4   |
| BCR         | ENSG00000186716 | 1.022±71798  | 2.66E-08  | 1.37E-4   |
| HIST1H2AG   | ENSG00000196787 | 1.020±71118  | 9.38E-08  | 0.0014881 |
| SSR2        | ENSG00000163479 | 1.019±15311  | 4.30E-08  | 3.79E-4   |
| EF5F1A1     | ENSG00000156330 | 1.012±47257  | 1.08E-07  | 4.62E-4   |
| PTEN        | ENSG00000115388 | 1.009±10007  | 0.0003374 | 0.0004115 |
| [C]2zvf57   | ENSG00000115678 | -1.009±09969 | 0.000472  | 0.0004226 |
| ELOB        | ENSG00000130363 | -1.970±0438  | 1.64E-05  | 0.0003451 |
| B2M         | ENSG00000166710 | -1.962±59858 | 3.78E-07  | 1.37E-4   |
| EF5F3K      | ENSG00000178935 | -2.966±4061  | 2.65E-06  | 7.30E-4   |
| PTEN        | ENSG00000120029 | -2.951±40615 | 3.00E-05  | 0.0003000 |
| SCARNA17    | ENSG00000251992 | -2.951±63979 | 1.74E-06  | 5.18E-4   |
| H1A-8       | ENSG00000234745 | -2.948±88318 | 6.68E-08  | 3.10E-4   |
| C7orf76     | ENSG00000146576 | -3.942±40446 | 0.000152  | 0.0002259 |
| J7          | ENSG00000143543 | -3.941±53986 | 1.89E-06  | 5.60E-4   |
| OSCRN       | ENSG00000143543 | -3.941±53986 | 1.89E-06  | 5.60E-4   |
| TMEM14C     | ENSG00000111843 | -3.637±88303 | 0.0002869 | 0.001151  |
| ATP5MGM     | ENSG00000167283 | -3.935±60803 | 0.0001484 | 0.0021779 |
| COXA1       | ENSG00000131133 | -4.919±46434 | 2.37E-06  | 6.68E-4   |
| CCT3        | ENSG00000163468 | -4.912±20265 | 1.55E-06  | 0.0003313 |
| S3R4        | ENSG00000163468 | -4.908±63545 | 0.0002000 | 0.0004460 |
| TMEM222     | ENSG00000197322 | -4.908±63544 | 1.02E-06  | 3.31E-4   |
| NDUF4A      | ENSG00000189043 | -5.857±93648 | 1.02E-06  | 3.31E-4   |
| NDUF5B      | ENSG00000110717 | -5.875±63243 | 0.0022648 | 0.017956  |
| ACTB        | ENSG00000075624 | -5.867±0115  | 4.30E-06  | 0.0001114 |



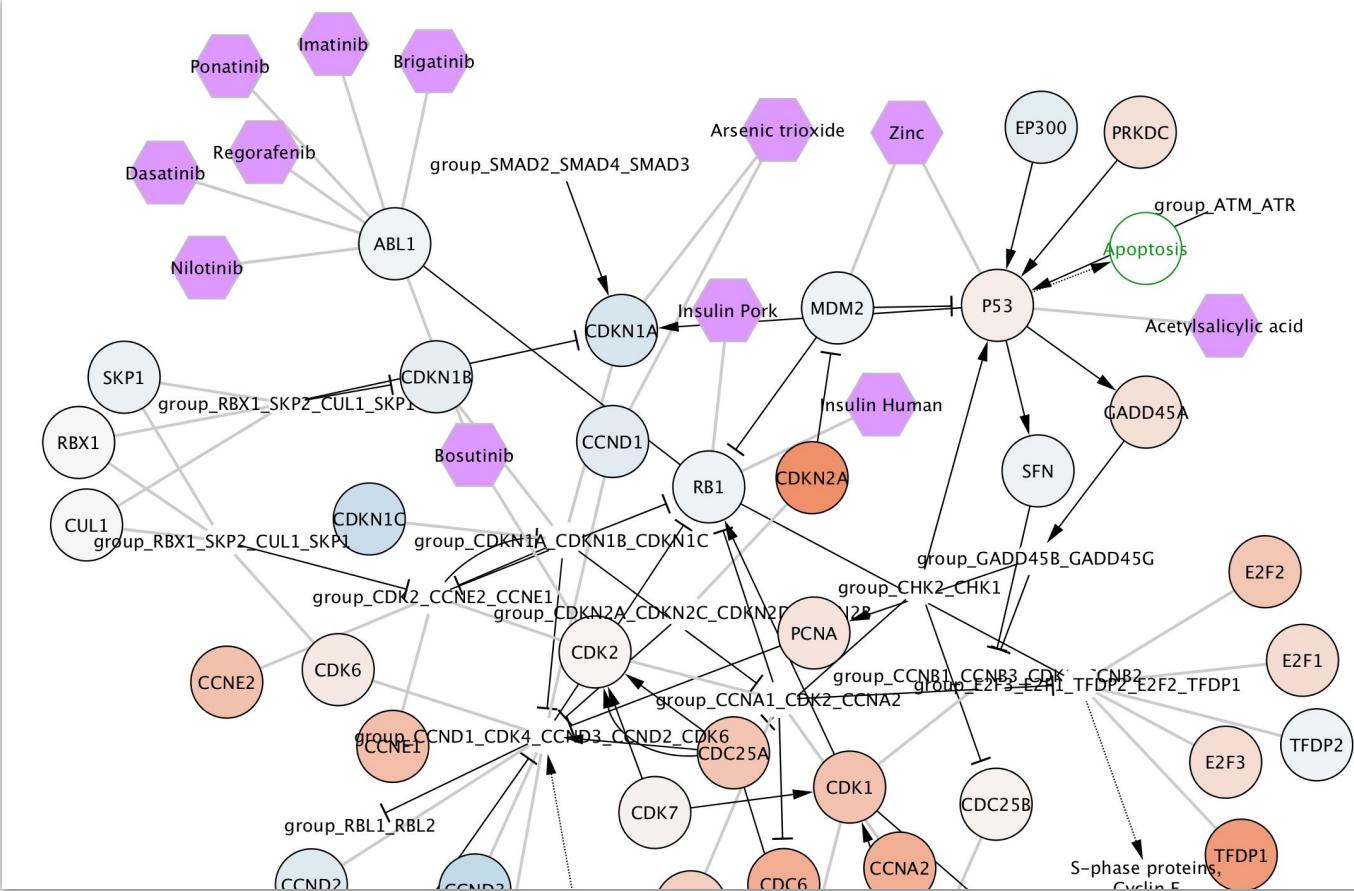
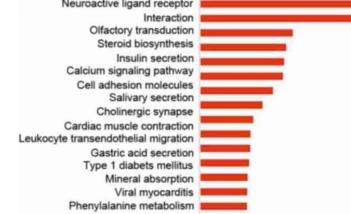
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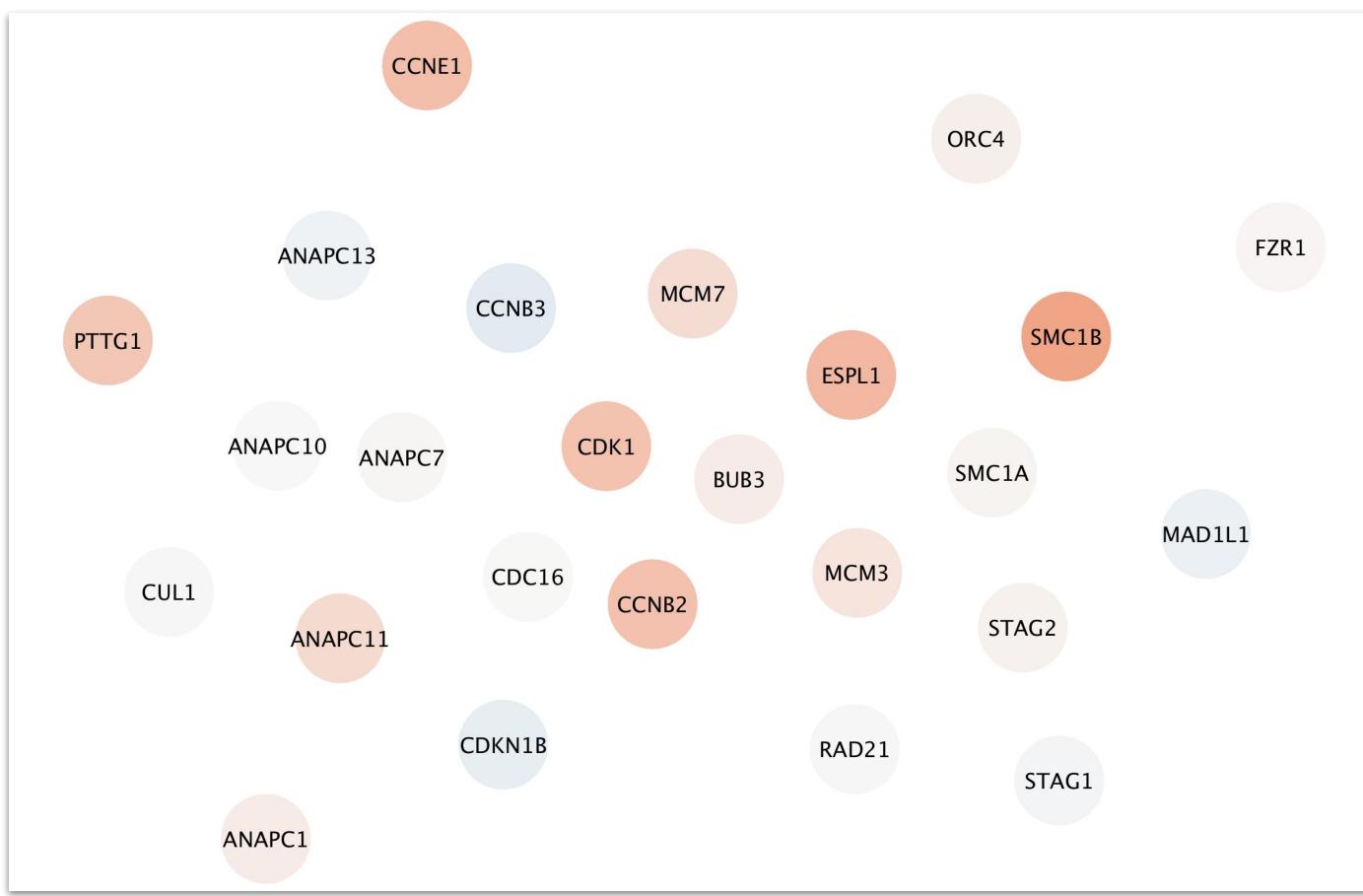
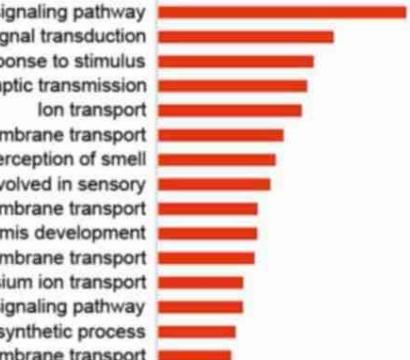
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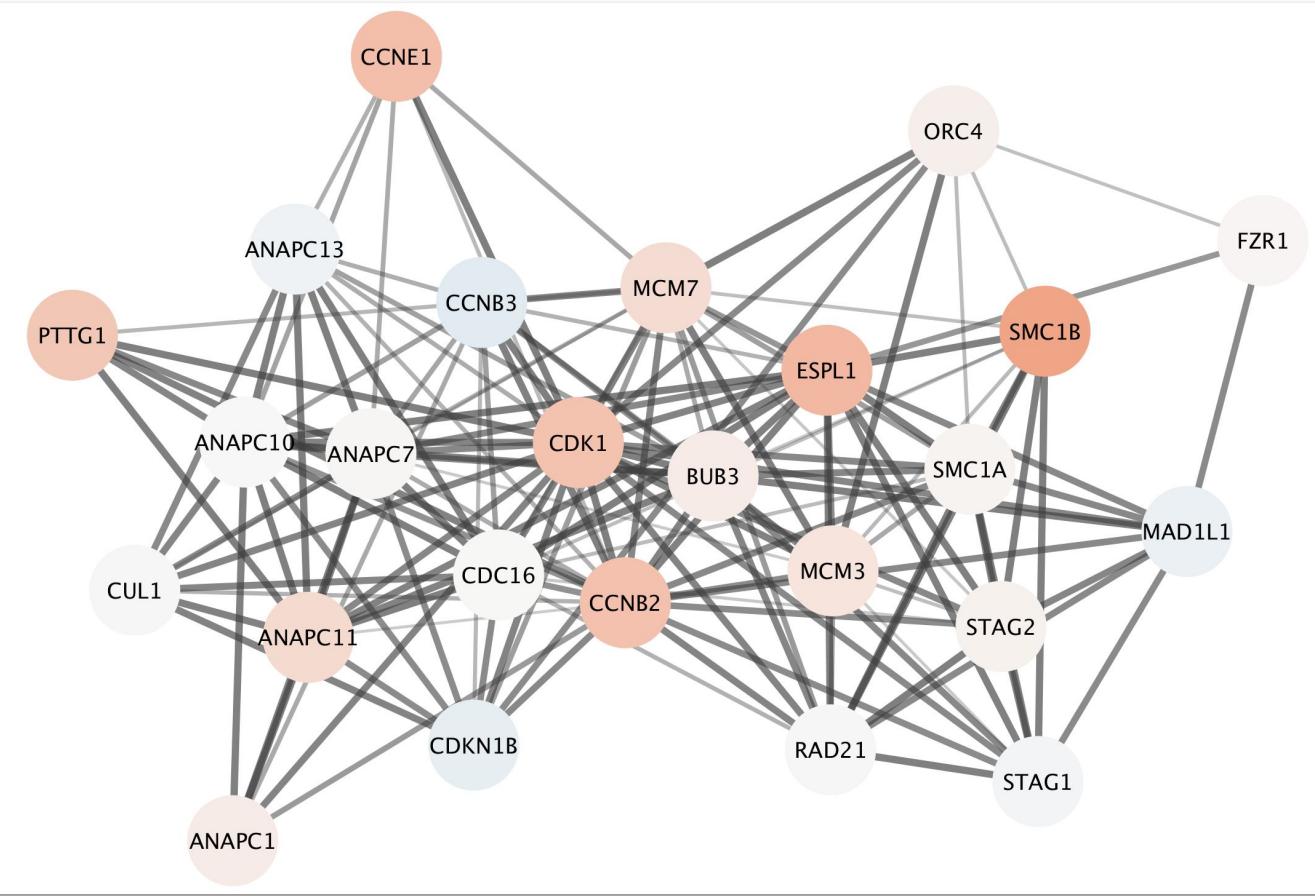
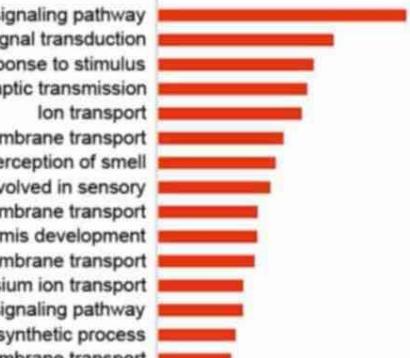
| A           | B                | C               | D           | E          |            |
|-------------|------------------|-----------------|-------------|------------|------------|
| hgnc_symbol | EnsemblID        | logFC           | Pvalue      | FDR        |            |
| FGFR2P2     | ENSG00000137441  | 4.95372148      | 2.07E-11    | 2.52E-4    |            |
| IIGK4       | ENSG00000211594  | 4.57014524      | 5.80E-13    | 1.02E-4    |            |
| GPR83       | ENSG00000181733  | 3.07384469      | 2.37E-06    | 6.68E-4    |            |
| RP52P10     | ENSG00000213697  | 3.01666907      | 1.59E-06    | 0.000153   |            |
| RP53AP1     | ENSG00000213504  | 2.97616767      | 1.00E-06    | 0.000565   |            |
| RP53AP44    | ENSG00000234031  | 2.87189316      | 2.02E-05    | 0.0004115  |            |
| RP521       | ENSG00000171858  | 1.78201017      | 5.40E-16    | 2.76E-4    |            |
| ERGIC3      | ENSG00000125981  | 1.04270392      | 4.08E-07    | 1.48E-4    |            |
| ATP5F1E     | ENSG000002142172 | 1.04309011      | 1.74E-07    | 6.57E-4    |            |
| LGR5        | ENSG00000186046  | 1.03865046      | 1.00E-06    | 0.000153   |            |
| MIR653AHG   | ENSG000002277195 | 1.03864596      | 1.15E-07    | 4.98E-4    |            |
| 3CR         | ENSG00000186716  | 1.02217159      | 2.66E-08    | 1.37E-4    |            |
| HIST1H2AG   | ENSG00000196787  | 1.02057115      | 9.38E-05    | 0.004881   |            |
| SSR2        | ENSG00000183479  | 1.01915312      | 4.30E-10    | 3.79E-4    |            |
| EP301       | ENSG00000183475  | 1.01915312      | 4.30E-10    | 3.79E-4    |            |
| TM4M159     | ENSG00000116158  | 1.00983307      | 0.0017788   | 0.0149854  |            |
| G12orf57    | ENSG00000116178  | 1.00960964      | 0.0009472   | 0.0094228  |            |
| ELOB        | ENSG00000103363  | 1.97004381      | 1.64E-05    | 0.000451   |            |
| B2M         | ENSG00000166710  | 1.96259859      | 3.78E-07    | 1.37E-4    |            |
| EP3K        | ENSG00000172500  | -2.96610099     | 2.65E-05    | 7.30E-4    |            |
| 3           | SCARNA17         | ENSG00000251992 | -2.95153973 | 1.74E-06   | 5.18E-4    |
| 4           | HLA-B            | ENSG00000234745 | 2.94688319  | 6.68E-08   | 3.10E-4    |
| 5           | C7orf26          | ENSG00000146576 | 3.94240446  | 0.000152   | 0.002259   |
| 7B          | ENSG00000154588  | 3.93505598      | 1.98E-05    | 5.62E-4    |            |
| 8           | OSCN             | ENSG00000111543 | 3.93738303  | 0.0001769  | 0.0001801  |
| 8           | TMEM14C          | ENSG00000111543 | 3.93738303  | 0.00018151 | 0.00018151 |
| 9           | ATP5MG           | ENSG00000167283 | -3.93536083 | 0.0001484  | 0.0021779  |
| 10          | COX4I1           | ENSG00000131143 | 4.91954634  | 2.37E-06   | 6.68E-4    |
| 11          | C1CT3            | ENSG00000130626 | 4.91954634  | 1.55E-05   | 0.0003331  |
| 12          | S3MK4            | ENSG00000180579 | 4.91954634  | 0.0002035  | 0.0002035  |
| 13          | SNHG22           | ENSG00000217122 | 4.90561554  | 9.03E-05   | 0.0004461  |
| 14          | NDUFV4           | ENSG00000189043 | 5.8779366   | 1.02E-06   | 3.31E-4    |
| 15          | NDUF58           | ENSG00000110717 | 5.87553243  | 0.0022648  | 0.0179561  |
| 16          | ACTB             | ENSG00000075624 | 5.8670115   | 4.30E-06   | 0.0001114  |

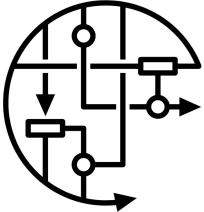


| A | B           | C                | D           | E                  |                    |
|---|-------------|------------------|-------------|--------------------|--------------------|
|   | hgnc_symbol | EnsemblID        | logFC       | Pvalue             | FDR                |
| 1 | FGBP2       | ENSG00000137441  | 4.95721448  | 2.07E-13           | 2.53%              |
| 1 | IGK4        | ENSG00000211594  | 4.57014526  | 5.80E-13           | 1.02%              |
| 1 | GPR3        | ENSG00000181773  | 3.07384469  | 2.37E-06           | 6.68%              |
| 1 | RPS20P10    | ENSG00000233973  | 3.07384469  | 1.59E-05           | 0.0003379          |
| 1 | RPS20P1     | ENSG00000234031  | 2.90201467  | 0.0000000000000005 | 0.0000000000000005 |
| 1 | RPS3AP44    | ENSG00000234031  | 1.87189316  | 2.01E-05           | 0.0000000000000011 |
| 1 | RPS21       | ENSG000002171838 | 1.78201017  | 5.40E-16           | 2.76%              |
| 1 | ERGIC3      | ENSG00000125991  | 1.04270392  | 4.08E-07           | 1.48%              |
| 1 | ATP5F1C     | ENSG00000124172  | 1.04191011  | 1.74E-07           | 6.97%              |
| 1 | CDC14A      | ENSG00000228268  | 1.00000000  | 4.83E-05           | 0.0000000000000013 |
| 2 | MMP9AHG     | ENSG000001795795 | 1.03684596  | 1.16E-05           | 0.98%              |
| 3 | BCR         | ENSG00000186716  | 1.02217198  | 2.66E-08           | 1.37%              |
| 4 | HIST1H2AG   | ENSG00000196787  | 1.02057118  | 9.38E-05           | 0.001488           |
| 5 | SSR2        | ENSG00000163479  | 1.01915131  | 4.30E-10           | 3.79%              |
| 6 | EF1F1A1     | ENSG00000163479  | 1.01915131  | 1.24E-05           | 1.08%              |
| 7 | TMM2L5P9    | ENSG00000156589  | 1.00900000  | 0.0000000000000005 | 0.0000000000000005 |
| 8 | C12orf57    | ENSG00000111578  | -1.00900006 | 0.0000472          | 0.0042420          |
| 9 | ELO1        | ENSG00000103363  | 1.9700433   | 1.64E-05           | 0.0003453          |
| 9 | B2M         | ENSG00000166710  | -1.96259859 | 3.78E-07           | 1.37%              |
| 1 | EIF3K       | ENSG00000178982  | -2.96000000 | 2.65E-06           | 7.30%              |
| 2 | TRBP        | ENSG00000178982  | -2.96000000 | 0.0000000000000005 | 0.0000000000000005 |
| 3 | SCARNA17    | ENSG00000251192  | -2.95163073 | 1.74E-06           | 5.18%              |
| 4 | H1A-B       | ENSG00000234745  | -2.94588319 | 6.68E-08           | 3.10%              |
| 5 | C7orf26     | ENSG00000146576  | -3.94240445 | 0.0001522          | 0.002225           |
| 6 | JTB         | ENSG00000143543  | -3.94165939 | 1.89E-06           | 5.60%              |
| 7 | OCSCN       | ENSG00000143543  | -3.94165939 | 0.0002326          | 0.0002326          |
| 8 | TMM2L4C     | ENSG00000111443  | -3.93798801 | 0.0002326          | 0.0002326          |
| 9 | ATP5M6G     | ENSG00000167283  | -3.93336083 | 0.0001484          | 0.0021771          |
| 0 | CDX41       | ENSG00000131283  | -4.91954634 | 2.37E-06           | 6.68%              |
| 1 | CCT3        | ENSG00000163468  | -4.91242065 | 1.58E-05           | 0.0003111          |
| 2 | SRSF1       | ENSG000001808975 | -4.90891154 | 0.0000000000000005 | 0.0000000000000005 |
| 3 | SNHG22      | ENSG000001808975 | -4.90891154 | 9.09E-08           | 0.0000000000000005 |
| 4 | NDUFV4      | ENSG00000189943  | -5.87879366 | 0.0000000000000005 | 0.0000000000000005 |
| 5 | NDUF58      | ENSG00000110717  | -5.87563243 | 0.0022648          | 0.017956           |
| 6 | ACTB        | ENSG00000075624  | -5.86701155 | 4.30E-06           | 0.000111           |



| A  | B           | C                | D           | E          |            |
|----|-------------|------------------|-------------|------------|------------|
|    | hgnc_symbol | EnsemblID        | logFC       | Pvalue     | FDR        |
| 1  | FGBP2       | ENSG00000137441  | 4.957021448 | 2.07E-11   | 2.53E-4    |
| 2  | IGK4        | ENSG00000211594  | 4.57014526  | 5.80E-13   | 1.02E-3    |
| 3  | GPR3        | ENSG00000181773  | 3.07384469  | 2.37E-06   | 6.68E-4    |
| 4  | RPS20P10    | ENSG00000233973  | 3.07384469  | 1.59E-05   | 0.0003379  |
| 5  | RPS20P1     | ENSG00000234031  | 2.90201467  | 2.01E-05   | 0.0003379  |
| 6  | RPS3AP44    | ENSG00000234031  | 1.87189316  | 1.02E-05   | 0.0003379  |
| 7  | RPS21       | ENSG000002171838 | 1.78201017  | 5.40E-16   | 2.76E-5    |
| 8  | ERGIC3      | ENSG00000125991  | 1.04270392  | 4.08E-07   | 1.48E-4    |
| 9  | ATP5F1C     | ENSG00000124172  | 1.04191011  | 1.74E-07   | 6.97E-4    |
| 10 | CDC14       | ENSG00000222846  | 1.00000000  | 4.83E-05   | 0.0003379  |
| 11 | MMP9AHG     | ENSG00000179579  | 1.03684596  | 1.16E-05   | 0.0003379  |
| 12 | BCR         | ENSG00000186716  | 1.02217198  | 2.66E-08   | 1.37E-4    |
| 13 | HIST1H2AG   | ENSG00000196787  | 1.02057118  | 9.38E-05   | 0.0003379  |
| 14 | SSR2        | ENSG00000163479  | 1.01915111  | 4.30E-10   | 3.79E-4    |
| 15 | EF1A1       | ENSG00000156259  | 1.00000000  | 1.08E-07   | 0.0003379  |
| 16 | TMSB15P     | ENSG00000156259  | 1.00000000  | 1.00E-05   | 0.0003379  |
| 17 | C12orf57    | ENSG00000111578  | -1.00900066 | 0.000472   | 0.0042420  |
| 18 | ELO1        | ENSG00000103363  | 1.9700433   | 1.64E-05   | 0.0003453  |
| 19 | B2M         | ENSG00000166710  | -1.96259859 | 3.78E-07   | 1.37E-4    |
| 20 | EIF3K       | ENSG00000178982  | -2.96000000 | 2.65E-06   | 7.30E-4    |
| 21 | TRBP        | ENSG00000178982  | -2.96000000 | 0.00027028 | 0.00027028 |
| 22 | SCARNA17    | ENSG00000235192  | -2.95163073 | 1.74E-06   | 5.18E-4    |
| 23 | H1A-B       | ENSG00000234745  | -2.94588319 | 6.68E-08   | 3.10E-4    |
| 24 | C7orf26     | ENSG00000146576  | -3.94240455 | 0.0001522  | 0.0022255  |
| 25 | JTB         | ENSG00000143543  | -3.94165939 | 1.89E-06   | 5.60E-4    |
| 26 | PTTG1       | ENSG00000143543  | -3.94165939 | 0.0001522  | 0.0022255  |
| 27 | ORC4        | ENSG00000111443  | -3.93798801 | 0.0001270  | 0.0018152  |
| 28 | TMM23AC     | ENSG00000167283  | -3.93336083 | 0.0001484  | 0.0021771  |
| 29 | ATP5M6G     | ENSG00000131143  | -4.91954634 | 2.37E-06   | 6.68E-4    |
| 30 | COX4I1      | ENSG00000163468  | -4.91240205 | 1.58E-05   | 0.0003111  |
| 31 | CCT3        | ENSG00000180897  | -4.90891154 | 0.00016668 | 0.00016668 |
| 32 | SRSF1       | ENSG00000180897  | -4.90891154 | 9.03E-08   | 3.31E-4    |
| 33 | SNHG22      | ENSG00000189943  | -5.87583243 | 1.02E-06   | 3.31E-4    |
| 34 | NDUFV4      | ENSG00000189943  | -5.87583243 | 0.0022643  | 0.017956   |
| 35 | NDUFV8      | ENSG00000110717  | -5.87583243 | 0.0022643  | 0.017956   |
| 36 | ACTB        | ENSG00000075624  | -5.86701155 | 4.30E-06   | 0.0001118  |





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