# Supplementary Appendix 1

## Analysis with DAVID Software

To assign annotations to the differentially expressed genes, as determined by empirical Bayes analysis, we used DAVID software (http://david.abcc.ncifcrf.gov/). The Mouse430_2 background was chosen as the background setting. For enrichment analysis, default settings were used (Count: 2, EASE: 0.1, #Records: 1000).

The levels in the GO annotation analysis were chosen to achieve a balance between capturing the global processes and providing some details.

## Molecular Function Level 2, Cellular Component Level 4, Biological Process Level 5

Before analysis, RefSeq accession numbers were mapped to NCBI Gene ID numbers to control for the possibility that multiple identifiers on the list refer to the same gene. The NCBI Gene ID numbers were then mapped to gene categories (e.g., Apoptosis) within various categorical systems (e.g., Molecular Function). The enrichment in each category was then calculated as the **Fisher exact probability**. These are the *P* values shown in Figure 3a.

To strongly penalize the significance of categories supported by few genes and negligibly penalize categories supported by many genes, we used the EASE score (the default metric in DAVID) to rank categories of genes in Figure 3a. The EASE score is described as the upper bound of the distribution of Jackknife Fisher exact probabilities.

For further information about the analysis methods please refer to the following two references.

1. Dennis G Jr et al. (2003) *DAVID:* Database for Annotation, Visualization, and Integrated Discovery. *Genome Biol* 4:P3.
2. http://david.abcc.ncifcrf.gov/

## Analysis with the Gene Set Enrichment Analysis (GSEA)

As detailed in the first reference below, the GSEA method tests groups of genes rather than individual genes, in contrast to the empirical Bayes test. The notion is that certain genes have a closer relationship than others by regulation, function, chromosomal context, etc. and therefore should be tested together. By manually screening the contribution of different database sources to the original gene set, we concluded that the pathways from KEGG and Biocarta were the most reliable and complete. Hence, we restricted our gene sets to those two databases. Also, to filter out highly incomplete pathways, we used a lower threshold of pathways consisting of fewer than 10 genes , leaving 202 pathways for testing (for a complete list, see below). Since many of the pathways were found in both databases, in general, the lower threshold only left the best-annotated pathway copy. As described in the parameter section below, the *t* test was used as the metric, and 250 phenotype permutations were run. Core enrichment for the proteasome degradation pathway is shown below. Leading edge analysis was not performed. For further information about the analysis methods, please refer to the following three references.

1. Subramanian A et al. (2005) Gene set enrichment analysis: a knowledge-based approach for interpreting genome-wide expression profiles. *Proc Natl Acad Sci USA* 102:15545-50.
2. Mootha VK et al. (2003) PGC-1alpha-responsive genes involved in oxidative phosphorylation are coordinately downregulated in human diabetes. *Nat Genet* 34:267-73.
3. http://www.broad.mit.edu/gsea/

## Parameters Used in the Analysis

| | | |
|---|---|---|
| param | norm | meandiv |
| param | save_rnd_lists | false |
| param | median | false |
| param | scoring_scheme | weighted |
| param | make_sets | true |
| param | gmx | C:\c2.refseq Biocarta KEGG.gmt |
| param | gui | true |
| param | chip | Mouse430_2 |
| param | metric | t-test |
| param | order | descending |
| param | permute | phenotype |

|  |  |  |
|---|---|---|
| param | rnd_type | no_balance |
| param | set_min | 10 |
| param | sort | real |
| param | rnd_seed | timestamp |
| param | nperm | 250 |
| param | set_max | 500 |

## Gene Set Used in the Analysis (KEGG + Biocarta)

| NAME | ORIGINAL SIZE | AFTER RESTRICTING |
|---|---|---|
| 41bbPathway | 18 | 18 |
| ace2Pathway | 10 | 10 |
| acetaminophenPathway | 5 | Rejected! |
| achPathway | 13 | 13 |
| actinYPathway | 15 | 15 |
| agpcrPathway | 12 | 12 |
| ahspPathway | 9 | Rejected! |
| akap13Pathway | 8 | Rejected! |
| akap96Pathway | 9 | Rejected! |
| akapCentrosomePathway | 8 | Rejected! |
| aktPathway | 14 | 14 |
| alkPathway | 32 | 32 |
| alternativePathway | 4 | Rejected! |
| amiPathway | 18 | 18 |
| arapPathway | 16 | 16 |
| arenrf2Pathway | 14 | 14 |
| arfPathway | 8 | Rejected! |
| argininecPathway | 5 | Rejected! |
| asbcellPathway | 6 | Rejected! |
| at1rPathway | 32 | 32 |
| atmPathway | 16 | 16 |
| atrbrcaPathway | 15 | 15 |
| badPathway | 18 | 18 |
| bbcellPathway | 2 | Rejected! |
| bcrPathway | 33 | 33 |
| biopeptidesPathway | 36 | 36 |
| blymphocytePathway | 7 | Rejected! |
| cacamPathway | 14 | 14 |
| calcineurinPathway | 18 | 18 |
| cardiacegfPathway | 15 | 15 |
| carm1Pathway | 12 | 12 |
| carm-erPathway | 26 | 26 |
| caspase_activity | 6 | Rejected! |
| caspasePathway | 20 | 20 |
| cblPathway | 13 | 13 |
| ccr3Pathway | 18 | 18 |
| ccr5Pathway | 17 | 17 |
| cd40Pathway | 13 | 13 |
| cdc25Pathway | 8 | Rejected! |
| cdc42racPathway | 12 | 12 |
| cdk5Pathway | 11 | 11 |
| cdmacPathway | 15 | 15 |
| cell2cellPathway | 13 | 13 |

| | | |
|---|---|---|
| cellcyclePathway | 21 | 21 |
| ceramidePathway | 22 | 22 |
| cftrPathway | 11 | 11 |
| chemicalPathway | 19 | 19 |
| chrebpPathway | 16 | 16 |
| circadianPathway | 6 | Rejected! |
| ck1Pathway | 15 | 15 |
| classicPathway | 11 | 11 |
| Complement_Activation_Classical | 11 | 11 |
| compPathway | 14 | 14 |
| crebPathway | 24 | 24 |
| cremPathway | 7 | Rejected! |
| cskPathway | 18 | 18 |
| ctla4Pathway | 15 | 15 |
| ctlPathway | 9 | Rejected! |
| cxcr4Pathway | 21 | 21 |
| cytokinePathway | 19 | 19 |
| d4gdiPathway | 10 | 10 |
| dbpbPathway | 3 | Rejected! |
| dcPathway | 21 | 21 |
| deathPathway | 29 | 29 |
| DNA_DAMAGE_SIGNALLING | 84 | 84 |
| dnafragmentPathway | 9 | Rejected! |
| dreamPathway | 12 | 12 |
| drug_resistance_and_metabolism | 83 | 83 |
| ecmPathway | 19 | 19 |
| edg1Pathway | 23 | 23 |
| eea1Pathway | 6 | Rejected! |
| EGF_receptor_signaling_pathway | 12 | 12 |
| egfPathway | 24 | 24 |
| egfr_smrtePathway | 10 | 10 |
| Eicosanoid_Synthesis | 13 | 13 |
| eif2Pathway | 8 | Rejected! |
| eif4Pathway | 21 | 21 |
| electron_transport | 48 | 48 |
| Electron_Transport_Chain | 78 | 78 |
| electron_transporter_activity | 91 | 91 |
| eosinophilsPathway | 6 | Rejected! |
| ephA4Pathway | 10 | 10 |
| eponfkbPathway | 10 | 10 |
| epoPathway | 16 | 16 |
| erbb3Pathway | 4 | Rejected! |
| erbb4Pathway | 5 | Rejected! |
| erk5Pathway | 13 | 13 |
| erkPathway | 28 | 28 |
| erythPathway | 13 | 13 |
| etcPathway | 9 | Rejected! |
| etsPathway | 17 | 17 |
| extrinsicPathway | 12 | 12 |
| fasPathway | 25 | 25 |
| Fatty_Acid_Degradation | 18 | 18 |
| fatty_acid_metabolism | 20 | 20 |
| Fatty_Acid_Synthesis | 12 | 12 |
| fbw7Pathway | 9 | Rejected! |

| | | |
|---|---|---|
| fcer1Pathway | 34 | 34 |
| feederPathway | 7 | Rejected! |
| fibrinolysisPathway | 12 | 12 |
| flumazenilPathway | 9 | Rejected! |
| Fmlppathway | 36 | 36 |
| freePathway | 8 | Rejected! |
| fxrPathway | 6 | Rejected! |
| G13_Signaling_Pathway | 28 | 28 |
| g1Pathway | 22 | 22 |
| g2Pathway | 20 | 20 |
| gabaPathway | 12 | 12 |
| gata3Pathway | 15 | 15 |
| gcrPathway | 16 | 16 |
| ghPathway | 21 | 21 |
| gleevecPathway | 19 | 19 |
| Glycogen_Metabolism | 30 | 30 |
| glycolysisPathway | 8 | Rejected! |
| gpcrPathway | 31 | 31 |
| gsk3Pathway | 25 | 25 |
| gsPathway | 6 | Rejected! |
| hbxPathway | 6 | Rejected! |
| hcmvPathway | 15 | 15 |
| hdacPathway | 28 | 28 |
| hifPathway | 11 | 11 |
| hivnefPathway | 51 | 51 |
| hsp27Pathway | 13 | 13 |
| ifnaPathway | 9 | Rejected! |
| ifngPathway | 6 | Rejected! |
| igf1mtorPathway | 18 | 18 |
| igf1Pathway | 17 | 17 |
| igf1rPathway | 12 | 12 |
| il10Pathway | 13 | 13 |
| Il12Pathway | 20 | 20 |
| il17Pathway | 9 | Rejected! |
| il18Pathway | 6 | Rejected! |
| il1rPathway | 31 | 31 |
| il22bpPathway | 11 | 11 |
| il2Pathway | 21 | 21 |
| il2rbPathway | 31 | 31 |
| il3Pathway | 13 | 13 |
| il4Pathway | 9 | Rejected! |
| il5Pathway | 8 | Rejected! |
| il6Pathway | 19 | 19 |
| il7Pathway | 15 | 15 |
| Inflammatory_Response_Pathway | 23 | 23 |
| inflamPathway | 26 | 26 |
| insulin_signalling | 83 | 83 |
| insulinPathway | 17 | 17 |
| integrinPathway | 31 | 31 |
| intrinsicPathway | 21 | 21 |
| ionPathway | 4 | Rejected! |
| keratinocytePathway | 40 | 40 |
| krebPathway | 7 | Rejected! |
| Krebs-TCA_Cycle | 25 | 25 |

| | | |
|---|---|---|
| lairPathway | 12 | 12 |
| ldlPathway | 6 | Rejected! |
| lechtinPathway | 10 | 10 |
| leptinPathway | 10 | 10 |
| longevityPathway | 11 | 11 |
| lymphocytePathway | 9 | Rejected! |
| mapkPathway | 77 | 77 |
| Matrix_Metalloproteinases | 22 | 22 |
| mcalpainPathway | 22 | 22 |
| mef2dPathway | 18 | 18 |
| metPathway | 32 | 32 |
| mitochondriaPathway | 20 | 20 |
| mitrPathway | 9 | Rejected! |
| monocytePathway | 11 | 11 |
| mprPathway | 20 | 20 |
| mRNA_binding_activity | 9 | Rejected! |
| mRNA_processing | 38 | 38 |
| mRNA_splicing | 38 | 38 |
| mrpPathway | 5 | Rejected! |
| mspPathway | 6 | Rejected! |
| mta3Pathway | 15 | 15 |
| mtorPathway | 20 | 20 |
| muscle_myosin | 10 | 10 |
| myosinPathway | 13 | 13 |
| ndkDynaminPathway | 18 | 18 |
| neutrophilPathway | 8 | Rejected! |
| nfatPathway | 46 | 46 |
| nfkbPathway | 23 | 23 |
| ngfPathway | 15 | 15 |
| nkcellsPathway | 17 | 17 |
| nktPathway | 27 | 27 |
| no1Pathway | 26 | 26 |
| no2il12Pathway | 15 | 15 |
| nos1Pathway | 20 | 20 |
| nthiPathway | 21 | 21 |
| p27Pathway | 13 | 13 |
| p35alzheimersPathway | 10 | 10 |
| p38mapkPathway | 38 | 38 |
| p53_signalling | 79 | 79 |
| p53hypoxiaPathway | 16 | 16 |
| p53Pathway | 14 | 14 |
| par1Pathway | 18 | 18 |
| parkinPathway | 9 | Rejected! |
| pdgfPathway | 24 | 24 |
| pelp1Pathway | 7 | Rejected! |
| pepiPathway | 5 | Rejected! |
| pgc1aPathway | 23 | 23 |
| pitx2Pathway | 14 | 14 |
| pkcPathway | 7 | Rejected! |
| plcdPathway | 5 | Rejected! |
| plcePathway | 11 | 11 |
| plcPathway | 6 | Rejected! |
| plk3Pathway | 5 | Rejected! |
| pmlPathway | 10 | 10 |

| | | |
|---|---|---|
| pparaPathway | 48 | 48 |
| ppargPathway | 8 | Rejected! |
| Proteasome_Degradation | 30 | 30 |
| proteasomePathway | 20 | 20 |
| ps1Pathway | 14 | 14 |
| ptc1Pathway | 9 | Rejected! |
| ptdinsPathway | 21 | 21 |
| ptenPathway | 16 | 16 |
| pyk2Pathway | 27 | 27 |
| rabPathway | 8 | Rejected! |
| rac1Pathway | 19 | 19 |
| raccycdPathway | 20 | 20 |
| radiation_sensitivity | 18 | 18 |
| ranklPathway | 13 | 13 |
| ranPathway | 4 | Rejected! |
| rarrxrPathway | 15 | 15 |
| rasPathway | 20 | 20 |
| rbPathway | 11 | 11 |
| reckPathway | 8 | Rejected! |
| reelinPathway | 7 | Rejected! |
| relaPathway | 16 | 16 |
| rhoPathway | 26 | 26 |
| rnaPathway | 8 | Rejected! |
| S1P_Signaling | 23 | 23 |
| s1pPathway | 6 | Rejected! |
| salmonellaPathway | 11 | 11 |
| sarsPathway | 9 | Rejected! |
| setPathway | 10 | 10 |
| shhPathway | 12 | 12 |
| skp2e2fPathway | 10 | 10 |
| slrp2Pathway | 4 | Rejected! |
| slrpPathway | 6 | Rejected! |
| soddPathway | 10 | 10 |
| sppaPathway | 21 | 21 |
| spryPathway | 17 | 17 |
| srcRPTPPathway | 10 | 10 |
| stat3Pathway | 8 | Rejected! |
| stemPathway | 12 | 12 |
| stressPathway | 25 | 25 |
| tall1Pathway | 14 | 14 |
| tcapoptosisPathway | 6 | Rejected! |
| tcraPathway | 8 | Rejected! |
| tcrPathway | 39 | 39 |
| tcytotoxicPathway | 10 | 10 |
| telPathway | 14 | 14 |
| tercPathway | 6 | Rejected! |
| tertPathway | 6 | Rejected! |
| TGF_Beta_Signaling_Pathway | 33 | 33 |
| tgfbPathway | 14 | 14 |
| th1th2Pathway | 14 | 14 |
| thelperPathway | 11 | 11 |
| tidPathway | 17 | 17 |
| tnf_and_fas_network | 17 | 17 |
| tnfr1Pathway | 27 | 27 |

|  |  |  |
|---|---:|---:|
| tnfr2Pathway | 18 | 18 |
| tob1Pathway | 16 | 16 |
| tollPathway | 33 | 33 |
| tpoPathway | 20 | 20 |
| trkaPathway | 9 | Rejected! |
| tRNA_Synthetases | 18 | 18 |
| tsp1Pathway | 7 | Rejected! |
| tubbyPathway | 7 | Rejected! |
| tumor_supressor | 18 | 18 |
| ucalpainPathway | 15 | 15 |
| ureacyclePathway | 4 | Rejected! |
| vegfPathway | 21 | 21 |
| vipPathway | 25 | 25 |
| vitcbPathway | 11 | 11 |
| vobesityPathway | 7 | Rejected! |
| VOXPHOS | 76 | 76 |
| Wnt_Signaling | 49 | 49 |
| wntPathway | 25 | 25 |

## GSEA Report and Statistics

### Enrichment in phenotype: CRP- (4 samples)

118/202 gene sets had enrichment in phenotype **CRP–**

9 gene sets are significant at nominal p-value <5%

0 gene sets are significant at FDR <25%

### Enrichment in phenotype: CRP+ (4 samples)

84/202 gene sets had enrichment in phenotype **CRP+**

8 gene sets are significant at nominal *P* value <5%

5 gene sets are significant at FDR <25%

### Gene markers for the CRP- *versus* CRP+ comparison

The dataset had 16607 features (genes)

# of markers for phenotype **CRP–**: 7454 (44.9%) with correlation area 40.0%

# of markers for phenotype **CRP+**: 9153 (55.1%) with correlation area 60.0%

### Advanced statistics and plots

Gene set size filters (min=10, max=500) resulted in filtering out 75/277 gene sets

### Enrichment in phenotype: CRP+ (4 samples)

| NAME | SIZE | ES | NES | NOM *P* value | FDR q value | FWER *P* value |
|---|---|---|---|---|---|---|
| Electron_Transport_Chain | 78 | -0.71472 | -1.7821 | 0 | 0.036 | 0 |
| VOXPHOS | 76 | -0.68304 | -1.63741 | 0 | 0.108741 | 0.192 |
| p27Pathway | 13 | -0.68279 | -1.62864 | 0 | 0.090894 | 0.224 |
| Proteasome_Degradation | 30 | -0.69531 | -1.60481 | 0 | 0.08432 | 0.224 |
| proteasomePathway | 20 | -0.7701 | -1.52154 | 0 | 0.190091 | 0.456 |
| skp2e2fPathway | 10 | -0.6821 | -1.46507 | 0.042781 | 0.298218 | 0.596 |

| | | | | | | |
|---|---|---|---|---|---|---|
| mitochondriaPathway | 20 | -0.58958 | -1.4581 | 0 | 0.290509 | 0.596 |
| th1th2Pathway | 14 | -0.58699 | -1.34132 | 0.078125 | 0.653106 | 0.768 |
| nkcellsPathway | 17 | -0.67354 | -1.29402 | 0.101064 | 0.790315 | 0.824 |
| caspasePathway | 20 | -0.6505 | -1.25519 | 0.078431 | 0.949387 | 0.888 |
| d4gdiPathway | 10 | -0.61116 | -1.24869 | 0.076389 | 0.896234 | 0.888 |
| setPathway | 10 | -0.64307 | -1.23894 | 0.137255 | 0.884141 | 0.888 |
| mta3Pathway | 15 | -0.40261 | -1.23315 | 0.202899 | 0.84278 | 0.888 |
| Eicosanoid_Synthesis | 13 | -0.61116 | -1.22767 | 0.171296 | 0.809175 | 0.888 |
| extrinsicPathway | 12 | -0.59612 | -1.18708 | 0.17561 | 0.988286 | 0.912 |
| ceramidePathway | 22 | -0.46642 | -1.17461 | 0.281609 | 0.993338 | 0.952 |
| cdk5Pathway | 11 | -0.39465 | -1.1594 | 0.164948 | 1 | 0.952 |
| Il12Pathway | 20 | -0.50286 | -1.09481 | 0.448052 | 1 | 0.972 |
| igf1mtorPathway | 18 | -0.3139 | -1.08105 | 0.258065 | 1 | 0.972 |
| ndkDynaminPathway | 18 | -0.32465 | -1.06283 | 0.29 | 1 | 0.972 |
| DNA_DAMAGE_SIGNALLING | 84 | -0.33138 | -1.03415 | 0.495652 | 1 | 1 |
| mRNA_processing | 38 | -0.37062 | -1.0296 | 0.402597 | 1 | 1 |
| deathPathway | 29 | -0.31416 | -1.02723 | 0.412214 | 1 | 1 |
| hsp27Pathway | 13 | -0.44428 | -1.02233 | 0.433526 | 1 | 1 |
| soddPathway | 10 | -0.43869 | -1.02179 | 0.348148 | 1 | 1 |
| rarrxrPathway | 15 | -0.30979 | -1.01704 | 0.47486 | 1 | 1 |
| cellcyclePathway | 21 | -0.50236 | -1.01658 | 0.416185 | 1 | 1 |
| cytokinePathway | 19 | -0.49454 | -1.01356 | 0.497076 | 1 | 1 |
| electron_transporter_activity | 91 | -0.3236 | -1.00227 | 0.391608 | 1 | 1 |
| Complement_Activation_Classical | 11 | -0.5834 | -0.98832 | 0.565957 | 1 | 1 |
| ctla4Pathway | 15 | -0.63321 | -0.98489 | 0.510345 | 1 | 1 |
| mRNA_splicing | 38 | -0.39429 | -0.98157 | 0.558442 | 1 | 1 |
| igf1rPathway | 12 | -0.42207 | -0.98089 | 0.440789 | 1 | 1 |
| ghPathway | 21 | -0.35247 | -0.97822 | 0.503597 | 1 | 1 |
| chemicalPathway | 19 | -0.38003 | -0.96369 | 0.466667 | 1 | 1 |
| classicPathway | 11 | -0.55566 | -0.95197 | 0.578261 | 1 | 1 |
| tnfr2Pathway | 18 | -0.3257 | -0.95133 | 0.539773 | 1 | 1 |
| no2il12Pathway | 15 | -0.54222 | -0.92704 | 0.61039 | 1 | 1 |
| mprPathway | 20 | -0.35818 | -0.90893 | 0.548077 | 1 | 1 |
| raccycdPathway | 20 | -0.37749 | -0.8996 | 0.734463 | 1 | 1 |
| il10Pathway | 13 | -0.60577 | -0.89772 | 0.675325 | 1 | 1 |
| G13_Signaling_Pathway | 28 | -0.25708 | -0.8882 | 0.59375 | 1 | 1 |
| ccr3Pathway | 18 | -0.41464 | -0.87646 | 0.786207 | 1 | 1 |
| eif4Pathway | 21 | -0.3066 | -0.87505 | 0.463158 | 1 | 1 |
| Krebs-TCA_Cycle | 25 | -0.35221 | -0.87418 | 0.613636 | 1 | 1 |
| il2rbPathway | 31 | -0.28072 | -0.8725 | 0.6875 | 1 | 1 |
| tnf_and_fas_network | 17 | -0.33103 | -0.85875 | 0.659864 | 1 | 1 |
| badPathway | 18 | -0.34588 | -0.85481 | 0.669355 | 1 | 1 |
| cdc42racPathway | 12 | -0.35936 | -0.83624 | 0.554545 | 1 | 1 |
| Glycogen_Metabolism | 30 | -0.22689 | -0.8334 | 0.736434 | 1 | 1 |
| compPathway | 14 | -0.45602 | -0.83287 | 0.703057 | 1 | 1 |
| cacamPathway | 14 | -0.22955 | -0.82467 | 0.681416 | 1 | 1 |
| muscle_myosin | 10 | -0.55949 | -0.82253 | 0.725191 | 1 | 1 |
| cd40Pathway | 13 | -0.30631 | -0.817 | 0.646552 | 1 | 1 |
| nfkbPathway | 23 | -0.27017 | -0.81639 | 0.609589 | 1 | 1 |
| p53Pathway | 14 | -0.38916 | -0.81289 | 0.810127 | 1 | 1 |
| thelperPathway | 11 | -0.54448 | -0.7976 | 0.737931 | 1 | 1 |
| ccr5Pathway | 17 | -0.37847 | -0.79617 | 0.618644 | 1 | 1 |
| cxcr4Pathway | 21 | -0.28114 | -0.79274 | 0.825397 | 1 | 1 |
| radiation_sensitivity | 18 | -0.31907 | -0.77817 | 0.809816 | 1 | 1 |

| | | | | | | |
|---|---|---|---|---|---|---|
| Fmlppathway | 36 | -0.26454 | -0.77599 | 0.780142 | 1 | 1 |
| longevityPathway | 11 | -0.33826 | -0.77431 | 0.747968 | 1 | 1 |
| tcytotoxicPathway | 10 | -0.55382 | -0.77296 | 0.786207 | 1 | 1 |
| fasPathway | 25 | -0.26731 | -0.76904 | 0.801047 | 1 | 1 |
| Matrix_Metalloproteinases | 22 | -0.33784 | -0.76768 | 0.891892 | 1 | 1 |
| nktPathway | 27 | -0.34462 | -0.75999 | 0.777778 | 1 | 1 |
| erythPathway | 13 | -0.41607 | -0.75379 | 0.755 | 1 | 1 |
| amiPathway | 18 | -0.43373 | -0.75174 | 0.889655 | 0.994983 | 1 |
| cskPathway | 18 | -0.43373 | -0.75174 | 0.889655 | 0.980563 | 1 |
| tob1Pathway | 16 | -0.37918 | -0.75036 | 0.786207 | 0.968504 | 1 |
| tall1Pathway | 14 | -0.29958 | -0.74698 | 0.719745 | 0.961188 | 1 |
| actinYPathway | 15 | -0.31039 | -0.74256 | 0.642276 | 0.953984 | 1 |
| insulin_signalling | 83 | -0.2289 | -0.73836 | 0.84375 | 0.945629 | 1 |
| gsk3Pathway | 25 | -0.30596 | -0.72764 | 0.832298 | 0.944724 | 1 |
| lechtinPathway | 10 | -0.37894 | -0.71796 | 0.767544 | 0.941425 | 1 |
| tcrPathway | 39 | -0.31695 | -0.71391 | 0.934783 | 0.935749 | 1 |
| aktPathway | 14 | -0.24468 | -0.7096 | 0.841379 | 0.93111 | 1 |
| electron_transport | 48 | -0.16965 | -0.69415 | 0.905263 | 0.936444 | 1 |
| fcer1Pathway | 34 | -0.26827 | -0.69351 | 0.923729 | 0.926649 | 1 |
| pyk2Pathway | 27 | -0.22202 | -0.68724 | 0.869565 | 0.924706 | 1 |
| salmonellaPathway | 11 | -0.29861 | -0.674 | 0.727273 | 0.927898 | 1 |
| inflamPathway | 26 | -0.20719 | -0.54621 | 0.919598 | 0.998637 | 1 |
| dcPathway | 21 | -0.25088 | -0.53811 | 0.923077 | 0.988171 | 1 |
| stemPathway | 12 | -0.22935 | -0.51588 | 0.853147 | 0.984842 | 1 |

## Enrichment in phenotype: CRP– (4 samples)

| NAME | SIZE | ES | NES | NOM *P* value | FDR q value | FWER *P* value |
|---|---|---|---|---|---|---|
| gata3Pathway | 15 | 0.532375 | 1.422452 | 0.055172 | 1 | 0.648 |
| egfr_smrtePathway | 10 | 0.487912 | 1.410871 | 0.049645 | 1 | 0.696 |
| ace2Pathway | 10 | 0.69609 | 1.360714 | 0.011429 | 1 | 0.84 |
| shhPathway | 12 | 0.574704 | 1.358746 | 0.05988 | 1 | 0.84 |
| ucalpainPathway | 15 | 0.627546 | 1.351219 | 0.051429 | 1 | 0.84 |
| relaPathway | 16 | 0.506285 | 1.336408 | 0.039106 | 1 | 0.84 |
| intrinsicPathway | 21 | 0.531106 | 1.31908 | 0 | 1 | 0.872 |
| no1Pathway | 26 | 0.522752 | 1.316834 | 0.122581 | 1 | 0.872 |
| il22bpPathway | 11 | 0.6043 | 1.313382 | 0.110236 | 1 | 0.872 |
| cell2cellPathway | 13 | 0.478184 | 1.310909 | 0.136095 | 0.997167 | 0.872 |
| pmlPathway | 10 | 0.574682 | 1.267221 | 0.176471 | 1 | 0.872 |
| TGF_Beta_Signaling_Pathway | 33 | 0.50251 | 1.266292 | 0.227979 | 1 | 0.872 |
| EGF_receptor_signaling_pathway | 12 | 0.497561 | 1.266182 | 0.218045 | 1 | 0.872 |
| carm1Pathway | 12 | 0.692132 | 1.264346 | 0.049689 | 0.974136 | 0.872 |
| mapkPathway | 77 | 0.385176 | 1.256506 | 0.058065 | 0.966233 | 0.872 |
| vitcbPathway | 11 | 0.705188 | 1.244235 | 0.089286 | 0.993023 | 0.92 |
| ps1Pathway | 14 | 0.534021 | 1.243824 | 0.133803 | 0.937129 | 0.92 |
| cardiacegfPathway | 15 | 0.60983 | 1.243451 | 0.195556 | 0.890459 | 0.92 |
| egfPathway | 24 | 0.524056 | 1.243386 | 0.22335 | 0.845488 | 0.92 |
| par1Pathway | 18 | 0.578763 | 1.210844 | 0.099379 | 0.951553 | 0.92 |
| Fatty_Acid_Synthesis | 12 | 0.602853 | 1.195687 | 0.259669 | 0.969199 | 0.92 |
| integrinPathway | 31 | 0.491597 | 1.194879 | 0.218935 | 0.928496 | 0.92 |
| pparaPathway | 48 | 0.503567 | 1.193528 | 0.150289 | 0.896399 | 0.92 |
| 41bbPathway | 18 | 0.506347 | 1.189958 | 0.244318 | 0.876778 | 0.92 |
| alkPathway | 32 | 0.510331 | 1.181609 | 0.226667 | 0.877702 | 0.92 |
| monocytePathway | 11 | 0.596332 | 1.177618 | 0.281879 | 0.854848 | 0.92 |

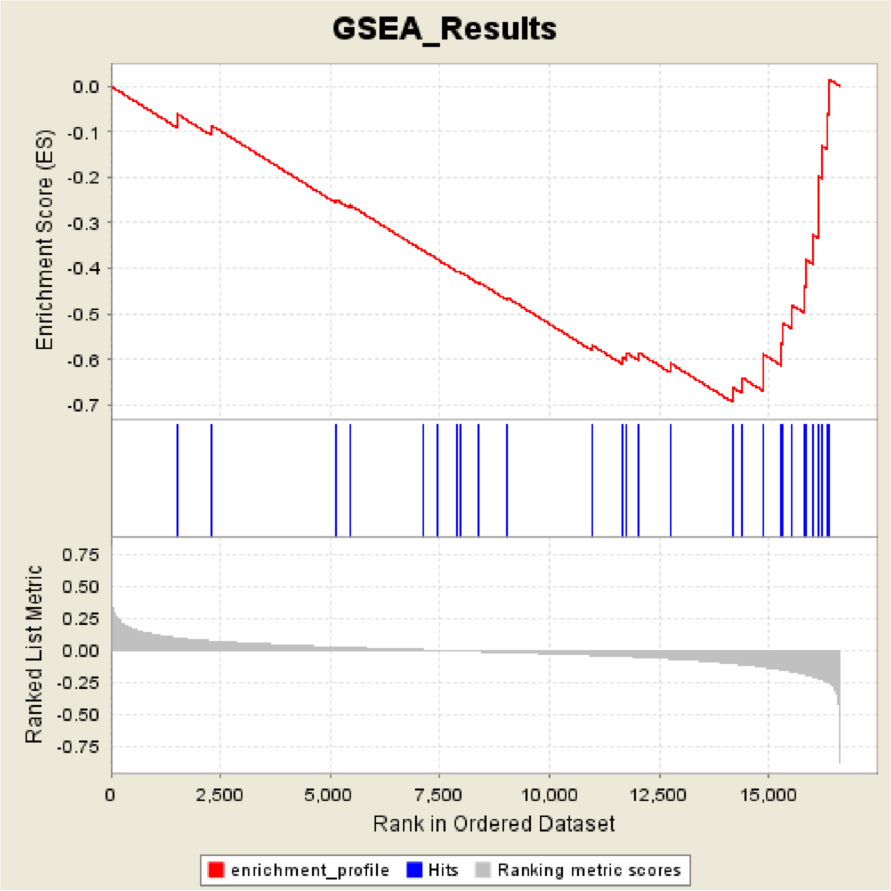
| | | | | | | |
|---|---|---|---|---|---|---|
| spryPathway | 17 | 0.421169 | 1.172166 | 0.185714 | 0.849242 | 0.952 |
| rhoPathway | 26 | 0.528389 | 1.170802 | 0.198758 | 0.82584 | 0.952 |
| atmPathway | 16 | 0.519718 | 1.168206 | 0.234375 | 0.812351 | 0.952 |
| tumor_supressor | 18 | 0.608874 | 1.162048 | 0.170732 | 0.805489 | 0.952 |
| pitx2Pathway | 14 | 0.505103 | 1.152855 | 0.385027 | 0.824298 | 0.952 |
| leptinPathway | 10 | 0.518603 | 1.144641 | 0.178771 | 0.833309 | 0.952 |
| pdgfPathway | 24 | 0.489255 | 1.143668 | 0.380435 | 0.81573 | 0.952 |
| fibrinolysisPathway | 12 | 0.489946 | 1.135537 | 0.235849 | 0.822775 | 0.952 |
| metPathway | 32 | 0.453117 | 1.123562 | 0.25 | 0.846069 | 0.952 |
| vipPathway | 25 | 0.453984 | 1.1224 | 0.36076 | 0.825517 | 0.952 |
| ranklPathway | 13 | 0.50644 | 1.120561 | 0.265432 | 0.812025 | 0.952 |
| vegfPathway | 21 | 0.399742 | 1.116635 | 0.294574 | 0.800628 | 0.952 |
| mcalpainPathway | 22 | 0.468105 | 1.109368 | 0.343374 | 0.799474 | 0.952 |
| nthiPathway | 21 | 0.398697 | 1.107173 | 0.1875 | 0.788747 | 0.952 |
| arapPathway | 16 | 0.42679 | 1.106316 | 0.384236 | 0.771846 | 0.952 |
| ck1Pathway | 15 | 0.448784 | 1.105801 | 0.337209 | 0.754806 | 0.952 |
| cblPathway | 13 | 0.437466 | 1.103004 | 0.179856 | 0.749516 | 0.952 |
| gpcrPathway | 31 | 0.443148 | 1.096304 | 0.2723 | 0.756221 | 0.952 |
| carm-erPathway | 26 | 0.453658 | 1.093224 | 0.406593 | 0.746655 | 0.952 |
| chrebpPathway | 16 | 0.441001 | 1.081818 | 0.352941 | 0.758918 | 0.952 |
| p35alzheimersPathway | 10 | 0.472375 | 1.068365 | 0.41206 | 0.792856 | 0.952 |
| pgc1aPathway | 23 | 0.419452 | 1.059521 | 0.360825 | 0.810267 | 1 |
| hdacPathway | 28 | 0.342839 | 1.058273 | 0.445714 | 0.79722 | 1 |
| tgfbPathway | 14 | 0.51476 | 1.056728 | 0.408163 | 0.787618 | 1 |
| srcRPTPPathway | 10 | 0.469867 | 1.047647 | 0.503704 | 0.800668 | 1 |
| il6Pathway | 19 | 0.492924 | 1.046281 | 0.43787 | 0.789746 | 1 |
| myosinPathway | 13 | 0.602226 | 1.040605 | 0.490683 | 0.793202 | 1 |
| hcmvPathway | 15 | 0.442352 | 1.040234 | 0.360294 | 0.780643 | 1 |
| ephA4Pathway | 10 | 0.462324 | 1.034778 | 0.48538 | 0.783571 | 1 |
| gleevecPathway | 19 | 0.431017 | 1.025967 | 0.537688 | 0.796589 | 1 |
| tpoPathway | 20 | 0.431599 | 1.022126 | 0.429319 | 0.791213 | 1 |
| hifPathway | 11 | 0.536749 | 1.017366 | 0.409091 | 0.790878 | 1 |
| eponfkbPathway | 10 | 0.376317 | 1.016504 | 0.526316 | 0.781658 | 1 |
| Fatty_Acid_Degradation | 18 | 0.500498 | 1.006381 | 0.429293 | 0.79535 | 1 |
| ecmPathway | 19 | 0.53835 | 0.99559 | 0.448052 | 0.810675 | 1 |
| calcineurinPathway | 18 | 0.454954 | 0.989843 | 0.455782 | 0.808431 | 1 |
| wntPathway | 25 | 0.386176 | 0.970229 | 0.599034 | 0.854754 | 1 |
| at1rPathway | 32 | 0.354295 | 0.96949 | 0.510791 | 0.843188 | 1 |
| Inflammatory_Response_Pathway | 23 | 0.377258 | 0.962229 | 0.492424 | 0.857342 | 1 |
| g2Pathway | 20 | 0.411088 | 0.94995 | 0.441176 | 0.871848 | 1 |
| agpcrPathway | 12 | 0.492267 | 0.949891 | 0.543624 | 0.859372 | 1 |
| g1Pathway | 22 | 0.33366 | 0.944804 | 0.51087 | 0.865307 | 1 |
| p53_signalling | 79 | 0.293789 | 0.92056 | 0.461538 | 0.911711 | 1 |
| keratinocytePathway | 40 | 0.359914 | 0.920556 | 0.508772 | 0.899201 | 1 |
| dreamPathway | 12 | 0.429488 | 0.910129 | 0.626263 | 0.905993 | 1 |
| il7Pathway | 15 | 0.444152 | 0.907254 | 0.503185 | 0.901541 | 1 |
| insulinPathway | 17 | 0.389503 | 0.898486 | 0.584541 | 0.909271 | 1 |
| biopeptidesPathway | 36 | 0.29324 | 0.897622 | 0.753425 | 0.898321 | 1 |
| nfatPathway | 46 | 0.343978 | 0.893846 | 0.646667 | 0.895924 | 1 |
| ptdinsPathway | 21 | 0.299784 | 0.893207 | 0.581522 | 0.885631 | 1 |
| etsPathway | 17 | 0.424847 | 0.888321 | 0.712766 | 0.887057 | 1 |
| telPathway | 14 | 0.261722 | 0.883881 | 0.710059 | 0.887558 | 1 |
| erk5Pathway | 13 | 0.383634 | 0.881278 | 0.632353 | 0.885908 | 1 |
| fatty_acid_metabolism | 20 | 0.34878 | 0.857707 | 0.605263 | 0.919992 | 1 |

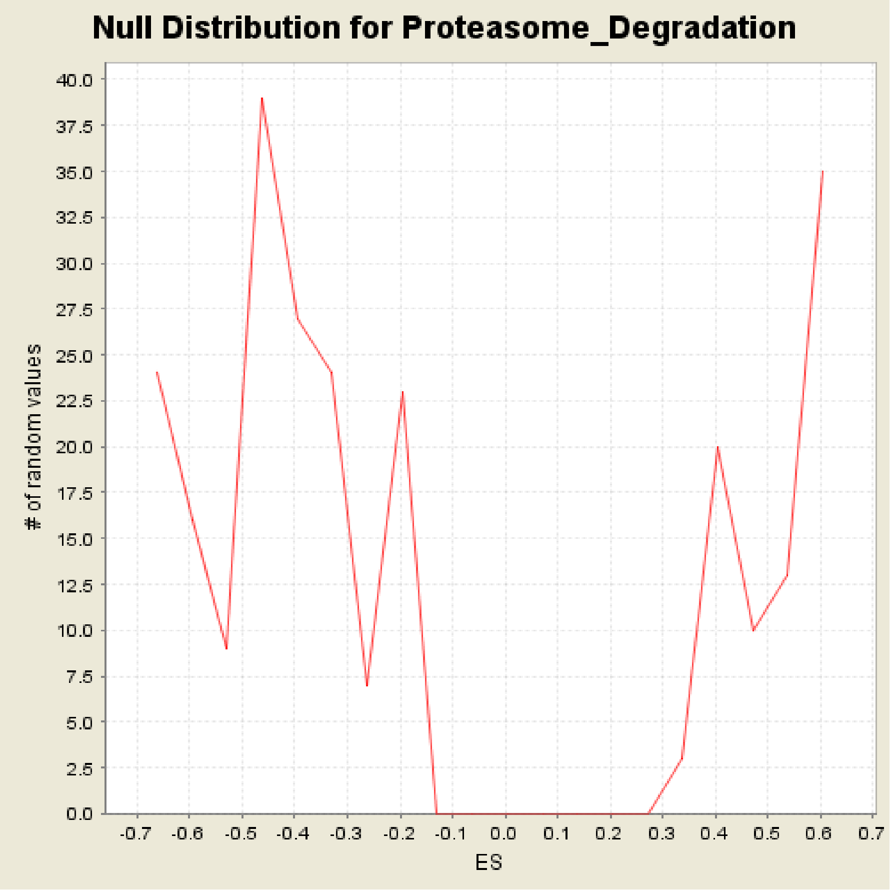
| | | | | | | |
|---|---|---|---|---|---|---|
| gcrPathway | 16 | 0.32965 | 0.855617 | 0.674603 | 0.916624 | 1 |
| rac1Pathway | 19 | 0.363311 | 0.852548 | 0.701031 | 0.915894 | 1 |
| rasPathway | 20 | 0.250126 | 0.850042 | 0.72381 | 0.914484 | 1 |
| drug_resistance_and_metabolism | 83 | 0.251829 | 0.838964 | 0.734568 | 0.925974 | 1 |
| ptenPathway | 16 | 0.270634 | 0.823333 | 0.716535 | 0.944771 | 1 |
| cdmacPathway | 15 | 0.34614 | 0.816073 | 0.873874 | 0.9486 | 1 |
| hivnefPathway | 51 | 0.236357 | 0.807027 | 0.754237 | 0.950246 | 1 |
| p38mapkPathway | 38 | 0.274314 | 0.806024 | 0.7 | 0.940117 | 1 |
| igf1Pathway | 17 | 0.38516 | 0.798036 | 0.711656 | 0.94586 | 1 |
| tnfr1Pathway | 27 | 0.262724 | 0.787446 | 0.836735 | 0.949306 | 1 |
| rbPathway | 11 | 0.298482 | 0.781657 | 0.73 | 0.950847 | 1 |
| tRNA_Synthetases | 18 | 0.291724 | 0.780106 | 0.71123 | 0.945686 | 1 |
| ngfPathway | 15 | 0.359079 | 0.765947 | 0.702128 | 0.969776 | 1 |
| tidPathway | 17 | 0.214772 | 0.758307 | 0.909091 | 0.97257 | 1 |
| tollPathway | 33 | 0.277455 | 0.742799 | 0.909774 | 0.984038 | 1 |
| mef2dPathway | 18 | 0.275013 | 0.740056 | 0.783333 | 0.979995 | 1 |
| erkPathway | 28 | 0.209314 | 0.738443 | 0.81203 | 0.972077 | 1 |
| stressPathway | 25 | 0.220453 | 0.735103 | 0.851282 | 0.967903 | 1 |
| edg1Pathway | 23 | 0.262612 | 0.726948 | 0.808511 | 0.967327 | 1 |
| plcePathway | 11 | 0.292775 | 0.720434 | 0.888112 | 0.970326 | 1 |
| nos1Pathway | 20 | 0.271675 | 0.714267 | 0.845638 | 0.969628 | 1 |
| atrbrcaPathway | 15 | 0.259317 | 0.707655 | 0.8125 | 0.971103 | 1 |
| achPathway | 13 | 0.232314 | 0.706929 | 0.837607 | 0.963044 | 1 |
| il1rPathway | 31 | 0.2418 | 0.69794 | 0.858333 | 0.96827 | 1 |
| sppaPathway | 21 | 0.283561 | 0.68957 | 0.879433 | 0.969245 | 1 |
| S1P_Signaling | 23 | 0.210321 | 0.684509 | 0.836207 | 0.970125 | 1 |
| epoPathway | 16 | 0.291768 | 0.676631 | 0.80625 | 0.969255 | 1 |
| gabaPathway | 12 | 0.272271 | 0.673282 | 0.871287 | 0.963285 | 1 |
| crebPathway | 24 | 0.256483 | 0.656746 | 0.88 | 0.971674 | 1 |
| il2Pathway | 21 | 0.265136 | 0.64108 | 0.918605 | 0.974494 | 1 |
| bcrPathway | 33 | 0.262399 | 0.635515 | 0.935714 | 0.969225 | 1 |
| p53hypoxiaPathway | 16 | 0.24596 | 0.617038 | 0.89697 | 0.97287 | 1 |
| Wnt_Signaling | 49 | 0.170635 | 0.613468 | 0.930233 | 0.967304 | 1 |
| lairPathway | 12 | 0.286678 | 0.605036 | 0.831579 | 0.970174 | 1 |
| mtorPathway | 20 | 0.256333 | 0.603488 | 0.928934 | 0.962752 | 1 |
| arenrf2Pathway | 14 | 0.268655 | 0.597831 | 0.941936 | 0.955974 | 1 |
| cftrPathway | 11 | 0.225728 | 0.555425 | 0.940397 | 0.975554 | 1 |
| il3Pathway | 13 | 0.250558 | 0.543795 | 0.935252 | 0.971287 | 1 |

## Proteasome Degradation Pathway

| PROBE | DESCRIPTION | GENE RANK | METRIC RANK | RES | CORE ENRICHM. |
|---|---|---|---|---|---|
| NM_009439 | proteasome 26S subunit, non-ATPase, 3 (Psmd3), mRNA. | 1509 | 0.095768 | -0.061 | No |
| NM_019639 | ubiquitin C (Ubc), mRNA. | 2285 | 0.071179 | -0.08543 | No |
| NM_008951 | proteasome 26S subunit, non-ATPase, 4 (Psmd4), mRNA. | 5137 | 0.024785 | -0.24964 | No |
| NM_134101 | proteasome 26S subunit, non-ATPase, 2 (Psmd2), mRNA. | 5441 | 0.021233 | -0.26126 | No |
| NM_011874 | proteasome 26S subunit, ATPase, 4 (Psmc4), mRNA. | 7111 | 0.003588 | -0.36081 | No |
| NM_023738 | ubiquitin-activating enzyme E1-like (Ube1l), mRNA. | 7434 | 2.16E-04 | -0.38017 | No |
| NM_010436 | H2A histone family, member X (H2afx), mRNA. | 7907 | -0.00486 | -0.40712 | No |
| NM_008950 | protease 26S subunit, ATPase 5 | 7985 | -0.00573 | -0.40997 | No |

| | | | | | |
|---|---|---|---|---|---|
| | (Psmc5), mRNA. | | | | |
| NM_001033865 | ribosomal protein S27a (Rps27a), mRNA. | 8389 | -0.00963 | -0.43126 | No |
| NM_019883 | ubiquitin A-52 residue ribosomal protein fusion product 1 (Uba52), mRNA. | 9031 | -0.01609 | -0.46489 | No |
| NM_008337 | interferon gamma (Ifng), mRNA. | 10952 | -0.03813 | -0.56875 | No |
| NM_145420 | ubiquitin-conjugating enzyme E2D 1, (Ube2d1), mRNA. | 11641 | -0.04775 | -0.59528 | No |
| NM_027357 | proteasome 26S subunit, non-ATPase, 1 (Psmd1), mRNA. | 11753 | -0.04918 | -0.58655 | No |
| NM_019912 | ubiquitin-conjugating enzyme E2D 2 (Ube2d2), mRNA. | 12034 | -0.05326 | -0.58674 | No |
| NM_011188 | proteasome 26S subunit, ATPase 2 (Psmc2), mRNA. | 12734 | -0.06565 | -0.60832 | No |
| NM_025356 | ubiquitin-conjugating enzyme E2D 3 (Ube2d3), mRNA. | 14177 | -0.10225 | -0.66324 | Yes |
| NM_008947 | protease 26S subunit, ATPase 1 (Psmc1), mRNA. | 14375 | -0.10924 | -0.64087 | Yes |
| NM_011968 | proteasome subunit, alpha type 6 (Psma6), mRNA. | 14855 | -0.12878 | -0.62938 | Yes |
| NM_008948 | proteasome 26S subunit, ATPase 3 (Psmc3), mRNA. | 14871 | -0.12961 | -0.58964 | Yes |
| NM_008946 | proteasome subunit, beta type 6 (Psmb6), mRNA. | 15271 | -0.15068 | -0.56645 | Yes |
| NM_001029855 | proteasome 28S subunit, beta (Psme2), mRNA. | 15314 | -0.15334 | -0.5209 | Yes |
| NM_025959 | proteasome 26S subunit, ATPase, 6 (Psmc6), mRNA. | 15523 | -0.16581 | -0.48145 | Yes |
| NM_016750 | H2A histone family, member Z (H2afz), mRNA. | 15802 | -0.18691 | -0.4396 | Yes |
| NM_026545 | proteasome 26S subunit, non-ATPase, 8 (Psmd8), mRNA. | 15848 | -0.19157 | -0.38224 | Yes |
| NM_011966 | proteasome subunit, alpha type 4 (Psma4), mRNA. | 16008 | -0.20581 | -0.32729 | Yes |
| NM_011965 | proteasome subunit, alpha type 1 (Psma1), mRNA. | 16110 | -0.21568 | -0.26574 | Yes |
| NM_011969 | proteasome subunit, alpha type 7 (Psma7), mRNA. | 16128 | -0.21758 | -0.19854 | Yes |
| NM_013585 | proteosome subunit, beta type 9 (Psmb9), mRNA. | 16198 | -0.22816 | -0.13115 | Yes |
| NM_080554 | proteasome 26S subunit, non-ATPase, 5 (Psmd5), mRNA. | 16303 | -0.24299 | -0.06122 | Yes |
| NM_011187 | proteasome subunit, beta type 7 (Psmb7), mRNA. | 16353 | -0.2533 | 0.015262 | Yes |


GSEA_Results
Enrichment Score (ES)
0.0
-0.1
-0.2
-0.3
-0.4
-0.5
-0.6
-0.7
Ranked List Metric
0.75
0.50
0.25
0.00
-0.25
-0.50
-0.75
0
2,500
5,000
7,500
10,000
12,500
15,000
Rank in Ordered Dataset
enrichment_profile
Hits
Ranking metric scores


Null Distribution for Proteasome_Degradation
# of random values
40.0
37.5
35.0
32.5
30.0
27.5
25.0
22.5
20.0
17.5
15.0
12.5
10.0
7.5
5.0
2.5
0.0
-0.7
-0.6
-0.5
-0.4
-0.3
-0.2
-0.1
0.0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
ES