**Answers to the Exercises**

1. Select significantly DEGs from the train dataset of AML (Acute Myelocytic Leukemia) and ALL (acute lymphoblastic leukemia) expression data (http://www.broadinstitute.org/cgi-bin/cancer/publications/pub\_paper.cgi?mode=view&paper\_id=43) and find enriched GO terms from an ontology analysis tool. Dataset and analysis functions are also included in R statistical package, golubEsets in Bioconductor.

2. List significantly enriched pathways using a pathway analysis tool with the dataset in Exercise 1

3. Find KEGG pathways significantly associated with leukemia subtype in the 2-sample comparison of AML and ALL by GSEA through the Kolmogorov-Smirnoff test. Analysis and data set are provided by SAFE R (<http://bioconductor.org/packages/2.0/bioc/html/safe.html>).

4. Identify the differentially co-expressed gene set pairs using dCoxS with simulated data in (<http://www.snubi.org/publication/dCoxS>). Compute interaction score between matrix M and M1 using ias fucntion. And, compute interaction score between M and M2. Finally, using compcorr function, estimate significance of difference of ias. Note that in compcorr function, n1 and n2 is the number of all possible sample pairs.

5. Report semantic relationships of pathways and GO terms using BioLattice (<http://www.snubi.org/software/biolattice/>). Use the result of *k*-means clustering (*k*=10) with DEG in Exercise 1. Select Category as ‘biological process’, p-value < 0.05.

**Answer 1:**

<DEG Gene List >

D87078\_at (PUM2), D88270\_at (VPREB1), J05243\_at (SPTAN1), L41870\_at (RB1), L47738\_at (CYFIP2), M11147\_at (FTL), M11722\_at (DNTT), M16038\_at (LYN), M21551\_rna1\_at (NMB), M23197\_at (CD33), M27891\_at (CST3), M29696\_at (IL7R), M37435\_at (CSF1), M55150\_at (FAH), M60527\_at (DCK), M62762\_at (ATP6V0C), M89957\_at (CD79B), M91432\_at (ACADM), M94633\_at (RAG2), S50223\_at (ZNF22), U05259\_rna1\_at (CD79A), U20998\_at (SRP9), U32944\_at (DYNLL1), U46499\_at (MGST1), U49844\_at (ATR), U50136\_rna1\_at (LTC4S), U50928\_at (PKD2), U62136\_at (UBE2V2), U73737\_at (MSH6), U82759\_at (HOXA9), X04085\_rna1\_at (CAT), X15949\_at (IRF2), X17042\_at (SRGN), X59350\_at (CD22), X61587\_at (RHOG), X62535\_at (DGKA), X62654\_rna1\_at (CD63), X63469\_at (GTF2E2), X74262\_at (RBBP4), X74801\_at (CCT3), X82240\_rna1\_at (TCL1A), X95735\_at (ZYX), Y12670\_at (LEPROT), Z69881\_at (ATP2A3), D38073\_at (MCM3), U31556\_at (E2F5), Z15115\_at (TOP2B), U22376\_cds2\_s\_at (MYB), L09209\_s\_at (APLP2), M12959\_s\_at (-), Y00787\_s\_at (IL8), M31211\_s\_at (MYL6B), U26266\_s\_at (DHPS), X85116\_rna1\_s\_at (STOM), U49020\_cds2\_s\_at (MEF2A), U72936\_s\_at (ATRX), J03801\_f\_at (LYZ), M19045\_f\_at (LYZ), M31523\_at (TCF3), U27460\_at (UGP2), U29175\_at (SMARCA4)  
\* The significant genes were selected by *t*-test (*p*-value < 1.0e-5)

<Enriched GO terms>

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| TermID | Term | Count | % | PValue |
| GO:0002520 | immune system development | 8 | 12.5 | 1.88E-04 |
| GO:0042113 | B cell activation | 5 | 7.8125 | 3.31E-04 |
| GO:0030097 | hemopoiesis | 7 | 10.9375 | 5.50E-04 |
| GO:0045321 | leukocyte activation | 7 | 10.9375 | 6.28E-04 |
| GO:0048534 | hemopoietic or lymphoid organ development | 7 | 10.9375 | 9.14E-04 |
| GO:0042100 | B cell proliferation | 3 | 4.6875 | 1.41E-03 |
| GO:0006259 | DNA metabolic process | 9 | 14.0625 | 1.50E-03 |
| GO:0001775 | cell activation | 7 | 10.9375 | 1.52E-03 |
| GO:0002521 | leukocyte differentiation | 5 | 7.8125 | 2.53E-03 |
| GO:0002377 | immunoglobulin production | 3 | 4.6875 | 7.52E-03 |
| GO:0002440 | production of molecular mediator of immune response | 3 | 4.6875 | 8.02E-03 |

**Answer 2:**

KEGG04640: Hematopoietic cell lineage (pvalue = 1.9E-3)  
KEGG05340: Primary immunodeficiency (pvalue = 1.9E -2)  
KEGG04110: Cell cycle (pvalue = 1.9E-2)  
KEGG04662: B cell receptor signaling pathway (pvalue = 1.9E-2)

**Answer 3:**

|  |  |  |  |
| --- | --- | --- | --- |
| KEGGID | Size | Global.Stat | Emp.pvalue |
| KEGG00860 | 15 | 110.39778 | 0.003 |
| KEGG04920 | 30 | 84.02642 | 0.011 |
| KEGG04110 | 51 | 99.95088 | 0.012 |
| KEGG00240 | 31 | 79.52313 | 0.022 |
| KEGG00564 | 10 | 66.96118 | 0.03 |
| KEGG00970 | 16 | 87.31489 | 0.03 |
| KEGG04640 | 70 | 94.99477 | 0.032 |

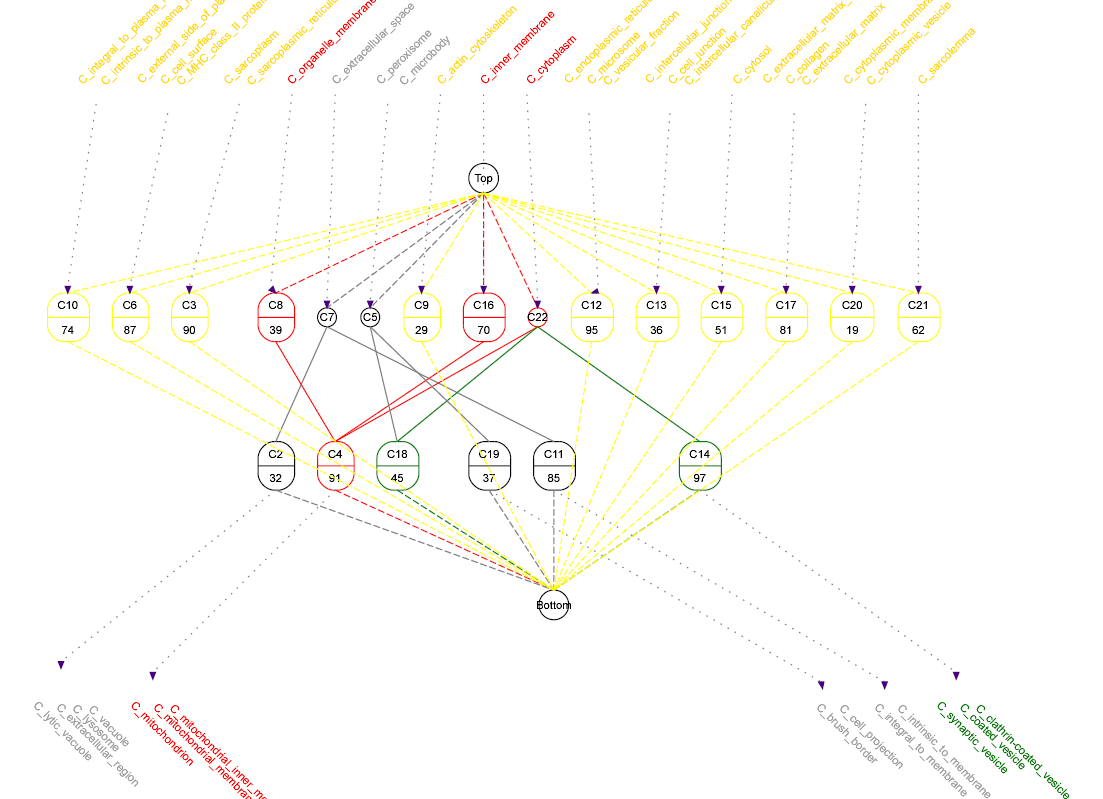
**Answer 4:**

R code:

> re1 <- ias(M, M1)  
> re2 <- ias(M, M2)  
> n1 <- n2 <- ncol(M)\*(ncol(M)-1)/2  
> re <- compcorr(n1, re1[[1]], n2, re2[[2]])

The difference of IS between the two conditions is13.56 and *p*-value of the difference is 0.

**Answer 5:**



**Order Table for concepts from experiment**

|  |  |  |
| --- | --- | --- |
| [**Concept 6**](http://cello.snubi.org/cgi-bin/biolattice/part.cgi?exp=test&concept=concept6)[**cluster 87**](http://cello.snubi.org/cgi-bin/biolattice/clsgene.cgi?cls=87&exp=test)  C\_external\_side\_of\_plasma\_membrane C\_cell\_surface C\_MHC\_class\_II\_protein\_complex | | |
| [**Concept 21**](http://cello.snubi.org/cgi-bin/biolattice/part.cgi?exp=test&concept=concept21)[**cluster 62**](http://cello.snubi.org/cgi-bin/biolattice/clsgene.cgi?cls=62&exp=test)  C\_sarcolemma | | |
| [**Concept 3**](http://cello.snubi.org/cgi-bin/biolattice/part.cgi?exp=test&concept=concept3)[**cluster 90**](http://cello.snubi.org/cgi-bin/biolattice/clsgene.cgi?cls=90&exp=test)  C\_sarcoplasm C\_sarcoplasmic\_reticulum | | |
| [**Concept 7**](http://cello.snubi.org/cgi-bin/biolattice/part.cgi?exp=test&concept=concept7)[**cluster 32,85**](http://cello.snubi.org/cgi-bin/biolattice/clsgene.cgi?cls=32,85&exp=test)  C\_extracellular\_space | [**Concept 2**](http://cello.snubi.org/cgi-bin/biolattice/part.cgi?exp=test&concept=concept2)[**cluster 32**](http://cello.snubi.org/cgi-bin/biolattice/clsgene.cgi?cls=32&exp=test)  C\_lytic\_vacuole C\_extracellular\_region C\_lysosome C\_vacuole |  |
| [**Concept 11**](http://cello.snubi.org/cgi-bin/biolattice/part.cgi?exp=test&concept=concept11)[**cluster 85**](http://cello.snubi.org/cgi-bin/biolattice/clsgene.cgi?cls=85&exp=test)  C\_integral\_to\_membrane C\_intrinsic\_to\_membrane |  |
| [**Concept 9**](http://cello.snubi.org/cgi-bin/biolattice/part.cgi?exp=test&concept=concept9)[**cluster 29**](http://cello.snubi.org/cgi-bin/biolattice/clsgene.cgi?cls=29&exp=test)  C\_actin\_cytoskeleton | | |
| [**Concept 17**](http://cello.snubi.org/cgi-bin/biolattice/part.cgi?exp=test&concept=concept17)[**cluster 81**](http://cello.snubi.org/cgi-bin/biolattice/clsgene.cgi?cls=81&exp=test)  C\_extracellular\_matrix\_(sensu\_Metazoa) C\_collagen C\_extracellular\_matrix | | |
| [**Concept 12**](http://cello.snubi.org/cgi-bin/biolattice/part.cgi?exp=test&concept=concept12)[**cluster 95**](http://cello.snubi.org/cgi-bin/biolattice/clsgene.cgi?cls=95&exp=test)  C\_endoplasmic\_reticulum C\_microsome C\_vesicular\_fraction | | |
| [**Concept 20**](http://cello.snubi.org/cgi-bin/biolattice/part.cgi?exp=test&concept=concept20)[**cluster 19**](http://cello.snubi.org/cgi-bin/biolattice/clsgene.cgi?cls=19&exp=test)  C\_cytoplasmic\_membrane-bound\_vesicle C\_cytoplasmic\_vesicle | | |
| [**Concept 15**](http://cello.snubi.org/cgi-bin/biolattice/part.cgi?exp=test&concept=concept15)[**cluster 51**](http://cello.snubi.org/cgi-bin/biolattice/clsgene.cgi?cls=51&exp=test)  C\_cytosol | | |
| [**Concept 22**](http://cello.snubi.org/cgi-bin/biolattice/part.cgi?exp=test&concept=concept22)[**cluster 45,91,97**](http://cello.snubi.org/cgi-bin/biolattice/clsgene.cgi?cls=45,91,97&exp=test)  C\_cytoplasm | [**Concept 4**](http://cello.snubi.org/cgi-bin/biolattice/part.cgi?exp=test&concept=concept4)[**cluster 91**](http://cello.snubi.org/cgi-bin/biolattice/clsgene.cgi?cls=91&exp=test)  C\_mitochondrion C\_mitochondrial\_membrane C\_mitochondrial\_inner\_membrane |  |
| [**Concept 14**](http://cello.snubi.org/cgi-bin/biolattice/part.cgi?exp=test&concept=concept14)[**cluster 97**](http://cello.snubi.org/cgi-bin/biolattice/clsgene.cgi?cls=97&exp=test)  C\_synaptic\_vesicle C\_coated\_vesicle C\_clathrin-coated\_vesicle |  |
| [**Concept 18**](http://cello.snubi.org/cgi-bin/biolattice/part.cgi?exp=test&concept=concept18)[**cluster 45**](http://cello.snubi.org/cgi-bin/biolattice/clsgene.cgi?cls=45&exp=test) |  |
| [**Concept 8**](http://cello.snubi.org/cgi-bin/biolattice/part.cgi?exp=test&concept=concept8)[**cluster 39,91**](http://cello.snubi.org/cgi-bin/biolattice/clsgene.cgi?cls=39,91&exp=test)  C\_organelle\_membrane | [**Concept 4**](http://cello.snubi.org/cgi-bin/biolattice/part.cgi?exp=test&concept=concept4)[**cluster 91**](http://cello.snubi.org/cgi-bin/biolattice/clsgene.cgi?cls=91&exp=test)  C\_mitochondrion C\_mitochondrial\_membrane C\_mitochondrial\_inner\_membrane |  |
| [**Concept 16**](http://cello.snubi.org/cgi-bin/biolattice/part.cgi?exp=test&concept=concept16)[**cluster 70,91**](http://cello.snubi.org/cgi-bin/biolattice/clsgene.cgi?cls=70,91&exp=test)  C\_inner\_membrane | [**Concept 4**](http://cello.snubi.org/cgi-bin/biolattice/part.cgi?exp=test&concept=concept4)[**cluster 91**](http://cello.snubi.org/cgi-bin/biolattice/clsgene.cgi?cls=91&exp=test)  C\_mitochondrion C\_mitochondrial\_membrane C\_mitochondrial\_inner\_membrane |  |
| [**Concept 10**](http://cello.snubi.org/cgi-bin/biolattice/part.cgi?exp=test&concept=concept10)[**cluster 74**](http://cello.snubi.org/cgi-bin/biolattice/clsgene.cgi?cls=74&exp=test)  C\_integral\_to\_plasma\_membrane C\_intrinsic\_to\_plasma\_membrane | | |
| [**Concept 13**](http://cello.snubi.org/cgi-bin/biolattice/part.cgi?exp=test&concept=concept13)[**cluster 36**](http://cello.snubi.org/cgi-bin/biolattice/clsgene.cgi?cls=36&exp=test)  C\_intercellular\_junction C\_cell\_junction C\_intercellular\_canaliculus | | |
| [**Concept 5**](http://cello.snubi.org/cgi-bin/biolattice/part.cgi?exp=test&concept=concept5)[**cluster 37,45**](http://cello.snubi.org/cgi-bin/biolattice/clsgene.cgi?cls=37,45&exp=test)  C\_peroxisome C\_microbody | [**Concept 18**](http://cello.snubi.org/cgi-bin/biolattice/part.cgi?exp=test&concept=concept18)[**cluster 45**](http://cello.snubi.org/cgi-bin/biolattice/clsgene.cgi?cls=45&exp=test) |  |
| [**Concept 19**](http://cello.snubi.org/cgi-bin/biolattice/part.cgi?exp=test&concept=concept19)[**cluster 37**](http://cello.snubi.org/cgi-bin/biolattice/clsgene.cgi?cls=37&exp=test)  C\_brush\_border C\_cell\_projection |  |