Roaming Around AML

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Abstract

Some random words placeholding the abstract

1. Introduction

This article conducts an unplanned investigation of bunch of data and research results about AML decease. As indicated by **?**, the fifth most affected site in body by cancer is the circulatory system, with about a hundred thousands estimated cases in total of a million cancer in the US, 2002. AML is one of the most suffered and fatal one with almost 35% of the cases resulting into death. Hence, piling up some results in this area will accelerate more experienced scientists toward a working solution. However, this field is not abandoned, and has been worked on extensively. Therefore, they are considered as rich sources of result validation. The process of the investigation begins with a beginner level differential expression analysis resulting in some gene lists with significant gene expression alterations. These lists are used as the input of the next pipeline component, gene enrichment. Extracting some pieces of information in this step will be the basis of some fact finding endeavors.

2. Differential Expression Analysis

This article has employed **?** data set and Limma tools **?**. The data set primarily consists of 170 samples having their expressions measured by 32321 probes and classified in two categories, having self-explanatory labels, "Normal" and "Leukemia." These samples were first examined in three prospectives, respectively independent of the cell source, cells of type T, cells of type B(Table 1.)

After having the data in this format, a basic visualization was employed to form an intuition about the comparability of the data. The data needed no normalization (figure1.) However, the heatmap and its interensic hierarchical clustering failed to assure the validity of the data.

extract some genes with significantly different expression levels in normal versus affected cells.

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Table 1: The samples were studied dependant and independant of their source.

Source Dependancy	Normal Sources	Leukemia Sources
Independent	B Cells, CD34+HSPC, Granulocytes, Monocytes, T Cells	AML Cell Line, AML Patient, B ALL Cell Line, B ALL Patient, T ALL Cell Line, T ALL Patient
T cells	T Cells	T ALL Cell Line, T ALL Patient
B cells	B Cells	B ALL Cell Line, B ALL Patient

3. Gene Set Enrichment Analysis

As the gene sets extracted, they were passed to EnrichR to find possible causes and cures for AML. The GSEA results were truncated not to be represent ideas elusive to naked eyes. So only results with adjusted p-value less than .05 were selected. Moreover, at most 5 top cases extracted from each database were kept and the rest were eliminated. The results were sorted by combined score before the elimination process. The databases that were exploited for each purpose are listed in Table B.48 . Appendix A would explain the reason of each database choice.

Table 2: Databases in Use for GSEA

Analysis	Databases
Transcription Factors	TRANSFAC and JASPAR PWMs, miRTarBase 2017
Pathways	KEGG2019 Human, NCI-Nature 2016, Reactome 2016
Gene Ontology	GO Biological Process 2018, GO Molecular Function 2018, GO Cellular Component 2018
Drugs	ARCHS4 IDG Coexp

The comprehensive genes outputed by GSEA can be viewed inAppendix B. Amongth the extracted genes, pathways, etc, some were more attractive and listed here with some details. The headers are represented in the format of ([Source_Change], Name, Adjusted P-value, Z-score, Combined Score, database.)

3.1. Transcription Factors (TFs)

This section has been widely influenced by proteinatlas and KEGG.

3.1.1. ETV4

Transcription regulator, e.g is unfavorable to liver cancer while favorable to thyroid cancer.

3.1.2. E2F4

Transcription facator, significant role in cell cycle regulation.

3.1.3. E2F1

Transcription factor of the E2F TF family.

3.1.4. NRF1

Nuclear respiratory factor 1, TF regulating key metabolic genes.

3.1.5. NFIC

TF in cells and replication factor for adenovirus.

3.1.6. NFYA

TF associated with a subunit of a high specified and affined DNA binding complex.

3.1.7. POU2F1

Of the same group of oct4 i.e octamer transcription factors.

3.2. Pathways (PWs)

3.2.1. Glycosaminoglycan degradation

Glycosaminoglycans are polar molecules found in extracellular matrix and interact with growth factors

3.2.2. Glycosphingolipid biosynthesis

Glycosphingolipids form a major part of lipid rafts in cell membrane, in which some receptors lay

3.2.3. RIG-I-like receptor signaling pathway

RIG-I-like receptors have accepted the role of pathogen sensing of RNA viruses

3.2.4. Autoimmune thyroid disease

A disease in which thyroid cells are defected and secrete antigens consequently, attracting B and T cells toward themselves, therefore, driven to necrosis/apoptosis.

3.2.5. Graft-versus-host disease

Allogeneic hematopoietic transplantations causes some disorders invoking donor cells against the host ones.

3.2.6. Endosomal/Vacuolar pathway

Antigenic peptides are generated and cross presented, resulting in loaded MHC-I cells through this pathway.

3.2.7. Interferon alpha/beta signaling

The Interferon alpha/beta signaling pathway results in some IFN-stimulated and -induced gene expressions and site bindings.

3.2.8. Antigen Presentation: Folding, assembly and peptide loading of class I MHC

Antigen peptides are loaded to MHC I molecules and cytotoxic T cells are invoked by them. This pathway deals with MHC since Folding in Golgi up to the peptide loading of it.

3.2.9. Immune System

Self explanatory.

3.2.10. Interferon gamma signaling

Interferon Gamma Receptors induce phosphorylation upon binding to IFNG and consequently activate genes containing gamma-interferon activation sequence (GAS) in their promoter along this pathway.

3.2.11. DNA replication

Self explanatory.

3.2.12. Homologous recombination

A pathway in which double strand breaks are fixed using the homologous DNA sequence, which is a necessary error correction mechanism for the DNA replication.

3.2.13. Oocyte meiosis

The process of forming mature female gametocyte.

3.2.14. Fanconi anemia pathway

A pathway in which some replication barriers are removed.

3.2.15. E2F transcription factor network

E2F factors are of the most important S-phase entry in the cell cycle, although their roles are not limited to the aforementioned one.

3.2.16. PLK1 signaling events

Yet another pathway to ensure the mitosis is done correctly.

3.2.17. FOXM1 transcription factor network

FOXM1 TFs have been found to be essential for mitotic progression and some gene encodings as well.

3.2.18. Aurora B signaling

Aurora B is assigned the duty of chromosome separation during cell divisions by the evolution. It is alleged that some aneuploidies are the consecuence of its malfunctioning.

3.2.19. ATR signaling pathway

DNA damage response is a mechanism in cell that maintains DNA integrity. This mechanism is mainly regulated by ATR signaling pathway.

3.2.20. Cell Cycle

A process including but not limited to DNA replication and organelle division in order to form daughter cells.

3.2.21. M Phase

A phase of cell cycle in which nuclear and cytoplasm are divided to form two daughter cells.

3.2.22. Cell Cycle Checkpoints

In order to have the cell cycle under control, evolution has defined some checkpoints between each two consecutive phases of cell cycle to ensure whether it is necessary to continue the cycle.

3.2.23. G2/M Checkpoints

Before entering mitosis phase, this checkpoint would check the DNA replication fidelity.

3.2.24. Th17 cell differentiation

Th17 cells are a subset of CD4+ T cells.

3.2.25. Allograft rejection

The process of recognizing donor cells as intruders and attacking them by T cells.

3.2.26. TNF receptor signaling pathway

Regulation of cell proliferation , differentiation, and apoptosis are processes in which TNF involves in.

3.2.27. TRAIL signaling pathway

TRIAL is a death ligand which binds to death receptors and causes apoptosis. Metastasis suppression is of its main roles.

3.2.28. IL12-mediated signaling events

IL12 is a protein defending cell against intracellular viral infections attracting imune system against the corrupted cell.

3.2.29. Downstream signaling in naive CD8+ T cells

3.2.30. Cytokine Signaling in Immune system

"Cytokines are small proteins that regulate and mediate immunity, inflammation, and hematopoiesis. They are secreted in response to immune stimuli, and usually act briefly, locally, at very low concentrations."

3.2.31. p73 transcription factor network

p73 is a TF with low frequency of mutation in cancer despite of overlapping gene targets with p53

3.2.32. Mitotic Prometaphase

A phase of mitosis in which the nuclear membrane breaks apart.

3.2.33. Resolution of Sister Chromatid Cohesion

Eliminating cohesin complexes from chromosomes having them still connected at centromeres

3.2.34. Intestinal immune network for IgA production

A mechanism of generating and differentiating noninflammatory immunoglobulin A originated from mucosal B cells.

3.2.35. TNF signaling pathway

TNFs play wide range of roles varying from apoptosis to survival reactions.

3.2.36. Asthma

A pathway in which allergens invoke T cells against themselves causing inflammation.

3.2.37. Immunoregulatory interactions between a Lymphoid and a non-Lymphoid cell

There are some receptors and surface attaching molecules which adjust the response of lymphoid cells to the environmental condition.

3.2.38. Adaptive Immune System

A major strategy of the immune system is to produce and devote a specific kind of cells to each pathogen. This is the responsibility of Adaptive Immune System.

3.2.39. CD22 mediated BCR regulation

Out of control BCR expression, which causes autoimmune disease, is avoided a set of mechanisms including CD22 receptors signaling.

3.2.40. TNF receptor superfamily (TNFSF) members mediating non-canonical NF-kB pathway

3.2.41. Human T-cell leukemia virus 1 infection

A retroviral infection mostly nonlethal and even asymptomatic.

3.2.42. Regulation of retinoblastoma protein

Of the main G0/G1 and G1/S regulators, Rb proteins can be made. They regulates target genes of E2F TFs.

3.2.43. Mitotic G1-G1/S phases

Respectively growth focused and transition states in which cell's commitment to the proliferation is ensured.

It can be obviously observed that the listed pathways are mainly concerning cell cycle and immune system. It can be guessed that cell cycle regulation errors are the causes of AML, while immune system deficiencies are the consequences of the cancer. The former is widely studied in , , , , and a handful of other articles. This article would follow the later to compile pieces of information about immune system deficiencies and AML relation.

3.3. Gene Ontology

Table up to Table would cover extracted Gene Ontologies which are in simple English and, therefore, intelligible using only high school biology knowledge. Skimming through tables entries, it was observed that highly scored ontologies are strongly linked to cell cycle regulation and fidelity mechanisms, and cellular components. While low scored ontologies, which are usually observed among genes which have been expressed less in AML affected cells, seems related to immune system regulation mechanisms and actions. Exploiting existing knowledge about AML, it could be inferred that due to failure of immune cells to differentiate and become mature, they lack the ability to accomplish their normal responsibility. Hence, the idea of immune deficiencies be side effects of AML is supported.

3.4. Consensus

As retroviral infections are not reported as significant causes of AML, it is not a strong suggestion to regard immune system weakness a major cause of AML. However, has indicated that autoimmune deficiencies can surge the risk of AML and supported this idea with a number of statistical tests. These tests approve the claim in some cases while stay wordless against others. Moreover, the immune system can be considered as a major therapy fails in AML. Bone marrow stem cell transplant is among the most well known therapies for AML while as indicated by it is suppressed by body immune system and donor cells are identified as intruders by the immune system. Previously reported pathways in this article has pointed this out. suggests immunotherapy methods to bypass the aforementioned problem.

3.5. Drugs

Usually cancer drugs target cell cycle phases to regulate the cell cycle, hoping to outperform mutational adaption of cancer cells , . A list of less studied drugs can be found in , but due to the god damn deadline, any investigation about docking capability and other related drug assessments are ignored.

Acknowledgments

Thank you dear everybody

Appendix A. GSEA Dataset Selection

place holder

Appendix B. GSEA Full Selected Genes

Table B.3: Databases in Use for GSEA

Name	Adj. P-value	Z-score	Combined Score
ETV4 (human)	0.043	-1.74	15.24

Table B.4: Databases in Use for GSEA

Name	Adj. P-value	Z-score	Combined Score
E2F4 (human)	6.248e-9	-1.97	48.40
E2F1 (human)	0.00002605	-1.55	23.43
NRF1 (human)	0.0001446	-1.71	22.44
NFIC (human)	0.001465	-1.69	18.00
NFYA (human)	0.002248	-1.60	16.03

Table B.5: Databases in Use for GSEA

Name	Adj. P-value	Z-score	Combined Score
hsa-miR-193b-3p	8.760050e-64	-6.364176	973.9777
hsa-miR-192-5p	2.501043e-31	-6.765765	522.3863
hsa-miR-215-5p	2.718386e-34	-5.184328	437.7653
hsa-miR-34a-5p	9.159129e-21	-5.117180	269.1568
hsa-miR-92a-3p	1.886866e-08	-9.381637	223.6528

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Table B.6: Databases in Use for GSEA

Name	Adj. P-value	Z-score	Combined Score
E2F4 (human)	0.006586	-1.95	18.87
E2F1 (human)	0.002198	-1.57	18.41

Table B.7: Databases in Use for GSEA

Name	Adj. P-value	Z-score	Combined Score
hsa-miR-193b-3p	1.574e-35	-6.36	558.85
hsa-miR-192-5p	4.991e-29	-6.77	485.40
hsa-miR-215-5p	6.399e-30	-5.18	384.69
hsa-miR-34a-5p	1.639e-7	-5.12	112.13
hsa-let-7b-5p	0.008490	-7.90	85.63

Table B.8: Databases in Use for GSEA

Name	Adj. P-value	Z-score	Combined Score
POU2F1 (human)	0.03246	-1.74	15.68

Table B.9: Databases in Use for GSEA

Name	Adj. P-value	Z-score	Combined Score
E2F4 (human)	3.861e-8	-1.97	44.58
E2F1 (human)	0.005012	-1.55	15.12
NRF1 (human)	0.01787	-1.71	14.02

Table B.10: Databases in Use for GSEA

Name	Adj. P-value	Z-score	Combined Score
hsa-miR-193b-3p	1.275e-39	-6.36	618.57
hsa-miR-192-5p	4.036e-18	-6.77	315.22
hsa-miR-215-5p	2.494e-19	-5.18	258.08
hsa-miR-34a-5p	5.211e-14	-5.12	188.50
hsa-let-7b-5p	0.00006949	-7.90	121.79

Table B.11: Databases in Use for GSEA

Name	Adj. P-value	Z-score	Combined Score
Glycosaminoglycan degradation	0.02246	-613.78	3210.85
Glycosphingolipid biosynthesis	0.4322	-900.86	1321.91
RIG-I-like receptor signaling pathway	0.004278	-97.67	704.97
Autoimmune thyroid disease	0.002948	-78.88	653.40
Graft-versus-host disease	0.001461	-68.48	636.28

Table B.12: Databases in Use for GSEA

Name	Adj. P-value	Z-score	Combined Score
Endosomal/Vacuolar pathway_Homo sapiens_R-HSA-1236977	0.000001320	-1.98	37.94
Interferon alpha/beta signaling_Homo sapiens_R-HSA-909733	0.00001904	-1.86	29.37
Antigen Presentation: Folding, assembly and peptide loading of class I MHC_Homo sapiens_R-HSA-983170	0.00002778	-1.93	28.99
Immune System_Homo sapiens_R-HSA-168256	0.0001276	-2.20	28.61
Interferon gamma signaling_Homo sapiens_R-HSA-877300	0.00008257	-1.76	24.06

Table B.13: Databases in Use for GSEA

Name	Adj. P-value	Z-score	Combined Score
DNA replication 6.096e-17	-49.69	1855.26	
Homologous recombination	5.327e-9	-49.65	1100.04
Oocyte meiosis	1.312e-10	-26.82	704.47
Fanconi anemia pathway	0.000001224	-41.92	687.64
Small cell lung cancer	0.0006399	-63.94	602.21

Table B.14: Databases in Use for GSEA

Name	Adj. P-value	Z-score	Combined Score
E2F transcription factor network_Homo sapiens_bb4d0fd3-6191-11e5-8ac5-06603eb7f303	1.616e-20	-1.73	85.49
PLK1 signaling events_Homo sapiens_e5e87977-6194-11e5-8ac5-06603eb7f303	1.127e-20	-1.66	83.87
FOXM1 transcription factor network_Homo sapiens_c51cda49-6192-11e5-8ac5-06603eb7f303	2.769e-16	-1.51	58.67
Aurora B signaling_Homo sapiens_304a75af-618c-11e5-8ac5-06603eb7f303	5.779e-18	-1.26	54.28
ATR signaling pathway_Homo sapiens_8991cbac-618b-11e5-8ac5-06603eb7f303	4.751e-15	-1.18	42.36

Table B.15: Databases in Use for GSEA

Name	Adj. P-value	Z-score	Combined Score
Cell Cycle_Homo sapiens_R-HSA-1640170	1.426e-117	-2.46	677.98
Cell Cycle, Mitotic_Homo sapiens_R-HSA-69278	1.227e-106	-2.47	616.03
M Phase_Homo sapiens_R-HSA-68886	2.552e-50	-2.43	290.68
Cell Cycle Checkpoints_Homo sapiens_R-HSA-69620	6.168e-44	-2.34	244.94
G2/M Checkpoints_Homo sapiens_R-HSA-69481	2.432e-40	-2.32	222.45

Table B.16: Databases in Use for GSEA

Name	Adj. P-value	Z-score	Combined Score
Glycosaminoglycan degradation	0.1424	-585.89	2091.24
Autoimmune thyroid disease	0.00003361	-80.82	1151.46
Th17 cell differentiation	0.00002734	-69.21	1041.32
Graft-versus-host disease	0.00004041	-68.48	923.26
Allograft rejection	0.00003361	-54.70	767.09

Table B.17: Databases in Use for GSEA

Name	Adj. P-value	Z-score	Combined Score
TNF receptor signaling pathway_Homo sapiens_316be05e-6196-11e5-8ac5-06603eb7f303	0.0001737	-1.53	19.39
TRAIL signaling pathway_Homo sapiens_3a79fddf-6196-11e5-8ac5-06603eb7f303	0.0001737	-1.41	18.49
IL12-mediated signaling events_Homo sapiens_7acdea19-6193-11e5-8ac5-06603eb7f303	0.0008804	-1.54	16.39
Downstream signaling in naive CD8+ T cells_Homo sapiens_92180cef-6191-11e5-8ac5-06603eb7f303	0.0009973	-1.43	14.59
IL2-mediated signaling events_Homo sapiens_a2a1883c-6193-11e5-8ac5-06603eb7f303	0.002484	-1.55	14.07

Table B.18: Databases in Use for GSEA

Name	Adj. P-value	Z-score	Combined Score
Immune System_Homo sapiens_R-HSA-168256	0.00001975	-2.23	37.84
Cytokine Signaling in Immune system_Homo sapiens_R-HSA-1280215	0.00003972	-2.40	37.28
Endosomal/Vacuolar pathway_Homo sapiens_R-HSA-1236977	0.00004649	-1.90	28.15
Interferon alpha/beta signaling_Homo sapiens_R-HSA-909733	0.00004649	-1.84	27.00
Interferon gamma signaling_Homo sapiens_R-HSA-877300	0.00006090	-1.75	24.90

Table B.19: Databases in Use for GSEA

Name	Adj. P-value	Z-score	Combined Score
Glyoxylate and dicarboxylate metabolism	0.5917	-701.48	867.99
Glycosaminoglycan biosynthesis	0.3410	-406.31	856.52
Homologous recombination	0.00001242	-50.16	744.50
Small cell lung cancer	0.001191	-67.62	628.70
DNA replication	0.00006099	-49.02	624.51

Table B.20: Databases in Use for GSEA

Name	Adj. P-value	Z-score	Combined Score
PLK1 signaling events_Homo sapiens_e5e87977-6194-11e5-8ac5-06603eb7f303	1.853e-13	-1.66	55.78
FOXM1 transcription factor network_Homo sapiens_c51cda49-6192-11e5-8ac5-06603eb7f303	1.887e-11	-1.65	46.63
E2F transcription factor network_Homo sapiens_bb4d0fd3-6191-11e5-8ac5-06603eb7f303	3.319e-11	-1.68	45.91
p73 transcription factor network_Homo sapiens_a88c505e-6194-11e5-8ac5-06603eb7f303	8.821e-10	-1.38	32.22
ATR signaling pathway_Homo sapiens_8991cbac-618b-11e5-8ac5-06603eb7f303	1.914e-10	-1.24	31.11

Table B.21: Databases in Use for GSEA

Name	Adj. P-value	Z-score	Combined Score
Cell Cycle_Homo sapiens_R-HSA-1640170	3.743e-54	-2.46	317.68
Cell Cycle, Mitotic_Homo sapiens_R-HSA-69278	5.027e-44	-2.47	259.31
Mitotic Prometaphase_Homo sapiens_R-HSA-68877	1.905e-22	-2.03	111.73
M Phase_Homo sapiens_R-HSA-68886	2.687e-18	-2.41	107.58
Resolution of Sister Chromatid Cohesion_Homo sapiens_R-HSA-2500257	1.644e-20	-2.06	103.70
Intestinal immune network for IgA production	0.000003880	-99.15	1739.13

Table B.22: Databases in Use for GSEA

Name	Adj. P-value	Z-score	Combined Score
Glycosphingolipid biosynthesis	0.8842	-781.54	574.04
TNF signaling pathway	0.06974	-74.45	391.55
Autoimmune thyroid disease	0.08780	-77.59	383.98
Asthma	0.09760	-81.53	76.60

Table B.23: Databases in Use for GSEA

Name	Adj. P-value	Z-score	Combined Score
Immune System_Homo sapiens_R-HSA-168256	0.0003718	-2.23	31.24
Immunoregulatory interactions between a Lymphoid and a non-Lymphoid cell_Homo sapiens_R-HSA-198933	0.0006682	-2.00	25.45
Adaptive Immune System_Homo sapiens_R-HSA-1280218	0.006699	2.27	22.67
CD22 mediated BCR regulation_Homo sapiens_R-HSA-5690714	0.009758	-1.94	17.65
TNF receptor superfamily (TNFSF) members mediating non-canonical NF-kB pathway_Homo sapiens_R-HSA-5676594	0.009595	-1.88	17.61

Table B.24: Databases in Use for GSEA

Name	Adj. P-value	Z-score	Combined Score
Small cell lung cancer	0.002421	-64.35	525.51
DNA replication	0.0004052	-48.35	515.36
Homologous recombination	0.0005634	-48.79	488.48
Fanconi anemia pathway	0.001818	-40.98	355.37
Human T-cell leukemia virus 1 infection	0.00003497	-18.10	242.43

Table B.25: Databases in Use for GSEA

Name	Adj. P-value	Z-score	Combined Score
E2F transcription factor network_Homo sapiens_bb4d0fd3-6191-11e5-8ac5-06603eb7f303	6.635e-13	-1.78	57.97
FOXM1 transcription factor network_Homo sapiens_c51cda49-6192-11e5-8ac5-06603eb7f303	6.102e-9	-1.65	37.63
PLK1 signaling events_Homo sapiens_e5e87977-6194-11e5-8ac5-06603eb7f303	2.976e-7	-1.47	26.78
Aurora B signaling_Homo sapiens_304a75af-618c-11e5-8ac5-06603eb7f303	9.910e-8	-1.26	24.67
Regulation of retinoblastoma protein_Homo sapiens_407a3468-6195-11e5-8ac5-06603eb7f303	0.000003482	-1.52	23.55

Table B.26: Databases in Use for GSEA

Name	Adj. P-value	Z-score	Combined Score
Cell Cycle_Homo sapiens_R-HSA-1640170	1.430e-40	-2.46	241.02
Cell Cycle, Mitotic_Homo sapiens_R-HSA-69278	7.756e-36	-2.47	213.08
Mitotic G1-G1/S phases_Homo sapiens_R-HSA-453279	1.077e-18	-2.11	98.22
G1/S Transition_Homo sapiens_R-HSA-69206	2.942e-15	-2.11	80.21
Mitotic Prometaphase_Homo sapiens_R-HSA-68877	1.569e-15	-2.02	78.71

Table B.27: Databases in Use for GSEA

Name	Adj. P-value	Z-score	Combined Score
antigen processing and presentation of exogenous peptide antigen via MHC class I, TAP-independent (GO:0002480)	0.0001851	-2.33	35.76
type I interferon signaling pathway (GO:0060337)	0.0002905	-2.32	30.11
retrograde transport, vesicle recycling within Golgi (GO:0000301)	0.02414	-4.03	29.32
regulation of necrotic cell death (GO:0010939)	0.003712	-2.48	23.91
regulation of necroptotic process (GO:0060544)	0.0002905	-1.62	20.96

Table B.28: Databases in Use for GSEA

Name	Adj. P-value	Z-score	Combined Score
death-inducing signaling complex (GO:0031264)	0.01076	-3.30	22.26
recycling endosome membrane (GO:0055038)	0.00003093	-1.46	21.80
integral component of lumenal side of endoplasmic reticulum membrane (GO:0071556)	0.001205	-1.95	20.60
COPII-coated ER to Golgi transport vesicle (GO:0030134)	0.001228	-2.06	19.47
MHC protein complex (GO:0042611)	0.001980	-2.05	17.74

Table B.29: Databases in Use for GSEA

Name	Adj. P-value	Z-score	Combined Score
DNA metabolic process (GO:0006259)	1.366e-44	-1.36	147.85
DNA replication (GO:0006260)	1.493e-35	-1.56	135.24
DNA repair (GO:0006281)	3.977e-26	-1.71	109.74
mitotic cell cycle phase transition (GO:0044772)	2.146e-32	-1.17	92.67
chromatin remodeling at centromere (GO:0031055)	1.246e-15	-2.28	88.85

Table B.30: Databases in Use for GSEA

Name	Adj. P-value	Z-score	Combined Score
DNA helicase activity (GO:0003678)	7.421e-10	-2.66	66.98
ATPase activity (GO:0016887)	4.563e-9	-2.31	53.57
DNA-dependent ATPase activity (GO:0008094)	3.454e-13	-1.53	51.82
DNA binding (GO:0003677)	1.223e-16	-1.20	50.97
3'-5' DNA helicase activity (GO:0043138)	0.000003135	-2.82	44.63

Table B.31: Databases in Use for GSEA

Name	Adj. P-value	Z-score	Combined Score
nuclear chromosome part (GO:0044454)	4.133e-37	-1.25	111.11
chromosome, centromeric region (GO:0000775)	5.429e-20	-2.25	108.81
microtubule organizing center (GO:0005815)	1.986e-18	-2.02	88.76
spindle (GO:0005819)	1.837e-29	-1.18	83.06
chromatin (GO:0000785)	1.158e-19	-1.66	78.42

Table B.32: Databases in Use for GSEA

Name	Adj. P-value	Z-score	Combined Score
retrograde transport, vesicle recycling within Golgi (GO:0000301)	0.009160	-4.03	37.61
cytokine-mediated signaling pathway (GO:0019221)	6.018e-9	-1.35	35.45
type I interferon signaling pathway (GO:0060337)	0.001496	-2.32	29.10
regulation of lymphocyte activation (GO:0051249)	0.005443	-2.70	27.84
antigen processing and presentation of exogenous peptide antigen via MHC class I, TAP-independent (GO:0002480)	0.001988	-2.33	27.55

Table B.33: Databases in Use for GSEA

Name	Adj. P-value	Z-score	Combined Score
cytokine receptor activity (GO:0004896)	0.0002861	-1.84	25.68
tumor necrosis factor-activated receptor activity (GO:0005031)	0.04099	-2.56	20.28

Table B.34: Databases in Use for GSEA

Name	Adj. P-value	Z-score	Combined Score
clathrin vesicle coat (GO:0030125)	0.03999	-3.52	19.54
integral component of lumenal side of endoplasmic reticulum membrane (GO:0071556)	0.002593	-1.94	19.08
MHC protein complex (GO:0042611)	0.003483	-2.08	18.73
T cell receptor complex (GO:0042101)	0.02267	-2.55	16.46
clathrin coat of trans-Golgi network vesicle (GO:0030130)	0.05913	-3.12	15.73

Table B.35: Databases in Use for GSEA

Name	Adj. P-value	Z-score	Combined Score
strand displacement (GO:0000732)	1.727e-11	-2.58	75.45
kinetochore organization (GO:0051383)	2.163e-11	-2.56	73.81
mitotic nuclear division (GO:0140014)	1.157e-11	-2.22	65.92
DNA biosynthetic process (GO:0071897)	1.520e-12	-1.97	62.81
DNA replication (GO:0006260)	2.687e-15	-1.55	61.43

Table B.36: Databases in Use for GSEA

Name	Adj. P-value	Z-score	Combined Score
DNA helicase activity (GO:0003678)	0.000009750	-2.62	38.96
microtubule motor activity (GO:0003777)	1.938e-7	-1.85	37.43
ATPase activity (GO:0016887)	0.000003774	-2.31	37.41
motor activity (GO:0003774)	2.992e-7	-1.58	30.62
DNA-dependent ATPase activity (GO:0008094)	4.744e-7	-1.52	28.12

Table B.37: Databases in Use for GSEA

Name	Adj. P-value	Z-score	Combined Score
chromosome, centromeric region (GO:0000775)	4.185e-16	-2.26	89.52
condensed chromosome, centromeric region (GO:0000779)	5.224e-12	-2.09	61.06
spindle microtubule (GO:0005876)	5.953e-12	-1.95	56.22
condensed chromosome kinetochore (GO:0000777)	3.066e-10	-2.22	54.12
spindle (GO:0005819)	1.758e-16	-1.18	48.64

Table B.38: Databases in Use for GSEA

Name	Adj. P-value	Z-score	Combined Score
renal filtration (GO:0097205)	0.002162	-3.50	38.03
phagocytosis, engulfment (GO:0006911)	0.0001266	-2.39	35.59
regulation of immune effector process (GO:0002697)	0.001193	-2.89	34.48
glomerular filtration (GO:0003094)	0.001895	-3.00	33.73
positive regulation of lymphocyte activation (GO:0051251	0.0001266	-2.21	32.93

Table B.39: Databases in Use for GSEA

Name	Adj. P-value	Z-score	Combined Score
immunoglobulin receptor binding (GO:0034987)	0.00008611	-2.41	36.35

Table B.40: Databases in Use for GSEA

Name	Adj. P-value	Z-score	Combined Score
DNA metabolic process (GO:0006259)	1.976e-20	-1.36	71.65
microtubule cytoskeleton organization involved in mitosis (GO:1902850)	4.370e-12	-1.65	53.05
sister chromatid segregation (GO:0000819)	3.095e-9	-2.04	50.33
mitotic spindle organization (GO:0007052)	3.027e-13	-1.39	49.10
DNA replication (GO:0006260)	1.211e-11	-1.55	47.77

Table B.41: Databases in Use for GSEA

Name	Adj. P-value	Z-score	Combined Score
histone kinase activity (GO:0035173)	0.0001513	-3.09	41.13
DNA helicase activity (GO:0003678)	0.0001706	-2.67	34.36
DNA polymerase binding (GO:0070182)	0.0004986	-2.31	25.27
3'-5' DNA helicase activity (GO:0043138)	0.004400	-2.80	22.77
DNA-dependent ATPase activity (GO:0008094)	0.00006878	-1.53	22.22

Table B.42: Databases in Use for GSEA

Name	Adj. P-value	Z-score	Combined Score
microtubule organizing center (GO:0005815)	1.411e-10	-2.07	54.44
chromosome, centromeric region (GO:0000775)	2.555e-8	-2.21	45.55
nuclear chromosome part (GO:0044454)	1.751e-13	-1.25	42.91
centrosome (GO:0005813), 1.411e-10	-1.61	42.58	
condensed chromosome kinetochore (GO:0000777)	5.286e-7	-2.27	39.74

Table B.43: Databases in Use for GSEA

Name	Adj. P-value	Z-score	Combined Score
STK17A_IDG_kinase_ARCHS4_coexpression	5.174e-28	-1.62	110.43
P2RY10_IDG_GPCR_ARCHS4_coexpression	1.710e-25	-1.55	95.41
MAP3K14_IDG_kinase_ARCHS4_coexpression	9.806e-18	-1.54	66.84
GPR25_IDG_GPCR_ARCHS4_coexpression	1.197e-15	-1.77	66.61
GPR174_IDG_GPCR_ARCHS4_coexpression	8.520e-17	-1.58	63.96

Table B.44: Databases in Use for GSEA

Name	Adj. P-value	Z-score	Combined Score
UCK2_IDG_kinase_ARCHS4_coexpression	9.315e-75	-1.61	283.39
PKMYT1_IDG_kinase_ARCHS4_coexpression	2.303e-65	-1.53	235.44
CHRNA9_IDG_ionchannel_ARCHS4_coexpression	2.957e-46	-1.54	168.06
RIOK1_IDG_kinase_ARCHS4_coexpression	7.258e-36	-1.60	136.09
PKN3_IDG_kinase_ARCHS4_coexpression	7.575e-35	-1.55	127.31

Table B.45: Databases in Use for GSEA

Name	Adj. P-value	Z-score	Combined Score
STK17A_IDG_kinase_ARCHS4_coexpression	6.729e-22	-1.62	88.38
GPR174_IDG_GPCR_ARCHS4_coexpression	2.546e-21	-1.62	84.65
P2RY10_IDG_GPCR_ARCHS4_coexpression	2.546e-21	-1.54	80.07
DYRK2_IDG_kinase_ARCHS4_coexpression	8.547e-12	-1.60	47.72
GPR171_IDG_GPCR_ARCHS4_coexpression	3.522e-10	-1.72	44.50

Table B.46: Databases in Use for GSEA

Name	Adj. P-value	Z-score	Combined Score
UCK2_IDG_kinase_ARCHS4_coexpression	1.384e-31	-1.60	121.31
PKMYT1_IDG_kinase_ARCHS4_coexpression	1.384e-31	-1.54	117.12
CHRNA9_IDG_ionchannel_ARCHS4_coexpression	1.934e-23	-1.54	87.25
PKN3_IDG_kinase_ARCHS4_coexpression	3.962e-15	-1.55	57.22
CSNK2A2_IDG_kinase_ARCHS4_coexpression	3.962e-15	-1.47	54.49

Table B.47: Databases in Use for GSEA

Name	Adj. P-value	Z-score	Combined Score
P2RY10_IDG_GPCR_ARCHS4_coexpression	2.375e-20	-1.56	79.30
MAP3K14_IDG_kinase_ARCHS4_coexpression	3.895e-7	-1.55	30.67
STK38L_IDG_kinase_ARCHS4_coexpression	0.000007491	-1.61	26.45
GPR174_IDG_GPCR_ARCHS4_coexpression	0.00002773	-1.60	23.70
GPR152_IDG_GPCR_ARCHS4_coexpression	0.003520	-1.98	17.89

Table B.48: Databases in Use for GSEA

Name	Adj. P-value	Z-score	Combined Score
PKMYT1_IDG_kinase_ARCHS4_coexpression	8.882e-32	-1.54	118.82
UCK2_IDG_kinase_ARCHS4_coexpression	1.443e-24	-1.60	95.40
CHRNA9_IDG_ionchannel_ARCHS4_coexpression	9.312e-17	-1.54	63.51
PKN3_IDG_kinase_ARCHS4_coexpression	9.496e-14	-1.56	52.99
CSNK2A2_IDG_kinase_ARCHS4_coexpression	6.583e-11	-1.46	39.83