

# Supplementary Material

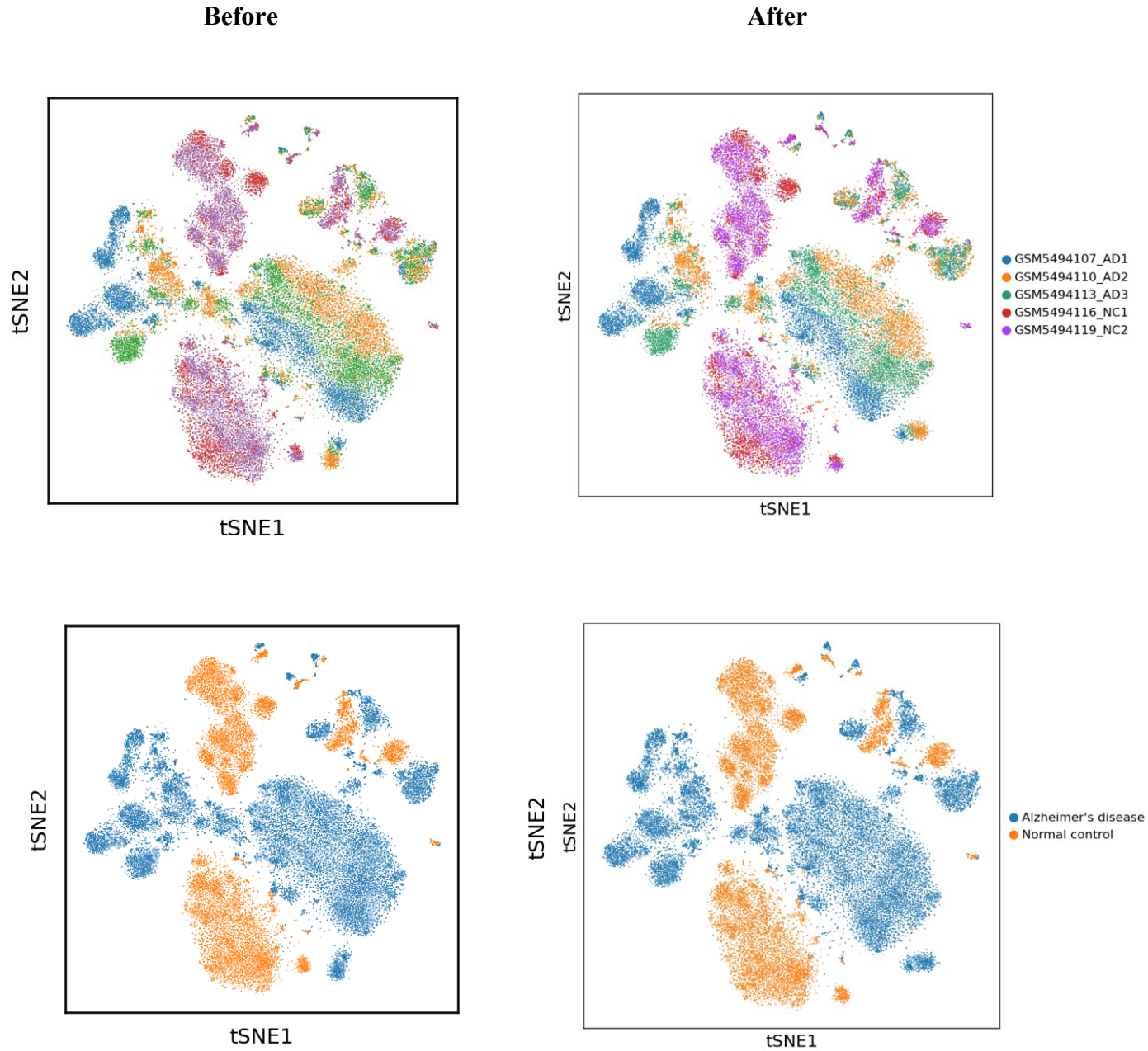
## Exploring Promising Biomarkers for Alzheimer's disease through the Computational Analysis of Peripheral Blood Single-Cell RNA Sequencing Data

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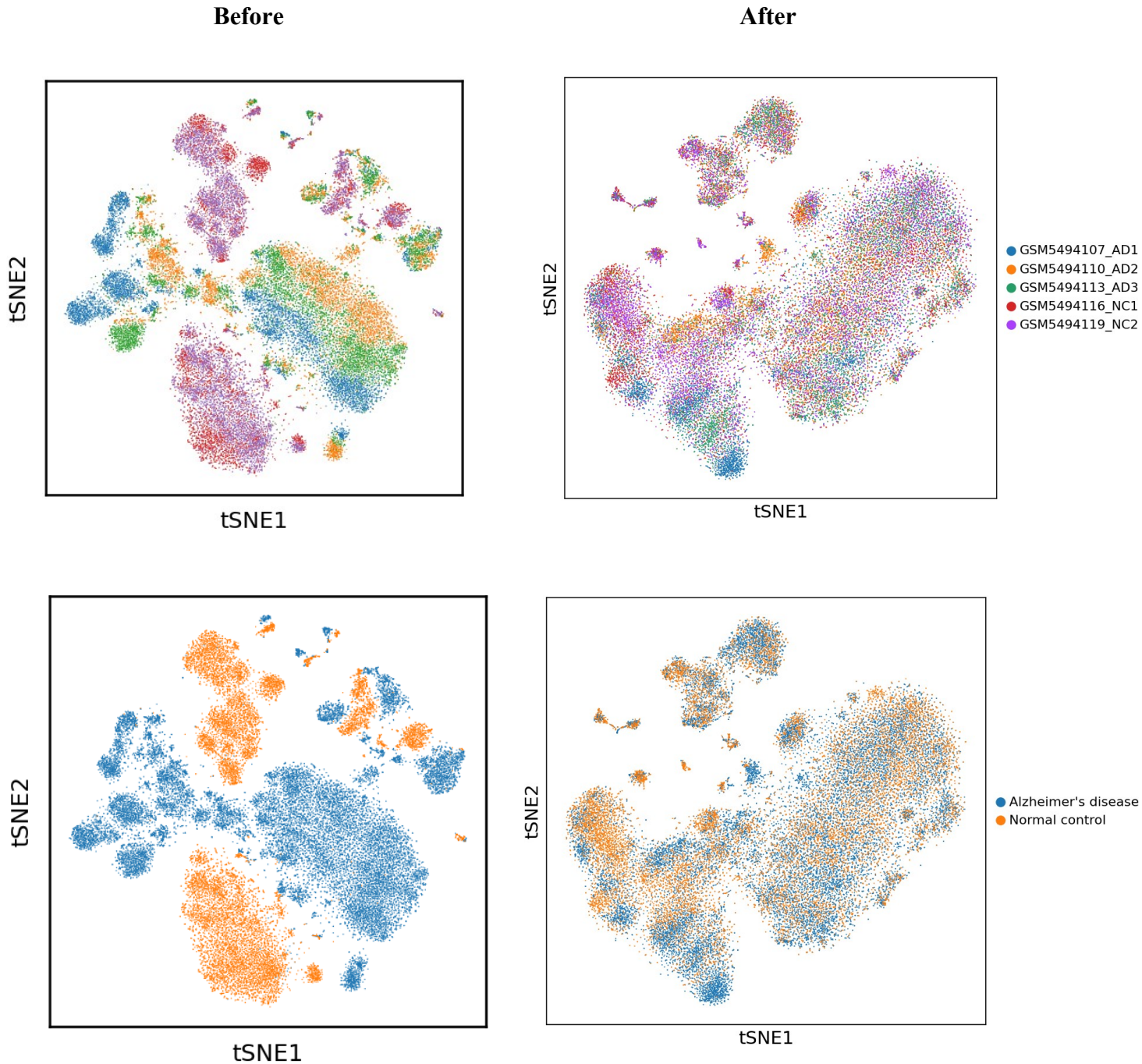
In this section, we provide an explanation of why we chose SCALEX as our preferred data integration algorithm for combining the five batches, over other potential algorithms. To validate our decision, we assessed the effectiveness of three alternative data integration algorithms, namely BBKNN, Scanorama, and Harmony (Harmony's Python implementation). It is worth mentioning that Scanorama and Harmony are among the integration algorithms that have demonstrated superior performance on pbmc single cell data, according to a benchmarking study by Luecken et al. [4].

**BBKNN:** This is an scRNA-seq data integration algorithm created by Polanski et al [1]. It can be used directly in any scapy workflow. It is essentially an alternative to scanpy's neighbor computation function (`scanpy.pp.neighbors`). The algorithm creates a neighbor graph of the cells available within the data. It begins by identifying the  $k$  nearest neighbors for each cell across the entire data. To counteract for batch effects within the data, the algorithm identifies a smaller set of  $k$  nearest neighbors for each batch separately, instead of the whole dataset. These nearest neighbors from each of the batches are then merged into the final neighbor list for each cell. That way, connections are created between analogous cells in different batches. The following are the tsne maps before and after integration with BBKNN:



**Figure S1.** tSNE embeddings of GSE181279 scRNA-seq dataset before (left) and after integration with BBKNN (right); A) tSNE embeddings colored by batch types. B) tSNE embeddings colored by disease types. Evidently, in both instances, BBKNN is unable to rectify batch effects present in the data. This likely suggests that the dataset used for this research is too intricate for the algorithm to handle effectively.

2. **Scanorama**: is a scRNA-seq data integration created by Hie et al [2]. It is a generalization of the mutual nearest neighbors matching algorithm that finds similar cells among many datasets instead of only 2 at a time. Randomized SVD is also used as a dimensionality reduction technique in order to improve the algorithm's robustness to noise. The following are the tsne maps before and after integration with Scanorama:

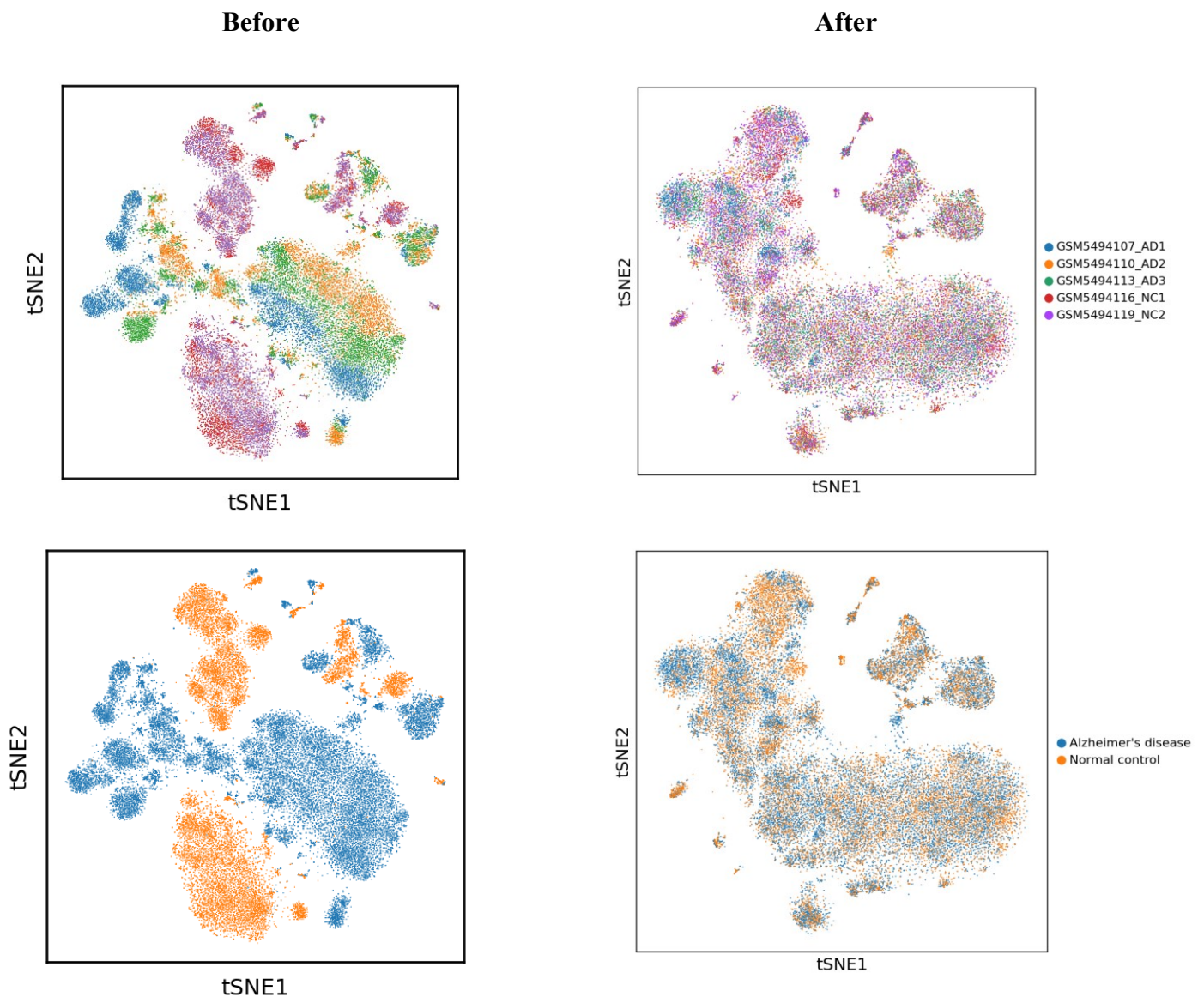


**Figure S2.** tSNE embeddings of GSE181279 scRNA-seq dataset before (left) and after integration with Scanorama (right); A) tSNE embeddings colored by batch types. B) tSNE embeddings colored by disease types. Scanorama manages to change the pattern of the data. This signifies that the algorithm has successfully addressed batch effects. Nonetheless, the complete mixing of cells might also imply overmixing or overcorrection. If the dataset's authors had supplied cell type labels, this issue could have been more definitively resolved.



**3. Harmony:** is a scRNA-seq data integration algorithm created by Korsunsky et al [3]. It was first implemented in R. Since its introduction, it has been implemented in python as well (harmonypy can be used directly through scanpy). Harmony accepts each cell's coordinates in a reduced feature space created through the use of PCA. It makes use of fuzzy clustering in order to assign each cell to multiple clusters (a penalty term is utilized to ensure that within cluster diversity is maximized).

A global centroid is calculated for each cluster along with data-specific centroids for each cluster. In each cluster, a correction factor for each dataset is calculated based on the centroids. Last but not least, the algorithm corrects each cell using a cell specific correction factor (it is a linear combination of dataset correction factors weighted by the cell's soft cluster assignments made in the first step of the algorithm). The following are the tsne maps before and after integration with Harmonypy:



**Figure S3.** tSNE embeddings of GSE181279 scRNA-seq dataset before (left) and after integration with Harmony (right); A) tSNE embeddings colored by batch types. B) tSNE embeddings colored by disease types. Harmony manages to change the pattern of the data. This is an indicator that it has managed to correct for batch effects. However, the fact that cells have now been completely mixed could also be an indicator of overmixing/overcorrection. This would have been clarified had the cell type labels been provided by the authors of the dataset.

## References:

- [1] Polański, K., Young, M. D., Miao, Z., Meyer, K. B., Teichmann, S. A., Park, J. E. BBKNN: fast batch alignment of single cell transcriptomes. *Bioinformatics*, **2020** 36, 964-965.
- [2] Hie, B., Bryson, B., & Berger, B. Efficient integration of heterogeneous single-cell transcriptomes using Scanorama. *Nature biotechnology*, **2019** 37, 685-691.
- [3] Abdelaal, T., Michielsen, L., Cats, D., Hoogduin, D., Mei, H., Reinders, M. J., & Mahfouz, A. A comparison of automatic cell identification methods for single-cell RNA sequencing data. *Genome biology*, **2019** 20, 1-19.
- [4] Luecken MD, Büttner M, Chaichoompu K, Danese A, Interlandi M, Mueller MF, Strobl DC, Zappia L, Dugas M, Colomé-Tatché M, Theis FJ. Benchmarking atlas-level data integration in single-cell genomics. *Nature methods*, **2022** 19, 41-50.

**Table S1.** The top 10 enriched Reactome pathways for DEGs

Index	Name	P-value	Adjusted p-value	Odds Ratio	Combined score
1	Translocation of ZAP-70 to immunological synapse R-HSA-202430	0.000001559	0.00009637	61.18	818.06
2	Endosomal/vacuolar pathway R-HSA-1236977	0.00002186	0.0005485	73.84	792.37
3	Phosphorylation of CD3 and TCR Zeta Chains R-HSA-202427	0.000003135	0.0001662	49.70	629.84
4	PD-1 signaling R-HSA-389948	0.000003857	0.0001789	46.77	583.07
5	Cross-presentation Of Particulate Exogenous Antigens (Phagosomes) R-HSA-1236973	0.0007347	0.01239	65.00	469.04
6	Immunoregulatory Interactions Between A Lymphoid And A non-Lymphoid Cell R-HSA-198933	8.566e-10	1.059e-7	18.62	388.84
7	Antigen presentation: Folding, Assembly, Peptide Loading of Class I MHC R-HSA-983170	0.00001283	0.0004760	33.12	373.05
8	Scavenging By Class A Receptors R-HSA-3000480	0.0001246	0.002568	36.91	331.81
9	Nef Mediated Downregulation of MHC Class I Complex Cell Surface Expression R-HSA-164940	0.001173	0.01856	48.75	328.95
10	Generation Of Second Messenger Molecules R-HSA-202433	0.00002218	0.0005485	28.38	304.16

**Table S2.** The top 10 enriched biological processes for DEGs

Index	Name	P-value	Adjusted p-value	Odds Ratio	Combined score
1	peptide antigen assembly with MHC protein complex (GO:0002501)	1.026e-8	0.000002669	397.88	7318.83
2	antigen processing and presentation of exogenous peptide antigen via MHC class I, TAP-independent (GO:0002480)	0.000007505	0.0004435	118.16	1394.33
3	antigen processing and presentation of endogenous peptide antigen (GO:0002483)	6.634e-7	0.00006996	79.54	1131.58
4	regulation of glial cell migration (GO:1903975)	0.0002651	0.005302	130.02	1070.77
5	regulation of hippocampal neuron apoptotic process (GO:0110089)	0.0002651	0.005302	130.02	1070.77
6	regulation of microglial cell mediated cytotoxicity (GO:1904149)	0.0002651	0.005302	130.02	1070.77
7	regulation of neutrophil activation (GO:1902563)	0.0002651	0.005302	130.02	1070.77
8	positive regulation of CD4-positive, CD25-positive, alpha-beta regulatory T cell differentiation (GO:0032831)	0.0002651	0.005302	130.02	1070.77
9	positive regulation of mast cell activation involved in immune response (GO:0033008)	0.0002651	0.005302	130.02	1070.77
10	intracellular sequestering of iron ion (GO:0006880)	0.0002651	0.005302	130.02	1070.77

**Table S3.** The top 10 enriched molecular functions for DEGs

Index	Name	P-value	Adjusted p-value	Odds Ratio	Combined score
1	MHC class II receptor activity (GO:0032395)	8.515e-10	1.379e-7	200.92	4196.00
2	C-X3-C chemokine binding (GO:0019960)	0.0002651	0.01431	130.02	1070.77
3	MHC class II protein complex binding (GO:0023026)	0.000001559	0.0001262	61.18	818.06
4	ferric iron binding (GO:0008199)	0.0005529	0.01639	78.00	585.05
5	superoxide-generating NADPH oxidase activator activity (GO:0016176)	0.0007347	0.01700	65.00	469.04
6	Tat protein binding (GO:0030957)	0.001173	0.02375	48.75	328.95
7	superoxide-generating NAD(P)H oxidase activity (GO:0016175)	0.001429	0.02571	43.33	283.84
8	oxidoreductase activity, acting on NAD(P)H, oxygen as acceptor (GO:0050664)	0.002690	0.03962	29.99	177.48
9	IgG binding (GO:0019864)	0.02573	0.1789	48.28	176.71
10	MHC class I protein complex binding (GO:0023024)	0.02573	0.1789	48.28	176.71

**Table S4.** The top 10 enriched cellular components for DEGs

Index	Name	P-value	Adjusted p-value	Odds Ratio	Combined score
1	MHC protein complex (GO:0042611)	1.640e-18	2.082e-16	211.55	8663.54
2	MHC class II protein complex (GO:0042613)	1.400e-13	8.890e-12	239.23	7080.42
3	MHC class I protein complex (GO:0042612)	0.000002701	0.00002450	196.96	2525.42
4	luminal side of endoplasmic reticulum membrane (GO:0098553)	1.159e-12	3.679e-11	82.82	2276.11
5	integral component of luminal side of endoplasmic reticulum membrane (GO:0071556)	1.159e-12	3.679e-11	82.82	2276.11
6	phagolysosome (GO:0032010)	0.0002651	0.001295	130.02	1070.77
7	secondary lysosome (GO:0005767)	0.000001197	0.00001169	66.28	903.79
8	ER to Golgi transport vesicle membrane (GO:0012507)	3.471e-10	8.561e-9	35.96	783.26
9	coated vesicle membrane (GO:0030662)	4.045e-10	8.561e-9	35.19	761.17
10	transport vesicle membrane (GO:0030658)	8.320e-10	1.510e-8	31.80	664.87

**Table S5.** The top 5 enriched Reactome pathways for *EFhd2*

Index	Name	P-value	Adjusted p-value	Odds Ratio	Combined score
1	RHOD GTPase Cycle R-HSA-9013405	0.002600	0.01300	19948.00	118735.70
2	RHO GTPase Cycle R-HSA-9012999	0.02205	0.04125	19559.00	74606.82
3	Signaling By Rho GTPases R-HSA-194315	0.03220	0.04125	19356.00	66503.24
4	Signaling By Rho GTPases, Miro GTPases and RHOBTB3 R-HSA-9716542	0.03300	0.04125	19340.00	65973.64
5	Signal Transduction R-HSA-162582	0.1232	0.1232	17535.00	36710.27

**Table S6.** The top 10 enriched Reactome pathways for *Rhoc*

Index	Name	P-value	Adjusted p-value	Odds Ratio	Combined score
1	RHO GTPases activate Rhotekin and Rhophilins R-HSA-5666185	0.0004500	0.004800	19991.00	154056.47
2	RHO GTPases activate ROCKs R-HSA-5627117	0.0009500	0.004800	19981.00	139049.21
3	RHO GTPases activate CIT R-HSA-5625900	0.0009500	0.004800	19981.00	139049.21
4	Sema4D induced Cell Migration and Growth-Cone Collapse R-HSA-416572	0.001000	0.004800	19980.00	138017.41
5	Sema4D in Semaphorin Signaling R-HSA-400685	0.001200	0.004800	19976.00	134347.69
6	RHO GTPases activate PKNs R-HSA-5625740	0.003100	0.008667	19938.00	115169.25
7	Semaphorin interactions R-HSA-373755	0.003200	0.008667	19936.00	114524.75
8	RHOC GTPase Cycle R-HSA-9013106	0.003650	0.008667	19927.00	111851.11
9	G Alpha (12/13) Signaling Events R-HSA-416482	0.003900	0.008667	19922.00	110503.22
10	RHO GTPases activate Formins R-HSA-5663220	0.005950	0.01190	19881.00	101877.73

**Table S7.** The top 10 enriched biological processes for *Rhoc*

Index	Name	P-value	Adjusted p-value	Odds Ratio	Combined score
1	positive regulation of lipase activity (GO:0060193)	0.0005000	0.008266	19990.00	151942.59
2	regulation of lipase activity (GO:0060191)	0.0007000	0.008266	19986.00	145187.41
3	epiboly involved in wound healing (GO:0090505)	0.0008000	0.008266	19984.00	142504.37
4	wound healing, spreading of cells (GO:0044319)	0.001200	0.008823	19976.00	134347.69
5	cortical cytoskeleton organization (GO:0030865)	0.002050	0.008823	19959.00	123544.89
6	positive regulation of stress fiber assembly (GO:0051496)	0.002200	0.008823	19956.00	122117.07
7	mitotic cytokinesis (GO:0000281)	0.002450	0.008823	19951.00	119939.12
8	positive regulation of actin filament bundle assembly (GO:0032233)	0.002550	0.008823	19949.00	119129.02
9	apical junction assembly (GO:0043297)	0.003000	0.008823	19940.00	115834.63
10	cell-cell junction assembly (GO:0007043)	0.003300	0.008823	19934.00	113899.85

**Table S8.** The top 10 enriched molecular functions for *Rhoc*

Index	Name	P-value	Adjusted p-value	Odds Ratio	Combined score
1	GTP binding (GO:0005525)	0.009450	0.02432	19811.00	92353.95
2	guanyl ribonucleotide binding (GO:0032561)	0.01070	0.02432	19786.00	89779.40
3	GTPase activity (GO:0003924)	0.01080	0.02432	19784.00	89586.28
4	nucleoside-triphosphatase activity (GO:0017111)	0.01390	0.02432	19722.00	84328.81
5	purine ribonucleoside triphosphate binding (GO:0035639)	0.02300	0.02530	19540.00	73710.11
6	kinase binding (GO:0019900)	0.02305	0.02530	19539.00	73663.91
7	protein kinase binding (GO:0019901)	0.02530	0.02530	19494.00	71678.61

**Table S9.** The top 10 enriched cellular components for *Rhoc*

Index	Name	P-value	Adjusted p-value	Odds Ratio	Combined score
1	neuron projection (GO:0043005)	0.02780	0.06000	19444.00	69662.51
2	cytoskeleton (GO:0005856)	0.03000	0.06000	19400.00	68027.34
3	intracellular non-membrane-bounded organelle (GO:0043232)	0.05790	0.07720	18842.00	53681.64
4	intracellular membrane-bounded organelle (GO:0043231)	0.2596	0.2596	14808.00	19970.28



**Table S10.** The top 10 enriched Reactome pathways for *LMNA*

Index	Name	P-value	Adjusted p-value	Odds Ratio	Combined score
1	Depolymerisation of Nuclear Lamina R-HSA-4419969	0.0007500	0.008066	19985.00	143801.31
2	Initiation of Nuclear Envelope (NE) Reformation R-HSA-2995383	0.0009500	0.008066	19981.00	139049.21
3	Deregulated CDK5 Triggers Neurodegenerative Pathways in Alzheimer's Disease Models R-HSA-8862803	0.001050	0.008066	19979.00	137035.71
4	Defective Intrinsic Pathway for Apoptosis R-HSA-9734009	0.001200	0.008066	19976.00	134347.69
5	Apoptotic cleavage of Cellular Proteins R-HSA-111465	0.001900	0.008066	19962.00	125080.30
6	XBP1(S) activates Chaperone Genes R-HSA-381038	0.002300	0.008066	19954.00	121217.83
7	IRE1alpha activates Chaperones R-HSA-381070	0.002400	0.008066	19952.00	120356.53
8	Apoptotic execution Phase R-HSA-75153	0.002600	0.008066	19948.00	118735.70
9	Nuclear envelope Breakdown R-HSA-2980766	0.002650	0.008066	19947.00	118349.79
10	Meiotic synapsis R-HSA-1221632	0.003000	0.008066	19940.00	115834.63

**Table S11.** The top 10 enriched Reactome pathways for *LMNA*

Index	Name	P-value	Adjusted p-value	Odds Ratio	Combined score
1	regulation of cardiac muscle hypertrophy in response to stress (GO:1903242)	0.0003000	0.003087	19994.00	162186.52
2	negative regulation of cardiac muscle hypertrophy (GO:0010614)	0.0006000	0.003087	19988.00	148283.12
3	positive regulation of cell aging (GO:0090343)	0.0006500	0.003087	19987.00	146675.88
4	regulation of cell aging (GO:0090342)	0.0006500	0.003087	19987.00	146675.88
5	mitotic nuclear membrane organization (GO:0101024)	0.002550	0.006412	19949.00	119129.02
6	mitotic nuclear membrane reassembly (GO:0007084)	0.002550	0.006412	19949.00	119129.02
7	IRE1-mediated unfolded protein response (GO:0036498)	0.002650	0.006412	19947.00	118349.79
8	nuclear membrane reassembly (GO:0031468)	0.002700	0.006412	19946.00	117971.02
9	cellular response to decreased oxygen levels (GO:0036294)	0.003450	0.007283	19931.00	112996.74
10	protein localization to nucleus (GO:0034504)	0.005300	0.01007	19894.00	104245.78

**Table S12.** The top 10 enriched biological processes for *FCER1G*

Index	Name	P-value	Adjusted p-value	Odds Ratio	Combined score
1	Platelet adhesion to Exposed Collagen R-HSA-75892	0.0006000	0.005867	19988.00	148283.12
2	Dectin-2 Family R-HSA-5621480	0.001450	0.005867	19971.00	130534.69
3	GPVI-mediated Activation Cascade R-HSA-114604	0.001600	0.005867	19968.00	128549.42
4	Fc Epsilon Receptor (FCERI) Signaling R-HSA-2454202	0.006500	0.01292	19870.00	100064.63
5	Cell Surface Interactions at Vascular Wall R-HSA-202733	0.006700	0.01292	19866.00	99442.44
6	C-type Lectin Receptors (CLRs) R-HSA-5621481	0.007050	0.01292	19859.00	98396.17
7	Platelet Activation, Signaling and Aggregation R-HSA-76002	0.01270	0.01996	19746.00	86214.24
8	Neutrophil Degranulation R-HSA-6798695	0.02340	0.03217	19532.00	73343.17
9	Hemostasis R-HSA-109582	0.02880	0.03520	19424.00	68904.42
10	Innate Immune System R-HSA-168249	0.05175	0.05692	18965.00	56161.72

**Table S13.** The top 10 enriched biological processes for *FCER1G*

Index	Name	P-value	Adjusted p-value	Odds Ratio	Combined score
1	regulation of cell activation (GO:0050865)	0.0005000	0.004920	19990.00	151942.59
2	immunoglobulin mediated immune response (GO:0016064)	0.0005000	0.004920	19990.00	151942.59
3	B cell mediated immunity (GO:0019724)	0.0005500	0.004920	19989.00	150029.82
4	cellular response to low-density lipoprotein particle stimulus (GO:0071404)	0.0007000	0.004920	19986.00	145187.41
5	neutrophil activation (GO:0042119)	0.0008000	0.004920	19984.00	142504.37
6	positive regulation of interleukin-4 production (GO:0032753)	0.0009000	0.004920	19982.00	140136.55
7	myeloid cell activation involved in immune response (GO:0002275)	0.0009500	0.004920	19981.00	139049.21
8	regulation of platelet activation (GO:0010543)	0.001100	0.004920	19978.00	136099.47
9	regulation of interleukin-4 production (GO:0032673)	0.001150	0.004920	19977.00	135204.64
10	immune response-activating cell surface receptor signaling pathway (GO:0002429)	0.001200	0.004920	19976.00	134347.69

**Table S14.** The top 10 enriched biological processes for *PELI1*

Index	Name	P-value	Adjusted p-value	Odds Ratio	Combined score
1	Toll signaling pathway (GO:0008063)	0.0002500	0.003850	19995.00	165840.18
2	negative regulation of necroptotic process (GO:0060546)	0.0004500	0.003850	19991.00	154056.47
3	negative regulation of programmed necrotic cell death (GO:0062099)	0.0005500	0.003850	19989.00	150029.82
4	regulation of programmed necrotic cell death (GO:0062098)	0.001000	0.004830	19980.00	138017.41
5	regulation of necroptotic process (GO:0060544)	0.001150	0.004830	19977.00	135204.64
6	protein K63-linked ubiquitination (GO:0070534)	0.002200	0.007700	19956.00	122117.07
7	protein K48-linked ubiquitination (GO:0070936)	0.002850	0.008550	19943.00	116875.01
8	response to molecule of bacterial origin (GO:0002237)	0.003650	0.009581	19927.00	111851.11
9	interleukin-1-mediated signaling pathway (GO:0070498)	0.004700	0.01097	19906.00	106700.27
10	response to lipid (GO:0033993)	0.005700	0.01197	19886.00	102756.96

**Table S15.** The top 10 enriched biological processes for *ZEB2*

Index	Name	P-value	Adjusted p-value	Odds Ratio	Combined score
1	positive regulation of secondary metabolite biosynthetic process (GO:1900378)	0.0004000	0.003667	19992.00	156418.91
2	positive regulation of melanin biosynthetic process (GO:0048023)	0.0004000	0.003667	19992.00	156418.91
3	regulation of melanin biosynthetic process (GO:0048021)	0.0005500	0.003667	19989.00	150029.82
4	positive regulation of transforming growth factor beta receptor signaling pathway (GO:0030511)	0.001200	0.004800	19976.00	134347.69
5	positive regulation of cellular response to transforming	0.001200	0.004800	19976.00	134347.69

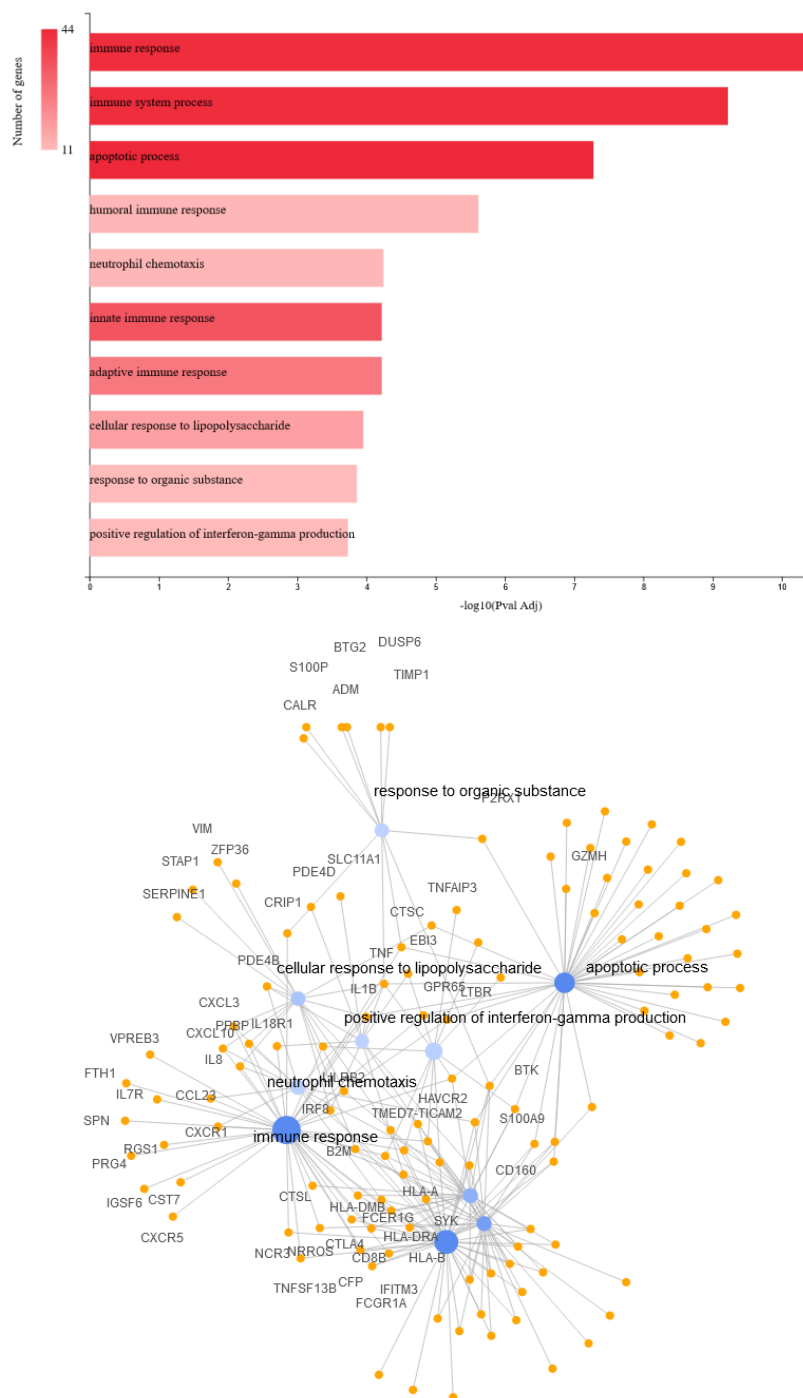
Index	Name	P-value	Adjusted p-value	Odds Ratio	Combined score
	growth factor beta stimulus (GO:1903846)				
6	epithelial cell migration (GO:0010631)	0.002050	0.006833	19959.00	123544.89
7	regulation of organelle organization (GO:0033043)	0.004000	0.01111	19920.00	109987.79
8	positive regulation of transmembrane receptor protein serine/threonine kinase signaling pathway (GO:0090100)	0.004600	0.01111	19908.00	107139.14
9	regulation of transforming growth factor beta receptor signaling pathway (GO:0017015)	0.005000	0.01111	19900.00	105436.78
10	positive regulation of canonical Wnt signaling pathway (GO:0090263)	0.006500	0.01300	19870.00	100064.63

**Table S16.** The top 10 enriched biological processes for *NR4A2*

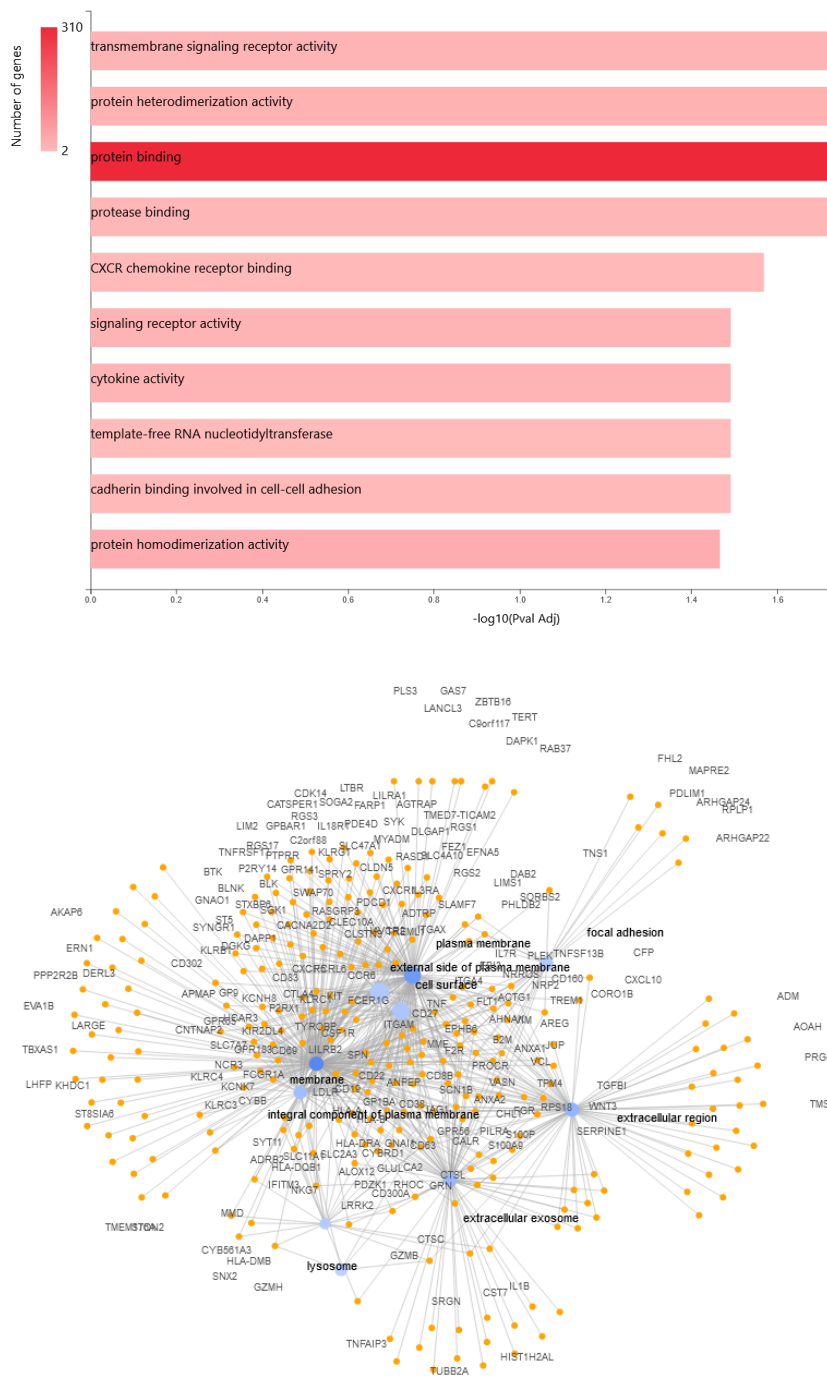
Index	Name	P-value	Adjusted p-value	Odds Ratio	Combined score
1	midbrain dopaminergic neuron differentiation (GO:1904948)	0.0005500	0.01160	19989.00	150029.82
2	dopaminergic neuron differentiation (GO:0071542)	0.001000	0.01160	19980.00	138017.41
3	central nervous system neuron differentiation (GO:0021953)	0.001700	0.01160	19966.00	127326.11
4	regulation of apoptotic signaling pathway (GO:2001233)	0.001900	0.01160	19962.00	125080.30
5	nucleic acid-templated transcription (GO:0097659)	0.002100	0.01160	19958.00	123057.76
6	neuron migration (GO:0001764)	0.002500	0.01160	19950.00	119530.06
7	fat cell differentiation (GO:0045444)	0.002900	0.01160	19942.00	116522.32
8	canonical Wnt signaling pathway (GO:0060070)	0.003400	0.01190	19932.00	113293.39
9	negative regulation of apoptotic signaling pathway (GO:2001234)	0.003900	0.01213	19922.00	110503.22
10	Wnt signaling pathway (GO:0016055)	0.004600	0.01288	19908.00	107139.14

**Table S17.** The top 10 enriched Reactome pathways for *LMNA*

Index	Name	P-value	Adjusted p-value	Odds Ratio	Combined score
1	RUNX3 Regulates Immune Response and Cell Migration R-HSA-8949275	0.0003000	0.004800	19994.00	162186.52
2	Integrin Cell Surface Interactions R-HSA-216083	0.003300	0.01787	19934.00	113899.85
3	Transcriptional Regulation by RUNX3 R-HSA-8878159	0.004750	0.01787	19905.00	106484.27
4	Potential Therapeutics for SARS R-HSA-9679191	0.004850	0.01787	19903.00	106058.91
5	Immunoregulatory Interactions Between a Lymphoid And A non-Lymphoid Cell R-HSA-198933	0.006150	0.01787	19877.00	101200.08
6	Cell Surface Interactions At Vascular Wall R-HSA-202733	0.006700	0.01787	19866.00	99442.44
7	Extracellular Matrix Organization R-HSA-1474244	0.01455	0.03326	19709.00	83372.48
8	SARS-CoV Infections R-HSA-9679506	0.01845	0.03690	19631.00	78380.66
9	Hemostasis R-HSA-109582	0.02880	0.05120	19424.00	68904.42
10	Adaptive Immune System R-HSA-1280218	0.03665	0.05864	19267.00	63703.39



**Figure S4.** GeneCodis ontological analysis and gene-annotation cluster networks. Visualizations generated for 10 top terms of related categories with our identified DEG list are presented here for GO biological process.



**Figure S5.** GeneCodis ontological analysis and gene-annotation cluster networks. Visualizations generated for 10 top terms of related categories with our identified DEG list are presented here for GO cellular component.





