

*Research Paper*

**CREB1<sup>K292</sup> and HINFP<sup>K330</sup> as putative common therapeutic targets in Alzheimer's and Parkinson's disease**

**Rohan Gupta<sup>1</sup> and Pravir Kumar<sup>1,\*</sup>**

<sup>1</sup>Molecular Neuroscience and Functional Genomics Laboratory, Department of Biotechnology, Delhi Technological University (Formerly DCE), Delhi 110042

\*Author to whom correspondence should be addressed:

**Pravir Kumar, PhD**

*Professor and Head, Department of Biotechnology*

*Molecular Neuroscience and Functional Genomics Laboratory*

*Former Dean, Delhi Technological University (Formerly Delhi College of Engineering)*

*Former Faculty, Tufts University School of Medicine, Boston, MA, USA*

*Room# FW4TF3, Mechanical Engineering Building*

*Shahbad Daulatpur, Bawana Road, Delhi 110042; Phone: +91- 9818898622*

*Email: [pravirkumar@dtu.ac.in](mailto:pravirkumar@dtu.ac.in); [kpravir@gmail.com](mailto:kpravir@gmail.com)*

*<https://www.ncbi.nlm.nih.gov/myncbi/1DW465XG9bp5p/bibliography/public/>*

*<https://scholar.google.co.in/citations?user=WVLI4i4AAAAJ&hl=en>*

**ORCID ID:** 0000-0001-7444-2344; **Scopus ID:** 14831447800; **ISI Research ID:** B-2164-2015

SUPPLEMENTARY FIGURES

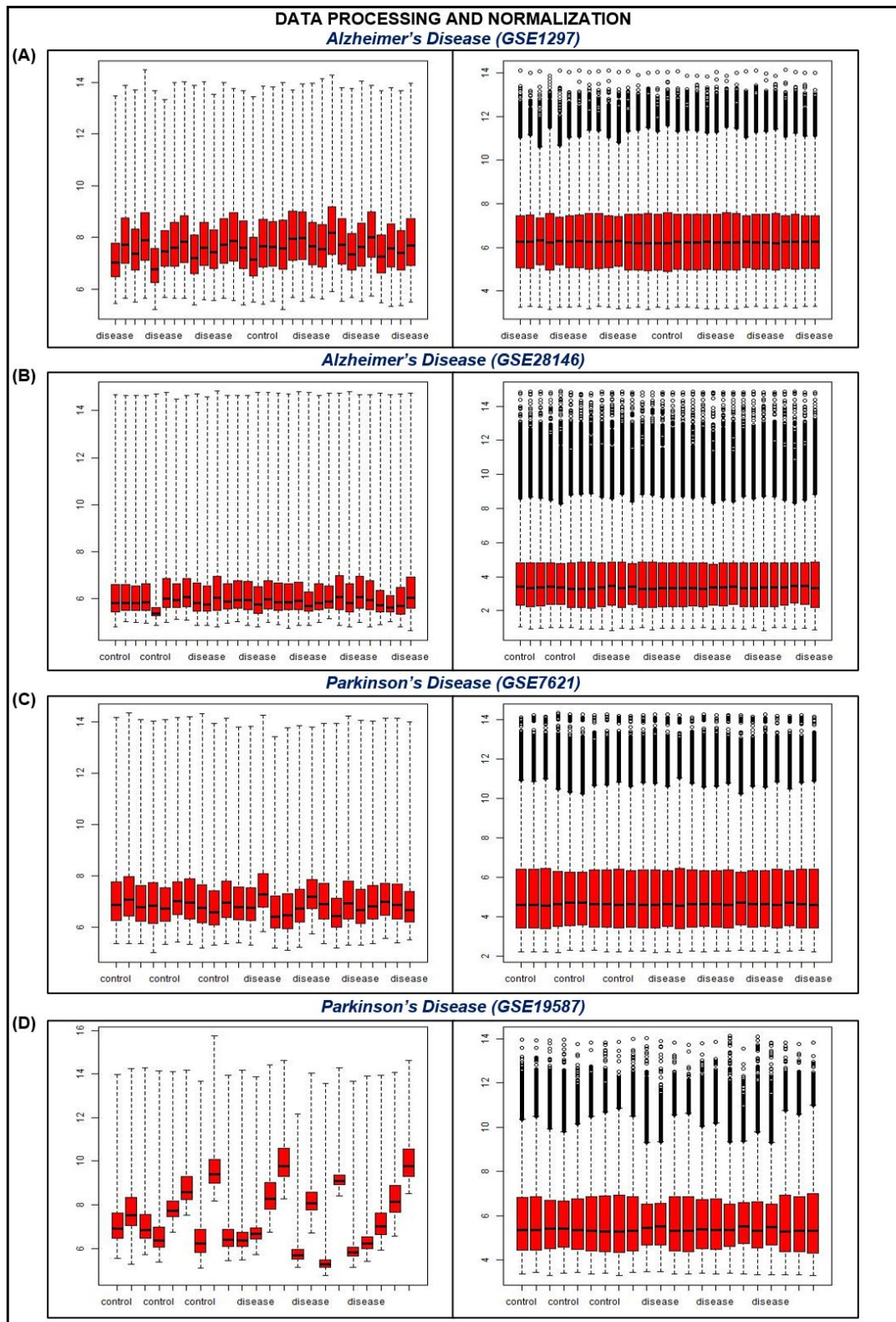
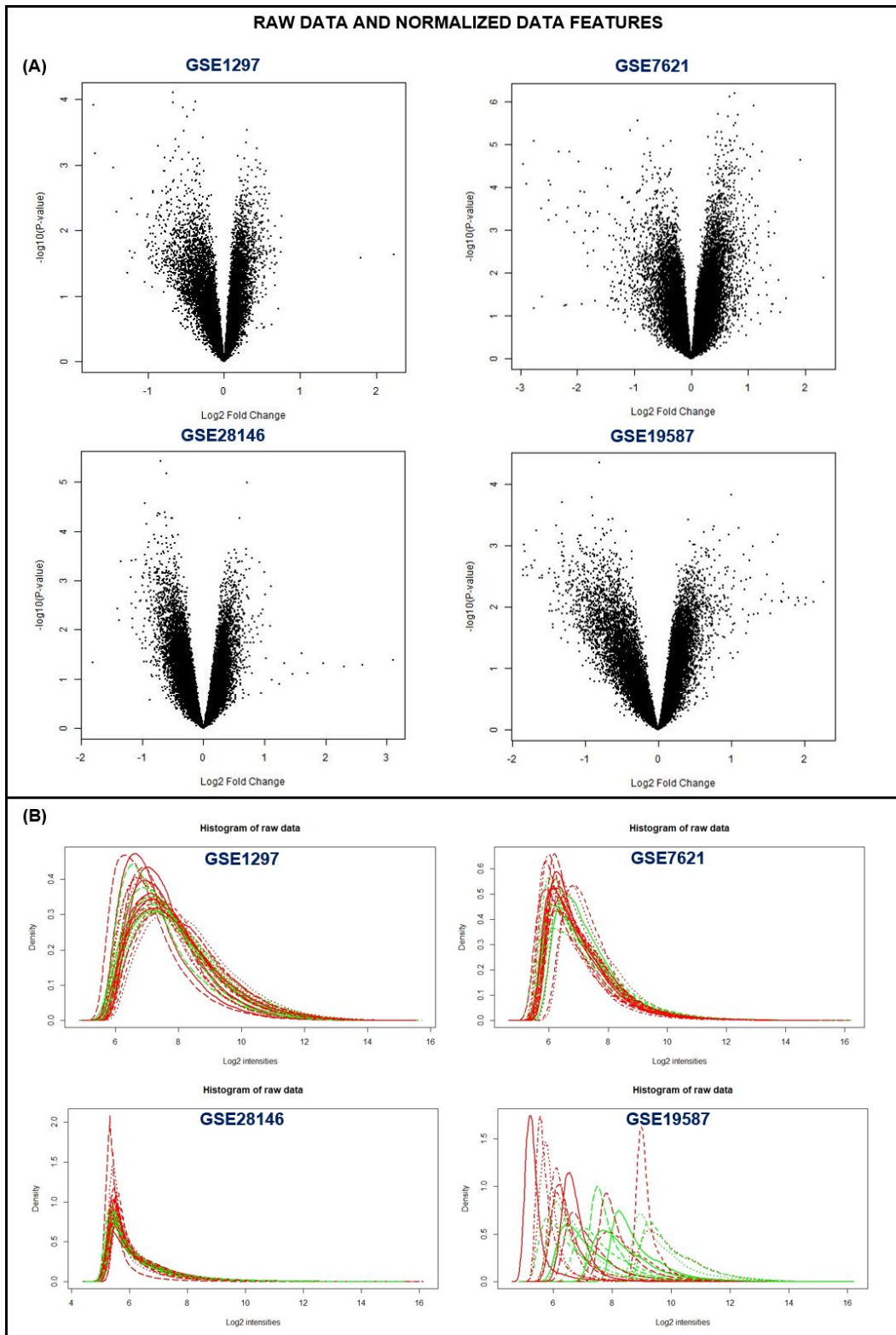


Figure S1: Box plots of Alzheimer's disease (GSE1297 and GSE28146) and Parkinson's disease (GSE7621 and GSE19587) before and after normalization of microarray datasets.



**Figure S2: (A) Volcano plots of publicly available microarray datasets for GSE1297, GSE28146, GSE7621, and GSE19587 (B) histograms of microarray datasets of Alzheimer's disease (GSE1297 and GSE28146) and Parkinson's disease (GSE7621 and GSE19587).**

RELATIVE EXPRESSION OF GENES WITH RESPECT TO HISTONE ACETYLATION

Genes	CDC42	TUBB4B	CD44	FGFR1	NUMA1	NFIA	INPP5D	NUP93	USP5	ARHGEF9	MYO5A
H2AK5	0	0	0	0.091	0	0	0	0.178	0.178	0	0
H2BK5	0.393	0	0	0	0.393	0	0	0.393	0	0.393	0.393
H2BK12	0	0	0.314	0.239	0.314	0	0	0.135	0.314	0	0.314
H2BK15	0	0	0.2	0.153	0.2	0	0	0.152	0.2	0	0.2
H2BK20	0	0	0.0965	0.096	0	0	0	0	0	0.096	0
H2BK120	0.348	0	0.348	0.174	0.174	0	0	0.347	0.174	0.174	0.174
H3K4	0.337	0	0.202	0.282	0.282	0	0	0.282	0.282	0.282	0.282
H3K9	0.584	0.239	0.252	0.269	0	0.584	0.212	0.251	0.584	0	0.584
H3K14	0.177	0.177	0.403	0	0	0	0	0.403	0.177	0.177	0.403
H3K18	0.366	0	0.484	0	0.484	0.439	0	0.484	0.484	0.484	0.484
H3K23	0	0	0	0	0.171	0	0.171	0.171	0.171	0	0.194
H3K27	0.513	0.234	0	0.236	0.294	0.294	0.513	0.513	0.513	0.513	0.513
H3K56	0	0.387	0.29	0	0.387	0.289	0	0.387	0.289	0.3871	0.387
H4K5	0.485	0.485	0.262	0.485	0.485	0.485	0	0.485	0.485	0.485	0.485
H4K8	0.516	0	0	0.516	0.516	0	0	0.229	0.516	0	0.516
H4K91	0.295	0	0.236	0.295	0.236	0.295	0.236	0.295	0.236	0.295	0

Figure S3: Relative expression of different HUB genes in the pathogenesis of AD and PD with respect to histone acetylation at particular lysine residue. Color scale goes from yellow (smaller values) to green (larger values).

SUPPLEMENTARY TABLES

Table S1: List of HUB genes identified in different PPI networks and lists of common proteins that were found in the cluster of all three PPI networks, such as AD, PD, and AD-PD union network.

Rank	HUB Genes	Alzheimer's Disease	Parkinson's Disease	Merged Network (Intersection)	Frequency
<b>Alzheimer's Disease PPI Network</b>					
1	SNAP25	Cluster 1		Cluster 1	2
2	CDC42	Cluster 2	Cluster 1	Cluster 5	3
3	GRIA2	Cluster 1		Cluster 1	2
4	GRM5	Cluster 1		Cluster 1	2
5	GRIA1	Cluster 1		Cluster 1	2
6	CAMK2A	Cluster 1		Cluster 1	2
7	GABRG2	Cluster 1		Cluster 1	2
8	SYT1	Cluster 1		Cluster 1	2
9	NRXN1	Cluster 1		Cluster 2	2
10	SYP	Cluster 1		Cluster 1	2
11	GFAP	Cluster 1		Cluster 1	2
12	CALM1	Cluster 1		Cluster 1	2
13	GAP43	Cluster 1		Cluster 1	2
14	SLC17A7	Cluster 1		Cluster 1	2
15	PLCB1	Cluster 1		Cluster 1	2
<b>Parkinson's Disease PPI Network</b>					
1	TP53		Cluster 1	Cluster 3	2
2	ACTB		Cluster 1	Cluster 3	2
3	HRAS		Cluster 1	Cluster 3	2
4	CDC42	Cluster 2	Cluster 1	Cluster 5	3
5	CAT		Cluster 1	Cluster 3	2
6	EEF2		Cluster 1	Cluster 3	2

7	PRKACA		Cluster 1	Cluster 3	2
8	ACTG1		Cluster 1	Cluster 3	2
9	TUBB		Cluster 1	Cluster 3	2
10	MDM2		Cluster 1	Cluster 3	2
11	GART		Cluster 1	Cluster 3	2
12	TUBB4B	Cluster 3	Cluster 1	Cluster 3	3
13	SMARCA4		Cluster 1	Cluster 3	2
14	TUFM		Cluster 1	Cluster 3	2
15	EIF4E		Cluster 1	Cluster 3	2
<b>AD-PD Union PPI Network</b>					
1	CDC42	Cluster 2	Cluster 1	Cluster 5	3
2	TP53		Cluster 1	Cluster 3	2
3	SNAP25	Cluster 1		Cluster 1	2
4	GRIA2	Cluster 1		Cluster 1	2
5	GRM5	Cluster 1		Cluster 1	2
6	GRIA1	Cluster 1		Cluster 1	2
7	CAMK2A	Cluster 1		Cluster 1	2
8	GABRG2	Cluster 1		Cluster 1	2
9	CD44	Cluster 3	Cluster 1	Cluster 1	3
10	NRXN1	Cluster 1		Cluster 1	2
11	SYT1	Cluster 1		Cluster 1	2
12	SYP	Cluster 1		Cluster 1	2
13	GFAP	Cluster 1		Cluster 1	2
14	CALM1	Cluster 4		Cluster 1	2
15	ACTB		Cluster 1	Cluster 3	2
<b>AD-PD Intersection PPI Network</b>					
1	CDC42	Cluster 2	Cluster 1	Cluster 5	3
2	CD44	Cluster 3	Cluster 1	Cluster 1	3
3	FGFR1	Cluster 4	Cluster 1	Cluster 3	3
4	MYO5A	Cluster 4	Cluster 1	Cluster 1	3
5	NUMA1	Cluster 3	Cluster 1	Cluster 3	3
6	TUBB4B	Cluster 3	Cluster 1	Cluster 3	3
7	ARHGEF9	Cluster 1	Cluster 1	Cluster 1	3
8	CDS2				0
9	KATNB1		Cluster 1	Cluster 3	2
10	USP5	Cluster 1	Cluster 3	Cluster 1	3
11	PKP4	Cluster 3		Cluster 3	2
12	NFIA	Cluster 1	Cluster 2	Cluster 1	3
13	APLNR	Cluster 2		Cluster 3	2
14	INPP5D	Cluster 3	Cluster 1	Cluster 3	3
15	NUP93	Cluster 2	Cluster 2	Cluster 2	3

Table S2: Prediction of putative lysine residues and HDAC enzymes in the CREB1

<b>MuSite Deep / Deep-PLA</b>				
Residue	Score	Confidence	Type	FPR (%)
91	0.25	Low	SIRT7	14.7
94	0.166	Low	SIRT7	13.26
123	0.12	Low	HDAC6	2.74
136	0.309	Moderate	SIRT1	0.03
155	0.162	Low	SIRT1	3.35
285	0.129	Low	SIRT7	9.68
292	0.139	Low	HDAC1	4.96
303	0.114	Low	SIRT7	12.54
304	0.133	Low	SIRT7	12.9
305	0.185	Low	SIRT7	13.98
309	0.29	Moderate	----	----
323	0.318	Moderate	----	----
330	0.557	High	HDAC2	10.67
333	0.288	Moderate	SIRT6	6.92



339	0.199	Low	SIRT6	2.31
<b>PSKAcePred / Deep-PLA</b>				
Residue	Score	Confidence	Type	FPR (%)
91	0.692	Moderate	SIRT7	14.7
94	0.872	High	SIRT7	13.26
136	0.659	Moderate	SIRT1	0.03
292	0.737	High	HDAC1	3.35
303	0.856	High	SIRT7	12.54
304	0.924	High	SIRT7	12.9
305	0.653	Moderate	SIRT7	13.98
309	0.994	High	----	----

Table S3: Prediction of putative lysine residues and HDAC enzymes in the HINFP

<b>MuSite Deep / Deep-PLA</b>				
Residue	Score	Confidence	Type	FPR (%)
6	0.318	Moderate	HDAC6	2.74
10	0.164	Low	HDAC6	3.84
31	0.163	Low	SIRT1	6.51
94	0.176	Low	----	----
96	0.159	Low	----	----
164	0.206	Low	SIRT3	14.56
174	0.191	Low	SIRT7	13.26
181	0.182	Low	----	----
185	0.177	Low	SIRT3	14.94
197	0.168	Low	----	----
213	0.311	Moderate	----	----
236	0.189	Low	----	----
256	0.191	Low	----	----
285	0.174	Low	----	----
294	0.186	Low	----	----
301	0.21	Low	----	----
330	0.42	Moderate	HDAC6	3.84
335	0.198	Low	HDAC6	2.74
346	0.178	Low	HDAC6	6.3
352	0.228	Low	HDAC3	8.6
366	0.175	Low	HDAC1	5.8
367	0.157	Low	HDAC1	4.23
371	0.354	Moderate	SIRT1	7.01
382	0.269	Moderate	HDAC1	6.53
439	0.153	Low	SIRT2	4.77
446	0.11	Low	SIRT2	0.95
504	0.154	Low	SIRT1	6
<b>PSKAcePred / Deep-PLA</b>				
Residue	Score	Confidence	Type	FPR (%)
31	0.73	High	SIRT1	6.51

96	0.766	High	----	----
174	0.779	High	SIRT7	13.26
185	0.591	Moderate	SIRT3	14.94
197	0.65	Moderate	----	----
213	0.616	Moderate	----	----
236	0.522	Moderate	----	----
330	0.726	High	HDAC6	3.84
335	0.93	High	HDAC6	2.74
352	0.5	Moderate	HDAC3	8.6
366	0.629	Moderate	HDAC1	5.8
367	0.904	High	HDAC1	4.23
371	0.911	High	SIRT1	7.01
446	0.719	High	SIRT2	0.95
504	0.506	Moderate	SIRT1	6

Table S4: Secondary structure of the protein acetylation sites predicted by PSIPRED: protein structure prediction server

CREB1			HNIFP					
Residue	Structure Prediction (PSIPRED)	Score (10)	Residue	Structure Prediction (PSIPRED)	Score (10)	Residue	Structure Prediction (PSIPRED)	Score (10)
91	Coil	4	6	Coil	9	301	Helix	9
94	Strand	3	10	Coil	8	330	Helix	3
123	Helix	8	31	Helix	6	335	Coil	5
136	Helix	9	94	Coil	8	346	Strand	4
155	Coil	5	96	Coil	1	352	Coil	9
285	Helix	9	164	Coil	8	366	Helix	3
292	Helix	9	174	Coil	9	367	Coil	1
303	Helix	9	181	Coil	4	371	Coil	9
304	Helix	9	185	Coil	1	382	Coil	4
305	Helix	9	197	Coil	9	439	Helix	6
309	Helix	9	213	Coil	6	446	Coil	9
323	Helix	9	236	Coil	8	504	Helix	9
330	Helix	9	256	Coil	8			
333	Helix	9	285	Coil	5			
339	Coil	0	294	Strand	1			