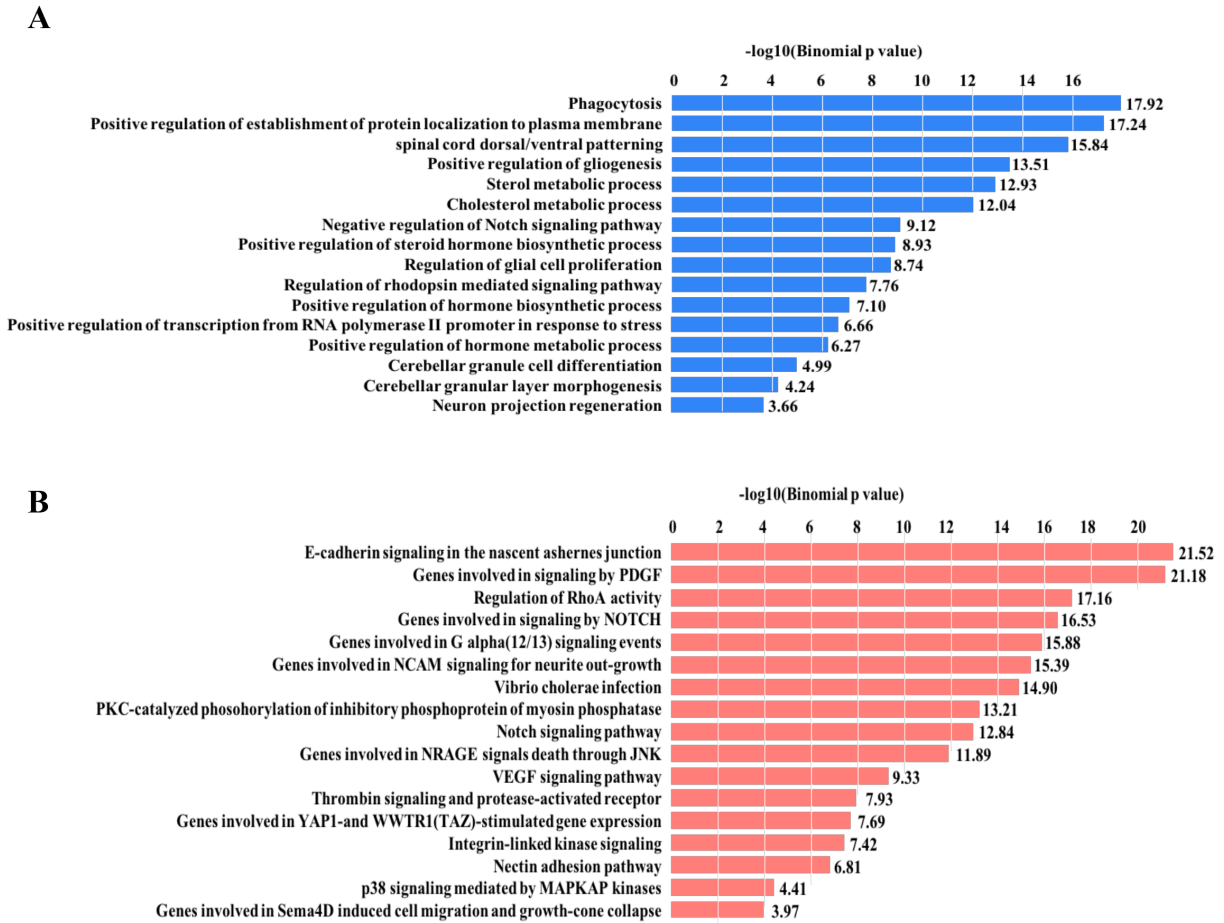


Supplementary Materials

Ethnicity-specific and overlapping alterations of brain hydroxymethylome in Alzheimer's disease

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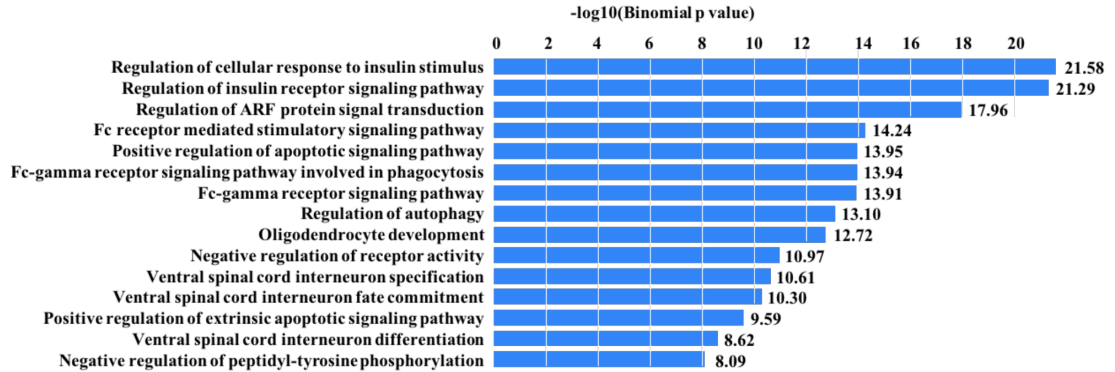
Supplementary Figure 1. GO and MSigDB pathway analysis of overlapped DhMRs. A. GO analysis of Chinese-Caucasian DhMRs overlap. B. MSigDB pathway analysis of the overlapping Chinese-Caucasian DhMRs. Blue and red bars represent $-\log_{10}$ (Binomial p-value).



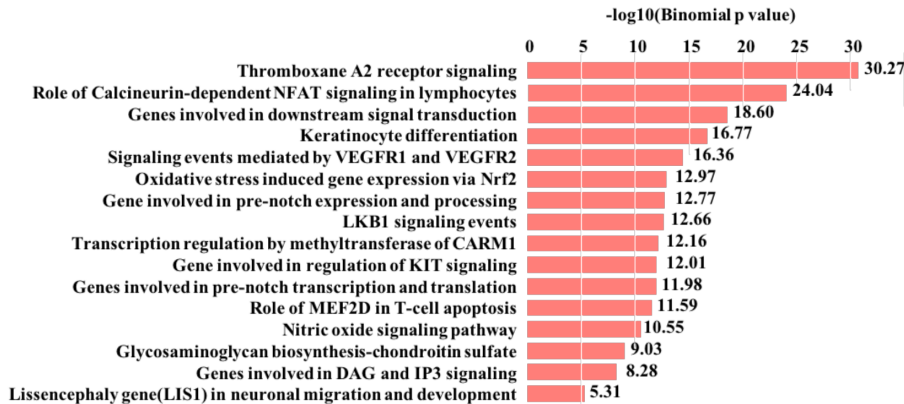
Supplementary Figure 2. GO and MSigDB pathway analysis of Chinese specific DhMRs. A.

GO analysis of Chinese specific DhMRs. **B.** MSigDB pathway analysis of Chinese specific DhMRs. Blue and red bars represent $-\log_{10}$ (Binomial p-value).

A



B



Supplementary Table 1. Demographic data of AD patients and controls

	AD	Control	<i>P</i> value
Number of subjects	5	5	
Gender-male/female	1/4	2/3	0.49
Age at death (yr)	87.4±7.9	84.0±3.5	0.403
PMI(hr)	4.6±1.2	5.7±2.0	0.305
Years in storage (yr)	1.2±0.4	1.0±0.4	0.484
Braak stage	V/VI	I/II	

Abbreviations: yr, year; hr, hour.

Supplementary Table 2. Details of AD patients and controls included in this study

	ID	Gender	Age at death (yr)	PMI (hr)	Years in storage (yr)	Braak stage	Diseases
AD	PTB048	F	82	4	1.5	V/VI	Chronic pulmonary emphysema, AD
	PTB050	F	80	4.5	1.4	V/VI	Coronary heart disease, AD
	PTB051	M	89	5	1.4	V/VI	Arrhythmias, AD
	PTB078	F	86	6.33	0.75	V/VI	AD
	PTB083	F	100	3	0.7	V/VI	Hypertension, AD
Control	PTB044	F	85	7.5	1.5	0	Hepatocellular cancer, Hypertension
	PTB055	F	84	5	1.25	I/II	Coronary heart disease
	PTB077	M	87	3.5	0.75	0	Colon cancer
	PTB080	F	86	4.5	0.75	V/VI	Diabetes, Coronary heart disease, Cerebral infarction
	PTB087	M	78	8	0.6	0	Diabetes, Liver Cirrhosis

Abbreviations: F, female; M, male; yr, year; PMI, postmortem interval; hr, hour.

Supplementary Table 3. Top 10 binding motifs identified in the DhMRs

Group	Motif Name	Consensus	P-value	Log P-value	q-value (Benjamini)	# of Target Sequences with Motif (of 7643)	% of Target Sequences with Motif	# of Background Sequences with Motif (of 41649)	% of Background Sequences with Motif
Chinese 16,165 DhMRs	c-Myc	VVCCACGTGG	1.00E-36	-8.52E+01	0	12471	79.92%	25799.8	75.62%
	bHLHE40	KCACGTGMCN	1.00E-34	-8.04E+01	0	9144	58.60%	18308.1	53.66%
	HIF-2a	GCACGTACCC	1.00E-33	-7.72E+01	0	9994	64.05%	20231.1	59.30%
	HIF-1a	TACGTGCV	1.00E-32	-7.46E+01	0	8275	53.03%	16462.3	48.25%
	Max	RCCACGTGGYYN	1.00E-31	-7.20E+01	0	13429	86.06%	28181.6	82.60%
	c-Myc	VCCACGTG	1.00E-30	-7.08E+01	0	11098	71.12%	22788.4	66.79%
	CLOCK	GHCACGTG	1.00E-29	-6.78E+01	0	12265	78.60%	25492.1	74.72%
	USF1	SGTCACGTGR	1.00E-26	-6.09E+01	0	11500	73.70%	23815.8	69.81%
	n-Myc	VRCCACGTGG	1.00E-23	-5.32E+01	0	13570	86.96%	28696.7	84.11%
Arnt:Ahr	TBGCACGCAA	1.00E-21	-4.87E+01	0	12490	80.04%	26227.7	76.87%	
Chinese-s pecific 9,665 DhMRs	c-Myc/m ES	VVCCACGTGG	1.00E-23	-5.44E+01	0	7226	78.09%	29795.9	73.54%
	c-Myc/L NCAP	VCCACGTG	1.00E-18	-4.27E+01	0	6343	68.54%	25992.1	64.15%
	bHLHE40	KCACGTGMCN	1.00E-17	-4.14E+01	0	5196	56.15%	20910.2	51.61%
	CLOCK	GHCACGTG	1.00E-16	-3.89E+01	0	7111	76.84%	29575.1	72.99%
	Max	RCCACGTGGYYN	1.00E-16	-3.74E+01	0	7825	84.56%	32930.8	81.27%

Supplementary Table 4. DEGs whose promoter regions binds to HIF-1 α / HIF-2 α

	MUC2	LRTOMT	NFE2L2	MARCH10	TRIM35
	STAC3	MIR3165	ERLIN1	MIR548W	NDUFA13
	CPXM1	NUMA1	SRMS	TANC2	CHST3
	C19orf57	PDCD1	CCSAP	DOC2GP	TEX29
	TRAIP	SSUH2	CRABP1	TCF20	RIPK4
	CEBPE	DLK1	ACTR1A	CYB561D2	CDK5
	FAM180A	URI1	RPS21	NPRL2	LINC00222
78 DEGs whose	TNNI2	LOC200772	DUOXA1	FKBP1A	DNAJB2
promoter regions	ZNF890P	MIER3	DUOXA2	FKBP1A-SDCBP2	ABCG8
binds to HIF-1 α	LRRC47	SETD9	HSPA8	SDCBP2	LOC284751
	LOC147093	LINC00163	DNHD1	SDCBP2-AS1	SDHAF1
	MUC1	IGFLR1	LOC100130348	KLF6	LOC151174
	ZNF786	ZNF648	ZFPL1	C1QTNF8	MAF1
	ANAPC15	CDH26	PUM1	ELFN1	RAB11FIP5
	IL18BP	TRA2B	SNORD103B	GLI3	
	LAMTOR1	MIR3128	SNORD85	ATP5SL	

	RAX2	NUMA1	NFE2L2	PNLIPRP2	RNF26
	C12orf43	ENPP7	RAPGEF5	PUM1	GLI3
	PBX4	RFX1	MIR5088	SNORD103B	TMEM115
	HIPK4	PDCD1	PRMT1	SNORD85	TRIM35
	RAPSN	PRR12	SRMS	10-Mar	NDUFA13
	FAM180A	SSUH2	ALOX15B	MIR548W	CHST3
	TNNI2	DLK1	HIST1H4H	TANC2	TEX29
	UTS2R	URI1	CRABP1	DOC2GP	PTTG1IP
90 DEGs whose	ZNF890P	SP7	ACTR1A	DCAF5	CDIPT
promoter regions	SLC6A19	RHOG	TRPM5	PSAP	CDK5
binds to HIF-2 α	LOC147093	RAC2	RPS21	UBR4	DNAJB2
	MUC1	LINC00163	DUOXA1	TCF20	PRDX5
	MUC5B	EVPL	DUOXA2	CYB561D2	ABCG8
	ANAPC15	ZNF648	LRCOL1	NPRL2	LOC284751
	IL18BP	GPR45	HSPA8	PDZRN3	SDHAF1
	LAMTOR1	CDH26	DNHD1	KLF6	LOC151174
	LRTOMT	TRA2B	LOC100130348	SSR2	MAF1
	MIR3165	MIR3128	ZFPL1	ELFN1	MT1DP

	FAM180A	PDCD1	CRABP1	SNORD85	TRIM35
	TNNI2	SSUH2	ACTR1A	MARCH10	NDUFA13
	ZNF890P	DLK1	RPS21	MIR548W	CHST3
	LOC147093	URI1	DUOXA1	TANC2	TEX29
Overlapped 55	MUC1	LINC00163	DUOXA2	DOC2GP	CDK5
DEGs	ANAPC15	ZNF648	HSPA8	TCF20	DNAJB2
	IL18BP	CDH26	DNHD1	CYB561D2	ABCG8
	LAMTOR1	TRA2B	LOC100130348	NPRL2	LOC284751
	LRTOMT	MIR3128	ZFPL1	KLF6	SDHAF1
	MIR3165	NFE2L2	PUM1	ELFN1	LOC151174
	NUMA1	SRMS	SNORD103B	GLI3	MAF1

Supplementary Table 5. Number of DhMRs by DSS and overlaps with DESeq2 results.

	# of DhMRs identified by DSS	# of DhMRs overlapped with DESeq2 results	Percentage of overlaps
Chinese cohort	16165	14201	88%
Chinese cohort overlapped with Caucasian cohort	6500	6147	95%