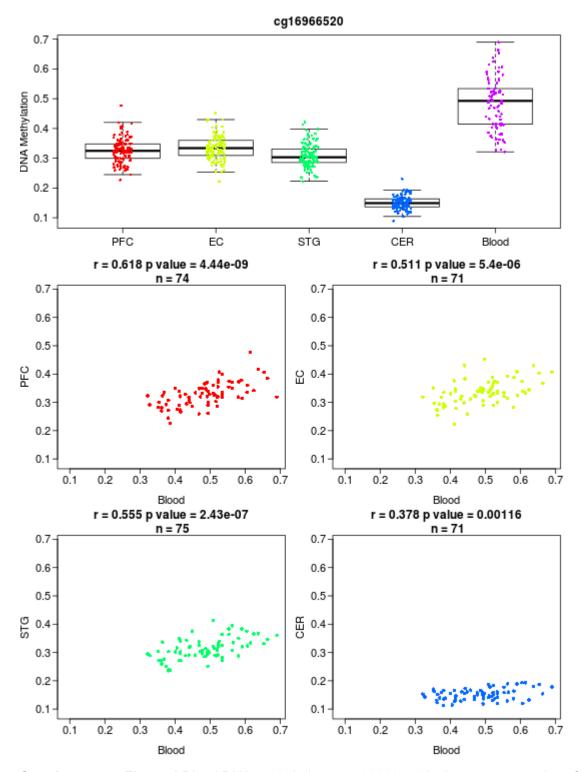
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Supplementary Figure 1 Blood DNA methylation at cg16966520 in the promoter region of the *EIF2D* gene is significantly associated with brain DNA methylation in the prefrontal cortex (PFC), entorhinal cortex (EC), superior temporal gyrus (STC), and cerebellum (CER). These results were obtained from the Blood Brain DNA Methylation Comparison Tool (https://epigenetics.essex.ac.uk/bloodbrain/).

MIAMI-AD About Genome-wide Query Gene Query	CpG Query Epigenetic Clock Query Downlo	oad Contact & Contribute		
Tour	Α	CpG Query		
Genome Version	Datasets Display Data Display Refresh Lownload Tables	ny Plot		
ligio	Show 10 + entries			Search:
CpGs Input Method Provide a list of CpGs	Dataset	Description	t Author t	Year PMID
 Upload a file Paste a list of comma-separated CpGs 		lood DNAm associated with Alzheimer's disease Blood DNAm associated with chronological age	Silva McCartney	2022 35982059 2020 31892350
cg13270055 Example Input	Showing 1 to 2 of 2 entries			Previous 1 Next
Phenotype	Show 10 ¢ entries			Search:
 ✓ Aging → MCI → Biomarkers → Sex ✓ Dementia 	CpG chr pos cg13270055 chr22 3696049		RefGene_Group mQTL Body mQTL	Blood-Brain comparison : Blood-Brain

Showing 1 to 1 of 1 entries

Show 10 🗢 entries Search:										
СрС	dataset 🕴	phenotype	sex_specific 🕴	sample_group	statistics	direction 🕴	statistics_value	pValue 🕴		
cg13270055	SIC	AD	No	ADNI + AIBL	OR for AD (meta- analysis)	-	0.967	1.65e-06		
cg13270055	SIC	AD	No	AIBL	OR for AD	-	0.97	9.79e-04		
cg13270055	SIC	AD	No	ADNI	OR for AD	-	0.964	4.58e- 04		
cg13270055	MCA	Aging	No	Generation Scotland, Discovery	estimate for age effect	+	0.008	1.89e-20		
cg13270055	MCA	Aging	No	Generation Scotland, Replication	estimate for age effect	+	0.006	6.89e-20		

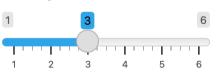
Showing 1 to 5 of 5 entries



Datasets Display Data Display Plot

Forest Plot

Plots per row



cg13270055 SIC (association with AD)

cg13270055 MCA (association with age)

Previous 1 Next

Previous 1 Next

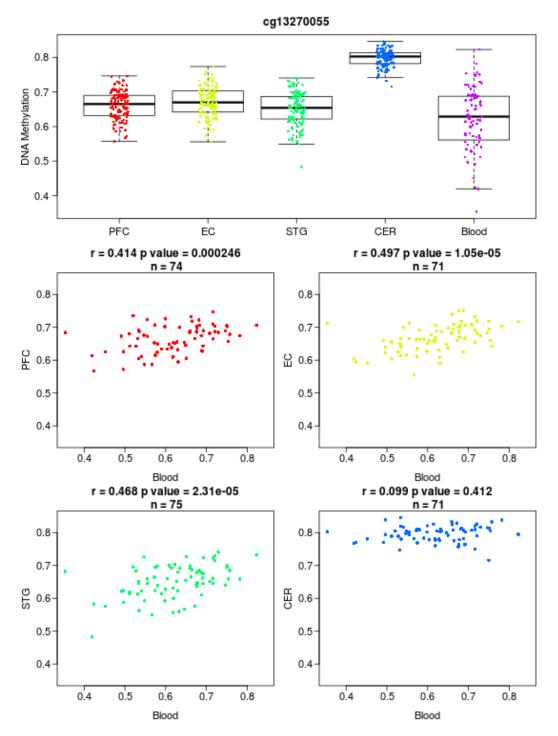
sample_group	Odds Ratio
	÷ 1



sample_group

Supplementary Figure 2 DNA methylation at cg13270055 located on the *CACNG2* gene increases with age ($P_{\text{discovery}} = 1.89 \times 10^{-20}$, $P_{\text{replication}} = 6.89 \times 10^{-20}$), but decreases in the blood samples of Alzheimer's subjects ($P_{\text{meta-analysis}} = 1.65 \times 10^{-6}$, $P_{\text{AIBL}} = 9.79 \times 10^{-4}$, $P_{\text{ADNI}} = 4.58 \times 10^{-4}$). The summary statistics are shown under (**A**) Display Data tab, and the forest plots are shown under (**B**) Display Plot tab.

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Supplementary Figure 3 Blood DNA methylation at cg13270055 located on the *CACNG2* gene is significantly associated with brain DNA methylation in the prefrontal cortex (PFC), entorhinal cortex (EC), superior temporal gyrus (STC), and cerebellum (CER). These results were obtained from the Blood Brain DNA Methylation Comparison Tool (https://epigenetics.essex.ac.uk/bloodbrain/).

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Datasets Dis	play Data Display Plot							
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select a different	set of CpGs level: double click on Threshold							
how 10 • entrie							Search:	
Dataset	Description	Author	Year	PMID	Source	Metric	Filter	Threshold
SIF	Blood DNAm associated with Alzheimer's disease in females	s Silva	2022	36109771	ADNI + AIBL	 pValue FDR 	● < than ○ > than	0.00001
SIM	Blood DNAm associated with Alzheimer's disease in males	Silva	2022	36109771	ADNI + AIBL	pValueFDR	● < than ○ > than	0.00001
nowing 1 to 2 of 2 e	ntries						Pre	vious 1 Nex
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CpG chr	pos : Illumina : dataset : sample_group	phenotype	sex_spec	ific stati	stics direc	tion st	atistics_value	pValue
	No significant CpGs There are no CpGs that me	eet all of the threshold o	utoffs. Pleas	e adjust the thre	sholds or the data	sets selected.		
howing 0 to 0 of 0 e	ntries							Previous Nex

B. Selecting female-specific CpGs associated with AD

Datasets	Display	Data Di	splay Plot									
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ow 10 + er	ntries										Search:	
Dataset			Description			Author	Year	PMID	Source	Metric	: Filter :	Threshold
IF	Blo	ood DNAm as	sociated with Alzhein	ner's disease	in females	Silva	2022	36109771	ADNI + AIBL	 pValue FDR 	● < than ○ > than	0.00001
IM	B	lood DNAm a	ssociated with Alzhei	mer's diseas	e in males	Silva	2022	36109771	ADNI + AIBL	 pValue FDR 	○ < than ● > than	0.05
Annotated		Explore To	op 10 CpGs									
how 10 ¢											Search:	
CpG	chr	pos	Illumina	dataset	sample_group	phenotype	sex_sp	ecific	statistics	direction	statistics_value	pValu
cg18020072	chr6	31590640	SNORA38;BAT2	SIF	ADNI + AIBL	AD	Yes, fe	males	OR for AD (meta- analysis)	+	1.328	3.02e
cg18020072	chr6	31590640	SNORA38;BAT2	SIM	ADNI + AIBL	AD	Yes, r	males	OR for AD (meta- analysis)	+	1.051	2.49e
cg24276069	chr1	45243927	RPS8;SNORD38B	SIF	ADNI + AIBL	AD	Yes, fe	emales	OR for AD (meta- analysis)	+	1.233	9.62e
cg24276069	chr1	45243927	RPS8;SNORD38B	SIM	ADNI + AIBL	AD	Yes, r	males	OR for AD (meta- analysis)	-	0.955	2.08e

C. Selecting male-specific CpGs associated with AD

Genome-wide Query

Datasets	Display I	Data Dis	play Plot									
Refresh	*	Download Tab	oles									
lected D	atasets											
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ataset			Descrip	tion		Author	Year	PMID	Source	Metric	Filter 1	hreshold
F	Blo	od DNAm ass	ociated with A	lzheimer's dis	ease in females	Silva	2022	36109771	ADNI + AIBL	 pValue FDR 	○ < than ● > than	0.05
м				Alzheimer's di	isease in males	Silva	2022	36109771	ADNI + AIBL	 pValue FDR 	● < than ○ > than	0.00001
how 10 •		Explore To	p 10 CpGs								Search:	
Срб	chr	pos	Illumina :	dataset	sample_group	phenotype	sex_specific	÷ (1	statistics	direction	statistics_valu	e pValue
cg02672643	chr11	110790527		SIF	ADNI + AIBL	AD	Yes, female	s OR for	AD (meta-analysis)	+	1.049	2.05e-0
cg02672643	chr11	110790527		SIM	ADNI + AIBL	AD	Yes, males	OR for	AD (meta-analysis)	+	1.19	1.62e-0
cg15757041	chr16	5115938	C16orf89	SIF	ADNI + AIBL	AD	Yes, female	s OR for	AD (meta-analysis)	+	1.058	4.70e-0
cg15757041	chr16	5115938	C16orf89	SIM	ADNI + AIBL	AD	Yes, males	OR for	AD (meta-analysis)		0.677	3.69e-0
cg15281611	chr1	54040884	GLIS1	SIF	ADNI + AIBL	AD	Yes, female	s OR for	AD (meta-analysis)	+	1.058	1.07e-0
cg15281611	chr1	54040884	GLIS1	SIM	ADNI + AIBL	AD	Yes, males	OR for	AD (meta-analysis)	+	1.181	6.66e-0
cg03827739	chr10	75401754	MYOZ1	SIF	ADNI + AIBL	AD	Yes, female	s OR for	AD (meta-analysis)	+	1.038	3.93e-0
cg03827739	chr10	75401754	MYOZ1	SIM	ADNI + AIBL	AD	Yes, males	OR for	AD (meta-analysis)	÷	1.199	8.03e-0

Supplementary Figure 4 Using Genome-wide Query to perform sex-specific analysis.

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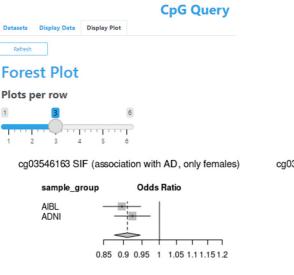
CpG Query

Refresh 🛃 Download Tables					
elected Datasets				Search:	
ataset	Description		Author	Year	PMID
IF	Blood DNAm associated with Alzheimer's disease in female	;	Silva	2022	36109771
м	Blood DNAm associated with Alzheimer's disease in males		Silva 2022 3610		
wing 1 to 2 of 2 entries				F	Previous 1 N
notations					
ow 10 ¢ entries				Search:	
CpG chr pos	Illumina Relation_to_Island	RefGene_Group	mQTL	Blood-Brain	comparison
cq03546163 chr6 35654363	FKBP5;FKBP5;FKBP5;FKBP5 N_Shore	5'UTR;5'UTR;5'UTR;5'UTR	mQTL	Bloor	d-Brain

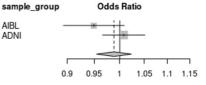
B Results under "Display Data" tab

ndividual Datasets how 10 • entries Search:									
CpG	dataset 🙏	sample_group	phenotype	sex_specific	statistics	direction	statistics_value	pValue	
cg03546163	SIF	ADNI + AIBL	AD	Yes, females	OR for AD (meta-analysis)		0.911	1.23e-06	
cg03546163	SIF	AIBL	AD	Yes, females	OR for AD		0.896	8.86e-05	
cg03546163	SIF	ADNI	AD	Yes, females	OR for AD	÷	0.924	3.02e-03	
cg03546163	SIM	ADNI + AIBL	AD	Yes, males	OR for AD (meta-analysis)		0.988	5.11e-01	
cg03546163	SIM	AIBL	AD	Yes, males	OR for AD	÷	0.95	9.45e-02	
cg03546163	SIM	ADNI	AD	Yes, males	OR for AD	+	1.008	7.16e-01	

C Results under the "Display Plot" tab



cg03546163 SIM (association with AD, only males)



Supplementary Figure 5 The CpG Query Tool can be used to explore details of DNA methylation at female-specific CpG cg03546163 associated with AD.