

Deep learning methods improve polygenic risk analysis and prediction for Alzheimer's disease

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Supplementary Methods

Alzheimer's Disease Neuroimaging Initiative cohort

We obtained genotype and phenotype data from the Alzheimer's Disease Neuroimaging Initiative (ADNI) database (adni.loni.usc.edu). The ADNI, led by Michael W. Weiner, MD, was launched in 2003 as a public-private partnership. It is a 4-stage study that aims to examine the brain's structure and function aided by biomarker and clinical data in people aged 55–90 years from the United States and Canada. For the present study, we included array genotype data obtained from ADNI-1, ADNI-2/GO, and ADNI-3 for analysis. After prefiltering, imputation, and postfiltering, 1,382 subjects (689 patients with Alzheimer's disease [AD] and 693 cognitively normal controls) were retained for downstream analysis. The phenotypes of the ADNI subjects are from the latest diagnostic records (updated January 2021).

National Institute on Aging Alzheimer's Disease Centers cohort

The clinical and neuropathology cores of the 29 National Institute on Aging (NIA)-funded Alzheimer's Disease Centers (ADCs) recruited and evaluated autopsy-confirmed and clinically confirmed patients with AD as well as cognitively normal elderly subjects. We retrieved the genotype and phenotype data of this AD cohort ($N = 6,065$) from the NIH dbGaP (accession number: phs000372.v2.p1). Genotype information was generated from the Illumina Human660W-Quad BeadChip or HumanOmniExpress Array. All autopsied subjects were ≥ 60 years old at death. Dementia in AD was determined according to the DSM-IV criteria or a Clinical Dementia Rating ≥ 1 . Further details can be found in publications arising from the corresponding dbGaP project^{1,2}. After prefiltering, imputation, and postfiltering, 5,692 subjects (3,946 patients with AD and 1,746 cognitively normal controls) were retained for downstream analysis.

Late Onset Alzheimer's Disease Family Study

The Late Onset Alzheimer's Disease (LOAD) Family Study recruited families with 2 or more siblings with late-onset AD as well as age- and ethnicity-matched, unrelated, nondemented controls. Patients with definite AD were diagnosed according to established neuropathological criteria (i.e., CERAD, Braak, Khachaturian, NIA-RI, or other established criteria). Probable AD or possible AD was ascertained according to the NINCDS-ADRDA criteria. Patients with AD with an age of onset or age at diagnosis ≥ 50 years old and normal controls ≥ 50 years old were recruited. We retrieved genotype and phenotype data from the NIH dbGaP (accession number: phs000168.v2.p2). Individual genotypes were generated from the Human 610Quadv1_B Beadchips (Illumina). After prefiltering, imputation, and postfiltering, 4,278 subjects (2,046 patients with AD and 2,232 cognitively normal controls) were retained for downstream analysis. Further details can be found in in publication arising from the corresponding dbGaP project³.

Filtering and imputation for the array datasets

We converted array genotype information from the ADNI, LOAD, and ADC datasets from PLINK to VCF format using VcfCooker (v1.1.1; <https://genome.sph.umich.edu/wiki/VcfCooker>). We applied prefiltering at both the individual and variant level, retaining individuals with a sample call rate $\geq 95\%$ and variants with a genotype call rate $\geq 80\%$ separately for each dataset. We submitted the filtered genotype data to the TOPMed Imputation Server⁴ (<https://imputation.biodatacatalyst.nih.gov>) using the TOPMed Imputation Reference panel (TOPMed r2)⁵ for phasing and imputation in the form of chromosome-separated VCF files generated by Eagle (v2.4)⁶. We performed post-imputation filtering by removing imputed variants with an imputation $r^2 < 0.4$ using the *bcftools filter* function. We further annotated the dbSNP ID (v154) using the *bcftools annotate* function. We retained single nucleotide polymorphisms with matched dbSNP IDs and alleles for subsequent polygenic score analysis. For part of the quality control analysis, we use PLINK to estimate the identity-by-descent (IBD) using variants with MAF > 0.01 and prune by R^2 of 0.2, and excluded suspected duplicated subjects using IBD > 0.90 .

Supplementary Note

For the ADNI dataset, data collection and sharing for this project were funded by the ADNI (National Institutes of Health Grant number: U01-AG024904) and the DoD ADNI (Department of Defense award number: W81XWH12-2-0012). The ADNI is funded by the NIA and the National Institute of Biomedical Imaging and Bioengineering as well as generous contributions from the following organizations: AbbVie; the Alzheimer's Association; the Alzheimer's Drug Discovery Foundation; Araclon Biotech; BioClinica, Inc.; Biogen; Bristol-Myers Squibb Company; CereSpir, Inc.; Cogstate; Eisai, Inc.; Elan Pharmaceuticals, Inc.; Eli Lilly and Company; EuroImmun; F. Hoffmann–La Roche Ltd. and its affiliated company Genentech, Inc.; Fujirebio; GE Healthcare; IXICO, Ltd.; Janssen Alzheimer Immunotherapy Research & Development, LLC; Johnson & Johnson Pharmaceutical Research & Development, LLC; Lumosity; Lundbeck; Merck & Co., Inc.; Meso Scale Diagnostics, LLC; NeuroRx Research; Neurotrack Technologies; Novartis 20 Pharmaceuticals Corporation; Pfizer, Inc.; Piramal Imaging; Servier; Takeda Pharmaceutical Company; and Transition Therapeutics. The Canadian Institutes of Health Research provides funding to support ADNI clinical sites in Canada. Private-sector contributions are facilitated by the Foundation for the National Institutes of Health (www.fnih.org). The grantee organization is the Northern California Institute for Research and Education, and the study is coordinated by the Alzheimer's Therapeutic Research Institute at the University of Southern California. The data generated by the ADNI are disseminated by the Laboratory for Neuro Imaging at the University of Southern California. For the Alzheimer's Disease Genetics Consortium (ADGC) Genome Wide Association Study–NIA Alzheimer's Disease Centers Cohort (i.e., the ADC dataset), funding support for the Alzheimer's Disease Genetics Consortium was provided through the NIA Division of Neuroscience (grant number: U01-AG032984). For the National Institute on Aging–Late Onset Alzheimer's Disease Family Study (i.e., the LOAD dataset), funding support for “the Genetic Consortium for Late Onset Alzheimer's Disease” was provided through the NIA Division of Neuroscience. The Genetic Consortium for Late Onset Alzheimer's Disease includes a genome-wide association study funded as part of the NIA Division of Neuroscience. The Genetic Consortium for Late Onset Alzheimer's Disease assisted with phenotype harmonization and genotype cleaning as well as general study coordination.

Alzheimer's Disease Neuroimaging Initiative

ADNI I, GO, II, and III studies

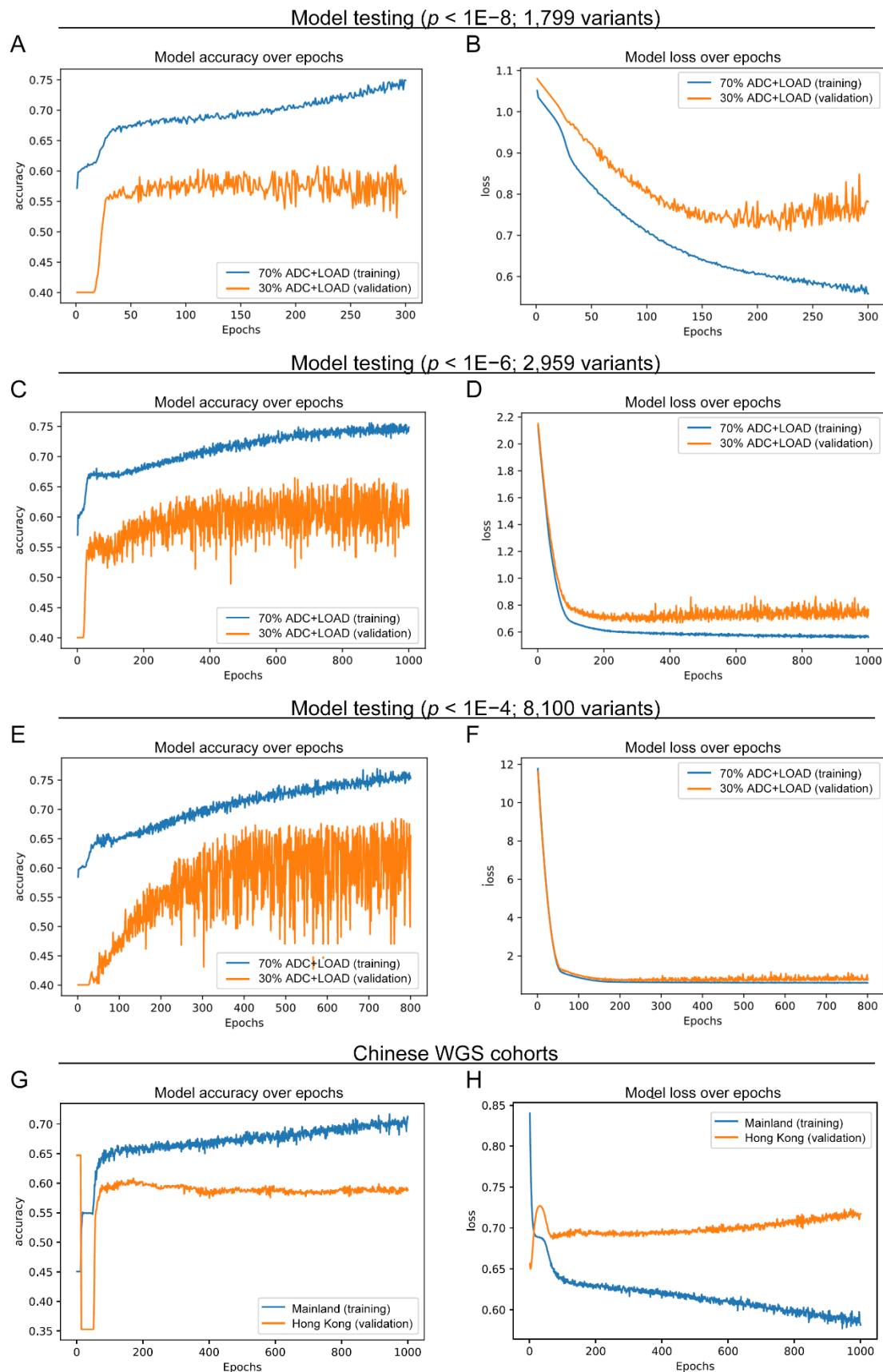
Andrew J. Saykin, Arthur W. Toga, Bret Borowski, Chad Ward, Charles DeCarli, Chet Mathis, Clifford R. Jack, Jr., Danielle Harvey, David Holtzman, David Jones, Devon Gessert, Eli Lilly, Eric M. Reiman, Erin Franklin, Franz Hefti, Greg Sorensen, Gustavo Jimenez, Howard Fillit, Jeff Gunter, Jennifer Salazar, John Hsiao, John Morris, John Q. Trojanowski, Karen Crawford, Scott Neu, Kejal Kantarci, Kelley Faber, Kelly Harless, Kewei Chen, Kwangsik Nho, Laurel Beckett, Lean Thal, Leon Thal, Leslie M. Shaw, Lew Kuller, Li Shen, Lindsey Hergesheimer, Lisa Taylor-Reinwald, M. Marcel Mesulam, Magdalena Korecka, Marc Raichle, Maria, Carrillo, Marilyn Albert, Matt Senjem, Matthew Bernstein, Michael Donohue, Michael Weiner, Michal Figurski, Neil Buckholtz, Nick Fox, Nigel J. Cairns, Norbert Schuff, Norm Foster, Paul Aisen, Paul Thompson, Peter Davies, Peter J. Snyder, Peter Snyder, Prashanthi Vemuri, Richard Frank, Robert A. Koeppe, Robert C. Green, Ronald Petersen, Sarah Walter, Steven Paul, Steven Potkin, Sungeun Kim, Tatiana M. Foroud, Tom Montine, Virginia Lee, William Jagust, William Potter, Yuliana Cabrera, Zaven Khachaturian

ADNI investigators from university and institutes

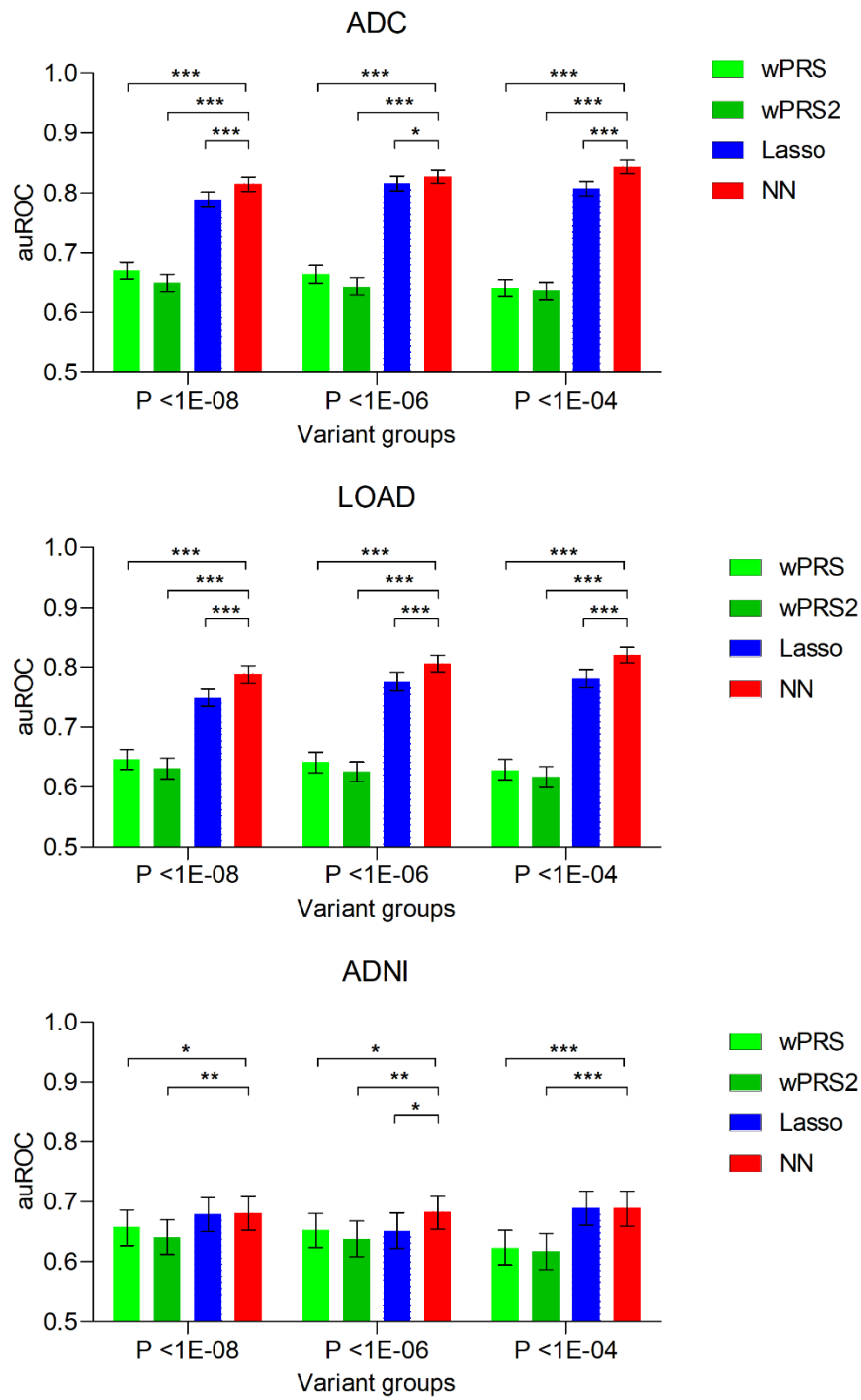
Adam Fleisher, Aimee Pierce, Akiva Mintz, Alan Lerner, Alexander Norbash, Allan I. Levey, Allyson Rosen, Amanda Smith, Anasztasia Ulysse, Andrew E. Budson, Andrew Kertesz, Angela Oliver, Ann Marie Hake, Anna Burke, Antero Sarrael, Anton P. Porsteinsson, Ashley Lamb, Athena Lee, Balebail Ashok Raj, Barton Lane, Beatriz Yanez, Beau Ances, Benita Mudge, Betty Lind, Bojana Stefanovic, Bonnie S. Goldstein, Borna Bonakdarpour, Brandy R. Matthews, Brian R. Ott, Brigid Reynolds, Bruce L. Miller, Bryan M. Spann, Carl Sadowsky, Charles Bernick, Charles D. Smith, Chiadi Onyike, Chris (Chinthaka) Heyn, Chris Hosein, Christi Leach, Christine M. Belden, Christopher H. van Dyck, Christopher M. Clark, Chuang-Kuo Wu, Colleen S. Albers, Connie Brand, Courtney Bodge, Curtis Tatsuoaka, Cynthia M. Carlsson, Dana Mathews, Daniel D'Agostino II, Daniel H.S. Silverman, Daniel Marson, David A. Wolk, David Bachman, David Clark, David Geldmacher, David Hart, David Knopman, David Perry, David Winkfield, Delwyn D. Miller, Diana Kerwin, Dick Drost, Donna M. Simpson, Donna Munic, Douglas W. Scharre, Dr Rob Bartha, Dzintra Celmins, Earl A. Zimmerman, Edmond Teng, Edward Coleman, Edward Zamrini, Effie Mitsis, Elizabeth Finger, Elizabeth Oates, Elizabeth Sosa, Ellen Woo, Emily Rogalski, Evan Fletcher, Francine Parfitt, Gaby Thai, Gad A. Marshall, Gary Conrad, Geoffrey Tremont, George Bartzokis, Ging-Yuek Robin Hsiung, Gloria Chiang, Godfrey D. Pearlson, Greg Jicha, Helen Vanderswag, Hillel Grossman, Horacio Capote, Howard Bergman, Howard Chertkow, Howard Feldman, Howard J. Rosen, Hristina Koleva, Hyungsub Shim, Irina Rachinsky, Jacobo Mintzer, Jaimie Ziolkowski, James Brewer, James J. Lah, Jamika, Singleton-Garvin, Janet S. Cellar, Jared R. Brosch, Jared Tinklenberg, Jason H. Karlawish, Javier Villanueva-Meyer, Jeffrey A. Kaye, Jeffrey M. Burns, Jeffrey R. Petrella, Jerome Yesavage, Joanne Allard, Joanne L. Lord, Joel Hetelle, John Brockington, John C. Morris, John Olichney, John Rogers, Joseph Quinn, Joseph S. Kass, Joy L. Taylor, Judith L. Heidebrink, Karen Anderson, Karen Blank, Karen Ekstam Smith, Karen L. Bell, Kathleen Johnson, Kathleen Tingus, Kathryn DeMarco, Kaycee M. Sink, Keith A. Johnson, Kelly M. Makino, Kenneth Spicer, Ki Won Nam, Kim Martin, Kim Poki-Walker, Kris Johnson, Kristin Fargher, Kristine Lipowski, Kyle Womack, Laura A. Flashman, Lawrence S. Honig, Liana Apostolova, Liberty Teodoro, Lisa C. Silbert, Lisa Ravdin, Lon S.

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Supplementary Figure 1. Optimization of the neural network model for classifying Alzheimer's disease

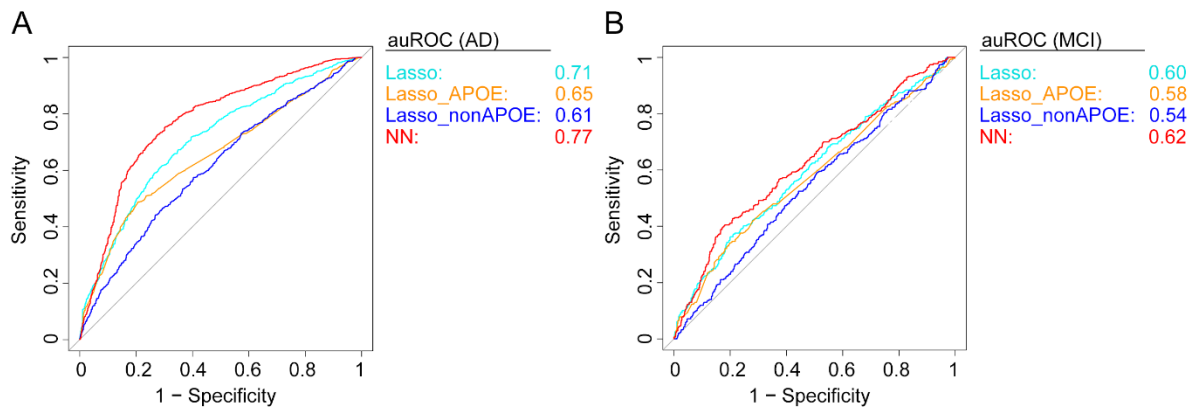


Supplementary Figure 2. Performance of different polygenic score models in the European-descent population AD cohorts

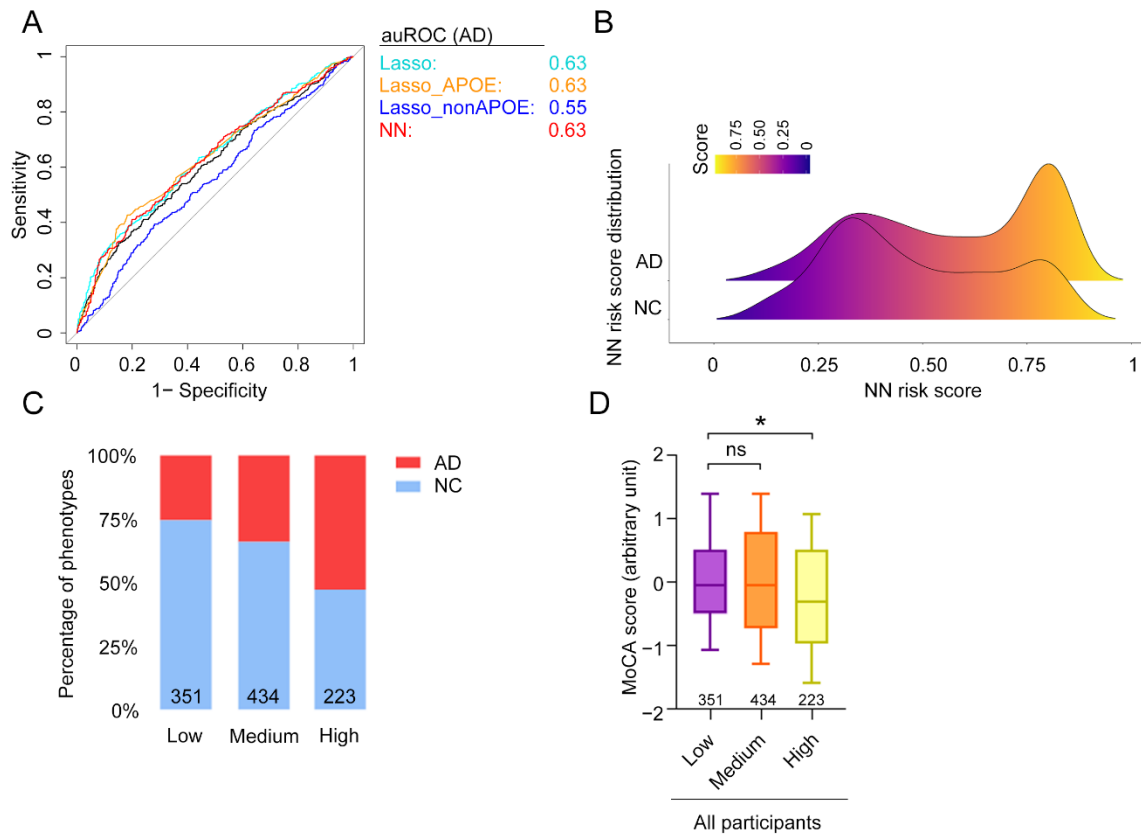


Comparing the values of auROCs of AD cohorts obtained by different models. The y-axis shows the mean auROC, with error bars represents the 95% CI. Bootstrap one-tailed test. ***P < 0.001, **P < 0.01, *P < 0.05.

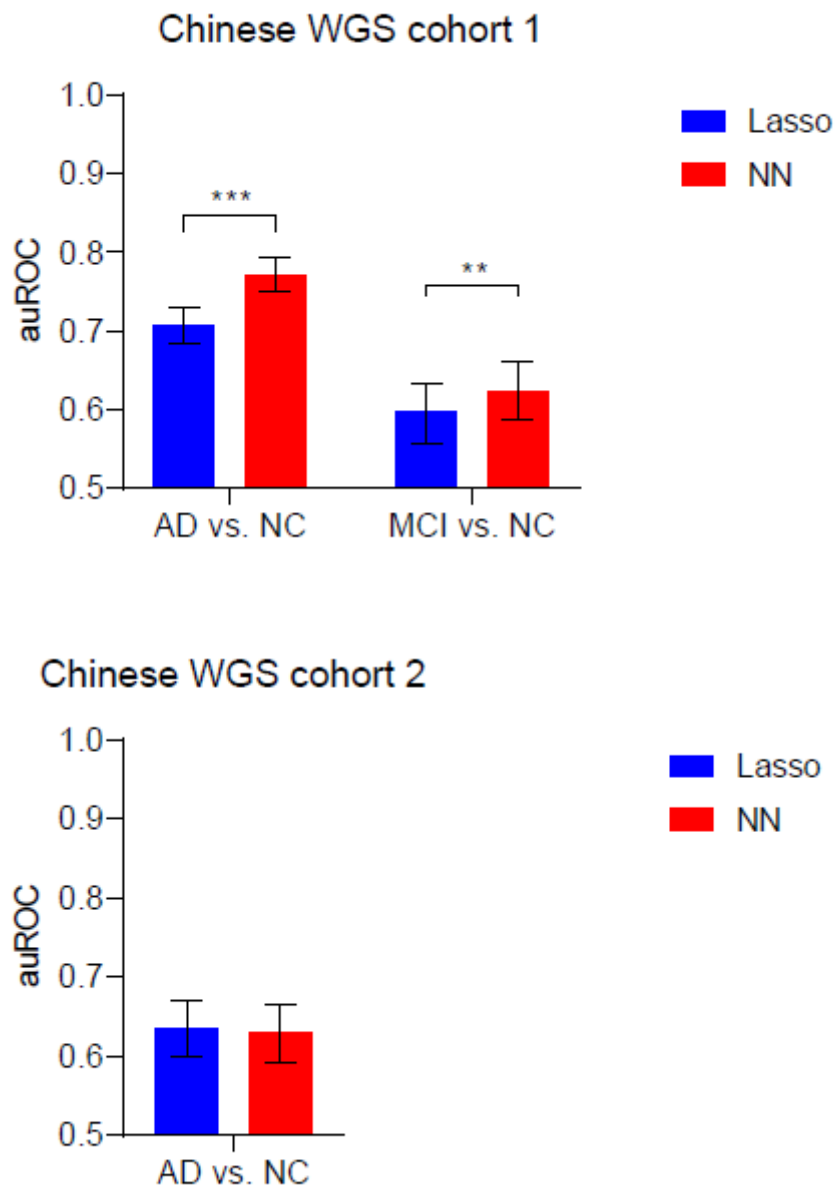
Supplementary Figure 3. Performance of polygenic risk models for classifying Alzheimer's disease risk in Chinese AD WGS cohort 1



Supplementary Figure 4. Performance of polygenic risk models for classifying Alzheimer's disease risk in Chinese AD WGS cohort 2



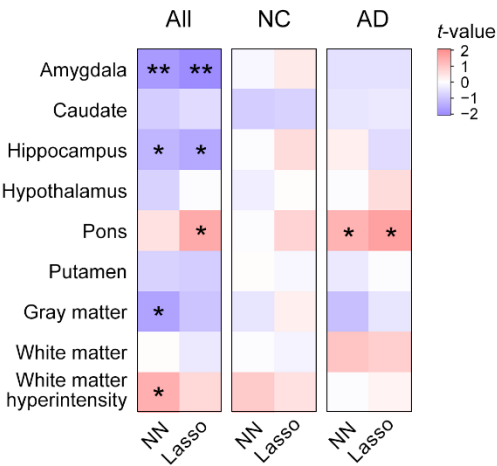
Supplementary Figure 5. Performance of different polygenic score models in the Chinese AD WGS cohorts



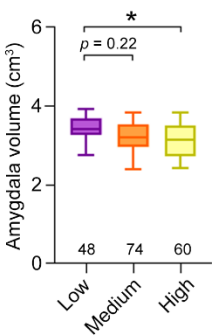
Comparing the values of auROCs of 2 Chinese AD cohorts by different models. The y-axis shows the mean auROC, with error bars represents the 95% CI. Bootstrap two-tailed test. *** $P < 0.001$, ** $P < 0.01$.

Supplementary Figure 6. Associations between polygenic scores and brain region volumes

A



B



Supplementary Table 1. Demographic and clinical characteristics of study cohorts

Cohorts for polygenic score model testing (N = 11,352)			
ADC (N = 5,692)			
	AD	NC	
Number of participants	3,946	1,746	
Mean age (SD)	79.72 (7.67)	75.51 (9.43)	
Female (%)	2,145 (54.36%)	1,138 (65.18%)	
LOAD (N = 4,278)			
	AD	NC	
Number of participants	2,046	2,232	
Mean age (SD)	89.15 (8.32)	80.67 (10.75)	
Female (%)	1,372 (67.06%)	1,361 (60.98%)	
ADNI (N = 1,382)			
	AD	NC	
Number of participants	689	693	
Mean age (SD)	77.65 (7.80)	75.29 (7.43)	
Female (%)	291 (42.24%)	387 (55.84%)	
Chinese WGS cohorts (N = 3,349)			
Chinese AD WGS cohort 1 (N = 2,340)			
	AD	NC	MCI
Number of participants	1,116	915	309
Mean age (SD)	67.22 (9.68)	67.44 (8.80)	69.07 (8.07)
Female (%)	629 (56.36%)	489 (53.44%)	149 (48.22%)
Mean MMSE (SD)	14.32 (6.25)	28.31 (2.20)	26.46 (1.90)
Mean education years (SD)	8.47 (4.90)	12.76 (3.08)	11.85 (3.46)
APOE-ε4 carriers (allele frequency)	471 (25.40%)	157 (9.23%)	98 (18.45%)
APOE-ε2 carriers (allele frequency)	99 (4.61%)	135 (7.87%)	38 (6.47%)
Chinese AD WGS cohort 2 (N = 1,009)			
	AD	NC	
Number of participants	356	653	
Mean age (SD)	80.31 (6.04)	78.78 (5.70)	
Female (%)	242 (67.97%)	311 (47.62%)	
Mean MoCA score (SD)	12.65 (5.43)	23.70 (2.80)	
Mean education years (SD)	4.79 (4.66)	8.13 (5.03)	
APOE-ε4 carriers (allele frequency)	132 (20.22%)	96 (7.73%)	
APOE-ε2 carriers (allele frequency)	36 (5.34%)	115 (9.34%)	

AD, Alzheimer's disease; ADC, National Institute on Aging Alzheimer's Disease Centers Cohort; ADNI, Alzheimer's Disease Neuroimaging Initiative (ADNI) database; LOAD, Late

Onset Alzheimer's Disease (LOAD) Family Study; MCI, mild cognitive impairment; MMSE, Mini-Mental State Examination; MoCA, Montreal Cognitive Assessment; NC, normal control; SD, standard deviation; WGS, whole-genome sequencing.

Supplementary Table 2. Performance of the polygenic score models in the European-descent population AD cohorts

<i>p</i> -value cutoff	Cohort	auROC (95% CI)			
		wPRS	wPRS2	Lasso	NN
<i>P</i> <1E−08	ADC	0.6708 (0.657-0.6849)	0.6503 (0.635-0.6648)	0.7892 (0.7761-0.8016)	0.8152 (0.8029-0.8266)
	LOAD	0.6462 (0.6294-0.6621)	0.6312 (0.6132-0.6481)	0.7496 (0.7342-0.7645)	0.7888 (0.7741-0.8024)
	ADNI	0.6572 (0.6268-0.6863)	0.6407 (0.612-0.6702)	0.679 (0.6504-0.7067)	0.6801 (0.6529-0.7087)
<i>P</i> <1E−06	ADC	0.6648 (0.6499-0.6794)	0.6435 (0.6286-0.6591)	0.8157 (0.8036-0.8280)	0.827 (0.8156-0.8382)
	LOAD	0.6411 (0.6237-0.6581)	0.6255 (0.6084-0.6419)	0.7764 (0.7618-0.7909)	0.8055 (0.7922-0.8196)
	ADNI	0.6528 (0.6236-0.6807)	0.6379 (0.608-0.668)	0.6515 (0.6218-0.6816)	0.6827 (0.6545-0.7091)
<i>P</i> <1E−04	ADC	0.6411 (0.6264-0.6555)	0.636 (0.6205-0.6511)	0.8072 (0.7951-0.8192)	0.8437 (0.8323-0.8547)
	LOAD	0.6283 (0.6113-0.6456)	0.6173 (0.5999-0.634)	0.7814 (0.7663-0.7961)	0.8202 (0.807-0.8326)
	ADNI	0.6228 (0.5942-0.6529)	0.617 (0.5868-0.6475)	0.6893 (0.6609-0.7179)	0.6891 (0.6594-0.7181)

Classification accuracy was measured as area under the receiver operating characteristic curve (auROC); AD, Alzheimer's disease; ADC, National Institute on Aging Alzheimer's Disease Centers Cohort; ADNI, Alzheimer's Disease Neuroimaging Initiative (ADNI) database; CI, confidence interval; LOAD, Late Onset Alzheimer's Disease (LOAD) Family Study; MCI, mild cognitive impairment; NN, neural network; wPRS, weight polygenic risk score.

Supplementary Table 3. Performance of polygenic score models in the European-descent population AD cohorts

<i>p</i> -value cutoff	Cohort	P-value for testing the difference in auROC		
		NN vs. wPRS	NN vs. wPRS2	NN vs. Lasso
<i>P</i> <1E−08	ADC	< 2.20E−16	< 2.20E−16	1.42E−13
	LOAD	< 2.20E−16	< 2.20E−16	1.85E−08
	ADNI	4.46E−02	3.61E−03	4.67E−01
<i>P</i> <1E−06	ADC	< 2.20E−16	< 2.20E−16	3.29E−02
	LOAD	< 2.20E−16	< 2.20E−16	3.66E−05
	ADNI	1.55E−02	1.17E−03	1.55E−02
<i>P</i> <1E−04	ADC	< 2.20E−16	< 2.20E−16	1.12E−05
	LOAD	< 2.20E−16	< 2.20E−16	1.55E−11
	ADNI	4.90E−06	1.36E−06	5.08E−01

Classification accuracy was measured as area under the receiver operating characteristic curve (auROC); AD, Alzheimer's disease; ADC, National Institute on Aging Alzheimer's Disease Centers Cohort; ADNI, Alzheimer's Disease Neuroimaging Initiative (ADNI) database; CI, confidence interval; LOAD, Late Onset Alzheimer's Disease (LOAD) Family Study; MCI, mild cognitive impairment; NN, neural network; wPRS, weight polygenic risk score. Bootstrap one-tailed test.

Supplementary Table 4. Sources of the variants for the replication analysis

Ethnicity	Index	Sample size	PMID	First author	DOI	Year
European descent	Number of variants retrieved: 183					
	1	788,989	N/A	Céline Bellenguez	10.1101/2020.10.01.20200659	2020 ⁷
	2	472,868	N/A	Jeremy Schwartzentruber	10.1101/2020.01.22.20018424	2020 ⁸
	3	1,126,563	N/A	Douglas P. Wightman	10.1101/2020.11.20.20235275	2020 ⁹
	4	455,258	30617256	Iris E. Jansen	10.1038/s41588-018-0311-9	2019 ¹⁰
	5	94,437	30820047	Brian W. Kunkle	10.1038/s41588-019-0358-2	2019 ¹¹
	6	25,580	29777097	Riccardo E. Marioni	10.1038/s41398-018-0150-6	2018 ¹²
African-American	Number of variants retrieved: 14					
	7	8,006	33074286	Brian W. Kunkle	10.1001/jamaneurol.2020.3536	2020 ¹³
Asian	Number of variants retrieved: 13					
	8	11,506	33188687	Longfei Jia	10.1093/brain/awaa364	2020 ¹⁴
Mixed	Number of variants retrieved: 6					
	9	59,556	28183528	Gyungah R. Jun	10.1016/j.jalz.2016.12.012	2017 ¹⁵

N/A, not applicable.

Supplementary Table 5. Variants included for the replication analysis in the Chinese population

Variants obtained from studies conducted in populations of European descent (number of variants retrieved: 183)					
Index	Variant	Chr.	Position	Gene	Source
1	rs113020870	1	985377	<i>AGRN</i>	3
2	rs141749679	1	109888432	<i>SORT1</i>	1
3	rs4575098	1	161155392	<i>ADAMTS4</i>	4
4	rs6656401	1	207692049	<i>CR1</i>	4, 6
5	rs679515	1	207750568	<i>CR1</i>	1, 3, 4
6	rs2093760	1	207786828	<i>CR1</i>	4
7	rs4844610	1	207802552	<i>CR1</i>	5
8	rs72777026	2	9699011	<i>ADAM17</i>	1
9	rs17020490	2	37531939	<i>PRKD3</i>	1
10	rs115186657	2	106235428	<i>FHL2</i>	3
11	rs143080277	2	106366056	<i>NCK2</i>	1
12	rs4663105	2	127891427	<i>BIN1</i>	3, 4
13	rs6733839	2	127892810	<i>BIN1</i>	1, 5, 6
14	rs139643391	2	203743439	<i>WDR12</i>	1
15	rs10933431	2	233981912	<i>INPP5D</i>	1, 2, 4, 5, 6
16	rs35349669	2	234068476	<i>INPP5D</i>	6
17	rs7597763	2	234082577	<i>INPP5D</i>	3
18	rs184384746	3	57226150	<i>HESX1</i>	4
19	rs16824536	3	154787511	<i>MME</i>	1
20	rs61762319	3	154801978	<i>MME</i>	1
21	rs3822030	4	987343	<i>IDUA</i>	1
22	rs4504245	4	11014822	<i>CLNK</i>	3
23	rs6448451	4	11024682	<i>CLNK</i>	4
24	rs6846529	4	11025131	<i>CLNK</i>	1
25	rs6448453	4	11026028	<i>CLNK</i>	4
26	rs7657553	4	11723235	<i>HS3ST1</i>	4
27	rs2245466	4	40198846	<i>RHOH</i>	1
28	rs112403360	5	14724413	<i>ANKH</i>	1
29	rs62374257	5	86223195	<i>COX7C</i>	1
30	rs190982	5	88223420	<i>MEF2C</i>	5
31	rs871269	5	150432388	<i>TNIP1</i>	1, 3
32	rs6891966	5	156526331	<i>HAVCR2</i>	3
33	rs113706587	5	179628150	<i>RASGEF1C</i>	1
34	rs9269853	6	32550322	<i>HLA-DRB1</i>	4
35	rs9271058	6	32575406	<i>HLA-DRB1</i>	5
36	rs6605556	6	32583099	<i>HLA-DQA1</i>	1
37	rs6931277	6	32583357	<i>HLA-DRB1</i>	4

38	rs1846190	6	32583813	<i>HLA-DRB1</i>	3
39	rs187370608	6	40942196	<i>TREM2</i>	3, 4
40	rs10947943	6	41004093	<i>UNC5CL</i>	1
41	rs143332484	6	41129207	<i>TREM2</i>	1
42	rs75932628	6	41129252	<i>TREM2</i>	1, 4, 5,
43	rs60755019	6	41149008	<i>TREML2</i>	1
44	rs9381040	6	41154650	<i>TREML2</i>	6
45	rs9473117	6	47431284	<i>CD2AP</i>	5
46	rs9381563	6	47432637	<i>CD2AP</i>	4, 6
47	rs7767350	6	47485126	<i>CD2AP</i>	1
48	rs9369716	6	47552180	<i>CD2AP</i>	3
49	rs785129	6	114612895	<i>HS3ST5</i>	1
50	rs6943429	7	7856894	<i>UMAD1</i>	1
51	rs10952097	7	8244012	<i>ICA1</i>	1
52	rs5011436	7	12268758	<i>TMEM106B</i>	3
53	rs13237518	7	12269593	<i>TMEM106B</i>	1
54	rs1160871	7	28168745	<i>JAZF1</i>	1
55	rs4723711	7	37844263	<i>NME8</i>	5
56	rs6966331	7	37883793	<i>EPDR1</i>	1
57	rs76928645	7	54941328	<i>SEC61G</i>	1
58	rs7384878	7	99932049	<i>SPDYE3</i>	1, 3, 4
59	rs1859788	7	99971834	<i>ZCWPW1</i>	2, 4
60	rs1476679	7	100004446	<i>ZCWPW1</i>	6
61	rs12539172	7	100091795	<i>NYAP1</i>	5
62	rs10808026	7	143099133	<i>EPHA1</i>	5, 6
63	rs3935067	7	143104331	<i>EPHA1</i>	3
64	rs12703526	7	143107588	<i>EPHA1</i>	2
65	rs7810606	7	143108158	<i>EPHA1</i>	4, 6
66	rs11763230	7	143108841	<i>EPHA1</i>	4
67	rs11771145	7	143110762	<i>EPHA1</i>	1, 6
68	rs114360492	7	145950029	<i>CNTNAP2</i>	4
69	rs1065712	8	11702122	<i>CTSB</i>	1
70	rs73223431	8	27219987	<i>PTK2B</i>	1, 2, 4, 5,
71	rs4236673	8	27464929	<i>CLU/PTK2B</i>	4, 6
72	rs11787077	8	27465312	<i>CLU</i>	1
73	rs1532278	8	27466315	<i>CLU</i>	3, 4
74	rs9331896	8	27467686	<i>CLU</i>	5
75	rs867230	8	27468503	<i>ECHDC3</i>	2
76	rs61732533	8	145108151	<i>SHARPIN</i>	3
77	rs34173062	8	145158607	<i>SHARPIN</i>	1
78	rs1800978	9	107665978	<i>ABCA1</i>	1
79	rs11257238	10	11717397	<i>ECHDC3</i>	4, 9

80	rs7912495	10	11718713	<i>USP6NL</i>	1, 3
81	rs7920721	10	11720308	<i>ECHDC3</i>	2, 5, 6, 9
82	rs11257242	10	11721119	<i>ECHDC3</i>	4, 9
83	rs1171814	10	61645833	<i>CCDC6</i>	2
84	rs7902657	10	61738152	<i>CCDC6</i>	3
85	rs7068231	10	61784928	<i>ANK3</i>	1
86	rs6586028	10	82253984	<i>TSPAN14</i>	1
87	rs1878036	10	82280137	<i>TSPAN14</i>	2
88	rs6584063	10	98026407	<i>BLNK</i>	1
89	rs7908662	10	124172912	<i>PLEKHA1</i>	1
90	rs3740688	11	47380340	<i>MADD</i>	3, 5, 6
91	rs10437655	11	47391948	<i>SPI1</i>	1, 2
92	rs12292911	11	47449072	<i>SPI1</i>	6
93	rs7933202	11	59936926	<i>MS4A2</i>	5
94	rs7935829	11	59942815	<i>MS4A6A</i>	4
95	rs2081545	11	59958380	<i>MS4A6A</i>	4
96	rs1582763	11	60021948	<i>MS4A4A</i>	1, 3, 4, 6
97	rs72924626	11	60095740	<i>MS4A6E</i>	2
98	rs867611	11	85776544	<i>PICALM</i>	4
99	rs561655	11	85800279	<i>PICALM</i>	3
100	rs3844143	11	85850243	<i>PICALM</i>	4
101	rs10792832	11	85867875	<i>PICALM</i>	2, 4, 6
102	rs3851179	11	85868640	<i>PICALM</i>	1, 5
103	rs74685827	11	121353077	<i>SORL1</i>	1
104	rs11218343	11	121435587	<i>SORL1</i>	1, 2, 3, 4, 5, 6
105	rs6489896	12	113719788	<i>TPCN1</i>	1
106	rs7146179	14	53298853	<i>FERMT2</i>	3
107	rs17125924	14	53391680	<i>FERMT2</i>	1, 2, 5, 6
108	rs7401792	14	92931261	<i>SLC24A4</i>	1
109	rs12881735	14	92932828	<i>SLC24A4</i>	5, 6
110	rs12590654	14	92938855	<i>SLC24A4</i>	1, 2, 3, 4, 6
111	rs7157106	14	106228095	<i>IGH gene cluster</i>	1
112	rs10131280	14	107121607	<i>IGH gene cluster</i>	1
113	rs12592778	15	50992311	<i>SLC24A4</i>	2
114	rs8025980	15	50994011	<i>SPPL2A</i>	1
115	rs59685680	15	51001534	<i>SPPL2A</i>	6
116	rs442495	15	59022615	<i>ADAM10</i>	2, 4
117	rs593742	15	59045774	<i>ADAM10</i>	6
118	rs602602	15	59057023	<i>MINDY2</i>	1, 3
119	rs117618017	15	63569902	<i>APH1B</i>	1, 2, 3, 4
120	rs3848143	15	64423506	<i>SNX1</i>	1
121	rs12592898	15	79229199	<i>CTSH</i>	1

122	rs1140239	16	30021402	<i>DOC2A</i>	1
123	rs889555	16	31122571	<i>BCKDK</i>	1, 6
124	rs2884738	16	31126321	<i>KAT8</i>	2
125	rs59735493	16	31133100	<i>KAT8</i>	4
126	rs4985556	16	70694000	<i>IL34</i>	1, 6
127	rs450674	16	79608408	<i>MAF</i>	1
128	rs12446759	16	81773003	<i>PLCG2</i>	1
129	rs12444183	16	81773209	<i>PLCG2</i>	2, 6
130	rs72824905	16	81942028	<i>PLCG2</i>	1
131	rs16941239	16	86454210	<i>FOXF1</i>	1
132	rs56407236	16	90170095	<i>PRDM7</i>	1
133	rs35048651	17	1631340	<i>WDR81</i>	1
134	rs7209200	17	4969940	<i>CHRNE</i>	3
135	rs9916042	17	4984447	<i>SCIMP</i>	4
136	rs61182333	17	5133128	<i>SCIMP</i>	2
137	rs7225151	17	5137047	<i>SCIMP</i>	1, 6
138	rs113260531	17	5138980	<i>SCIMP</i>	4
139	rs2242595	17	18059454	<i>MYO15A</i>	1
140	rs5848	17	42430244	<i>GRN</i>	1
141	rs708382	17	42442344	<i>GRN</i>	3
142	rs199515	17	44856641	<i>WNT3</i>	1
143	rs616338	17	47297297	<i>ABI3</i>	1
144	rs28394864	17	47450775	<i>ABI3</i>	3, 4
145	rs2526378	17	56404349	<i>TSPOAP1</i>	2
146	rs2632516	17	56409089	<i>AC004687.2</i>	3, 4, 9
147	rs2526377	17	56410041	<i>TSPOAP1</i>	1
148	rs138190086	17	61538148	<i>ACE</i>	5, 6
149	rs6504163	17	61545779	<i>ACE</i>	3, 6
150	rs4277405	17	61548918	<i>ACE</i>	1
151	rs4311	17	61560763	<i>ACE</i>	2
152	rs8093731	18	29088958	<i>SUZ12P1</i>	4
153	rs76726049	18	56189459	<i>ALPK2</i>	4
154	rs111278892	19	1039323	<i>ABCA7</i>	4, 6
155	rs3752231	19	1043638	<i>ABCA7</i>	6
156	rs12151021	19	1050874	<i>ABCA7</i>	1, 2, 3, 6
157	rs3752241	19	1053524	<i>ABCA7</i>	4
158	rs3752246	19	1056492	<i>ABCA7</i>	5
159	rs4147929	19	1063443	<i>ABCA7</i>	4, 6
160	rs149080927	19	1854253	<i>KLF16</i>	1
161	rs41289512	19	45351516	<i>APOE</i>	4, 6
162	rs146275714	19	45365447	<i>APOE</i>	2
163	rs769450	19	45410444	<i>APOE</i>	3

164	rs429358	19	45411941	<i>APOE</i>	2, 5
165	rs75627662	19	45413576	<i>APOE</i>	4
166	rs76320948	19	46241841	<i>AC074212.3</i>	4
167	rs2452170	19	49213504	<i>NTN5</i>	3
168	rs9304690	19	50453317	<i>SIGLEC11</i>	1
169	rs3865444	19	51727962	<i>CD33</i>	2, 4
170	rs12459419	19	51728477	<i>CD33</i>	6
171	rs1354106	19	51737991	<i>CD33</i>	3
172	rs587709	19	54771451	<i>LILRB2</i>	1
173	rs1761461	19	54825174	<i>KIR3DL2</i>	3
174	rs1358782	20	393978	<i>RBCK1</i>	1
175	rs6069736	20	54983075	<i>CASS4</i>	6
176	rs6069737	20	54995699	<i>CASS4</i>	3
177	rs6024870	20	54997568	<i>CASS4</i>	5
178	rs6014724	20	54998544	<i>CASS4</i>	1, 2, 4
179	rs6742	20	62374441	<i>SLC2A4RG</i>	1
180	rs2154481	21	27473875	<i>APP</i>	1
181	rs2154482	21	27520931	<i>APP</i>	3
182	rs4817090	21	27534261	<i>ADAMTS1</i>	2
183	rs2830489	21	28148191	<i>ADAMTS1</i>	1, 2

Variants obtained from studies conducted in African-American populations
(number of variants retrieved: 14)

Index	Variant	Chr.	Position	Gene	Source
184	rs115684722	1	232376163	<i>SIPAIL2</i>	7
185	rs168193	3	5302077	<i>EDEM1</i>	7
186	rs2633682	3	104409208	<i>ALCAM</i>	7
187	rs184179037	5	37483940	<i>WDR70</i>	7
188	rs145848414	5	174014114	<i>NSG2-MSX2</i>	7
189	rs569584007	11	43166842	<i>API5</i>	7
190	rs115816806	11	76541840	<i>ACER3</i>	7
191	rs75739461	12	18471546	<i>PIK3C2G</i>	7
192	rs9516245	13	94159800	<i>GPC6</i>	7
193	rs570487962	15	97992685	<i>ARRDC4-IGF1R</i>	7
194	rs79537509	16	8288401	<i>RBFOX1</i>	7
195	rs115550680	19	1050420	<i>ABCA7</i>	7
196	rs157591	19	45423934	<i>APOE</i>	7
197	rs3745495	19	50524332	<i>VRK3</i>	7

Variants obtained from studies conducted in Asian populations
(number of variants retrieved: 13)

Index	Variant	Chr.	Position	Gene	Source
198	rs6859823	5	105554384	<i>CTC-278L1.1</i>	8
199	rs3777215	5	95122000	<i>RHOBTB3, GLRX</i>	8
200	rs234434	14	97821020	<i>CTD-2506J14.1</i>	8

201	rs11668861	19	45380970	<i>NECTIN2</i>	8
202	rs6859	19	45382034	<i>NECTIN2</i>	8
203	rs3852860	19	45382966	<i>NECTIN2</i>	8
204	rs71352238	19	45394336	<i>TOMM40</i>	8
205	rs157580	19	45395266	<i>TOMM40</i>	8
206	rs2075650	19	45395619	<i>TOMM40</i>	8
207	rs157582	19	45396219	<i>TOMM40</i>	8
208	rs439401	19	45414451	<i>APOE</i>	8
209	rs4420638	19	45422946	<i>APOC1</i>	8
210	rs2255835	21	19491664	<i>CHODL</i>	8
Variants obtained from studies conducted in mixed populations (number of variants retrieved: 6)					
Index	Variant	Chr.	Position	Gene	Source
211	rs11168036	5	139707439	<i>PFDN1/HBEGF</i>	9
212	rs4150233	5	139714837	<i>PFDN1/HBEGF</i>	9
213	rs2011704	10	11718331	<i>USP6NL/ECHDC3</i>	9
214	rs11257240	10	11719074	<i>USP6NL/ECHDC3</i>	9
215	rs12358692	10	11721102	<i>USP6NL/ECHDC3</i>	9
216	rs9749589	19	3405592	<i>NFIC</i>	9

Chr., chromosome. Sources correspond to the index numbers in Supplementary Table 2.

Supplementary Table 6. Replication results of the associations of variants with Alzheimer's disease in the Chinese population

Variants				Chinese AD WGS cohort 1			Chinese AD WGS cohort 2		
Index	Variant	Gene	EA	β (SE)	p	EAf (AD/NC)	β (SE)	p	EAf (AD/NC)
1	rs113020870	<i>AGRN</i>	N/A	N/A	N/A	N/A	N/A	N/A	N/A
2	rs141749679	<i>SORT1</i>	N/A	N/A	N/A	N/A	N/A	N/A	N/A
3	rs4575098	<i>ADAMTS4</i>	A	0.065 (0.067)	3.35E−01	0.324/0.309	0.170 (0.150)	2.57E−01	0.332/0.317
4	rs6656401	<i>CR1</i>	A	−0.282 (0.202)	1.63E−01	0.023/0.030	0.035 (0.332)	9.15E−01	0.045/0.047
5	rs679515	<i>CR1</i>	T	−0.284 (0.204)	1.64E−01	0.022/0.029	0.035 (0.332)	9.15E−01	0.045/0.047
6	rs2093760	<i>CR1</i>	A	−0.124 (0.066)	5.94E−02	0.362/0.391	0.089 (0.147)	5.43E−01	0.340/0.350
7	rs4844610	<i>CR1</i>	A	−0.234 (0.200)	2.43E−01	0.023/0.029	−0.001 (0.335)	9.99E−01	0.044/0.047
8	rs72777026	<i>ADAM17</i>	G	0.063 (0.088)	4.77E−01	0.154/0.146	0.376 (0.214)	7.84E−02	0.135/0.121
9	rs17020490	<i>PRKD3</i>	T	0.061 (0.064)	3.43E−01	0.432/0.416	−0.295 (0.139)	3.37E−02	0.405/0.422
10	rs115186657	<i>FHL2</i>	N/A	N/A	N/A	N/A	N/A	N/A	N/A
11	rs143080277	<i>NCK2</i>	N/A	N/A	N/A	N/A	N/A	N/A	N/A
12	rs4663105	<i>BIN1</i>	C	0.206 (0.064)	1.25E−03	0.513/0.463	0.112 (0.141)	4.27E−01	0.485/0.462
13	rs6733839	<i>BIN1</i>	T	0.172 (0.064)	7.41E−03	0.469/0.428	0.153 (0.142)	2.80E−01	0.423/0.405
14	rs139643391	<i>WDR12</i>	N/A	N/A	N/A	N/A	N/A	N/A	N/A
15	rs10933431	<i>INPP5D</i>	G	−0.095 (0.067)	1.56E−01	0.309/0.328	0.077 (0.153)	6.16E−01	0.292/0.293
16	rs35349669	<i>INPP5D</i>	T	−0.218 (0.231)	3.45E−01	0.017/0.021	N/A	N/A	N/A
17	rs7597763	<i>INPP5D</i>	C	−0.236 (0.217)	2.76E−01	0.019/0.025	N/A	N/A	N/A
18	rs184384746	<i>HESX1</i>	N/A	N/A	N/A	N/A	N/A	N/A	N/A
19	rs16824536	<i>MME</i>	A	−0.311 (0.311)	3.16E−01	0.009/0.013	−2.097 (0.916)	2.21E−02	0.004/0.010
20	rs61762319	<i>MME</i>	N/A	N/A	N/A	N/A	N/A	N/A	N/A
21	rs3822030	<i>IDUA</i>	T	−0.010 (0.063)	8.69E−01	0.484/0.488	0.076 (0.140)	5.85E−01	0.441/0.433
22	rs4504245	<i>CLNK</i>	A	0.133 (0.085)	1.19E−01	0.177/0.159	0.308 (0.193)	1.11E−01	0.177/0.155
23	rs6448451	<i>CLNK</i>	G	0.064 (0.080)	4.22E−01	0.199/0.188	0.329 (0.182)	7.16E−02	0.205/0.187
24	rs6846529	<i>CLNK</i>	C	0.077 (0.077)	3.15E−01	0.225/0.210	0.263 (0.172)	1.28E−01	0.229/0.212
25	rs6448453	<i>CLNK</i>	A	0.048 (0.079)	5.41E−01	0.207/0.198	0.349 (0.179)	5.17E−02	0.216/0.195
26	rs7657553	<i>HS3ST1</i>	A	0.002 (0.065)	9.79E−01	0.341/0.341	0.029 (0.144)	8.39E−01	0.326/0.315
27	rs2245466	<i>RHOH</i>	C	0.080 (0.064)	2.12E−01	0.472/0.452	−0.106 (0.135)	4.31E−01	0.504/0.494
28	rs112403360	<i>ANKH</i>	A	0.081 (0.187)	6.65E−01	0.030/0.027	0.116 (0.400)	7.72E−01	0.038/0.030
29	rs62374257	<i>COX7C</i>	C	0.022 (0.072)	7.64E−01	0.270/0.267	0.196 (0.159)	2.18E−01	0.281/0.256
30	rs190982	<i>MEF2C</i>	G	0.154 (0.089)	8.33E−02	0.155/0.135	−0.171 (0.197)	3.84E−01	0.146/0.135
31	rs871269	<i>TNIP1</i>	C	0.072 (0.065)	2.67E−01	0.411/0.396	0.037 (0.140)	7.90E−01	0.462/0.416
32	rs6891966	<i>HAVCR2</i>	A	−0.061 (0.121)	6.14E−01	0.072/0.075	0.044 (0.320)	8.90E−01	0.049/0.048
33	rs113706587	<i>RASGEF1C</i>	A	0.074 (0.768)	9.23E−01	0.002/0.002	−0.353 (1.158)	7.61E−01	0.001/0.007
34	rs9269853	<i>HLA-DRB1</i>	A	0.121 (0.093)	1.91E−01	0.147/0.132	0.421 (0.269)	1.18E−01	0.197/0.232
35	rs9271058	<i>HLA-DRB1</i>	A	0.043 (0.088)	6.24E−01	0.150/0.144	0.644 (0.251)	1.05E−02	0.222/0.196

36	rs6605556	<i>HLA-DQA1</i>	G	−0.145 (0.093)	1.18E−01	0.116/0.132	−0.464 (0.265)	7.96E−02	0.081/0.119
37	rs6931277	<i>HLA-DRB1</i>	T	−0.145 (0.095)	1.27E−01	0.114/0.130	−0.287 (0.261)	2.73E−01	0.091/0.118
38	rs1846190	<i>HLA-DRB1</i>	A	−0.025 (0.072)	7.23E−01	0.253/0.255	−0.111 (0.156)	4.78E−01	0.221/0.256
39	rs187370608	<i>TREM2</i>	N/A	N/A	N/A	N/A	N/A	N/A	N/A
40	rs10947943	<i>UNC5CL</i>	A	0.083 (0.102)	4.14E−01	0.112/0.104	0.172 (0.219)	4.34E−01	0.119/0.114
41	rs143332484	<i>TREM2</i>	N/A	N/A	N/A	N/A	N/A	N/A	N/A
42	rs75932628	<i>TREM2</i>	N/A	N/A	N/A	N/A	N/A	N/A	N/A
43	rs60755019	<i>TREML2</i>	G	1.324 (0.786)	9.22E−02	0.004/0.001	0.370 (0.920)	6.88E−01	0.007/0.005
44	rs9381040	<i>TREML2</i>	T	0.164 (0.068)	1.57E−02	0.349/0.314	0.318 (0.150)	3.39E−02	0.379/0.361
45	rs9473117	<i>CD2AP</i>	C	0.096 (0.098)	3.27E−01	0.130/0.120	0.171 (0.200)	3.95E−01	0.143/0.142
46	rs9381563	<i>CD2AP</i>	C	0.132 (0.085)	1.19E−01	0.192/0.173	0.063 (0.174)	7.17E−01	0.218/0.210
47	rs7767350	<i>CD2AP</i>	T	0.085 (0.096)	3.77E−01	0.131/0.122	0.135 (0.199)	4.96E−01	0.146/0.145
48	rs9369716	<i>CD2AP</i>	T	0.093 (0.096)	3.36E−01	0.133/0.122	0.142 (0.199)	4.75E−01	0.146/0.145
49	rs785129	<i>HS3ST5</i>	C	−0.095 (0.069)	1.69E−01	0.320/0.340	0.038 (0.137)	7.82E−01	0.389/0.388
50	rs6943429	<i>UMAD1</i>	T	0.008 (0.064)	9.05E−01	0.414/0.410	−0.027 (0.140)	8.49E−01	0.482/0.470
51	rs10952097	<i>ICA1</i>	T	0.088 (0.109)	4.19E−01	0.097/0.089	−0.014 (0.217)	9.49E−01	0.125/0.136
52	rs5011436	<i>TMEM106B</i>	A	0.068 (0.064)	2.89E−01	0.335/0.318	−0.218 (0.140)	1.20E−01	0.355/0.364
53	rs13237518	<i>TMEM106B</i>	C	0.083 (0.066)	2.08E−01	0.338/0.319	−0.216 (0.144)	1.33E−01	0.358/0.365
54	rs1160871	<i>JAZF1</i>	N/A	N/A	N/A	N/A	N/A	N/A	N/A
55	rs4723711	<i>NME8</i>	T	−0.015 (0.075)	8.43E−01	0.235/0.238	0.069 (0.176)	6.96E−01	0.192/0.188
56	rs6966331	<i>EPDR1</i>	C	−0.040 (0.063)	5.30E−01	0.469/0.478	0.106 (0.133)	4.24E−01	0.514/0.492
57	rs76928645	<i>SEC61G</i>	T	−0.177 (1.426)	9.01E−01	0/0.001	N/A	N/A	N/A
58	rs7384878	<i>SPDYE3</i>	T	0.071 (0.065)	2.72E−01	0.418/0.401	0.146 (0.142)	3.06E−01	0.360/0.335
59	rs1859788	<i>ZCWPW1</i>	G	0.084 (0.064)	1.93E−01	0.431/0.410	0.191 (0.143)	1.83E−01	0.371/0.341
60	rs1476679	<i>ZCWPW1</i>	C	−0.052 (0.068)	4.46E−01	0.309/0.320	−0.042 (0.144)	7.69E−01	0.351/0.353
61	rs12539172	<i>NYAP1</i>	T	−0.05 (0.068)	4.62E−01	0.306/0.317	−0.038 (0.145)	7.90E−01	0.350/0.352
62	rs10808026	<i>EPHA1</i>	A	−0.023 (0.094)	8.07E−01	0.132/0.134	0.304 (0.208)	1.44E−01	0.138/0.126
63	rs3935067	<i>EPHA1</i>	C	0.126 (0.198)	5.24E−01	0.027/0.024	0.400 (0.418)	3.39E−01	0.037/0.027
64	rs12703526	<i>EPHA1</i>	T	0.039 (0.090)	6.63E−01	0.150/0.145	−0.263 (0.192)	1.71E−01	0.146/0.166
65	rs7810606	<i>EPHA1</i>	C	0.026 (0.090)	7.76E−01	0.148/0.145	−0.263 (0.192)	1.71E−01	0.146/0.165
66	rs11763230	<i>EPHA1</i>	T	0.018 (0.093)	8.49E−01	0.143/0.142	0.356 (0.209)	8.77E−02	0.139/0.126
67	rs11771145	<i>EPHA1</i>	G	0.038 (0.063)	5.41E−01	0.464/0.454	−0.062 (0.133)	6.40E−01	0.483/0.479
68	rs114360492	<i>CNTNAP2</i>	N/A	N/A	N/A	N/A	N/A	N/A	N/A
69	rs1065712	<i>CTSB</i>	N/A	N/A	N/A	N/A	N/A	N/A	N/A
70	rs73223431	<i>PTK2B</i>	T	0.056 (0.070)	4.26E−01	0.280/0.268	0.199 (0.145)	1.70E−01	0.320/0.287
71	rs4236673	<i>CLU/PTK2B</i>	A	−0.117 (0.083)	1.56E−01	0.176/0.192	−0.262 (0.161)	1.03E−01	0.236/0.250
72	rs11787077	<i>CLU</i>	T	−0.131 (0.080)	1.03E−01	0.186/0.206	−0.262 (0.161)	1.03E−01	0.236/0.253
73	rs1532278	<i>CLU</i>	T	−0.136 (0.080)	9.01E−02	0.185/0.206	−0.263 (0.159)	9.74E−02	0.237/0.254
74	rs9331896	<i>CLU</i>	C	−0.117 (0.080)	1.46E−01	0.186/0.203	−0.248 (0.161)	1.23E−01	0.239/0.255
75	rs867230	<i>ECHDC3</i>	C	−0.129 (0.080)	1.06E−01	0.188/0.208	−0.188 (0.162)	2.46E−01	0.242/0.252
76	rs61732533	<i>SHARPIN</i>	A	−2.840 (1.038)	6.20E−03	0.000/0.008	N/A	N/A	N/A

77	rs34173062	<i>SHARPIN</i>	N/A	N/A	N/A	N/A	N/A	N/A	N/A
78	rs1800978	<i>ABCA1</i>	G	0.100 (0.089)	2.64E−01	0.151/0.138	0.086 (0.182)	6.37E−01	0.170/0.179
79	rs11257238	<i>ECHDC3</i>	C	0.001 (0.073)	9.85E−01	0.249/0.249	0.047 (0.158)	7.67E−01	0.244/0.260
80	rs7912495	<i>USP6NL</i>	G	−0.021 (0.069)	7.63E−01	0.288/0.292	−0.002 (0.147)	9.90E−01	0.313/0.319
81	rs7920721	<i>ECHDC3</i>	G	−0.006 (0.073)	9.31E−01	0.247/0.249	0.047 (0.158)	7.67E−01	0.243/0.258
82	rs11257242	<i>ECHDC3</i>	G	−0.025 (0.064)	6.93E−01	0.323/0.330	−0.076 (0.142)	5.94E−01	0.323/0.348
83	rs1171814	<i>CCDC6</i>	G	0.106 (0.067)	1.15E−01	0.376/0.353	−0.098 (0.137)	4.77E−01	0.388/0.365
84	rs7902657	<i>CCDC6</i>	T	0.136 (0.071)	5.46E−02	0.288/0.262	−0.183 (0.151)	2.25E−01	0.294/0.299
85	rs7068231	<i>ANK3</i>	G	0.135 (0.071)	5.80E−02	0.289/0.262	−0.149 (0.150)	3.21E−01	0.296/0.295
86	rs6586028	<i>TSPAN14</i>	C	−0.096 (0.239)	6.86E−01	0.017/0.019	−0.302 (0.423)	4.76E−01	0.021/0.033
87	rs1878036	<i>TSPAN14</i>	T	−0.072 (0.303)	8.11E−01	0.011/0.011	−0.337 (0.441)	4.45E−01	0.020/0.027
88	rs6584063	<i>BLNK</i>	G	−0.274 (0.278)	3.24E−01	0.012/0.015	1.090 (0.636)	8.65E−02	0.020/0.009
89	rs7908662	<i>PLEKHA1</i>	A	0.087 (0.066)	1.91E−01	0.38/0.359	−0.156 (0.147)	2.87E−01	0.369/0.383
90	rs3740688	<i>MADD</i>	G	0.028 (0.068)	6.79E−01	0.345/0.340	−0.316 (0.151)	3.64E−02	0.249/0.316
91	rs10437655	<i>SPI1</i>	A	0.026 (0.069)	7.13E−01	0.297/0.290	0.277 (0.141)	5.02E−02	0.427/0.386
92	rs12292911	<i>SPI1</i>	A	0.016 (0.068)	8.09E−01	0.329/0.325	0.198 (0.140)	1.58E−01	0.440/0.410
93	rs7933202	<i>MS4A2</i>	C	−0.128 (0.134)	3.39E−01	0.055/0.063	0.292 (0.319)	3.61E−01	0.065/0.051
94	rs7935829	<i>MS4A6A</i>	G	0.031 (0.082)	7.08E−01	0.183/0.179	−0.015 (0.165)	9.25E−01	0.253/0.236
95	rs2081545	<i>MS4A6A</i>	A	0.040 (0.082)	6.29E−01	0.185/0.179	−0.016 (0.164)	9.20E−01	0.253/0.235
96	rs1582763	<i>MS4A4A</i>	A	−0.211 (0.092)	2.12E−02	0.119/0.145	0.217 (0.225)	3.35E−01	0.121/0.103
97	rs72924626	<i>MS4A6E</i>	C	−0.187 (0.084)	2.71E−02	0.154/0.181	0.130 (0.193)	4.99E−01	0.167/0.147
98	rs867611	<i>PICALM</i>	G	−0.204 (0.066)	2.13E−03	0.343/0.390	0.024 (0.144)	8.67E−01	0.385/0.400
99	rs561655	<i>PICALM</i>	G	−0.169 (0.064)	8.64E−03	0.450/0.491	−0.060 (0.142)	6.72E−01	0.442/0.486
100	rs3844143	<i>PICALM</i>	C	−0.176 (0.066)	7.43E−03	0.366/0.408	0.020 (0.144)	8.92E−01	0.389/0.414
101	rs10792832	<i>PICALM</i>	A	−0.169 (0.066)	1.01E−02	0.358/0.398	0.001 (0.144)	9.92E−01	0.383/0.413
102	rs3851179	<i>PICALM</i>	T	−0.169 (0.066)	1.01E−02	0.358/0.398	0.001 (0.144)	9.92E−01	0.383/0.413
103	rs74685827	<i>SORL1</i>	G	0.161 (0.102)	1.15E−01	0.119/0.104	0.341 (0.243)	1.60E−01	0.101/0.087
104	rs11218343	<i>SORL1</i>	C	−0.182 (0.072)	1.22E−02	0.246/0.282	−0.306 (0.151)	4.19E−02	0.264/0.304
105	rs6489896	<i>TPCN1</i>	C	0.136 (0.079)	8.66E−02	0.214/0.193	−0.082 (0.176)	6.39E−01	0.194/0.201
106	rs7146179	<i>FERMT2</i>	A	−0.029 (0.079)	7.11E−01	0.208/0.213	−0.047 (0.171)	7.84E−01	0.184/0.196
107	rs17125924	<i>FERMT2</i>	G	−0.114 (0.074)	1.23E−01	0.252/0.272	−0.115 (0.162)	4.76E−01	0.240/0.244
108	rs7401792	<i>SLC24A4</i>	A	−0.007 (0.066)	9.19E−01	0.359/0.360	0.122 (0.142)	3.90E−01	0.378/0.397
109	rs12881735	<i>SLC24A4</i>	C	0.023 (0.105)	8.25E−01	0.101/0.099	0.364 (0.253)	1.49E−01	0.090/0.097
110	rs12590654	<i>SLC24A4</i>	A	0.034 (0.064)	5.91E−01	0.484/0.475	−0.041 (0.137)	7.65E−01	0.423/0.441
111	rs7157106	<i>IGH gene cluster</i>	G	0.110 (0.113)	3.34E−01	0.090/0.081	−0.274 (0.349)	4.33E−01	0.035/0.044
112	rs10131280	<i>IGH gene cluster</i>	A	−0.038 (0.084)	6.53E−01	0.164/0.170	0.041 (0.178)	8.18E−01	0.198/0.188
113	rs12592778	<i>SLC24A4</i>	A	−0.035 (0.063)	5.79E−01	0.467/0.474	−0.232 (0.141)	9.98E−02	0.471/0.518
114	rs8025980	<i>SPPL2A</i>	A	0.035 (0.063)	5.78E−01	0.456/0.449	0.193 (0.145)	1.86E−01	0.426/0.385
115	rs59685680	<i>SPPL2A</i>	G	−0.051 (0.063)	4.19E−01	0.483/0.495	0.142 (0.141)	3.16E−01	0.500/0.469
116	rs442495	<i>ADAM10</i>	T	−0.087 (0.082)	2.91E−01	0.164/0.178	0.479 (0.184)	9.06E−03	0.211/0.161
117	rs593742	<i>ADAM10</i>	A	−0.099 (0.075)	1.90E−01	0.225/0.243	0.411 (0.173)	1.71E−02	0.239/0.200

118	rs602602	MINDY2	T	−0.101 (0.072)	1.60E−01	0.250/0.271	0.454 (0.167)	6.44E−03	0.273/0.217
119	rs117618017	APH1B	N/A	N/A	N/A	N/A	N/A	N/A	N/A
120	rs3848143	SNX1	G	0.122 (0.079)	1.23E−01	0.203/0.183	0.046 (0.175)	7.94E−01	0.164/0.181
121	rs12592898	CTSH	A	−0.200 (0.149)	1.80E−01	0.044/0.052	0.123 (0.280)	6.61E−01	0.067/0.070
122	rs1140239	DOC2A	T	0.116 (0.065)	7.43E−02	0.411/0.383	−0.121 (0.138)	3.84E−01	0.441/0.445
123	rs889555	BCKDK	T	0.073 (0.123)	5.52E−01	0.075/0.071	0.075 (0.208)	7.19E−01	0.132/0.126
124	rs2884738	KAT8	A	0.074 (0.123)	5.47E−01	0.075/0.071	0.076 (0.208)	7.13E−01	0.132/0.125
125	rs59735493	KAT8	A	0.083 (0.123)	5.00E−01	0.075/0.070	0.111 (0.210)	5.97E−01	0.132/0.124
126	rs4985556	IL34	A	0.184 (0.131)	1.58E−01	0.069/0.057	0.213 (0.253)	4.00E−01	0.093/0.074
127	rs450674	MAF	C	−0.179 (0.158)	2.58E−01	0.037/0.044	−0.555 (0.353)	1.15E−01	0.032/0.046
128	rs12446759	PLCG2	G	−0.130 (0.078)	9.46E−02	0.185/0.205	−0.021 (0.161)	8.95E−01	0.218/0.231
129	rs12444183	PLCG2	A	−0.087 (0.077)	2.58E−01	0.200/0.214	−0.098 (0.155)	5.28E−01	0.235/0.257
130	rs72824905	PLCG2	N/A	N/A	N/A	N/A	N/A	N/A	N/A
131	rs16941239	FOXF1	A	−0.089 (0.090)	3.24E−01	0.133/0.145	−0.063 (0.204)	7.56E−01	0.125/0.126
132	rs56407236	PRDM7	A	0.111 (0.196)	5.71E−01	0.029/0.025	0.701 (0.479)	1.44E−01	0.027/0.021
133	rs35048651	WDR81	N/A	N/A	N/A	N/A	N/A	N/A	N/A
134	rs7209200	CHRNE	T	0.010 (0.077)	8.93E−01	0.226/0.224	0.055 (0.161)	7.32E−01	0.244/0.228
135	rs9916042	SCIMP	A	−0.005 (0.074)	9.49E−01	0.246/0.246	0.012 (0.157)	9.40E−01	0.256/0.247
136	rs61182333	SCIMP	T	−0.058 (0.110)	5.95E−01	0.093/0.099	0.977 (0.317)	2.09E−03	0.081/0.053
137	rs7225151	SCIMP	A	0.126 (0.141)	3.75E−01	0.056/0.051	0.794 (0.417)	5.72E−02	0.038/0.026
138	rs113260531	SCIMP	A	0.114 (0.141)	4.18E−01	0.056/0.052	0.794 (0.417)	5.72E−02	0.038/0.026
139	rs2242595	MYO15A	G	−0.005 (0.064)	9.43E−01	0.476/0.478	−0.148 (0.139)	2.86E−01	0.482/0.487
140	rs5848	GRN	T	−0.030 (0.067)	6.58E−01	0.332/0.338	0.213 (0.149)	1.53E−01	0.420/0.383
141	rs708382	GRN	C	−0.097 (0.064)	1.33E−01	0.427/0.450	0.087 (0.142)	5.39E−01	0.492/0.456
142	rs199515	WNT3	G	N/A	N/A	0.000/0.001	3.593 (4.438)	4.18E−01	0.001/0.001
143	rs616338	ABI3	T	N/A	N/A	0.000/0.000	N/A	N/A	N/A
144	rs28394864	ABI3	A	0.026 (0.066)	6.94E−01	0.369/0.364	−0.041 (0.131)	7.55E−01	0.444/0.450
145	rs2526378	TSPOAP1	G	−0.105 (0.064)	9.83E−02	0.464/0.490	−0.020 (0.138)	8.83E−01	0.485/0.485
146	rs2632516	AC004687.2	C	−0.101 (0.064)	1.15E−01	0.464/0.489	0.006 (0.139)	9.65E−01	0.478/0.476
147	rs2526377	TSPOAP1	G	−0.110 (0.064)	8.35E−02	0.456/0.483	0.018 (0.137)	8.97E−01	0.479/0.474
148	rs138190086	ACE	A	−0.125 (0.325)	7.02E−01	0.009/0.010	0.638 (0.872)	4.65E−01	0.010/0.008
149	rs6504163	ACE	C	−0.056 (0.067)	4.03E−01	0.367/0.380	0.087 (0.147)	5.53E−01	0.364/0.353
150	rs4277405	ACE	C	−0.061 (0.066)	3.54E−01	0.337/0.353	−0.013 (0.150)	9.28E−01	0.334/0.339
151	rs4311	ACE	T	−0.031 (0.070)	6.56E−01	0.319/0.327	0.034 (0.149)	8.19E−01	0.323/0.323
152	rs8093731	SUZ12P1	T	−0.056 (0.184)	7.60E−01	0.028/0.031	0.484 (0.416)	2.45E−01	0.024/0.021
153	rs76726049	ALPK2	N/A	N/A	N/A	N/A	N/A	N/A	N/A
154	rs111278892	ABCA7	G	−2.188 (1.074)	4.17E−02	0.000/0.004	N/A	N/A	0.000/0.002
155	rs3752231	ABCA7	T	0.204 (0.064)	1.52E−03	0.449/0.400	−0.299 (0.145)	3.97E−02	0.406/0.436
156	rs12151021	ABCA7	G	−0.189 (0.064)	3.34E−03	0.478/0.524	0.219 (0.139)	1.16E−01	0.466/0.473
157	rs3752241	ABCA7	G	−0.077 (0.082)	3.49E−01	0.172/0.184	−0.015 (0.169)	9.32E−01	0.225/0.201
158	rs3752246	ABCA7	G	0.208 (0.067)	1.82E−03	0.375/0.326	−0.234 (0.143)	1.03E−01	0.351/0.372

159	rs4147929	ABCA7	A	0.213 (0.067)	1.34E−03	0.372/0.322	−0.251 (0.143)	7.88E−02	0.353/0.371
160	rs149080927	KLF16	N/A	N/A	N/A	N/A	N/A	N/A	N/A
161	rs41289512	APOE	G	N/A	N/A	0/0	N/A	N/A	N/A
162	rs146275714	APOE	A	0.456 (1.231)	7.11E−01	0.001/0.001	N/A	N/A	N/A
163	rs769450	APOE	A	−0.191 (0.083)	2.06E−02	0.175/0.203	−0.353 (0.163)	3.06E−02	0.188/0.234
164	rs429358	APOE	C	1.152 (0.093)	1.33E−35	0.273/0.099	1.348 (0.220)	9.05E−10	0.205/0.078
165	rs75627662	APOE	T	0.672 (0.076)	5.83E−19	0.313/0.184	0.621 (0.166)	1.84E−04	0.277/0.189
166	rs76320948	AC074212.3	T	N/A	N/A	0.001/0.000	N/A	N/A	N/A
167	rs2452170	NTN5	A	−0.493 (0.543)	3.64E−01	0.003/0.004	−1.643 (1.363)	2.28E−01	0.001/0.003
168	rs9304690	SIGLEC11	T	0.105 (0.078)	1.77E−01	0.228/0.210	0.267 (0.156)	8.64E−02	0.294/0.267
169	rs3865444	CD33	A	0.025 (0.084)	7.64E−01	0.181/0.177	−0.289 (0.192)	1.33E−01	0.138/0.171
170	rs12459419	CD33	T	0.026 (0.084)	7.59E−01	0.180/0.176	−0.258 (0.192)	1.81E−01	0.138/0.171
171	rs1354106	CD33	G	0.035 (0.077)	6.50E−01	0.221/0.215	−0.145 (0.166)	3.83E−01	0.207/0.228
172	rs587709	LILRB2	T	−0.074 (0.083)	3.72E−01	0.177/0.186	0.425 (0.149)	4.47E−03	0.372/0.338
173	rs1761461	KIR3DL2	A	−0.038 (0.091)	6.76E−01	0.135/0.139	0.141 (0.166)	3.93E−01	0.194/0.204
174	rs1358782	RBCK1	A	0.027 (0.111)	8.06E−01	0.089/0.087	−0.080 (0.240)	7.39E−01	0.088/0.082
175	rs6069736	CASS4	T	−0.051 (0.066)	4.37E−01	0.340/0.351	−0.190 (0.144)	1.89E−01	0.378/0.394
176	rs6069737	CASS4	N/A	N/A	N/A	N/A	N/A	N/A	N/A
177	rs6024870	CASS4	N/A	N/A	N/A	N/A	N/A	N/A	N/A
178	rs6014724	CASS4	G	−0.088 (0.065)	1.73E−01	0.355/0.375	−0.196 (0.143)	1.71E−01	0.392/0.395
179	rs6742	SLC2A4RG	T	0.271 (0.236)	2.49E−01	0.022/0.016	0.164 (0.488)	7.36E−01	0.024/0.022
180	rs2154481	APP	T	0.005 (0.064)	9.39E−01	0.470/0.469	0.036 (0.139)	7.98E−01	0.448/0.446
181	rs2154482	APP	T	0.027 (0.067)	6.82E−01	0.341/0.336	0.035 (0.144)	8.10E−01	0.341/0.376
182	rs4817090	ADAMTS1	C	−0.038 (0.064)	5.51E−01	0.445/0.454	0.069 (0.139)	6.21E−01	0.466/0.444
183	rs2830489	ADAMTS1	T	−0.096 (0.242)	6.92E−01	0.017/0.019	−0.336 (0.514)	5.14E−01	0.020/0.018
184	rs115684722	SIPAIL2	T	0.358 (0.366)	3.29E−01	0.009/0.007	0.169 (0.685)	8.05E−01	0.010/0.012
185	rs168193	EDEM1	G	−0.313 (0.201)	1.19E−01	0.022/0.030	−0.119 (0.304)	6.96E−01	0.052/0.044
186	rs2633682	ALCAM	A	−0.105 (0.086)	2.26E−01	0.164/0.179	−0.187 (0.187)	3.16E−01	0.149/0.157
187	rs184179037	WDR70	T	0.613 (0.605)	3.11E−01	0.004/0.002	0.209 (0.610)	7.32E−01	0.011/0.014
188	rs145848414	NSG2-MSX2	N/A	N/A	N/A	N/A	N/A	N/A	N/A
189	rs569584007	API5	N/A	N/A	N/A	N/A	N/A	N/A	N/A
190	rs115816806	ACER3	N/A	N/A	N/A	N/A	N/A	N/A	N/A
191	rs75739461	PIK3C2G	N/A	N/A	N/A	N/A	N/A	N/A	N/A
192	rs9516245	GPC6	C	−0.525 (0.400)	1.90E−01	0.005/0.008	−1.225 (1.100)	2.66E−01	0.001/0.009
193	rs570487962	ARRDC4-IGF1R	N/A	N/A	N/A	N/A	N/A	N/A	N/A
194	rs79537509	RBFOX1	N/A	N/A	N/A	N/A	14.04 (2048)	9.95E−01	0.001/0.000
195	rs115550680	ABCA7	N/A	N/A	N/A	N/A	N/A	N/A	N/A
196	rs157591	APOE	N/A	N/A	N/A	N/A	N/A	N/A	N/A
197	rs3745495	VRK3	G	0.021 (0.090)	8.14E−01	0.147/0.144	0.008 (0.207)	9.69E−01	0.131/0.126
198	rs6859823	CTC-278L1.1	T	−0.022 (0.068)	7.46E−01	0.315/0.319	−0.063 (0.141)	6.57E−01	0.379/0.391
199	rs3777215	RHOBTB3, GLRX	A	0.101 (0.090)	2.58E−01	0.150/0.138	0.177 (0.163)	2.78E−01	0.230/0.192

200	rs234434	<i>CTD-2506J14.1</i>	G	−0.036 (0.071)	6.12E−01	0.261/0.268	0.120 (0.164)	4.66E−01	0.251/0.227
201	rs11668861	<i>NECTIN2</i>	G	0.562 (0.073)	1.86E−14	0.326/0.215	0.365 (0.157)	2.01E−02	0.305/0.227
202	rs6859	<i>NECTIN2</i>	A	0.437 (0.068)	1.12E−10	0.405/0.306	0.539 (0.146)	2.28E−04	0.417/0.301
203	rs3852860	<i>NECTIN2</i>	C	0.557 (0.072)	1.46E−14	0.339/0.226	0.312 (0.153)	4.06E−02	0.310/0.233
204	rs71352238	<i>TOMM40</i>	C	1.041 (0.094)	1.50E−28	0.244/0.097	1.067 (0.218)	1.02E−06	0.185/0.082
205	rs157580	<i>TOMM40</i>	A	0.371 (0.064)	5.08E−09	0.537/0.442	0.170 (0.135)	2.07E−01	0.500/0.456
206	rs2075650	<i>TOMM40</i>	G	1.055 (0.094)	5.94E−29	0.243/0.096	1.021 (0.216)	2.38E−06	0.184/0.083
207	rs157582	<i>TOMM40</i>	T	0.717 (0.076)	3.46E−21	0.324/0.185	0.537 (0.165)	1.11E−03	0.289/0.202
208	rs439401	<i>APOE</i>	C	0.468 (0.065)	6.85E−13	0.529/0.414	0.221 (0.136)	1.04E−01	0.506/0.454
209	rs4420638	<i>APOC1</i>	G	1.065 (0.088)	1.07E−33	0.286/0.116	1.133 (0.197)	8.83E−09	0.226/0.102
210	rs2255835	<i>CHODL</i>	C	−0.010 (0.069)	8.90E−01	0.295/0.298	−0.088 (0.153)	5.65E−01	0.274/0.293
211	rs11168036	<i>PFDN1/HBEGF</i>	T	0.060 (0.065)	3.53E−01	0.415/0.401	0.119 (0.141)	3.97E−01	0.445/0.454
212	rs4150233	<i>PFDN1/HBEGF</i>	C	0.048 (0.062)	4.39E−01	0.408/0.396	0.061 (0.142)	6.65E−01	0.448/0.458
213	rs2011704	<i>USP6NL/ECHDC3</i>	C	−0.007 (0.073)	9.27E−01	0.248/0.249	0.039 (0.158)	8.04E−01	0.243/0.260
214	rs11257240	<i>USP6NL/ECHDC3</i>	G	−0.007 (0.073)	9.26E−01	0.248/0.249	0.039 (0.158)	8.04E−01	0.243/0.262
215	rs12358692	<i>USP6NL/ECHDC3</i>	T	−0.025 (0.064)	6.93E−01	0.323/0.330	−0.065 (0.142)	6.46E−01	0.324/0.348
216	rs9749589	<i>NFIC</i>	A	0.499 (0.551)	3.65E−01	0.004/0.003	1.066 (1.354)	4.31E−01	0.003/0.002

AD, Alzheimer’s disease; β , effect size; EA, effect allele; EAF, effect allele frequency; N/A, not applicable; NC, normal control; SE, standard error; WGS, whole-genome sequencing. Variants significantly associated with AD ($p < 0.05$) are displayed in bold text

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Supplementary Table 7. Variants significantly associated with Alzheimer's disease in the Chinese population

Variants				Chinese AD WGS cohort 1			Chinese AD WGS cohort 2		
Index	Variant	Gene	EA	β (SE)	<i>p</i>	EAf (AD/NC)	β (SE)	<i>p</i>	EAf (AD/NC)
Populations of European descent									
9	rs17020490	<i>PRKD3</i>	T	0.061 (0.064)	3.43E-01	0.432/0.416	-0.295 (0.139)	3.37E-02	0.405/0.422
12	rs4663105	<i>BIN1</i>	C	0.206 (0.064)	1.25E-03	0.513/0.463	0.112 (0.141)	4.27E-01	0.485/0.462
13	rs6733839	<i>BIN1</i>	T	0.172 (0.064)	7.41E-03	0.469/0.428	0.153 (0.142)	2.80E-01	0.423/0.405
19	rs16824536	<i>MME</i>	A	-0.311 (0.311)	3.16E-01	0.009/0.013	-2.097 (0.916)	2.21E-02	0.004/0.010
35	rs9271058	<i>HLA-DRB1</i>	A	0.043 (0.088)	6.24E-01	0.150/0.144	0.644 (0.251)	1.05E-02	0.222/0.196
44	rs9381040	<i>TREML2</i>	T	0.164 (0.068)	1.57E-02	0.349/0.314	0.318 (0.150)	3.39E-02	0.379/0.361
76	rs61732533	<i>SHARPIN</i>	A	-2.840 (1.038)	6.20E-03	0.000/0.008	N/A	N/A	N/A
90	rs3740688	<i>MADD</i>	G	0.028 (0.068)	6.79E-01	0.345/0.340	-0.316 (0.151)	3.64E-02	0.249/0.316
96	rs1582763	<i>MS4A4A</i>	A	-0.211 (0.092)	2.12E-02	0.119/0.145	0.217 (0.225)	3.35E-01	0.121/0.103
97	rs72924626	<i>MS4A6E</i>	C	-0.187 (0.084)	2.71E-02	0.154/0.181	0.130 (0.193)	4.99E-01	0.167/0.147
98	rs867611	<i>PICALM</i>	G	-0.204 (0.066)	2.13E-03	0.343/0.390	0.024 (0.144)	8.67E-01	0.385/0.400
99	rs561655	<i>PICALM</i>	G	-0.169 (0.064)	8.64E-03	0.450/0.491	-0.060 (0.142)	6.72E-01	0.442/0.486
100	rs3844143	<i>PICALM</i>	C	-0.176 (0.066)	7.43E-03	0.366/0.408	0.020 (0.144)	8.92E-01	0.389/0.414
101	rs10792832	<i>PICALM</i>	A	-0.169 (0.066)	1.01E-02	0.358/0.398	0.001 (0.144)	9.92E-01	0.383/0.413
102	rs3851179	<i>PICALM</i>	T	-0.169 (0.066)	1.01E-02	0.358/0.398	0.001 (0.144)	9.92E-01	0.383/0.413
104	rs11218343	<i>SORL1</i>	C	-0.182 (0.072)	1.22E-02	0.246/0.282	-0.306 (0.151)	4.19E-02	0.264/0.304
116	rs442495	<i>ADAM10</i>	T	-0.087 (0.082)	2.91E-01	0.164/0.178	0.479 (0.184)	9.06E-03	0.211/0.161
117	rs593742	<i>ADAM10</i>	A	-0.099 (0.075)	1.90E-01	0.225/0.243	0.411 (0.173)	1.71E-02	0.239/0.200
118	rs602602	<i>MINDY2</i>	T	-0.101 (0.072)	1.60E-01	0.250/0.271	0.454 (0.167)	6.44E-03	0.273/0.217
136	rs61182333	<i>SCIMP</i>	T	-0.058 (0.110)	5.95E-01	0.093/0.099	0.977 (0.317)	2.09E-03	0.081/0.053
154	rs111278892	<i>ABCA7</i>	G	-2.188 (1.074)	4.17E-02	0.000/0.004	N/A	N/A	0/0.002
155	rs3752231	<i>ABCA7</i>	T	0.204 (0.064)	1.52E-03	0.449/0.400	-0.299 (0.145)	3.97E-02	0.406/0.436
156	rs12151021	<i>ABCA7</i>	G	-0.189 (0.064)	3.34E-03	0.478/0.524	0.219 (0.139)	1.16E-01	0.466/0.473
158	rs3752246	<i>ABCA7</i>	G	0.208 (0.067)	1.82E-03	0.375/0.326	-0.234 (0.143)	1.03E-01	0.351/0.372
159	rs4147929	<i>ABCA7</i>	A	0.213 (0.067)	1.34E-03	0.372/0.322	-0.251 (0.143)	7.88E-02	0.353/0.371
163	rs769450	<i>APOE</i>	A	-0.191 (0.083)	2.06E-02	0.175/0.203	-0.353 (0.163)	3.06E-02	0.188/0.234
164	rs429358	<i>APOE</i>	C	1.152 (0.093)	1.33E-35	0.273/0.099	1.348 (0.220)	9.05E-10	0.205/0.078
165	rs75627662	<i>APOE</i>	T	0.672 (0.076)	5.83E-19	0.313/0.184	0.621 (0.166)	1.84E-04	0.277/0.189
172	rs587709	<i>LILRB2</i>	T	-0.074 (0.083)	3.72E-01	0.177/0.186	0.425 (0.149)	4.47E-03	0.372/0.338
Asian populations									
201	rs11668861	<i>NECTIN2</i>	G	0.562 (0.073)	1.86E-14	0.326/0.215	0.365 (0.157)	2.01E-02	0.305/0.227
202	rs6859	<i>NECTIN2</i>	A	0.437 (0.068)	1.12E-10	0.405/0.306	0.539 (0.146)	2.28E-04	0.417/0.301
203	rs3852860	<i>NECTIN2</i>	C	0.557 (0.072)	1.46E-14	0.339/0.226	0.312 (0.153)	4.06E-02	0.310/0.233
204	rs71352238	<i>TOMM40</i>	C	1.041 (0.094)	1.50E-28	0.244/0.097	1.067 (0.218)	1.02E-06	0.185/0.082

205	rs157580	<i>TOMM40</i>	A	0.371 (0.064)	5.08E-09	0.537/0.442	0.170 (0.135)	2.07E-01	0.500/0.456
206	rs2075650	<i>TOMM40</i>	G	1.055 (0.094)	5.94E-29	0.243/0.096	1.021 (0.216)	2.38E-06	0.184/0.083
207	rs157582	<i>TOMM40</i>	T	0.717 (0.076)	3.46E-21	0.324/0.185	0.537 (0.165)	1.11E-03	0.289/0.202
208	rs439401	<i>APOE</i>	C	0.468 (0.065)	6.85E-13	0.529/0.414	0.221 (0.136)	1.04E-01	0.506/0.454
209	rs4420638	<i>APOC1</i>	G	1.065 (0.088)	1.07E-33	0.286/0.116	1.133 (0.197)	8.83E-09	0.226/0.102

AD, Alzheimer's disease; β , effect size; EA, effect allele; EAF, effect allele frequency; N/A, not applicable; NC, normal control; SE, standard error; WGS, whole-genome sequencing.

Supplementary Table 8. Meta-analysis results of the effects of variants on Alzheimer's disease in the Chinese population

Index	Variant	Gene	EA	β (SE)	Meta- <i>p</i>	EAF (AD/NC)	<i>I</i> ²
1	rs113020870	<i>AGRN</i>	N/A	N/A	N/A	N/A	N/A
2	rs141749679	<i>SORT1</i>	N/A	N/A	N/A	N/A	N/A
3	rs4575098	<i>ADAMTS4</i>	A	0.082 (0.061)	1.78E−01	0.325/0.313	0.00
4	rs6656401	<i>CR1</i>	A	−0.196 (0.173)	2.55E−01	0.028/0.037	0.00
5	rs679515	<i>CR1</i>	T	−0.197 (0.174)	2.58E−01	0.028/0.036	0.00
6	rs2093760	<i>CR1</i>	A	−0.088 (0.06)	1.43E−01	0.356/0.374	42.77
7	rs4844610	<i>CR1</i>	A	−0.173 (0.172)	3.14E−01	0.028/0.036	0.00
8	rs72777026	<i>ADAM17</i>	G	0.108 (0.081)	1.83E−01	0.149/0.136	45.35
9	rs17020490	<i>PRKD3</i>	T	−0.001 (0.058)	9.83E−01	0.425/0.419	81.52
10	rs115186657	<i>FHL2</i>	N/A	N/A	N/A	N/A	N/A
11	rs143080277	<i>NCK2</i>	N/A	N/A	N/A	N/A	N/A
12	rs4663105	<i>BIN1</i>	C	0.190 (0.058)	1.12E−03	0.506/0.463	0.00
13	rs6733839	<i>BIN1</i>	T	0.169 (0.058)	3.82E−03	0.458/0.418	0.00
14	rs139643391	<i>WDR12</i>	N/A	N/A	N/A	N/A	N/A
15	rs10933431	<i>INPP5D</i>	G	−0.068 (0.061)	2.72E−01	0.305/0.318	5.35
16	rs35349669	<i>INPP5D</i>	T	N/A	N/A	N/A	N/A
17	rs7597763	<i>INPP5D</i>	C	N/A	N/A	N/A	N/A
18	rs184384746	<i>HESX1</i>	N/A	N/A	N/A	N/A	N/A
19	rs16824536	<i>MME</i>	A	−0.496 (0.294)	9.24E−02	0.008/0.011	70.66
20	rs61762319	<i>MME</i>	N/A	N/A	N/A	N/A	N/A
21	rs3822030	<i>IDUA</i>	T	0.004 (0.057)	9.38E−01	0.474/0.465	0.00
22	rs4504245	<i>CLNK</i>	A	0.161 (0.078)	3.80E−02	0.177/0.157	0.00
23	rs6448451	<i>CLNK</i>	G	0.107 (0.073)	1.44E−01	0.200/0.188	43.72
24	rs6846529	<i>CLNK</i>	C	0.108 (0.070)	1.24E−01	0.226/0.211	0.00
25	rs6448453	<i>CLNK</i>	A	0.097 (0.072)	1.79E−01	0.209/0.196	57.75
26	rs7657553	<i>HS3ST1</i>	A	0.007 (0.059)	9.12E−01	0.338/0.330	0.00
27	rs2245466	<i>RHOH</i>	C	0.046 (0.058)	4.28E−01	0.48/0.469	35.48
28	rs112403360	<i>ANKH</i>	A	0.087 (0.169)	6.06E−01	0.032/0.028	0.00
29	rs62374257	<i>COX7C</i>	C	0.052 (0.066)	4.31E−01	0.272/0.262	0.00
30	rs190982	<i>MEF2C</i>	G	0.099 (0.081)	2.23E−01	0.153/0.135	55.76
31	rs871269	<i>TNIP1</i>	C	0.066 (0.059)	2.64E−01	0.423/0.404	0.00
32	rs6891966	<i>HAVCR2</i>	A	−0.048 (0.113)	6.72E−01	0.066/0.064	0.00
33	rs113706587	<i>RASGEF1C</i>	A	−0.056 (0.640)	9.30E−01	0.002/0.004	0.00
34	rs9269853	<i>HLA-DRB1</i>	A	0.153 (0.088)	8.17E−02	0.159/0.174	9.99
35	rs9271058	<i>HLA-DRB1</i>	A	0.109 (0.083)	1.90E−01	0.167/0.165	80.41
36	rs6605556	<i>HLA-DQA1</i>	G	−0.18 (0.088)	4.03E−02	0.107/0.127	22.49

37	rs6931277	<i>HLA-DRB1</i>	T	−0.162 (0.089)	7.02E−02	0.109/0.125	0.00
38	rs1846190	<i>HLA-DRB1</i>	A	−0.040 (0.065)	5.40E−01	0.245/0.255	0.00
39	rs187370608	<i>TREM2</i>	N/A	N/A	N/A	N/A	N/A
40	rs10947943	<i>UNC5CL</i>	A	0.099 (0.092)	2.85E−01	0.114/0.108	0.00
41	rs143332484	<i>TREM2</i>	N/A	N/A	N/A	N/A	N/A
42	rs75932628	<i>TREM2</i>	N/A	N/A	N/A	N/A	N/A
43	rs60755019	<i>TREML2</i>	G	0.921 (0.598)	1.23E−01	0.005/0.003	0.00
44	rs9381040	<i>TREML2</i>	T	0.190 (0.062)	2.13E−03	0.356/0.333	0.00
45	rs9473117	<i>CD2AP</i>	C	0.111 (0.088)	2.09E−01	0.133/0.129	0.00
46	rs9381563	<i>CD2AP</i>	C	0.119 (0.076)	1.20E−01	0.198/0.188	0.00
47	rs7767350	<i>CD2AP</i>	T	0.094 (0.086)	2.75E−01	0.135/0.131	0.00
48	rs9369716	<i>CD2AP</i>	T	0.102 (0.086)	2.37E−01	0.136/0.132	0.00
49	rs785129	<i>HS3ST5</i>	C	−0.068 (0.062)	2.69E−01	0.337/0.360	0.00
50	rs6943429	<i>UMAD1</i>	T	0.002 (0.058)	9.73E−01	0.430/0.435	0.00
51	rs10952097	<i>ICA1</i>	T	0.067 (0.097)	4.89E−01	0.104/0.109	0.00
52	rs5011436	<i>TMEM106B</i>	A	0.019 (0.058)	7.50E−01	0.340/0.337	71.03
53	rs13237518	<i>TMEM106B</i>	C	0.031 (0.060)	6.04E−01	0.343/0.338	71.93
54	rs1160871	<i>JAZF1</i>	N/A	N/A	N/A	N/A	N/A
55	rs4723711	<i>NME8</i>	T	−0.002 (0.069)	9.76E−01	0.225/0.218	0.00
56	rs6966331	<i>EPDR1</i>	C	−0.013 (0.057)	8.16E−01	0.480/0.484	0.00
57	rs76928645	<i>SEC61G</i>	T	N/A	N/A	N/A	N/A
58	rs7384878	<i>SPDYE3</i>	T	0.084 (0.059)	1.55E−01	0.404/0.373	0.00
59	rs1859788	<i>ZCWPW1</i>	G	0.102 (0.058)	8.12E−02	0.416/0.381	0.00
60	rs1476679	<i>ZCWPW1</i>	C	−0.050 (0.061)	4.14E−01	0.319/0.334	0.00
61	rs12539172	<i>NYAP1</i>	T	−0.048 (0.062)	4.37E−01	0.316/0.331	0.00
62	rs10808026	<i>EPHA1</i>	A	0.032 (0.086)	7.05E−01	0.133/0.131	51.28
63	rs3935067	<i>EPHA1</i>	C	0.176 (0.179)	3.25E−01	0.030/0.025	0.00
64	rs12703526	<i>EPHA1</i>	T	−0.015 (0.081)	8.50E−01	0.149/0.154	50.70
65	rs7810606	<i>EPHA1</i>	C	−0.026 (0.081)	7.49E−01	0.148/0.153	46.16
66	rs11763230	<i>EPHA1</i>	T	0.074 (0.085)	3.85E−01	0.142/0.135	54.19
67	rs11771145	<i>EPHA1</i>	G	0.020 (0.057)	7.30E−01	0.469/0.464	0.00
68	rs114360492	<i>CNTNAP2</i>	N/A	N/A	N/A	N/A	N/A
69	rs1065712	<i>CTSB</i>	N/A	N/A	N/A	N/A	N/A
70	rs73223431	<i>PTK2B</i>	T	0.083 (0.063)	1.88E−01	0.290/0.276	0.00
71	rs4236673	<i>CLU/PTK2B</i>	A	−0.147 (0.074)	4.56E−02	0.190/0.216	0.00
72	rs11787077	<i>CLU</i>	T	−0.157 (0.072)	2.85E−02	0.198/0.225	0.00
73	rs1532278	<i>CLU</i>	T	−0.162 (0.071)	2.37E−02	0.197/0.226	0.00
74	rs9331896	<i>CLU</i>	C	−0.143 (0.072)	4.60E−02	0.198/0.225	0.00
75	rs867230	<i>ECHDC3</i>	C	−0.141 (0.072)	5.00E−02	0.201/0.226	0.00
76	rs61732533	<i>SHARPIN</i>	A	N/A	N/A	N/A	N/A
77	rs34173062	<i>SHARPIN</i>	N/A	N/A	N/A	N/A	N/A

78	rs1800978	<i>ABCA1</i>	G	0.097 (0.080)	2.24E-01	0.156/0.155	0.00
79	rs11257238	<i>ECHDC3</i>	C	0.009 (0.066)	8.91E-01	0.248/0.253	0.00
80	rs7912495	<i>USP6NL</i>	G	-0.018 (0.062)	7.78E-01	0.294/0.304	0.00
81	rs7920721	<i>ECHDC3</i>	G	0.003 (0.066)	9.60E-01	0.246/0.253	0.00
82	rs11257242	<i>ECHDC3</i>	G	-0.034 (0.058)	5.65E-01	0.323/0.337	0.00
83	rs1171814	<i>CCDC6</i>	G	0.067 (0.060)	2.68E-01	0.379/0.358	44.11
84	rs7902657	<i>CCDC6</i>	T	0.078 (0.064)	2.23E-01	0.289/0.277	72.64
85	rs7068231	<i>ANK3</i>	G	0.083 (0.064)	1.96E-01	0.29/0.276	65.85
86	rs6586028	<i>TSPAN14</i>	C	-0.146 (0.208)	4.83E-01	0.018/0.025	0.00
87	rs1878036	<i>TSPAN14</i>	T	-0.157 (0.250)	5.30E-01	0.013/0.018	0.00
88	rs6584063	<i>BLNK</i>	G	-0.055 (0.255)	8.28E-01	0.014/0.013	74.10
89	rs7908662	<i>PLEKHA1</i>	A	0.046 (0.060)	4.43E-01	0.377/0.369	56.03
90	rs3740688	<i>MADD</i>	G	-0.030 (0.062)	6.28E-01	0.322/0.330	76.82
91	rs10437655	<i>SPI1</i>	A	0.074 (0.062)	2.29E-01	0.328/0.330	60.89
92	rs12292911	<i>SPI1</i>	A	0.051 (0.061)	4.07E-01	0.356/0.360	26.87
93	rs7933202	<i>MS4A2</i>	C	-0.065 (0.124)	5.99E-01	0.057/0.058	32.13
94	rs7935829	<i>MS4A6A</i>	G	0.022 (0.073)	7.66E-01	0.200/0.202	0.00
95	rs2081545	<i>MS4A6A</i>	A	0.029 (0.073)	6.95E-01	0.201/0.202	0.00
96	rs1582763	<i>MS4A4A</i>	A	-0.150 (0.085)	7.88E-02	0.120/0.127	67.74
97	rs72924626	<i>MS4A6E</i>	C	-0.137 (0.077)	7.63E-02	0.157/0.167	55.91
98	rs867611	<i>PICALM</i>	G	-0.164 (0.060)	6.14E-03	0.353/0.394	51.73
99	rs561655	<i>PICALM</i>	G	-0.151 (0.058)	9.85E-03	0.448/0.489	0.00
100	rs3844143	<i>PICALM</i>	C	-0.142 (0.060)	1.80E-02	0.372/0.410	34.68
101	rs10792832	<i>PICALM</i>	A	-0.139 (0.060)	2.01E-02	0.364/0.404	13.18
102	rs3851179	<i>PICALM</i>	T	-0.139 (0.060)	2.01E-02	0.364/0.404	13.18
103	rs74685827	<i>SORL1</i>	G	0.188 (0.094)	4.57E-02	0.115/0.097	0.00
104	rs11218343	<i>SORL1</i>	C	-0.205 (0.065)	1.61E-03	0.251/0.291	0.00
105	rs6489896	<i>TPCN1</i>	C	0.099 (0.072)	1.68E-01	0.209/0.196	21.69
106	rs7146179	<i>FERMT2</i>	A	-0.032 (0.072)	6.54E-01	0.202/0.206	0.00
107	rs17125924	<i>FERMT2</i>	G	-0.114 (0.067)	8.98E-02	0.249/0.260	0.00
108	rs7401792	<i>SLC24A4</i>	A	0.016 (0.060)	7.90E-01	0.363/0.375	0.00
109	rs12881735	<i>SLC24A4</i>	C	0.073 (0.097)	4.51E-01	0.098/0.098	35.47
110	rs12590654	<i>SLC24A4</i>	A	0.021 (0.058)	7.23E-01	0.469/0.461	0.00
111	rs7157106	<i>IGH gene cluster</i>	G	0.074 (0.108)	4.94E-01	0.076/0.066	8.74
112	rs10131280	<i>IGH gene cluster</i>	A	-0.024 (0.076)	7.56E-01	0.173/0.178	0.00
113	rs12592778	<i>SLC24A4</i>	A	-0.068 (0.058)	2.39E-01	0.468/0.493	38.55
114	rs8025980	<i>SPPL2A</i>	A	0.060 (0.058)	2.98E-01	0.449/0.422	0.00
115	rs59685680	<i>SPPL2A</i>	G	-0.019 (0.058)	7.43E-01	0.487/0.484	35.97
116	rs442495	<i>ADAM10</i>	T	0.007 (0.075)	9.28E-01	0.175/0.171	87.33
117	rs593742	<i>ADAM10</i>	A	-0.018 (0.069)	7.90E-01	0.228/0.225	86.33
118	rs602602	<i>MINDY2</i>	T	-0.014 (0.066)	8.32E-01	0.255/0.248	89.26

119	rs117618017	<i>APH1B</i>	N/A	N/A	N/A	N/A	N/A
120	rs3848143	<i>SNX1</i>	G	0.109 (0.072)	1.30E−01	0.194/0.182	0.00
121	rs12592898	<i>CTSH</i>	A	−0.129 (0.132)	3.28E−01	0.05/0.060	3.57
122	rs1140239	<i>DOC2A</i>	T	0.073 (0.059)	2.15E−01	0.418/0.408	58.57
123	rs889555	<i>BCKDK</i>	T	0.074 (0.106)	4.87E−01	0.089/0.094	0.00
124	rs2884738	<i>KAT8</i>	A	0.075 (0.106)	4.82E−01	0.089/0.093	0.00
125	rs59735493	<i>KAT8</i>	A	0.090 (0.106)	3.96E−01	0.089/0.093	0.00
126	rs4985556	<i>IL34</i>	A	0.190 (0.116)	1.02E−01	0.075/0.064	0.00
127	rs450674	<i>MAF</i>	C	−0.242 (0.144)	9.37E−02	0.036/0.045	0.00
128	rs12446759	<i>PLCG2</i>	G	−0.109 (0.070)	1.20E−01	0.193/0.216	0.00
129	rs12444183	<i>PLCG2</i>	A	−0.089 (0.069)	1.96E−01	0.209/0.232	0.00
130	rs72824905	<i>PLCG2</i>	N/A	N/A	N/A	N/A	N/A
131	rs16941239	<i>FOXF1</i>	A	−0.085 (0.082)	3.03E−01	0.131/0.137	0.00
132	rs56407236	<i>PRDM7</i>	A	0.196 (0.181)	2.81E−01	0.028/0.023	23.05
133	rs35048651	<i>WDR81</i>	N/A	N/A	N/A	N/A	N/A
134	rs7209200	<i>CHRNE</i>	T	0.018 (0.069)	7.91E−01	0.230/0.226	0.00
135	rs9916042	<i>SCIMP</i>	A	−0.002 (0.067)	9.77E−01	0.248/0.246	0.00
136	rs61182333	<i>SCIMP</i>	T	0.053 (0.104)	6.08E−01	0.090/0.080	89.49
137	rs7225151	<i>SCIMP</i>	A	0.195 (0.134)	1.45E−01	0.052/0.041	56.58
138	rs113260531	<i>SCIMP</i>	A	0.184 (0.134)	1.69E−01	0.052/0.041	58.09
139	rs2242595	<i>MYO15A</i>	G	−0.030 (0.058)	6.06E−01	0.478/0.482	0.00
140	rs5848	<i>GRN</i>	T	0.011 (0.061)	8.59E−01	0.353/0.357	54.80
141	rs708382	<i>GRN</i>	C	−0.066 (0.058)	2.58E−01	0.442/0.452	28.34
142	rs199515	<i>WNT3</i>	G	N/A	N/A	0/0.001	N/A
143	rs616338	<i>ABI3</i>	T	N/A	N/A	N/A	N/A
144	rs28394864	<i>ABI3</i>	A	0.012 (0.059)	8.33E−01	0.387/0.400	0.00
145	rs2526378	<i>TSPOAP1</i>	G	−0.090 (0.058)	1.21E−01	0.469/0.488	0.00
146	rs2632516	<i>AC004687.2</i>	C	−0.082 (0.058)	1.57E−01	0.467/0.483	0.00
147	rs2526377	<i>TSPOAP1</i>	G	−0.087 (0.058)	1.33E−01	0.461/0.479	0.00
148	rs138190086	<i>ACE</i>	A	−0.032 (0.305)	9.16E−01	0.009/0.010	0.00
149	rs6504163	<i>ACE</i>	C	−0.031 (0.061)	6.06E−01	0.366/0.369	0.00
150	rs4277405	<i>ACE</i>	C	−0.053 (0.060)	3.78E−01	0.337/0.347	0.00
151	rs4311	<i>ACE</i>	T	−0.019 (0.063)	7.61E−01	0.32/0.326	0.00
152	rs8093731	<i>SUZ12P1</i>	T	0.032 (0.168)	8.48E−01	0.027/0.027	29.04
153	rs76726049	<i>ALPK2</i>	N/A	N/A	N/A	N/A	N/A
154	rs111278892	<i>ABCA7</i>	G	N/A	N/A	0/0.003	N/A
155	rs3752231	<i>ABCA7</i>	T	0.122 (0.059)	3.72E−02	0.439/0.415	90.07
156	rs12151021	<i>ABCA7</i>	G	−0.118 (0.058)	4.30E−02	0.475/0.503	85.93
157	rs3752241	<i>ABCA7</i>	G	−0.065 (0.074)	3.77E−01	0.185/0.191	0.00
158	rs3752246	<i>ABCA7</i>	G	0.128 (0.061)	3.43E−02	0.369/0.345	87.24
159	rs4147929	<i>ABCA7</i>	A	0.129 (0.061)	3.28E−02	0.368/0.343	88.42

160	rs149080927	<i>KLF16</i>	N/A	N/A	N/A	N/A	N/A
161	rs41289512	<i>APOE</i>	G	N/A	N/A	N/A	N/A
162	rs146275714	<i>APOE</i>	A	N/A	N/A	N/A	N/A
163	rs769450	<i>APOE</i>	A	−0.224 (0.074)	2.42E−03	0.178/0.216	0.00
164	rs429358	<i>APOE</i>	C	1.182 (0.086)	2.72E−43	0.256/0.090	0.00
165	rs75627662	<i>APOE</i>	T	0.663 (0.069)	8.24E−22	0.304/0.186	0.00
166	rs76320948	<i>AC074212.3</i>	T	N/A	N/A	N/A	N/A
167	rs2452170	<i>NTN5</i>	A	−0.651 (0.504)	1.97E−01	0.002/0.004	0.00
168	rs9304690	<i>SIGLEC11</i>	T	0.137 (0.070)	4.89E−02	0.244/0.233	0.00
169	rs3865444	<i>CD33</i>	A	−0.025 (0.077)	7.41E−01	0.170/0.174	55.45
170	rs12459419	<i>CD33</i>	T	−0.020 (0.077)	7.99E−01	0.170/0.174	45.55
171	rs1354106	<i>CD33</i>	G	0.003 (0.070)	9.64E−01	0.218/0.220	0.00
172	rs587709	<i>LILRB2</i>	T	0.044 (0.073)	5.42E−01	0.224/0.249	88.32
173	rs1761461	<i>KIR3DL2</i>	A	0.003 (0.080)	9.66E−01	0.149/0.166	0.00
174	rs1358782	<i>RBCK1</i>	A	0.008 (0.101)	9.36E−01	0.089/0.085	0.00
175	rs6069736	<i>CASS4</i>	T	−0.075 (0.060)	2.10E−01	0.349/0.369	0.00
176	rs6069737	<i>CASS4</i>	N/A	N/A	N/A	N/A	N/A
177	rs6024870	<i>CASS4</i>	N/A	N/A	N/A	N/A	N/A
178	rs6014724	<i>CASS4</i>	G	−0.106 (0.059)	7.19E−02	0.364/0.384	0.00
179	rs6742	<i>SLC2A4RG</i>	T	0.251 (0.212)	2.38E−01	0.022/0.019	0.00
180	rs2154481	<i>APP</i>	T	0.010 (0.058)	8.58E−01	0.465/0.459	0.00
181	rs2154482	<i>APP</i>	T	0.028 (0.061)	6.40E−01	0.341/0.353	0.00
182	rs4817090	<i>ADAMTS1</i>	C	−0.019 (0.058)	7.40E−01	0.450/0.450	0.00
183	rs2830489	<i>ADAMTS1</i>	T	−0.140 (0.219)	5.24E−01	0.018/0.018	0.00
184	rs115684722	<i>SIPAIL2</i>	T	0.316 (0.323)	3.28E−01	0.010/0.009	0.00
185	rs168193	<i>EDEM1</i>	G	−0.254 (0.168)	1.30E−01	0.029/0.036	0.00
186	rs2633682	<i>ALCAM</i>	A	−0.119 (0.078)	1.27E−01	0.161/0.170	0.00
187	rs184179037	<i>WDR70</i>	T	0.413 (0.430)	3.37E−01	0.006/0.007	0.00
188	rs145848414	<i>NSG2-MSX2</i>	N/A	N/A	N/A	N/A	N/A
189	rs569584007	<i>API5</i>	N/A	N/A	N/A	N/A	N/A
190	rs115816806	<i>ACER3</i>	N/A	N/A	N/A	N/A	N/A
191	rs75739461	<i>PIK3C2G</i>	N/A	N/A	N/A	N/A	N/A
192	rs9516245	<i>GPC6</i>	C	−0.607 (0.376)	1.07E−01	0.004/0.009	0.00
193	rs570487962	<i>ARRDC4-IGF1R</i>	N/A	N/A	N/A	N/A	N/A
194	rs79537509	<i>RBFOX1</i>	N/A	N/A	N/A	N/A	N/A
195	rs115550680	<i>ABCA7</i>	N/A	N/A	N/A	N/A	N/A
196	rs157591	<i>APOE</i>	N/A	N/A	N/A	N/A	N/A
197	rs3745495	<i>VRK3</i>	G	0.019 (0.083)	8.19E−01	0.143/0.137	0.00
198	rs6859823	<i>CTC-278L1.1</i>	T	−0.030 (0.061)	6.27E−01	0.331/0.349	0.00
199	rs3777215	<i>RHOBTB3, GLRX</i>	A	0.119 (0.079)	1.32E−01	0.169/0.160	0.00
200	rs234434	<i>CTD-2506J14.1</i>	G	−0.011 (0.065)	8.61E−01	0.259/0.251	0.00

201	rs11668861	<i>NECTIN2</i>	G	0.527 (0.066)	1.71E−15	0.321/0.220	22.76
202	rs6859	<i>NECTIN2</i>	A	0.455 (0.062)	1.53E−13	0.408/0.304	0.00
203	rs3852860	<i>NECTIN2</i>	C	0.513 (0.065)	3.60E−15	0.332/0.229	52.36
204	rs71352238	<i>TOMM40</i>	C	1.045 (0.086)	9.66E−34	0.230/0.091	0.00
205	rs157580	<i>TOMM40</i>	A	0.334 (0.058)	7.58E−09	0.528/0.448	44.75
206	rs2075650	<i>TOMM40</i>	G	1.050 (0.086)	4.11E−34	0.229/0.090	0.00
207	rs157582	<i>TOMM40</i>	T	0.685 (0.069)	3.07E−23	0.315/0.192	0.00
208	rs439401	<i>APOE</i>	C	0.422 (0.059)	6.16E−13	0.523/0.431	62.76
209	rs4420638	<i>APOC1</i>	G	1.076 (0.080)	6.41E−41	0.272/0.110	0.00
210	rs2255835	<i>CHODL</i>	C	−0.023 (0.063)	7.12E−01	0.290/0.296	0.00
211	rs11168036	<i>PFDN1/HBEGF</i>	T	0.070 (0.059)	2.33E−01	0.422/0.423	0.00
212	rs4150233	<i>PFDN1/HBEGF</i>	C	0.050 (0.057)	3.78E−01	0.418/0.422	0.00
213	rs2011704	<i>USP6NL/ECHDC3</i>	C	0.001 (0.066)	9.87E−01	0.247/0.254	0.00
214	rs11257240	<i>USP6NL/ECHDC3</i>	G	0.001 (0.066)	9.87E−01	0.247/0.254	0.00
215	rs12358692	<i>USP6NL/ECHDC3</i>	T	−0.032 (0.058)	5.86E−01	0.323/0.337	0.00
216	rs9749589	<i>NFIC</i>	A	0.580 (0.510)	2.56E−01	0.004/0.003	0.00

AD, Alzheimer's disease; β , effect size; EA, effect allele; EAF, effect allele frequency; N/A, not applicable; NC, normal control; SE, standard error; WGS, whole-genome sequencing. The meta-analysis was conducted using a fixed-effects model. Variants significantly associated with AD ($p < 0.05$) are displayed in bold text.

Supplementary Table 9. Variants used to construct polygenic score models

Variants				Chinese AD WGS cohort 1			Chinese AD WGS cohort 2		
Index	Variant	Gene	EA	β (SE)	p	EAF (AD/NC)	β (SE)	p	EAF (AD/NC)
Non-APOE AD genetic risk ($n = 25$)									
12	rs4663105	<i>BIN1</i>	C	0.206 (0.064)	1.25E-03	0.513/0.463	0.112 (0.141)	4.27E-01	0.485/0.462
13	rs6733839	<i>BIN1</i>	T	0.172 (0.064)	7.41E-03	0.469/0.428	0.153 (0.142)	2.80E-01	0.423/0.405
19	rs16824536	<i>MME</i>	A	-0.311 (0.311)	3.16E-01	0.009/0.013	-2.097 (0.916)	2.21E-02	0.004/0.010
22	rs4504245	<i>CLNK</i>	A	0.133 (0.085)	1.19E-01	0.177/0.159	0.308 (0.193)	1.11E-01	0.177/0.155
35	rs9271058	<i>HLA-DRB1</i>	A	0.043 (0.088)	6.24E-01	0.150/0.144	0.644 (0.251)	1.05E-02	0.222/0.196
36	rs6605556	<i>HLA-DQA1</i>	G	-0.145 (0.093)	1.18E-01	0.116/0.132	-0.464 (0.265)	7.96E-02	0.081/0.119
44	rs9381040	<i>TREML2</i>	T	0.164 (0.068)	1.57E-02	0.349/0.314	0.318 (0.150)	3.39E-02	0.379/0.361
71	rs4236673	<i>CLU/PTK2B</i>	A	-0.117 (0.083)	1.56E-01	0.176/0.192	-0.262 (0.161)	1.03E-01	0.236/0.250
72	rs11787077	<i>CLU</i>	T	-0.131 (0.080)	1.03E-01	0.186/0.206	-0.262 (0.161)	1.03E-01	0.236/0.253
73	rs1532278	<i>CLU</i>	T	-0.136 (0.080)	9.01E-02	0.185/0.206	-0.263 (0.159)	9.74E-02	0.237/0.254
74	rs9331896	<i>CLU</i>	C	-0.117 (0.080)	1.46E-01	0.186/0.203	-0.248 (0.161)	1.23E-01	0.239/0.255
76	rs61732533	<i>SHARPIN</i>	A	-2.840 (1.038)	6.20E-03	0.000/0.008	N/A	N/A	N/A
98	rs867611	<i>PICALM</i>	G	-0.204 (0.066)	2.13E-03	0.343/0.390	0.024 (0.144)	8.67E-01	0.385/0.400
99	rs561655	<i>PICALM</i>	G	-0.169 (0.064)	8.64E-03	0.450/0.491	-0.060 (0.142)	6.72E-01	0.442/0.486
100	rs3844143	<i>PICALM</i>	C	-0.176 (0.066)	7.43E-03	0.366/0.408	0.020 (0.144)	8.92E-01	0.389/0.414
101	rs10792832	<i>PICALM</i>	A	-0.169 (0.066)	1.01E-02	0.358/0.398	0.001 (0.144)	9.92E-01	0.383/0.413
102	rs3851179	<i>PICALM</i>	T	-0.169 (0.066)	1.01E-02	0.358/0.398	0.001 (0.144)	9.92E-01	0.383/0.413
103	rs74685827	<i>SORL1</i>	G	0.161 (0.102)	1.15E-01	0.119/0.104	0.341 (0.243)	1.60E-01	0.101/0.087
104	rs11218343	<i>SORL1</i>	C	-0.182 (0.072)	1.22E-02	0.246/0.282	-0.306 (0.151)	4.19E-02	0.264/0.304
154	rs111278892	<i>ABCA7</i>	G	-2.188 (1.074)	4.17E-02	0.000/0.004	N/A	N/A	0.000/0.002
155	rs3752231	<i>ABCA7</i>	T	0.204 (0.064)	1.52E-03	0.449/0.400	-0.299 (0.145)	3.97E-02	0.406/0.436
156	rs12151021	<i>ABCA7</i>	G	-0.189 (0.064)	3.34E-03	0.478/0.524	0.219 (0.139)	1.16E-01	0.466/0.473
158	rs3752246	<i>ABCA7</i>	G	0.208 (0.067)	1.82E-03	0.375/0.326	-0.234 (0.143)	1.03E-01	0.351/0.372
159	rs4147929	<i>ABCA7</i>	A	0.213 (0.067)	1.34E-03	0.372/0.322	-0.251 (0.143)	7.88E-02	0.353/0.371
168	rs9304690	<i>SIGLEC11</i>	T	0.105 (0.078)	1.77E-01	0.228/0.210	0.267 (0.156)	8.64E-02	0.294/0.267
APOE AD genetic risk ($n = 12$)									
163	rs769450	<i>APOE</i>	A	-0.191 (0.083)	2.06E-02	0.175/0.203	-0.353 (0.163)	3.06E-02	0.188/0.234
164	rs429358	<i>APOE</i>	C	1.152 (0.093)	1.33E-35	0.273/0.099	1.348 (0.220)	9.05E-10	0.205/0.078
165	rs75627662	<i>APOE</i>	T	0.672 (0.076)	5.83E-19	0.313/0.184	0.621 (0.166)	1.84E-04	0.277/0.189
201	rs11668861	<i>NECTIN2</i>	G	0.562 (0.073)	1.86E-14	0.326/0.215	0.365 (0.157)	2.01E-02	0.305/0.227
202	rs6859	<i>NECTIN2</i>	A	0.437 (0.068)	1.12E-10	0.405/0.306	0.539 (0.146)	2.28E-04	0.417/0.301
203	rs3852860	<i>NECTIN2</i>	C	0.557 (0.072)	1.46E-14	0.339/0.226	0.312 (0.153)	4.06E-02	0.310/0.233
204	rs71352238	<i>TOMM40</i>	C	1.041 (0.094)	1.50E-28	0.244/0.097	1.067 (0.218)	1.02E-06	0.185/0.082
205	rs157580	<i>TOMM40</i>	A	0.371 (0.064)	5.08E-09	0.537/0.442	0.170 (0.135)	2.07E-01	0.500/0.456
206	rs2075650	<i>TOMM40</i>	G	1.055 (0.094)	5.94E-29	0.243/0.096	1.021 (0.216)	2.38E-06	0.184/0.083

207	rs157582	<i>TOMM40</i>	T	0.717 (0.076)	3.46E-21	0.324/0.185	0.537 (0.165)	1.11E-03	0.289/0.202
208	rs439401	<i>APOE</i>	C	0.468 (0.065)	6.85E-13	0.529/0.414	0.221 (0.136)	1.04E-01	0.506/0.454
209	rs4420638	<i>APOC1</i>	G	1.065 (0.088)	1.07E-33	0.286/0.116	1.133 (0.197)	8.83E-09	0.226/0.102

AD, Alzheimer's disease; β , effect size; EA, effect allele; EAF, effect allele frequency; N/A, not applicable; NC, normal control; SE, standard error; WGS, whole-genome sequencing.

Supplementary Table 10. Performance of the polygenic score models in the Chinese WGS cohorts

	Chinese AD WGS cohort 1		Chinese AD WGS cohort 2
Models	AD vs. NC (1,116 AD, 915 NC)	MCI vs. NC (309 MCI, 915 NC)	AD vs. NC (356 AD, 653 NC)
Lasso regression model			
Lasso	0.7069 (0.6840-0.7298)	0.5963 (0.5574-0.6327)	0.6348 (0.5997-0.6700)
Lasso_APOE	0.6528 (0.6297-0.6761)	0.5777 (0.5406-0.6158)	0.6323 (0.5959-0.6697)
Lasso_nonAPOE	0.6114 (0.5874-0.6354)	0.5412 (0.5050-0.5786)	0.5539 (0.5187-0.5904)
Neural network model			
NN	0.7718 (0.7507-0.7923)	0.6241 (0.5867-0.6614)	0.6299 (0.5924-0.6656)

Classification accuracy was measured as area under the receiver operating characteristic curve (auROC). AD, Alzheimer's disease; MCI, mild cognitive impairment; NC, normal control; NN, neural network; WGS, whole-genome sequencing; wPRS, weight polygenic risk score.

Supplementary Table 11. Test of the polygenic score models performance in the Chinese WGS cohorts

	Chinese AD WGS cohort 1		Chinese AD WGS cohort 2
Models	AD vs. NC (1,116 AD, 915 NC)	MCI vs. NC (309 MCI, 915 NC)	AD vs. NC (356 AD, 653 NC)
NN vs. Lasso (<i>P</i> -value)	< 2.20E-16	6.24E-03	6.39E-01

Testing for classification accuracy was measured as area under the receiver operating characteristic curve (auROC); AD, Alzheimer's disease; MCI, mild cognitive impairment; NC, normal control; NN, neural network; wPRS, weight polygenic risk score. Bootstrap two-tailed test

Supplementary Table 12. Individual disease risk stratification based on polygenic scores and their associations with phenotypes

	Chinese AD WGS cohort 1			Chinese AD WGS cohort 2	
	AD	MCI	NC	AD	NC
Low risk (<i>n</i>)	155	101	443	90	261
Medium risk (<i>n</i>)	466	120	357	148	287
High risk (<i>n</i>)	495	88	115	118	105
Dataset	Phenotype	Group	β	SE	<i>p</i> -value
Chinese AD WGS cohort 1	AD vs. NC	High vs. Low	2.525	0.141	<2E-16
		High vs. Medium	1.191	0.126	<2E-16
		Medium vs. Low	1.320	0.117	<2E-16
	MCI vs. NC	High vs. Low	1.263	0.184	6.16E-12
		High vs. Medium	0.819	0.179	5.06E-06
		Medium vs. Low	0.384	0.153	1.25E-02
Chinese AD WGS cohort 2	AD vs. NC	High vs. Low	1.322	0.272	1.13E-06
		High vs. Medium	0.982	0.258	1.44E-04
		Medium vs. Low	0.384	0.238	0.107

AD, Alzheimer's disease; β , effect size; MCI, mild cognitive impairment; NC, normal control; SE, standard error; WGS, whole-genome sequencing.

Supplementary Table 13. Association between polygenic scores and cognitive performance

Dataset	Group	β	SE	p-value
Chinese AD WGS cohort 1	All participants	-1.768	0.082	<2E-16
	Non-AD participants	-0.298	0.082	3.10E-04
	APOE- ϵ 3 carriers	-2.145	0.128	<2E-16
	APOE- ϵ 4 carriers	-1.753	0.335	2.18E-07
Chinese AD WGS cohort 2	All participants	-0.287	0.107	7.38E-03
	Non-AD participants	0.171	0.135	0.206
	APOE- ϵ 3 carriers	-0.071	0.166	0.668
	APOE- ϵ 4 carriers	0.116	0.452	0.798

AD, Alzheimer's disease; β , effect size; SE, standard error; WGS, whole-genome sequencing. Significant associations ($p < 0.05$) are displayed in bold text.

Supplementary Table 14. Associations between polygenic scores and the plasma ATN biomarker panel

Group	Biomarker	NN				PRS_Full			
All		β	SE	<i>t</i>	<i>p</i> -value	β	SE	<i>t</i>	<i>p</i> -value
	A β ₄₂	-3.614	0.957	-3.776	<u>1.96E-04</u>	-1.261	0.334	-3.780	<u>1.93E-04</u>
	A β ₄₀	21.945	16.767	1.309	1.92E-01	7.139	6.030	1.184	2.37E-01
	A β ₄₂ /A β ₄₀	-0.016	0.004	-3.628	<u>3.42E-04</u>	-0.005	0.002	-3.250	<u>1.30E-03</u>
	tau	-0.051	0.276	-0.185	8.53E-01	0.076	0.097	0.777	4.38E-01
	p-tau181	1.536	0.355	4.322	<u>2.20E-05</u>	0.618	0.141	4.379	<u>1.72E-05</u>
	NfL	5.388	2.167	2.487	<u>1.35E-02</u>	1.587	0.739	2.148	<u>3.26E-02</u>
		PRS_APOE				PRS_nonAPOE			
		β	SE	<i>t</i>	<i>p</i> -value	β	SE	<i>t</i>	<i>p</i> -value
	A β ₄₂	-1.664	0.354	-4.708	<u>4.01E-06</u>	0.030	0.588	0.051	9.59E-01
	A β ₄₀	5.355	7.355	0.728	4.67E-01	11.423	9.584	1.192	2.34E-01
	A β ₄₂ /A β ₄₀	-0.007	0.002	-3.897	<u>1.23E-04</u>	0.000	0.003	0.012	9.91E-01
	tau	0.022	0.106	0.211	8.33E-01	0.203	0.150	1.352	1.78E-01
	p-tau181	0.657	0.168	3.901	<u>1.22E-04</u>	0.465	0.253	1.839	<u>6.71E-02</u>
	NfL	1.704	0.914	1.864	<u>6.34E-02</u>	0.854	1.168	0.731	4.65E-01
Group	Biomarker	NN				PRS_Full			
NC		β	SE	<i>t</i>	<i>p</i> -value	β	SE	<i>t</i>	<i>p</i> -value
	A β ₄₂	-3.936	1.276	-3.086	<u>2.55E-03</u>	-1.524	0.526	-2.894	<u>4.55E-03</u>
	A β ₄₀	24.432	22.467	1.087	2.79E-01	10.729	8.618	1.245	2.16E-01
	A β ₄₂ /A β ₄₀	-0.023	0.007	-3.145	<u>2.12E-03</u>	-0.009	0.003	-3.022	<u>3.09E-03</u>
	tau	-0.454	0.384	-1.183	2.39E-01	-0.113	0.179	-0.633	5.28E-01
	p-tau181	0.629	0.278	2.265	<u>2.55E-02</u>	0.309	0.190	1.625	1.07E-01
	NfL	4.749	2.229	2.130	<u>3.53E-02</u>	1.110	0.811	1.368	1.74E-01
		PRS_APOE				PRS_nonAPOE			
		β	SE	<i>t</i>	<i>p</i> -value	β	SE	<i>t</i>	<i>p</i> -value
	A β ₄₂	-2.229	0.493	-4.520	<u>1.52E-05</u>	0.336	0.879	0.383	7.03E-01
	A β ₄₀	2.541	8.667	0.293	7.70E-01	30.349	12.515	2.425	<u>1.69E-02</u>
	A β ₄₂ /A β ₄₀	-0.011	0.003	-3.533	<u>5.94E-04</u>	-0.004	0.006	-0.782	4.36E-01
	tau	-0.160	0.177	-0.901	3.70E-01	0.105	0.245	0.428	6.69E-01
	p-tau181	0.293	0.222	1.324	1.88E-01	0.275	0.228	1.205	2.31E-01
	NfL	0.697	0.850	0.820	4.14E-01	1.724	1.223	1.409	1.61E-01
Group	Biomarker	NN				PRS_Full			
AD		β	SE	<i>t</i>	<i>p</i> -value	β	SE	<i>t</i>	<i>p</i> -value
	A β ₄₂	-2.457	1.475	-1.665	9.80E-02	-0.910	0.486	-1.872	6.32E-02
	A β ₄₀	9.025	22.723	0.397	6.92E-01	-1.704	8.015	-0.213	8.32E-01
	A β ₄₂ /A β ₄₀	-0.006	0.004	-1.460	1.46E-01	-0.002	0.002	-1.408	1.61E-01
	tau	0.306	0.386	0.791	4.30E-01	0.162	0.121	1.331	1.85E-01
	p-tau181	0.711	0.708	1.005	3.17E-01	0.132	0.227	0.579	5.63E-01
	NfL	0.953	3.698	0.258	7.97E-01	0.002	1.044	0.002	9.99E-01
		PRS_APOE				PRS_nonAPOE			
		β	SE	<i>t</i>	<i>p</i> -value	β	SE	<i>t</i>	<i>p</i> -value
	A β ₄₂	-1.181	0.519	-2.276	<u>2.43E-02</u>	0.031	0.774	0.040	9.68E-01
	A β ₄₀	3.290	9.693	0.339	7.35E-01	-13.761	15.093	-0.912	3.63E-01
	A β ₄₂ /A β ₄₀	-0.003	0.002	-1.718	8.79E-02	0.002	0.002	0.702	4.84E-01
	tau	0.089	0.151	0.590	5.56E-01	0.274	0.191	1.432	1.54E-01
	p-tau181	0.190	0.268	0.710	4.79E-01	0.000	0.506	0.000	1.00E+00
	NfL	0.741	1.284	0.577	5.65E-01	-2.297	1.821	-1.261	2.09E-01

A β , amyloid-beta; AD, Alzheimer's disease; β , effect size; NC, normal control; NfL, neurofilament light polypeptide; NN, neural network; PRS, polygenic risk score; SE, standard error. Bold underlined text indicates $p < 0.05$; underlined text indicates $p < 0.10$.

Supplementary Table 15. Associations between polygenic scores and regional brain volumes

Group	Brain region	NN				PRS_Full			
All		β	SE	<i>t</i>	<i>p</i> -value	β	SE	<i>t</i>	<i>p</i> -value
	Amygdala	−0.373	0.135	−2.753	<u>6.53E−03</u>	−0.161	0.050	−3.201	<u>1.63E−03</u>
	Caudate	−0.362	0.274	−1.319	1.89E−01	−0.093	0.102	−0.912	3.63E−01
	Gray matter	−17.116	6.750	−2.536	<u>1.21E−02</u>	−4.037	2.569	−1.571	1.18E−01
	Hippocampus	−0.634	0.320	−1.981	<u>4.92E−02</u>	−0.271	0.113	−2.393	<u>1.78E−02</u>
	Hypothalamus	−0.023	0.018	−1.237	2.18E−01	−0.001	0.006	−0.117	9.07E−01
	Pons	0.361	0.434	0.831	4.07E−01	0.348	0.151	2.311	<u>2.20E−02</u>
	Putamen	−0.394	0.310	−1.269	2.06E−01	−0.143	0.109	−1.303	1.94E−01
	White matter	0.023	9.787	0.002	9.98E−01	−1.66	3.191	−0.52	6.04E−01
	White matter hyperintensity	2.559	1.146	2.232	<u>2.69E−02</u>	0.747	0.675	1.107	2.70E−01
		PRS_APOE				PRS_nonAPOE			
		β	SE	<i>t</i>	<i>p</i> -value	β	SE	<i>t</i>	<i>p</i> -value
	Amygdala	−0.132	0.053	−2.481	<u>1.41E−02</u>	−0.237	0.096	−2.468	<u>1.46E−02</u>
	Caudate	−0.074	0.114	−0.653	5.14E−01	−0.042	0.177	−0.235	8.15E−01
	Gray matter	−4.448	2.759	−1.612	1.09E−01	−3.394	4.511	−0.752	4.53E−01
	Hippocampus	−0.277	0.122	−2.274	<u>2.42E−02</u>	−0.293	0.226	−1.296	1.97E−01
	Hypothalamus	0.003	0.006	0.436	6.64E−01	−0.011	0.012	−0.962	3.37E−01
	Pons	0.298	0.176	1.688	<u>9.33E−02</u>	0.487	0.281	1.733	<u>8.49E−02</u>
	Putamen	−0.243	0.137	−1.774	<u>7.79E−02</u>	0.235	0.183	1.289	1.99E−01
	White matter	0.307	4.029	0.076	9.39E−01	−8.283	6.089	−1.36	1.76E−01
	White matter hyperintensity	0.809	0.666	1.215	2.26E−01	0.937	0.864	1.085	2.80E−01
Group	Region	NN				PRS_Full			
NC		β	SE	<i>t</i>	<i>p</i> -value	β	SE	<i>t</i>	<i>p</i> -value
	Amygdala	−0.026	0.118	−0.223	8.24E−01	0.033	0.063	0.529	5.98E−01
	Caudate	−0.467	0.344	−1.357	1.78E−01	−0.174	0.143	−1.213	2.28E−01
	Gray matter	−4.507	6.939	−0.65	5.18E−01	1.288	3.353	0.384	7.02E−01
	Hippocampus	−0.002	0.226	−0.008	9.93E−01	0.092	0.092	1.001	3.20E−01
	Hypothalamus	−0.011	0.023	−0.483	6.30E−01	0.000	0.008	0.051	9.59E−01
	Pons	−0.071	0.558	−0.127	8.99E−01	0.266	0.226	1.178	2.42E−01
	Putamen	0.003	0.358	0.009	9.93E−01	−0.049	0.202	−0.244	8.08E−01
	White matter	−1.585	14.016	−0.113	9.10E−01	−1.995	6.764	−0.295	7.69E−01
	White matter hyperintensity	0.946	0.652	1.452	1.50E−01	0.227	0.276	0.821	4.14E−01
		PRS_APOE				PRS_nonAPOE			
		β	SE	<i>t</i>	<i>p</i> -value	β	SE	<i>t</i>	<i>p</i> -value
	Amygdala	0.040	0.060	0.675	5.01E−01	0.087	0.137	0.638	5.25E−01
	Caudate	−0.168	0.166	−1.012	3.14E−01	0.028	0.226	0.125	9.00E−01
	Gray matter	0.972	3.219	0.302	7.63E−01	2.260	5.925	0.381	7.04E−01
	Hippocampus	0.055	0.106	0.522	6.03E−01	0.228	0.213	1.074	2.86E−01
	Hypothalamus	0.001	0.009	0.083	9.34E−01	0.006	0.019	0.324	7.46E−01

	Pons	0.131	0.261	0.500	6.18E-01	0.778	0.418	1.860	<u>6.61E-02</u>
	Putamen	-0.163	0.272	-0.6	5.50E-01	0.462	0.234	1.977	<u>5.10E-02</u>
	White matter	1.475	8.261	0.178	8.59E-01	-13.225	8.292	-1.595	1.14E-01
	White matter hyperintensity	0.233	0.311	0.750	4.55E-01	-0.026	0.574	-0.046	9.64E-01
Group	Region	NN				PRS_Full			
AD		β	SE	t	p -value	β	SE	t	p -value
	Amygdala	-0.27	0.339	-0.796	4.29E-01	-0.096	0.117	-0.815	4.18E-01
	Caudate	-0.403	0.553	-0.73	4.68E-01	-0.1	0.167	-0.598	5.52E-01
	Gray matter	-22.958	13.366	-1.718	<u>9.04E-02</u>	-2.554	3.767	-0.678	5.00E-01
	Hippocampus	0.213	0.476	0.449	6.55E-01	-0.112	0.122	-0.914	3.64E-01
	Hypothalamus	0.000	0.029	-0.006	9.96E-01	0.008	0.009	0.927	3.57E-01
	Pons	1.683	0.803	2.097	<u>3.97E-02</u>	0.631	0.245	2.579	<u>1.21E-02</u>
	Putamen	-0.44	0.777	-0.566	5.73E-01	-0.015	0.194	-0.077	9.39E-01
	White matter	24.228	15.221	1.592	1.16E-01	5.036	3.795	1.327	1.89E-01
	White matter hyperintensity	-0.17	3.799	-0.045	9.64E-01	0.307	0.929	0.331	7.42E-01
		PRS_APOE				PRS_nonAPOE			
		β	SE	t	p -value	β	SE	t	p -value
	Amygdala	0.009	0.106	0.085	9.33E-01	-0.381	0.185	-2.062	<u>4.31E-02</u>
	Caudate	-0.055	0.195	-0.283	7.78E-01	-0.209	0.345	-0.606	5.46E-01
	Gray matter	-2.061	5.388	-0.382	7.03E-01	-4.721	6.714	-0.703	4.84E-01
	Hippocampus	-0.004	0.158	-0.026	9.79E-01	-0.371	0.228	-1.626	1.09E-01
	Hypothalamus	0.013	0.009	1.462	1.48E-01	-0.004	0.014	-0.267	7.90E-01
	Pons	0.761	0.276	2.756	<u>7.52E-03</u>	0.314	0.358	0.878	3.83E-01
	Putamen	-0.033	0.237	-0.139	8.90E-01	0.115	0.403	0.284	7.77E-01
	White matter	7.957	4.945	1.609	1.12E-01	-2.487	6.679	-0.372	7.11E-01
	White matter hyperintensity	0.446	0.925	0.482	6.32E-01	-0.363	1.787	-0.203	8.40E-01

AD, Alzheimer's disease; β , effect size; NC, normal control; NN, neural network; PRS, polygenic risk score; SE, standard error. Bold underlined text indicates $p < 0.05$; underlined text indicates $p < 0.10$.

Supplementary Table 16. Plasma proteins significantly associated with neural network model risk score in normal controls

Protein	Uniprot_ID	β	SE	t	p -value	FDR
MMP-1	P03956	2033.208	750.694	2.708	8.80E-03	0.677
VEGFA	P15692	642.467	267.060	2.406	1.92E-02	0.706
CCL19	Q99731	609.755	109.720	5.557	6.65E-07	0.001
VEGFA	P15692	324.745	133.149	2.439	1.78E-02	0.706
PGF	P49763	95.135	39.392	2.415	1.88E-02	0.706
WFDC2	Q14508	44.616	16.481	2.707	8.86E-03	0.677
MIF	P14174	44.494	22.039	2.019	4.80E-02	0.728
PGF	P49763	43.780	20.917	2.093	4.06E-02	0.709
TNFRSF9	Q07011	41.782	17.534	2.383	2.04E-02	0.706
VWC2	Q2TAL6	36.690	17.242	2.128	3.75E-02	0.709
GM-CSF-R-alpha	P15509	35.085	17.406	2.016	4.83E-02	0.728
CST3	P01034	31.845	15.863	2.008	4.92E-02	0.728
TNF-R1	P19438	31.034	11.214	2.767	7.51E-03	0.677
SYND1	P18827	27.210	8.760	3.106	2.91E-03	0.438
VEGFR-2	P35968	26.336	12.157	2.166	3.43E-02	0.709
TNFRSF19	Q9NS68	21.594	10.049	2.149	3.58E-02	0.709
IL-18BP	O95998	18.224	8.782	2.075	4.23E-02	0.721
TNF-R2	P20333	17.334	7.564	2.292	2.55E-02	0.709
U-PAR	Q03405	12.966	6.280	2.065	4.33E-02	0.728
EDA2R	Q9HAV5	10.523	4.643	2.266	2.71E-02	0.709
EPHB4	P54760	10.175	3.884	2.620	1.11E-02	0.700
TFF3	Q07654	9.059	3.855	2.350	2.21E-02	0.709
TNFRSF14	Q92956	8.622	2.615	3.296	1.65E-03	0.438
CLEC14A	Q86T13	7.568	3.538	2.139	3.66E-02	0.709
ANXA1	P04083	7.133	3.552	2.008	4.92E-02	0.728
NOS3	P29474	6.630	2.111	3.141	2.63E-03	0.438
NPPC	P23582	5.689	2.712	2.097	4.03E-02	0.709
GZMB	P10144	5.670	2.787	2.035	4.64E-02	0.728
SIT1	Q9Y3P8	5.512	2.601	2.119	3.83E-02	0.709
CAPG	P40121	4.568	2.060	2.217	3.05E-02	0.709
PARK7	Q99497	4.398	1.821	2.415	1.89E-02	0.706
CSTB	P04080	4.386	1.787	2.454	1.71E-02	0.706
CDSN	Q15517	4.353	2.083	2.089	4.10E-02	0.709
LTBR	P36941	4.325	1.425	3.035	3.55E-03	0.471
ITM2A	O43736	4.188	1.516	2.763	7.63E-03	0.677
LAIR1	Q6GTX8	4.083	1.550	2.634	1.07E-02	0.700
CLEC1A	Q8NC01	3.883	1.677	2.316	2.41E-02	0.709
FUT3/FUT5	Q11128,P21217	3.464	1.632	2.123	3.79E-02	0.709
UBAC1	Q9BSL1	3.446	1.639	2.102	3.98E-02	0.709
hK11	Q9UBX7	2.987	1.400	2.134	3.70E-02	0.709
SRP14	P37108	2.463	1.080	2.281	2.62E-02	0.709
PSMD9	O00233	2.276	0.776	2.931	4.80E-03	0.573
CLEC6A	Q6EIG7	2.061	0.764	2.699	9.07E-03	0.677
AARSD1	Q9BTE6	1.974	0.962	2.052	4.46E-02	0.728
FCRLB	Q6BAA4	1.877	0.923	2.034	4.65E-02	0.728
FGR	P09769	1.874	0.762	2.460	1.69E-02	0.706
ESAM	Q96AP7	1.780	0.840	2.119	3.83E-02	0.709
PRDX1	Q06830	1.661	0.672	2.471	1.64E-02	0.706
NINJ1	Q92982	1.406	0.453	3.101	2.93E-03	0.438
PI3	P19957	1.366	0.631	2.165	3.43E-02	0.709
PTK7	Q13308	1.306	0.472	2.765	7.59E-03	0.677
IL12RB1	P42701	1.260	0.563	2.237	2.91E-02	0.709

IFNLR1	Q8IU57	1.060	0.521	2.036	4.62E-02	0.728
CCL21	O00585	0.770	0.345	2.229	2.96E-02	0.709
PDCD1	Q15116	0.670	0.276	2.422	1.85E-02	0.706
SIRT5	Q9NXA8	0.569	0.178	3.195	2.24E-03	0.438
IL3RA	P26951	0.565	0.238	2.377	2.07E-02	0.706
PPM1B	O75688	0.456	0.215	2.116	3.85E-02	0.709
TPPP3	Q9BW30	0.427	0.184	2.316	2.41E-02	0.709
ATP6V1D	Q9Y5K8	0.394	0.170	2.312	2.43E-02	0.709
NDRG1	Q92597	0.331	0.134	2.474	1.63E-02	0.706
PADI2	Q9Y2J8	0.315	0.153	2.058	4.40E-02	0.728
ATP6AP2	O75787	0.248	0.102	2.438	1.78E-02	0.706
PDP1	Q9P0J1	0.201	0.089	2.253	2.80E-02	0.709
TPMT	P51580	0.167	0.073	2.288	2.58E-02	0.709
GSTP1	P09211	0.156	0.049	3.165	2.46E-03	0.438
LYAR	Q9NX58	-0.248	0.112	-2.209	3.10E-02	0.709
DGKZ	Q13574	-0.249	0.102	-2.426	1.84E-02	0.706
BST1	Q10588	-0.337	0.138	-2.439	1.77E-02	0.706
SEZ6L2	Q6UXD5	-0.611	0.291	-2.101	3.99E-02	0.709
PLTP	P55058	-1.457	0.465	-3.134	2.67E-03	0.438
AGR3	Q8TD06	-3.677	1.641	-2.241	2.87E-02	0.709
GGT5	P36269	-4.900	2.333	-2.100	4.00E-02	0.709
TMPRSS5	Q9H3S3	-4.928	2.056	-2.397	1.97E-02	0.706
LEPR	P48357	-6.315	2.683	-2.353	2.19E-02	0.709
GPNMB	Q14956	-8.849	4.092	-2.163	3.46E-02	0.709
BOC	Q9BWV1	-15.032	5.721	-2.628	1.09E-02	0.700
LRRN1	Q6UXK5	-15.436	6.016	-2.566	1.28E-02	0.706
GPNMB	Q14956	-16.663	7.292	-2.285	2.59E-02	0.709
PON3	Q15166	-48.715	23.231	-2.097	4.02E-02	0.709

β , effect size; FDR, false discovery rate; SE, standard error.

Supplementary Table 17. Gene Ontology analysis of plasma proteins associated with polygenic scores in normal controls (i.e., positively associated with polygenic risk)

Category	Term	Gene count	p-value	FDR
GOTERM_BP_ALL	Cell surface receptor signaling pathway	34	2.20E-11	5.60E-08
GOTERM_BP_ALL	Cytokine-mediated signaling pathway	16	1.40E-09	1.30E-06
GOTERM_BP_ALL	Cellular response to tumor necrosis factor	12	1.50E-09	1.30E-06
GOTERM_BP_ALL	Immune system process	30	2.70E-09	1.60E-06
GOTERM_BP_ALL	Response to tumor necrosis factor	12	3.40E-09	1.60E-06
GOTERM_BP_ALL	Response to cytokine	18	3.80E-09	1.60E-06
GOTERM_BP_ALL	Cellular response to cytokine stimulus	17	4.70E-09	1.70E-06
GOTERM_BP_ALL	Regulation of response to external stimulus	17	6.30E-09	2.00E-06
GOTERM_BP_ALL	Defense response	23	1.30E-08	3.50E-06
GOTERM_BP_ALL	Cellular response to chemical stimulus	30	1.40E-08	3.50E-06
GOTERM_BP_ALL	Cellular response to organic substance	27	2.30E-08	4.70E-06
GOTERM_BP_ALL	Regulation of response to stress	21	2.30E-08	4.70E-06
GOTERM_BP_ALL	Tumor necrosis factor-mediated signaling pathway	9	4.80E-08	9.10E-06
GOTERM_BP_ALL	Response to organic substance	30	6.10E-08	1.10E-05
GOTERM_BP_ALL	Immune response	22	1.00E-07	1.70E-05
GOTERM_BP_ALL	Response to stress	34	1.10E-07	1.70E-05
GOTERM_BP_ALL	Response to external stimulus	25	1.70E-07	2.50E-05
GOTERM_BP_ALL	Regulation of I-kappaB kinase/NF-kappaB signaling	10	2.40E-07	3.30E-05
GOTERM_BP_ALL	Protein phosphorylation	23	4.50E-07	5.70E-05
GOTERM_BP_ALL	I-kappaB kinase/NF-kappaB signaling	10	4.60E-07	5.70E-05
GOTERM_BP_ALL	Regulation of programmed cell death	20	5.60E-07	6.70E-05
GOTERM_BP_ALL	Response to reactive oxygen species	9	1.10E-06	1.30E-04
GOTERM_BP_ALL	Regulation of cell death	20	1.50E-06	1.60E-04
GOTERM_BP_ALL	Protein metabolic process	40	1.50E-06	1.60E-04
GOTERM_BP_ALL	Response to chemical	34	1.80E-06	1.60E-04
GOTERM_BP_ALL	Response to external biotic stimulus	15	1.80E-06	1.60E-04
GOTERM_BP_ALL	Response to other organism	15	1.80E-06	1.60E-04
GOTERM_BP_ALL	Programmed cell death	22	2.00E-06	1.70E-04
GOTERM_BP_ALL	MAPK cascade	15	2.10E-06	1.80E-04
GOTERM_BP_ALL	Signal transduction	41	2.20E-06	1.90E-04
GOTERM_BP_ALL	Regulation of apoptotic process	19	2.30E-06	1.90E-04
GOTERM_BP_ALL	Response to lipid	15	2.70E-06	2.10E-04
GOTERM_BP_ALL	Apoptotic process	21	3.30E-06	2.30E-04
GOTERM_BP_ALL	Response to biotic stimulus	15	3.30E-06	2.30E-04
GOTERM_BP_ALL	Cellular protein metabolic process	37	3.30E-06	2.30E-04
GOTERM_BP_ALL	Signal transduction by protein phosphorylation	15	3.50E-06	2.40E-04
GOTERM_BP_ALL	Regulation of response to stimulus	31	4.30E-06	2.90E-04
GOTERM_BP_ALL	Response to oxygen-containing compound	19	4.50E-06	2.90E-04
GOTERM_BP_ALL	Cell death	22	4.80E-06	3.10E-04
GOTERM_BP_ALL	Cell migration	17	5.20E-06	3.30E-04
GOTERM_BP_ALL	Positive regulation of phosphorus metabolic process	16	5.60E-06	3.30E-04
GOTERM_BP_ALL	Positive regulation of phosphate metabolic process	16	5.60E-06	3.30E-04
GOTERM_BP_ALL	Peptidyl-tyrosine phosphorylation	10	5.70E-06	3.30E-04
GOTERM_BP_ALL	Peptidyl-tyrosine modification	10	6.00E-06	3.40E-04
GOTERM_BP_ALL	Regulation of MAPK cascade	13	6.90E-06	3.80E-04
GOTERM_BP_ALL	Regulation of immune system process	18	8.40E-06	4.50E-04
GOTERM_BP_ALL	Regulation of cytokine production	12	8.70E-06	4.60E-04
GOTERM_BP_ALL	Apoptotic signaling pathway	12	9.60E-06	4.90E-04
GOTERM_BP_ALL	Regulation of stress-activated MAPK cascade	8	9.60E-06	4.90E-04
GOTERM_BP_ALL	Regulation of cell proliferation	19	9.90E-06	4.90E-04

GOTERM_BP_ALL	Regulation of stress-activated protein kinase signaling cascade	8	1.00E-05	4.90E-04
GOTERM_BP_ALL	Phosphorylation	23	1.00E-05	4.90E-04
GOTERM_BP_ALL	Leukocyte migration	10	1.00E-05	4.90E-04
GOTERM_BP_ALL	Cellular protein modification process	31	1.20E-05	5.40E-04
GOTERM_BP_ALL	Protein modification process	31	1.20E-05	5.40E-04
GOTERM_BP_ALL	Positive regulation of cell adhesion	10	1.30E-05	5.60E-04
GOTERM_BP_ALL	Positive regulation of signal transduction	18	1.30E-05	5.80E-04
GOTERM_BP_ALL	Response to stimulus	49	1.40E-05	5.90E-04
GOTERM_BP_ALL	Response to lipopolysaccharide	9	1.60E-05	6.70E-04
GOTERM_BP_ALL	Regulation of phosphate metabolic process	19	1.60E-05	6.70E-04
GOTERM_BP_ALL	Regulation of phosphorus metabolic process	19	1.70E-05	6.70E-04
GOTERM_BP_ALL	Single organism signaling	41	1.70E-05	6.70E-04
GOTERM_BP_ALL	Regulation of protein phosphorylation	17	1.70E-05	6.70E-04
GOTERM_BP_ALL	Regulation of signaling	27	1.80E-05	7.00E-04
GOTERM_BP_ALL	Phosphate-containing compound metabolic process	27	2.00E-05	7.40E-04
GOTERM_BP_ALL	Cytokine production	12	2.00E-05	7.40E-04
GOTERM_BP_ALL	Phosphorus metabolic process	27	2.00E-05	7.40E-04
GOTERM_BP_ALL	Regulation of protein metabolic process	24	2.00E-05	7.40E-04
GOTERM_BP_ALL	Regulation of cytokine secretion	7	2.10E-05	7.40E-04
GOTERM_BP_ALL	Signaling	41	2.10E-05	7.40E-04
GOTERM_BP_ALL	Inflammatory response	12	2.20E-05	7.40E-04
GOTERM_BP_ALL	Multi-organism process	23	2.20E-05	7.40E-04
GOTERM_BP_ALL	Cell motility	17	2.30E-05	7.40E-04
GOTERM_BP_ALL	Localization of cell	17	2.30E-05	7.40E-04
GOTERM_BP_ALL	Cell communication	41	2.30E-05	7.40E-04
GOTERM_BP_ALL	Response to molecule of bacterial origin	9	2.30E-05	7.40E-04
GOTERM_BP_ALL	Regulation of cellular protein metabolic process	23	2.30E-05	7.50E-04
GOTERM_BP_ALL	Regulation of signal transduction	25	2.40E-05	7.70E-04
GOTERM_BP_ALL	Regulation of leukocyte migration	7	2.60E-05	8.10E-04
GOTERM_BP_ALL	Cell activation	14	2.70E-05	8.30E-04
GOTERM_BP_ALL	Positive regulation of intracellular signal transduction	14	2.80E-05	8.70E-04
GOTERM_BP_ALL	Positive regulation of response to stimulus	21	3.10E-05	9.40E-04
GOTERM_BP_ALL	Locomotion	18	3.30E-05	9.80E-04
GOTERM_BP_ALL	Cell adhesion	19	3.40E-05	1.00E-03
GOTERM_BP_ALL	Positive regulation of phosphorylation	14	3.40E-05	1.00E-03
GOTERM_BP_ALL	Cytokine secretion	7	3.50E-05	1.00E-03
GOTERM_BP_ALL	Biological adhesion	19	3.60E-05	1.00E-03
GOTERM_BP_ALL	Regulation of intracellular signal transduction	19	3.80E-05	1.10E-03
GOTERM_BP_ALL	Regulation of phosphorylation	17	4.00E-05	1.10E-03
GOTERM_BP_ALL	Positive regulation of cell communication	18	4.00E-05	1.10E-03
GOTERM_BP_ALL	Cell chemotaxis	8	4.20E-05	1.10E-03
GOTERM_BP_ALL	Positive regulation of signaling	18	4.30E-05	1.10E-03
GOTERM_BP_ALL	Regulation of cell communication	26	4.30E-05	1.10E-03
GOTERM_BP_ALL	Single-organism metabolic process	31	4.30E-05	1.10E-03
GOTERM_BP_ALL	Macromolecule modification	31	4.40E-05	1.10E-03
GOTERM_BP_ALL	Stress-activated protein kinase signaling cascade	8	4.50E-05	1.20E-03
GOTERM_BP_ALL	Single-multicellular organism process	39	4.70E-05	1.20E-03
GOTERM_BP_ALL	Intracellular signal transduction	24	5.10E-05	1.30E-03
GOTERM_BP_ALL	Regulation of multicellular organismal process	24	5.10E-05	1.30E-03
GOTERM_BP_ALL	Positive regulation of I-kappaB kinase/NF-kappaB signaling	7	6.10E-05	1.50E-03
GOTERM_BP_ALL	Regulation of chemotaxis	7	6.90E-05	1.70E-03
GOTERM_BP_ALL	Positive regulation of MAPK cascade	10	7.70E-05	1.90E-03
GOTERM_BP_ALL	Positive regulation of cytokine production	9	9.30E-05	2.20E-03
GOTERM_BP_ALL	Leukocyte activation	12	9.30E-05	2.20E-03
GOTERM_BP_ALL	Regulation of protein modification process	18	9.50E-05	2.20E-03
GOTERM_BP_ALL	Regulation of cell activation	10	9.80E-05	2.30E-03

GOTERM_BP_ALL	Positive regulation of protein phosphorylation	13	1.00E-04	2.30E-03
GOTERM_BP_ALL	Cellular response to reactive oxygen species	6	1.00E-04	2.40E-03
GOTERM_BP_ALL	Response to oxidative stress	9	1.10E-04	2.40E-03
GOTERM_BP_ALL	Negative regulation of cell death	13	1.10E-04	2.40E-03
GOTERM_BP_ALL	Cellular response to stimulus	42	1.10E-04	2.50E-03
GOTERM_BP_ALL	Negative regulation of hydrolase activity	9	1.20E-04	2.70E-03
GOTERM_BP_ALL	Positive regulation of cellular process	33	1.30E-04	2.80E-03
GOTERM_BP_ALL	Regulation of cell adhesion	11	1.30E-04	2.80E-03
GOTERM_BP_ALL	Positive regulation of leukocyte activation	8	1.60E-04	3.40E-03
GOTERM_BP_ALL	Positive regulation of stress-activated MAPK cascade	6	1.70E-04	3.70E-03
GOTERM_BP_ALL	Positive regulation of stress-activated protein kinase signaling cascade	6	1.80E-04	3.80E-03
GOTERM_BP_ALL	Response to bacterium	10	1.80E-04	3.90E-03
GOTERM_BP_ALL	Positive regulation of cell activation	8	1.90E-04	4.00E-03
GOTERM_BP_ALL	Regulation of defense response	11	1.90E-04	4.00E-03
GOTERM_BP_ALL	Extrinsic apoptotic signaling pathway	7	1.90E-04	4.00E-03
GOTERM_BP_ALL	Chemotaxis	10	2.00E-04	4.00E-03
GOTERM_BP_ALL	Positive regulation of multicellular organismal process	16	2.00E-04	4.00E-03
GOTERM_BP_ALL	Negative regulation of apoptotic process	12	2.10E-04	4.00E-03
GOTERM_BP_ALL	Regulation of protein localization	13	2.10E-04	4.00E-03
GOTERM_BP_ALL	Taxis	10	2.10E-04	4.00E-03
GOTERM_BP_ALL	Regulation of biological process	55	2.10E-04	4.00E-03
GOTERM_BP_ALL	Regulation of immune effector process	8	2.10E-04	4.00E-03
GOTERM_BP_ALL	Regulation of establishment of protein localization	12	2.10E-04	4.10E-03
GOTERM_BP_ALL	Negative regulation of programmed cell death	12	2.30E-04	4.40E-03
GOTERM_BP_ALL	Movement of cell or subcellular component	18	2.40E-04	4.50E-03
GOTERM_BP_ALL	Negative regulation of endopeptidase activity	7	2.50E-04	4.60E-03
GOTERM_BP_ALL	Regulation of leukocyte apoptotic process	5	2.60E-04	5.00E-03
GOTERM_BP_ALL	Positive regulation of protein modification process	14	2.70E-04	5.00E-03
GOTERM_BP_ALL	Stress-activated MAPK cascade	7	2.90E-04	5.30E-03
GOTERM_BP_ALL	Regulation of cellular response to stress	10	3.00E-04	5.50E-03
GOTERM_BP_ALL	Negative regulation of peptidase activity	7	3.20E-04	5.80E-03
GOTERM_BP_ALL	Regulation of leukocyte activation	9	3.50E-04	6.20E-03
GOTERM_BP_ALL	Response to inorganic substance	9	3.50E-04	6.30E-03
GOTERM_BP_ALL	Regulation of JNK cascade	6	3.60E-04	6.40E-03
GOTERM_BP_ALL	Positive regulation of immune effector process	6	3.70E-04	6.60E-03
GOTERM_BP_ALL	Immune effector process	11	4.10E-04	7.20E-03
GOTERM_BP_ALL	Regulation of protein transport	11	4.30E-04	7.40E-03
GOTERM_BP_ALL	Positive regulation of biological process	34	4.40E-04	7.70E-03
GOTERM_BP_ALL	Positive regulation of cytokine secretion	5	4.80E-04	8.20E-03
GOTERM_BP_ALL	T-helper 1 type immune response	4	4.80E-04	8.20E-03
GOTERM_BP_ALL	Negative regulation of response to external stimulus	7	4.90E-04	8.20E-03
GOTERM_BP_ALL	Positive regulation of response to external stimulus	7	4.90E-04	8.20E-03
GOTERM_BP_ALL	Positive regulation of cell-matrix adhesion	4	5.20E-04	8.60E-03
GOTERM_BP_ALL	Regulation of glycoprotein metabolic process	4	5.20E-04	8.60E-03
GOTERM_BP_ALL	Negative regulation of biological process	31	5.20E-04	8.60E-03
GOTERM_BP_ALL	Regulation of leukocyte chemotaxis	5	5.40E-04	8.80E-03
GOTERM_BP_ALL	Positive regulation of transport	12	5.60E-04	9.20E-03
GOTERM_BP_ALL	Leukocyte apoptotic process	5	5.80E-04	9.40E-03
GOTERM_BP_ALL	Negative regulation of immune system process	8	6.10E-04	9.70E-03
GOTERM_BP_ALL	JNK cascade	6	6.10E-04	9.80E-03
GOTERM_BP_ALL	Regulation of protein secretion	8	6.40E-04	1.00E-02
GOTERM_BP_ALL	Cellular response to stress	17	6.60E-04	1.00E-02
GOTERM_BP_ALL	Positive regulation of cell-substrate adhesion	5	6.70E-04	1.00E-02
GOTERM_BP_ALL	Positive regulation of lymphocyte activation	7	7.10E-04	1.10E-02
GOTERM_BP_ALL	Positive regulation of leukocyte migration	5	7.50E-04	1.20E-02
GOTERM_BP_ALL	Leukocyte chemotaxis	6	8.00E-04	1.20E-02
GOTERM_BP_ALL	Positive regulation of immune system process	12	8.00E-04	1.20E-02

GOTERM_BP_ALL	Regulation of lymphocyte activation	8	8.50E-04	1.30E-02
GOTERM_BP_ALL	Regulation of T-cell activation	7	8.80E-04	1.30E-02
GOTERM_BP_ALL	Single-organism developmental process	34	9.00E-04	1.30E-02
GOTERM_BP_ALL	Response to toxic substance	6	9.60E-04	1.40E-02
GOTERM_BP_ALL	Regulation of cell migration	10	9.80E-04	1.40E-02
GOTERM_BP_ALL	Innate immune response	11	1.00E-03	1.50E-02
GOTERM_BP_ALL	Multicellular organismal process	40	1.00E-03	1.50E-02
GOTERM_BP_ALL	Positive regulation of JNK cascade	5	1.00E-03	1.50E-02
GOTERM_BP_ALL	Negative regulation of catalytic activity	11	1.10E-03	1.50E-02
GOTERM_BP_ALL	Regulation of leukocyte proliferation	6	1.10E-03	1.60E-02
GOTERM_BP_ALL	Positive regulation of chemotaxis	5	1.10E-03	1.60E-02
GOTERM_BP_ALL	Regulation of leukocyte cell-cell adhesion	7	1.10E-03	1.60E-02
GOTERM_BP_ALL	Positive regulation of T-cell activation	6	1.10E-03	1.60E-02
GOTERM_BP_ALL	Cell-cell adhesion	13	1.10E-03	1.60E-02
GOTERM_BP_ALL	Positive chemotaxis	4	1.10E-03	1.60E-02
GOTERM_BP_ALL	Negative regulation of proteolysis	7	1.20E-03	1.70E-02
GOTERM_BP_ALL	Regulation of cellular process	52	1.20E-03	1.70E-02
GOTERM_BP_ALL	Positive regulation of protein secretion	6	1.20E-03	1.70E-02
GOTERM_BP_ALL	Response to hydrogen peroxide	5	1.20E-03	1.70E-02
GOTERM_BP_ALL	Superoxide metabolic process	4	1.30E-03	1.70E-02
GOTERM_BP_ALL	Positive regulation of lipid metabolic process	5	1.30E-03	1.70E-02
GOTERM_BP_ALL	Peptidyl-amino acid modification	13	1.30E-03	1.80E-02
GOTERM_BP_ALL	Regulation of localization	20	1.30E-03	1.80E-02
GOTERM_BP_ALL	Positive regulation of leukocyte cell-cell adhesion	6	1.30E-03	1.80E-02
GOTERM_BP_ALL	Positive regulation of secretion by cell	7	1.40E-03	1.80E-02
GOTERM_BP_ALL	Positive regulation of T-helper 1 type immune response	3	1.40E-03	1.90E-02
GOTERM_BP_ALL	Negative regulation of response to stimulus	14	1.50E-03	1.90E-02
GOTERM_BP_ALL	Developmental process	34	1.50E-03	2.00E-02
GOTERM_BP_ALL	Removal of superoxide radicals	3	1.60E-03	2.10E-02
GOTERM_BP_ALL	Regulation of cell motility	10	1.60E-03	2.10E-02
GOTERM_BP_ALL	Cellular response to oxidative stress	6	1.60E-03	2.10E-02
GOTERM_BP_ALL	Biological regulation	55	1.70E-03	2.10E-02
GOTERM_BP_ALL	Positive regulation of organelle organization	9	1.70E-03	2.20E-02
GOTERM_BP_ALL	Epithelium development	12	1.80E-03	2.30E-02
GOTERM_BP_ALL	Protein secretion	8	1.80E-03	2.30E-02
GOTERM_BP_ALL	Carbohydrate derivative biosynthetic process	10	1.90E-03	2.40E-02
GOTERM_BP_ALL	Cellular response to oxygen-containing compound	11	2.00E-03	2.50E-02
GOTERM_BP_ALL	Cellular response to oxygen radical	3	2.00E-03	2.50E-02
GOTERM_BP_ALL	Cellular response to superoxide	3	2.00E-03	2.50E-02
GOTERM_BP_ALL	Positive regulation of cellular protein metabolic process	14	2.00E-03	2.50E-02
GOTERM_BP_ALL	Anatomical structure development	33	2.10E-03	2.50E-02
GOTERM_BP_ALL	Negative regulation of cellular process	28	2.10E-03	2.50E-02
GOTERM_BP_ALL	Positive regulation of secretion	7	2.10E-03	2.50E-02
GOTERM_BP_ALL	Regulation of locomotion	10	2.20E-03	2.60E-02
GOTERM_BP_ALL	ERK1 and ERK2 cascade	6	2.20E-03	2.60E-02
GOTERM_BP_ALL	Regulation of transport	16	2.20E-03	2.60E-02
GOTERM_BP_ALL	Sprouting angiogenesis	4	2.30E-03	2.70E-02
GOTERM_BP_ALL	Regulation of secretion by cell	9	2.40E-03	2.80E-02
GOTERM_BP_ALL	Positive regulation of cell-cell adhesion	6	2.40E-03	2.80E-02
GOTERM_BP_ALL	Regulation of ERK1 and ERK2 cascade	6	2.40E-03	2.80E-02
GOTERM_BP_ALL	Regulation of alpha-beta T-cell activation	4	2.50E-03	2.90E-02
GOTERM_BP_ALL	Positive regulation of T-helper cell differentiation	3	2.50E-03	2.90E-02
GOTERM_BP_ALL	Regulation of endopeptidase activity	7	2.70E-03	3.10E-02
GOTERM_BP_ALL	Lymphocyte activation	9	2.70E-03	3.10E-02
GOTERM_BP_ALL	Response to superoxide	3	2.80E-03	3.20E-02
GOTERM_BP_ALL	Positive regulation of cellular metabolic process	21	2.80E-03	3.20E-02
GOTERM_BP_ALL	Cellular response to lipid	8	2.90E-03	3.20E-02

GOTERM_BP_ALL	Regulation of cellular component movement	10	2.90E-03	3.20E-02
GOTERM_BP_ALL	Regulation of apoptotic signaling pathway	7	3.00E-03	3.30E-02
GOTERM_BP_ALL	Myeloid leukocyte migration	5	3.00E-03	3.30E-02
GOTERM_BP_ALL	Regulation of T-helper 1 type immune response	3	3.00E-03	3.40E-02
GOTERM_BP_ALL	Multicellular organism development	30	3.10E-03	3.40E-02
GOTERM_BP_ALL	Cell proliferation	16	3.10E-03	3.40E-02
GOTERM_BP_ALL	Cellular response to hydrogen peroxide	4	3.10E-03	3.40E-02
GOTERM_BP_ALL	Regulation of cell-cell adhesion	7	3.20E-03	3.50E-02
GOTERM_BP_ALL	Extrinsic apoptotic signaling pathway via death domain receptors	4	3.20E-03	3.50E-02
GOTERM_BP_ALL	Lymphocyte migration	4	3.40E-03	3.60E-02
GOTERM_BP_ALL	Positive regulation of protein metabolic process	14	3.50E-03	3.70E-02
GOTERM_BP_ALL	T-cell costimulation	4	3.50E-03	3.70E-02
GOTERM_BP_ALL	Positive regulation of cell migration	7	3.60E-03	3.80E-02
GOTERM_BP_ALL	Lymphocyte costimulation	4	3.60E-03	3.80E-02
GOTERM_BP_ALL	Positive regulation of leukocyte chemotaxis	4	3.60E-03	3.80E-02
GOTERM_BP_ALL	Regulation of peptidase activity	7	3.60E-03	3.80E-02
GOTERM_BP_ALL	Response to oxygen radical	3	3.60E-03	3.80E-02
GOTERM_BP_ALL	Regulation of hydrolase activity	13	3.70E-03	3.80E-02
GOTERM_BP_ALL	Glycoprotein metabolic process	7	3.80E-03	3.90E-02
GOTERM_BP_ALL	Regulation of secretion	9	3.90E-03	4.00E-02
GOTERM_BP_ALL	Intrinsic apoptotic signaling pathway	6	3.90E-03	4.00E-02
GOTERM_BP_ALL	Positive regulation of positive chemotaxis	3	3.90E-03	4.00E-02
GOTERM_BP_ALL	Leukocyte proliferation	6	4.00E-03	4.10E-02
GOTERM_BP_ALL	Cellular oxidant detoxification	4	4.00E-03	4.10E-02
GOTERM_BP_ALL	Positive regulation of cellular component organization	12	4.20E-03	4.30E-02
GOTERM_BP_ALL	Positive regulation of cell motility	7	4.20E-03	4.30E-02
GOTERM_BP_ALL	Regulation of positive chemotaxis	3	4.20E-03	4.30E-02
GOTERM_BP_ALL	Positive regulation of CD4-positive, alpha-beta T-cell differentiation	3	4.20E-03	4.30E-02
GOTERM_BP_ALL	Cellular detoxification	4	4.30E-03	4.30E-02
GOTERM_BP_ALL	Positive regulation of ERK1 and ERK2 cascade	5	4.40E-03	4.40E-02
GOTERM_BP_ALL	Regulation of lipid metabolic process	6	4.40E-03	4.40E-02
GOTERM_BP_ALL	Regulation of cell-substrate adhesion	5	4.60E-03	4.50E-02
GOTERM_BP_ALL	Regulation of proteolysis	9	4.80E-03	4.70E-02
GOTERM_BP_ALL	Positive regulation of cellular component movement	7	4.80E-03	4.70E-02
GOTERM_BP_ALL	Adaptive immune response	7	4.80E-03	4.70E-02
GOTERM_BP_ALL	Detoxification	4	4.80E-03	4.70E-02
GOTERM_BP_ALL	Tissue development	15	4.80E-03	4.70E-02
GOTERM_BP_ALL	Regulation of T-helper cell differentiation	3	4.90E-03	4.70E-02
GOTERM_BP_ALL	Regulation of cgmp metabolic process	3	4.90E-03	4.70E-02
GOTERM_BP_ALL	Positive regulation of locomotion	7	4.90E-03	4.70E-02
GOTERM_BP_ALL	Regulation of cell-matrix adhesion	4	5.10E-03	4.90E-02
GOTERM_CC_ALL	Extracellular region part	41	1.10E-12	2.50E-10
GOTERM_CC_ALL	Extracellular region	44	2.30E-12	2.50E-10
GOTERM_CC_ALL	Extracellular exosome	32	5.40E-10	2.40E-08
GOTERM_CC_ALL	Extracellular vesicle	32	6.10E-10	2.40E-08
GOTERM_CC_ALL	Extracellular organelle	32	6.20E-10	2.40E-08
GOTERM_CC_ALL	Membrane-bounded vesicle	36	6.50E-10	2.40E-08
GOTERM_CC_ALL	Vesicle	36	1.90E-09	6.10E-08
GOTERM_CC_ALL	Extracellular space	18	6.60E-06	1.80E-04
GOTERM_CC_ALL	Plasma membrane part	24	1.60E-05	3.80E-04
GOTERM_CC_ALL	Plasma membrane	35	2.30E-05	4.80E-04
GOTERM_CC_ALL	External side of plasma membrane	8	2.40E-05	4.80E-04
GOTERM_CC_ALL	Cell periphery	35	3.80E-05	7.00E-04
GOTERM_CC_ALL	Integral component of plasma membrane	17	1.30E-04	2.10E-03
GOTERM_CC_ALL	Side of membrane	9	1.60E-04	2.50E-03

GOTERM_CC_ALL	Intrinsic component of plasma membrane	17	2.00E-04	2.90E-03
GOTERM_CC_ALL	Cell surface	11	3.10E-04	4.30E-03
GOTERM_CC_ALL	Extracellular matrix	9	5.10E-04	6.60E-03
GOTERM_CC_ALL	Anchoring junction	10	8.00E-04	9.80E-03
GOTERM_CC_ALL	Proteinaceous extracellular matrix	7	1.70E-03	1.90E-02
GOTERM_CC_ALL	Adherens junction	9	2.90E-03	3.10E-02
Category	Term	Gene count	p-value	FDR
GOTERM_MF_ALL	Tumor necrosis factor-activated receptor activity	7	2.20E-10	3.40E-08
GOTERM_MF_ALL	Death receptor activity	7	2.20E-10	3.40E-08
GOTERM_MF_ALL	Signal transducer activity	18	1.20E-04	9.00E-03
GOTERM_MF_ALL	Signaling receptor activity	16	1.20E-04	9.00E-03
GOTERM_MF_ALL	Molecular transducer activity	17	2.30E-04	1.20E-02
GOTERM_MF_ALL	Receptor activity	17	2.30E-04	1.20E-02
GOTERM_MF_ALL	Cytokine binding	5	3.80E-04	1.70E-02
GOTERM_MF_ALL	Transmembrane signaling receptor activity	14	6.80E-04	2.60E-02
GOTERM_MF_ALL	Transmembrane receptor activity	14	9.90E-04	3.30E-02
Category	Term	Gene count	p-value	FDR
KEGG_PATHWAY	Cytokine–cytokine receptor interaction	13	1.70E-09	1.30E-07

FDR, false discovery rate.

Supplementary Table 18. Gene Ontology analysis of plasma proteins associated with polygenic scores in normal controls (i.e., negatively associated with polygenic risk)

Category	Term	Gene count	<i>p</i>-value	FDR
GOTERM_BP_ALL	Cell activation	4	1.90E-02	1.00E+00
GOTERM_BP_ALL	Small molecule biosynthetic process	3	3.90E-02	1.00E+00
GOTERM_BP_ALL	Regulation of tissue remodeling	2	4.40E-02	1.00E+00
GOTERM_CC_ALL	Plasma membrane	8	2.80E-02	1.00E+00
GOTERM_CC_ALL	Cell periphery	8	3.10E-02	1.00E+00

FDR, false discovery rate.

Supplementary Table 19. Summary of protein–protein interaction network analysis for plasma proteins associated with polygenic scores

Statistic	Value
Number of nodes	19 (14 + 5 interactors)
Number of edges	113
Average node degree	11.9
Average local clustering coefficient	0.844
Expected number of edges	22
Protein–protein interaction enrichment <i>p</i> -value	<1.0E–16

Supplementary Table 20. Plasma proteins associated with individual modules in the neural network model

Index	Protein_name	UniprotID	OlinkID	β	SE	t-value	p-value	Module	Cluster
1	GCNT1	Q02742	OID01349	-160.25	33.21	-4.83	1.11E-05	4	1
2	ECE1	P42892	OID05132	-15.26	3.32	-4.60	2.54E-05	2	1
3	AARSD1	Q9BTE6	OID05202	-59.50	14.01	-4.25	8.39E-05	4	1
4	KRT19	P08727	OID00967	77.45	19.22	4.03	1.74E-04	2	1
5	IL15	P40933	OID05169	33.55	8.97	3.74	4.38E-04	4	1
6	UNC5C	O95185	OID00292	-1020.97	289.30	-3.53	8.41E-04	3	1
7	CRADD	P78560	OID05129	-337.67	95.87	-3.52	8.69E-04	4	1
8	BST1	Q10588	OID01436	23.87	6.84	3.49	9.56E-04	3	1
9	USO1	O60763	OID05443	-116.60	35.80	-3.26	1.93E-03	4	1
10	VASH1	Q7L8A9	OID01073	-17.78	5.50	-3.23	2.06E-03	4	1
11	LAMP3	Q9UQV4	OID01015	-402.07	124.47	-3.23	2.09E-03	4	1
12	SPRY2	O43597	OID00998	-275.43	85.65	-3.22	2.18E-03	4	1
13	SRPK2	P78362	OID00994	-57.95	18.02	-3.22	2.18E-03	4	1
14	EIF4G1	Q04637	OID00976	-768.16	242.52	-3.17	2.51E-03	4	1
15	LGMN	Q99538	OID01460	-62.77	19.83	-3.16	2.53E-03	4	1
16	CNTN4	Q8I WV2	OID01476	278.35	88.85	3.13	2.77E-03	5	1
17	ICA1	Q05084	OID01003	-75.12	24.22	-3.10	3.04E-03	5	1
18	NUB1	Q9Y5A7	OID01092	-114.23	39.39	-2.90	5.36E-03	4	1
19	HAGH	Q16775	OID00322	-310.39	109.41	-2.84	6.33E-03	4	1
20	CRX	O43186	OID01315	158.55	56.53	2.80	6.91E-03	2	1
21	DNAJB1	P25685	OID01342	-861.51	307.18	-2.80	6.91E-03	4	1
22	PRDX5	P30044	OID00955	-363.08	129.87	-2.80	7.12E-03	4	1
23	IL3RA	P26951	OID05211	-12.30	4.40	-2.79	7.14E-03	4	1
24	LSP1	P33241	OID05440	-161.82	59.11	-2.74	8.33E-03	4	1
25	CASP2	P42575	OID05437	-27.01	9.91	-2.73	8.59E-03	4	1
26	NFKBIE	O00221	OID01310	-89.95	33.12	-2.72	8.76E-03	5	1
27	LGALS7	P47929	OID01344	-29.91	11.01	-2.72	8.76E-03	2	1
28	5'-NT	P21589	OID00708	-16980.87	6264.00	-2.71	8.93E-03	5	1
29	CCT5	P48643	OID05436	-6.46	2.41	-2.68	9.62E-03	4	1
30	DAPP1	Q9UN19	OID01011	-2250.82	839.12	-2.68	9.63E-03	5	1
31	MIF	P14174	OID01453	-974.70	364.03	-2.68	9.76E-03	4	1
32	HSP90B1	P14625	OID05159	8.73	3.30	2.64	1.07E-02	4	1
33	AIMP1	Q12904	OID05448	-121.93	46.39	-2.63	1.11E-02	4	1
34	NFATC1	O95644	OID01325	-109.37	42.09	-2.60	1.19E-02	5	1
35	EDA2R	Q9HAV5	OID00370	-606.17	234.43	-2.59	1.23E-02	1	1
36	DRG2	P55039	OID05463	-15.84	6.17	-2.57	1.29E-02	4	1
37	PRDX1	Q06830	OID00952	-24.71	9.62	-2.57	1.30E-02	4	1
38	TR-AP	P13686	OID00606	135.52	53.81	2.52	1.47E-02	2	1
39	PTPN6	P29350	OID01446	-19.47	7.75	-2.51	1.49E-02	4	1
40	FGF-5	P12034	OID00509	-11.14	4.45	-2.50	1.53E-02	4	1
41	SCAMP3	O14828	OID00668	-1480.72	592.37	-2.50	1.54E-02	5	1
42	AMIGO2	Q86SJ2	OID01365	-211.54	88.56	-2.39	2.03E-02	5	1
43	IL-18R1	Q13478	OID00517	-5805.20	2504.28	-2.32	2.41E-02	1	1
44	TGM2	P21980	OID00462	-5031.06	2196.58	-2.29	2.58E-02	2	1
45	CD38	P28907	OID00308	-398.30	174.15	-2.29	2.60E-02	4	1
46	PRKRA	O75569	OID01068	-22.34	9.90	-2.26	2.81E-02	4	1
47	STXBP3	O00186	OID01106	-7.12	3.16	-2.25	2.82E-02	4	1
48	ADAM 22	Q9P0K1	OID00317	213.73	95.70	2.23	2.95E-02	2	1
49	KLRD1	Q13241	OID00995	-3313.70	1484.47	-2.23	2.97E-02	5	1
50	IL-12B	P29460	OID00523	-1754.96	787.98	-2.23	3.00E-02	5	1
51	ARHGEF12	Q9NZN5	OID01390	-423.42	190.31	-2.22	3.01E-02	4	1
52	XCL1	P47992	OID00433	-658.44	296.56	-2.22	3.05E-02	5	1
53	PEBP1	P30086	OID01483	-81.20	36.65	-2.22	3.09E-02	4	1
54	HTRA2	O43464	OID01402	-25.59	11.55	-2.22	3.09E-02	5	1
55	RASSF2	P50749	OID01094	-10.01	4.53	-2.21	3.11E-02	4	1
56	CA1	P00915	OID01223	-1867.31	851.31	-2.19	3.24E-02	4	1
57	ZBTB16	Q05516	OID01350	-197.63	90.26	-2.19	3.27E-02	5	1
58	PLXNB2	O15031	OID01218	-20.61	9.45	-2.18	3.34E-02	2	1
59	STX6	O43752	OID01318	-142.48	66.16	-2.15	3.56E-02	5	1
60	GFR-alpha-1	P56159	OID00333	-2865.28	1331.29	-2.15	3.57E-02	3	1
61	IL17F	Q96PD4	OID05407	18.96	8.89	2.13	3.75E-02	5	1
62	TIMP1	P01033	OID01224	-126.70	60.11	-2.11	3.95E-02	2	1
63	SPINK1	P00995	OID01415	221.54	106.85	2.07	4.28E-02	5	1
64	TNFSF14	O43557	OID00506	-166.30	80.26	-2.07	4.29E-02	4	1
65	ENO2	P09104	OID01138	-154.61	75.17	-2.06	4.45E-02	4	1

66	TSHB	P01222	OID01196	295.29	144.22	2.05	4.54E-02	3	1
67	ERBB2	P04626	OID00682	-259.20	126.91	-2.04	4.59E-02	4	1
68	PRELP	P51888	OID00431	1625.41	802.98	2.02	4.77E-02	5	1
69	4E-BP1	Q13541	OID00536	-11598.21	2181.97	-5.32	1.91E-06	4	2
70	PFKM	P08237	OID01333	-96.77	21.05	-4.60	2.48E-05	4	2
71	FUCA1	P04066	OID01433	-715.50	161.08	-4.44	4.35E-05	4	2
72	PRDX6	P30041	OID01343	-75.79	17.58	-4.31	6.67E-05	4	2
73	MetAP 2	P50579	OID00692	-859.40	217.47	-3.95	2.23E-04	4	2
74	S100A11	P31949	OID00727	-73.48	18.64	-3.94	2.31E-04	4	2
75	FLI1	Q01543	OID01348	-56.27	14.32	-3.93	2.37E-04	4	2
76	GLO1	Q04760	OID00419	-420.91	112.77	-3.73	4.45E-04	4	2
77	IL4	P05112	OID00546	-31.71	8.57	-3.70	4.92E-04	5	2
78	BACH1	O14867	OID00996	-65.22	17.89	-3.64	5.94E-04	4	2
79	SIRT2	Q8IXJ6	OID00538	-709.00	195.40	-3.63	6.18E-04	4	2
80	ADAM 8	P78325	OID00707	-708.01	202.00	-3.51	9.16E-04	4	2
81	CTSV	O60911	OID00702	-51.03	14.83	-3.44	1.12E-03	4	2
82	DFFA	O00273	OID01004	-308.50	90.47	-3.41	1.22E-03	4	2
83	FCRL6	Q6DN72	OID01006	-543.39	159.62	-3.40	1.24E-03	5	2
84	IL-4RA	P24394	OID00387	24.79	7.31	3.39	1.29E-03	4	2
85	DCTPP1	Q9H773	OID05421	-205.46	61.38	-3.35	1.48E-03	4	2
86	TOP2B	Q02880	OID01036	-264.18	79.83	-3.31	1.65E-03	5	2
87	NBN	O60934	OID01087	-30.78	9.34	-3.29	1.73E-03	4	2
88	CD22	P20273	OID05400	-2715.47	828.06	-3.28	1.81E-03	5	2
89	AKT1S1	Q96B36	OID05192	-98.38	30.32	-3.25	2.00E-03	4	2
90	GOPC	Q9HD26	OID05442	-153.90	47.78	-3.22	2.15E-03	4	2
91	NT5C3A	Q9H0P0	OID05415	-144.33	45.37	-3.18	2.41E-03	4	2
92	PIK3AP1	Q6ZUJ8	OID00997	-142.28	44.99	-3.16	2.54E-03	4	2
93	PECAM-1	P16284	OID00652	-597.01	192.12	-3.11	2.96E-03	5	2
94	PSMD9	O00233	OID05480	-46.80	15.07	-3.10	3.01E-03	4	2
95	ATG4A	Q8WYN0	OID01370	-198.85	64.63	-3.08	3.24E-03	4	2
96	STIP1	P31948	OID01465	-6.43	2.10	-3.07	3.33E-03	4	2
97	CD48	P09326	OID00667	-686.08	224.49	-3.06	3.46E-03	4	2
98	PSME1	Q06323	OID05187	-159.28	52.48	-3.04	3.67E-03	4	2
99	CLEC6A	Q6EIG7	OID01017	-133.56	44.11	-3.03	3.74E-03	5	2
100	EIF4B	P23588	OID05128	-1281.88	423.51	-3.03	3.76E-03	4	2
101	IL6	P05231	OID00482	222.31	73.54	3.02	3.77E-03	5	2
102	PLXNA4	Q9HCM2	OID00982	-1043.57	345.34	-3.02	3.81E-03	4	2
103	CD2AP	Q9Y5K6	OID01133	-1331.47	442.40	-3.01	3.94E-03	2	2
104	GDNFR-alpha-3	O60609	OID00343	490.54	164.32	2.99	4.19E-03	2	2
105	MUC-16	Q8WXI7	OID00741	-82.21	27.53	-2.99	4.22E-03	2	2
106	CLIP2	Q9UDT6	OID05465	-474.42	159.60	-2.97	4.38E-03	4	2
107	INPPL1	O15357	OID01056	-766.53	258.00	-2.97	4.39E-03	4	2
108	LY9	Q9HBG7	OID00669	-963.32	327.49	-2.94	4.77E-03	5	2
109	TANK	Q92844	OID01020	-105.69	36.43	-2.90	5.33E-03	4	2
110	SELL	P14151	OID01249	-6185.23	2137.76	-2.89	5.42E-03	5	2
111	HCLS1	P14317	OID00942	-1011.58	349.89	-2.89	5.49E-03	4	2
112	COL4A1	P02462	OID01330	-418.34	146.57	-2.85	6.04E-03	2	2
113	STX8	Q9UNK0	OID01076	-248.04	86.92	-2.85	6.08E-03	5	2
114	SPARC	P09486	OID00685	-5198.06	1828.99	-2.84	6.28E-03	4	2
115	LYN	P07948	OID00715	-181.03	63.84	-2.84	6.39E-03	4	2
116	CDHR2	Q9BYE9	OID05477	-169.53	59.84	-2.83	6.43E-03	2	2
117	STK4	Q13043	OID00392	-722.32	257.03	-2.81	6.81E-03	4	2
118	ITGB1BP2	Q9UKP3	OID00443	-507.42	181.31	-2.80	7.03E-03	4	2
119	TNFRSF9	Q07011	OID00553	-2250.48	819.41	-2.75	8.09E-03	1	2
120	TBCB	Q99426	OID05181	-1057.95	388.06	-2.73	8.58E-03	4	2
121	SOD1	P00441	OID01222	-9.16	3.36	-2.72	8.58E-03	4	2
122	ATP6V1D	Q9Y5K8	OID05468	-7.38	2.71	-2.72	8.62E-03	4	2
123	ERBB2IP	Q96RT1	OID01077	-200.35	73.67	-2.72	8.73E-03	4	2
124	CCL3	P10147	OID00532	-250.74	93.01	-2.70	9.26E-03	4	2
125	NT-proBNP	P16860	OID00131	552.56	205.04	2.69	9.28E-03	5	2
126	NAMPT	P43490	OID05406	-18.56	6.90	-2.69	9.49E-03	4	2
127	CLEC11A	Q9Y240	OID01416	-225.79	84.50	-2.67	9.90E-03	4	2
128	FASLG	P48023	OID00694	-6460.37	2421.04	-2.67	9.99E-03	2	2
129	SRC	P12931	OID00388	-3290.36	1234.37	-2.67	1.00E-02	4	2
130	CA12	O43570	OID01066	98.48	37.02	2.66	1.02E-02	5	2
131	IGSF3	O75054	OID01321	38.57	14.60	2.64	1.07E-02	2	2
132	CDH15	P55291	OID05134	2632.97	1001.53	2.63	1.11E-02	1	2
133	ARHGAP25	P42331	OID05434	-9.86	3.78	-2.61	1.17E-02	4	2
134	BCR	P11274	OID01336	-613.35	235.97	-2.60	1.19E-02	5	2
135	MGMT	P16455	OID00990	-616.34	237.13	-2.60	1.20E-02	4	2
136	SCARB2	Q14108	OID00300	-383.79	147.88	-2.60	1.20E-02	1	2

137	RASA1	P20936	OID01078	-11.37	4.47	-2.54	1.38E-02	1	2
138	LAP3	P28838	OID05469	-55.47	21.82	-2.54	1.39E-02	5	2
139	SERPINA9	Q86WD7	OID01100	-332.40	131.35	-2.53	1.43E-02	1	2
140	GLB1	P16278	OID00937	-62.56	24.85	-2.52	1.48E-02	5	2
141	DIABLO	Q9NR28	OID01145	-57.36	22.86	-2.51	1.51E-02	2	2
142	SIT1	Q9Y3P8	OID01013	-218.91	87.36	-2.51	1.52E-02	5	2
143	PARK7	Q99497	OID01423	-76.33	30.48	-2.50	1.53E-02	4	2
144	ARG1	P05089	OID01199	-8.13	3.28	-2.48	1.63E-02	4	2
145	TNFRSF10A	O00220	OID01309	-193.78	78.27	-2.48	1.64E-02	1	2
146	VIM	P08670	OID00717	-193.89	78.99	-2.45	1.73E-02	5	2
147	ADA	P00813	OID00560	-367.88	150.02	-2.45	1.73E-02	4	2
148	LRRN1	Q6UXK5	OID01362	-349.64	143.60	-2.43	1.81E-02	4	2
149	FCGR2A	P12318	OID01244	-88.23	36.26	-2.43	1.82E-02	2	2
150	TXLNA	P40222	OID00655	-789.44	326.63	-2.42	1.90E-02	4	2
151	CDNF	Q49AH0	OID01359	-14.35	5.99	-2.40	1.99E-02	4	2
152	IFN-gamma-R1	P15260	OID00670	-788.26	329.05	-2.40	2.00E-02	5	2
153	CGA	P01215	OID01450	1173.96	490.87	2.39	2.02E-02	3	2
154	CLEC7A	Q9BXN2	OID01016	-285.55	119.68	-2.39	2.05E-02	3	2
155	BCAN	Q96GW7	OID00325	-284.37	119.82	-2.37	2.11E-02	4	2
156	EDAR	Q9UNE0	OID00946	-128.58	54.30	-2.37	2.14E-02	5	2
157	ITGB2	P05107	OID00565	-331.19	140.01	-2.37	2.15E-02	4	2
158	LCN2	P80188	OID01278	-11.68	4.98	-2.35	2.26E-02	5	2
159	ANGPT2	O15123	OID01132	62.62	26.70	2.34	2.27E-02	4	2
160	YES1	P07947	OID01070	-931.28	403.61	-2.31	2.48E-02	4	2
161	AGR2	O95994	OID01045	150.78	65.58	2.30	2.53E-02	2	2
162	SULT2A1	Q06520	OID01351	-18.63	8.11	-2.30	2.54E-02	4	2
163	IL-15RA	Q13261	OID00514	-22.36	9.75	-2.29	2.56E-02	4	2
164	LAT	O43561	OID00371	-3219.46	1409.19	-2.28	2.61E-02	4	2
165	AXIN1	O15169	OID00487	-838.55	367.37	-2.28	2.63E-02	5	2
166	PRTFDC1	Q9NRG1	OID05176	-307.40	134.72	-2.28	2.64E-02	4	2
167	SOD2	P04179	OID00413	-1714.09	754.07	-2.27	2.69E-02	4	2
168	HSP 27	P04792	OID00465	-9795.90	4321.72	-2.27	2.73E-02	2	2
169	SHPS-1	P78324	OID00628	-185.83	82.50	-2.25	2.82E-02	5	2
170	IFN-gamma	P01579	OID05547	-4495.03	1997.02	-2.25	2.83E-02	1	2
171	BAG6	P46379	OID01197	-88.40	39.26	-2.25	2.84E-02	2	2
172	ICAM1	P05362	OID01230	-1145.19	516.30	-2.22	3.06E-02	5	2
173	CDC27	P30260	OID05450	-17.35	7.86	-2.21	3.14E-02	4	2
174	EFNA4	P52798	OID00299	-128.60	58.32	-2.21	3.16E-02	1	2
175	PTPRM	P28827	OID05486	-92.78	42.12	-2.20	3.18E-02	4	2
176	PLA2G7	Q13093	OID01283	-51.41	23.41	-2.20	3.23E-02	5	2
177	uPA	P00749	OID00481	-23994.82	10934.22	-2.19	3.24E-02	5	2
178	ACTN4	O43707	OID05481	-4.67	2.13	-2.19	3.28E-02	4	2
179	ICAM4	Q14773	OID05479	662.19	302.91	2.19	3.31E-02	1	2
180	SERPINA12	Q8IW75	OID00422	163.28	75.40	2.17	3.46E-02	1	2
181	IRF9	Q00978	OID00945	-38.07	17.59	-2.16	3.48E-02	4	2
182	SIGLEC10	Q96LC7	OID01375	-128.90	59.92	-2.15	3.58E-02	5	2
183	TNFRSF6B	O95407	OID00663	-575.10	267.52	-2.15	3.60E-02	1	2
184	PDGF subunit A	P04085	OID00648	-292.00	136.89	-2.13	3.73E-02	4	2
185	S100P	P25815	OID01131	-6.94	3.27	-2.13	3.80E-02	4	2
186	GFER	P55789	OID05423	-85.22	40.15	-2.12	3.83E-02	4	2
187	MCP-4	Q99616	OID00504	-119210.06	56363.51	-2.12	3.89E-02	2	2
188	TGF-alpha	P01135	OID00687	-19.70	9.33	-2.11	3.93E-02	4	2
189	EPHA10	Q5JZY3	OID05184	42.37	20.14	2.10	3.99E-02	3	2
190	BLVRB	P30043	OID01424	-3.89	1.85	-2.10	4.00E-02	4	2
191	TNF	P01375	OID05548	-236.16	113.35	-2.08	4.18E-02	3	2
192	LRP1	Q07954	OID01030	-58.10	27.92	-2.08	4.21E-02	3	2
193	EREG	O14944	OID05151	-11.53	5.55	-2.08	4.23E-02	4	2
194	GZMA	P12544	OID00339	-828.14	399.53	-2.07	4.28E-02	4	2
195	FAS	P25445	OID00615	-737.72	356.25	-2.07	4.30E-02	1	2
196	SERPINB8	P50452	OID01141	27.83	13.46	2.07	4.34E-02	3	2
197	AFP	P02771	OID05441	-519.35	251.78	-2.06	4.39E-02	2	2
198	QDPR	P09417	OID01162	-216.87	106.32	-2.04	4.62E-02	4	2
199	CASP-3	P42574	OID00630	-1149.27	563.97	-2.04	4.63E-02	4	2
200	SIRT5	Q9NXA8	OID01057	-17.71	8.72	-2.03	4.71E-02	1	2
201	CCL15	Q16663	OID00629	7062.59	3478.32	2.03	4.71E-02	5	2
202	CR2	P20023	OID01258	-514.36	253.39	-2.03	4.71E-02	4	2
203	RPS6KB1	P23443	OID05150	-25.58	12.61	-2.03	4.74E-02	5	2
204	STX16	O14662	OID01312	-132.31	65.50	-2.02	4.82E-02	5	2
205	CNTNAP2	Q9UHC6	OID00943	-70.77	35.07	-2.02	4.85E-02	5	2
206	PSG1	P11464	OID05186	405.67	201.40	2.01	4.89E-02	1	2
207	ITGB6	P18564	OID01026	-47.53	23.66	-2.01	4.94E-02	4	2

208	RP2	O75695	OID05424	-37.22	9.43	-3.95	2.27E-04	4	3
209	PLXNB3	Q9ULL4	OID00306	-820.06	248.82	-3.30	1.71E-03	5	3
210	GZMH	P20718	OID00686	-327.16	105.91	-3.09	3.15E-03	4	3
211	GZMB	P10144	OID00743	-138.88	47.44	-2.93	4.96E-03	4	3
212	GP6	Q9HCN6	OID05026	-48.42	16.63	-2.91	5.16E-03	4	3
213	NCF2	P19878	OID01102	-289.86	101.16	-2.87	5.89E-03	4	3
214	CD27	P26842	OID00703	2047.49	717.40	2.85	6.07E-03	2	3
215	GDF-8	O14793	OID00328	678.66	239.45	2.83	6.38E-03	1	3
216	STAMBP	O95630	OID00558	-939.72	334.46	-2.81	6.82E-03	4	3
217	BOC	Q9BWV1	OID00386	178.84	65.37	2.74	8.32E-03	1	3
218	FUS	P35637	OID05453	-32.12	11.78	-2.73	8.56E-03	4	3
219	WWP2	O00308	OID05219	-371.85	137.86	-2.70	9.26E-03	5	3
220	NID1	P14543	OID01250	-98.78	37.32	-2.65	1.05E-02	2	3
221	TCL1A	P56279	OID00720	-2429.00	932.64	-2.60	1.18E-02	1	3
222	TIMD4	Q96H15	OID01298	388.60	154.40	2.52	1.47E-02	3	3
223	ADM	P35318	OID00381	724.70	288.01	2.52	1.48E-02	4	3
224	ARTN	Q5T4W7	OID00526	-14.89	6.03	-2.47	1.66E-02	4	3
225	AZU1	P20160	OID00597	-53.47	23.04	-2.32	2.40E-02	4	3
226	CEACAM3	P40198	OID05164	-4.28	1.86	-2.30	2.54E-02	1	3
227	CXCL1	P09341	OID00496	-16001.80	7008.09	-2.28	2.62E-02	5	3
228	PMVK	Q15126	OID05218	-513.51	226.06	-2.27	2.70E-02	4	3
229	HLA-E	P13747	OID05493	-64.22	28.42	-2.26	2.78E-02	3	3
230	RGMB	Q6NW40	OID00314	469.92	213.61	2.20	3.20E-02	2	3
231	ACE2	Q9BYF1	OID00457	-150.59	69.67	-2.16	3.50E-02	2	3
232	PVALB	P20472	OID01113	-6024.34	2787.74	-2.16	3.51E-02	5	3
233	MAX	P61244	OID01088	-17.18	7.95	-2.16	3.51E-02	4	3
234	ITGA6	P23229	OID00959	-21.03	9.75	-2.16	3.53E-02	4	3
235	IL-24	Q13007	OID00524	-42.17	19.57	-2.15	3.55E-02	4	3
236	CD69	Q07108	OID01467	-318.16	148.13	-2.15	3.61E-02	5	3
237	EDIL3	O43854	OID01064	24.88	11.73	2.12	3.85E-02	5	3
238	KIRREL2	Q6UWL6	OID05188	43.45	20.65	2.10	4.00E-02	1	3
239	IDUA	P35475	OID00393	-945.16	453.28	-2.09	4.16E-02	5	3
240	SPINK4	O60575	OID05475	18.19	8.80	2.07	4.34E-02	2	3
241	KLK6	Q92876	OID00647	-106.12	52.04	-2.04	4.61E-02	1	3
242	KIF1BP	Q96EK5	OID05213	-124.31	60.96	-2.04	4.63E-02	4	3
243	CA2	P00918	OID01477	-332.85	165.51	-2.01	4.92E-02	4	3
244	TRIM21	P19474	OID00964	-197.17	46.23	-4.27	7.92E-05	4	4
245	LYAR	Q9NX58	OID01388	-17.61	4.20	-4.20	9.74E-05	1	4
246	CD5	P06127	OID00531	-342.74	84.56	-4.05	1.58E-04	4	4
247	FHIT	P49789	OID05157	-21.40	5.35	-4.00	1.91E-04	4	4
248	CST6	Q15828	OID01437	284.65	75.30	3.78	3.88E-04	5	4
249	FOXO3	O43524	OID05455	-41.97	11.34	-3.70	4.96E-04	4	4
250	CSNK1D	P48730	OID01035	-9.48	2.61	-3.63	6.29E-04	4	4
251	Alpha-2-MRAP	P30533	OID00311	-4557.75	1338.60	-3.40	1.23E-03	4	4
252	LAIR-2	Q6ISS4	OID00373	3150.52	934.84	3.37	1.37E-03	5	4
253	SH2B3	Q9UQQ2	OID00983	-866.13	257.64	-3.36	1.41E-03	4	4
254	ANXA1	P04083	OID00745	-182.34	55.25	-3.30	1.70E-03	4	4
255	ARHGAP1	Q07960	OID01352	-83.74	26.04	-3.22	2.16E-03	4	4
256	ESM-1	Q9NQ30	OID00729	-7163.81	2238.94	-3.20	2.29E-03	4	4
257	TIGAR	Q9NQ88	OID01041	-20.36	6.41	-3.17	2.46E-03	4	4
258	FOXO1	Q12778	OID01065	-129.11	41.56	-3.11	2.99E-03	4	4
259	HBQ1	P09105	OID05471	-69.61	22.52	-3.09	3.13E-03	4	4
260	UBAC1	Q9BSL1	OID05484	-71.77	23.35	-3.07	3.29E-03	4	4
261	MANF	P55145	OID00374	-6285.32	2056.51	-3.06	3.43E-03	4	4
262	LAT2	Q9GZY6	OID01074	-469.51	155.25	-3.02	3.78E-03	4	4
263	VCAM1	P19320	OID01257	-541.27	179.13	-3.02	3.78E-03	5	4
264	HS6ST1	O60243	OID01320	-427.57	143.00	-2.99	4.14E-03	5	4
265	HEXIM1	O94992	OID00987	-707.22	236.61	-2.99	4.18E-03	4	4
266	CCL16	O15467	OID00654	1040.85	355.84	2.93	4.96E-03	2	4
267	FAM3C	Q92520	OID01175	-1550.63	535.10	-2.90	5.39E-03	1	4
268	IRAK4	Q9NWZ3	OID00940	-320.41	110.64	-2.90	5.41E-03	4	4
269	CD200R1	Q8TD46	OID00376	-535.82	186.00	-2.88	5.61E-03	4	4
270	IL-18BP	O95998	OID00640	-1280.22	445.05	-2.88	5.68E-03	1	4
271	BNP	P16860	OID00455	193.12	68.42	2.82	6.59E-03	5	4
272	LACTB2	Q53H82	OID05470	-321.42	114.05	-2.82	6.70E-03	4	4
273	IL-17D	Q8TAD2	OID00403	-66.35	23.70	-2.80	7.01E-03	2	4
274	RETN	Q9HD89	OID00603	-1181.71	427.90	-2.76	7.76E-03	2	4
275	CBL	P22681	OID01340	-390.70	141.62	-2.76	7.82E-03	5	4
276	ARSB	P15848	OID01337	-39.67	14.42	-2.75	7.99E-03	4	4
277	Beta-NGF	P01138	OID00335	-8.88	3.25	-2.73	8.36E-03	4	4
278	TDGF1	P13385	OID05131	8.86	3.27	2.71	8.96E-03	4	4

279	DRAXIN	Q8NBI3	OID00341	-357.76	133.51	-2.68	9.66E-03	1	4
280	LILRB2	Q8N423	OID01296	-84.52	31.77	-2.66	1.02E-02	2	4
281	GDNF	P39905	OID00475	-93.33	35.43	-2.63	1.09E-02	4	4
282	CCl4	P13236	OID00498	-957.43	365.06	-2.62	1.12E-02	4	4
283	LAIR1	Q6GTX8	OID01488	-178.70	69.57	-2.57	1.30E-02	1	4
284	VEGFR-3	P35916	OID00740	-491.70	193.56	-2.54	1.39E-02	4	4
285	PRKAB1	Q9Y478	OID01046	-28.01	11.12	-2.52	1.47E-02	4	4
286	GALNT7	Q86SF2	OID05487	-440.15	175.33	-2.51	1.50E-02	3	4
287	Dkk-4	Q9UBT3	OID00369	-320.89	129.86	-2.47	1.65E-02	3	4
288	PPP1R9B	Q96SB3	OID00936	-309.24	126.28	-2.45	1.75E-02	4	4
289	SORCS2	Q96PQ0	OID01377	-127.53	52.27	-2.44	1.79E-02	1	4
290	FCRLB	Q6BAA4	OID00744	-52.49	21.80	-2.41	1.94E-02	4	4
291	IGLC2	P0DOY2	OID01240	-2035.29	848.24	-2.40	1.98E-02	3	4
292	CDKN1A	P38936	OID00709	-940.96	392.54	-2.40	2.00E-02	5	4
293	CLEC4C	Q8WTT0	OID00949	-375.15	157.71	-2.38	2.09E-02	5	4
294	DCTN1	Q14203	OID00958	-647.15	272.39	-2.38	2.10E-02	4	4
295	ANGPTL4	Q9BY76	OID01413	53.65	22.62	2.37	2.13E-02	2	4
296	TLT-2	Q5T2D2	OID00588	-434.40	183.71	-2.36	2.15E-02	5	4
297	IRAK1	P51617	OID00950	-79.10	33.67	-2.35	2.24E-02	4	4
298	CD160	Q95971	OID00721	-386.18	166.44	-2.32	2.41E-02	5	4
299	CLEC1B	Q9P126	OID00318	-56118.32	24220.30	-2.32	2.42E-02	5	4
300	ICAM3	P32942	OID01267	-231.25	99.84	-2.32	2.42E-02	5	4
301	NAA10	P41227	OID05168	-173.06	74.73	-2.32	2.43E-02	4	4
302	CTSF	Q9UBX1	OID01400	-59.54	25.84	-2.30	2.50E-02	5	4
303	CD63	P08962	OID05222	-970.49	422.72	-2.30	2.55E-02	4	4
304	CARHSP1	Q9Y2V2	OID05198	-12.77	5.66	-2.26	2.81E-02	4	4
305	GCG	P01275	OID01329	77.10	34.35	2.24	2.87E-02	4	4
306	HMBS	P08397	OID05464	-115.62	51.86	-2.23	2.99E-02	4	4
307	TR	P02786	OID00593	-2233.37	1003.01	-2.23	3.00E-02	5	4
308	SMPD1	P17405	OID00309	-772.78	348.71	-2.22	3.08E-02	5	4
309	DCN	P07585	OID00444	413.43	186.97	2.21	3.11E-02	3	4
310	TFF3	Q07654	OID00573	-400.86	181.71	-2.21	3.15E-02	1	4
311	AIFM1	Q95831	OID01048	-151.53	68.86	-2.20	3.20E-02	5	4
312	THPO	P40225	OID00452	169.31	77.42	2.19	3.29E-02	5	4
313	SERPINA7	P05543	OID01232	-588.22	269.46	-2.18	3.32E-02	5	4
314	CRISP2	P16562	OID01338	-1509.54	695.91	-2.17	3.43E-02	2	4
315	WFDC2	Q14508	OID00732	-2478.47	1144.44	-2.17	3.47E-02	3	4
316	EPHB6	Q15197	OID00313	-369.82	171.23	-2.16	3.51E-02	1	4
317	SEMA7A	Q75326	OID01461	-181.26	84.83	-2.14	3.71E-02	5	4
318	CES1	P23141	OID01263	-379.40	179.29	-2.12	3.88E-02	1	4
319	NEMO	Q9Y6K9	OID00467	-659.64	312.26	-2.11	3.91E-02	4	4
320	IL-5R-alpha	Q01344	OID00354	-398.66	190.11	-2.10	4.05E-02	4	4
321	S100A4	P26447	OID00680	1024.42	489.00	2.09	4.08E-02	1	4
322	IFNGR2	P38484	OID05410	-1188.68	568.10	-2.09	4.10E-02	5	4
323	OMG	P23515	OID01341	-171.10	82.01	-2.09	4.15E-02	4	4
324	PDGFC	Q9NRA1	OID01044	-109.99	52.72	-2.09	4.16E-02	1	4
325	SKAP1	Q86WV1	OID01366	-679.39	326.04	-2.08	4.18E-02	4	4
326	ZBTB17	Q13105	OID01355	-26.78	12.88	-2.08	4.21E-02	4	4
327	GNLY	P22749	OID01262	-14.23	6.88	-2.07	4.32E-02	4	4
328	RGMA	Q96B86	OID00305	-14001.19	6783.91	-2.06	4.37E-02	4	4
329	SIGLEC6	Q43699	OID01317	-648.50	314.30	-2.06	4.37E-02	4	4
330	CEACAM1	P13688	OID00659	-1390.02	674.66	-2.06	4.41E-02	4	4
331	YTHDF3	Q7Z739	OID05476	-20.37	9.99	-2.04	4.63E-02	4	4
332	EZR	P15311	OID00296	-145.94	71.80	-2.03	4.69E-02	4	4
333	WAS	P42768	OID01109	-34.20	16.88	-2.03	4.76E-02	2	4
334	TNFRSF4	P43489	OID00722	-188.34	93.06	-2.02	4.78E-02	1	4
335	IFNLR1	Q8IU57	OID01010	-41.78	20.65	-2.02	4.79E-02	1	4
336	METAP1D	Q6UB28	OID01360	-559.19	278.56	-2.01	4.95E-02	5	4

Plasma proteins significantly associated with neural network risk scores are shown. β , effect size; FDR, false discovery rate; SE, standard error.

Supplementary Table 21. Cell-type enrichment analysis of the plasma proteins in each cluster

	Cluster 1			Cluster 2		
	Tissue-specific genes	Fold change	<i>p</i> -value	Tissue-specific genes	Fold change	<i>p</i> -value
B cells	10	2.8407	0.0195	6	0.8338	0.8041
Dendritic cells	7	1.0749	0.9769	11	0.8263	0.8041
Endothelial cells	7	0.5681	0.9769	27	1.0720	0.5852
Eosinophils	4	0.5588	0.9769	23	1.5719	0.0489
Erythroblasts	2	0.5980	0.9769	18	2.6331	0.0003
Macrophages	5	0.6360	0.9769	20	1.2445	0.3372
Megakaryocytes	3	0.5063	0.9769	28	2.3116	0.0001
Monocytes	5	0.7222	0.9769	12	0.8479	0.8041
Neutrophils	7	1.2174	0.9769	15	1.2762	0.3372
Natural killer cells	4	1.1555	0.9769	10	1.4132	0.3372
T cells	3	1.1363	0.9769	5	0.9265	0.8041
	Cluster 3			Cluster 4		
	Tissue-specific genes	Fold change	<i>p</i> -value	Tissue-specific genes	Fold change	<i>p</i> -value
B cells	1	0.5366	0.9426	13	2.7295	0.0033
Dendritic cells	4	1.1602	0.9426	19	2.1564	0.0033
Endothelial cells	7	1.0731	0.9426	13	0.7799	0.8826
Eosinophils	3	0.7917	0.9426	18	1.8587	0.0183
Erythroblasts	1	0.5648	0.9426	4	0.8841	0.7466
Macrophages	3	0.7208	0.9426	14	1.3162	0.3013
Megakaryocytes	2	0.6375	0.9426	9	1.1226	0.5629
Monocytes	4	1.0913	0.9426	11	1.1744	0.5183
Neutrophils	4	1.3141	0.9426	8	1.0284	0.6417
Natural killer cells	2	1.0913	0.9426	8	1.7082	0.1940
T cells	0	0.0000	1.0000	7	1.9597	0.1625

Cell types with significant enrichment of the identified plasma proteins ($p < 0.05$) are displayed in bold text.

Supplementary Table 22. Plasma proteins in each cluster that are significantly enriched in corresponding cell types

	Cluster 1	Cluster 2		Cluster 4		
Index	B cells	Erythroblasts	Megakaryocytes	B cells	Dendritic cells	Eosinophils
1	CD27	CRADD	PARK7	CD69	IRF9	AXIN1
2	IFNLR1	PARK7	ARHGAP1	LY9	GLB1	IRF9
3	FAM3C	CCT5	QDPR	SIT1	VIM	BACH1
4	TNF	GLO1	CCT5	ADA	NFKBIE	CBL
5	CD38	ARHGEF12	GLO1	BACH1	ZBTB17	ICAM3
6	IGLC2	EIF4G1	USO1	LAT2	PLAU	TREML2
7	IL4R	SOD1	ARHGEF12	HSP90B1	VCAM1	SIRPA
8	SERPINA9	PRKAB1	EIF4G1	TOP2B	CDKN1A	TNFSF14
9	TCL1A	AKT1S1	SOD1	NFKBIE	COCH	ZBTB17
10	TNFRSF10A	ATG4A	CASP2	ZBTB17	DAPP1	NFATC1
11		BLVRB	MAX	NFATC1	ICAM1	ADAM8
12		FOXO3	TXLNA	CD22	IL15	CLEC4C
13		HAGH	CLIP2	FOXO1	IL15RA	LRPAP1
14		HMBS	MANF		IL6	SEMA7A
15		METAP2	YES1		LAP3	TGFA
16		PSMD9	GOPC		NUB1	WWP2
17		UBAC1	EIF4EBP1		TANK	ARSB
18		EIF4EBP1	ENO2		ARSB	HS6ST1
19			GP6		FOXO1	
20			HEXIM1			
21			ITGA6			
22			LAT			
23			NT5C3A			
24			PLXNA4			
25			PMVK			
26			PRTFDC1			
27			SH2B3			
28			SRC			

Supplementary Table 23. Summary of protein–protein interaction network analysis for plasma proteins enriched in specific cell types

Statistic/cell type	B cells	Dendritic cells	Eosinophils	Erythroblasts	Megakaryocytes
Number of nodes	22	19	18	18	28
Number of edges	64	50	20	41	58
Average node degree	5.82	5.26	2.22	4.56	4.14
Average local clustering coefficient	0.646	0.665	0.369	0.678	0.558
Expected number of edges	23	21	6	19	40
Protein–protein interaction enrichment <i>p</i> -value	1E–12	5.34E–08	5.1E–06	7.82E–06	0.00501

Supplementary Table 24. Transcript abundance of plasma proteins enriched in B cells

Gene symbol	B cells	Dendritic cells	Endothelial cells	Eosinophils	Erythroblasts	Macrophages
<i>SERPINA9</i>	30.0	0.0	0.0	0.0	0.0	0.0
<i>IGLC2</i>	9998.7	1.3	0.0	11.1	0.1	0.0
<i>TCL1A</i>	246.1	0.3	0.0	1.4	0.0	0.0
<i>CD22</i>	422.0	2.1	0.1	4.3	0.1	13.2
<i>CD38</i>	64.5	5.5	0.2	0.5	0.0	4.4
<i>CD27</i>	52.5	0.0	0.0	1.8	0.0	0.0
<i>SIT1</i>	22.6	0.4	0.0	1.7	0.1	2.0
<i>IFNLR1</i>	9.4	1.9	0.0	0.1	0.0	11.6
<i>LY9</i>	47.8	1.9	0.0	2.6	0.3	10.9
<i>IL4R</i>	163.4	84.4	28.9	94.0	8.3	21.4
<i>FAM3C</i>	46.5	15.9	31.8	0.9	7.2	13.6
<i>CD69</i>	297.3	8.5	1.6	45.4	35.4	0.0
<i>ADA</i>	29.8	2.4	13.8	0.6	5.8	11.5
<i>TNF</i>	12.8	11.8	0.0	0.7	0.4	1.7
<i>LAT2</i>	124.1	18.7	0.4	20.2	10.9	39.0
<i>NFATC1</i>	18.0	3.5	8.9	14.8	4.5	3.6
<i>NFKBIE</i>	37.7	26.7	14.2	19.4	2.9	37.6
<i>FOXO1</i>	28.2	39.8	30.6	4.4	6.1	2.7
<i>HSP90B1</i>	415.3	186.1	500.0	56.7	125.5	273.8
<i>ZBTB17</i>	34.0	34.1	13.3	25.5	11.9	15.8
<i>TNFRSF10A</i>	10.4	4.2	9.4	8.4	3.3	11.5
<i>BACH1</i>	64.4	25.4	10.3	83.0	38.5	38.3
<i>TOP2B</i>	103.4	72.5	62.4	67.6	57.1	34.6

Gene symbol	Megakaryocytes	Monocytes	Neutrophils	Natural killer cells	T cells
<i>SERPINA9</i>	0.0	0.0	0.0	0.0	0.0
<i>IGLC2</i>	0.0	0.7	27.5	0.4	5.8
<i>TCL1A</i>	0.0	0.3	0.5	0.4	0.0
<i>CD22</i>	0.4	0.7	0.3	0.2	0.1
<i>CD38</i>	0.0	2.8	7.1	24.9	3.9
<i>CD27</i>	0.0	0.1	0.3	0.4	60.8
<i>SIT1</i>	0.0	0.1	0.2	0.1	29.2
<i>IFNLR1</i>	0.0	0.0	0.0	0.1	0.4
<i>LY9</i>	0.1	0.8	0.1	24.5	43.4
<i>IL4R</i>	15.4	26.2	87.1	10.7	45.7
<i>FAM3C</i>	23.3	4.4	1.4	17.7	4.8
<i>CD69</i>	261.3	21.7	4.9	117.3	367.5
<i>ADA</i>	8.6	3.6	2.3	25.1	13.9
<i>TNF</i>	6.7	7.1	3.7	1.1	4.7
<i>LAT2</i>	69.4	115.4	64.5	76.3	1.6
<i>NFATC1</i>	10.9	2.7	1.9	5.9	8.0
<i>NFKBIE</i>	5.3	22.6	4.6	4.2	4.0
<i>FOXO1</i>	7.9	8.2	7.0	4.2	24.9
<i>HSP90B1</i>	370.2	124.6	118.3	165.7	120.8
<i>ZBTB17</i>	12.1	8.7	17.7	13.5	15.5
<i>TNFRSF10A</i>	2.4	3.3	4.7	0.7	13.8
<i>BACH1</i>	40.2	86.2	82.0	11.0	13.9
<i>TOP2B</i>	143.6	38.0	69.4	81.6	71.2

Transcript abundance is indicated as the FPKM values obtained from the RNA sequencing data. FPKM, fragments per kilobase per million mapped fragments.

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