Table 1 | The 38 genomic risk loci identified from 90,338 (46,613 proxy) cases and 1,036,225 (318,246 proxy) controls

Genomic locus	Gene	Position (GRCh37)	Lead variant	A1	A1 frequency	*P* value	*N*
1	***AGRN***	**1:985,377**	**rs113020870**	**T**	**0.0041**	$\mathbf{3.83\times10^{-8}}$	**776,379**
2	*CR1*	1:207,750,568	rs679515	C	0.82	2.42×10^{-25}	762,176
3	*NCK2*	2:106,235,428	rs115186657	C	0.0035	1.33×10^{-8}	727,537
4	*BIN1*	2:127,891,427	rs4663105	C	0.41	3.92×10^{-58}	1,078,540
5	*INPPD5*	2:234,082,577	rs7597763	C	0.45	4.65×10^{-9}	819,541
6	*CLNK*	4:11,014,822	rs4504245	G	0.79	5.23×10^{-12}	1,080,458
7	***TNIP1***	**5:150,432,388**	**rs871269**	**T**	**0.32**	$\mathbf{1.37\times10^{-9}}$	**1,089,904**
8	***HAVCR2***	**5:156,526,331**	**rs6891966**	**G**	**0.77**	$\mathbf{7.91\times10^{-10}}$	**1,089,230**
9	*HLA-DRB1*	6:32,583,813	rs1846190	A	0.30	2.66×10^{-14}	754,040
10	*TREM2*	6:40,942,196	rs187370608	G	0.997	1.26×10^{-25}	791,668
11	*CD2AP*	6:47,552,180	rs9369716	T	0.27	1.70×10^{-17}	1,052,285
12	***TMEM106B***	**7:12,268,758**	**rs5011436**	**C**	**0.41**	$\mathbf{2.70\times10^{-9}}$	**1,123,678**
13	*ZCWPW1/NYAP1*	7:99,932,049	rs7384878	T	0.69	9.41×10^{-16}	1,084,138
14	*EPHA1-AS1*	7:143,104,331	rs3935067	G	0.62	4.69×10^{-11}	1,117,025
15	*CLU*	8:27,466,315	rs1532278	T	0.39	1.57×10^{-22}	1,126,563
16	*SHARPIN*	8:145,108,151	rs61732533	G	0.95	3.14×10^{-9}	1,122,653
17	*USP6NL/ECHDC3*	10:11,718,713	rs7912495	G	0.46	7.68×10^{-15}	1,120,367
18	*CCDC6*	10:61,738,152	rs7902657	T	0.54	3.68×10^{-8}	1,126,388
19	*MADD/SPI1*	11:47,380,340	rs3740688	T	0.54	8.78×10^{-9}	1,123,185
20	*MS4A4A*	11:60,021,948	rs1582763	G	0.62	3.40×10^{-33}	1,125,804
21	*PICALM*	11:85,800,279	rs561655	G	0.35	1.24×10^{-26}	1,126,563
22	*SORL1*	11:121,435,587	rs11218343	T	0.96	1.33×10^{-13}	1,125,100
23	*FERMT2*	14:53,298,853	rs7146179	G	0.89	6.99×10^{-11}	1,089,904
24	*RIN3*	14:92,938,855	rs12590654	G	0.67	6.63×10^{-17}	1,116,967
25	*ADAM10*	15:59,057,023	rs602602	T	0.70	6.22×10^{-15}	1,124,268
26	*APH1B*	15:63,569,902	rs117618017	T	0.13	7.00×10^{-12}	889,854
27	*SCIMP/RABEP1*	17:4,969,940	rs7209200	T	0.33	3.18×10^{-8}	1,125,637
28	***GRN***	**17:42,442,344**	**rs708382**	**T**	**0.61**	$\mathbf{1.98\times10^{-9}}$	**1,125,622**
29	*ABI3*	17:47,450,775	rs28394864	G	0.54	4.90×10^{-10}	1,084,218
30	*TSPOAP1-AS1*	17:56,409,089	rs2632516	G	0.54	7.46×10^{-10}	1,082,451
31	*ACE*	17:61,545,779	rs6504163	T	0.61	1.23×10^{-9}	1,083,145
32	*ABCA7*	19:1,050,874	rs12151021	G	0.68	2.81×10^{-15}	1,082,434
33	*APOE*	19:45,411,941	rs429358	T	0.84	$<1.0\times10^{-300}$	1,126,190
34	***NTN5***	**19:49,213,504**	**rs2452170**	**G**	**0.47**	$\mathbf{1.72\times10^{-8}}$	**1,088,626**
35	*CD33*	19:51,737,991	rs1354106	G	0.37	2.21×10^{-10}	716,038
36	***LILRB2***	**19:54,825,174**	**rs1761461**	**C**	**0.49**	$\mathbf{1.56\times10^{-9}}$	**1,116,336**
37	*CASS4*	20:54,995,699	rs6069737	T	0.083	6.73×10^{-16}	1,087,703
38	*APP*	21:27,520,931	rs2154482	T	0.44	7.66×10^{-10}	1,124,606

The *P* values were identified through a meta-analysis (two-sided test) of summary statistics generated by linear/logistic regressions (two-sided test) and were not adjusted for multiple testing. The previously unidentified loci are highlighted in bold. The genes were assigned on the basis of colocalization results, fine-mapping results and previous literature. A1, tested allele; *N*, sample size.

by Bcl3 in mouse microglia[20], where this module was implicated in prolonged exposure to inflammation and aging of microglia. The gene encoding Bcl3 (*BCL3*) was found to be significantly associated with cerebrospinal fluid amyloid-beta1–42 peptide after conditioning for *APOE*[21] and was observed as upregulated postmortem in the brain of patients with LOAD[22]. Further investigation into this locus in nonEuropean populations may yield more support for the lead variant and improve the fine-mapping analysis.

The lead variant of locus 8 (rs6891966; $P=7.91\times10^{-10}$) is located in an intron of *HAVCR2* (Supplementary Fig. 6). *HAVCR1* and *TIMD4* also map to this region on the basis of brain eQTLs (PsychENCODE). *HAVCR2* was significantly differentially expressed in bulk brain tissue of patients with LOAD compared to controls[23]. *HAVCR2* is preferentially expressed in aged microglia[24], was included as one of the top 100 enriched transcripts in brain and microglia and was included in a cluster of transcripts that are involved in sensing endogenous ligands and microbes[25]. The protein encoded by *HAVCR2* (Havcr2) has been suggested to bind to phosphatidylserine on cell surfaces to mediate apoptosis[26] and to interact with amyloid precursor protein[27]. *TIMD4* is another gene in this region that encodes a protein (TIM-4) with a similar function to Havcr2; it binds to phosphatidylserine on cell surfaces to medi-