Table 1 | Summary of association results in the stage I and stage II analysis for known loci with a genome-wide significant signal

Variant[a]	Chromosome	Position[b]	Gene[c]	Known locus	Minor/major allele	MAF[d]	OR[e]	95% CI	P value
rs679515	1	207577223	*CR1*	*CR1*	T/C	0.188	1.13	1.11–1.15	7.2×10^{-46}
rs6733839	2	127135234	*BIN1*	*BIN1*	T/C	0.389	1.17	1.16–1.19	6.1×10^{-118}
rs10933431	2	233117202	*INPP5D*	*INPP5D*	G/C	0.234	0.93	0.92–0.95	3.6×10^{-18}
rs6846529	4	11023507	*CLNK*	*CLNK/HS3ST1*	C/T	0.283	1.07	1.05–1.08	2.2×10^{-17}
rs6605556	6	32615322	*HLA-DQA1*	*HLA*	G/A	0.161	0.91	0.90–0.93	7.1×10^{-20}
rs10947943	6	41036354	*UNC5CL*	*TREM2*	A/G	0.142	0.94	0.93–0.96	1.1×10^{-9}
rs143332484	6	41161469	*TREM2*	*TREM2*	T/C	0.013	1.41	1.32–1.50	2.8×10^{-25}
rs75932628	6	41161514	*TREM2*	*TREM2*	T/C	0.003	2.39	2.09–2.73	2.5×10^{-37}
rs60755019	6	41181270	*TREML2*	*TREM2*	G/A	0.004	1.55	1.33–1.80	2.1×10^{-8}
rs7767350	6	47517390	*CD2AP*	*CD2AP*	T/C	0.271	1.08	1.06–1.09	7.9×10^{-22}
rs6966331	7	37844191	*EPDR1*	*NME8*	T/C	0.349	0.96	0.94–0.97	4.6×10^{-10}
rs7384878	7	100334426	*SPDYE3*	*ZCWPW1/NYAP1*	C/T	0.31	0.92	0.91–0.94	1.1×10^{-26}
rs11771145	7	143413669	*EPHA1*	*EPHA1*	A/G	0.348	0.95	0.93–0.96	3.3×10^{-14}
rs73223431	8	27362470	*PTK2B*	*PTK2B*	T/C	0.369	1.07	1.06–1.08	4.0×10^{-22}
rs11787077	8	27607795	*CLU*	*CLU*	T/C	0.392	0.91	0.90–0.92	1.7×10^{-44}
rs7912495	10	11676714	*USP6NL*	*ECHDC3*	G/A	0.462	1.06	1.05–1.08	9.7×10^{-19}
rs10437655	11	47370397	*SPI1*	*CELF1/SPI1*	A/G	0.399	1.06	1.04–1.07	5.3×10^{-14}
rs1582763	11	60254475	*MS4A4A*	*MS4A*	A/G	0.371	0.91	0.90–0.92	3.7×10^{-42}
rs3851179	11	86157598	*EED*	*PICALM*	T/C	0.358	0.9	0.89–0.92	3.0×10^{-48}
rs74685827	11	121482368	*SORL1*	*SORL1*	G/T	0.019	1.19	1.13–1.25	2.8×10^{-11}
rs11218343	11	121564878	*SORL1*	*SORL1*	C/T	0.039	0.84	0.81–0.87	1.4×10^{-21}
rs17125924	14	52924962	*FERMT2*	*FERMT2*	G/A	0.089	1.1	1.07–1.12	8.3×10^{-16}
rs7401792	14	92464917	*SLC24A4*	*SLC24A4/RIN3*	G/A	0.371	1.04	1.02–1.05	4.8×10^{-8}
rs12590654	14	92472511	*SLC24A4*	*SLC24A4/RIN3*	A/G	0.328	0.93	0.92–0.95	4.2×10^{-21}
rs8025980	15	50701814	*SPPL2A*	*SPPL2A*	G/A	0.345	0.96	0.94–0.97	1.3×10^{-8}
rs602602	15	58764824	*MINDY2*	*ADAM10*	A/T	0.28	0.94	0.93–0.96	2.1×10^{-15}
rs117618017	15	63277703	*APH1B*	*APH1B*	T/C	0.144	1.11	1.09–1.13	2.2×10^{-25}
rs889555	16	31111250	*BCKDK*	*KAT8*	T/C	0.281	0.95	0.94–0.97	2.0×10^{-11}
rs4985556	16	70660097	*IL34*	*IL34*	A/C	0.115	1.07	1.05–1.09	6.0×10^{-10}
rs12446759	16	81739398	*PLCG2*	*PLCG2*	G/A	0.403	0.95	0.94–0.96	1.2×10^{-13}
rs72824905	16	81908423	*PLCG2*	*PLCG2*	G/C	0.008	0.74	0.68–0.81	8.5×10^{-12}
rs7225151	17	5233752	*SCIMP*	*SCIMP/RABEP1*	A/G	0.124	1.08	1.05–1.10	4.1×10^{-13}
rs199515	17	46779275	*WNT3*	*MAPT*	G/C	0.219	0.94	0.93–0.96	9.3×10^{-13}
rs616338	17	49219935	*ABI3*	*ABI3*	T/C	0.012	1.32	1.23–1.42	2.8×10^{-14}
rs2526377	17	58332680	*TSPOAP1*	*TSPOAP1*	G/A	0.445	0.95	0.94–0.97	1.6×10^{-12}
rs4277405	17	63471557	*ACE*	*ACE*	C/T	0.384	0.94	0.93–0.95	8.8×10^{-20}
rs12151021	19	1050875	*ABCA7*	*ABCA7*	A/G	0.336	1.1	1.09–1.12	1.6×10^{-37}
rs6014724	20	56423488	*CASS4*	*CASS4*	G/A	0.09	0.89	0.87–0.91	4.1×10^{-21}
rs2830489	21	26775872	*ADAMTS1*	*ADAMTS1*	T/C	0.281	0.95	0.94–0.97	1.7×10^{-10}

P values are two-sided raw *P* values derived from a fixed-effect meta-analysis. CI, confidence interval; OR, odds ratio; MAF, minor allele frequency. [a]Reference single-nucleotide polymorphism (SNP) (rs) number, according to dbSNP build 153. [b]GRCh38 assembly. [c]Nearest protein-coding gene according to GENCODE release 33. [d]Weighted average MAF across all discovery studies. [e]Approximate OR calculated with respect to the minor allele.

colocalization between association signals for the ADD risk and those for the molecular phenotypes and the association between the ADD risk and these phenotypes by integrating *cis*-QTL information into our ADD GWAS. Moreover, we considered the lead variant annotation (the allele frequency, protein-altering effects and nearest protein-coding gene) and a genome-wide, high-content short interfering RNA screen for APP metabolism[17]. Based on this evidence, we developed a systematic gene prioritization strategy that yielded a total weighted score of between 0 and 100 for each gene (Supplementary Fig. 34 and Supplementary Note). This score was used to compare and prioritize genes in the new loci within 1 Mb upstream and 1 Mb downstream of the lead variants. Genes either were ranked as tier 1 (greater likelihood of being the causal risk gene responsible for the ADD signal) or tier 2 (lower likelihood and the absence of a minimum level of evidence as a causal risk gene) or were not ranked.

Table 2 | Summary of association results in the stage I and stage II analysis for new loci at the time of analysis with a genome-wide significant signal

Locus number	Variant[a]	Chromosome	Position[b]	Gene[c]	Minor/major allele	MAF[d]	OR[e]	95% CI	P value
1	rs141749679	1	109345810	SORT1	C/T	0.004	1.38	1.24–1.54	7.5×10^{-9}
2	rs72777026	2	9558882	ADAM17	G/A	0.144	1.06	1.04–1.08	2.7×10^{-8}
3	rs17020490	2	37304796	PRKD3	C/T	0.145	1.06	1.04–1.08	3.3×10^{-9}
4	rs143080277	2	105749599	NCK2	C/T	0.005	1.47	1.33–1.63	2.1×10^{-13}
5	rs139643391	2	202878716	WDR12	T/TC	0.131	0.94	0.92–0.96	1.1×10^{-8}
6	rs16824536	3	155069722	MME	A/G	0.054	0.92	0.89–0.95	3.6×10^{-8}
6	rs61762319	3	155084189	MME	G/A	0.026	1.16	1.11–1.21	2.2×10^{-11}
7	rs3822030	4	993555	IDUA	G/T	0.429	0.95	0.94–0.96	8.3×10^{-12}
8	rs2245466	4	40197226	RHOH	G/C	0.343	1.05	1.03–1.06	1.2×10^{-9}
9	rs112403360	5	14724304	ANKH	A/T	0.073	1.09	1.06–1.12	2.3×10^{-9}
10	rs62374257	5	86927378	COX7C	C/T	0.23	1.07	1.05–1.09	1.4×10^{-15}
11	rs871269	5	151052827	TNIP1	T/C	0.326	0.96	0.95–0.97	8.7×10^{-9}
12	rs113706587	5	180201150	RASGEF1C	A/G	0.11	1.09	1.07–1.12	2.2×10^{-16}
13	rs785129	6	114291731	HS3ST5	T/C	0.35	1.04	1.03–1.06	2.4×10^{-9}
14	rs6943429	7	7817263	UMAD1	T/C	0.42	1.05	1.03–1.06	1.0×10^{-10}
15	rs10952097	7	8204382	ICA1	T/C	0.114	1.07	1.05–1.10	6.8×10^{-9}
16	rs13237518	7	12229967	TMEM106B	A/C	0.411	0.96	0.94–0.97	4.9×10^{-11}
17	rs1160871	7	28129126	JAZF1	G/GTCTT	0.222	0.95	0.93–0.97	9.8×10^{-9}
18	rs76928645	7	54873635	SEC61G	T/C	0.103	0.93	0.91–0.95	1.6×10^{-10}
19	rs1065712	8	11844613	CTSB	C/G	0.053	1.09	1.06–1.12	1.9×10^{-9}
20	rs34173062	8	144103704	SHARPIN	A/G	0.081	1.13	1.09–1.16	1.7×10^{-16}
21	rs1800978	9	104903697	ABCA1	G/C	0.13	1.06	1.04–1.08	1.6×10^{-9}
22	rs7068231	10	60025170	ANK3	T/G	0.403	0.95	0.94–0.96	3.3×10^{-13}
23	rs6586028	10	80494228	TSPAN14	C/T	0.196	0.93	0.91–0.94	2.0×10^{-19}
24	rs6584063	10	96266650	BLNK	G/A	0.043	0.89	0.86–0.92	6.7×10^{-11}
25	rs7908662	10	122413396	PLEKHA1	G/A	0.467	0.96	0.95–0.97	2.6×10^{-9}
26	rs6489896	12	113281983	TPCN1	C/T	0.076	1.08	1.05–1.10	1.8×10^{-9}
27	rs7157106	14	105761758	IGH gene cluster	A/G	0.36	1.05	1.03–1.07	2.0×10^{-8}
27	rs10131280	14	106665591	IGH gene cluster	A/G	0.133	0.94	0.92–0.96	4.3×10^{-10}
28	rs3848143	15	64131307	SNX1	G/A	0.22	1.05	1.04–1.07	8.4×10^{-11}
29	rs12592898	15	78936857	CTSH	A/G	0.133	0.94	0.92–0.96	4.2×10^{-9}
30	rs1140239	16	30010081	DOC2A	T/C	0.379	0.94	0.93–0.96	2.6×10^{-13}
31	rs450674	16	79574511	MAF	C/T	0.373	0.96	0.95–0.98	3.2×10^{-8}
32	rs16941239	16	86420604	FOXF1	A/T	0.029	1.13	1.08–1.17	1.3×10^{-8}
33	rs56407236	16	90103687	PRDM7	A/G	0.069	1.11	1.08–1.14	6.5×10^{-15}
34	rs35048651	17	1728046	WDR81	T/TGAG	0.214	1.06	1.04–1.08	7.7×10^{-11}
35	rs2242595	17	18156140	MYO15A	A/G	0.112	0.94	0.92–0.96	1.1×10^{-9}
36	rs5848	17	44352876	GRN	T/C	0.289	1.07	1.06–1.09	2.4×10^{-20}
37	rs149080927	19	1854254	KLF16	G/GC	0.48	1.05	1.04–1.07	5.1×10^{-10}
38	rs9304690	19	49950060	SIGLEC11	T/C	0.24	1.05	1.03–1.07	4.7×10^{-9}
39	rs587709	19	54267597	LILRB2	C/T	0.325	1.05	1.04–1.07	3.6×10^{-11}
40	rs1358782	20	413334	RBCK1	A/G	0.246	0.95	0.94–0.97	1.6×10^{-8}
41	rs6742	20	63743088	SLC2A4RG	T/C	0.221	0.95	0.93–0.97	2.6×10^{-9}
42	rs2154481	21	26101558	APP	C/T	0.476	0.95	0.94–0.97	1.0×10^{-12}

P values are two-sided raw P values derived from a fixed-effect meta-analysis. [a]rs number, according to dbSNP build 153. [b]GRCh38 assembly. [c]Nearest protein-coding gene according to GENCODE release 33. [d]Weighted average MAF across all discovery studies. [e]Approximate OR calculated with respect to the minor allele.