Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Jonsson T, Stefansson H, Steinberg S, et al. Variant of *TREM2* associated with the risk of Alzheimer's disease. N Engl J Med 2013;368:107-16. DOI: 10.1056/NEJMoa1211103

Supplementary Appendix

A coding variant in the *TREM2* gene confers risk of Alzheimer's disease

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Table S1. Association results for sequence variants in TREM2 that are likely to affect protein function.

Marker	P-value	OR (95% CI)	Minor allele	Major allele	MAF	Effect
rs79011726	0.59	1.21 (0.60-2.46)	T	C	0.17	E151K
chr6:41236977	0.42	0.78 (0.43-1.42)	C	A	0.37	splicing
rs142232675	0.28	1.56 (0.70-3.51)	T	C	0.12	D87N
rs143332484	0.48	1.13 (0.80-1.59)	T	C	0.78	R62H
rs75932628	3.42×10^{-10}	2.92 (2.09-4.09)	T	C	0.46	R47H
chr6:41237236	0.78	0.81 (0.18-3.62)	T	C	0.05	G45E

Association with Alzheimer‘s disease in Iceland is shown, using population controls age 85 or greater. Variants are indicated by their rs-names, with the exception of two novel variants, which are indicated by their chromosomal location (NCBI Build 36). In each case, odds ratios are reported for the minor allele. Minor allelic frequencies (MAF) are reported for controls in %.

Table S2. Association results for rs75932628-T based on imputation.

cohort	N_{case}/N_{cont}	P-value	OR (95% CI)	frequency (%)
NIA-LOAD	1,026/851	0.095	1.93 (0.89-4.18)	0.70
eMERGE	566/1,851	0.0026	4.29 (1.66-11.06)	0.34
Combined	**1,592/2,702**	**0.0014**	**2.66 (1.46-4.84)**	**-**

Shown is the frequency of rs75932628-T in controls.

Table S3. Effect of ApoE ε4 on the association of rs75932628-T with Alzheimer's disease in Iceland.

Patient group	N	freq (%)	OR (95% CI)	P-value
AD all	2,773	1.42	3.10 (2.18-4.43)	3.93×10^{-10}
ApoE ε4+	1,511	1.09	2.38 (1.45-3.89)	0.00056
ApoE ε4-	1,262	1.81	4.03 (2.63-6.16)	1.28×10^{-10}
ApoE ε4+ vs ApoE ε4-	N/A	N/A	0.60 (0.37-0.98)	0.040

Frequency of risk allele and association results are shown using population controls age 85 or greater (N = 8,888).

Table S4. ApoE ε4 analysis in replication cohorts.

cohort	$N_{\varepsilon 4+}$	$N_{\varepsilon 4-}$	frequency (%)	$OR_{\varepsilon 4+ \text{ vs } \varepsilon 4-}$ (95% CI)	P-value
Emory	233	147	0.39	1.26 (0.10-36.74)	1
Munich	309	205	0.58	3.34 (0.46-77.77)	0.41
NIA-LOAD	754	271	1.17	2.42 (0.77-7.59)	0.13
eMERGE	187	310	0.90	0.70 (0.12-3.96)	0.69
Norway	364	323	0.36	inf (0.89-inf)	0.064
Combined	**1,847**	**1,256**	**-**	**1.79**	**0.2**

Frequency of risk allele in affected individuals with ApoE ε4 information and the OR comparing ε4+ vs ε4- AD patients are shown. The OR value is infinity for the Norwegian cohort due to the fact that there are no carriers of the rs75932628-T allele in the ε4- group. Results for the eMERGE data set are based on imputation of ApoE ε4.