Supplementary Tables and Figures for "African Ancestry GWAS of Dementia in a Large Military Cohort Identifies Significant Risk Loci"

by Richard Sherva et al.

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Supplemental Table 1. ICD Codes used for ADRD Case/Control Definitions

Diagnostic Category	ICD Codes
Alzheimer's Disease	ICD-9: 331.0; ICD-10: G30.1, 30.8, and 30.9.
Non-Specific Dementia	ICD 9 Codes
	294.20: Unspecified dementia without behavioral disturbance
	294.21: Unspecified dementia with behavioral disturbance
	294.8: Other persistent mental disorders/Other specified organic brain syndromes
	290.0: Senile dementia uncomplicated
	290.20: Senile dementia with delusional features,
	290.21: Senile dementia with depressive features
	290.3: Senile dementia with delirium
	331.2: Senile degeneration of the brain
	ICD 10 codes
	F03.90: Unspecified dementia without behavioral disturbance
	F03.91 Unspecified dementia with behavioral disturbance
	G31.1: Senile degeneration of the brain
Related Dementia	290.40, 290.41, 290.42, 290.43, F01.50, F01.51: Vascular dementia
	331.82; G31.83: Lewy Body dementia
	331.1, G31.0; 331.19, G31.09: Frontotemporal/Other Fronto-Dementia
	290.10, 290.10, 290.11, 290.12, 290.13, G30.0: Presenile/Early onset dementia
	331.5, G91.2: Idiopathic Normal Pressure Hydrocephalus
Other Dementias	333.4; G10: Huntington's Disease
	332, G20: Parkinson's Disease Dementia
	A81.00: Creutzfeldt-Jakob Disease
	331.11, G31.01: Pick's Disease of the Brain
	F10.96: Korsakoff Syndrome
	294.10, 294.11 Dementia in conditions classified elsewhere with/without behavioral disturbance.
	F02.80, F2.81 Dementia in other diseases classified elsewhere with/without behavioral disturbance
Mild Cognitive Impairment (MCI)	ICD 9: 331.83; ICD10: G31.84

Note: To qualify as an ADRD case, a participant must have received at least two ICD codes from any of the "Alzheimer's Disease", "Non-specific Dementia", or "Related Dementia" categories. Controls must not have received any of the ADRD ICD codes, any codes from the "Other Dementias" or "Mild Cognitive Impairment" category or have been prescribed AD medication.

Supplementary Table 2: Associations effect sizes and significance for the association between ApoE genotypes and AD, ADRD, and proxy dementia in African ancestry (AFR) MVP participants.

APOE Genotype	3/3 (reference)	2/2	2/3	2/4	3/4	4/4
N (ADRD cases/controls)	10,167	130	2366	701	6036	854
N (%) ADRD cases	1950 (17.52%)	29 (19.33%)	437 (16.74%)	170 (22.25%)	1502 (22.74%)	334 (36.07%)
ADRD						
OR vs 33	NA	1.20	0.93	1.45	1.44	2.90
Pvalue	NA	0.43	0.25	0.0001	2.66×10^{-18}	3.18×10^{-43}
AD strict						
OR	NA	0.35	0.81	1.68	2.06	5.52
Pvalue	NA	0.30	0.21	0.02	3.45×10^{-15}	1.41×10^{-46}
Maternal						
OR	NA	0.78	0.99	1.43	1.37	2.07
Pvalue	NA	0.31	0.88	1.82×10^{-5}	1.64×10^{-16}	2.19×10^{-25}
Paternal						
OR	NA	0.97	1.0004	1.03	1.30	1.43
Pvalue	NA	0.91	0.99	0.83	3.72×10^{-7}	0.0009

OR=odds ratio

Supplementary table 3: Suggestive (p<5x10-7) associations between common variants and ADRD in an APOE E4 adjusted analysis meta-analysis

Chr	Position	SNP	Effect Allele	OR	P-value	Gene
6	10358477	rs116443000	T	2.22	1.63E-07	Intergenic
9	78131027	rs73650172	G	1.22	4.25E-07	Intergenic
9	1.25E+08	rs181518405	A	1.85	3.90E-07	LHX6
10	1.35E+08	rs146777408	T	1.34	3.34E-07	CFAP46
12	1.07E+08	rs11610873	C	0.75	2.64E-07	LOC100287944
20	45165858	rs202380	T	0.86	2.98E-07	near OCSTAMP
20	59454012	rs34197461	A	1.33	2.71E-07	near CDH4

Supplementary Table 4: Associations between variants with minor allele frequency less than 0.01 in the full meta-analysis (MVP ADRD, MVP proxy dementia, and ADGC AD).

SNP	Effect allele	ADRD OR	ADRD P	Proxy P	MVP P	ADGC P	Meta P	Dir	MAF	r2
rs569876967	A	1.56	1.89E-01	1.51E-08	1.86E-07	NA	1.86E-07	++?	0.002	0.70
rs115837776	T	1.92	2.77E-02	7.07E-05	7.83E-06	5.83E-03	2.07E-07	+++	0.002	0.72
rs117435266	A	2.15	2.82E-03	3.93E-05	3.91E-07	NA	3.91E-07	++?	0.002	0.90
rs567572378	A	1.89	2.21E-04	2.63E-04	2.42E-07	NA	2.42E-07	++?	0.006	0.75
rs73581622	A	1.58	2.24E-03	3.73E-05	2.94E-07	6.98E-01	4.98E-06	++-	0.006	0.86
rs116329346	A	1.66	7.93E-04	9.13E-05	2.57E-07	6.97E-01	4.46E-06	++-	0.007	0.77
rs145008711	A	0.63	3.03E-03	4.67E-05	4.94E-07	8.97E-01	4.75E-06	--+	0.007	0.76

The direction of effect represents the direction of the effect allele in the MVP ADRD, MVP proxy, and the ADGC AD GWASs, in that order.

Supplementary table 5: Suggestive (p<5x10-7) associations between common variants in the APOE-adjusted meta analysis (MVP ADRD and ADGC AD)

Chr	POS	SNP	Effect Allele	P	Dir	Gene
6	41136086	rs73427289	T	8.25E-08	++	LOC105375056
8	119904557	rs10955908	A	3.24E-07	--	Intergenic
9	13220518	rs141610415	T	4.27E-07	?-	Intergenic
11	43166842	rs569584007	T	8.81E-08	?-	Intergenic
12	106951385	rs114572990	A	4.97E-07	-?	Near TTC17
15	97992685	rs570487962	A	1.69E-09	?+	LINC02254
17	72273608	rs9893381	A	4.89E-07	++	DNAI2

The direction of effect represents the direction of the effect allele in the MVP ADRD and ADGC AD APOE-adjusted GWASs, in that order.

Supplementary Table 6: Associations between common, coding variants in LD with suggestive (p<5.0x10-7) variants in the MVP-ADGC AFR meta-analysis

Chr	Pos	Effect Allele	Alternate Allele	Pvalue	Direction	SNP	Gene
6	41126655	A	G	4.64E-09	---	rs2234256	TREM2
6	41129105	T	G	2.23E-07	++?	rs2234253	TREM2
19	1000665	A	G	7.12E-07	+++	rs144440136	GRIN3B
19	1047336	A	G	3.22E-08	+++	rs59851484	ABCA7
19	1058635	T	C	4.40E-10	+++	rs73505232	ABCA7
19	45391454	T	C	4.94E-06	+++	rs145654351	PVRL2
19	45404579	T	G	8.63E-62	+++	rs394819	APOE
19	45409167	C	G	3.21E-07	---	rs7122067	APOE
19	45411941	T	C	6.09E-150	---	rs429358	APOE
19	45412079	T	C	5.02E-12	---	rs7412	APOE

The direction of effect represents the direction of the effect allele in the MVP ADRD, MVP proxy, and the ADGC AD GWASs, in that order.

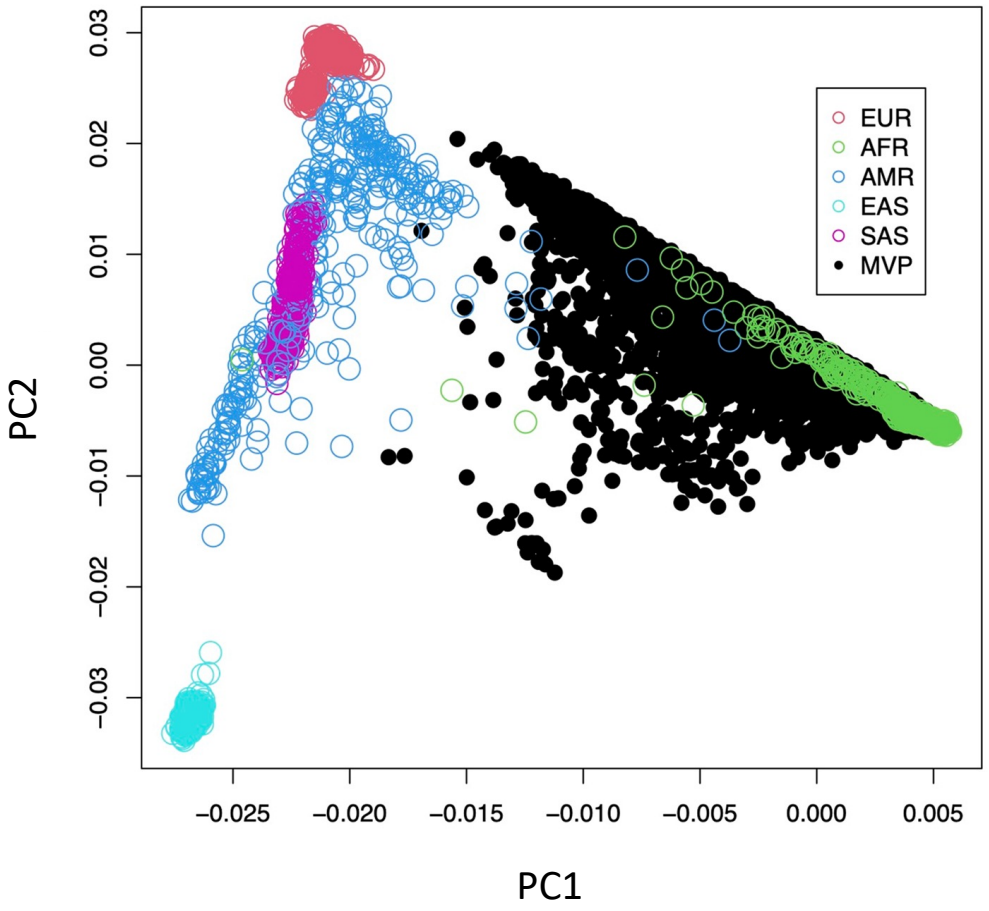
Supplementary table 7. SNPs with regulatory effects in African ancestry Cortex tissue according to the Metabrain Network database

Chr	Pos	rsID*	Effect Allele	Alternate Allele	Gene	P eQTL	FDR eQTL	Z eQTL	Z Dementia GWAS	P Dementia Meta
8	10278248	rs12677754	a	g	PRSS51	1.08E-15	0	-8.0	4.14	3.45E-05
8	10279483	rs10113408	c	g	PRSS51	4.11E-17	0	-8.4	-4.9	9.83E-07
8	10279503	rs10112584	a	g	PRSS51	6.4E-17	0	-8.4	4.88	1.09E-06
8	10279626	rs4607615	c	g	PRSS51	3.6E-17	0	-8.4	-5.38	7.37E-08
8	10280217	rs11250006	a	t	PRSS51	1.73E-13	0	-7.4	-4.5	6.95E-06
8	10280818	rs6985267	a	c	PRSS51	3.18E-15	0	-7.9	-4.53	5.99E-06
8	10283233	rs34629088	a	t	PRSS51	5.51E-11	0	-6.6	-3.15	1.62E-03
8	10283761	rs3750313	a	g	PRSS51	2.5E-11	0	-6.7	3.04	2.37E-03
8	10285497	rs11250008	t	c	PRSS51	9.28E-22	0	-9.6	4.26	2.03E-05
8	10285810	rs3750314	t	c	PRSS51	1.6E-22	0	-9.8	-4.44	8.94E-06
19	991171	rs114066284	t	g	CNN2	7.42E-06	5.47E-02	-4.5	2.55	1.09E-02
19	1004709	rs76827013	a	g	ABCA7	4.08E-07	4.75E-03	-5.1	-4.43	9.24E-06
19	1005186	rs61740285	a	g	ABCA7	3.97E-07	4.65E-03	-5.1	4.47	7.88E-06
19	1010027	rs77386938	a	t	ABCA7	3.31E-07	3.87E-03	-5.1	-5.06	4.27E-07
19	1010115	rs116247697	t	c	ABCA7	3.2E-07	3.69E-03	-5.1	5.1	3.44E-07
19	1010183	rs115454056	t	c	ABCA7	3.2E-07	3.69E-03	-5.1	5.09	3.55E-07
19	1012024	rs114980668	c	g	ABCA7	3.27E-07	3.80E-03	-5.1	-5.11	3.23E-07
19	1013963	rs114895164	a	g	ABCA7	2.62E-07	3.19E-03	-5.1	5.18	2.18E-07
19	1022261	rs142732532	c	g	ABCA7	1.29E-06	1.30E-02	-4.8	5.23	1.73E-07
19	1024909	rs114555712	a	g	ABCA7	2.64E-07	3.22E-03	-5.1	-5.05	4.39E-07
19	1050420	rs115550680	a	g	ABCA7	1.78E-07	2.36E-03	-5.2	-5.7	1.17E-08

*SNPs in bold are independent lead SNPs in the region in the GWAS.

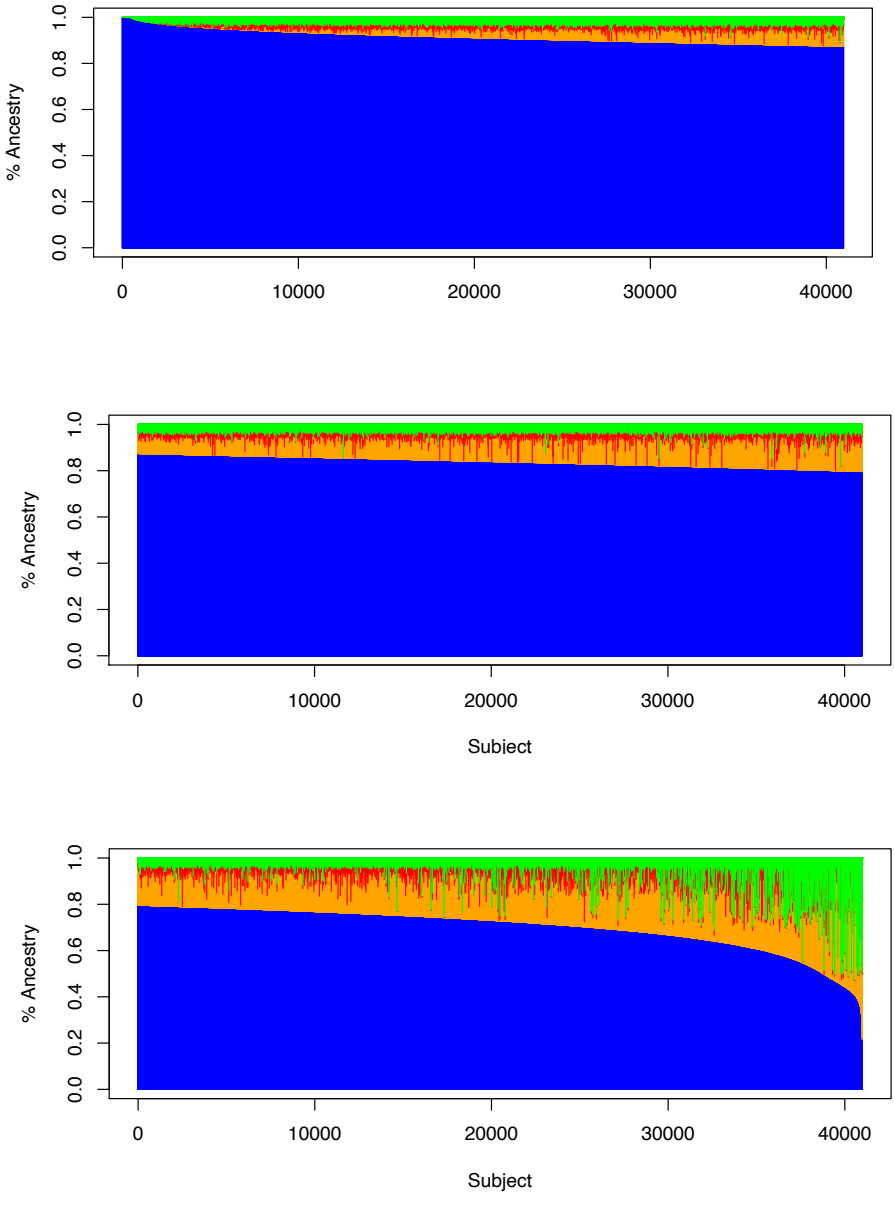
The Z-scores for A/T and G/C SNPs are not possible to comapre in the eQTL and GWAS results due to strand ambiguity

Supplementary Figure 1: Plot of the first two principal components of ancestry in MVP AFR participants relative to 1000 Genomes reference populations

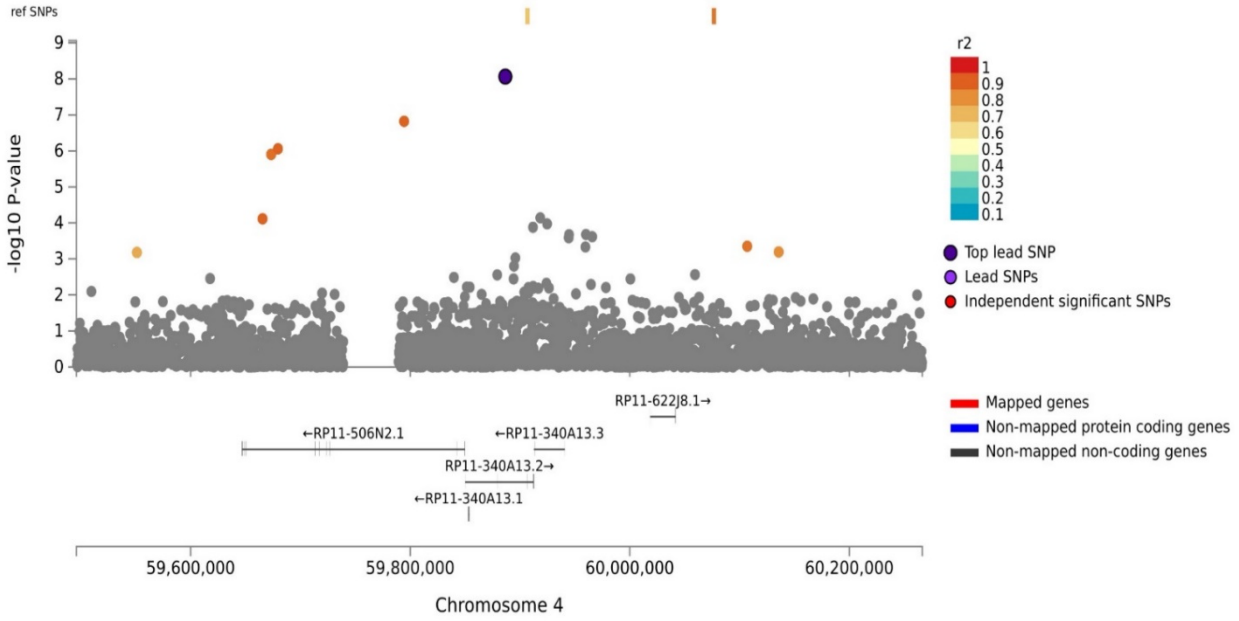


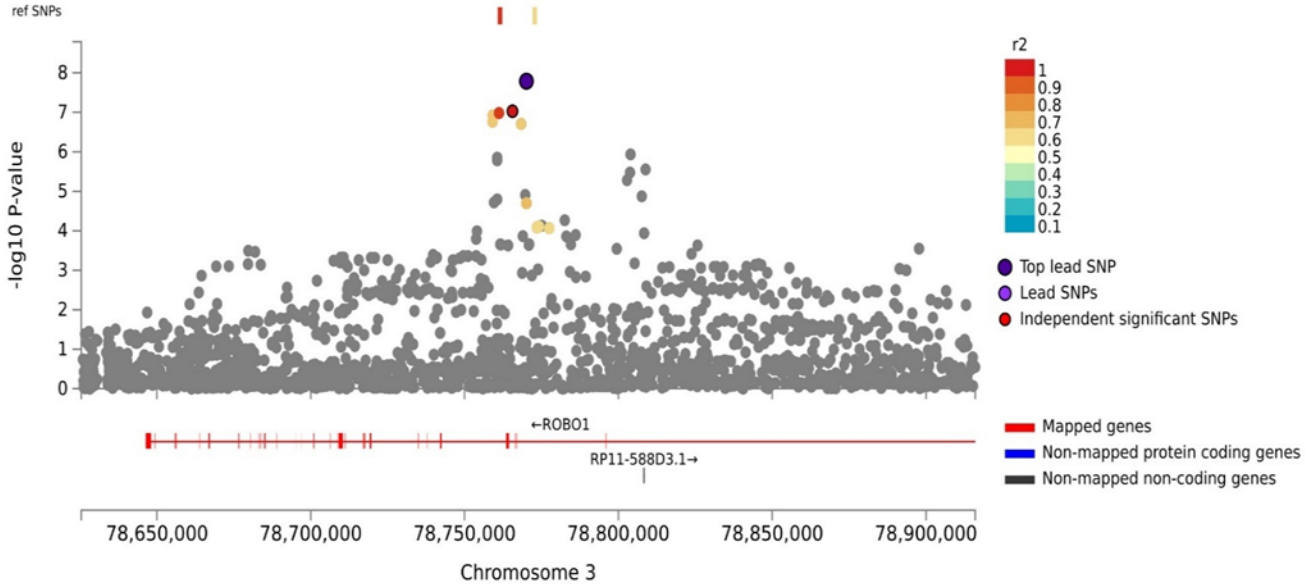
AFR=African, EUR=European, SAS=South Asian, EAS=East Asian, AMR=admixed American, MVP=Million Veterans Project HARE-defined African Ancestry Participants

Supplementary Figure 2: Ancestry Plot (proportion of ancestry) relative to 1000 Genomes reference samples for MVP HARE-defined AFR participants. Sorted in order of estimated % African Ancestry. Blue=African Ancestry (YRI and LWK), Orange=European Ancestry (GBR), Red=American Ancestry (PEL), Green = Asian Ancestry (CHB).

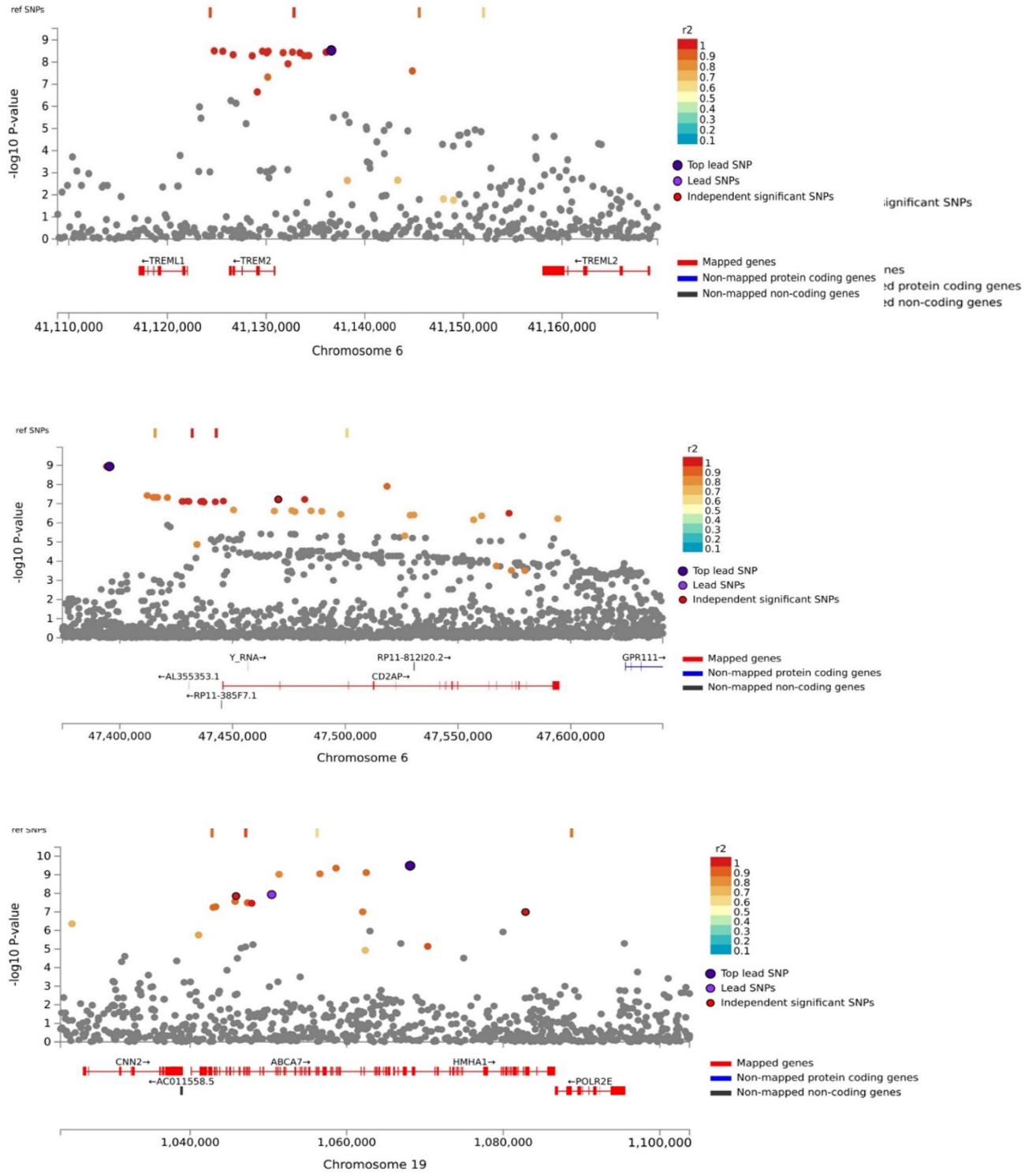


Supplementary Figure 3: Regional Manhattan plots for the two non-APOE regions containing genome-wide significant associations in MVP AFR ADRD case-control analysis.

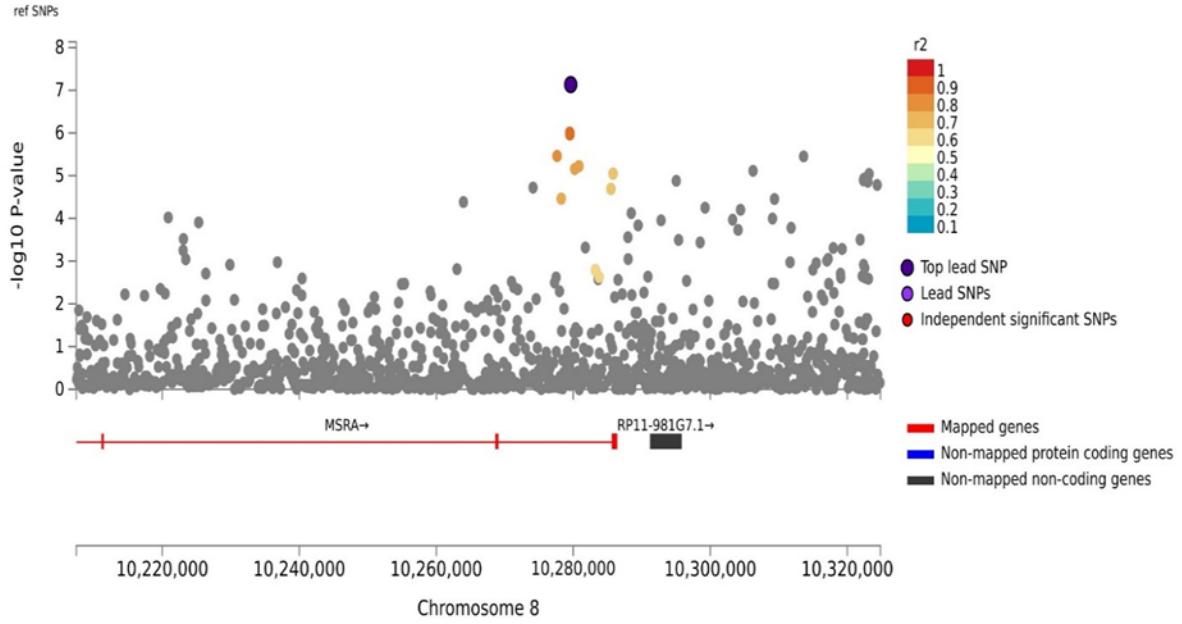


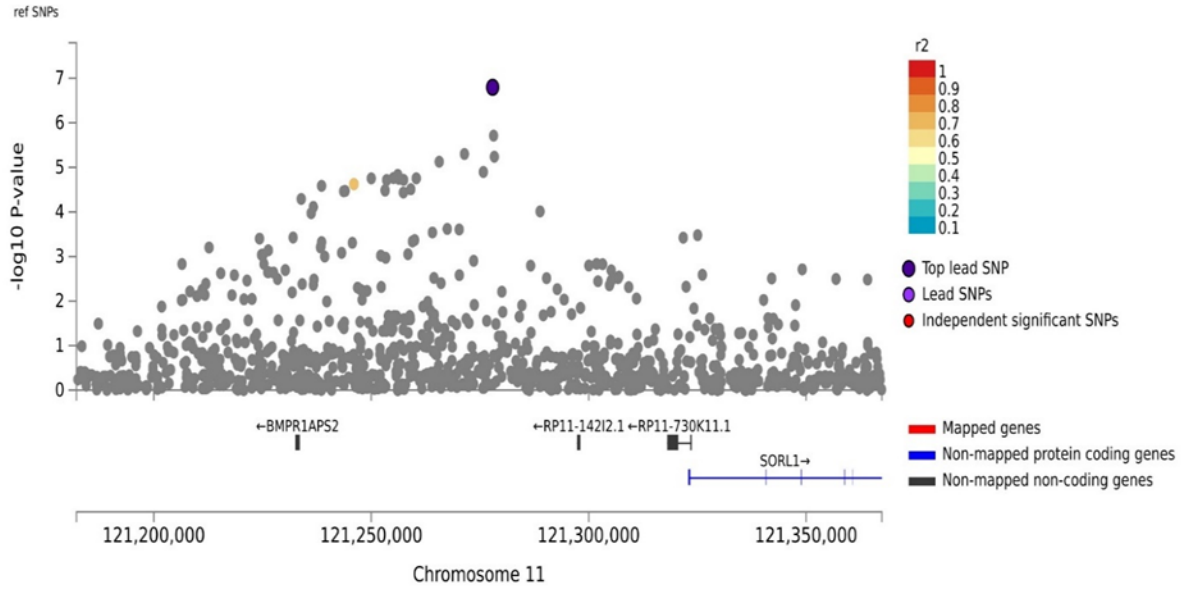


Supplementary Figure 4: Regional Manhattan plots for the three non-APOE regions containing genome-wide significant associations in the full meta-analysis (MVP ADRD, MVP proxy, and ADGC AD GWASs).



Supplementary Figure 5: Regional Manhattan plots for the MRSA and SORL1 regions in the full meta-analysis (MVP ADRD, MVP proxy, and ADGC AD GWASs).





Supplementary Figure 6: Canonical pathways with significant enrichment of association signals in the MVP/ADGC meta-analysis.