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Supplementary Data

Is the Urea Cycle Involved in Alzheimer's Disease?

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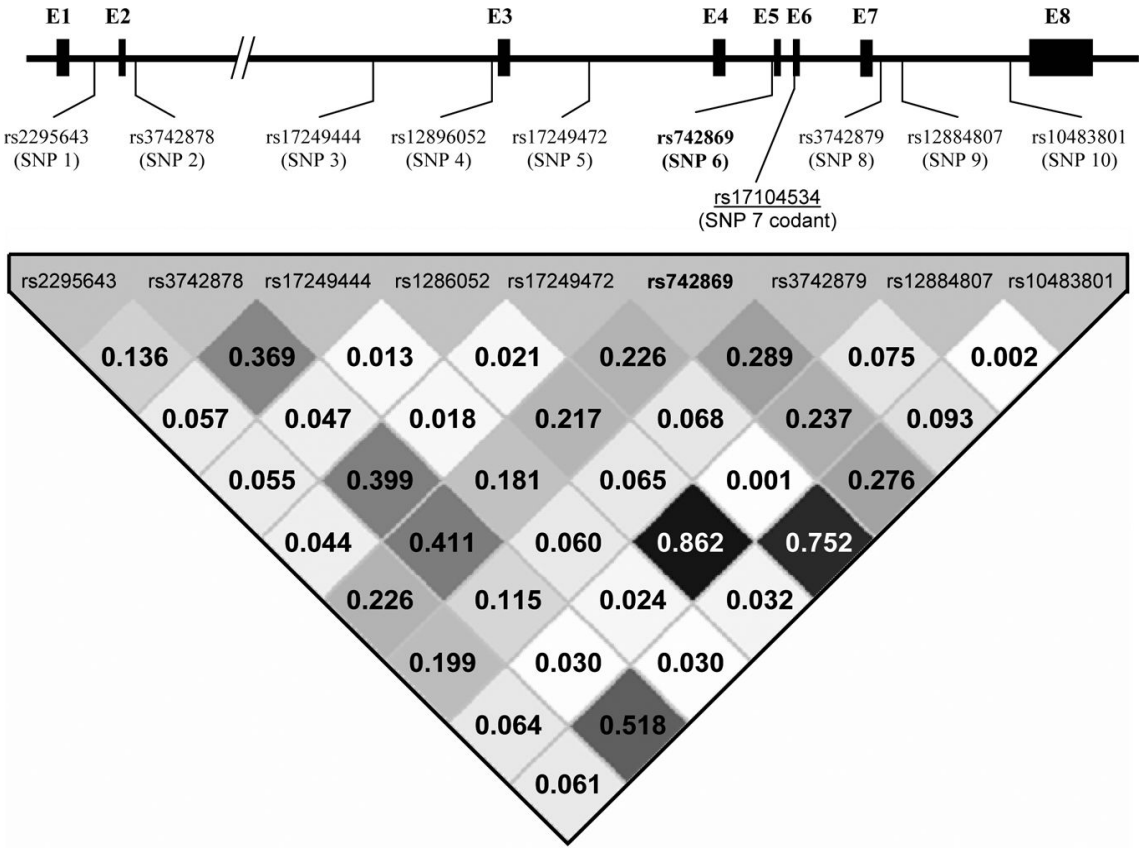
Supplementary Table 1. Differences in the genotypes distributions between cases and controls for each Tag-SNP studied in GS, CPS1, ASS, ASL, Arg1, and Arg2 genes. The p value corresponds to the statistical significance of the differences in genotype distribution of each SNP in the combined test population (France + USA) for men and women (M+W), men only (M), or women only (W). Significant differences are in bold and SNPs of interest are marked in grey.

Genes	SNP	p value M+W	p value M	p value W
GS (Chr2) 7 SNPs	rs9347	0.25	0.74	0.19
	rs4652704	0.55	0.35	0.51
	rs12403634	0.35	0.30	0.61
	rs12136955	**0.048**	0.08	0.40
	rs2296520	0.22	0.74	0.16
	rs17462824	0.98	0.08	0.23
	rs912900	0.16	0.21	0.30
CPS1 (Chr2) 32 SNPs	rs7598448	0.27	0.80	0.36
	rs13005394	0.36	0.96	0.20
	rs2371001	0.18	0.75	**0.029**
	rs2287604	0.42	0.24	0.84
	rs12468557	0.47	0.99	0.19
	rs10172081	0.55	0.50	0.52
	rs12997383	0.06	0.18	0.07
	rs2287596	**0.034**	0.17	0.15
	rs2371015	0.43	0.25	0.65
	rs10804185	0.51	0.87	0.27
	rs4420657	0.44	0.50	0.24
	rs4142154	0.54	0.38	0.88
	rs12623361	0.74	0.26	0.79
	rs2287598	0.63	0.99	0.43
	rs7607205	0.23	0.63	0.24
	rs16844779	0.29	0.70	0.40
	rs7422339	0.98	0.26	0.44
	rs6752652	0.10	0.35	0.32
	rs7599931	0.21	0.39	0.28
	rs3213784	0.42	0.56	0.52
	rs4325692	0.90	0.90	0.91
	rs2371011	0.15	0.14	0.64
	rs13022335	0.57	0.77	0.64
	rs13388400	0.37	0.87	0.37
	rs4567871	0.43	0.36	0.13
	rs17775871	0.47	0.25	0.96
	rs10469763	0.70	0.96	0.31
	rs11903219	0.68	**0.032**	0.43
	rs6750325	0.23	0.74	0.30
	rs13010668	0.14	0.59	0.17
	rs17774535	0.33	0.65	0.35
	rs2287603	0.57	0.19	0.97
ASS (Chr9) 23 SNPs	rs474330	0.13	0.90	0.06
	rs7860909	0.19	0.60	0.16
	rs506705	0.31	0.97	0.12
	rs634432	0.51	0.82	0.43
	rs1215985	0.88	0.95	0.88
	rs1215988	0.87	0.48	0.90
	rs10901072	0.90	0.90	0.98
	rs590086	0.08	0.21	0.19
	rs1215972	0.07	0.12	0.51
	rs688430	0.68	0.71	0.85
	rs17147023	0.95	0.73	0.56
	rs10901047	0.06	0.63	**0.021**
	rs602924	0.64	0.89	0.45
	rs2282219	0.94	0.32	0.13
	rs544701	0.93	0.74	0.93
	rs4740158	0.54	0.60	0.56
	rs666971	0.41	0.73	0.08
	rs486889	0.95	0.44	0.68
	rs11243372	0.48	0.93	0.23
	rs928518	0.52	0.98	0.31
	rs652313	0.95	0.67	0.95
	rs10793902	0.85	0.51	0.78
	rs914983	0.86	0.73	0.70
ASL (Chr7) 4 SNPs	rs1183245	0.81	1.00	0.74
	rs313831	0.60	0.91	0.69
	rs313830	0.31	0.80	0.23
	rs313829	0.74	0.85	0.86
ArgI (Chr6) 5 SNPs	rs2781659	0.41	0.55	0.34
	rs17184300	0.06	0.82	**0.031**
	rs2246012	0.79	0.89	0.91
	rs2781666	0.97	0.63	0.66
	rs17599586	0.09	0.76	0.07
Arg2 (Chr14) 10 SNPs	rs17249472	0.87	0.21	0.39
	rs3742878	**0.017**	**0.036**	0.06
	rs12884807	0.35	0.09	0.94
	rs17249444	**0.050**	0.09	0.21
	rs2295643	0.62	0.24	0.96
	rs3742879	0.36	0.08	0.44
	rs10483801	0.60	0.10	0.84
	rs742869	**0.022**	**0.0002**	0.94
	rs17104534	Absence of the SNP		
	rs12896052	0.15	0.07	0.84

Supplementary Table 2. Arginase 2 expression in AD cases according to rs742869 genotypes. The mean of the amount of ARG2 mRNA relative to β-actin was calculated for each rs742869 genotype ($\pm$ standard deviation) in the whole population, in men only, or women only. Differences were tested using the Kruskal-Wallis test

Genotypes	M+W		M		W	
	Relative expression	p value	Relative expression	p value	Relative expression	p value
AA	0.061 ± 0.035	0.388	0.056 ± 0.028	0.223	0.066 ± 0.045	0.499
AG	0.045 ± 0.022		0.041 ± 0.020		0.046 ± 0.024	
GG	0.046 ± 0.029		0.026 ± 0.008		0.065 ± 0.031	



Supplementary Figure 1. Localization of the 10 tag-SNPs in the Arg2 genes and linkage Disequilibrium (r^2 value) between the 9 polymorphic tag-SNPs of the Arg2 gene in the whole combined "discovery" sample. (No minor allele for rs17104534 were observed in the population).