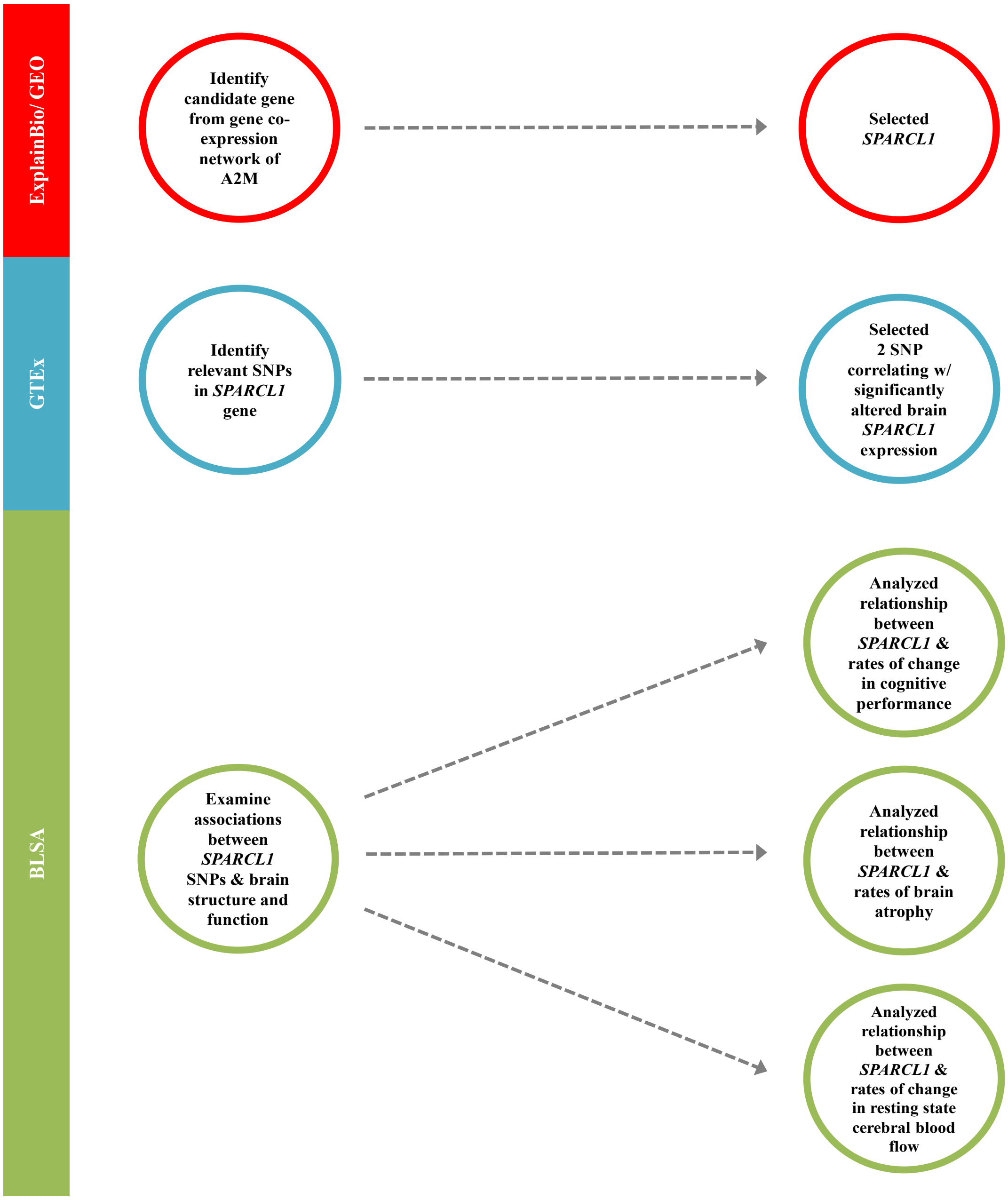
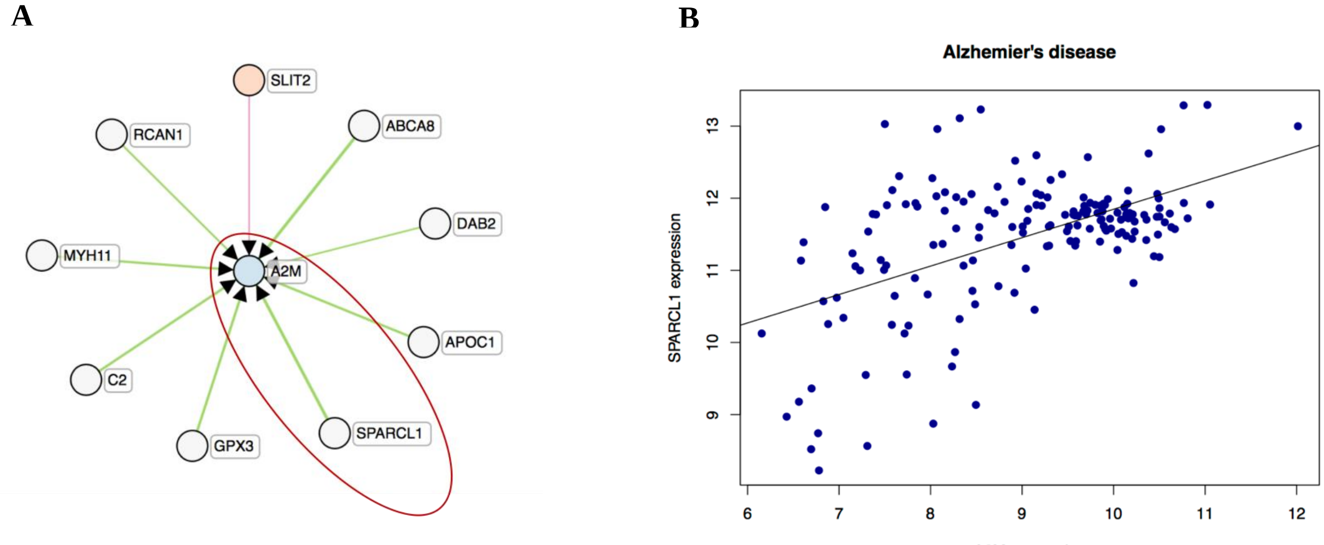
Supplementary Material



Supplementary Fig. 1. Datasets used in this study.From left to right: tool/dataset utilized,study objective, and outcome(s). GEO, Gene Expression Omnibus (https://www.explainbio.com); GTEx, Gene-Tissue Expression Project; BLSA, Baltimore Longitudinal Study of Aging



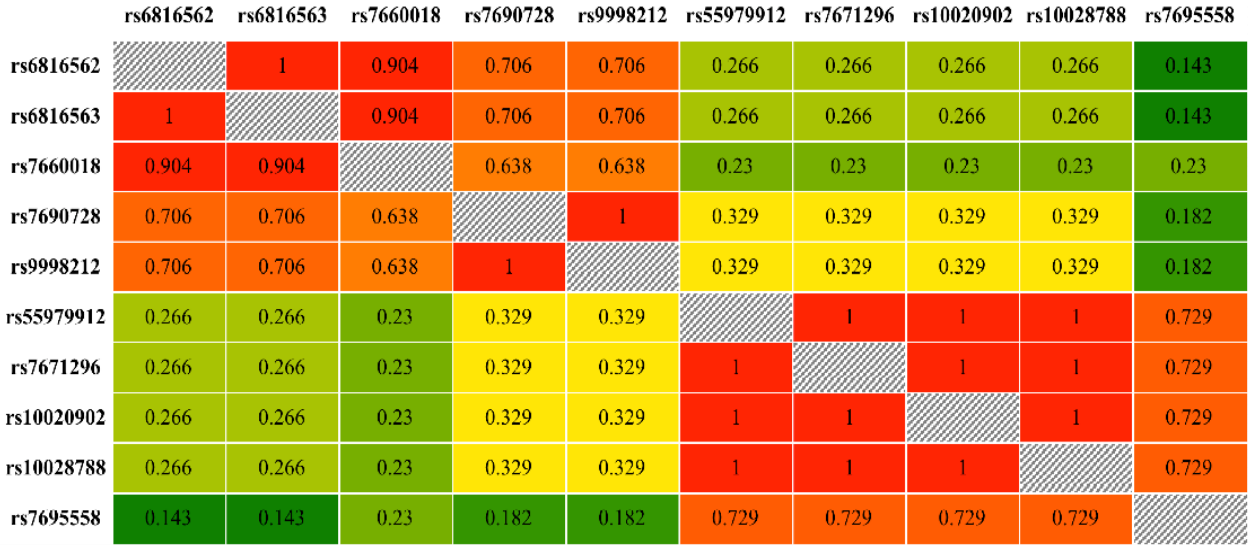
Supplementary Fig. 2. Gene co-expression network of *A2M*. A) Gene network illustrating the expression of *A2M* gene as a product of the expression of its 9 source genes. Secreted protein acidic and rich in cysteine- like1 (*SPARCL1*) was identified as a promising target for its roles in the formation and maintenance of synapses. B) Scatterplot of *A2M* versus*SPARCL1* expression in AD (Pearson correlation= 0.532; p-value=1.07x10^{-13}) [1].

[1] Varma VR, Varma S, An Y, Hohman TJ, Seddighi S, Casanova R, Beri A, Dammer EB, Seyfried NT, Pletnikova O, Moghekar A, Wilson MR, Lah JJ, O'Brien RJ, Levey AI, Troncoso JC, Albert MS, Thambisetty M (2017) Alpha-2 macroglobulin in Alzheimer's disease: A marker of neuronal injury through the RCAN1 pathway. *Mol Psychiatry***22**, 13-23.

Supplementary Table 1. SPARCL1 SNPs influencing *SPARCL1* gene expression in brain tissue. Using expression quantitative trait (eQTL) data from the Gene Tissue Expression (GTEx) project, we identified 11 *SPARCL1* SNPs that are significantly associated with reduced *SPARCL1* expression in the brain.

***SPARCL1* SNP**	**Beta value**	**Tissue**
rs7695558	-0.617	Frontal Cortex (BA9)
rs10020902	-0.599	Frontal Cortex (BA9)
rs10028788	-0.599	Frontal Cortex (BA9)
rs7671296	-0.598	Frontal Cortex (BA9)
rs55979912	-0.463	Frontal Cortex (BA9)
rs9998212	-0.464	Hippocampus
rs7690728	-0.458	Hippocampus
rs60614311	-0.413	Hippocampus
rs6816562	-0.406	Hippocampus
rs6816563	-0.406	Hippocampus
rs7660018	-0.371	Hippocampus

Supplementary Fig. 3. Linkage disequilibrium for SNPs with eQTLs in brain tissue.Heatmap representation of linkage disequilibrium (LD) values reflecting the degree of non-random association between SNPs identified through GTEx (r^2 values shown). Orange/red represent r^2 >0.6. Yellow/green represent r^2 <0.6. SNPs associated with *SPARCL1* expression in the cortex are in high LD, and SNPs associated with *SPARCL1* expression in the hippocampus are in high LD.



	rs6816562	**rs6816563**	**rs7660018**	**rs7690728**	**rs9998212**	**rs55979912**	**rs7671296**	**rs10020902**	**rs10028788**	**rs7695558**
rs6816562	▨	1	0.904	0.706	0.706	0.266	0.266	0.266	0.266	0.143
rs6816563	1	▨	0.904	0.706	0.706	0.266	0.266	0.266	0.266	0.143
rs7660018	0.904	0.904	▨	0.638	0.638	0.23	0.23	0.23	0.23	0.23
rs7690728	0.706	0.706	0.638	▨	1	0.329	0.329	0.329	0.329	0.182
rs9998212	0.706	0.706	0.638	1	▨	0.329	0.329	0.329	0.329	0.182
rs55979912	0.266	0.266	0.23	0.329	0.329	▨	1	1	1	0.729
rs7671296	0.266	0.266	0.23	0.329	0.329	1	▨	1	1	0.729
rs10020902	0.266	0.266	0.23	0.329	0.329	1	1	▨	1	0.729
rs10028788	0.266	0.266	0.23	0.329	0.329	1	1	1	▨	0.729
rs7695558	0.143	0.143	0.23	0.182	0.182	0.729	0.729	0.729	0.729	▨