Our previous studies have identified 3 potential cerebro-spinal fluid (CSF) biomarkers in late-onset Alzheimers Disease (LOAD); Fibrinogen α-chain (FGA), Contactin-1 (CNTN1), SPARC-like-1 (SPARCL1), all of which have been implicated in LOAD pathophysiology suggesting they may be involved in a novel pathway in LOAD pathogenesis.

Using a ‘gene-centric’ approach, SNPs falling within biomarker genes and extended linkage disequilibrium (LD) blocks were analysed for LOAD association in three previously published genome-wide association studies (GWAS) (Reiman et al, Li et al and Carrasquillo et al). Candidate SNPs showing suggestive association (P<0.25) were compared across platform using the genes LD architecture (established using Hapmap CEU population, release 22).

Using this approach we have identified a 24kb LD block in CNTN1 where SNPs show suggestive recessive association (p=0.03) across platform, with consistent OR (1.1-3.2). Although insufficient SNP coverage does not permit cross-platform comparison in FGA, one suggestive SNP (p=0.032, OR=1.3) tags a potentially functional variant. SPARCL1 does not show any consistency across platform.

In-depth analysis of genes at the SNP level, incorporating multiple datasets, may prioritise regions potentially harbouring rare variants in preparation for resequencing projects. Adopting a ‘multiple rare variant approach’ may identify causative variants missed at the genome-wide level.