**APPENDIX 1**

**Variant-level Quality Control**

Variant-level quality control (QC) included removal of variants with a low mapping score (QUAL score < 22, Prob < 0.95), variants not labeled “Pass”, variants with low read depth (<6), variants with out-of-range variant read count(<3 reads or <10% alternate read for heterozygotes), and variants represented by a single strand (>0.99). Additional filtering included removal of monomorphic variants, variants with high missingness (>20%), variants with excessive heterozygosity (|z|>1.22 for MAF <0.2, |z|> 5 st.dev for MAF >= 0.2) [14], and variants with very high read depth (>500 reads).

**Validation Sequencing**

Genomic DNA (~50ng) was amplified using a SimpliAmp Thermal Cycler (Applied Biosystems) in a 20ul reaction volume with HotStarTaq Master Mix (Qiagen) in the presence of 2uM primers (IDT). The PCR conditions used were: 95°C 15min followed by 30 cycles of 95°C 20sec, 55°C 30sec, 72°C 2min with a final extension of 72°C 7min. The amplified PCR products were prepared for Sanger sequencing by adding ExoSAP-IT (USB) and incubating at 37°C for 45min followed by a 80°C 15min. The PCR products were then Sanger sequenced using the BigDye® Terminator v3.1 Cycle Sequencing kit (Part No. 4337457 Applied Biosystems). The sequencing reaction contained BigDye® Terminator v3.1 Ready Reaction Mix, 5X Sequencing Buffer, 5M Betaine solution (Part No. B0300 Sigma) and 0.64uM sequencing primer (IDT) in a total volume of 5ul. The sequencing reaction was performed in a SimpliAmp Thermal Cycler (Applied Biosystems) using the following program: 96°C 1min followed by 25 cycles of 96°C 10sec, 50°C 5sec, 60°C 1min15sec. The products were cleaned using XTerminator and SAM Solution (Applied Biosystems) with 30min of shaking at 1800rpm followed by centrifugation at 1000 rpm for 2min. The sequencing products were analyzed on a 3130xl Genetic Analyzer (Applied Biosystems) and the sequencing traces were compared using Sequencher 4.1 (Gene Code).

**Candidate genes evaluated**Candidate genes evaluated included: *APP, PSEN1, PSEN2, GRN, MAPT, TREM2, PLD3, APOE, ABCA7, SORL1, CR1, BIN1, CD2AP, EPHA1, CLU, MS4A6A, PICALM, CD33, HLA-DRB5, HLA-DRB1, PTK2B, SLC24A4, RIN3, INPP5D, MEF2C, NME8, ZCWPW1, CELF1, FERMT2, CASS4, TREML2,* and *AKAP9*.