NHS Lothian
South East Scotland Genetic Laboratories

# COGNITIVE GENE PANEL - TECHNICAL INFORMATION V2.0

**Design:** The cognitive gene panel was designed as part of a custom probe set from Twist Bioscience (TE-91014499) to cover 26 genes associated with neurodegeneration. This panel design provides coverage of 100% of the target coding regions and flanking intronic sequences (+/- 15bp) for the 26 genes listed below.

**Method:** Library preparation and target enrichment was performed using the custom designed TE-91014499 probe set (Twist Bioscience) and Nextera Flex for Enrichment (Illumina). Sequencing was performed using a 150bp paired-end sequencing kit on a MiSeq (Illumina). All stages of the workflow were performed according to the manufacturer's instructions.

**Coverage criteria:** For each sample reported, >95% of the target coding and flanking intronic regions of the 26 genes was covered to a minimum depth of 20 reads (20x). Any regions of the SOD1 gene for motor neurone disease/amyotrophic lateral sclerosis referrals and any regions of the PSEN1 gene for Alzheimer disease referrals not covered to 20x depth were flagged for follow-up Sanger sequencing. Specific details of coverage and depth for individual tests are available from the laboratory on request.

**Variant identification and interpretation:** Sequence data were mapped and variants identified using GenomeAnalysisToolKit (GATK) and NextGENe (Softgenetics) with hg19 (GRCh37) human genome as the reference. Variants identified were subsequently classified according to recent ACGS Best Practice Guidelines for Variant Classification using all available evidence. Any clinically significant variants were confirmed by Sanger sequencing.

**Variant reporting:** Variants were reported according to HGVS guidelines using the accession numbers listed below. Variants categorised as non-pathogenic or likely non-pathogenic were filtered out at the variant interpretation stage and were not included in the clinical report. Details of these variants are available from the laboratory on request.

## Genes included and associated sequence accession numbers:

ALS2 (NM_020919.3); ANG (NM_001145.4); ANXA11 (NM_145869.1); APP (NM_000484.3); CHMP2B (NM_014043.3); CSF1R (NM_005211.3); DCTN1 (NM_004082.4); FIG4 (NM_014845.5); FUS (NM_004960.3); GRN (NM_002087.2); ITM2B (NM_021999.4); MAPT (NM_001123066.3); NEK1 (NM_001199397.1); OPTN (NM_001008211.1); PFN1 (NM_005022.3); PRNP (NM_000311.3); PSEN1 (NM_000021.3); PSEN2 (NM_000447.2); SETX (NM_015046.5); SOD1 (NM_000454.4); SQSTM1 (NM_003900.4); TARDBP (NM_007375.3); TBK1 (NM_013254.3); UBQLN2 (NM_013444.3); VAPB (NM_004738.4); VCP (NM_007126.3).