NHS Lothian
South East Scotland
Genetic Laboratories

CORNELIA DE LANGE SYNDROME PANEL – TECHNICAL INFORMATION v2.0

Design: The Cornelia de Lange syndrome (CdLS) gene panel was designed as part of a custom probe set from Twist Bioscience (ID TE-98414269) to cover nine genes and two genomic intervals associated with CdLS and CdLS-like disorders. This panel predicts coverage of 100% for the coding regions and flanking intronic sequences (+/- 15bp) of the *NIPBL, SMC1A, SMC3, HDAC8, RAD21, ANKRD11, KMT2A, BRD4, PUF60* genes, as well as, *AFF4* exon 03 and *NAA10* exon 05.

Method: Library preparation and target enrichment was performed using the custom designed TE-98414269 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 regions were covered to a minimum depth of 20 reads (20X). 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 not included in the clinical report. Details of these variants are available from the laboratory on request.

Genes included and associated sequence accession numbers:
NIPBL (NM_133433.3); *SMC1A* (NM_006306.2); *SMC3* (NM_005445.3); *HDAC8* (NM_018486.2); *RAD21* (NM_006265.2); *ANKRD11* (NM_001256183.1); *KMT2A*, formerly known as MLL (NM_001197104.1); *BRD4* (NM_058243.2); *PUF60* (NM_078480.2); *AFF4* (E03 only; NM_014423.3); *NAA10* (E05 only; NM_003491.3).