MEDPACE®

GERMLINE EXOME SERVICES

TEST OVERVIEW

Whole exome sequencing (WES) is a test that evaluates patients with suspected genetic disorders for variants within the protein-coding regions (exons) of their genes. Due to its broad coverage, WES enables a comprehensive approach for identifying genetic variants that may contribute to obtaining a diagnosis or guiding treatment decisions. Given that exons are significantly enriched for clinically significant variants compared to non-coding regions of the genome, WES often offers higher read depth and efficiency compared to whole genome sequencing (WGS). For these reasons, WES is frequently employed to provide a comprehensive assessment of potentially pathogenic variants. Furthermore, if more targeted interrogation of specific genes is desired, WES-derived sequencing data can be bioinformatically filtered to only assess the targets of interest.

The Medpace whole exome platform is designed to detect germline variants including single nucleotide variants (SNVs) and insertions/deletions (indels) from genomic DNA extracted from whole blood.

TEST DETAILS

The Medpace whole exome platform is a CE-IVDR assay utilizing the Twist Precision Exome Dx Kit. This panel covers 36.5 Mb of human protein coding regions and the immediately flanking intronic regions, including variants from major genetic databases (RefSeq, CCDS, GenCode, Clinvar, ACMG73 and more) and additional curated clinical content such as clinically-relevant non-coding pathogenic and likely pathogenic variants. The Twist Precision Prep and Enrichment Dx Kit, Twist Precision Exome Dx Panel, Twist Precision Exome Dx Kit, and Qiagen QCI Interpret software used for variant annotation comply with the requirements of the EU Regulation: In-Vitro Diagnostic Regulation (2017/746). Sequencing is performed on the Illumina NextSeq 2000, which uses sequencing by-synthesis (SBS) technology to perform cluster generation and next-generation sequencing from enriched DNA libraries.

SPECIMEN TYPES

The preferred specimen for the assay is genomic DNA (gDNA) extracted from whole blood collected in K2 EDTA tubes.

SENSITIVITY, SPECIFICITY AND LIMIT OF DETECTION (LOD)

The analytical sensitivity determined from internal validation data is 96.4% for single-nucleotide polymorphisms, 96.3% for small indels (≤ 10 bp), and 93.9% for large indels (> 10 bp). The analytical specificity is >99% for all variant types.

REPORTABLE OUTCOME

Detected variants are interpreted following the American College of Medical Genetics and Genomics (ACMG) guidelines, which recommends that the clinical pathogenicity of a variant be evaluated using multiple lines of evidence from available literature, structural/ functional data, population frequencies, and statistical analysis of clinical data, with the possibility to report pathogenic, likely pathogenic, and variants of uncertain significance; variants determined to be benign or likely benign are only reported upon request.

REFERENCE RANGE

Click here to download the .bed files with all covered targets of the Twist Exome.

NGS AT MEDPACE

Medpace uses several Illumina-based NGS instruments including the MiSeqDx, NextSeq 550 and NextSeq 2000 at both our US and Belgium laboratories. Medpace is capable of performing several NGS techniques including whole exome sequencing (WES), RNA-sequencing (RNA-seq) and targeted gene sequencing (both germline and somatic). Our validated targeted sequencing panels include a Pan Cancer panel, Familial Hypercholesterolemia (FH) panel, a Myeloid Malignancies panel, and a Dyslipidemia panel. Targeted panels have the advantage of providing increased depth of coverage while generating sequencing information in a cost-effective manner.

FULL SERVICE CLINICAL DEVELOPMENT

Medpace is a scientifically driven, global, full-service clinical contract research organization (CRO) providing Phase I-IV clinical development services to the biotechnology, pharmaceutical and medical device industries. Medpace's mission is to accelerate the global development of safe and effective medical therapeutics through its high science and disciplined operating approach that leverages local regulatory and deep therapeutic expertise across all major areas including oncology, cardiology, metabolic disease, endocrinology, central nervous system and anti-viral and anti-infective.

MAKING THE COMPLEX SEAMLESS®