MEDPACE

MYELOID PANEL SERVICES

TEST OVERVIEW

The Medpace Myeloid panel uses next-generation sequencing (NGS) technology to assess variants in tumor suppressor genes and oncogenic hotspots frequently mutated in hematological malignancies, focusing on leukemia and myeloproliferative disorders. The Myeloid panel is designed to detect variants including single nucleotide variants (SNVs) and insertions/deletions (indels) from genomic DNA extracted from whole blood. Testing from bone marrow and FFPE slides is pending validation.

TEST DETAILS

The Myeloid panel utilizes custom Roche KAPA HyperChoice probes designed to target 54 genes (Table 1) with diagnostic or prognostic association with myeloid malignancies. The panel targets somatic variants with known involvement in acute myeloid leukemia (AML), myelodysplastic syndrome (MDS), myeloproliferative neoplasms (MPN), chronic myelogenous leukemia (CML), chronic myelomonocytic leukemia (CMML), and juvenile myelomonocytic leukemia (JMML), including single nucleotide variants (SNVs), insertions/deletions (indels), and small duplications. The probes in the custom panel target part or whole exonic sequence of the genes. Sequencing is performed on the Illumina NextSeq 550 or NextSeq 2000, which uses sequencing-by-synthesis (SBS) technology to perform cluster generation a nd next-generation sequencing from enriched DNA libraries.

SPECIMEN TYPES

The preferred specimen for the assay is whole blood (3mL, EDTA). testing of formalin-fixed, paraffin-embedded tissue and bone marrow samples needs to be validated. The genomic DNA input required for the assay is 100 ng.

SENSITIVITY, SPECIFICITY AND LIMIT OF DETECTION (LOD)

The overall sensitivity of the assay for somatic variant detection is >90% and for germline variant detection is >95%. The overall specificity of the assay for both somatic and germline variants is >99.99%.

REPORTABLE RANGES AND OUTCOME

The reportable ranges of targeted regions are listed in Table 1 below. These regions are based on the Human Genome Reference Consortium GRCh38 genome build. Within the reportable ranges, there are several reportable outcomes for SNVs and indels. Variants will be interpreted and classified into one of the following categories: Tier I (variants of strong clinical significance), Tier II (variants of potential clinical significance), Tier III (variants of unknown clinical significance), and Tier IV (benign or likely benign variants).[1] Only Tier I, II, and III variants will be reported. The VAF (%) of Tier I, II, and III variants will also be reported.

GENE	EXONS COVERED- includes intron/exon boundaries
ABL1	4-6
ASXL1	13 (sometimes known as exon 12)
ATRX	8-10, 17-31
BCOR	2-15
BCORL1	1-12
BRAF	15
CALR	9
CBL	8,9
CBLB	9,10
CBLC	9,10
CDKN2A	1-3
CEBPA	1
CSF3R	14-17
CUX1	1-24
DNMT3A	2-23
ETV6/TEL	1-8
EZH2	2-20
FBXW7	9-11
FLT3	14,15,20
GATA1	2
GATA2	2-6
GNAS	8,9
HRAS	2,3
IDH1	4
IDH2	4
IKZF1	2-8
JAK2	12,14

GENE	EXONS COVERED- includes intron/exon boundaries
JAK3	13
KDM6A	1-30
KIT	2,8-11,13,17
KRAS	2,3
MLL/KMT2A	5-8
MPL	10
MYD88	3-5
NOTCH1	26-28,34
NPM1	11 (sometimes known as exon 12)
NRAS	2,3
PDGFRA	12,14,18
PHF6	2-10
PTEN	5,7
PTPN11	3,13
RAD21	2-14
RUNX1	2-9
SETBP1	4
SF3B1	13-16
SMC1A	2,11,16,17
SMC3	10,13,19,23,25,28
SRSF2	1
STAG2	3-35
TET2	3-11
TP53	2-11
U2AF1	2, 6
WT1	7,9
ZRSR2	1-11

Table 1: The reportable ranges of targeted regions in the Myeloid Panel.

REFERENCE RANGE

Each gene targeted in this assay has an associated wildtype reference sequence. The references used in this assay are based on the Genome Reference Consortium GRCh38 build and established gene reference sequences (RefSeqs) listed in Table 2 below (National Center for Biotechnology Information: https://www.ncbi.nlm.nih.gov/refseq/).

GENE	REFSEQ TRANSCRIPT	GENE	REFSEQ TRANSCRIPT
ABL 1	NM_005157.6	*JAK3*	NM_000215.3
ASXL 1	NM_015338.6	*KDM6A*	NM_001291415.1
ATRX	NM_000489.5	*KIT*	NM_000222.2
BCOR	NM_001123385.2	*KRAS*	NM_004985.5
BCORL 1	NM_021946.4	*KMT2A/MLL*	NM_001197104.1
BRAF	NM_004333.6	*MPL*	NM_005373.3
CALR	NM_004343.3	*MYD88*	NM_001172567.2
CBL	NM_005188.4	*NOTCH1*	NM_017617.5
CBLB	NM_170662.5	*NPM1*	NM_002520.6
CBLC	NM_012116.4	*NRAS*	NM_002524.5
CDKN2A	NM_000077.4	*PDGFRA*	NM_006206.6
CEBPA	NM_004364.4	*PHF6*	NM_001015877.2
CSF3R	NM_156039.3	*PTEN*	NM_000314.8
CUX1	NM_181552.4	*PTPN11*	NM_002834.4
DNMT3A	NM_175629.2	*RAD21*	NM_006265.3
ETV6/TEL	NM_001987.5	*RUNX1*	NM_001754.4
EZH2	NM_004456.5	*SETBP1*	NM_015559.3
FBXW7	NM_001349798.2	*SF3B1*	NM_012433.3
FLT3	NM_004119.3	*SMC1A*	NM_006306.4
GATA1	NM_002049.4	*SMC3*	NM_005445.3
GATA2	NM_032638.5	*SRSF2*	NM_003016.4
GNAS	NM_000516.6	*STAG2*	NM_001042749.2
HRAS	NM_005343.4	*TET2*	NM_001127208.2
IDH1	NM_005896.3	*TP53*	NM_000546.5
IDH2	NM_002168.3	*U2AF1*	NM_006758.2
IKZF1	NM_006060.6	*WT1*	NM_024426.6
JAK2	NM_004972.3	*ZRSR2*	NM_005089.3

Table 2: Reference sequences of the genes included in the myeloid panel.

NGS AT MEDPACE

Medpace uses several Illumina-based sequencing instruments including the MiSeqDx, NextSeq 550, and NextSeq 2000 at both our US and Belgium laboratories. Medpace can perform several NGS techniques including whole exome sequencing (WES), RNA-sequencing (RNA-seq) and targeted gene sequencing. Our validated sequencing panels include a 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.

REFERENCE

1. Li, M., et al. Standards and Guidelines for the Interpretation and Reporting of Sequence Variants in Cancer. Journal of Molecular Diagnostics, 19(1), 4-23 (2017).