Myeloid Malignancies and Acute Myeloid Leukemia Mutation Panels by Next Generation Sequencing

Myeloid malignancies are clonal disorders of hematopoietic stem and progenitor cells that include myelodysplastic syndromes (MDS), myeloproliferative neoplasms (MPN), myelodysplastic/myeloproliferative neoplasms (MDS/MPN), and acute myeloid leukemia (AML). Recent studies have identified recurrently mutated genes with diagnostic and/or prognostic impact in myeloid malignancies. The presence of certain mutations may inform clinical management. This multigene panel by massively parallel sequencing (next generation sequencing) is a more cost-effective approach when compared to the cost of multiple single gene tests. This test can be used to complement the morphologic and cytogenetic workup of myeloid malignancies.

Tests to Consider

Myeloid Malignancies Mutation Panel by Next Generation Sequencing 2011117

Method: Massively Parallel Sequencing

Myeloid Malignancies Somatic Mutation and Copy Number Analysis Panel 2012182

Method: Massively Parallel Sequencing/Genomic Microarray (Oligo-SNP Array)

Acute Myeloid Leukemia Mutation Panel by Next Generation Sequencing 3002714

Method: Massively Parallel Sequencing

For more information on genomic microarray testing in oncology, see the additional technical information document, Cytogenomic Microarray – Oncology

See Related Tests

For additional test information, including information on individual tests, refer to the Acute Myeloid Leukemia Molecular Genetic Testing Test Fact Sheet.

Disease Overview

Diagnostic Issues

- Genetic targets contained in panels are relevant across the spectrum of myeloid malignancies
- Identification of one or more clonal genetic abnormalities may aid in establishing the diagnosis and subclassification of a myeloid neoplasm
- Identification of certain variants or patterns of variants may aid in prognostication and clinical management of patients with a diagnosis of myeloid malignancy

Prognostic and Treatment Issues

- Certain variants or patterns of variants may have diagnostic or prognostic significance
- Certain variants may inform clinical management

Genetics

Genes Tested: Myeloid Malignancies Mutation Panel by Next Generation Sequencing

ANKRD26, *ASXL1*, *ASXL2*, *BCOR*, *BCORL1*, *BRAF*, *CALR*, *CBL*, *CBLB*, *CEBPA*, *CSF3R*, *CUX1*[a], *DDX41*, *DNMT1*[a], *DNMT3A*, *ELANE*, *ETNK1*, *ETV6*, *EZH2*, *FBXW7*, *FLT3*, *GATA1*, *GATA2*, *GNAS*, *HNRNPK*, *IDH1*, *IDH2*, *IL7R*, *JAK1*, *JAK2*, *JAK3*, *KDM6A*[a], *KIT*, *KMT2A*, *KRAS*, *LUC7L2*, *MPL*, *NOTCH1*, *NPM1*[a], *NRAS*, *NSD1*, *PHF6*, *PIGA*, *PRPF40B*, *PRPF8*, *PTPN11*, *RAD21*, *RUNX1*, *SETBP1*, *SF3B1*, *SH2B3*, *SMC1A*, *SMC3*, *SRSF2*, *STAG2*, *STAT3*, *STAT5B*[a], *SUZ12*[a], *TET2*, *TP53*, *U2AF1*, *U2AF2*, *WT1*, *ZRSR2*

Genes Tested: Acute Myeloid Leukemia Mutation Panel by Next Generation Sequencing

ANKRD26, *ASXL1*, *CEBPA*, *DDX41*, *DNMT3A*, *ETV6*, *FLT3*, *GATA2*, *IDH1*, *IDH2*, *KIT*, *KRAS*, *NPM1*[a], *NRAS*, *RUNX1*, *TP53*, *WT1*

([a]One or more exons of the preferred transcript are not covered by sequencing for the indicated gene. See Genes Tested table below for full list of targeted regions and exclusions.)

Test Interpretation

Results

- Positive: a somatic variant in one of the tested genes was detected
  - Clinical relevance will be described, if known
- Negative: no variants were detected in the sequenced genes

Limitations

- Not intended to detect minimal residual disease (MRD)
- Variants may be present below the limit of detection (LOD) of 5% allele frequency
- Variants greater than 24 base pairs may be detected at LOD, but the analytical sensitivity may be reduced
- Variants may not be identified due to technical limitations in the presence of pseudogenes or in repetitive or homologous regions
- Variants in regions that are not included in the preferred transcript for the targeted genes will not be detected; see Genes Tested table below for full list of targeted regions and exclusions

Analytical Sensitivity

Variant Class	Analytical Sensitivity (PPA)[a] Estimate (%)	Analytical Sensitivity (PPA) 95% Credibility Region[a] (%)
SNVs	96.9%	95.1-98.1%
Insertions/Duplications (1-24bp)	98.1%	95.5-99.3%
Insertions/Duplications (>24bp)	> 99%	92.9-100.0%
Deletions (1-24bp)	96.7%	92.8-98.7%
Deletions (>24bp)	90%	79.5-96.1%
MNVs	97%	93.0-99.0%
FLT3 ITDs	>99%	97.1-100.0%

[a]Genes included on this test are a subset of a larger methods-based validation from which the PPA values are derived.

bp, base pairs; ITDs, internal tandem duplications; MNVs, multinucleotide variants; PPA, positive percent agreement; SNVs, single nucleotide variants

Genes Tested by Myeloid Malignancies Mutation Panel by Next Generation Sequencing

(The subset of genes tested by Acute Myeloid Leukemia Mutation Panel by Next Generation Sequencing are bolded)

Gene	Preferred Transcript[a]	Excluded Exons[b]
ANKRD26	NM_014915	
ASXL1	NM_015338	
ASXL2	NM_018263	
BCOR	NM_001123385	
BCORL1	NM_021946	
BRAF	NM_004333	
CALR	NM_004343	

[a]This is the transcript number used for analyzing and reporting variants. The transcript version number may change periodically and thus is not listed here. The transcript with version number will be included on the patient's report if a variant is detected in the gene.

[b]Noncoding exons are not analyzed, except for regions containing known clinically relevant variants in the ANKRD26 5'UTR and NOTCH1 3'UTR. In addition, coding exons noted here are not sequenced due to technical limitations of the assay.

Gene	Preferred Transcript[a]	Excluded Exons[b]
CBL	NM_005188	
CBLB	NM_170662	
CEBPA	NM_004364	
CSF3R	NM_156039	
CUX1	NM_181552	24
DDX41	NM_016222	
DNMT1	NM_001130823	5
DNMT3A	NM_175629	
ELANE	NM_001972	
ETNK1	NM_018638	
ETV6	NM_001987	
EZH2	NM_004456	
FBXW7	NM_033632	
FLT3	NM_004119	
GATA1	NM_002049	
GATA2	NM_032638	
GNAS	NM_000516	
HNRNPK	NM_002140	
IDH1	NM_005896	
IDH2	NM_002168	
IL7R	NM_002185	
JAK1	NM_002227	
JAK2	NM_004972	
JAK3	NM_000215	
KDM6A	NM_001291415	13

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[b]Noncoding exons are not analyzed, except for regions containing known clinically relevant variants in the ANKRD26 5'UTR and NOTCH1 3'UTR. In addition, coding exons noted here are not sequenced due to technical limitations of the assay.

Gene	Preferred Transcript[a]	Excluded Exons[b]
KIT	NM_000222	
KMT2A	NM_001197104	
KRAS	NM_004985	
LUC7L2	NM_016019	
MPL	NM_005373	
NOTCH1	NM_017617	
NPM1	NM_002520	1
NRAS	NM_002524	
NSD1	NM_022455	
PHF6	NM_001015877	
PIGA	NM_002641	
PRPF40B	NM_001031698	
PRPF8	NM_006445	
PTPN11	NM_002834	
RAD21	NM_006265	
RUNX1	NM_001754	
SETBP1	NM_015559	
SF3B1	NM_012433	
SH2B3	NM_005475	
SMC1A	NM_006306	
SMC3	NM_005445	
SRSF2	NM_003016	
STAG2	NM_001042749	
STAT3	NM_139276	
STAT5B	NM_012448	6-9

[a]This is the transcript number used for analyzing and reporting variants. The transcript version number may change periodically and thus is not listed here. The transcript with version number will be included on the patient's report if a variant is detected in the gene.

[b]Noncoding exons are not analyzed, except for regions containing known clinically relevant variants in the ANKRD26 5'UTR and NOTCH1 3'UTR. In addition, coding exons noted here are not sequenced due to technical limitations of the assay.

Gene	Preferred Transcript[a]	Excluded Exons[b]
SUZ12	NM_015355	1-9
TET2	NM_001127208	
TP53	NM_000546	
U2AF1	NM_006758	
U2AF2	NM_007279	
WT1	NM_024426	
ZRSR2	NM_005089	

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[b]Noncoding exons are not analyzed, except for regions containing known clinically relevant variants in the ANKRD26 5'UTR and NOTCH1 3'UTR. In addition, coding exons noted here are not sequenced due to technical limitations of the assay.

Related Information

Acute Myeloid Leukemia - AML
Myelodysplastic Syndromes
Myeloproliferative Neoplasms

Related Tests

CEBPA Mutation Detection 2004247

Method: Polymerase Chain Reaction/Sequencing

NPM1 Mutation Detection by RT-PCR, Quantitative 3000066

Method: Quantitative Reverse-Transcription Polymerase Chain Reaction

IDH1 and IDH2 Mutation Analysis, exon 4 2006444

Method: Polymerase Chain Reaction/Sequencing

KIT Mutations in AML by Fragment Analysis and Sequencing 2002437

Method: Capillary Electrophoresis

FLT3 ITD and TKD Mutation Detection 3001161

Method: Capillary Electrophoresis

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