Myeloid Malignancies Mutation Panel by Next Generation Sequencing

Indications for Ordering

Assess for single gene variants, including substitutions and insertions and deletions, that may have diagnostic, prognostic, and/or therapeutic significance in

- Acute myeloid leukemia
- Myelodysplastic syndromes (MDS)
- Myeloproliferative neoplasms (MPN)
- MDS/MPN overlap disorders such as chronic myelomonocytic leukemia

Test Description

Myeloid Malignancies Mutation Panel by Next Generation Sequencing

- Next generation sequencing (NGS) library construction from genomic DNA
- Enrichment for regions of interest by hybridization
- Massively parallel sequencing

Tests to Consider

Primary tests

- Myeloid Malignancies Mutation Panel by Next Generation Sequencing 2011117
- Myeloid Malignancies Somatic Mutation and Copy Number Analysis Panel 2012182

Related tests

- *CEBPA* Mutation Detection 2004247
- *NPM1* Mutation Detection by RT-PCR, Quantitative 3000066
- *IDH1* and *IDH2* Mutation Analysis, exon 4 2006444
- *KIT* Mutations in AML by Fragment Analysis and Sequencing 2002437

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 of a neoplasm
- Identification of certain variants or patterns of variants may aid in diagnostic subclassification

Prognostic and treatment issues

- Certain variants or patterns of variants may have prognostic significance
- Certain variants may allow for the use of targeted therapies

Genetics

Genes – *ASXL1, ASXL2, BCOR, BCORL1, BRAF, CALR, CBL, CEBPA, CSF3R, DNMT1, DNMT3A, EED, ELANE, ETNK1, ETV6, EZH2, FAM5C, FLT3, GATA1, GATA2, HNRNPK, IDH1, IDH2, JAK2, JAK3, KDM6A, KIT, KRAS, LUC7L2, MAP2K1, MLL, MPL, NOTCH1, NPM1, NRAS, NSD1, PHF6, PRPF40B, PRPF8, PTPN11, RAD21, RUNX1, SETBP1, SF1, SF3A1, SF3B1, SMC1A, SMC3, SRSF2, STAG2, SUZ12, TET2, TP53, U2AF1, U2AF2, WT1, ZRSR2*

- See Myeloid Panel Coordinates table below for full list of targeted regions

Test Interpretation

Results

- Positive – a somatic variant in one of the 57 tested genes was detected
  - Clinical relevance (diagnosis, prognosis, therapy) will be correlated, if known
- Negative result – no variants were detected in the sequenced genes

Limitations

- Variants may be present below the limit of detection (LOD) of 5% allele frequency
- Lower limit of detection for large variants (>30bp) has not been validated
- Not intended to detect minimal residual disease

Analytical Sensitivity

Variant Class	No. Variants Tested	PPA	95% Tolerance Interval at 95% Reliability
SNV	414	96%	94-97%
Insertions and duplications (small,[a] medium,[b] large[c])	281	100%	94-100%
Deletions (small[a] and medium[b])	132	100%	97-100%
Deletions (large[d])	5	80%	37-98%

[a]Small variant (<30 bp)
[b]Medium variant (30-60 bp)
[C]Large variant, insertions/duplications (60-224 bp)
[d]Large variant, deletions (60-1675 bp)

Myeloid Panel Coordinates

Gene	Accession No.	Sequenced Exons
ASXL1	NM_015338.5	12
ASXL2	NM_018263.4	10, 11, 12
BCOR	NM_001123385.1	All[a]
BCORL1	NM_021946.4	All
BRAF	NM_004333.4	15
BRINP3/FAM5C	NM_199051.1	All[a]
CALR	NM_004343.3	9
CBL	NM_005188.3	8, 9
CEBPA	NM_004364.4	All
CSF3R	NM_156039.3	14, 17
DNMT1	NM_001130823.1	1-4, 6-41
DNMT3A	NM_175629.2	All[a]
EED	NM_003797.4	All
ELANE	NM_001972.2	All
ETNK1	NM_018638.4	3
ETV6	NM_001987.4	All
EZH2	NM_004456.4	All[a]
FLT3	NM_004119.2	14,15, 16, 20
GATA1	NM_002049.3	2
GATA2	NM_001145661.1	4-7
HNRNPK	NM_002140.3	3-17
IDH1	NM_005896.3	4
IDH2	NM_002168.3	4
JAK2	NM_004972.3	12-14
JAK3	NM_000215.3	2-4, 11, 15-22
KDM6A	NM_001291415.1	All
KIT	NM_000222.2	8, 9, 11, 13, 17, 18
KMT2A/MLL	NM_001197104.1	All
KRAS	NM_004985.4	2-4
LUC7L2	NM_016019.4	All
MAP2K1	NM_002755.3	2,3
MPL	NM_005373.2	10
NOTCH1	NM_017617.3	26-28, 34
NPM1	NM_002520.6	10, 11
NRAS	NM_002524.4	2-4
NSD1	NM_022455.4	All[a]
PHF6	NM_001015877.1	All[a]
PRPF40B	NM_001031698.2	All
PRPF8	NM_006445.3	All[a]
PTPN11	NM_002834.3	3, 4, 12, 13
RAD21	NM_006265.2	All[a]
RUNX1	NM_001754.4	All
SETBP1	NM_015559.2	4(codons 799-965)
SF1	NM_004630.3	All
SF3A1	NM_005877.5	All
SF3B1	NM_012433.3	6-8, 12-18
SMC1A	NM_006306.3	All
SMC3	NM_005445.3	All
SRSF2	NM_003016.4	All
STAG2	NM_001042749.2	All[a]
SUZ12	NM_015355.2	10-16
TET2	NM_001127208.2	All[a]
TP53	NM_000546.5	All[a]
U2AF1	NM_006758.2	2, 6
U2AF2	NM_007279.2	All
WT1	NM_024426.4	3, 6-9
ZRSR2	NM_005089.3	All

[a]Excludes noncoding exons