CENTOGENE
THE RARE DISEASE COMPANY

Myeloid Tumor Panel

The Targeted Approach to Detecting Myeloid Malignancies

PRODUCT SHEET

Myeloid Tumor Panel Somatic Mutation Testing

Myeloid tumors represent the fourth most frequently diagnosed cancer in economically developed countries. The majority of myeloid tumors contain high numbers of somatic mutations, which significantly contribute to the pathogenesis, progression, and prognosis of myeloid malignancies. Sequencing and identification of the genetic variants can provide valuable information for diagnostic decisions, prognosis, therapeutic approaches and patient counseling.

CENTOGENE'S Myeloid Tumor Panel has been designed to target important regions within 35 genes that are frequently mutated in myeloid malignancies. Our panel helps physicians identify patients who are less likely to respond well to conventional treatment, enables the identification of patients who will benefit from biomarker targeted therapies, supports in determining the intensity of treatment each patient should receive, and enables rapid eligibility identification and patient stratification for clinical trials.

The CENTOGENE Advantage

- Curated to **provide the most valuable information** for diagnostic decisions, prognosis, and therapeutic approaches
- The most **up-to-date panel gene content** including the latest medical and in-house findings
- **World-class expertise** and life-long commitment to our patients
- **High-quality analysis for precise clinical interpretation** using advanced bioinformatics and artificial intelligence-powered tools
- **First-class medical reports** powered by CentoMD® database, containing > 12.7 million unique variants and multiomics data from over 120 countries

Diseases Covered

Acute myeloid leukemia (AML), Chronic myeloid leukemia (CML), Myelodysplastic syndrome (MDS), Myeloproliferative neoplasms (MPN), Chronic myelomonocytic leukemia (CMML), and Juvenile myelomonocytic leukemia (JMML)

Key Features and Performance

COVERAGE	• ≥ 97.0 % targeted regions covered at ≥ 200 x • Mean depth coverage ≥ 1000 x • 1.8 – 2 Gb of sequencing data generated for each patient
VARIANT TYPES	• Sensitivity SNVs and InDels (≤ 50 bp) > 99.7 % • Accuracy of > 99.7 % • Specificity of ≥ 99.9 % guaranteed for all reported variant. Variants with low quality and/or unclear zygosity are confirmed by orthogonal methods*
REPORTING	Pathogenic and likely pathogenic variants are reported following ACMG classification guidelines recommendations. Additionally, these variants are reported according to their actionability into Tier 1 (strong clinical significance) or Tier 2 (potential clinical significance), following the standards and guidelines for the Interpretation and reporting of sequence variants in cancer**
REQUESTED MATERIAL	≥ 1 µg DNA or 1 ml bone marrow or 1 ml blood or 1 filtercard (CentoCard®)
TAT	10 business days

SNVs: single nucleotide variants; InDels: small insertions/deletions; CNVs: copy number variations

* Variants with low quality and / or unclear zygosity are confirmed by orthogonal methods, i.e.: SNVs and InDels by Sanger sequencing; CNVs by Multiplex ligationdependent probe amplification (MPLA), quantitative polymerase chain reaction (qPCR)

** Li et al. 2017, PMID: 27993330

GENE	ASSOCIATED SOMATIC PHENOTYPES	RELEVANCE [1–3]	Percentange of acute myeloid leukemia patients with ALTERED GENE [4]
ASXL1	Myelodysplastic syndrome	Related with poor prognosis in AML (Predictive biomarker)	18.18%
ATM	B-cell non-Hodgkin Lymphoma, Mantle cell lymphoma, T-cell prolymphocytic leukemia	(Predictive biomarker)	2.66%
CBL	Juvenile myelomonocytic leukemia	Eligibility criterion for clinical trials	2.32%
CDKN2A	Multiple myeloma, Acute lymphoblastic leukemia	Eligibility criterion for clinical trials	6.70%
CEBPA	Acute myeloid leukemia	Biallelic mutations related with favourable prognosis (Predictive biomarker)	4.03%
CREBBP	Lung adenocarcinomas, Colon adenocarcinomas, Acute myeloid leukemia	Eligibility criterion for clinical trials	3.19%
DNMT3A	Somatic acute myeloid leukemia	related with adverse prognosis (Predictive biomarker)	19.73%
ETV6	Acute myeloid leukemia	Eligibility criterion for clinical trials	16.81%
EZH2	Myelodysplastic syndromes, Lymphoma, Colorectal cancer, Endometrial cancer	Eligibility criterion for clinical trials	4.22%
FLT3	Acute lymphoblastic leukemia, Acute myeloid leukemia	Related with reduced survival in Acute lymphoblastic leukemia, (Predictive biomarker), biomarker-directed therapy available	11.13%
GATA2	Acute myeloid leukemia	related with adverse prognosis (Predictive biomarker)	5.33%
HRAS	Follicular thyroid carcinoma	(Predictive biomarker)	2.28%
IDH1	Glioma	biomarker-directed therapy available (Predictive biomarker)	7.95%
IDH2	Acute myeloid leukemia, Breast cancer, Colon adenocarcinoma, Lung adenocarcinoma, Myelodysplasic syndromes	biomarker-directed therapy available (Predictive biomarker)	10.50%
JAK2	Acute myeloid leukemia, Myelofibrosis, Polycythemia vera	Eligibility criterion for clinical trials	3.04%
KIT	Acute myeloid leukemia, Germ cell tumors	(Predictive biomarker)	2.14%
KRAS	Acute myeloid leukemia, Bladder cancer, Breast cancer, Gastric cancer, Lung cancer, Pancreatic carcinoma	(Predictive biomarker)	3.87%
NF1	Juvenile myelomonocytic leukemia	(Predictive biomarker)	7.45%
NOTCH1	Colon adenocarcinoma, Lung adenocarcinoma, Breast cancer	Eligibility criterion for clinical trials	2.79%
NPM1	Acute myeloid leukemia	(Predictive biomarker) related with favourable prognosis	16.38%
NRAS	Colorectal cancer, Follicular thyroid carcinoma	Eligibility criterion for clinical trials	9.68%
PDGFRB	Myeloproliferative disorder	Eligibility criterion for clinical trials	2.13%
PHF6	Acute myeloid leukemia, Lung adenocarcinoma, Myelodysplastic syndromes, Endometrial endometrioid adenocarcinoma	Eligibility criterion for clinical trials	4.21%
PTPN11	Juvenile myelomonocytic leukemia	Eligibility criterion for clinical trials	4.84%
RAD21	Breast cancer, Lung adenocarcinoma, Prostate adenocarcinoma, Colon adenocarcinoma, Acute myeloid leukemia	Eligibility criterion for clinical trials	2.65%
RUNX1	Acute myeloid leukemia	(Predictive biomarker) related with adverse prognosis	14.75%
SF3B1	Myelodysplastic syndrome	Eligibility criterion for clinical trials	3.34%
SMC1A	Lung adenocarcinoma, Endometrial adenocarcinoma, Colon adenocarcinoma, Acute myeloid leukemia	Eligibility criterion for clinical trials	1.02%
SMC3	Lung adenocarcinoma, Colon adenocarcinoma, Acute myeloid leukemia	Eligibility criterion for clinical trials	1.27%
SRSF2	Acute myeloid leukemia, Myelodysplastic syndromes, Breast cancer, Chronic myelomonocytic leukemia	Eligibility criterion for clinical trials	10.38%
STAG2	Lung adenocarcinoma, Bladder urothelial carcinoma, Colon adenocarcinoma, Acute myeloid leukemia	Eligibility criterion for clinical trials	5.88%
TET2	Myelodysplastic syndrome	(Predictive biomarker)	16.98%
TP53	Breast cancer, Hepatocellular carcinoma, Nasopharyngeal carcinoma, Pancreatic cancer, Osteosarcoma, Glioma	(Predictive biomarker) related with adverse prognosis	12.30%
U2AF1	Lung adenocarcinoma, Myelodysplastic syndromes, Acute myeloid leukemia	Eligibility criterion for clinical trials	4.63%
WT1	Mesothelioma, Wilms tumor	(Predictive biomarker) related with adverse prognosis	4.29%

1 https://www.mycancergenome.org/content/disease/acute-myeloid-leukemia/
2 World Health Organization classification of myeloid neoplasms and acute leukemia (2016)
3 ELN recommendations from an international expert panel (2017)
4 The AACR Project GENIE Consortium. AACR Project GENIE: powering precision medicine through an international consortium. Cancer Discovery. 2017;7(8):818-831. Dataset Version 8. This dataset does not represent the totality of the genetic landscape; see paper for more information.