Product Profile

QIAact Myeloid DNA UMI Panel

For detection of key mutations in myeloid malignancies from blood and bone marrow

Myeloid malignancies are complex clonal diseases arising in hematopoietic stem or progenitor cells. There is an increasing need for molecular identification of key mutations characterizing these blood and bone marrow disorders. The application of next generation sequencing (NGS) affords clinical researchers with rapid and unprecedented insights into the genetic drivers of disease. Numerous molecular markers of known significance to clonal myeloid malignancy have been identified including single nucleotide variants (SNVs) and insertion/deletion mutations (InDels). These heterogenous blood disorders comprise many different subtypes such as myeloproliferative neoplasms (MPN), myelodysplastic syndrome (MDS) and acute myeloid leukemia (AML).

Current approaches for analyzing hematological disorders often require multiple sequential analyses using varying technologies, entailing extensive effort and investment to implement in a laboratory. Given the genetic complexity of these blood disorders and the large number of genetic variants that have been associated with myeloid malignancies, researchers need a well-designed NGS assay, including data analysis and interpretation, to effectively capture key variants from the most informative genes in a single experiment. Targeted NGS approaches offer the potential to screen multiple biomarkers in a single reaction, while excluding irrelevant regions of the genome from the analysis. ▷

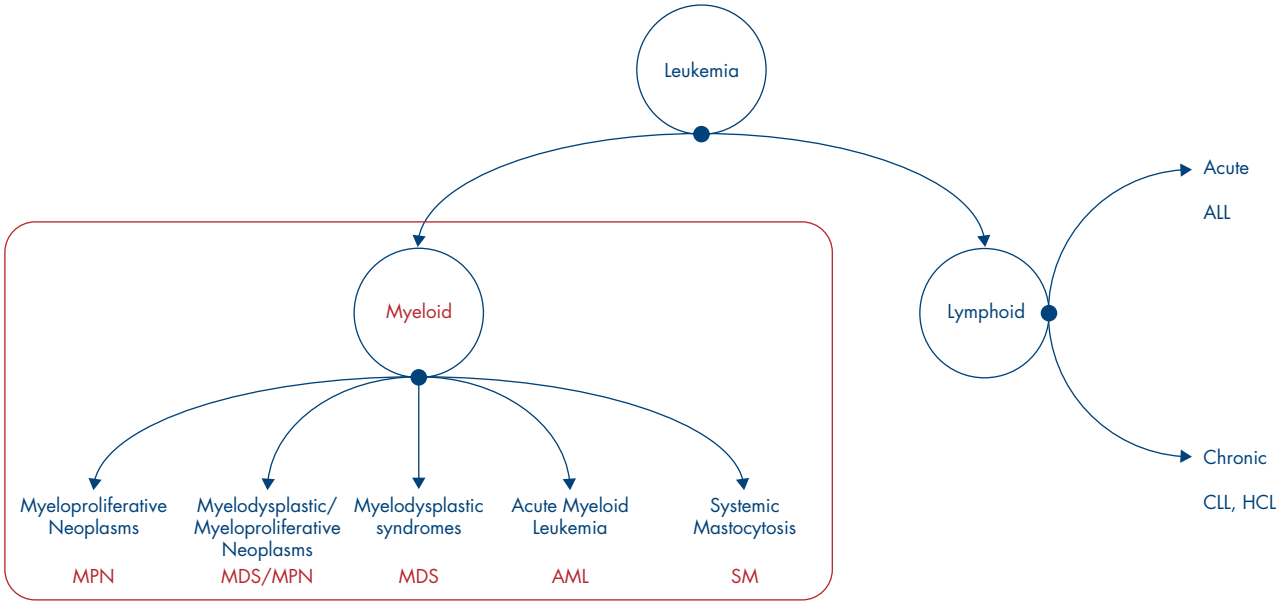


Figure 1. Molecular Characterization of Myeloid Neoplasms. The QIAact Myeloid DNA UMI Panel helps molecular characterization for the presence of a clonal neoplasm in several myeloid subtypes.

The QIAact Myeloid DNA UMI Panel in combination with the QIAGEN GeneReader™ NGS System provides a single integrated solution to simultaneously test for actionable mutations and requires only a small amount of sample material. This Sample to Insight® solution can detect pathogenic and actionable variants, including those that are difficult-to-detect, from both blood and bone marrow. Myeloid neoplasm subtypes targeted by the QIAact Myeloid DNA UMI Panel are shown in Figure 1.

An optimized panel design process

The QIAact Myeloid DNA UMI Panel builds on the success of the *ipsogen*® product portfolio and leverages QIAGEN's extensive knowledge of blood cancers. The panel was developed in collaboration with a team of internationally recognized onco-hematology experts and covers 25 genes with known significance to clonal myeloid malignancies (Table 1 and Figure 2). Furthermore, the genomic regions included in the panel span approximately 9,000 previously reported variants that have been recorded as pathogenic in the QIAGEN Knowledge Base.

Incorporating Unique Molecular Index technology for increased accuracy and analytical sensitivity

Unique Molecular Index (UMI) technology is the process by which short sequences or "barcodes" are added to each original DNA molecule. This enables the identification and removal of false positive DNA variants introduced by DNA amplification or the sequencing process. UMI technology, in combination with an amplicon-based NGS panel and optimized bioinformatics, results in a high level of analytical sensitivity and specificity and allows for the capture of SNVs as well as larger mutations such as InDels and frame-shifts.

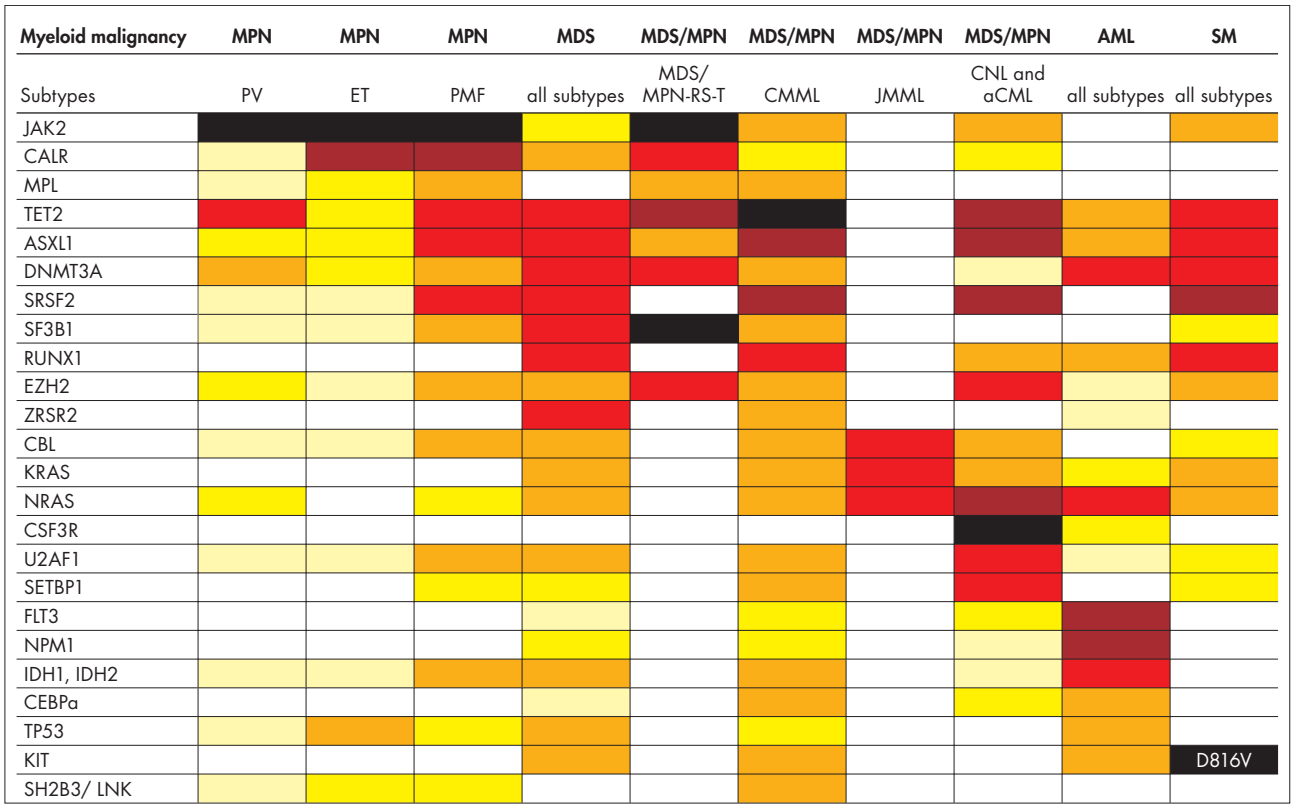
UMI incorporation into the QIAact Myeloid DNA UMI Panel enables detection of low frequency variants associated with clonal myeloid malignancies, including those below the 1% variant allele frequency (VAF) such as mutations within JAK2 and KIT genes (for the other genes, the panel supports mutation detection with a VAF of 5%). Accurate reporting of usually challenging-to-detect mutations including the large CALR Type 1 (52 bp deletion), FLT3 ITDs (with identified insertion site), and GC-rich sequences, such as in the CEBPA gene, are also possible due to this digital sequencing approach paired with optimized bioinformatics.

Table 1. Details of regions covered by the QIAact Myeloid DNA UMI Panel. The panel covers single nucleotide variants (SNVs) and insertions/deletions (InDels) in 25 genes of known significance to myeloid malignancies.

	Full exon covered (exon numbers are according to transcript ID)	Transcript ID
ASXL1	Exons 12, 13	NM_015338
CALR	Exon 9	NM_004343
CBL	Exons 8, 9	NM_005188
CEBPa	Exon 1	NM_004364
CSF3R	Exons 14 to 17	NM_156039
DNMT3A	Exons 2 to 23	NM_022552
EZH2	Exons 2 to 20	NM_004456
FLT3	Exons 14, 15, 20	NM_004119
IDH1	Exon 4	NM_005896
IDH2	Exon 4	NM_002168
JAK2	Exons 12 to 15	NM_004972
KIT	Exons 8, 9, 10, 11, 17	NM_000222
KRAS	Exons 2, 3, 4	NM_004985
MPL	Exons 1 to 12	NM_005373
NPM1	Exon 11	NM_002520
NRAS	Exons 2, 3, 4	NM_002524
RUNX1	Exons 2 to 9	NM_001754
SETBP1	Exon 4	NM_015559
SF3B1	Exons 11 to 16	NM_012433
SH2B3 / LNK	Exons 2 to 8	NM_005475.2
SRSF2	Exon 1	NM_003016
TET2	Exons 3 to 11	NM_001127208
TP53	Exons 3 to 11	NM_000546
U2AF1	Exons 2, 6	NM_006758
ZRSR2	Exons 1 to 11	NM_005089

Part of a complete Sample to Insight NGS workflow

The QIAact Myeloid DNA UMI panel is designed and verified as a complete assay on the QIAGEN GeneReader NGS System. This means that all steps from DNA extraction (either automated using QIAcube® or QIAsymphony® SP, or performed manually) to sequencing and result interpretation and reporting have been developed and optimized in synchronization. The result is an assay and workflow that is truly "end to end" and ready for implementation in any laboratory (Figure 3).



Frequency:
0
rare (<1)
1–5
5–10
10–25
25–50
>50

MPN myeloproliferative neoplasm
PV polycythemia vera
ET essential thrombocythemia
PMF primary myelofibrosis
MDS myelodysplastic syndrome
MDS/MPN myelodysplastic/myeloproliferative neoplasms
MDS/MPN-RS-T MDS/MPN with ring sideroblasts and thrombocytosis (MDS/MPN-RS-T; previously known as RARS-T*)

CMML chronic myelomonocytic leukemia
JMML juvenile myelomonocytic leukemia
CNL chronic neutrophilic leukemia
aCML atypical CML
AML acute myeloid leukemia
SM systemic mastocytosis

* RARS-T (refractory anemia with ring sideroblasts associated with marked thrombocytosis).

Figure 2. Mutation Frequency in Myeloid Malignancies. The QIAact Myeloid DNA UMI Panel is a core pan-myeloid panel that targets markers of known significance to myeloid malignancies and includes the most common mutations.

Note: Listed frequency estimates are from reports in the literature.

Integrated bioinformatics for interpretation at the push of a button

The QIAact Myeloid DNA UMI Panel workflow incorporates an optimized and fully integrated bioinformatics pipeline, comprising QCI® Analyze for variant identification, and QCI Interpret for standardized classification, evidence-sourced interpretation and reporting of detected variants. QCI Interpret uses QIAGEN's comprehensive Knowledge Base with manually curated literature updated daily. Interpretation is applied according to international guidelines established for variant classification and actionability such as the latest AMP/ASCO/CAP guidelines.

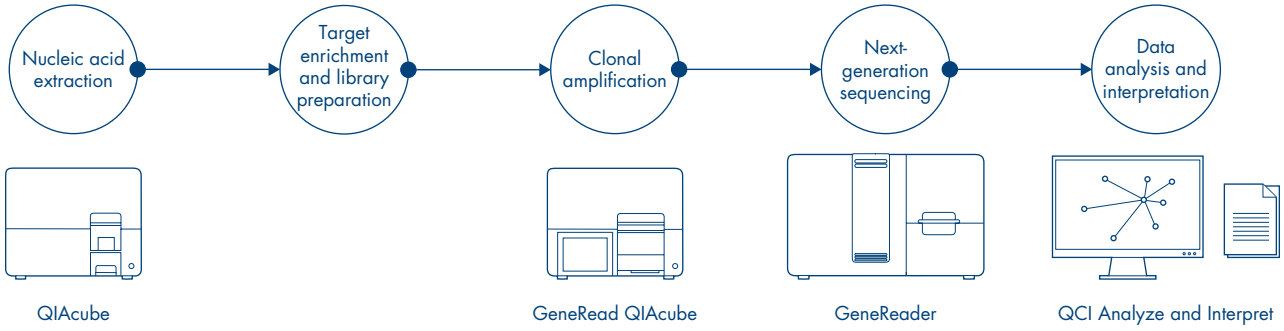


Figure 3. The complete GeneReader NGS System workflow. The GeneRead family of products allows seamless integration of QIAGEN automated solutions along with manual target enrichment and library preparation.

Highlights of the QIAact Myeloid DNA UMI Panel

- **Targets**: 25 genes of known significance to myeloid malignancies, covering genomic regions containing about 9,000 variants reported to be pathogenic
- **High Sensitivity**: detection of variants in JAK2 and KIT (1% VAF), KIT D816V (0.4% VAF), enabled by digital sequencing using UMIs
- **Detection of Challenging Mutations**: including FLT3 ITDs, CALR deletions and CEBPA mutations
- **Sample Input**: 40 ng DNA, extracted from blood or bone marrow
- **Flexibility**: multiple QIAact DNA UMI Panels may be combined on the same flowcell
- **Automated Analysis**: integrated bioinformatics, interpretation and reporting with QCI

Ordering Information

Product	Contents	Cat. no.
QIAact Myeloid DNA UMI Panel	Generates target enriched DNA libraries for digital sequencing on the GeneReader NGS System, to deliver myeloid malignancy research insights	181950

The GeneReader NGS System is for Research Use Only. Not intended for diagnostic procedures.

NOTE: Reporting on FLT3 ITDs will not be available in the USA before December 17, 2018.