HemaTarget Profile Test – Information Sheet

A comprehensive genomic profiling test for hematologic cancers

CURRENT GENE LIST:**

ABCB1	*ABCC3*	*ABL**	*ABL2**	*ADD3**	*AFF1**	*ALK**	*ASXL1*	*BCL2**	*BCL3**
*BCL6**	*BCL9 **	*BCOR*	*BCR**	*BIRC3**	*CALR*	*CAPRIN1**	*CBFA2T3**	*CBFB**	*CBL*
*CCDC28A**	*CCDC6**	*CCDC88C**	*CCND1**	*CCND3**	*CD33*	*CDA*	*CEBPA*	*CEP85L**	*CLTC**
*CRLF2**	*DCK*	*DDX10**	*DNMT3A*	*ERC1**	*ERCC2*	*ETV6**	*EZH2*	*FBXW7*	*FCRL4**
*FGFR1**	*FGFR3**	*FIP1L1**	*FLT3*	*GIT2**	*GOLGA4**	*HHEX**	*HIP1**	*HMGB3**	*HOXA11**
*HOXA13**	*HOXA9**	*HOXC11**	*HOXC13**	*HOXD13**	*IDH1*	*IDH2*	*IGHD3**	*IGHE**	*IGHJ3**
*IGHV1**	*IGHV2**	*IGHV3**	*IGLL5**	*IKZF1*	*IL1B*	*IL6R*	*IL7R*	*IQCG**	*IRF3*
*JAK2**	*KDM5A**	*KIT*	*KMT2A**	*LNP1**	*MAFB**	*MALT1**	*MECOM**	*MLH1*	*MLLT1**
*MLLT10**	*MLLT3**	*MLLT4**	*MPL*	*MTHFR*	*MUC1**	*MYC**	*MYD88*	*MYH11**	*NDE1**
*NIN**	*NOTCH1**	*NPM1*	*NRAS*	*NSD1**	*NT5C2*	*NUP98**	*PAX5*	*PBX1**	*PCM1**
*PDGFRA**	*PDGFRB**	*PHF6*	*PRKG2**	*PRRX1**	*PRRX2**	*PSIP1**	*RABEP1**	*RAP1GDS1**	*RPN1**
*RUNX1**	*RUNX1T1**	*SETBP1**	*SF3B1*	*SLCO1B1*	*SPECC1**	*SRSF2*	*STAG2*	*TCF3**	*TET2*
*TOP1**	*TP53*	*TP53BP1**	*TRIP11**	*TYMS*	*U2AF1*	*WDR48**	*WHSC1L1**	*WT1*	*ZMYM2**
ZRSR2									

* These genes undergo genomic rearrangements detected by RNA sequencing technology.
** This gene list is updated from time to time, and is current as to this version of the information sheet.

OVERVIEW

Personalized medicine does not rely on the “one-size-fits-all” treatment approach but rather takes into account individual patients' genomic uniqueness. Next generation sequencing (NGS) of patients' tumor DNA has greatly enhanced the identification of patient-tumor specific variants, and has enabled oncologists to make more informed personalized treatment decisions for their cancer patients based on their cancer's genomic profile.

The GeneSort HemaTarget Profile Test (HemaTarget) is a comprehensive genomic profiling gene panel for blood cancers (hematologic malignancies) designed to assist physicians with disease stratification, prognosis and targeted therapy decisions. The test simultaneously sequences 131 cancer related genes and examines the genomic changes associated with the development of blood cancers. The panel includes but is not limited to, acute and chronic leukemia (AML/ALL and CML), lymphomas, myelodysplastic syndrome (MDS) and multiple myeloma. This panel profiles genes and selected non-coding regions related to drug metabolism, efficiency and toxicity and chemotherapy. Using NGS technology the HemaTarget tests all classes of genomic alterations: base changes, insertions/deletions, copy number variations and fusions (translocations) which can then be targeted by matched drug therapies.

The HemaTarget is a single comprehensive assay that provides valuable information relevant for:

- Diagnosis
- Disease stratification
- First line treatment decisions (chemotherapy)
- Prognosis

- Therapeutic course

Uniquely, the HemaTarget includes detection of variants associated with:

- Drug response
- Drug metabolism: guides treatment dose
- Chemotherapy response: toxicity, dosage
- Dose associated event free survival (EFS)
- Risk for graft versus host disease post allogenic stem cell transplantation

METHODS

DNA and RNA are extracted from bone marrow samples and enriched for the selected cancer-related genes/regions of the panel using a proprietary targeted capture system developed by GeneSort. The captured products are sequenced on an Illumina HiSeq 2500/1500 platform with 2X100 paired-end reads with a median depth of coverage ≥750X. Deep sequencing (or many reads of the same region) enables characterization of rare tumor variants (≥5% variant allele frequency). Data analysis is performed using proprietary bioinformatics tools developed at GeneSort.

THE REPORT

The HemaTarget's final report provides a table of variants with possible therapies and relevant technical information regarding sequence depth of coverage, variant frequency and annotation of variants according to clinical databases. In the core of the report, detailed information about the genomic alterations is provided with its etiology along with data regarding the possible treatments and detailed references to sustain the results which appear in the report.

Several result outcomes are possible including:

- **Positive result – includes the following scenarios of reportable variables:**
  - Variants with FDA approved drugs for the patient's cancer type, or variants included in professional guidelines, are identified.
  - Variants predicting response to treatment for the patient's cancer type based on well-powered studies are identified.
  - Variants predicting response to treatment approved by the FDA for a different type of tumor or variants that serve as inclusion criteria for clinical trials are identified.
  - Variants with plausible therapeutic significance based on preclinical trials are identified.
  - Variants with no known therapies are identified.
- **Negative result** – a negative result indicates that no reportable variants were detected.

REPORTING VARIANTS OF UNKNOWN SIGNIFICANCE (VUS).

VUS represents variants for which clinical decision making is not well defined at the time the report was generated. GeneSort reports include VUS findings so evolving evidence and updated interpretations may be considered for these variants.

CONFIRMATION

Confirmation of NGS-identified variants is performed by golden standard, Sanger sequencing. Confirmations are performed when possible (variant allele frequency ≥20% and sufficient DNA is available).

SAMPLE TYPES

Bone marrow, FFPE (formalin fixed paraffin embedded), peripheral blood

SUMMARY OF HEMATARGET PROFILE TEST SPECIFICATIONS

Technical Parameters	Test Specifications
Number of Genes	131
Gene Rearrangements	>30
Analytical Accuracy	99%
Analytical Specificity	100%
Analytical Sensitivity Threshold	≥ 5%
Average Depth of Coverage	≥ 750X
Sample Requirements	Bone Marrow/Peripheral Blood/FFPE
Turn Around Time	< 30 Working Days

FURTHER INFORMATION

For further information please contact GeneSort by email at info@genesort.com

HemaTarget Profile Test Selected Publications:

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AID GENOMICS

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(21) Hubmann, M., Köhnke, T., et al. (2014). *Haematologica 99*, 1317–1325.
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