This test uses cell-free DNA (cfDNA) for detecting abnormalities in hematologic diseases. The test is particularly designed and offered to reduce the need for bone marrow biopsy. It is highly useful for patients presenting with cytopenia and to rule out MDS/CMML, MPN or other hematologic neoplasms. It can also be used for monitoring patients with hematologic neoplasms. Based on multiple studies, cfDNA can be more accurate in detecting abnormalities in bone marrow than bone marrow actual biopsy. Bone marrow biopsy might be limited to site of the biopsy, while the cfDNA reflects abnormalities in the entire body. Furthermore, based on our investigation, plasma is enriched by cancer-specific DNA/RNA due to the high turnover of tumor cells as compared with normal cells. This test is recommended for the diagnosis and follow up of:

GTC-Liquid Biopsy, Hematology

Diagnosis and Monitoring

-**Myelodysplastic syndrome (MDS)/Chronic myelomonocytic leukemia (CMML):** To determine if the patient has reactive cytopenia and to distinguish between CHIP (Clonal Hematopoiesis of Indeterminate Potential) or CCUS (Clonal Cytopenia of Unknown Significance) and MDS.

**-Acute Myeloid Leukemia (AML):** To confirm diagnosis of AML and helps in determining eligibility for treatment with FLT3 and IDH1/2 inhibitors and evaluate minimal/measurable residual disease (MRD). It is particularly useful for pediatric and elderly patients.

**-Myeloproliferative Neoplasms (MPN):** To confirm diagnosis and monitor MPN and evaluate levels of JAK2, CALR and MPL mutations.

**-Lymphoma:** Liquid biopsy and cfDNA analysis is recommended for patients with lymphoma and specific mutations. The levels of the detected mutations can be used to monitor these diseases and evaluate therapy. Analysis of the original diagnostic sample is required for proper and sensitive monitoring of lymphoma.

Specimen Requirements:

Peripheral blood: 5-10 mL. EDTA tube is preferred.

Shipping:

Ship using cold pack. The cold pack should not directly contact Blood. Ship As soon as sample collected with overnight delivery.

Turn Around Time:

5-7 days

Tested Genes

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Hematology Genes Tested for Abnormalities in coding sequence** | | | | | | | | | | | | |
| ABL1 | BCL2 | CBL | CDKN2C | DICER1 | FAS | IDH2 | KMT2A | MPL | PAX5 | PTCH1 | SMAD2 | TGFBR2 |
| AKT1 | BCL2L1 | CBLB | CEBPA | DNMT3A | FBXW7 | IGF1R | KMT2B | MRE11A | PBRM1 | PTEN | SMAD4 | TP53 |
| AKT2 | BCL6 | CBLC | CHEK1 | EP300 | FLT3 | IKZF1 | KMT2C | MTOR | PDGFRA | PTPN11 | SMARCA4 | TSC1 |
| AKT3 | BCOR | CCND1 | CHEK2 | ERG | GATA1 | IKZF3 | KMT2D | MUTYH | PDGFRB | RAD21 | SMARCB1 | TSC2 |
| ALK | BCORL1 | CCND3 | CIC | ETV6 | GATA2 | IRF4 | KRAS | MYC | PHF6 | RAD50 | SMC1A | TSHR |
| AMER1 | BCR | CD274 | CREBBP | EZH2 | GATA3 | JAK1 | MAP2K1 | MYD88 | PIK3CA | RAD51 | SMO | WT1 |
| APC | BIRC3 | CD79A | CRLF2 | FAM175A | GEN1 | JAK2 | MAP2K2 | NFKBIA | PIK3R1 | RB1 | SOCS1 | ZNF217 |
| ARID1A | BLM | CD79B | CSF1R | FAM46C | GNAQ | JAK3 | MAP2K4 | NOTCH1 | PIK3R2 | RHOA | SRC | ZRSR2 |
| ARID1B | BRAF | CDH1 | CSF3R | FANCA | GNAS | KAT6A | MAP3K1 | NOTCH2 | PIM1 | RNF43 | SRSF2 | MEF2B |
| ARID2 | BRCA1 | CDK12 | CTNNA1 | FANCC | H3F3A | KDM5C | MAP3K14 | NOTCH3 | PLCG1 | RUNX1 | STAG2 |  |
| ASXL1 | BRCA2 | CDK4 | CTNNB1 | FANCD2 | HNF1A | KDM6A | MAPK1 | NPM1 | POLD1 | SDHB | STAT3 |  |
| ATM | BTK | CDK6 | CUX1 | FANCE | HOXB13 | KDR | MCL1 | NRAS | POLE | SETBP1 | STK11 |  |
| ATRX | CALR | CDKN2A | CXCR4 | FANCF | HSP90AA1 | KEAP1 | MDM2 | NSD1 | PPM1D | SETD2 | TERT |  |
| B2M | CARD11 | CDKN2B | DDR2 | FANCG | IDH1 | KIT | MDM4 | PALB2 | PPP2R1A | SF3B1 | TET2 |  |

**References:**

1. Rogers A, Joe Y, Manshouri T, Dey A, Jilani I, Giles F, Estey E, Freireich E, Keating M, Kantarjian H, Albitar M. Relative increase in leukemia-specific DNA in peripheral blood plasma from patients with acute myeloid leukemia and myelodysplasia. Blood. 2004;103:2799–801.

2. Nakamura S, Yokoyama K, Shimizu E, Yusa N, Kondoh K, Ogawa M, Takei T, Kobayashi A, Ito M, Isobe M, Konuma T, Kato S, Kasajima R, Wada Y, Nagamura-Inoue T, Yamaguchi R, Takahashi S, Imoto S, Miyano S, Tojo A. Prognostic impact of circulating tumor DNA status post-allogeneic hematopoietic stem cell transplantation in AML and MDS. Blood. 2019 Jun 20;133(25):2682-2695. doi: 10.1182/blood-2018-10-880690.

3. Paul Yeh, Michael Dickinson, Sarah Ftouni, Tane Hunter, Devbarna Sinha, Stephen Q. Wong, Rishu Agarwal, Ravikiran Vedururu, Kenneth Doig, Chun Yew Fong, Piers Blombery, David Westerman, Mark A. Dawson and Sarah-Jane Dawson. Molecular disease monitoring using circulating tumor DNA in myelodysplastic syndromes. Blood. 2017;129(12):1685-1690.

4. Albitar A, Ma W, DeDios I, Estella J, Ahn I, Farooqui M, Wiestner A, Albitar M. Using high-sensitivity sequencing for the detection of mutations in BTK and PLCγ2 genes in cellular and cell-free DNA and correlation with progression in patients treated with BTK inhibitors. Oncotarget. 2017 Mar 14;8(11):17936-17944. doi: 10.18632/oncotarget.15316. PMID: 28212557

5. Albitar F, Ma W, Diep K, De Dios I, Agersborg S, Thangavelu M, Brodie S, Albitar M. Deep Sequencing of Cell-Free Peripheral Blood DNA as a Reliable Method for Confirming the Diagnosis of Myelodysplastic Syndrome. Genet Test Mol Biomarkers. 2016 Jul;20(7):341-5. doi: 10.1089/gtmb.2015.0278. PMID: 27248906

6. Aljurf M, Abalkhail H, Alseraihy A, Mohamed SY, Ayas M, Alsharif F, Alzahrani H, Al-Jefri A, Aldawsari G, Al-Ahmari A, Belgaumi AF, Walter CU, El-Solh H, Rasheed W, Albitar M. Chimerism Analysis of Cell-Free DNA in Patients Treated with Hematopoietic Stem Cell Transplantation May Predict Early Relapse in Patients with Hematologic Malignancies. Biotechnol Res Int. 2016;2016:8589270. doi: 10.1155/2016/8589270.

7. Ma W, Kantarjian H, Zhang X, Jilani I, Sheikholeslami MR, Donahue AC, Ravandi F, Estey E, O'Brien S, Keating M, Giles FJ, Albitar M. Detection of nucleophosmin gene mutations in plasma from patients with acute myeloid leukemia: clinical significance and implications. Cancer Biomark. 2009;5(1):51-8. doi: 10.3233/CBM-2009-0583. PMID: 19242062

8. Yeh CH, Tseng R, Albitar M. Plasma-based detection of clonality in lymphoid malignancies. Eur J Haematol. 2009 Jun;82(6):450-3. doi: 10.1111/j.1600-0609.2009.01231.x. PMID: 19187275.

9. Ma W, Kantarjian H, Zhang X, Sun W, Buller AM, Jilani I, Schwartz JG, Giles F, Albitar M. Higher detection rate of JAK2 mutation using plasma. Blood. 2008 Apr 1;111(7):3906-7. doi: 10.1182/blood-2008-02-139188. PMID: 18362222.

10. Giles FJ, Albitar M. Plasma-based testing as a new paradigm for clinical testing in hematologic diseases. Expert Rev Mol Diagn. 2007 Sep;7(5):615-23. Review. PMID: 17892367.

11. Ma W, Tseng R, Gorre M, Jilani I, Keating M, Kantarjian H, Cortes J, O'Brien S, Giles F, Albitar M. Plasma RNA as an alternative to cells for monitoring molecular response in patients with chronic myeloid leukemia. Haematologica. 2007 Feb;92(2):170-5. PMID: 17296565.

12. Ma W, Kantarjian H, Jilani I, Gorre M, Bhalla K, Ottmann O, Giles F, Albitar M. Heterogeneity in detecting Abl kinase mutations and better sensitivity using circulating plasma RNA. Leukemia. 2006 Nov;20(11):1989-91. Epub 2006 Aug 24. PMID: 16932346.

13. Ma W, Jilani I, Gorre M, Keating M, Chan H, Tseng R, Kantarjian H, O'Brien S, Giles FJ, Albitar M. Plasma as a source of mRNA for determining IgV(H) mutation status in patients with chronic lymphocytic leukaemia. Br J Haematol. 2006 Jun;133(6):690-2.

14. Jilani I, Estey E, Manshuri T, Caligiuri M, Keating M, Giles F, Thomas D, Kantarjian H, Albitar M. Better detection of FLT3 internal tandem duplication using peripheral blood plasma DNA. Leukemia. 2003 Jan;17(1):114-9.

15. Kurtz DM, Green MR, Bratman SV, Scherer F, Liu CL, Kunder CA, Takahashi K, Glover C, Keane C, Kihira S, Visser B, Callahan J, Kong KA, Faham M, Corbelli KS, Miklos D, Advani RH, Levy R, Hicks RJ, Hertzberg M, Ohgami RS, Gandhi MK, Diehn M, Alizadeh AA.Noninvasive monitoring of diffuse large B-cell lymphoma by immunoglobulin high-throughput sequencing. Blood. 2015 Jun 11;125(24):3679-87.