JAK2 V617F

- **BCR-ABL genotyping**

General:

The exact chromosomal defect in Philadelphia chromosome is a translocation. Parts of two chromosomes, 9 and 22, switch places. The result is a fusion gene, created by juxtapositioning of a part of the BCR ("breakpoint cluster region") gene from chromosome 22 (region q11) to the Abl1 gene on chromosome 9 (region q34). In agreement with the International System for Human Cytogenetic Nomenclature (ISCN), this chromosomal translocation is designated as t(9;22)(q34;q11). Abl stands for "Abelson", the name of a leukemia virus which carries a similar protein.

The presence of this translocation is a highly sensitive marker for CML, since 95% of the patients with CML show this abnormality. However, the presence of the Philadelphia chromosome is not sufficiently specific to diagnose CML, since it is also found in acute lymphoblastic leukemia (ALL, 25–30% in adult and 2–10% in pediatric cases) and occasionally in acute myelogenous leukemia (AML).

Indication:	clarification CML, B-ALL
Material:	4 x 2.5 ml blood in PAX Gene tubes
Preanalytics:	PAX Gene tubes are highly recommended for dispatch! Please order in advance. Store at ambient temperature (Do not freeze!)
TAT:	2 weeks*
Method:	PCR
Ref.- range:	negative

- **BCR-ABL quantification/monitoring**

General:

By measuring the gene expression of the BCR-ABL fusion gene it is possible to monitor the success of the chemotherapy of BCR-ABL positive patients. The qPCR-technology is very sensitive and is, therefore, able to detect molecular relapses at a very low level of disease (MRD). Generally accepted guidelines recommend the monitoring every three months.

Indication:	monitoring of therapy
Material:	4 x 2.5 ml blood in PAX Gene tubes
Preanalytics:	PAX Gene tubes are highly recommended for dispatch! Please order in

advance. Store at ambient temperature (Do not freeze!)

TAT: 2 weeks*

Method: PCR

- **BCR-ABL mutation screening after resistance to therapy**

General:

Patients treated with Glivec can develop mutations in the BCR-ABL fusion gene (e.g. in the active center of the ABL part) which can result in a resistance to therapy. A resistance leads to a progression of the disease. This specifically designed screening can detect mutations at a very low level of disease.

Indication: resistance to the Glivec therapy

Material: 4 x 2.5 ml blood in PAX Gene tubes

Preanalytic: PAX Gene tubes are highly recommended for dispatch! Please order in advance. Store at ambient temperature (Do not freeze!)

TAT: 2 weeks, Germany

Method: sequencing

- **JAK2-V617F mutation**

General:

Janus kinase 2 (commonly called JAK2) has been implicated in signaling by members of the type II cytokine receptor family (e.g. interferon receptors), the GM-CSF receptor family (IL-3R, IL-5R and GM-CSF-R), the gp130 receptor family (e.g. IL-6R), and the single chain receptors.

JAK2 signaling is activated downstream from the prolactin receptor. JAK2 gene fusions with the TEL(ETV6) (TEL-JAK2) and PCM1 genes have been found in leukemia patients. Furthermore, mutations in JAK2 have been implicated in polycythemia vera, essential thrombocythemia, and other myelo-proliferative disorders.

The mutation changes a valine into phenylalanine at position 167 and appears to make hematopoietic cells more sensitive to growth factors such as erythropoietin and thrombopoietin.

Indication: risk of Philadelphia negative myeloproliferative syndrome

Material: 10 ml EDTA blood

Preanalytics: Blood shipment at ambient temperature (Do not freeze!)

TAT: 2 weeks*

Method: PCR

- **JAK2-V617F quantification**

General:

see above, JAK2-V617 mutation

Indication: monitoring of therapy, support of the prognosis
Material: 10 ml EDTA blood
Preanalytics: Blood shipment at ambient temperature (Do not freeze!)
TAT: 2 weeks*
Method: PCR

- **JAK2 misc. mutations Exon 12**

General:

see above, JAK2

Indication: risk of polycythemia vera, Jak2 negative
Material: 10 ml EDTA blood
Preanalytics: Blood shipment at ambient temperature (Do not freeze!)
TAT: 2 weeks*
Method: PCR

- **PRV-1 mRNA expression**

General:

Polycythemia rubra vera–1 (PRV-1) is a GPI-linked protein that is expressed on a subgroup of neutrophils. The number of PRV-1–expressing neutrophils increases in pregnancy and sepsis, or after administration of granulocyte colony-stimulating factor. Expression of the PRV-1 gene is also increased in patients with polycythemia vera (PV, 95 %) and essential thrombocythemia (ET, 50 %) and primitive myelofibrosis (PMF, 50%).

Indication: risk of myleoproliferative syndrome
Material: 40 ml EDTA blood
Preanalytics: Blood shipment at ambient temperature (Do not freeze, do no cool!), blood should be in the lab 48h after extraction!!!
TAT: 2 weeks*
Method: qPCR

- **MPL- (W515L/K) mutation**

General:

The MPL (W515L and W515K) mutations have been detected in granulocytes of patients suffering from certain types of primitive myelofibrosis (PMF). It is still unknown whether this molecular event is also present in lymphoid cells and therefore potentially at the hematopoietic stem cell (HSC) level.

Indication:	risk of primitive myelofibrosis, Jak2 negative essential thrombocythemia.
Material:	10 ml EDTA blood
Preanalytics:	Blood shipment at ambient temperature (Do not freeze!)
TAT:	2 weeks*
Method:	PCR

- **c-Kit- (D816V) mutation**

General:

The receptor tyrosine kinase c-Kit plays a critical role in hematopoiesis, and gain-of-function mutations of the receptor are frequently seen in several malignancies, including acute myeloid leukemia, gastrointestinal stromal tumors, and testicular carcinoma. The most common mutation of c-Kit in these disorders is a substitution of the aspartic acid residue in position 816 to a valine (D816V), leading to constitutive activation of the receptor.

Indication:	risk of systemic mastocytosis
Material:	10 ml EDTA blood
Preanalytics:	Blood shipment at ambient temperature (not frozen!)
TAT:	2 weeks*
Method:	PCR

- **WT1 quantification**

General:

WT1 is a 52- to 54-kda transcription factor, is the gene product of Wilms' tumor 1 (wt1) and a reliable marker for the detection of the presence of leukemic cell clones as well as myelodysplastic syndromes.

Indication:	prognosis of acute lymphatic leukemia, risk management
Material:	4 x 2.5 ml blood in PAX Gene tubes
Preanalytics:	PAX Gene tubes are highly recommended for dispatch ! Please order in

advance. Blood shipment at ambient temperature (do not freeze)
TAT: 2 weeks*
Method: qPCR

- **TET2 mutation (Ten-eleven translocation-2)**
  Indication: Somatic mutations in TET2 occur in about 15% of patients with various myeloid cancers
  Material: 2 ml tissue
  Preanalytics: Blood shipment at ambient temperature (not frozen!)
  TAT: 2 weeks*
  Method: PCR, sequencing of exons 3 to 11

- **FIP1L1-PDGFRA fusion gene**
  Material: 10 ml EDTA blood
  Preanalytics: Blood shipment at ambient temperature (not frozen!)
  TAT: 2 weeks*
  Method: PCR

- **Cytochemical stains (peroxidase, esterase, PAS, ALP)**
  Material: 10 ml EDTA blood
  Preanalytics: Blood shipment at ambient temperature (not frozen!)
  TAT: 2 weeks*
  Method: microscopy

- **Immunophenotyping (lymphocyte differentiation, ZAP-70)**
  Material: 10 ml EDTA blood or bone marrow blood
  Preanalytics: Blood shipment at ambient temperature (not frozen!)
  TAT: 2 weeks*
  Method: Flow cytometry

For complete list of laboratory test offered at Freiburg Medical Laboratory, please visit http://www.fml-dubai.com/parameter-listings/