

MLL Münchner Leukämie Labor GmbH
 Max-Lebsche-Platz 31
 81377 München
 Postfach 20 14 53, 80014 München

T: +49 (0)89 99017-0
 F: +49 (0)89 99017-111
 info@mll.com
 www.mll.com

MLL MVZ GmbH
 Medizinisches Versorgungszentrum
 für Innere Medizin, Hämatologie und
 Internistische Onkologie

T: +49 (0)89 99015-0
 F: +49 (0)89 99015-111
 info@mll-mvz.com
 www.mll-mvz.com



Akkreditiert:
 DIN EN ISO/IEC 17025



Akkreditiert:
 DIN EN ISO 15189

Prof. Dr. med. Dr. phil. Torsten Haferlach, Prof. Dr. med. Wolfgang Kern, Prof. Dr. med. Claudia Haferlach

Request form

Material Reception: Monday to Saturday,
 Sunday after telephone
 registration

Shipping: If possible by 24h Express,
 for shipping on Friday please
 order **Saturday delivery** from
 the courier service

Required test material:

- **Chromosome analysis:** 5 ml **heparin** bone marrow (500 I.E. Hep./ml bone marrow, **no** EDTA/citrate, in exceptional cases heparin blood)
- **Cytomorphology:** 4-6 unstained smears of bone marrow and blood each (anticoagulant **EDTA** or **citrate**, **no** heparin)
- **Molecular genetics/Immunophenotyping:** 10 – 15 ml bone marrow/peripheral blood each (EDTA/heparin/citrate)

Name, first name:

Date of Birth:

Sex: female male

Address:

Frame for patient label

- Material:** Bone marrow (10 ml in total)
 Peripheral blood (20 ml in total)

Number of bone marrow smears:
 Number of peripheral blood smears:

- Analysis:** Cytomorphology
 Immunophenotyping (Flow cytometry)
 Chromosome analysis (Cytogenetics)
 FISH
 Molecular genetics (PCR, Mutation analysis, NGS)

Date of material withdrawal:

Time of material withdrawal:

- Initial diagnosis Follow-up
 Study:

or/and (step-by-step) diagnostics according to guidelines/recommendation of the professional societies

- Hemoglobinopathies incl. thalassemias
 (separate request form at www.mll.com/en)

Laboratory

Values:

Blood count

Leukocytes:
 Hemoglobin:
 Thrombocytes:

Differential blood count

/µl Myeloblasts:
 g/dl Promyeloblasts:
 /µl Myelocytes:
 Metamyelocytes:

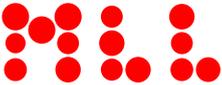
% Band neutrophils:
 % Mature neutrophils:
 % Eosinophiles:
 % Basophiles:

% Monocytes:
 % Lymphocytes:
 %
 %

**(Suspected) Diagnosis,
 other pathological findings:**

**Therapy (incl. previous radio-/
 chemotherapy):**

**Requesting physician (stamp) with
 telephone number and fax number:**



Please send the enclosure to:

MLL MVZ GmbH
Postfach 20 14 53
80014 München

Telefon: +49 (0)89 99017-0
E-Mail: info@mll.com

Patient Consent – MLL Research Projects

I have been informed of the research activities of MLL through MLL's information sheet on data processing and the use of biomaterial as well as the additional information available at www.mll.com. I would like to support the research activities of MLL and consent to the use of my excess biomaterial for research purposes. Based on the information of MLL, I understand that I am donating my biomaterial for research purposes and will not share in any financial proceeds from the research using my biomaterial or health data.

Additional (please tick the box, if desired):

If MLL gains any new medical knowledge about me, I agree that MLL will inform me of this knowledge without prior request.

I may revoke my consent and agreement to be contacted in the case of new knowledge at any time and also separately with effect for the future. Notice of my revocation may be sent by mail to MLL Münchner Leukämielabor GmbH, Max-Lebsche-Platz 31, 81377 Munich, electronically using the email address info@mll.com or by fax to 089-99017111.

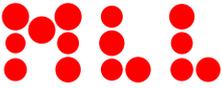
Date, Signature:

First name, Last name:

Date of birth:

Street:

Postal code, City:



MLL Münchner Leukämielabor GmbH
MLL MVZ GmbH

Münchner Leukämielabor (MLL)

Information on Data Processing and the Use of Biomaterial

Münchner Leukämielabor (MLL¹) is a medically and scientifically interdisciplinary practice with a specialized laboratory. MLL focuses on optimized, safe and rapid leukemia diagnostics for a large number of leukemia cases using a comprehensive spectrum of diagnostic methods. Hand in hand with providing medical care to patients from Germany and abroad, the physicians and scientists of MLL are continuously engaged in research with great success in order to improve leukemia diagnostics and the treatment of leukemia. The medical scientific research projects of MLL and its cooperation partners serve to improve the understanding of the origin, development and diagnosis of disease. On this basis, MLL develops new and improved approaches for prevention, care and treatment.

Cooperation and Research. The members of MLL cooperate closely in providing medical care to patients and in medical scientific research. In addition, MLL cooperates with selected institutions in the analysis and research of tissue samples and body fluids (biomaterials) and medical databases. This takes place in the context of scientific studies or projects (research projects) in order to be able to detect, prevent and combat disease better. These research projects are indispensable in order to be able to treat leukemia and other serious diseases even better in the future. Insights gained from the analysis of patient data and biomaterials are extremely important for the further development of diagnostic capabilities and the treatment of disease, including drug therapy.

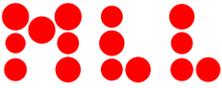
For research projects, MLL uses biomaterial and health data from patients in coordination with the responsible bodies, in particular the responsible independent ethics committee(s). In the context of collaborations, MLL receives expense allowances or fees from public bodies or private cooperation partners, depending on the nature and objective of the research project, for its contributions to the research project.

Processing of Health Data and Biomaterial. When providing medical care to patients and conducting its research activities, MLL processes health data of patients and biomaterial. The biomaterial used for research is obtained from blood samples, biopsies or surgical procedures performed on patients; so-called “excess” biomaterial that is not needed for medical care is used for research.

MLL analyzes health data and biomaterials depending on the request for testing and medical necessity. Health data includes, for example, information arising from the examination and treatment of patients, such as the results of a blood pressure measurement or laboratory tests, but above all also genetic data of patients. In particular, MLL analyzes combinations (chromosomes) and components (nucleic acids) of genetic material specifically for genetic changes in blood or bone marrow cells.

MLL stores all health data in a protected database. Likewise, MLL securely stores biomaterials (tissue samples and body fluids) of its patients. The quality-controlled and state-of-the-art long-term storage of biomaterials takes place in biobanks and archives of MLL.

¹ “MLL” includes: MLL Münchner Leukämielabor GmbH, MLL MVZ GmbH, MLLI GmbH and MLL Dx GmbH, all in Munich, Max-Lebsche-Platz 31; only MLL MVZ GmbH practices „medicine“ within the meaning of medical patient care.



MLL Münchner Leukämie Labor GmbH
MLL MVZ GmbH

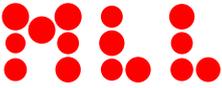
Identity Protection of Patients. Not only during the course of medical treatment, but also in the context of research projects, MLL processes and protects personal data and biomaterial in such a way that reference to a patient can only be established by using special information keys, which MLL keeps safe and protects against access by third parties, for example, by assigning a specific allocation code and storing personally identifiable data separately. Because only MLL has the corresponding allocation key, MLL is still able to provide medical treatment without MLL's cooperation partners or others being able to identify patients. This also applies in particular for research partners in the medical or pharmaceutical industry who would like to engage MLL to conduct medical research studies or use MLL's patient research data to develop diagnostic methods or drugs. Scientific publications of MLL and its cooperation partners are made exclusively in a form that does not allow for any conclusions to be drawn about individual persons.

However, it is possible that in the course of further analyzing health data and biomaterial, chromosomal characteristics may be discovered that may be relevant for both the patient's medical care and that of his or her descendants. Patients can decide whether they would like to be actively contacted in the case of such new findings.

Use of Biomaterial and Health Data for Research with the Consent of Patients. Excess biomaterial and health data, especially genetic data, are - as described - of great importance for medical scientific research projects. Our patients decide whether they want to give excess biomaterial to MLL so that it can be used for research. With the patient's consent, the biomaterial becomes the property of MLL and is retained by MLL for a time period during which the material may be useful for research to a reasonable extent. The biomaterial is used for MLL's own research and is made available to third parties for research purposes. Consenting patients "donate" excess biomaterial and data for scientific research. Patients do not receive any financial consideration for their consent even if the research results are used commercially (e.g., by selling newly developed drugs or diagnostic procedures). Patients who do not give their consent naturally do not suffer any disadvantages in terms of their medical care provided by MLL.

MLL processes patients' health data for research purposes, applying the privileges granted by law, in particular by data protection law, in the interests of further developing the diagnosis and treatment of disease as described above.

Further Information. Our patients can find more detailed information about MLL on the website <https://www.mll.com/datenschutz.html>. The above explanations together with further information on the processing of patient data can be found on the website through which MLL provides information on the processing of patient data in accordance with the applicable data protection regulations. The data protection information is also available in the reception area of MLL.



Supplemental order form: Fluorescence in situ hybridization

Material:

Depending on the respective disease, bone marrow and/or peripheral blood can be used. In case of normal cellularity 2 – 3 ml bone marrow or 10 ml peripheral blood are sufficient. EDTA or heparin should be used as stabilizer. Already prepared, not fixed, unstained smears can be examined as well.

Analyses:

The analyses offered are oriented towards recommendations according to the GenQA guidelines (Rack et al., Leukemia 2019) and the current scientific literature (further information and references at mll.com). Depending on the respective disease we carry out step-wise diagnostics as appropriate.

Acute myeloid leukemia (AML)

Recurrent genetic abnormalities (WHO 2022)

- | | |
|--|--|
| <input type="checkbox"/> PML::RARA rearrangement / t(15;17)(q24;q21) | <input type="checkbox"/> MECOM (EVI1) rearrangement (3q26) |
| <input type="checkbox"/> RUNX1::RUNX1T1 rearrangement / t(8;21)(q22;q22) | <input type="checkbox"/> DEK::NUP214 rearrangement / t(6;9)(p23;q34) |
| <input type="checkbox"/> CBFβ::MYH11 rearrangement / inv(16)(p13q22)/t(16;16)(p13;q22) | <input type="checkbox"/> BCR::ABL1 rearrangement / t(9;22)(q34;q11) |
| <input type="checkbox"/> KMT2A (MLL) rearrangement (11q23) | <input type="checkbox"/> NUP98 rearrangement (11p15) |

Additional abnormalities with prognostic relevance (Döhner et al. Blood, 2022; Grimwade et al. Blood, 2016)

- | | |
|--|--|
| <input type="checkbox"/> 5q31 deletion (CDC25C, EGR1) | <input type="checkbox"/> Validation of other abnormalities detected by chromosome analysis as a baseline for follow-up controls, e.g. trisomy 8, 12p deletion, trisomy 13, 20q deletion etc. |
| <input type="checkbox"/> 5q33 deletion (RPS14) | |
| <input type="checkbox"/> 7q31 deletion bzw. Monosomie 7 (D7S486, cen7) | |
| <input type="checkbox"/> 17p13 deletion (TP53) | |

Myelodysplastic neoplasms (MDS)

Abnormalities with relevance for diagnosis and prognostic risk classification according to IPSS-R (Greenberg et al. Blood, 2012, Schanz et al. JCO, 2012)

- | | |
|--|--|
| <input type="checkbox"/> 5q31 deletion (CDC25C, EGR1) | <input type="checkbox"/> 20q12 deletion (D20S108) |
| <input type="checkbox"/> 5q33 deletion (RPS14) | <input type="checkbox"/> Y-loss (cenY) |
| <input type="checkbox"/> 7q31 deletion bzw. Monosomie 7 (D7S486, cen7) | <input type="checkbox"/> Validation of other abnormalities detected by chromosome analysis as a baseline for follow up controls, e.g. 1q gain, 11q deletion, 12p deletion, trisomy 19 etc. |
| <input type="checkbox"/> Trisomy 8 (cen8) | |
| <input type="checkbox"/> 17p13 deletion (TP53) | |

Cytogenetically cryptic abnormalities

- | | |
|--|---|
| <input type="checkbox"/> 4q24 deletion (TET2) | <input type="checkbox"/> 21q22 deletion (RUNX1) |
| <input type="checkbox"/> 7q36 deletion (EZH2) | |
| <input type="checkbox"/> 12p13 deletion (ETV6) | |

Aplastic anemia (AA)

- | | |
|---|---|
| <input type="checkbox"/> 13q14 deletion (DLEU) | <input type="checkbox"/> 7q31 deletion or monosomy 7 (D7S486, cen7) |
| <input type="checkbox"/> 17p13 deletion (TP53) | <input type="checkbox"/> Trisomy 8 (cen8) |
| <input type="checkbox"/> Trisomy 6 (6q21 / SEC63, 6q23 / MYB) | <input type="checkbox"/> Trisomy 21 (21q22 / RUNX1) |

Myelodysplastic/myeloproliferative neoplasms (MDS/MPN)

- | | |
|---|---|
| <input type="checkbox"/> 7q31 deletion or monosomy 7 (D7S486, cen7) | <input type="checkbox"/> 13q14 deletion (DLEU) |
| <input type="checkbox"/> Trisomy 8 (cen8) | <input type="checkbox"/> 20q12 deletion (D20S108) |
| <input type="checkbox"/> 17p13 deletion (TP53) | <input type="checkbox"/> Trisomy 21 (21q22 / RUNX1) |

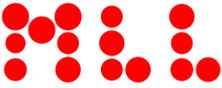
Chronic myelomonocytic leukemia (CMML)

Prognostically relevant abnormalities

- | |
|---|
| <input type="checkbox"/> 7q31 deletion or monosomy 7 (D7S486, cen7) |
| <input type="checkbox"/> Trisomy 8 (cen8) |

Cytogenetically cryptic abnormalities

- | |
|--|
| <input type="checkbox"/> ETV6 rearrangement or ETV6-Deletion (12p13) |
| <input type="checkbox"/> 4q24 deletion (TET2) |
| <input type="checkbox"/> 17q11 deletion (NF1) |



Supplemental order form: Fluorescence in situ hybridization

Chronic myeloid leukemia (CML)

Diagnosis

- BCR::ABL1 rearrangement / t(9;22)(q34;q11)

High-risk additional aberrations according to ELN 2020 (Hochhaus et al. Leukemia, 2020)

- | | |
|---|--|
| <input type="checkbox"/> MECOM (EVI1) rearrangement (3q26) | <input type="checkbox"/> Isochromosome 17q (17p13 / TP53 deletion, 17q11 / NF1 gain) |
| <input type="checkbox"/> Trisomy 8 (cen 8) | <input type="checkbox"/> Trisomy 19 (19p13 / ZNF44+ZNF443, 19q13 / BICRA+NOP53) |
| <input type="checkbox"/> 7q31 deletion or monosomy 7 (D7S486, cen7) | <input type="checkbox"/> KMT2A (MLL) rearrangements (11q23) |

Myeloproliferative neoplasms (MPN)

- | | |
|---|---|
| <input type="checkbox"/> BCR::ABL1 rearrangement / t(9;22)(q34;q11) | <input type="checkbox"/> Trisomy 9 (cen9) |
| <input type="checkbox"/> Trisomy 1 or 1q gain (1p32 / CDKN2C, 1q21 / CKS1B) | <input type="checkbox"/> 4q24 deletion (TET2) |
| <input type="checkbox"/> Trisomy 8 (cen8) | <input type="checkbox"/> 20q12 deletion (D20S108) |

Hypereosinophilia (HE, HES)

Myeloid/lymphoid neoplasms with eosinophilia and gene rearrangements

- | | |
|---|---|
| <input type="checkbox"/> CHIC2 deletion (4q12, correlate to FIP1L1::PDGFRA rearrangement) | <input type="checkbox"/> FGFR1 rearrangement (8p11) |
| <input type="checkbox"/> other PDGFRA rearrangements (4q12) | <input type="checkbox"/> JAK2 rearrangement (9p24) |
| <input type="checkbox"/> PDGFRB rearrangement (5q32-33) | <input type="checkbox"/> ETV6 rearrangement (12p13) |

Blastic plasmacytoid dendritic cell neoplasm (BPDCN)

- | | |
|--|---|
| <input type="checkbox"/> 5q31 deletion (CDC25C / EGR1) | <input type="checkbox"/> 13q14 deletion (DLEU) |
| <input type="checkbox"/> 9p21 deletion (CDKN2A) | <input type="checkbox"/> 17p13 deletion (TP53) |
| <input type="checkbox"/> 12p13 deletion (CDKN1B) | <input type="checkbox"/> MYC rearrangement (8q24) |

Acute lymphoblastic leukemia (ALL): B-cell line

Diagnostically and prognostically relevant abnormalities according to WHO 2022

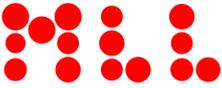
- | | |
|--|---|
| <input type="checkbox"/> BCR::ABL1 rearrangement / t(9;22)(q34;q11) | <input type="checkbox"/> TCF3 (E2A)::PBX1 rearrangement / t(1;19)(q23;p13) |
| <input type="checkbox"/> KMT2A (MLL) rearrangement (11q23) | <input type="checkbox"/> RUNX1 amplifications (iAMP21) / further RUNX1 rearrangements (21q22) |
| <input type="checkbox"/> ETV6::RUNX1 rearrangement / t(12;21)(p13;q22) | <input type="checkbox"/> MYC rearrangement (8q24) |
| <input type="checkbox"/> Polysomies 4, 10, 13, 14, 17 und 21 (hochhyperdiploider Karyotyp) | <input type="checkbox"/> 9p21 deletion (CDKN2A) |
| <input type="checkbox"/> Monosomies 3, 7, 9, 13 und 17 (hypodiploider Karyotyp) | |
| <input type="checkbox"/> IGH rearrangement (14q32) | |

„Philadelphia-like“ ALL

- | | |
|--|---|
| <input type="checkbox"/> CRLF2 rearrangement (Xp22 / Yp11) | <input type="checkbox"/> JAK2 rearrangement (9p24) |
| <input type="checkbox"/> P2RY8 rearrangement (Xp22 / Yp11) | <input type="checkbox"/> ETV6 rearrangement (12p13) |
| <input type="checkbox"/> PDGFRB rearrangement (5q32-33) | |

Acute lymphoblastic leukemia (ALL): T-cell line

- | | |
|--|--|
| <input type="checkbox"/> TRA/D rearrangement (14q11) | <input type="checkbox"/> KMT2A (MLL) rearrangement (11q23) |
| <input type="checkbox"/> TRB rearrangement (7q34) | <input type="checkbox"/> 6q21/6q23 deletion (SEC63 / MYB) |
| <input type="checkbox"/> TLX3 rearrangement (5q35) | <input type="checkbox"/> 9p21 deletion (CDKN2A) |
| <input type="checkbox"/> TLX1 rearrangement (10q24) | <input type="checkbox"/> Monosomy 7 (cen7) |



Supplemental order form: Fluorescence in situ hybridization

Highly malignant mature B-cell neoplasms, diffuse large B-cell lymphoma (DLBCL)

- | | |
|---|--|
| <input type="checkbox"/> <i>IGH::BCL2</i> rearrangement / t(14;18)(q32;q21) | <input type="checkbox"/> <i>MYC</i> rearrangement (8q24) |
| <input type="checkbox"/> <i>IGH::MYC</i> rearrangement / t(8;14)(q24;q32) | <input type="checkbox"/> 13q14 deletion (<i>DLEU</i>) |
| <input type="checkbox"/> <i>BCL6</i> rearrangement (3q27) | <input type="checkbox"/> 17p13 deletion (<i>TP53</i>) |

CD5-negative mature B-cell neoplasms

- | | |
|--|---|
| <input type="checkbox"/> 6q deletion (<i>SEC63</i> / 6q21, <i>MYB</i> / 6q23) | <input type="checkbox"/> Trisomy 12 (cen12) |
| <input type="checkbox"/> 3q gain (<i>BCL6</i> / 3q27) | <input type="checkbox"/> Trisomy 18 or <i>IGH::BCL2</i> rearrangement / t(14;18)(q32;q21) |
| <input type="checkbox"/> 11q deletion (<i>ATM</i> / 11q22) | <input type="checkbox"/> (<i>IGH</i> / 14q32, <i>BCL2</i> / 18q21) |
| <input type="checkbox"/> 17p13 deletion (<i>TP53</i>) | <input type="checkbox"/> 7q deletion (<i>D7S486</i> / 7q31) |
| <input type="checkbox"/> 13q deletion (<i>DLEU</i> / 13q14) | |

Mantle cell lymphoma (MCL)

- | |
|--|
| <input type="checkbox"/> <i>IGH::CCND1</i> rearrangement / t(11;14)(q13;q32) |
| <input type="checkbox"/> 17p13 deletion (<i>TP53</i>) |
| <input type="checkbox"/> 9p21 deletion (<i>CDKN2A</i>) |

Chronic lymphocytic leukemia (CLL)

Diagnosis

- | |
|---|
| <input type="checkbox"/> <i>IGH::CCND1</i> rearrangement / t(11;14)(q13;q32) |
| <input type="checkbox"/> <i>IGH::BCL2</i> rearrangement / t(14;18)(q32;q21) |
| <input type="checkbox"/> <i>IGH</i> rearrangement independent of partner gene (14q32) |

Prognosis

- | | |
|---|--|
| <input type="checkbox"/> 11q22 deletion (<i>ATM</i>) | <input type="checkbox"/> 13q14 deletion (<i>D13S319</i> / <i>D13S25</i>) |
| <input type="checkbox"/> 13q14 deletion (<i>RB1</i>) | <input type="checkbox"/> 17p13 deletion (<i>TP53</i>) |
| <input type="checkbox"/> 13q14 deletion (<i>DLEU</i>) | <input type="checkbox"/> Trisomy 12 (cen12) |

Waldenström's Macroglobulinemia

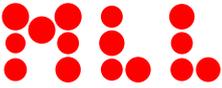
- | | |
|--|--|
| <input type="checkbox"/> 3q-gain (<i>BCL6</i> / 3q27) | <input type="checkbox"/> 11q deletion (<i>ATM</i> / 11q22) |
| <input type="checkbox"/> Trisomy 4 (4q12 / 4q24) | <input type="checkbox"/> 13q deletion (<i>DLEU</i> / 13q14) |
| <input type="checkbox"/> 6q deletion (<i>SEC63</i> / 6q21, <i>MYB</i> / 6q23) | <input type="checkbox"/> 17p13 deletion (<i>TP53</i>) |
| <input type="checkbox"/> 8q gain (<i>MYC</i> / 8q24) | <input type="checkbox"/> Trisomy 18 (<i>BCL2</i> / 18q21) |

Persistent polyclonal B-cell lymphocytosis (PPBL)

- | |
|---|
| <input type="checkbox"/> 3q-gain (<i>BCL6</i> / 3q27) |
| <input type="checkbox"/> 8q-gain (<i>MYC</i> / 8q24) |
| <input type="checkbox"/> <i>IGH::BCL2</i> rearrangement / t(14;18)(q32;q21) |

Mature T-cell neoplasms (T-NHL)

- | | |
|---|---|
| <input type="checkbox"/> <i>TRA/D</i> rearrangement (14q11) | <input type="checkbox"/> 8q24-gain (<i>MYC</i>) |
| <input type="checkbox"/> <i>TRB</i> rearrangement (7q34) | <input type="checkbox"/> 6q21 / 6q23 deletion (<i>SEC63</i> / <i>MYB</i>) |
| <input type="checkbox"/> 11q22 deletion (<i>ATM</i>) | <input type="checkbox"/> <i>ALK</i> rearrangement (2p23) |
| <input type="checkbox"/> 17p13 deletion (<i>TP53</i>) | |



Supplemental order form: Fluorescence in situ hybridization

T-prolymphocytic leukemia

- | | |
|--|---|
| <input type="checkbox"/> <i>TRA/D</i> rearrangement (14q11) | <input type="checkbox"/> 11q22 deletion (<i>ATM</i>) |
| <input type="checkbox"/> <i>TCL1A (TCL1)</i> rearrangement (14q32) | <input type="checkbox"/> 17p13 deletion (<i>TP53</i>) |
| <input type="checkbox"/> 8q24 gain (<i>MYC</i>) | |

T-prolymphocytic leukemia

- | | |
|--|---|
| <input type="checkbox"/> 11q22 deletion (<i>ATM</i>) | <input type="checkbox"/> 6q21 / 6q23 deletion (<i>SEC63 / MYB</i>) |
| <input type="checkbox"/> 11q23 deletion (<i>KMT2A</i>) | <input type="checkbox"/> Abnormalities affecting chromosome 7 (7q31 / D7S486, cen7) |
| <input type="checkbox"/> 13q14 deletion (<i>DLEU</i>) | <input type="checkbox"/> Trisomy 8 (cen8) |
| <input type="checkbox"/> 17p13 deletion (<i>TP53</i>) | |

Multiple Myeloma

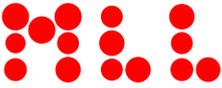
(FISH after enrichment of CD138+ cell fraction by „Magnet Activated Cell Sorting“/MACS)

Diagnostic and prognostic panel (according to EMN/Caers et al. *Haematologica*, 2018)

- | | |
|---|--|
| <input type="checkbox"/> 17p13 deletion (<i>TP53</i>) | <input type="checkbox"/> 1p32 deletion / 1q21 gain (<i>CDKN2C, CKS1B</i>) |
| <input type="checkbox"/> <i>IGH::FGFR3</i> rearrangement / t(4;14)(p16;q32) | <input type="checkbox"/> <i>IGH::CCND1</i> rearrangement / t(11;14)(q13;q32) |
| <input type="checkbox"/> <i>IGH::MAF</i> rearrangement / t(14;16)(q32;q23) | <input type="checkbox"/> <i>IGH::MAFB</i> rearrangement / t(14;20)(q32;q12) |

Further recurrent abnormalities in plasma cell neoplasms

- | | |
|---|---|
| <input type="checkbox"/> <i>IGH</i> rearrangement independent of partner gene (14q32) | <input type="checkbox"/> Trisomy 9 (cen9) |
| <input type="checkbox"/> <i>IGH::CCND3</i> rearrangement / t(6;14)(p21;q32) | <input type="checkbox"/> Trisomy 11 (cen11) |
| <input type="checkbox"/> <i>IGH::MYC</i> rearrangement / t(8;14)(q24;q32) | <input type="checkbox"/> Trisomy 5 (5p15 / <i>CDC25C, 5q31 / EGR1</i>) |
| <input type="checkbox"/> <i>MYC</i> rearrangement (8q24) independent of partner gene | <input type="checkbox"/> Trisomy 19 (19p13 / <i>ZNF44+ZNF443, 19q13 / BICRA+NOP53</i>) |
| <input type="checkbox"/> 13q14 deletion / monosomy 13 (<i>DLEU</i>) | <input type="checkbox"/> 12p13 deletion (<i>ETV6</i>) |
| <input type="checkbox"/> Trisomy 3 (cen3) | |



Supplemental order form: Molecular genetics

Material:

Depending on the disease, bone marrow and/or blood can be used. 10-15 ml bone marrow or 10-15 ml blood are sufficient in case of normal cellularity. Both EDTA and heparin can be used as stabilizers.

Analyses:

The analyses offered are based on the recommendations of the WHO, the European Leukemia Network and the current scientific literature (further information and references at www.mll.com). Depending on the respective disease, we may carry out step-wise diagnostics.

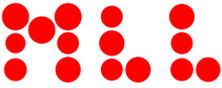
Myeloid neoplasms

Myeloid markers (complete)

- | | | | |
|----------------------------------|-----------------------------------|---------------------------------|--------------------------------|
| <input type="checkbox"/> ASXL1 | <input type="checkbox"/> FBXW7 | <input type="checkbox"/> NRAS | <input type="checkbox"/> SMC3 |
| <input type="checkbox"/> ASXL2 | <input type="checkbox"/> FLT3 | <input type="checkbox"/> PDGFRA | <input type="checkbox"/> SRSF2 |
| <input type="checkbox"/> ATRX | <input type="checkbox"/> FLT3-ITD | <input type="checkbox"/> PDGFRB | <input type="checkbox"/> STAG2 |
| <input type="checkbox"/> BCOR | <input type="checkbox"/> GATA1 | <input type="checkbox"/> PHF6 | <input type="checkbox"/> SUZ12 |
| <input type="checkbox"/> BCORL1 | <input type="checkbox"/> GATA2 | <input type="checkbox"/> PIGA | <input type="checkbox"/> TET2 |
| <input type="checkbox"/> BRAF | <input type="checkbox"/> GNB1 | <input type="checkbox"/> PPM1D | <input type="checkbox"/> TP53 |
| <input type="checkbox"/> CALR | <input type="checkbox"/> IDH1 | <input type="checkbox"/> PRPF8 | <input type="checkbox"/> UBA1 |
| <input type="checkbox"/> CBL | <input type="checkbox"/> IDH2 | <input type="checkbox"/> PTEN | <input type="checkbox"/> U2AF1 |
| <input type="checkbox"/> CEBPA | <input type="checkbox"/> IL6R | <input type="checkbox"/> PTPN11 | <input type="checkbox"/> U2AF2 |
| <input type="checkbox"/> CSF3R | <input type="checkbox"/> JAK2 | <input type="checkbox"/> RAD21 | <input type="checkbox"/> WT1 |
| <input type="checkbox"/> CSNK1A1 | <input type="checkbox"/> KIT | <input type="checkbox"/> RUNX1 | <input type="checkbox"/> ZEB2 |
| <input type="checkbox"/> CUX1 | <input type="checkbox"/> KRAS | <input type="checkbox"/> SETBP1 | <input type="checkbox"/> ZRSR2 |
| <input type="checkbox"/> DDX41 | <input type="checkbox"/> MPL | <input type="checkbox"/> SF1 | |
| <input type="checkbox"/> DNMT3A | <input type="checkbox"/> MYD88 | <input type="checkbox"/> SF3A1 | |
| <input type="checkbox"/> ETV6 | <input type="checkbox"/> NF1 | <input type="checkbox"/> SF3B1 | |
| <input type="checkbox"/> EZH2 | <input type="checkbox"/> NOTCH1 | <input type="checkbox"/> SH2B3 | |
| | <input type="checkbox"/> NPM1 | <input type="checkbox"/> SMC1A | |

Tumor profiling

- Transcriptome analysis (RNA-Seq, detection of fusion transcripts, expression, expression patterns)



Supplemental order form: Molecular genetics

Acute myeloid leukemia (AML)

AML ELN panel (Döhner et al., Blood 2022)

- | | |
|------------------------------------|---------------------------------|
| <input type="checkbox"/> ASXL1 | <input type="checkbox"/> NF1 |
| <input type="checkbox"/> BCOR | <input type="checkbox"/> NPM1 |
| <input type="checkbox"/> BCORL1 | <input type="checkbox"/> NRAS |
| <input type="checkbox"/> BRAF | <input type="checkbox"/> PHF6 |
| <input type="checkbox"/> CBL | <input type="checkbox"/> PPM1D |
| <input type="checkbox"/> CEBPA | <input type="checkbox"/> PTPN11 |
| <input type="checkbox"/> CSF3R | <input type="checkbox"/> RAD21 |
| <input type="checkbox"/> DDX41 | <input type="checkbox"/> RUNX1 |
| <input type="checkbox"/> DNMT3A | <input type="checkbox"/> SETBP1 |
| <input type="checkbox"/> ETV6 | <input type="checkbox"/> SF3B1 |
| <input type="checkbox"/> EZH2 | <input type="checkbox"/> SRSF2 |
| <input type="checkbox"/> FLT3-ITD | <input type="checkbox"/> STAG2 |
| <input type="checkbox"/> FLT3-TKD | <input type="checkbox"/> TET2 |
| <input type="checkbox"/> GATA2 | <input type="checkbox"/> TP53 |
| <input type="checkbox"/> IDH1 | <input type="checkbox"/> U2AF1 |
| <input type="checkbox"/> IDH2 | <input type="checkbox"/> WT1 |
| <input type="checkbox"/> JAK2 | <input type="checkbox"/> ZRSR2 |
| <input type="checkbox"/> KIT | |
| <input type="checkbox"/> KMT2A-PTD | |
| <input type="checkbox"/> KRAS | |

AML/targeted therapy

- FLT3-ITD
 FLT3-TKD
 IDH1
 IDH2

Fusion genes

- CBFβ::MYH11
 DEK::NUP214 (DEK::CAN)
 KMT2A (MLL) translocations
 KMT2A-PTD (MLL-PTD)
 PML::RARA
 RUNX1::RUNX1T1 (AML1::ETO)
 other fusion genes, if cytogenetics is available for corresponding rearrangement
 other:

Quantitative follow-up monitoring (MRD)

- CBFβ::MYH11
 DEK::NUP214 (DEK::CAN)
 FLT3-ITD
 KMT2A (MLL) translocations
 KMT2A-PTD (MLL-PTD)
 NPM1
 PML::RARA
 RUNX1::RUNX1T1 (AML1::ETO)
 other:

Resistance mutations

- BAX mutations in venetoclax resistance
 BCL2 mutations in venetoclax resistance
 IDH2 mutations in enasidenib (IDH2 inhibitor) resistance

Myelodysplastic neoplasms (MDS) and Clonal cytopenia of undetermined significance (CCUS)

Diagnostic and prognostic panel in suspected MDS

incl. base genes „CCUS“/Clonal cytopenia of undetermined significance, according to WHO 2022

incl. base genes IPSS-M-Panel according to Bernard et al.

- | | | | | |
|---------------------------------|-----------------------------------|--------------------------------|---------------------------------|--------------------------------|
| <input type="checkbox"/> ASXL1 | <input type="checkbox"/> ETV6 | <input type="checkbox"/> IDH2 | <input type="checkbox"/> PRPF8 | <input type="checkbox"/> TET2 |
| <input type="checkbox"/> BCOR | <input type="checkbox"/> EZH2 | <input type="checkbox"/> KRAS | <input type="checkbox"/> PTPN11 | <input type="checkbox"/> TP53 |
| <input type="checkbox"/> BCORL1 | <input type="checkbox"/> FLT3 | <input type="checkbox"/> NF1 | <input type="checkbox"/> RUNX1 | <input type="checkbox"/> U2AF1 |
| <input type="checkbox"/> CBL | <input type="checkbox"/> FLT3-ITD | <input type="checkbox"/> NPM1 | <input type="checkbox"/> SETBP1 | <input type="checkbox"/> WT1 |
| <input type="checkbox"/> CEBPA | <input type="checkbox"/> GATA2 | <input type="checkbox"/> NRAS | <input type="checkbox"/> SF3B1 | <input type="checkbox"/> ZRSR2 |
| <input type="checkbox"/> DNMT3A | <input type="checkbox"/> GNB1 | <input type="checkbox"/> PHF6 | <input type="checkbox"/> SRSF2 | |
| <input type="checkbox"/> ETNK1 | <input type="checkbox"/> IDH1 | <input type="checkbox"/> PPM1D | <input type="checkbox"/> STAG2 | |

Supplementary gene panel „CCUS“/Clonal cytopenia of undetermined significance (according to WHO 2022)

- | | | | | |
|--------------------------------|--------------------------------|---------------------------------|--------------------------------|--------------------------------|
| <input type="checkbox"/> BRAF | <input type="checkbox"/> DDX41 | <input type="checkbox"/> MYD88 | <input type="checkbox"/> RAD21 | <input type="checkbox"/> SMC3 |
| <input type="checkbox"/> CALR | <input type="checkbox"/> JAK2 | <input type="checkbox"/> NOTCH1 | <input type="checkbox"/> SF1 | <input type="checkbox"/> U2AF2 |
| <input type="checkbox"/> CSF3R | <input type="checkbox"/> KIT | <input type="checkbox"/> PIGA | <input type="checkbox"/> SF3A1 | <input type="checkbox"/> UBA1 |
| <input type="checkbox"/> CUX1 | <input type="checkbox"/> MPL | <input type="checkbox"/> PTEN | <input type="checkbox"/> SMC1A | |

IPSS-M-Panel (complete) according to Bernard et al. (NEJM Evidence 2022)

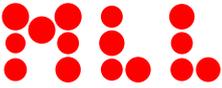
- IPSS-M genes (blood count values, cytogenetics and cytomorphology of the bone marrow are required to complete the IPSS-M! Link to the IPSS-M Web Calculator: <https://mds-risk-model.com>)

MDS with isolated del(5q)

- TP53 (prognostic) CSNK1A1 (10% mutation frequency)

Aplastic anemia (AA)

- BCOR BCORL1 PIGA



Supplemental order form: Molecular genetics

Chronic myelomonocytic leukemia (CMML)

Panel according to ELN/EHA guidelines (Itzykson et al., HemaSphere 2018)

- | | | | |
|---------------------------------------|---|-------------------------------------|--|
| <input type="checkbox"/> ASXL1 | <input type="checkbox"/> FIP1L1::PDGFRA | <input type="checkbox"/> NF1 | <input type="checkbox"/> SRSF2 |
| <input type="checkbox"/> BCOR | <input type="checkbox"/> FLT3-ITD | <input type="checkbox"/> NPM1 | <input type="checkbox"/> TET2 |
| <input type="checkbox"/> BCR::ABL1 | <input type="checkbox"/> FLT3-TKD | <input type="checkbox"/> NRAS | <input type="checkbox"/> U2AF1 |
| <input type="checkbox"/> CBL | <input type="checkbox"/> IDH1 | <input type="checkbox"/> PCM1::JAK2 | <input type="checkbox"/> ZNF198::FGFR1 |
| <input type="checkbox"/> DNMT3A | <input type="checkbox"/> IDH2 | <input type="checkbox"/> RUNX1 | <input type="checkbox"/> ZRSR2 |
| <input type="checkbox"/> ETV6::PDGFRB | <input type="checkbox"/> JAK2 | <input type="checkbox"/> SETBP1 | |
| <input type="checkbox"/> EZH2 | <input type="checkbox"/> KRAS | <input type="checkbox"/> SF3B1 | |

Prognostic panel according to Elena et al. (Blood 2016)

- | | | | |
|--------------------------------|-------------------------------|--------------------------------|---------------------------------|
| <input type="checkbox"/> ASXL1 | <input type="checkbox"/> NRAS | <input type="checkbox"/> RUNX1 | <input type="checkbox"/> SETBP1 |
|--------------------------------|-------------------------------|--------------------------------|---------------------------------|

Myelodysplastic/myeloproliferative neoplasm with neutrophilia (MDS/MPN-N)

- | | | | | |
|--------------------------------|------------------------------|--------------------------------|--------------------------------|---------------------------------|
| <input type="checkbox"/> ASXL1 | <input type="checkbox"/> CBL | <input type="checkbox"/> CSF3R | <input type="checkbox"/> ETNK1 | <input type="checkbox"/> SETBP1 |
|--------------------------------|------------------------------|--------------------------------|--------------------------------|---------------------------------|

Chronic myeloid leukemia (CML)

- | | |
|--|--|
| <input type="checkbox"/> BCR::ABL1 quantification | <input type="checkbox"/> BCR::ABL1 detection |
| <input type="checkbox"/> BCR::ABL1 mutation in case of TKI resistance | <input type="checkbox"/> other: |
| <input type="checkbox"/> BCR::ABL1 mutation in case of Asciminib (ABL001) resistance | |

Polycythaemia vera (PV)

Diagnosis

- | | |
|--------------------------------------|---|
| <input type="checkbox"/> BCR::ABL1 | <input type="checkbox"/> CALR (only if BCR::ABL1/JAK2 negative) |
| <input type="checkbox"/> JAK2 V617F | <input type="checkbox"/> MPL (only if BCR::ABL1/JAK2 negative) |
| <input type="checkbox"/> JAK2 exon12 | |

JAK2-negative erythrocytosis*/polyglobulia (Wouters et al., Blood Advances 2020)

- | | | |
|---------------------------------|--------------------------------|--------------------------------|
| <input type="checkbox"/> ASXL1 | <input type="checkbox"/> EZH2 | <input type="checkbox"/> SRSF2 |
| <input type="checkbox"/> BCOR | <input type="checkbox"/> IDH1 | <input type="checkbox"/> TP53 |
| <input type="checkbox"/> BCORL1 | <input type="checkbox"/> IDH2 | <input type="checkbox"/> TET2 |
| <input type="checkbox"/> DNMT3A | <input type="checkbox"/> SF3B1 | <input type="checkbox"/> U2AF1 |

*If familial erythrocytosis is suspected, refer to the respective panel on page 15 „Hereditary diseases“.

Prognostic panel according to WHO 2022

- | | | |
|--------------------------------|--------------------------------|-------------------------------|
| <input type="checkbox"/> ASXL1 | <input type="checkbox"/> IDH1 | <input type="checkbox"/> IDH2 |
| <input type="checkbox"/> RUNX1 | <input type="checkbox"/> SRSF2 | <input type="checkbox"/> TP53 |

Essential thrombocythaemia (ET)

Diagnosis

- | | | | |
|------------------------------------|-------------------------------|-------------------------------------|-----------------------------------|
| <input type="checkbox"/> BCR::ABL1 | <input type="checkbox"/> CALR | <input type="checkbox"/> JAK2 V617F | <input type="checkbox"/> MPL W515 |
|------------------------------------|-------------------------------|-------------------------------------|-----------------------------------|

Prognostic panel according to WHO 2022

- | | | |
|--------------------------------|--------------------------------|--------------------------------|
| <input type="checkbox"/> ASXL1 | <input type="checkbox"/> RUNX1 | <input type="checkbox"/> SF3B1 |
| <input type="checkbox"/> SRSF2 | <input type="checkbox"/> TP53 | <input type="checkbox"/> U2AF1 |

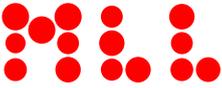
Primary myelofibrosis (PMF)

Diagnosis

- | | | | |
|------------------------------------|-------------------------------|-------------------------------------|-----------------------------------|
| <input type="checkbox"/> BCR::ABL1 | <input type="checkbox"/> CALR | <input type="checkbox"/> JAK2 V617F | <input type="checkbox"/> MPL W515 |
|------------------------------------|-------------------------------|-------------------------------------|-----------------------------------|

Prognostic panel according to Tefferi A. et al, JCO 2018 (MIPSS70+ version 2.0 score)

- | | | |
|--------------------------------|--------------------------------|--------------------------------|
| <input type="checkbox"/> ASXL1 | <input type="checkbox"/> EZH2 | <input type="checkbox"/> IDH1 |
| <input type="checkbox"/> IDH2 | <input type="checkbox"/> SRSF2 | <input type="checkbox"/> U2AF1 |



Supplemental order form: Molecular genetics

Chronic neutrophilic leukemia (CNL)

- CSF3R ASXL1

Myeloproliferative neoplasms (MPN) in general

Diagnosis

- BCR::ABL1 CALR JAK2 V617F MPL W515

MPN-triple-negative panel (if ET/PMF is suspected and after exclusion of classical mutations in JAK2, MPL, CALR)

- | | | |
|---------------------------------|--|--------------------------------|
| <input type="checkbox"/> ASXL1 | <input type="checkbox"/> IDH1 | <input type="checkbox"/> SRSF2 |
| <input type="checkbox"/> BCOR | <input type="checkbox"/> IDH2 | <input type="checkbox"/> TET2 |
| <input type="checkbox"/> BCORL1 | <input type="checkbox"/> JAK2 (entire coding region) | <input type="checkbox"/> TP53 |
| <input type="checkbox"/> DNMT3A | <input type="checkbox"/> MPL (entire coding region) | <input type="checkbox"/> U2AF1 |
| <input type="checkbox"/> EZH2 | <input type="checkbox"/> SF3B1 | |

Hyper eosinophilia (HE, HES)

Myeloid/lymphoid neoplasms with eosinophilia und gene rearrangement

- | | |
|--|--|
| <input type="checkbox"/> FIP1L1::PDGFRA | <input type="checkbox"/> ZNF198::FGFR1 |
| <input type="checkbox"/> PDGFRA expression | <input type="checkbox"/> PCM1::JAK2 |
| <input type="checkbox"/> ETV6::PDGFRB | |

Other clonality markers

- | | |
|---------------------------------------|--|
| <input type="checkbox"/> BCR::ABL1 | <input type="checkbox"/> DNMT3A |
| <input type="checkbox"/> JAK2 V617F | <input type="checkbox"/> SRSF2 |
| <input type="checkbox"/> JAK2 exon 13 | <input type="checkbox"/> TET2 |
| <input type="checkbox"/> KIT D816V | <input type="checkbox"/> STAT5B |
| <input type="checkbox"/> ASXL1 | <input type="checkbox"/> Target search by means of transcriptome analysis (RNA-Seq, detection of fusion transcripts, expression) |

Mastocytosis and SM-AHN (Systemic mastocytosis with an associated hematological neoplasm)

Diagnosis

- KIT D816V
 KIT (complete coding region) (from bone marrow in case of KIT D816V negativity)

Diagnostic panel according to Schwaab et al. (Blood 2014)

- | | | |
|--------------------------------|------------------------------------|--------------------------------|
| <input type="checkbox"/> ASXL1 | <input type="checkbox"/> KIT D816V | <input type="checkbox"/> SRSF2 |
| <input type="checkbox"/> CBL | <input type="checkbox"/> KRAS | <input type="checkbox"/> TET2 |
| <input type="checkbox"/> EZH2 | <input type="checkbox"/> NRAS | <input type="checkbox"/> U2AF1 |
| <input type="checkbox"/> JAK2 | <input type="checkbox"/> RUNX1 | |

Prognostic panel according to Jawhar et al. (Leukemia 2015), Pardanani et al. (Blood Cancer J. 2019) and Muñoz-González et al. (Blood 2019)

- | | | |
|---------------------------------|--------------------------------|--------------------------------|
| <input type="checkbox"/> ASXL1 | <input type="checkbox"/> NRAS | <input type="checkbox"/> SRSF2 |
| <input type="checkbox"/> DNMT3A | <input type="checkbox"/> RUNX1 | |

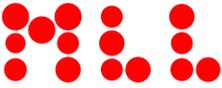
Hereditary alpha-tryptasemia (HaT)

- TPSAB1

Blastic plasmacytoid dendritic cell neoplasm (BPDCN)

Panel according to Menezes et al. (Leukemia 2014)

- | | |
|-----------------------------------|--------------------------------|
| <input type="checkbox"/> ASXL1 | <input type="checkbox"/> NPM1 |
| <input type="checkbox"/> ETV6 | <input type="checkbox"/> NRAS |
| <input type="checkbox"/> EZH2 | <input type="checkbox"/> SRSF2 |
| <input type="checkbox"/> FLT3-ITD | <input type="checkbox"/> TET2 |
| <input type="checkbox"/> FLT3-TKD | <input type="checkbox"/> TP53 |
| <input type="checkbox"/> IDH2 | <input type="checkbox"/> ZRSR2 |
| <input type="checkbox"/> KRAS | |



Supplemental order form: Molecular genetics

Lymphoid neoplasms

Lymphoid markers (complete)

- | | | | |
|---------------------------------|--------------------------------|---------------------------------|----------------------------------|
| <input type="checkbox"/> ARID1A | <input type="checkbox"/> EGR1 | <input type="checkbox"/> KLHL6 | <input type="checkbox"/> RPS15 |
| <input type="checkbox"/> ATM | <input type="checkbox"/> EP300 | <input type="checkbox"/> KMT2D | <input type="checkbox"/> RUNX1 |
| <input type="checkbox"/> ATR | <input type="checkbox"/> ETV6 | <input type="checkbox"/> KRAS | <input type="checkbox"/> SF3B1 |
| <input type="checkbox"/> BCL10 | <input type="checkbox"/> EZH2 | <input type="checkbox"/> MAP2K1 | <input type="checkbox"/> SGK1 |
| <input type="checkbox"/> BCL2 | <input type="checkbox"/> FBXW7 | <input type="checkbox"/> MEF2B | <input type="checkbox"/> SOCS1 |
| <input type="checkbox"/> BIRC3 | <input type="checkbox"/> FLT3 | <input type="checkbox"/> MYC | <input type="checkbox"/> STAT3 |
| <input type="checkbox"/> BRAF | <input type="checkbox"/> FOXO1 | <input type="checkbox"/> MYD88 | <input type="checkbox"/> STAT5B |
| <input type="checkbox"/> BTK | <input type="checkbox"/> FYN | <input type="checkbox"/> NOTCH1 | <input type="checkbox"/> STAT6 |
| <input type="checkbox"/> CARD11 | <input type="checkbox"/> ID3 | <input type="checkbox"/> NOTCH2 | <input type="checkbox"/> TET2 |
| <input type="checkbox"/> CCL22 | <input type="checkbox"/> IDH2 | <input type="checkbox"/> NRAS | <input type="checkbox"/> TNFAIP3 |
| <input type="checkbox"/> CCND1 | <input type="checkbox"/> IKZF1 | <input type="checkbox"/> PAX5 | <input type="checkbox"/> TP53 |
| <input type="checkbox"/> CD28 | <input type="checkbox"/> IL7R | <input type="checkbox"/> PHF6 | <input type="checkbox"/> UBR5 |
| <input type="checkbox"/> CD79B | <input type="checkbox"/> IRF4 | <input type="checkbox"/> PLCG1 | <input type="checkbox"/> VAV1 |
| <input type="checkbox"/> CREBBP | <input type="checkbox"/> JAK1 | <input type="checkbox"/> PLCG2 | <input type="checkbox"/> XPO1 |
| <input type="checkbox"/> CXCR4 | <input type="checkbox"/> JAK2 | <input type="checkbox"/> POT1 | <input type="checkbox"/> ZEB2 |
| <input type="checkbox"/> DIS3 | <input type="checkbox"/> JAK3 | <input type="checkbox"/> PTEN | |
| <input type="checkbox"/> DNMT3A | <input type="checkbox"/> KLF2 | <input type="checkbox"/> RHOA | |

Acute lymphoblastic leukemia (ALL): B-cell line

Diagnosis

- | | |
|--|---|
| <input type="checkbox"/> BCR::ABL1 | <input type="checkbox"/> IKZF1 deletion |
| <input type="checkbox"/> KMT2A::AFF1 (MLL::MLLT2) | <input type="checkbox"/> other translocation: |
| <input type="checkbox"/> KMT2A::MLLT1 (MLL::MLLT1) | <input type="checkbox"/> Establishment of clone-specific markers |
| <input type="checkbox"/> ETV6::RUNX1 (TEL::AML1) | <input type="checkbox"/> Clarification BCR::ABL-like ALL |
| <input type="checkbox"/> TCF3::PBX1 (E2A::PBX1) | <input type="checkbox"/> Target search by means of transcriptome analysis
(RNA-Seq, fusion transcript detection, expression, expression pattern) |

Follow-up (MRD)

- | | |
|---|--|
| <input type="checkbox"/> BCR::ABL1 quantification | <input type="checkbox"/> TCF3::PBX1 (E2A::PBX1) quantification |
| <input type="checkbox"/> KMT2A::AFF1 (MLL::MLLT2) quantification | <input type="checkbox"/> IKZF1 deletion quantification |
| <input type="checkbox"/> KMT2A::MLLT1 (MLL::MLLT1) quantification | <input type="checkbox"/> Clone-specific MRD |
| <input type="checkbox"/> ETV6::RUNX1 (TEL::AML1) quantification | |

Resistance mutations

- BCR::ABL1 mutation in case of TKI-resistance

Acute lymphoblastic leukemia (ALL): T-cell line

Diagnosis/fusion genes

- STIL::TAL1
 PICALM::MLLT10 (CALM::AF10)
 NUP214::ABL1
 SET::NUP214

Diagnosis/molecular markers

- DNMT3A
 NOTCH1
 FBXW7
 RUNX1
 PHF6
 PTEN
 Establishment of clone-specific markers

Follow up (MRD)

- Clone-specific MRD

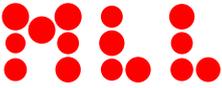
Mature B-cell neoplasms (B-NHL)

Diagnosis

- B-cell receptor rearrangement

Diagnostic panel for differentiation of CD5-negative mature B-cell neoplasms

- | | |
|---------------------------------|---------------------------------|
| <input type="checkbox"/> BRAF | <input type="checkbox"/> MYD88 |
| <input type="checkbox"/> CXCR4 | <input type="checkbox"/> NOTCH2 |
| <input type="checkbox"/> KLF2 | <input type="checkbox"/> TP53 |
| <input type="checkbox"/> MAP2K1 | |



Supplemental order form: Molecular genetics

Mantle cell lymphoma (MCL)

Diagnosis

- | | |
|---|--------------------------------------|
| <input type="checkbox"/> <i>IGH::CCND1 (BCL1::IGH) / t(11;14)</i> | <input type="checkbox"/> <i>TP53</i> |
| <input type="checkbox"/> (Cyclin D1) expression | <input type="checkbox"/> <i>UBR5</i> |
| <input type="checkbox"/> <i>SOX11</i> expression | |

Resistance mutations

- BCL2* mutation in case of Venetoclax resistance

Follicular lymphoma (FL)

Diagnosis

- IGH::BCL2 (BCL2::IGH) / t(14;18)*

Other prognostically relevant genes

- BCL2*
 TP53

Prognosis according to m7-FLIPI-Score (Pastore et al., Lancet Oncology 2016)

- ARID1A*
 CARD11
 CREBBP
 EP300
 EZH2
 FOXO1
 MEF2B

Resistance mutations

- BCL2* mutation in case of Venetoclax resistance

Diffuse large B-cell lymphoma (DLBCL)

Prognosis

- | | | | |
|---------------------------------------|--|---------------------------------------|---------------------------------------|
| <input type="checkbox"/> <i>BCL2</i> | <input type="checkbox"/> <i>KLHL6</i> | <input type="checkbox"/> <i>SGK1</i> | <input type="checkbox"/> <i>STAT6</i> |
| <input type="checkbox"/> <i>CD79B</i> | <input type="checkbox"/> <i>MYD88</i> | <input type="checkbox"/> <i>SOCS1</i> | <input type="checkbox"/> <i>TP53</i> |
| <input type="checkbox"/> <i>FOXO1</i> | <input type="checkbox"/> <i>NOTCH1</i> | <input type="checkbox"/> <i>STAT3</i> | |

Chronic lymphocytic leukemia (CLL)

Panel according to Onkopedia guidelines

- TP53* *IGHV* mutation status

Prognostic panel according to Rossi et al. (Blood 2013)

- BIRC3* *SF3B1*
 NOTCH1 *TP53*

Recurrent mutations

- | | | |
|--|--|---------------------------------------|
| <input type="checkbox"/> <i>IGHV</i> mutation status | <input type="checkbox"/> <i>KRAS</i> | <input type="checkbox"/> <i>SF3B1</i> |
| <input type="checkbox"/> <i>ATM</i> | <input type="checkbox"/> <i>NOTCH1</i> | <input type="checkbox"/> <i>TP53</i> |
| <input type="checkbox"/> <i>BIRC3</i> | <input type="checkbox"/> <i>POT1</i> | |
| <input type="checkbox"/> <i>BRAF</i> | <input type="checkbox"/> <i>RPS15</i> | |

Resistance mutations

- BTK* mutation in case of Ibrutinib resistance
 PLCG2 mutation in case of Ibrutinib resistance
 BCL2 mutation in case of Venetoclax resistance

Waldenström's Macroglobulinemia

- CXCR4* *MYD88*

Splenic marginal zone lymphoma (SMZL)

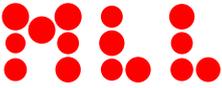
- NOTCH2* *KLF2* *TP53*

Hairy cell leukemia

- BRAF V600E*

Multiple myeloma

- BRAF* *KRAS* *NRAS* *TP53*



Supplemental order form: Molecular genetics

Mature T-cell neoplasms (T-NHL)

- T-cell receptor rearrangement

T-LGL-leukemia and NK-LGL-leukemia/chronic lymphoproliferative disorders of NK-cells (CLPD-NK)

- STAT3 STAT5B CCL22 TET2

Differentiation of peripheral T-cell lymphomas (PTCL)

- CCL22 IDH2 STAT3 VAV1
 CD28 PLCC1 STAT5B
 FYN RHOA TET2

Chimerism analysis

- Before allogeneic stem cell transplantation
 Donor
 After allogeneic stem cell transplantation

Hereditary diseases

In the following analyses, genes, in which mutations occur constitutionally, are examined (germline mutations) in the indicated diseases.

Myeloid neoplasms with germline predisposition without a pre-existing disorder or organ dysfunction

- AML with germline CEBPA mutation
 Myeloid neoplasms with germline DDX41 mutation*

Myeloid neoplasms with germline predisposition and pre-existing platelet disorders

- Myeloid neoplasms with germline RUNX1 mutation*
 Myeloid neoplasms with germline ANKRD26 mutation*
 Myeloid neoplasms with germline ETV6 mutation*

Other myeloid neoplasms with germline predisposition

- Myeloid neoplasms with germline GATA2 mutation
 Myeloid neoplasms associated of telomere biology disorders and mutations in the genes TERT and TERC

Familial erythrocytoses – basic screening

- BPGM EPAS1 JAK2 (entire coding region)
 EGLN1 EPOR VHL

Familial erythrocytosis - extended screening according to Camps et al. (Haematologica 2016)

- BHLHE41 EPOR HIF3A
 BPGM GFI1B JAK2 (entire coding region)
 EGLN1 HBA1 KDM6A
 EGLN2 HBA2 OS9
 EGLN3 HBB SH2B3
 EPAS1 HIF1A VHL
 EPO HIF1AN ZNF197

Hereditary hemochromatosis

- HFE - p.(Cys282Tyr) and p.(His63Asp)

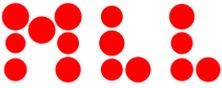
Hereditary alpha-tryptasemia (HaT)

- TPSAB1

Cyclic neutropenia

- ELANE

* Known in lymphoid neoplasms as well.



MLL Münchner Leukämie Labor GmbH
MLL MVZ GmbH

Supplemental order form: Immunophenotyping

Material:

Immunophenotyping can be performed on peripheral blood and bone marrow aspirate as well as other liquid sample material such as effusion fluids. For sole immunophenotyping, each anticoagulant is suitable, for further analyses see the main order form.

Analyses:

In addition to classical suspected diagnoses and indications (mature B-cell neoplasms incl. CLL, acute leukemia, detection/exclusion of immature cells/blasts, multiple myeloma, myelodysplastic syndromes, CMML, mature T-cell neoplasms, immune status), immunophenotyping is offered for the following special diagnostics:

- Hereditary spherocytosis, EMA test
- Blastic plasmacytoid dendritic cell neoplasm (BPDCN)
- MRD (minimal/measurable residual disease): CLL, multiple myeloma, ALL, AML
- Paroxysmal nocturnal hemoglobinuria (PNH)
- Systemic mastocytosis
- Investigation for Sézary syndrome in confirmed mycosis fungoides according to EORTC (Olsen et al., Blood 2022)