MLL Münchner Leukämielabor GmbH
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Akkreditiert:
DIN EN ISO/IEC 17025
DAkkS Deutsche Akkreditierungsstelle D-PL-13227-01-00

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

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Akkreditiert:
DIN EN ISO 15189
DAkkS Deutsche Akkreditierungsstelle D-ML-13228-01-00

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

Request form

Material Receiption: 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/periphal 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)
☐ Periphal blood (20 ml in total)

Number of bone marrow smears:
Number of periphal blood smears:

Date of material withdrawal:
Time of material withdrawal:
☐ Initial diagnosis ☐ Follow-up
Study:

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

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		**Differential blood count**					
Leukocytes:	/µl	Myeloblasts:	%	Band neutrophils:	%	Monocytes:	%
Hemoglobin:	g/dl	Promyeloblasts:	%	Mature neutrophils:	%	Lymphocytes:	%
Thrombocytes:	/µl	Myelocytes:	%	Eosinophiles:	%		
		Metamyelocytes:	%	Basophiles:	%		

(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:

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Münchner Leukämielabor (MLL)

Information on Data Processing and the Use of Biomaterial

Münchner Leukämielabor (MLL[1]) 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.

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 descendents. 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.

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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)**
- ☐ *PML::RARA* rearrangement / t(15;17)(q24;q21)
- ☐ *RUNX1::RUNX1T1* rearrangement / t(8;21)(q22;q22)
- ☐ *CBFB::MYH11* rearrangement / inv(16)(p13q22)/t(16;16)(p13;q22)
- ☐ *KMT2A (MLL)* rearrangement (11q23)
- ☐ *MECOM (EVI1)* rearrangement (3q26)
- ☐ *DEK::NUP214* rearrangement / t(6;9)(p23;q34)
- ☐ *BCR::ABL1* rearrangement / t(9;22)(q34;q11)
- ☐ *NUP98* rearrangement (11p15)

☐ **Additional abnormalities with prognostic relevance (Döhner et al. Blood, 2022; Grimwade et al. Blood, 2016)**
- ☐ 5q31 deletion (*CDC25C*, *EGR1*)
- ☐ 5q33 deletion (*RPS14*)
- ☐ 7q31 deletion bzw. Monosomie 7 (*D7S486*, cen7)
- ☐ 17p13 deletion (*TP53*)
- ☐ 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.

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)**
- ☐ 5q31 deletion (*CDC25C*, *EGR1*)
- ☐ 5q33 deletion (*RPS14*)
- ☐ 7q31 deletion bzw. Monosomie 7 (*D7S486*, cen7)
- ☐ Trisomy 8 (cen8)
- ☐ 17p13 deletion (*TP53*)
- ☐ 20q12 deletion (*D20S108*)
- ☐ Y-loss (cenY)
- ☐ 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.

☐ **Cytogenetically cryptic abnormalities**
- ☐ 4q24 deletion (*TET2*)
- ☐ 7q36 deletion (*EZH2*)
- ☐ 12p13 deletion (*ETV6*)
- ☐ 21q22 deletion (*RUNX1*)

Aplastic anemia (AA)

- ☐ 13q14 deletion (*DLEU*)
- ☐ 17p13 deletion (*TP53*)
- ☐ Trisomy 6 (6q21 / *SEC63*, 6q23 / *MYB*)
- ☐ 7q31 deletion or monosomy 7 (*D7S486*, cen7)
- ☐ Trisomy 8 (cen8)
- ☐ Trisomy 21 (21q22 / *RUNX1*)

Myelodysplastic/myeloproliferative neoplasms (MDS/MPN)

- ☐ 7q31 deletion or monosomy 7 (*D7S486*, cen7)
- ☐ Trisomy 8 (cen8)
- ☐ 17p13 deletion (*TP53*)
- ☐ 13q14 deletion (*DLEU*)
- ☐ 20q12 deletion (*D20S108*)
- ☐ Trisomy 21 (21q22 / *RUNX1*)

Chronic myelomonocytic leukemia (CMML)

☐ **Prognostically relevant abnormalities**
- ☐ 7q31 deletion or monosomy 7 (*D7S486*, cen7)
- ☐ Trisomy 8 (cen8)

☐ **Cytogenetically cryptic abnormalities**
- ☐ *ETV6* rearrangement or *ETV6*-Deletion (12p13)
- ☐ 4q24 deletionen (*TET2*)
- ☐ 17q11 deletion (*NF1*)

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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)

☐ *MECOM* (*EVI1*) rearrangement (3q26)
☐ Trisomy 8 (cen 8)
☐ 7q31 deletion or monosomy 7 (D7S486, cen7)
☐ Isochromosome 17q (17p13 / *TP53* deletion, 17q11 / *NF1* gain)
☐ Trisomy 19 (19p13 / *ZNF44+ZNF443*, 19q13 / *BICRA+NOP53*)
☐ *KMT2A (MLL)* rearrangements (11q23)

Myeloproliferative neoplasms (MPN)

☐ *BCR::ABL1* rearrangement / t(9;22)(q34;q11)
☐ Trisomy 1 or 1q gain (1p32 / *CDKN2C*, 1q21 / *CKS1B*)
☐ Trisomy 8 (cen8)
☐ Trisomy 9 (cen9)
☐ 4q24 deletion (*TET2*)
☐ 20q12 deletion (*D20S108*)

Hypereosinophilia (HE, HES)

Myeloid/lymphoid neoplasms with eosinophilia and gene rearrangements

☐ *CHIC2 deletion (4q12, correlate to FIP1L1::PDGFRA rearrangement)*
☐ other *PDGFRA* rearrangements (4q12)
☐ *PDGFRB* rearrangement (5q32-33)
☐ *FGFR1* rearrangement (8p11)
☐ *JAK2* rearrangement (9p24)
☐ *ETV6* rearrangement (12p13)

Blastic plasmocytoid dendritic cell neoplam (BPDCN)

☐ 5q31 deletion (*CDC25C / EGR1*)
☐ 9p21 deletion (*CDKN2A*)
☐ 12p13 deletion (*CDKN1B*)
☐ 13q14 deletion (*DLEU*)
☐ 17p13 deletion (*TP53*)
☐ *MYC* rearrangement (8q24)

Acute lymphoblastic leukemia (ALL): B-cell line

☐ **Diagnostically and prognostically relevant abnormalities according to WHO 2022)**

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

☐ **„Philadelphia-like“ ALL**

☐ *CRLF2* rearrangement (Xp22 / Yp11)
☐ *P2RY8* rearrangement (Xp22 / Yp11)
☐ *PDGFRB* rearrangement (5q32-33)
☐ *JAK2* rearrangement (9p24)
☐ *ETV6* rearrangement (12p13)

Acute lymphoblastic leukemia (ALL): T-cell line

☐ *TRA/D* rearrangement (14q11)
☐ *TRB* rearrangement (7q34)
☐ *TLX3* rearrangement (5q35)
☐ *TLX1* rearrangement (10q24)
☐ *KMT2A (MLL)* rearrangement (11q23)
☐ 6q21/6q23 deletion (*SEC63 / MYB*)
☐ 9p21 deletion (*CDKN2A*)
☐ Monosomy 7 (cen7)

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Supplemental order form: Fluorescence in situ hybridization

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

- ☐ *IGH::BCL2* rearrangement / t(14;18)(q32;q21)
- ☐ *IGH::MYC* rearrangement / t(8;14)(q24;q32)
- ☐ *BCL6* rearrangement (3q27)
- ☐ *MYC* rearrangement (8q24)
- ☐ 13q14 deletion (*DLEU*)
- ☐ 17p13 deletion (*TP53*)

CD5-negative mature B-cell neoplasms

- ☐ 6q deletion (*SEC63* / 6q21, *MYB* / 6q23)
- ☐ 3q gain (*BCL6* / 3q27)
- ☐ 11q deletion (*ATM* / 11q22)
- ☐ 17p13 deletion (*TP53*)
- ☐ 13q deletion (*DLEU* / 13q14)
- ☐ Trisomy 12 (cen12)
- ☐ Trisomy 18 or *IGH::BCL2* rearrangement / t(14;18)(q32;q21) (*IGH* / 14q32, *BCL2* / 18q21)
- ☐ 7q deletion (*D7S486* / 7q31)

Mantle cell lymphoma (MCL)

- ☐ *IGH::CCND1* rearrangement / t(11;14)(q13;q32)
- ☐ 17p13 deletion (*TP53*)
- ☐ 9p21 deletion (*CDKN2A*)

Chronic lymphocytic leukemia (CLL)

☐ **Diagnosis**

- ☐ *IGH::CCND1* rearrangement / t(11;14)(q13;q32)
- ☐ *IGH::BCL2* rearrangement / t(14;18)(q32;q21)
- ☐ *IGH* rearrangement independent of partner gene (14q32)

☐ **Prognosis**

- ☐ 11q22 deletion (*ATM*)
- ☐ 13q14 deletion (*RB1*)
- ☐ 13q14 deletion (*DLEU*)
- ☐ 13q14 deletion (*D13S319* / *D13S25*)
- ☐ 17p13 deletion (*TP53*)
- ☐ Trisomy 12 (cen12)

Waldenström's Macroglobulinemia

- ☐ 3q-gain (*BCL6* / 3q27)
- ☐ Trisomy 4 (4q12 / 4q24)
- ☐ 6q deletion (*SEC63* / 6q21, *MYB* / 6q23)
- ☐ 8q gain (*MYC* / 8q24)
- ☐ 11q deletion (*ATM* / 11q22)
- ☐ 13q deletion (*DLEU* / 13q14)
- ☐ 17p13 deletion (*TP53*)
- ☐ Trisomy 18 (*BCL2* / 18q21)

Persistent polyclonal B-cell lymphocytosis (PPBL)

- ☐ 3q-gain (*BCL6* / 3q27)
- ☐ 8q-gain (*MYC* / 8q24)
- ☐ *IGH::BCL2* rearrangement / t(14;18)(q32;q21)

Mature T-cell neoplasms (T-NHL)

- ☐ *TRA/D* rearrangement (14q11)
- ☐ *TRB* rearrangement (7q34)
- ☐ 11q22 deletion (*ATM*)
- ☐ 17p13 deletion (*TP53*)
- ☐ 8q24-gain (*MYC*)
- ☐ 6q21 / 6q23 deletion (*SEC63* / *MYB*)
- ☐ *ALK* rearrangement (2p23)

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Supplemental order form: Fluorescence in situ hybridization

T-prolymphocytic leukemia

- ☐ *TRA/D* rearrangement (14q11)
- ☐ *TCL1A* (*TCL1*) rearrangement (14q32)
- ☐ 8q24 gain (*MYC*)
- ☐ 11q22 deletion (*ATM*)
- ☐ 17p13 deletion (*TP53*)

T-prolymphocytic leukemia

- ☐ 11q22 deletion (*ATM*)
- ☐ 11q23 d*eletion (KMT2A)*
- ☐ 13q14 deletion (*DLEU*)
- ☐ 17p13 deletion (*TP53*)
- ☐ 6q21 / 6q23 deletion (*SEC63 / MYB*)
- ☐ Abnormalities affecting chromosome 7 (7q31 / D7S486, cen7)
- ☐ Trisomy 8 (cen8)

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)**

- ☐ 17p13 deletion (*TP53*)
- ☐ *IGH::FGFR3* rearrangement / t(4;14)(p16;q32)
- ☐ *IGH::MAF* rearrangement / t(14;16)(q32;q23)
- ☐ 1p32 deletion / 1q21 gain (CDKN2C, CKS1B)
- ☐ *IGH::CCND1* rearrangement / t(11;14)(q13;q32)
- ☐ *IGH::MAFB* rearrangement / t(14;20)(q32;q12)

☐ **Further recurrent abnormalities in plasma cell neoplasms**

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

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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)**

☐ *ASXL1*	☐ *FBXW7*	☐ *NRAS*	☐ *SMC3*
☐ *ASXL2*	☐ *FLT3*	☐ *PDGFRA*	☐ *SRSF2*
☐ *ATRX*	☐ *FLT3-ITD*	☐ *PDGFRB*	☐ *STAG2*
☐ *BCOR*	☐ *GATA1*	☐ *PHF6*	☐ *SUZ12*
☐ *BCORL1*	☐ *GATA2*	☐ *PIGA*	☐ *TET2*
☐ *BRAF*	☐ *GNB1*	☐ *PPM1D*	☐ *TP53*
☐ *CALR*	☐ *IDH1*	☐ *PRPF8*	☐ *UBA1*
☐ *CBL*	☐ *IDH2*	☐ *PTEN*	☐ *U2AF1*
☐ *CEBPA*	☐ *IL6R*	☐ *PTPN11*	☐ *U2AF2*
☐ *CSF3R*	☐ *JAK2*	☐ *RAD21*	☐ *WT1*
☐ *CSNK1A1*	☐ *KIT*	☐ *RUNX1*	☐ *ZEB2*
☐ *CUX1*	☐ *KRAS*	☐ *SETBP1*	☐ *ZRSR2*
☐ *DDX41*	☐ *MPL*	☐ *SF1*	
☐ *DNMT3A*	☐ *MYD88*	☐ *SF3A1*	
☐ *ETNK1*	☐ *NF1*	☐ *SF3B1*	
☐ *ETV6*	☐ *NOTCH1*	☐ *SH2B3*	
☐ *EZH2*	☐ *NPM1*	☐ *SMC1A*	

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

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Supplemental order form: Molecular genetics

Acute myeloid leukemia (AML)

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

- ☐ *ASXL1*
- ☐ *BCOR*
- ☐ *BCORL1*
- ☐ *BRAF*
- ☐ *CBL*
- ☐ *CEBPA*
- ☐ *CSF3R*
- ☐ *DDX41*
- ☐ *DNMT3A*
- ☐ *ETV6*
- ☐ *EZH2*
- ☐ *FLT3*-ITD
- ☐ *FLT3*-TKD
- ☐ *GATA2*
- ☐ *IDH1*
- ☐ *IDH2*
- ☐ *JAK2*
- ☐ *KIT*
- ☐ *KMT2A*-PTD
- ☐ *KRAS*
- ☐ *NF1*
- ☐ *NPM1*
- ☐ *NRAS*
- ☐ *PHF6*
- ☐ *PPM1D*
- ☐ *PTPN11*
- ☐ *RAD21*
- ☐ *RUNX1*
- ☐ *SETBP1*
- ☐ *SF3B1*
- ☐ *SRSF2*
- ☐ *STAG2*
- ☐ *TET2*
- ☐ *TP53*
- ☐ *U2AF1*
- ☐ *WT1*
- ☐ *ZRSR2*

☐ **AML/targeted therapy**

- ☐ *FLT3*-ITD
- ☐ *FLT3*-TKD
- ☐ *IDH1*
- ☐ *IDH2*

☐ **Fusion genes**

- ☐ *CBFB::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)

- ☐ *CBFB::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.

- ☐ *ASXL1*
- ☐ *BCOR*
- ☐ *BCORL1*
- ☐ *CBL*
- ☐ *CEBPA*
- ☐ *DNMT3A*
- ☐ *ETNK1*
- ☐ *ETV6*
- ☐ *EZH2*
- ☐ *FLT3*
- ☐ *FLT3*-ITD
- ☐ *GATA2*
- ☐ *GNB1*
- ☐ *IDH1*
- ☐ *IDH2*
- ☐ *KRAS*
- ☐ *NF1*
- ☐ *NPM1*
- ☐ *NRAS*
- ☐ *PHF6*
- ☐ *PPM1D*
- ☐ *PRPF8*
- ☐ *PTPN11*
- ☐ *RUNX1*
- ☐ *SETBP1*
- ☐ *SF3B1*
- ☐ *SRSF2*
- ☐ *STAG2*
- ☐ *TET2*
- ☐ *TP53*
- ☐ *U2AF1*
- ☐ *WT1*
- ☐ *ZRSR2*

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

- ☐ *BRAF*
- ☐ *CALR*
- ☐ *CSF3R*
- ☐ *CUX1*
- ☐ *DDX41*
- ☐ *JAK2*
- ☐ *KIT*
- ☐ *MPL*
- ☐ *MYD88*
- ☐ *NOTCH1*
- ☐ *PIGA*
- ☐ *PTEN*
- ☐ *RAD21*
- ☐ *SF1*
- ☐ *SF3A1*
- ☐ *SMC1A*
- ☐ *SMC3*
- ☐ *U2AF2*
- ☐ *UBA1*

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*

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Supplemental order form: Molecular genetics

Chronic myelomonocytic leukemia (CMML)

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

☐ *ASXL1*	☐ *FIP1L1::PDGFRA*	☐ *NF1*	☐ *SRSF2*
☐ *BCOR*	☐ *FLT3*-ITD	☐ *NPM1*	☐ *TET2*
☐ *BCR::ABL1*	☐ *FLT3*-TKD	☐ *NRAS*	☐ *U2AF1*
☐ *CBL*	☐ *IDH1*	☐ *PCM1::JAK2*	☐ *ZNF198::FGFR1*
☐ *DNMT3A*	☐ *IDH2*	☐ *RUNX1*	☐ *ZRSR2*
☐ *ETV6::PDGFRB*	☐ *JAK2*	☐ *SETBP1*	
☐ *EZH2*	☐ *KRAS*	☐ *SF3B1*	

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

☐ *ASXL1*	☐ *NRAS*	☐ *RUNX1*	☐ *SETBP1*

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

☐ ASXL1	☐ *CBL*	☐ *CSF3R*	☐ *ETNK1*	☐ *SETBP1*

Chronic myeloid leukemia (CML)

☐ *BCR::ABL1* quantification
☐ *BCR::ABL1* mutation in case of TKI resistance
☐ *BCR::ABL1 mutation in case of Asciminib (ABL001) resistance*
☐ *BCR::ABL1* detection
☐ other:

Polycythaemia vera (PV)

☐ **Diagnosis**

☐ *BCR::ABL1*	☐ *CALR (only if BCR::ABL1/JAK2 negative)*
☐ *JAK2* V617F	☐ *MPL (only if BCR::ABL1/JAK2 negative)*
☐ *JAK2* exon12	

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

☐ *ASXL1*	☐ *EZH2*	☐ *SRSF2*
☐ *BCOR*	☐ *IDH1*	☐ *TP53*
☐ *BCORL1*	☐ *IDH2*	☐ *TET2*
☐ *DNMT3A*	☐ *SF3B1*	☐ *U2AF1*

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

☐ **Prognostic panel according to WHO 2022**

☐ *ASXL1*	☐ *IDH1*	☐ *IDH2*
☐ *RUNX1*	☐ *SRSF2*	☐ *TP53*

Essential thrombocythaemia (ET)

☐ **Diagnosis**

☐ *BCR::ABL1*	☐ *CALR*	☐ *JAK2* V617F	☐ *MPL* W515

☐ **Prognostic panel according to WHO 2022**

☐ *ASXL1*	☐ *RUNX1*	☐ *SF3B1*
☐ *SRSF2*	☐ *TP53*	☐ *U2AF1*

Primary myelofibrosis (PMF)

☐ **Diagnosis**

☐ *BCR::ABL1*	☐ *CALR*	☐ *JAK2* V617F	☐ *MPL* W515

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

☐ *ASXL1*	☐ *EZH2*	☐ *IDH1*
☐ *IDH2*	☐ *SRSF2*	☐ *U2AF1*

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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)**

- ☐ *ASXL1*
- ☐ *BCOR*
- ☐ *BCORL1*
- ☐ *DNMT3A*
- ☐ *EZH2*
- ☐ *IDH1*
- ☐ *IDH2*
- ☐ *JAK2* (entire coding region)
- ☐ *MPL* (entire coding region)
- ☐ *SF3B1*
- ☐ *SRSF2*
- ☐ *TET2*
- ☐ *TP53*
- ☐ *U2AF1*

Hypereosinophilia (HE, HES)

☐ **Myeloid/lymphoid neoplasms with eosinophilia und gene rearrangement**

- ☐ *FIP1L1::PDGFRA*
- ☐ *PDGFRA* expression
- ☐ *ETV6::PDGFRB*
- ☐ *ZNF198::FGFR1*
- ☐ *PCM1::JAK2*

☐ **Other clonality markers**

- ☐ *BCR::ABL1*
- ☐ *JAK2* V617F
- ☐ *JAK2* exon 13
- ☐ *KIT* D816V
- ☐ *ASXL1*
- ☐ *DNMT3A*
- ☐ *SRSF2*
- ☐ *TET2*
- ☐ *STAT5B*
- ☐ 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)**

- ☐ *ASXL1*
- ☐ *CBL*
- ☐ *EZH2*
- ☐ *JAK2*
- ☐ *KIT* D816V
- ☐ *KRAS*
- ☐ *NRAS*
- ☐ *RUNX1*
- ☐ *SRSF2*
- ☐ *TET2*
- ☐ *U2AF1*

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

- ☐ *ASXL1*
- ☐ *DNMT3A*
- ☐ *NRAS*
- ☐ *RUNX1*
- ☐ *SRSF2*

Hereditary alpha-tryptasemia (HaT)

- ☐ *TPSAB1*

Blastic plasmacytoid dendritic cell neoplasm (BPDCN)

☐ **Panel according to Menezes et al. (Leukemia 2014)**

- ☐ *ASXL1*
- ☐ *ETV6*
- ☐ *EZH2*
- ☐ *FLT3*-ITD
- ☐ *FLT3*-TKD
- ☐ *IDH2*
- ☐ *KRAS*
- ☐ *NPM1*
- ☐ *NRAS*
- ☐ *SRSF2*
- ☐ *TET2*
- ☐ *TP53*
- ☐ *ZRSR2*

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Supplemental order form: Molecular genetics

Lymphoid neoplasms

☐ **Lymphoid markers (complete)**

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

Acute lymphoblastic leukemia (ALL): B-cell line

☐ **Diagnosis**

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

Follow-up (MRD)

- ☐ *BCR::ABL1* quantification
- ☐ *KMT2A::AFF1* (*MLL::MLLT2*) quantification
- ☐ *KMT2A::MLLT1* (*MLL::MLLT1*) quantification
- ☐ *ETV6::RUNX1* (*TEL::AML1*) quantification
- ☐ *TCF3::PBX1* (*E2A::PBX1*) quantification
- ☐ *IKZF1* deletion quantification
- ☐ Clone-specific MRD

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-specif 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-cellneoplasms**

- ☐ *BRAF*
- ☐ *CXCR4*
- ☐ *KLF2*
- ☐ *MAP2K1*
- ☐ *MYD88*
- ☐ *NOTCH2*
- ☐ *TP53*

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Supplemental order form: Molecular genetics

Mantle cell lymphoma (MCL)

☐ **Diagnosis**
☐ *IGH::CCND1* (*BCL1::IGH*) / t(11;14)
☐ (Cyclin D1) expression
☐ *SOX11* expression
☐ *TP53*
☐ *UBR5*

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**
☐ *BCL2*
☐ *CD79B*
☐ *FOXO1*
☐ *KLHL6*
☐ *MYD88*
☐ *NOTCH1*
☐ *SGK1*
☐ *SOCS1*
☐ *STAT3*
☐ *STAT6*
☐ *TP53*

Chronic lymphocytic leukemia (CLL)

☐ **Panel according to Onkopedia guidelines**
☐ *TP53*
☐ *IGHV* mutation status

☐ **Prognostic panel according to Rossi et al. (Blood 2013)**
☐ *BIRC3*
☐ *NOTCH1*
☐ *SF3B1*
☐ *TP53*

☐ **Recurrent mutations**
☐ *IGHV* mutation status
☐ *ATM*
☐ *BIRC3*
☐ *BRAF*
☐ *KRAS*
☐ *NOTCH1*
☐ *POT1*
☐ *RPS15*
☐ *SF3B1*
☐ *TP53*

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*

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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* ☐ *PLCG1* ☐ *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.

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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)