Molecular genetics

Catalogue of Services

State-of-the-art methods for the identification of gene mutations with the highest sensitivity; preparation of genetic tumor profiles and determination of minimal residual disease (MRD).

Molecular genetics combines a variety of different methods using either genomic DNA or cellular RNA (reverse transcribed into cDNA) as template. The spectrum of analyses ranges from the isolation of white blood cells and extraction of nucleic acids as sample preparation to PCR, quantitative PCR, digital PCR, Next generation sequencing (NGS), fragment length analysis, clonality detection and chimerism. Each of these methods comprises a variety of specific assays. Through panel diagnostics, a broad portfolio of gene mutations can be examined in parallel using a single approach, whereas highly sensitive methods such as quantitative PCR achieve detection limits of 10^{-5}.

Examinations:

- Isolation of white blood cells from bone marrow and peripheral blood
- Extraction of genomic DNA and RNA, reverse transcription to cDNA
- PCR - Polymerase chain reaction
- Quantitative PCR
- Digital PCR
- NGS - Next generation sequencing, single amplicons, genes or gene panels
- Fragment length analysis (gene scan)
- Clonality assay (B-/T-cell receptor rearrangements)
- Chimerism
- MRD - Minimal residual disease detection, using the most sensitive available assay

Explorative assays (Research use only):

- WES - Whole exome sequencing
- WGS - Whole genome sequencing
- WTS - Whole transcriptome sequencing (RNA-Seq)

Molecular genetics

Catalogue of Services

Disease specific diagnostics:

Chronic myeloid neoplasms (CMN)

- O *ASXL1*
- O *BCOR*
- O *BCORL1*
- O *CALR*
- O *CBL*
- O *CEBPA*
- O *CSF3R*
- O *DNMT3A*
- O *ETV6*
- O *EZH2*
- O *FLT3*
- O *IDH1*
- O *IDH2*
- O *JAK2*
- O *KIT*
- O *KRAS*
- O *MPL*
- O *NF1*
- O *NPM1*
- O *NRAS*
- O *PHF6*
- O *PPM1D*
- O *PTPN11*
- O *RAD21*
- O *RUNX1*
- O *SETBP1*
- O *SF3B1*
- O *SMC3*
- O *SRSF2*
- O *STAG2*
- O *TET2*
- O *TP53*
- O *U2AF1*
- O *ZRSR2*

Myeloid marker (complete)

- O *ASXL1*
- O *ASXL2*
- O *ATRX*
- O *BCOR*
- O *BCORL1*
- O *BRAF*
- O *BRCC3*
- O *CALR*
- O *CBL*
- O *CDH23*
- O *CDKN2A*
- O *CEBPA*
- O *CREBBP*
- O *CSF3R*
- O *CSNK1A1*
- O *CTCF*
- O *CUX1*
- O *DDX41*
- O *DDX54*
- O *DHX29*
- O *DNMT3A*
- O *EP300*
- O *ETNK1*
- O *ETV6*
- O *EZH2*
- O *FLT3*
- O *GATA1*
- O *GATA2*
- O *GNAS*
- O *GNB1*
- O *IDH1*
- O *IDH2*
- O *JAK2*
- O *KDM5A*
- O *KDM6A*
- O *KIT*
- O *KMT2D*
- O *KRAS*
- O *MPL*
- O *MYC*
- O *NF1*
- O *NPM1*
- O *NRAS*
- O *PHF6*
- O *PIGA*
- O *PPM1D*
- O *PRPF8*
- O *PTPN11*
- O *RAD21*
- O *RUNX1*
- O *SETBP1*
- O *SF1*
- O *SF3A1*
- O *SF3B1*
- O *SH2B3*
- O *SMC1A*
- O *SMC3*
- O *SRSF2*
- O *STAG2*
- O *SUZ12*
- O *TET2*
- O *TP53*
- O *U2AF1*
- O *U2AF2*
- O *WT1*
- O *ZBTB7A*
- O *ZRSR2*

Molecular genetics

Catalogue of Services

AML, Acute myeloid leukemia – ELN guidelines

- O *ASXL1*
- O *CEBPA*
- O *FLT3*-ITD
- O *FLT3*-TKD
- O *NPM1*
- O *RUNX1*
- O *TP53*
- O *BCR-ABL1*
- O *CBFB-MYH11*
- O *DEK-NUP214*
- O *KMT2A*-Fusions
- O *PML-RARA*
- O *RUNX1-RUNX1T1*

AML, Acute myeloid leukemia – diagnosis, prognosis, therapy decision

- O *ASXL1*
- O *CEBPA*
- O *DNMT3A*
- O *FLT3*-ITD
- O *FLT3*-TKD
- O *IDH1*
- O *IDH2*
- O *KIT*
- O *KMT2A*-PTD
- O *NPM1*
- O *RUNX1*
- O *TP53*

AML, Acute myeloid leukemia – fusion genes

- O *CBFB-MYH11*
- O *DEK-NUP214*
- O *KMT2A*-Fusions
- O *KMT2A*-PTD
- O *PML-RARA*
- O *RUNX1-RUNX1T1*

AML, Acute myeloid leukemia – quantitative analyses (MRD)

- O *CBFB-MYH11*
- O *CEBPA*
- O *DEK-NUP214*
- O *FLT3*-ITD
- O *KMT2A*-Fusions
- O *KMT2A*-PTD
- O *NPM1*
- O *PML-RARA*
- O *RUNX1*
- O *RUNX1-RUNX1T1*

AML, Acute myeloid leukemia – resistance mutations

- O *IDH2* at Edasidenib (IDH2-inhibitor) resistance

MDS, Myelodysplastic syndrome – diagnosis and prognosis

- O *ASXL1*
- O *CBL*
- O *DNMT3A*
- O *EZH2*
- O *JAK2*
- O *RUNX1*
- O *SF3B1*
- O *SRSF2*
- O *TET2*
- O *TP53*
- O *U2AF1*
- O *ZRSR2*

MDS, Myelodysplastic syndrome – isolated 5q deletion

- O *TP53*
- O *CSNK1A1*

Aplastic anemia

- O *BCOR*
- O *BCORL1*
- O *PIGA*

Molecular genetics

Catalogue of Services

CMML, Chronic myelomonocytic leukemia – ELN/EHA guidelines

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

CMML, Chronic myelomonocytic leukemia – prognosis

O *ASXL1*	O *NRAS*	O *RUNX1*	O *SETBP1*

aCML, Atypical chronic myeloid leukemia

O *CBL*	O *CSF3R*	O *ETNK1*	O *SETBP1*

CML, Chronic myeloid leukemia

O *BCR-ABL1* (diagnosis)	O *BCR-ABL1* mutation (at TKI resistance)
O *BCR-ABL1* (quantitative, follow-up)	O *BCR-ABL1* mutation (at Asciminib resistance)

PV, Polycytemia vera - diagnosis

O *BCR-ABL1*	O *JAK2* V617F	O *JAK2* exon 12

PV, Polycytemia vera - prognosis

O *ASXL1*	O *IDH2*	O *SRSF2*

ET, Essential thrombocytemia - diagnosis

O *BCR-ABL1*	O *CALR*	O *JAK2* V617F	O *MPL* W515

ET, Essential thrombocytemia - prognosis

O *EZH2*	O *SF3B1*	O *U2AF1*
O *IDH2*	O *TP53*	

PMF, Primary myelofibrosis - diagnosis

O *BCR-ABL1*	O *CALR*	O *JAK2* V617F	O *MPL* W515

Molecular genetics

Catalogue of Services

PMF, Primary myelofibrosis - prognosis

O *ASXL1* O *IDH1* O *SRSF2*

O *EZH2* O *IDH2*

CNL, Chronic neutrophilic leukemia

O *ASXL1* O *CSF3R*

MPN, Myeloproliferative neoplasm

O *BCR-ABL1* O *CALR* O *JAK2* V617F O *MPL* W515

MPN, Myeloproliferative neoplasm – triple negative

O *ASXL1* O *IDH2* O *SF3B1* O *TET2*

O *EZH2* O *JAK2* (complete) O *SRSF2* O *U2AF1*

O *IDH1* O *MPL* (complete) O *TP53*

MLN eo, Myeloid/lymphoid neoplasm with eosinophilia and gene rearrangement

O *ETV6-PDGFRB* O *PDGFRB*-Expression O *ZNF198- FGFR1*

O *FIP1L1-PDGFRA* O *PCM1-JAK2*

Eosinophilia - Clonality marker

O *ASXL1* O *DNMT3A* O *KIT* D816V O *TET2*

O *BCR-ABL1* O *JAK2* O *SRSF2*

SM and SM-AHN, Systemic mastocytosis and associated hematologic neoplasms - diagnosis

O *KIT* D816V O other *KIT* mutations

SM and SM-AHN, Systemic mastocytosis and associated hematologic neoplasms – diagnosis extended

O *ASXL1* O *JAK2* O *NRAS* O *TET2*

O *CBL* O *KIT* D816V O *RUNX1* O *U2AF1*

O *EZH2* O *KRAS* O *SRSF2*

SM and SM-AHN, Systemic mastocytosis and associated hematologic neoplasms – prognosis

O *ASXL1* O *RUNX1* O *SRSF2*

Molecular genetics

Catalogue of Services

BPDCN, Blastic plasmacytoid dendritic cell neoplasm

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

Lymphoid marker (complete)

- O *ARID1A*
- O *ATM*
- O *BCL2*
- O *BIRC3*
- O *BRAF*
- O *BTK*
- O *CARD11*
- O *CCND1*
- O *CD79A*
- O *CD79B*
- O *CREBBP*
- O *CXCR4*
- O *DDX3X*
- O *DIS3*
- O *DNMT3A*
- O *EP300*
- O *EZH2*
- O *FAM46C*
- O *FAS*
- O *FAT4*
- O *FBXW7*
- O *FOXO1*
- O *GPR98*
- O *ID3*
- O *IKBKB*
- O *IL2RG*
- O *JAK1*
- O *JAK3*
- O *KLF2*
- O *KLHL6*
- O *KMT2D*
- O *KRAS*
- O *LRP1B*
- O *MAP2K1*
- O *MAPK1*
- O *MEF2B*
- O *MYBBP1A*
- O *MYD88*
- O *NFKBIE*
- O *NOTCH1*
- O *NOTCH2*
- O *NRAS*
- O *PHF6*
- O *PLCG2*
- O *POT1*
- O *PTPRD*
- O *RPS15*
- O *SF3B1*
- O *STAT3*
- O *STAT5B*
- O *TBL1XR1*
- O *TCF3*
- O *TET2*
- O *TLR2*
- O *TNFAIP3*
- O *TNFRSF14*
- O *TP53*
- O *TRAF3*
- O *UBR5*
- O *WHSC1*
- O *YPO1*
- O *ZMYM3*

B-ALL, Acute B-lymphoblastic leukemia – diagnosis (PCR) and follow-up (quantitative PCR)

- O *BCR-ABL1*
- O *KMT2A-AFF1*
- O *KMT2A-MLLT1*
- O *ETV6-RUNX1*
- O *TCF3-PBX1*
- O Clone-specific MRD (B-cell receptor rearrangement)
- O *IKZF1*-Deletion

B-ALL, Acute B-lymphoblastic leukemia – resistance mutation

- O *BCR-ABL1* mutation (at TKI resistance)

Molecular genetics

Catalogue of Services

T-ALL, Acute T-lymphoblastic leukemia - diagnosis

O *DNMT3A* O *NUP214-ABL1* O *PICALM-MLLT10* O *SET-NUP214*
O *FBXW7* O *PHF6* O *RUNX1* O *STIL-TAL1*
O *NOTCH1*

T-ALL, Acute T-lymphoblastic leukemia – follow-up

O Clone-specific MRD (T-cell receptor rearrangement)

Mature B-cell neoplasm - diagnosis

O B-cell receptor rearrangement

Mature B-cell neoplasms – CD5 negative

O *BRAF* O *KLF2* O *MYD88* O *TP53*
O *CXCR4* O *MAP2K1* O *NOTCH2*

MCL, Mantle cell lymphoma – diagnosis, prognosis

O *IGH-CCND1* O *SOX11*-Expression O *UBR5*
O *CCND1*-Expression O *TP53* O *BCL2* mutation (at Venetoclax resistance)

FL, Follicular lymphoma – diagnosis, prognosis

O *IGH-BCL2* O *BCL2* O *TP53*
O *BCL2* mutation (at Venetoclax resistance)

FL, Follicular lymphoma – m7-FLIPI-score

O *ARID1A* O *CREBBP* O *EZH2* O *MEF2B*
O *CARD11* O *EP300* O *FOXO1*

DLBCL, Diffuse large B-cell lymphoma - prognosis

O *CD79B* O *NOTCH1* O *TP53*
O *MYD88* O *STAT3*

CLL, Chronic lymphocytic leukemia – diagnosis, prognosis

O *IGHV* mutation status O *TP53* O *SF3B1*

Molecular genetics

Catalogue of Services

CLL, Chronic lymphocytic leukemia – prognosis extended

O *BIRC3* O *NOTCH1* O *SF3B1* O *TP53*

CLL, Chronic lymphocytic leukemia – resistance mutations

O *BTK* mutation (at Ibrutinib resistance) O *BCL2* mutation (at Venetoclax resistance)

O *PLCG2* mutation (at Ibrutinib resistance)

CLL, Chronic lymphocytic leukemia – recurrent mutations

O *ATM* O *FBXW7* O *NFKBIE* O *TP53*

O *BCL2* O *ID3* O *NOTCH1* O *UBR5*

O *BIRC3* O *KLHL6* O *NRAS* O *XPO1*

O *BRAF* O *KRAS* O *PLDG2* O *ZMYM3*

O *BTK* O *MAP2K1* O *POT1*

O *CARD11* O *MAPK1* O *RPS15*

O *DDX3X* O *MYD88* O *SF3B1*

Waldenström macroglobulinemia (M. Waldenström)

O *CXCR4* O *MYD88*

SMZL, Splenic marginal zone lymphoma

O *KLF2* O *NOTCH2*

Hairy cell leukemia

O *BRAF* V600E

Hairy cell leukemia, variant

O *MAP2K1*

Multiple myeloma (CD138+ sorted cells)

O *BRAF* O *KRAS* O *NRAS* O *TP53*

Mature T-cell neoplasms

O T-cell receptor rearrangement

T-/NK-LGL, Large granular lymphocytic leukemia

O *STAT3* O *STAT5B*

Molecular genetics

Catalogue of Services

Chimerism

O Before stem cell transplantation
O After stem cell transplantation
O Donor

Hereditary diseases

Informed consent in accordance with the German Genetic Diagnosis Act (GenDG) is required.

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

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

Myeloid neoplasms with germline predisposition and pre-existing platelet disorders

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

Other

O Myeloid neoplasms with germline *GATA2* mutation
O Myeloid neoplasms with germline predisposition associated with telomere biology disorders and mutations in *TERC* and *TERT*

Familial erythrocytosis – screening

O *BPGM*
O *EGLN1*
O *EPAS1*
O *EPOR*
O *JAK2* (complete)
O *VHL*

Familial erythrocytosis – screening extended

O *BHLHE41*
O *BPGM*
O *EGLN1*
O *EGLN2*
O *EGLN3*
O *EPAS1*
O *EPO*
O *EPOR*
O *GFI1B*
O *HBA1*
O *HBA2*
O *HBB*
O *HIF1A*
O *HIF1AN*
O *HIF3A*
O *JAK2* (complete)
O *KDM6A*
O *OS9*
O *SH2B3*
O *VHL*
O *ZNF197*

Cyclic neutropenia

O *ELANE*