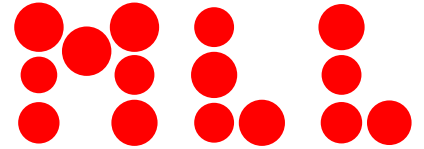


Molecular genetics

Catalogue of Services



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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:

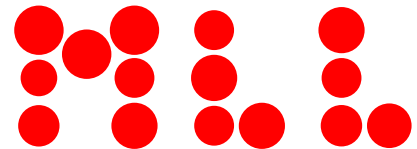
- Isolation of white blood cells from bone marrow and peripheral blood
- Extraction of genomic DNA and RNA, reverse transcription to cDNA
- PCR - Polymerase chain reaction
- Quantitative PCR
- Digital PCR
- NGS - Next generation sequencing, single amplicons, genes or gene panels
- Fragment length analysis (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)

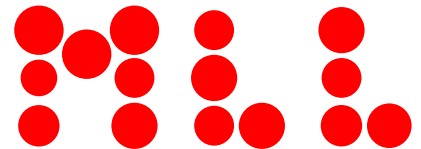
| | | | |
|------------------------------|----------------------------|------------------------------|-----------------------------|
| <input type="radio"/> ASXL1 | <input type="radio"/> EZH2 | <input type="radio"/> NPM1 | <input type="radio"/> SMC3 |
| <input type="radio"/> BCOR | <input type="radio"/> FLT3 | <input type="radio"/> NRAS | <input type="radio"/> SRSF2 |
| <input type="radio"/> BCORL1 | <input type="radio"/> IDH1 | <input type="radio"/> PHF6 | <input type="radio"/> STAG2 |
| <input type="radio"/> CALR | <input type="radio"/> IDH2 | <input type="radio"/> PPM1D | <input type="radio"/> TET2 |
| <input type="radio"/> CBL | <input type="radio"/> JAK2 | <input type="radio"/> PTPN11 | <input type="radio"/> TP53 |
| <input type="radio"/> CEBPA | <input type="radio"/> KIT | <input type="radio"/> RAD21 | <input type="radio"/> U2AF1 |
| <input type="radio"/> CSF3R | <input type="radio"/> KRAS | <input type="radio"/> RUNX1 | <input type="radio"/> ZRSR2 |
| <input type="radio"/> DNMT3A | <input type="radio"/> MPL | <input type="radio"/> SETBP1 | |
| <input type="radio"/> ETV6 | <input type="radio"/> NF1 | <input type="radio"/> SF3B1 | |

Myeloid marker (complete)

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

Molecular genetics

Catalogue of Services



AML, Acute myeloid leukemia – ELN guidelines

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

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

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

AML, Acute myeloid leukemia – fusion genes

- CBFβ-MYH11
- DEK-NUP214
- KMT2A-Fusions
- KMT2A-PTD
- PML-RARA
- RUNX1-RUNX1T1

AML, Acute myeloid leukemia – quantitative analyses (MRD)

- CBFβ-MYH11
- CEBPA
- DEK-NUP214
- FLT3-ITD
- KMT2A-Fusions
- KMT2A-PTD
- NPM1
- PML-RARA
- RUNX1
- RUNX1-RUNX1T1

AML, Acute myeloid leukemia – resistance mutations

- IDH2 at Edasidenib (IDH2-inhibitor) resistance
-

MDS, Myelodysplastic syndrome – diagnosis and prognosis

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

MDS, Myelodysplastic syndrome – isolated 5q deletion

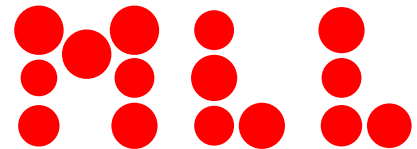
- TP53
 - CSNK1A1
-

Aplastic anemia

- BCOR
- BCORL1
- PIGA

Molecular genetics

Catalogue of Services



CMML, Chronic myelomonocytic leukemia – ELN/EHA guidelines

- | | | | |
|-----------------------------------|-------------------------------------|---------------------------------|------------------------------------|
| <input type="radio"/> ASXL1 | <input type="radio"/> FIP1L1-PDGFR4 | <input type="radio"/> NF1 | <input type="radio"/> SRSF2 |
| <input type="radio"/> BCOR | <input type="radio"/> FLT3-ITD | <input type="radio"/> NPM1 | <input type="radio"/> TET2 |
| <input type="radio"/> BCR-ABL1 | <input type="radio"/> FLT3-TKD | <input type="radio"/> NRAS | <input type="radio"/> U2AF1 |
| <input type="radio"/> CBL | <input type="radio"/> IDH1 | <input type="radio"/> PCM1-JAK2 | <input type="radio"/> ZNF198-FGFR1 |
| <input type="radio"/> DNMT3A | <input type="radio"/> IDH2 | <input type="radio"/> RUNX1 | <input type="radio"/> ZRSR2 |
| <input type="radio"/> ETV6-PDGFRB | <input type="radio"/> JAK2 | <input type="radio"/> SETBP1 | |
| <input type="radio"/> EZH2 | <input type="radio"/> KRAS | <input type="radio"/> SF3B1 | |

CMML, Chronic myelomonocytic leukemia – prognosis

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

αCML, Atypical chronic myeloid leukemia

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

CML, Chronic myeloid leukemia

- | | |
|--|---|
| <input type="radio"/> BCR-ABL1 (diagnosis) | <input type="radio"/> BCR-ABL1 mutation (at TKI resistance) |
| <input type="radio"/> BCR-ABL1 (quantitative, follow-up) | <input type="radio"/> BCR-ABL1 mutation (at Asciminib resistance) |
-

PV, Polycythemia vera - diagnosis

- | | | |
|--------------------------------|----------------------------------|------------------------------------|
| <input type="radio"/> BCR-ABL1 | <input type="radio"/> JAK2 V617F | <input type="radio"/> JAK2 exon 12 |
|--------------------------------|----------------------------------|------------------------------------|

PV, Polycythemia vera - prognosis

- | | | |
|-----------------------------|----------------------------|-----------------------------|
| <input type="radio"/> ASXL1 | <input type="radio"/> IDH2 | <input type="radio"/> SRSF2 |
|-----------------------------|----------------------------|-----------------------------|
-

ET, Essential thrombocythemia - diagnosis

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

ET, Essential thrombocythemia - prognosis

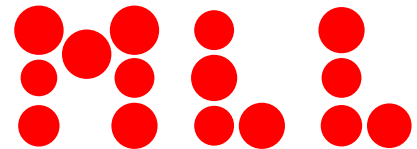
- | | | |
|----------------------------|-----------------------------|-----------------------------|
| <input type="radio"/> EZH2 | <input type="radio"/> SF3B1 | <input type="radio"/> U2AF1 |
| <input type="radio"/> IDH2 | <input type="radio"/> TP53 | |
-

PMF, Primary myelofibrosis - diagnosis

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

Molecular genetics

Catalogue of Services



PMF, Primary myelofibrosis - prognosis

- ASXL1
 - EZH2
 - IDH1
 - IDH2
 - SRSF2
-

CNL, Chronic neutrophilic leukemia

- ASXL1
 - CSF3R
-

MPN, Myeloproliferative neoplasm

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

MPN, Myeloproliferative neoplasm – triple negative

- ASXL1
 - EZH2
 - IDH1
 - IDH2
 - JAK2 (complete)
 - MPL (complete)
 - SF3B1
 - SRSF2
 - TP53
 - TET2
 - U2AF1
-

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

- ETV6-PDGFRB
 - FIP1L1-PDGFR A
 - PDGFRB-Expression
 - PCM1-JAK2
 - ZNF198- FGFR1
-

Eosinophilia - Clonality marker

- ASXL1
 - BCR-ABL1
 - DNMT3A
 - JAK2
 - KIT D816V
 - SRSF2
 - TET2
-

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

- KIT D816V
 - other KIT mutations
-

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

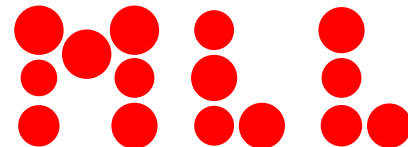
- ASXL1
 - CBL
 - EZH2
 - JAK2
 - KIT D816V
 - KRAS
 - NRAS
 - RUNX1
 - SRSF2
 - TET2
 - U2AF1
-

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

- ASXL1
- RUNX1
- SRSF2

Molecular genetics

Catalogue of Services



BPDCN, Blastic plasmacytoid dendritic cell neoplasm

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

Lymphoid marker (complete)

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

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

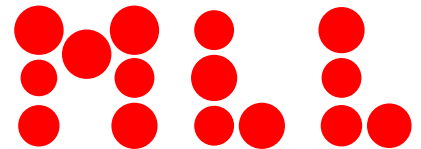
- | | | | |
|----------------------------------|-----------------------------------|--|--------------------------------------|
| <input type="radio"/> BCR-ABL1 | <input type="radio"/> KMT2A-MLLT1 | <input type="radio"/> TCF3-PBX1 | <input type="radio"/> IKZF1-Deletion |
| <input type="radio"/> KMT2A-AFF1 | <input type="radio"/> ETV6-RUNX1 | <input type="radio"/> Clone-specific MRD (B-cell receptor rearrangement) | |

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

- BCR-ABL1 mutation (at TKI resistance)

Molecular genetics

Catalogue of Services



T-ALL, Acute T-lymphoblastic leukemia - diagnosis

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

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

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

Mature B-cell neoplasm - diagnosis

- B-cell receptor rearrangement

Mature B-cell neoplasms – CD5 negative

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

MCL, Mantle cell lymphoma – diagnosis, prognosis

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

FL, Follicular lymphoma – diagnosis, prognosis

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

FL, Follicular lymphoma – m7-FLIPI-score

- ARID1A
 - CARD11
 - CREBBP
 - EP300
 - EZH2
 - FOXO1
 - MEF2B
-

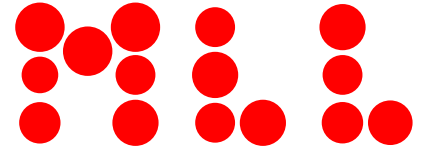
DLBCL, Diffuse large B-cell lymphoma - prognosis

- CD79B
 - MYD88
 - NOTCH1
 - STAT3
 - TP53
-

CLL, Chronic lymphocytic leukemia – diagnosis, prognosis

- IGHV mutation status
- TP53
- SF3B1

Molecular genetics



Catalogue of Services

CLL, Chronic lymphocytic leukemia – prognosis extended

BIRC3 *NOTCH1* *SF3B1* *TP53*

CLL, Chronic lymphocytic leukemia – resistance mutations

BTK mutation (at Ibrutinib resistance) *BCL2* mutation (at Venetoclax resistance)
 PLCG2 mutation (at Ibrutinib resistance)

CLL, Chronic lymphocytic leukemia – recurrent mutations

| | | | |
|-------------------------------------|-------------------------------------|-------------------------------------|------------------------------------|
| <input type="radio"/> <i>ATM</i> | <input type="radio"/> <i>FBXW7</i> | <input type="radio"/> <i>NFKBIE</i> | <input type="radio"/> <i>TP53</i> |
| <input type="radio"/> <i>BCL2</i> | <input type="radio"/> <i>ID3</i> | <input type="radio"/> <i>NOTCH1</i> | <input type="radio"/> <i>UBR5</i> |
| <input type="radio"/> <i>BIRC3</i> | <input type="radio"/> <i>KLHL6</i> | <input type="radio"/> <i>NRAS</i> | <input type="radio"/> <i>XPO1</i> |
| <input type="radio"/> <i>BRAF</i> | <input type="radio"/> <i>KRAS</i> | <input type="radio"/> <i>PLDG2</i> | <input type="radio"/> <i>ZMYM3</i> |
| <input type="radio"/> <i>BTK</i> | <input type="radio"/> <i>MAP2K1</i> | <input type="radio"/> <i>POT1</i> | |
| <input type="radio"/> <i>CARD11</i> | <input type="radio"/> <i>MAPK1</i> | <input type="radio"/> <i>RPS15</i> | |
| <input type="radio"/> <i>DDX3X</i> | <input type="radio"/> <i>MYD88</i> | <input type="radio"/> <i>SF3B1</i> | |

Waldenström macroglobulinemia (M. Waldenström)

CXCR4 *MYD88*

SMZL, Splenic marginal zone lymphoma

KLF2 *NOTCH2*

Hairy cell leukemia

BRAF V600E

Hairy cell leukemia, variant

MAP2K1

Multiple myeloma (CD138+ sorted cells)

BRAF *KRAS* *NRAS* *TP53*

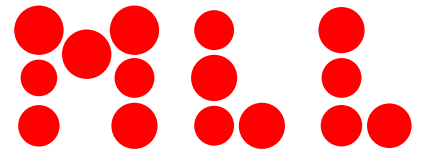
Mature T-cell neoplasms

T-cell receptor rearrangement

T-/NK-LGL, Large granular lymphocytic leukemia

STAT3 *STAT5B*

Molecular genetics



Catalogue of Services

Chimerism

- Before stem cell transplantation
 - After stem cell transplantation
 - 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

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

Familial erythrocytosis – screening

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

Familial erythrocytosis – screening extended

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

Cyclic neutropenia

- ELANE*