Cytogenetics & FISH

Catalogue of Services

Cytogenetics: Identification and characterization of chromosome aberrations of prognostic relevance by means of chromosome banding analysis.

Determining the karyotype is based on chromosome banding analysis. This requires a sufficient number of metaphases in good quality. The bone marrow or blood cells are cultivated for 24 to 72 hours dependent on the cell type and then arrested at the metaphase stage by adding colcemid. Cytokines can be added to stimulate the malignant cell population and increase the metaphase yield during cultivation. Swelling of the cells is induced by adding a hypotonic potassium chloride solution; they are then fixed in this state by a methanol/glacial acetic acid solution. The cell suspension is then dripped onto the slide. It is mandatory to conduct chromosome banding in order to ensure an unequivocal identification of the individual chromosomes. The most frequently used techniques are G- (giemsa), Q- (quinacrine) and R- (reverse) banding. The various banding techniques produce light and dark bands on the chromosomes that are specific to each one and that hence permit unequivocal identification of the individual chromosomes. According to international consensus, 20–25 metaphases should be fully analyzed in order to produce a reliable diagnosis (ISCN).

Examinations:

- Chromosome banding analysis for determination of the karyotype

Fluorescence in situ hybridization (FISH): Use of fluorescence probes for the identification of aberrant chromosome in metaphases and distinct genetic abnormalities in interphase nuclei.

The FISH technique is based on the hybridization of DNA probes that identify specific chromosomal structures. It is possible to use probes that mark specific centromere regions of individual chromosomes, genes or entire chromosomes. 24-color FISH is performed to resolve complex karyotypes as with this technique all 24 different chromosomes (1-22, X and Y) can be “colored” in one hybridization and thus identified within complex rearrangements.

Examinations:

- Interphase FISH
- Metaphase FISH
- 24-color FISH
- Locus specific or centromere specific probes (interphase or metaphase FISH)
- Chromosome painting (metaphase FISH)
- CD138 based purification of plasma cells, MACS

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Disease specific diagnostics:

AML, Acute myeloid leukemia – recurrent genetic aberrations (WHO 2017)

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

AML, Acute myeloid leukemia – other prognostic relevant aberrations

- O 5q31-Deletion (*CDC25C*, *EGR1*)
- O 5q33-Deletion (*RPS14*)
- O 7q31-Deletion / Monosomy 7 (*D7S486*, cen7)
- O 17p13-Deletion (*TP53*)
- *O NUP98*-Rearrangements (11p15)

MDS, Myelodysplastic syndrome – diagnostic and for IPSS-R relevant aberrations

- O 5q31-Deletion (*CDC25C*, *EGR1*)
- O 5q33-Deletion (*RPS14*)
- O 7q31-Deletion / Monosomy 7 (*D7S486*, cen7)
- O Trisomy 8 (cen8)
- O 17p13-Deletion (*TP53*)
- O 20q12-Deletion (*D20S108*)
- O Loss of Y (cenY)

MDS, Myelodysplastic syndrome – cytogenetic cryptic aberrations

- O 4q24-Deletion (*TET2*)
- O 7q36-Deletion (*EZH2*)
- O 12p13-Deletion (*ETV6*)
- O 21q22-Deletion (*RUNX1*)
- O *MECOM* (*EVI1*)-Rearrangements (3q26)

Aplastic anemia

- O 13q14-Deletion (*DLEU*)
- O 17p13-Deletion (*TP53*)
- O Trisomy 6 (6q21 / *SEC63*, 6q23 / *MYB*)
- O 7q31-Deletion / Monosomy 7 (*D7S486*, cen7)
- O Trisomy 8 (cen8)
- O Trisomy 21 (21q22 / *RUNX1*)

MDS/MPN, Myelodysplastic/myeloproliferative neoplasms

- O 7q31-Deletion / Monosomy 7 (*D7S486*, cen7)
- O Trisomy 8 (cen8)
- O 17p13-Deletion (*TP53*)
- O 13q14-Deletion *(DLEU)*
- O 20q12-Deletion *(D20S108)*
- O Trisomy 21 (21q22 / *RUNX1*)

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CMML, Chronic myelomonocytic leukemia – prognostic relevant aberrations

O 7q31-Deletion / Monosomy 7 (*D7S486*, cen7)
O Trisomy 8 (cen8)

CMML, Chronic myelomonocytic leukemia – cytogenetic cryptic aberrations

O *ETV6*-Rearrangement / *ETV6*-Deletion (12p13)
O 17q11-Deletion (*NF1*)
O 4q24-Deletionen (*TET2*)

CML, Chronic myeloid leukemia – diagnosis

O *BCR-ABL1*-Rearrangement / t(9;22)(q34;q11)

CML, Chronic myeloid leukemia – prognostic relevant aberrations

O 7q31-Deletion / Monosomy 7 (*D7S486*, cen7)
O *MECOM* (EVI1)-Rearrangements (3q26)

CML, Chronic myeloid leukemia – „major route“ additional aberrations

O Isochromosome 17q (17p13 / *TP53*-Deletion, 17q11 / *NF1*-Gain)
O Trisomy 19 (19p13 / *ZNF44* + *ZNF443*, 19q13 / *BICRA* + *NOP53*)
O Trisomy 8 (cen8)

MPN, Myeloproliferative neoplasms

O *BCR-ABL1*-Rearrangement / t(9;22)(q34;q11)
O Trisomy 9 (cen9)
O Trisomy 1 / 1q-Gain (1p32 / *CDKN2C*, 1q21 / *CKS1B*)
O 4q24-Deletion (*TET2*)
O Trisomy 8 (cen8)
O 20q12-Deletion (*D20S108*)

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

O *CHIC2*-Deletion (4q12, *FIP1L1-PDGFRA*-Rearrangement)
O *FGFR1*-Rearrangements (8p11)
O *JAK2*-Rearrangements (9p24)
O other *PDGFRA*-Rearrangements (4q12)
O *ETV6*-Rearrangements (12p13)
O *PDGFRB*-Rearrangement (5q32)

BPDCN, Blastic plasmacytoid dendritic cell neoplasm

O 5q31-Deletion (*CDC25C / EGR1*)
O 13q14-Deletion (*DLEU*)
O 6q21 / 6q23-Deletion (*SEC63 / MYB*)
O 17p13-Deletion (*TP53*)
O 9p21-Deletion (*CDKN2A*)
O *MYC*-Rearrangements (8q24)
O 12p13-Deletion (*CDKN1B*)

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B-ALL, Acute B-lymphoblastic leukemia – diagnostic and prognostic aberrations

- O *BCR-ABL1*-Rearrangement / t(9;22)(q34;q11)
- O *KMT2A (MLL)*-Rearrangements (11q23)
- O *ETV6-RUNX1*-Rearrangement / t(12;21)(p13;q22)
- O Polysomies 4, 10, 13, 14, 17 and 21 (high hyperdiploid karyotype)
- O Monosomies 3, 7, 9, 13 and 17 (hypo diploid karyotype)
- O *IGH*-Rearrangements (14q32)
- O *TCF3 (E2A)-PBX1*-Rearrangement / t(1;19)(q23;p13)
- O *RUNX1*-Amplification (iAMP21)
- O other *RUNX1*-Rearrangements (21q22)
- O *MYC*-Rearrangement (8q24)
- O 9p21-Deletion (*CDKN2A*)

B-ALL, Acute B-lymphoblastic leukemia – philadelphia like

- O *CRLF2*-Rearrangements (Xp22 / Yp11)
- O *P2RY8*-Rearrangements (Xp22 / Yp11)
- O *PDGFRB*-Rearrangements (5q32)
- O *JAK2*-Rearrangements (9p24)
- O *ETV6*-Rearrangements (12p13)

T-ALL, Acute T-lymphoblastic leukemia

- O *TRA/D*-Rearrangements (14q11)
- O *TRB*-Rearrangements (7q34)
- O *TLX3*-Rearrangements (5q35)
- O *TLX1*-Rearrangements (10q24)
- O *KMT2A (MLL)*-Rearrangements (11q23)
- O 6q21/6q23-Deletion (*SEC63 / MYB*)
- O 9p21-Deletion (*CDKN2A*)
- O Monosomy 7 (7cen)

Mature B-cell neoplasms – recurrent aberrations

- O *IGH-CCND1*-Rearrangement / t(11;14)(q13;q32)
- O *IGH-BCL2*-Rearrangement / t(14;18)(q32;q21)
- O *IGH-MYC*-Rearrangement / t(8;14)(q24;q32)
- O other *IGH*-Rearrangements (14q32)
- O *BCL6*-Rearrangements (3q27)
- O *MYC*-Rearrangements (8q24)
- O 6q21 / 6q23-Deletion (*SEC63 / MYB*)
- O 11q22-Deletion (*ATM*)
- O 13q14-Deletion (*DLEU; D13S319 / D13S25*)
- O 17p13-Deletion (*TP53*)
- O Trisomy 3 / 3q-Gain (*BCL6 / 3q27*)
- O Trisomy 12 (cen12)

Mature B-cell neoplasms – CD5 negative

- O 6q-Deletion (*SEC63* / 6q21, *MYB* / 6q23)
- O 3q-Gain (*BCL6* / 3q27)
- O 11q-Deletion (*ATM* / 11q22)
- O 17p13-Deletion (*TP53*)
- O 13q-Deletion (*DLEU* / 13q14)
- O 7q-Deletion (*D7S486* / 7q31)
- O Trisomy 12 (cen12)
- O Trisomy 18 / *IGH-BCL2*-Rearrangement / t(14;18)(q32;q21) (*IGH* / 14q32, *BCL2* / 18q21)

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MCL, Mantle cell lymphoma

O *IGH-CCND1*-Rearrangement / t(11;14)(q13;q32)
O 17p13-Deletion (*TP53*)
O 9p21-Deletion (*CDKN2A*)
O 13q14-Deletion (*RB1*)
O 12p13-Deletion (*CDKN1B*)

CLL, Chronic lymphocytic leukemia - diagnosis

O *IGH-CCND1*-Rearrangement / t(11;14)(q13;q32)
O *IGH-BCL2*-Rearrangement / t(14;18)(q32;q21)
O other *IGH*-Rearrangements (14q32)

CLL, Chronic lymphocytic leukemia - prognosis

O 6q21 / 6q23-Deletion (*SEC63 / MYB*)
O 11q22-Deletion (*ATM*)
O 13q14-Deletion (*RB1*)
O 13q14-Deletion (*DLEU*)
O 13q14-Deletion (*D13S319 / D13S25*)
O 17p13-Deletion (*TP53*)
O Trisomy 12 (cen12)

Waldenström macroglobulinemia (M. Waldenström)

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

HCL, Hairy cell leukemia

O Chromosome 5 aberrations
O 6q21 / 6q23-Deletion (*SEC63 / MYB*)
O Chromosome 7 aberrations
O 11q22-Deletion (*ATM*)
O 17p13-Deletion (*TP53*)
O other IGH Aberrations (14q32)

PPBL, persistent polyclonal B-cell lymphocytosis

O 3q-Gain (*BCL6* / 3q27)
O 8q-Gain (*MYC* / 8q24)
O *IGH-BCL2*-Rearrangement / t(14;18)(q32;q21)

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Catalogue of Services

Mature T-cell neoplasms

- O *TRA/D*-Rearrangements (14q11)
- O *TRB*-Rearrangements (7q34)
- O 11q22-Deletion (*ATM*)
- O 17p13-Deletion (*TP53*)
- O 8q24-Gain (*MYC*)
- O 6q21 / 6q23-Deletion (*SEC63 / MYB*)
- O ALK-Rearrangements (*2p23*)

T-PLL, T-cell prolymphocytic leukemia

- O *TRA/D*-Rearrangements (14q11)
- O *TCL1A (TCL1)*-Rearrangements (14q32)
- O 8q24-Gain (*MYC*)
- O 11q22-Deletion (*ATM*)
- O 17p13-Deletion (*TP53*)

T-/NK-LGL, Large granular lymphocytic leukemia

- O 11q22-Deletion (*ATM*)
- O 11q23-Deletion *(KMT2A)*
- O 13q14-Deletion (*DLEU*)
- O 17p13-Deletion (*TP53*)
- O 6q21 / 6q23-Deletion (*SEC63 / MYB*)
- O Chromosome 7 aberrations
- O Trisomy 8 (8cen)

Multiple myeloma (CD138+ sorted cells) – diagnostic and prognostic relevant aberrations

- O 17p13-Deletion (*TP53*)
- O *IGH-FGFR3*-Rearrangement / t(4;14)(p16;q32)
- O *IGH-MAF*-Rearrangement / t(14;16)(q32;q23)
- O 1p32-Deletion / 1q21-Gain (CDKN2C, CKS1B)
- O *IGH-CCND1*-Rearrangement / t(11;14)(q13;q32)
- O *IGH-MAFB*-Rearrangement / t(14;20)(q32;q12)

Multiple myeloma (CD138+ sorted cells) – other recurrent aberrations

- O other *IGH*-Rearrangements (14q32)
- O *IGH-CCND3*-Rearrangement / t(6;14)(p21;q32)
- O *IGH-MYC*-Rearrangement / t(8;14)(q24;q32)
- O other *MYC*-Rearrangements (8q24)
- O 13q14-Deletion / Monosomy 13 (*DLEU*)
- O Trisomy 3 (cen3)
- O Trisomy 9 (cen9)
- O Trisomy 11 (cen11)
- O Trisomy 15 (cen15)
- O Trisomy 5 (5p15 / *CDC25C*, 5q31 / *EGR1*)
- O Trisomy 19 (19p13 / *ZNF44* + *ZNF443*, 19q13 / *BICRA* + *NOP53*)
- O 12p13-Deletion (*ETV6*)