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HEMATOLOGY PANEL

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HEMATOLOGY PANEL

17-001-A del (13q14) (D13S319) /LAMP1 (13q34) / Cent 12

Deletions covering the 13q14 region are frequently seen in a wide range of hematological disorders. Chromosome 13q deletions occur in 16-40% of multiple myeloma (MM) cases, and most are completely monosomy 13 (85%); the remaining 15% constitutes the deletion of 13q14. A case study of patients with multiple myeloma narrowed the critically deleted region to 13q14. Historically, deletions of 13q have been associated with poor prognosis in MM, but its prognostic relevance is now believed to be related to its association with other concomitant genetic lesions. Deletions in the long arm of chromo some 13 are also frequently detected in patients with aggressive nonHodgkin lymphoma (NHL).

Trisomy 12 is another common chromo somal abnormality seen in CLL and is de tected in approximately 20% of CLL cases. Trisomy 12 is associated with a moderate prognostic outcome when there is only one abnormality. Therefore, when used in conjunction with other biomarkers, mor phology, and clinical information, FISH is a valuable tool for predicting disease progression and overall survival in CLL patients.

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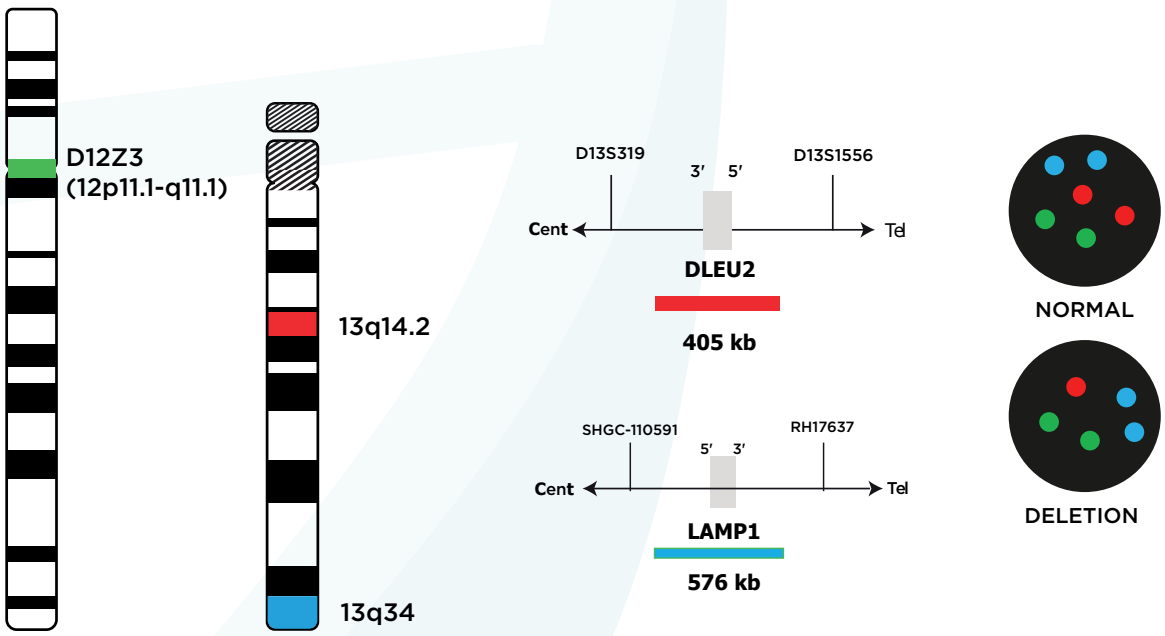

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HEMATOLOGY PANEL

17-052 ATM/ TP53 / Cent 17

The tumor suppressor TP53 gene in the 17p13.1 region and the protein kinase ATM gene in the 11q22.3 region are frequently deleted in chronic lymphocytic leukemia (CLL) conditions. Deletions of the TP53 (tumor protein 53; alsa known as p53) gene have been detected in patients with CLL, multiple myeloma (MM), and acute myeloid leukemia (AML). Allelic loss of the short arm of chromosome 17 in CLL patients is associated with failure of treatment with alkylating agents and shorter survival times. The ATM (ataxia telangiectasia mutated) gene is located at 11q22.3, and encodes a protein kinase involved in cell cycle regulation, including TP53 activation. CLL patients with 11q deletion show rapid disease progression and low-grade survival.

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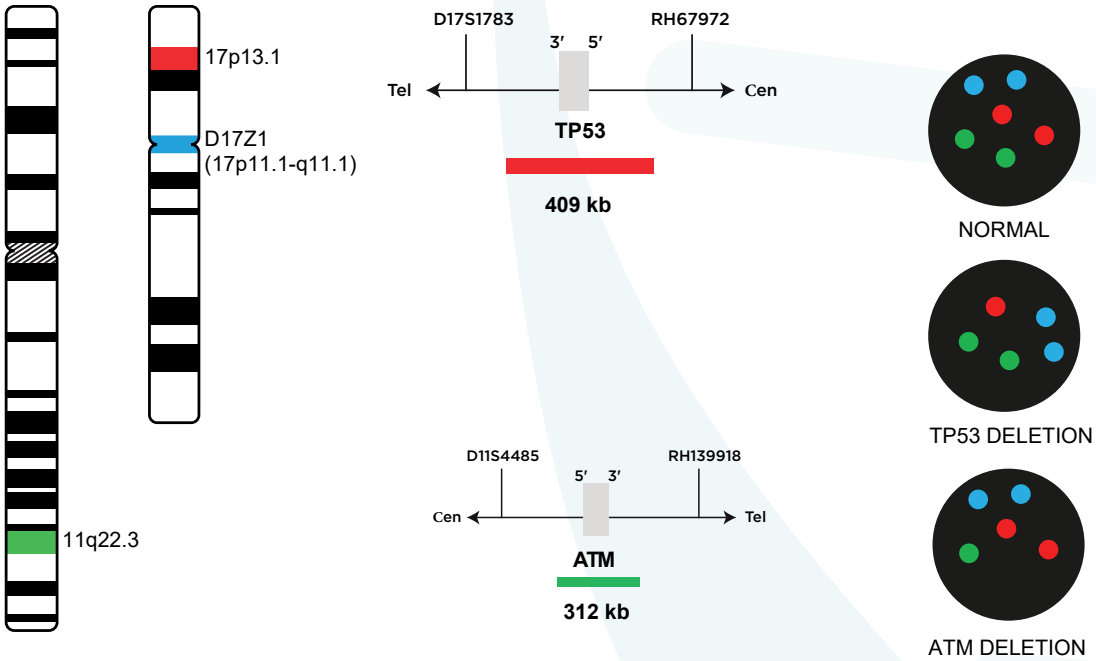

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HEMATOLOGY PANEL

17-040 BCR-ABL t(9;22)

Rearrangements involving t(9;22)(q34.1q11.2) are observed in approximately 90% of adults with chronic myeloid leukemia (CML) and approximately 25% of adults with acute lymphobalstic leukemia (ALL). The presence of a BCR-ABL1 fusion has important diagnostic and prognostic implications in various hematological diseases. Rearrangements are characterized cytogenetically by the presence of the Philadelphia (Ph) chromosome.

This translocation often results in a chimeric BCR/ ABL1 fusion gene on the derivative 22nd chromosome. The product of this gene is the BCR/ ABL1 protein with abnormal tyrosine kinase activity. in normal cells, ABL1 kinase activity is well regulated in response to growth factors and other stimulant.

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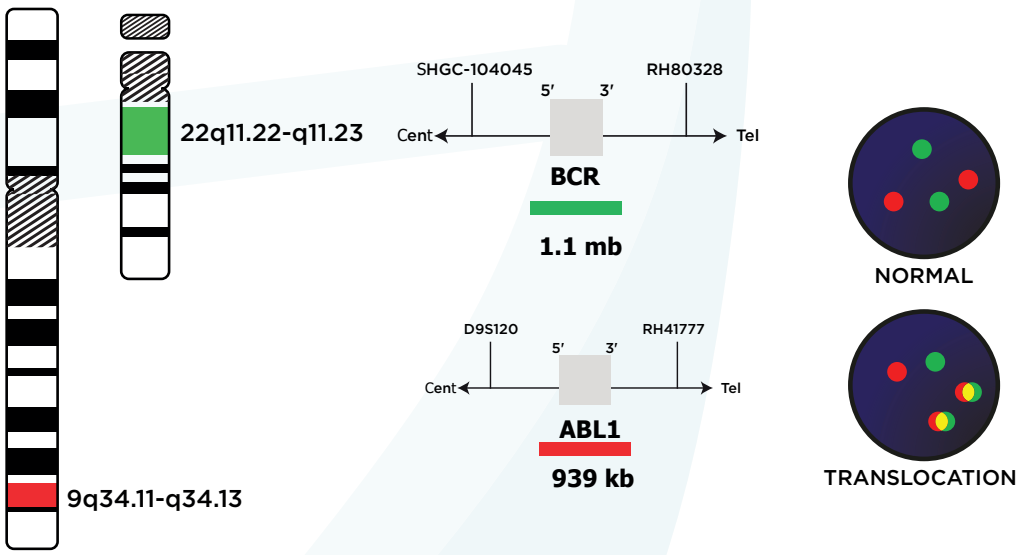

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17-068 EGR1 del(5q31.2)

Deletions covering the 5q31.2 region are one of the most common karyotypic abnormalities in myelodysplastic syndrome (MDS) and acute myeloid leukemia (AML) with changes due to myelodysplasia in therapy-associated MDS or AML, 40% of patients show a 5q deletion. The fact that EGRl deletion is associated with higher tumor grade in estrogen receptor negative (ER-negative) breast carcino-mas suggests that loss of the EGRl gene may contribute to the pathogenesis of ER-negative breast carcinomas. Transfusion-independent, lower-risk MDS patients with

A 5q deletion are treated with the FDA-approved lenalid-omide, a thalidomide analogue. Dicentric chromosomes, including chromosome 5, have often been observed in patients with de nova or therapy-associated MDS and AML. These patients often show a complex karyotype. In such conditions, characterization of rearrangement by conventional cytogenetics is hardly feasible. Therefore, FISH can be a useful tool for diagnosis and treatment decisions.

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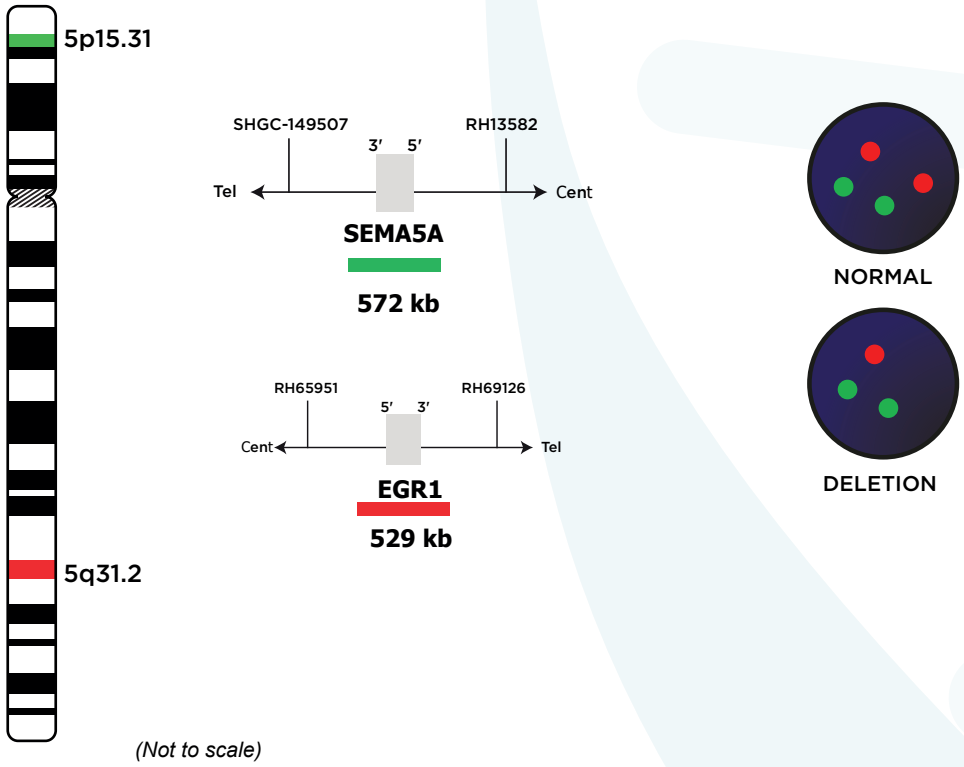

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HEMATOLOGY PANEL

17-054 del(7q31.2)

Chromosome 7 monosomy and deletion of the long arm of chromosome 7 are recurrent chromosomal abnormalities frequently seen in myeloid diseases. Monosomy 7 and de1(7q); it is seen in many myeloid diseases, including myelodysplastic syndrome (MDS), acute myeloid leukemia (AML), and juvenile myelomonocytic leukemia (JMML). The presence of Monosomy 7 or del (7q) as karyotypic changes is associated with worse out comes in myeloid malignancies.

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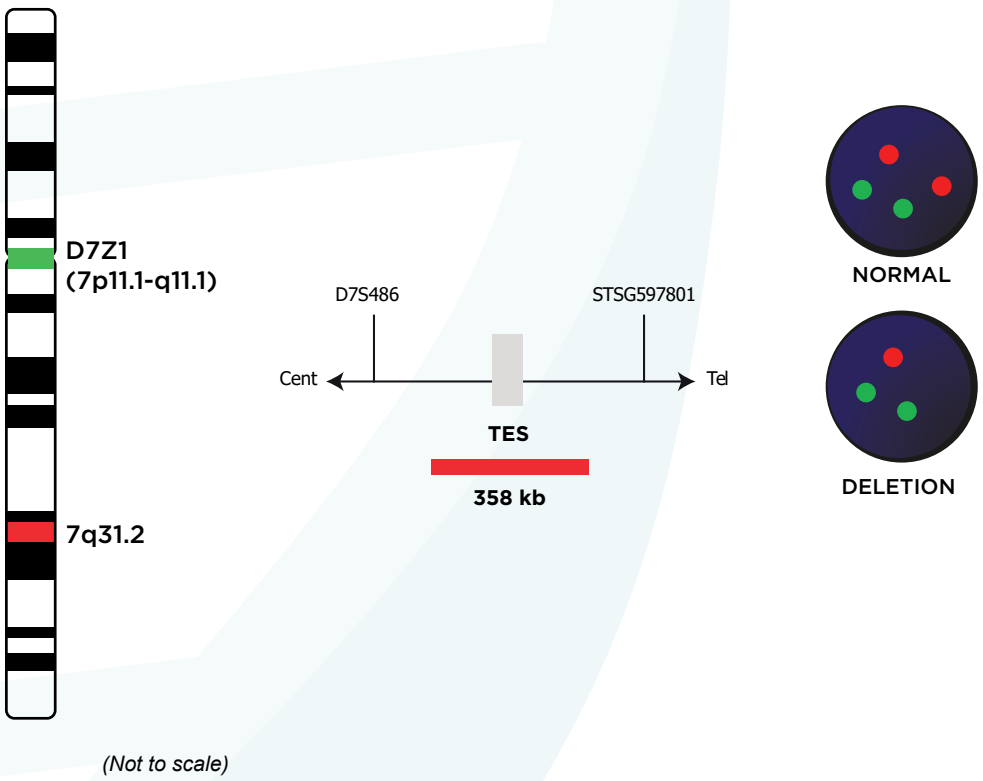

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17-059 del(20q12-13)

Chromosome 20q deletions can occur in a variety of myeloid disorders; for example, myelodysplastic syndromes (MDS), acute myeloid leukemia (AML) and myeloproliferative neoplasms (MPNs). in MDS, del(20q) as the only cytogenetic abnormality is associated with a favorable prognosis, better survival, anda lower risk of conversion to AML. Del(20q) with additional cytogenetic abnormalities predicts a poor prognosis.

The 20q deletion is seen in approximately 2% of MDS cases. Patients with del(20q) base have an advantageous outcome compared to patients with additional abnormalities such as del(5q), del(7q), monosomy 7 and trisomy 8. Most del(20q) patients have interstitial deletion between 20q11.2 and 20q13.3.

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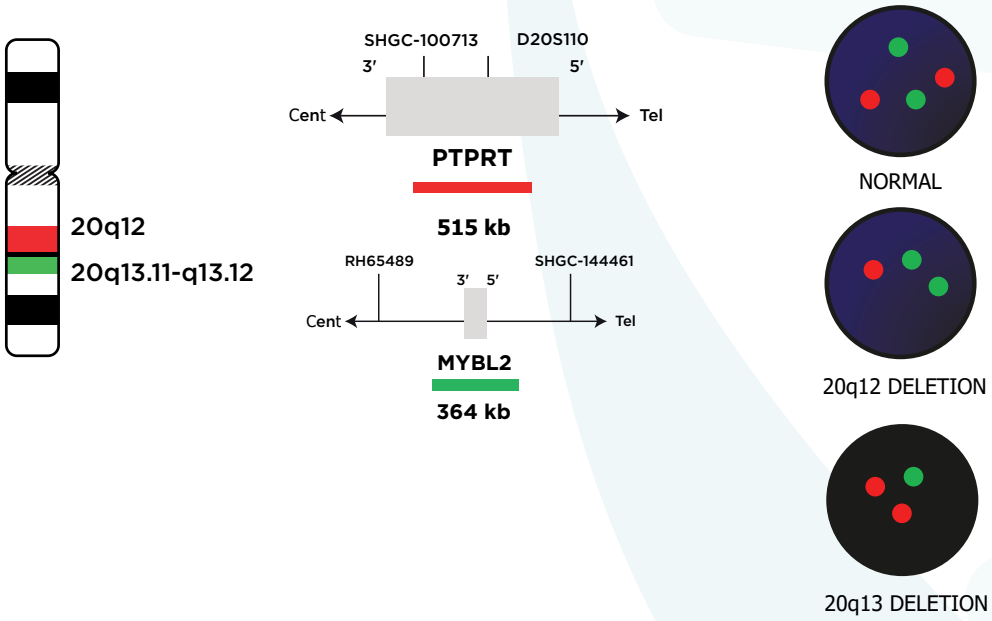

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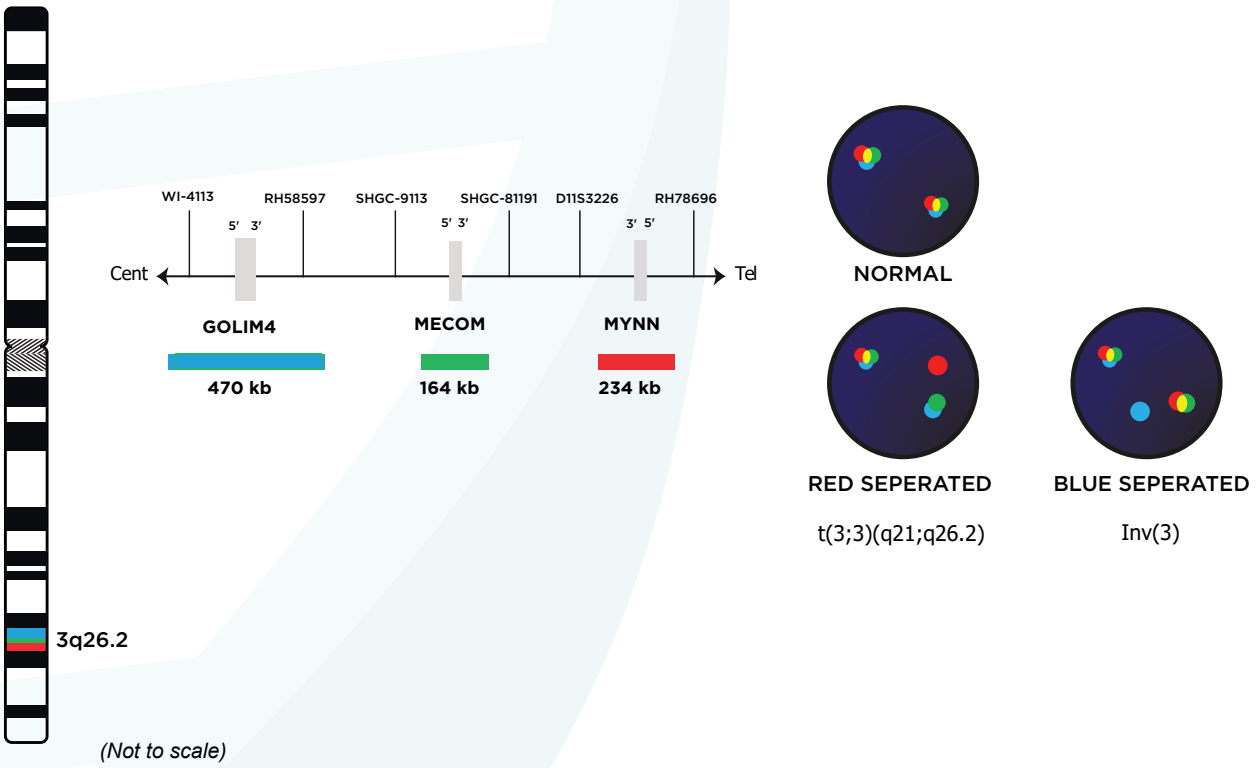
HEMATOLOGY PANEL

17-091 EVI1 (3q26.2) Breakapart

Inv(3)/t(3;3) and less commonly inv(3;3)(q26.2;q21q26.2) occur in 1-2.5% of acute myeloid leukemia (AML) and occur in myelodysplastic syndromes and chronic it is alsa observed in the blastic stage of myeloid leukemia. Various other MECOM translocations involving other fusion partner genes have alsa been reported in various types of myeloid malig nancies. 3q26.2 rearrangements are associated with minimal or no response to chemotherapy and poor clinical outcome. Chromosomal rearrangements involving the 3q26.2 region are associated with myeloid malignancies, abnormal expression of the MECOM gene, an unfavorable prognosis, and an aggressive clinical course.

INVERTION



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17-004 p16 (9p21)

The CDKN2A (cyclin dependent kinase inhibitor 2A) gene, often referred to as p16 or INK4a/ ARF, is located in the 9p21.3 chromosome region. Using alternative first exons and an alternative reading frame, the gene encodes two different tumor suppressor proteins p161NK4a and p14ARF, both of which are involved in cell cycle regulation. CDKN2A has been identified as a major susceptibility gene for melanoma. The tumor suppressor gene CDKN2A is inactivated by homozygous deletions with high frequency in various human primary tumors such as bladder and renal cell carcinomas, prostate and ovarian adeno carcinomas, non-small cell lung cancer, sarcoma, glioma, mesothelioma, and melanoma. Furthermore, deletion of the CDKN2A gene is found in up to 80% of T-cell acute lymphoblastic leukemia cases and is associated with poor prognosis and disease relapse.

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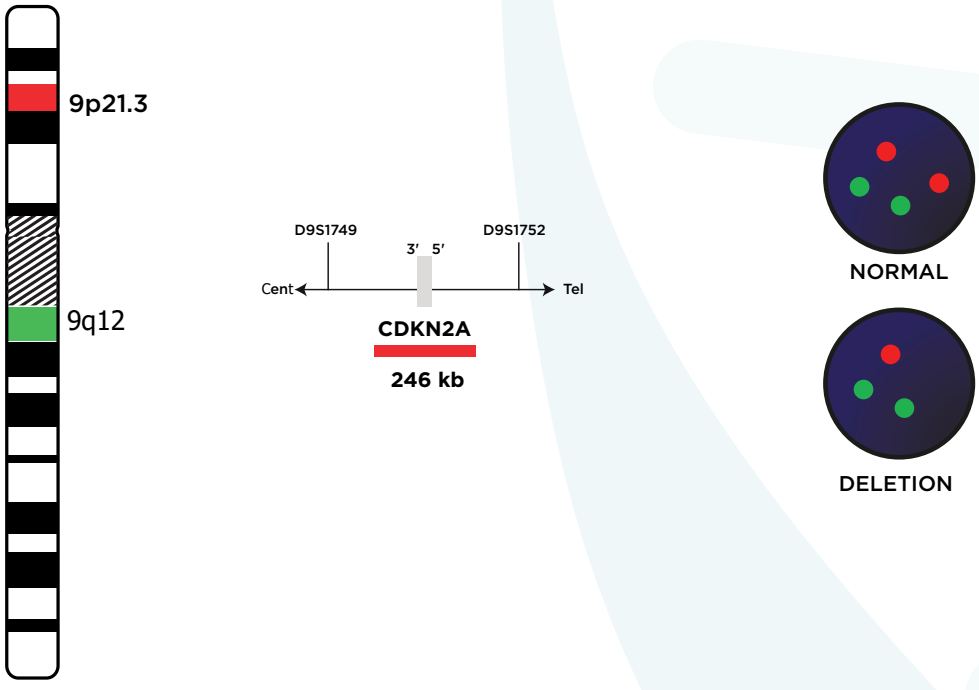

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HEMATOLOGY PANEL

17-043 PML-RARA t(15;17)

Translocations involving the PML (promyelocytic leukemia, also known as MYL) gene and the PARA (retinoic acid receptor alpha, RARa) gene are thought to be characteristic of acute promyelocyt ic leukemia (APL), a subtype of acute myeloid leukemia. The PML-RARA fusion gene is created by the t(15;17)(q24;q21) translocation found in 90% of APL cases, a leukemia that accounts for 5-8% of acute myeloid leukemia (AML) cases. Variant RARA translocations may be observed in a subset of cases. Known fusion partners are NPMl at 5q35, NUMAl at 11q13, ZBTB16 (PLZF) at 11q23, STAT5B at 17q21, PRKARlA at 17q24, FIPlll at 4q12, and BCOR at Xpll. Because the PML/RARA fusion is responsible for the response of these neoplasms to alltrans retinoic acid (ATRA) therapy and other conventional chemotherapy, it is important to correctly distinguish between t(15;17) translocations and those involving other RARA partners.

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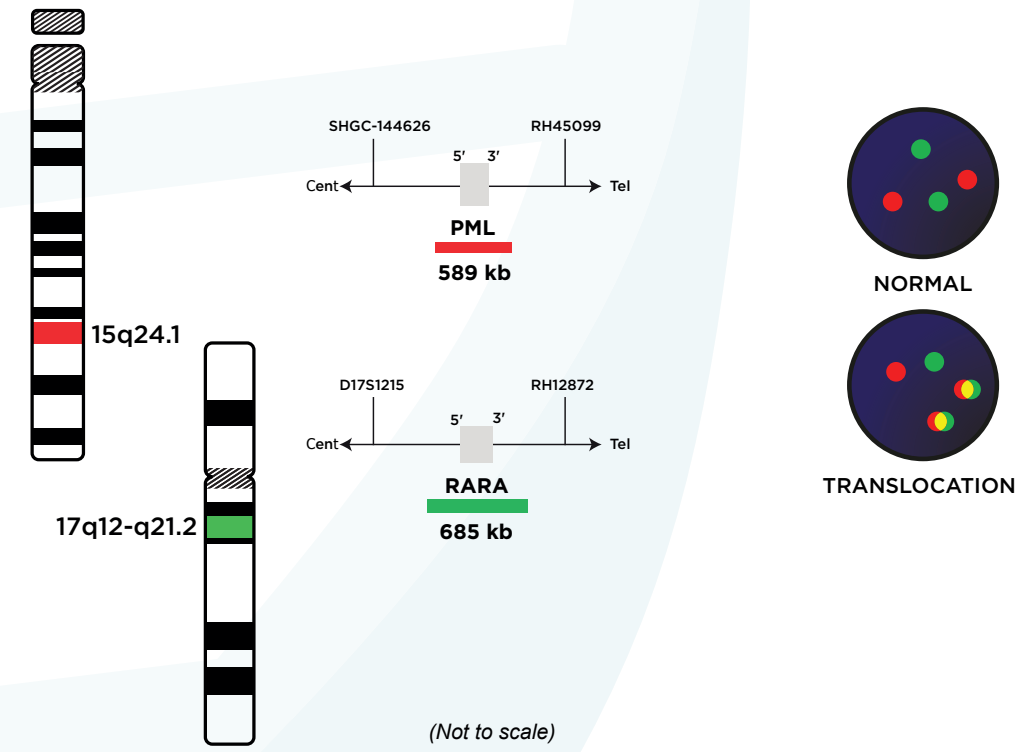

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17-032 AML1-ETO t(8;21)

The t(8;21) balanced chromosomal translocation is found in approximately 90% of patients with acute myeloid leukemia (AML). AML is a heterogeneous clonal disorder of hematopoietic progenitor cells and is one of the most common malignant myeloid disorders in adults. Run t-associated transcription factor 1 gene (RUNX1) and RUNX1 translocation partner 1 gene (RUNX1T1) are involved in the transcriptional regulation of genes during normal hematopoiesis.

Translocation occurs in 10% to 22% of patients with AML FAB type M2 and in 5% to 10% of AML cases; it is most common in children and young adults2 and is a good prognostic indicator.

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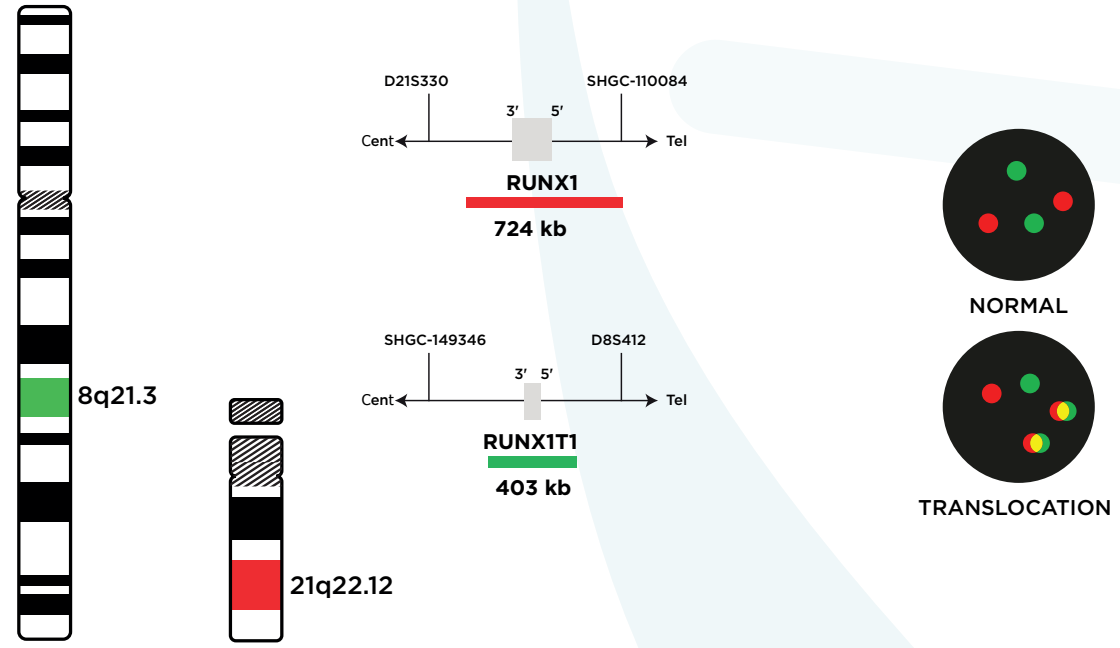

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HEMATOLOGY PANEL

17-033 TEL-AML t(12;21)

t(12;21)(p13.2;q22.1) balanced chromosome translocation childhood onset B-cell precursor (BCP) is the most common genetic rearrangement in acute lymphoblastic leukemia (ALL) (19-27% of BCP-ALL) occurs in the early stages of pregnancy) and has been associated with a good prognosis. In ETV6/ RUNX1 positive ALL, three secondary abnormalities have been found to impair the clinical course: deletion of the second non-translocation ETV6 allele, gains of the RUNX1 gene, and duplication of derivation 21. Detection of t(12;21) by fluorescent in situ hybridization (FISH) allows simultaneous detection of the most common secondary changes and provides additional infor mation about the likely outcome of the disease in ALL patients.

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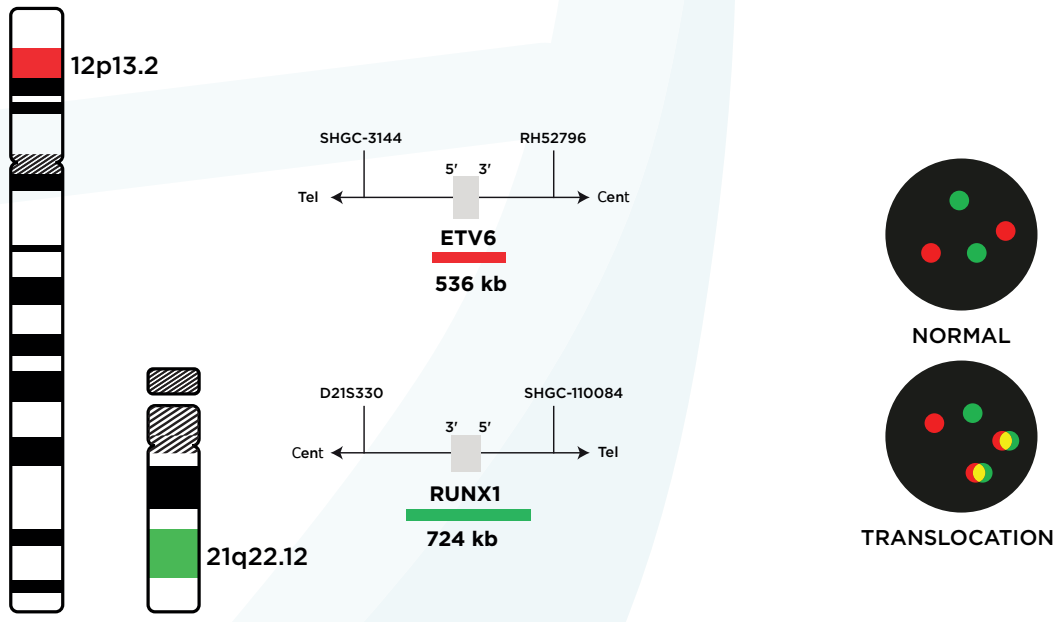

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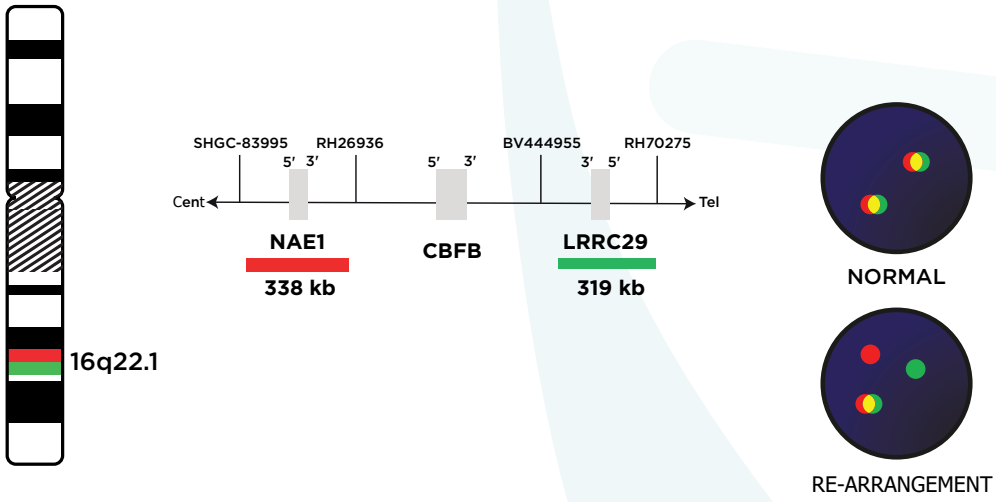
17-050 CBFB Breakapart

CBFB encodes the beta subunit of the CBFA/CBFB transcription factor complex involved in myeloid differentiation. Chromosomal abnormalities of inv(16)(p13;1q22.1) and its associated t(16;16)(p13.1q22.1) translocation detected in approximately 10% of AML (acute myeloblastic leukemia) patients it causes its fusion with the MYH11 (smooth muscle myosin heavy chain) gene at 16p13.1. Rearrangements of the CBFB gene are frequently found in patients with the myelomonocytic subtype with increased bone marrow eosinophils, termed AML FAB (French-American-British classification) type M4Eo, and are found in 5-8% of AMLs. This rearrangement may also occur in cases of treatment-related AML. Inversion inv(16)(p13.11q22.1) or translocation t(16;16)(p13;11q22.1) produces CBFB-MYH11 gene rearrangements and is classified as a favorable cytogenetic risk group in patients with AML.

BREAKAPART



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HEMATOLOGY PANEL

17-002 MLL (11q23) Breakapart

Up to 1-15% of cancer patients treated with KMT2A gene rearrangements with a DNA topoisomerase II inhibitor develop therapy-associated leukemia (t-AML) associated with KMT2A translocations. Translocations involving the KMT2A gene are detected in 5-6% of all acute myeloid leukemias (AML) and 5-10% of all acute lymphoblastic leukemias (ALL). The frequency of translocations involving the KMT2A gene is significantly higher in infants with AML (50%) and ALL (80%). Over 30 fusion partners have been documented tor KMT2A; the most common translocations are t(4;11) and t(11;19) in ALL patients, t(6;11), t(9;11) and t(11;19) in AML patients. Overall, the finding of KMT2A re-arrangements in patients with acute leukemia indicates a less favorable prognosis. However, recent studies suggest that the specific KMT2A translocation partner may have an impact on response to therapy and overall prognosis, depending on the clinical concept.

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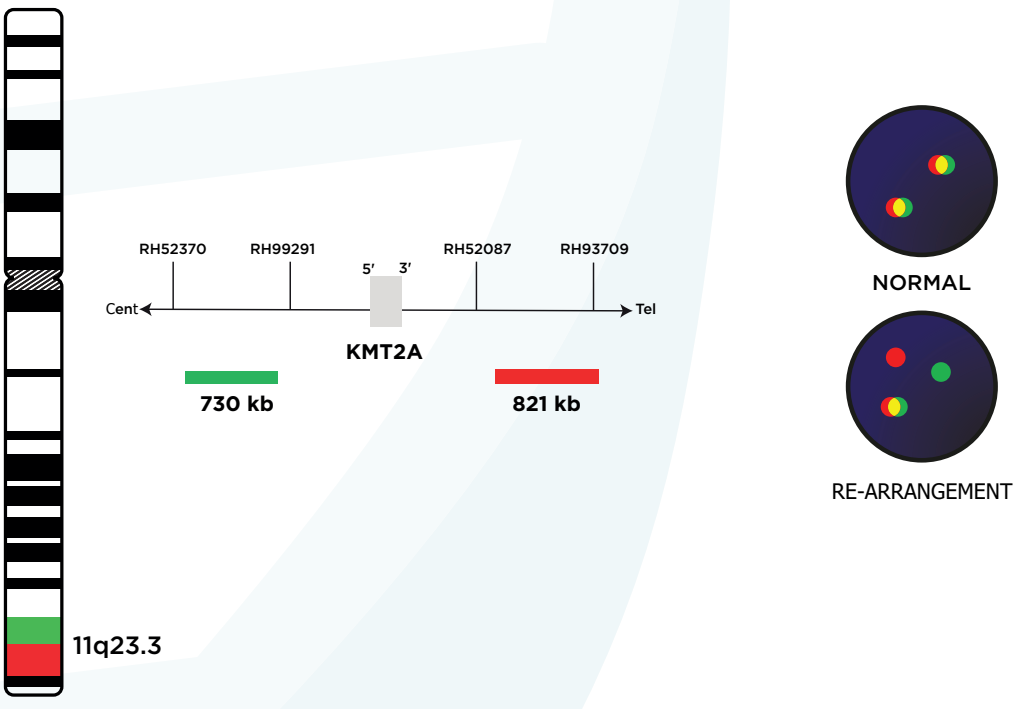

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17-066 c-MYC (8q24) Breakapart

The MYC proto-oncogene (MYC proto-oncogene, bHLH transcription factor, a.k.a. CMYC) encodes a transcription factor required tor cell growth and proliferation and is extensively involved in tumorigenesis. Translocations involving the MYC gene are thought to be the cyto genetic hallmark of Burkitt's lymphoma, but are also found in other lymphoma types. MYC rearrangements that activate MYC by translocation with one of the three immunoglobulin loci (IGH, IGL, or IGK) are detected in nearly all cases of Burkitt lymphoma at diagnosis. They are also seen in diffuse large B-cell lymphoma (DLBCL), multiple myeloma, and plasmablastic lymphoma, among other diseases.

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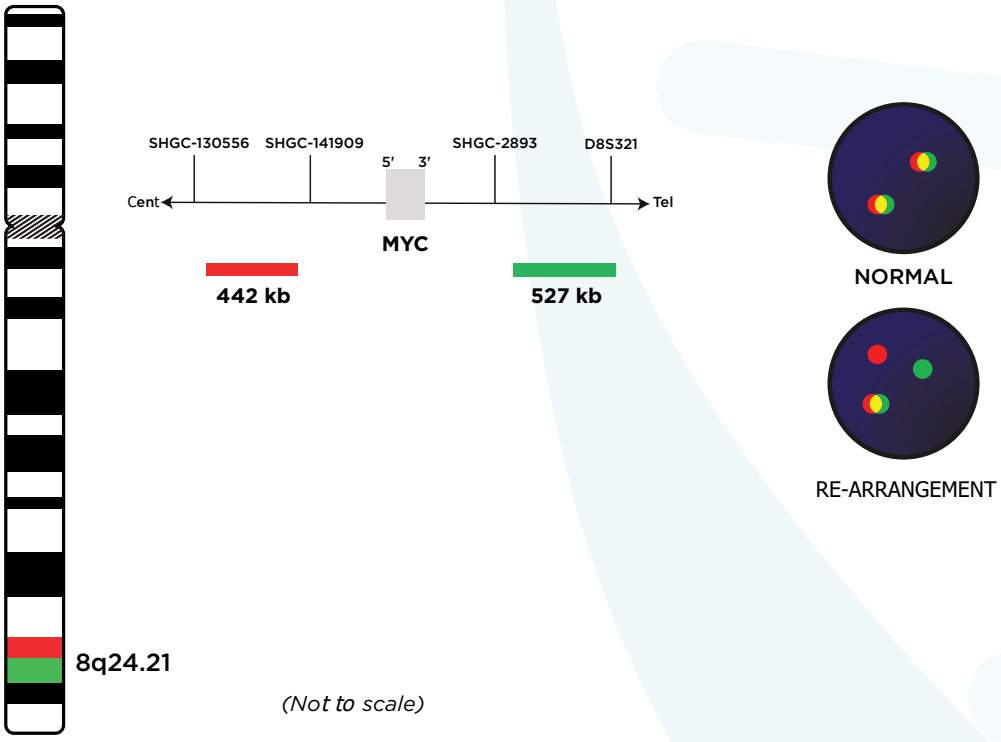

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HEMATOLOGY PANEL

17-073 IGH (14q32) Breakapart

Rearrangements involving the IGH (immunoglobulin heavy chain) gene are considered to be cytogenetic markers of non-Hodgkin lymphoma (NHL). NHLs represent 50% of all hematological malignancies. IGH gene rearrangements have been identified in approximately 50% of NHLs and are associated with specific subtypes of NHLs. Translocation of t(11;14)(q13.3;q32.3) in approximately 95% of mantle cell lymphoma (MCL), 80% of t(14;18)(q32.3;q21.3) follicular lymphoma (FL) in , t(3;14)(q27;q32.3) is found in diffuse large B-cell lymphoma (DLBCL) and t(8;14)(q24.21;q32.3) Burkitt's lymphoma. In all of these translocations, an oncogene located near the breakpoint of the translocation partner is activated by passing near the IGH regula tory sequences.

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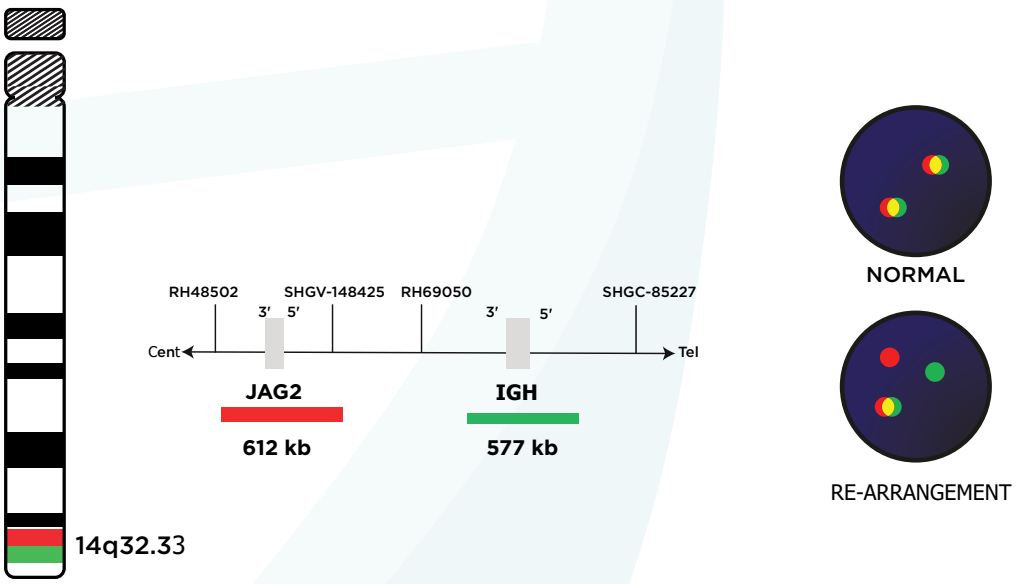

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17-069 IGH-FGFR3 t(4;14)

The FGFR3 (fibroblast growth factor receptor 3) gene is located in the 4p16.3 region, and the IGH (immunoglobulin heavy locus) is located in the 14q32.33 region. FGFR3 encodes a receptor tyrosine kinase that regulates the downstream signaling chain after ligand binding. Fusion of several part ner genes (including the IGH locus), often found in multiple myeloma (MM), can lead to ligand-in dependent activation of the tyrosine kinase of the re-sulting FGFR3 fusion protein. FGFR3/IGH trans locations are observed in approximately 15-20% of MM patients. Breakpoints for the 4p16.3 locus are located between the FGFR3 gene and the 5′ end of the NSD2 gene. The t(4;14)(p16.3;q32.3) translocation is associated with up-regulation of FGFR3 and myeloma NSD2 (also known as MMSET) portion protein. Patients with the FGFR3/IGH translocation show an overall poor prognosis, which is only partially alleviated by the use of the newer agents bortezomib and lenalidomide.

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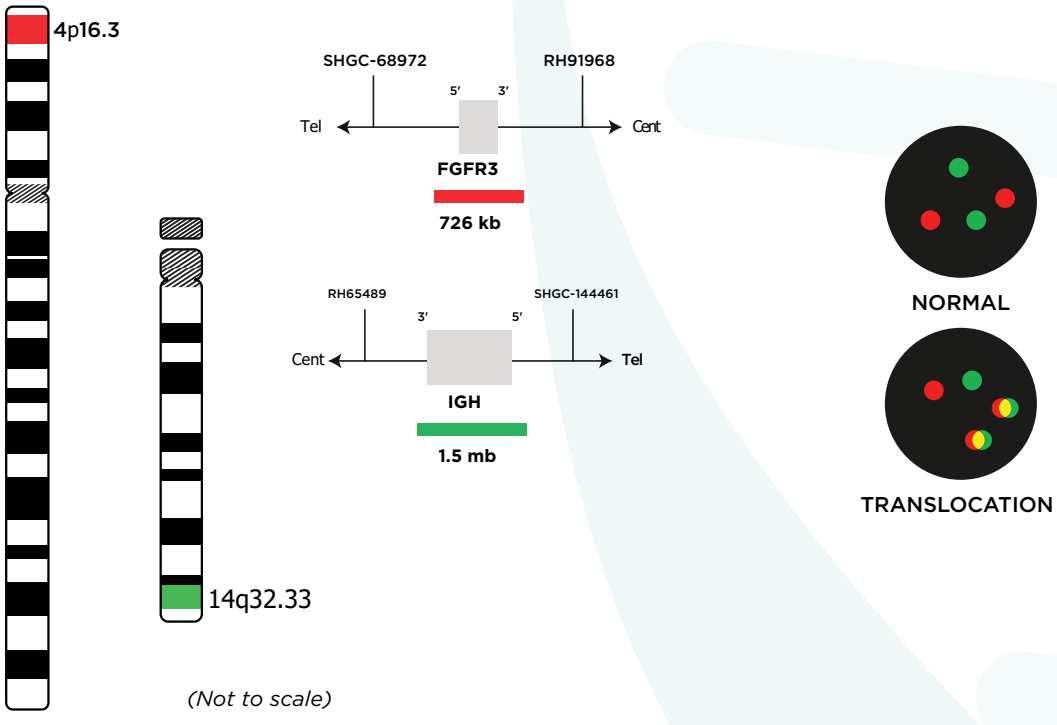

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HEMATOLOGY PANEL

17-074 IGH-cMYC t(8;14)

MYC proto-oncogene (MYC proto-oncogene, bHLH transcription factor) encodes a transcrip tion factor required for celi growth and proliferation and is extensively involved in tumorigenesis. Burkitt lymphoma has the cMYC/IGH translocation, t(8;14)(q24;q32) and variant forms t(2;8)(p13;q24) and t(8;22)(q24;q11) and is a mature B cell or Burkitt type Acute Lymphoblastic Leukemia (ALL) is also observed.

The most common translocation t(8;14)(q24.21;q32.3) involving the MYC gene region can be found in approximately 80% of Burkitt lymphoma cases and moves the MYC gene near the lgH (immunoglobulin heavy chain) locus. Other translocations affecting the MYC gene are t(8;22)(q24.21;q11.2) and t(2;8)(p11.2;q24.21), both of which involve one of two immunoglobulin light chain loci.

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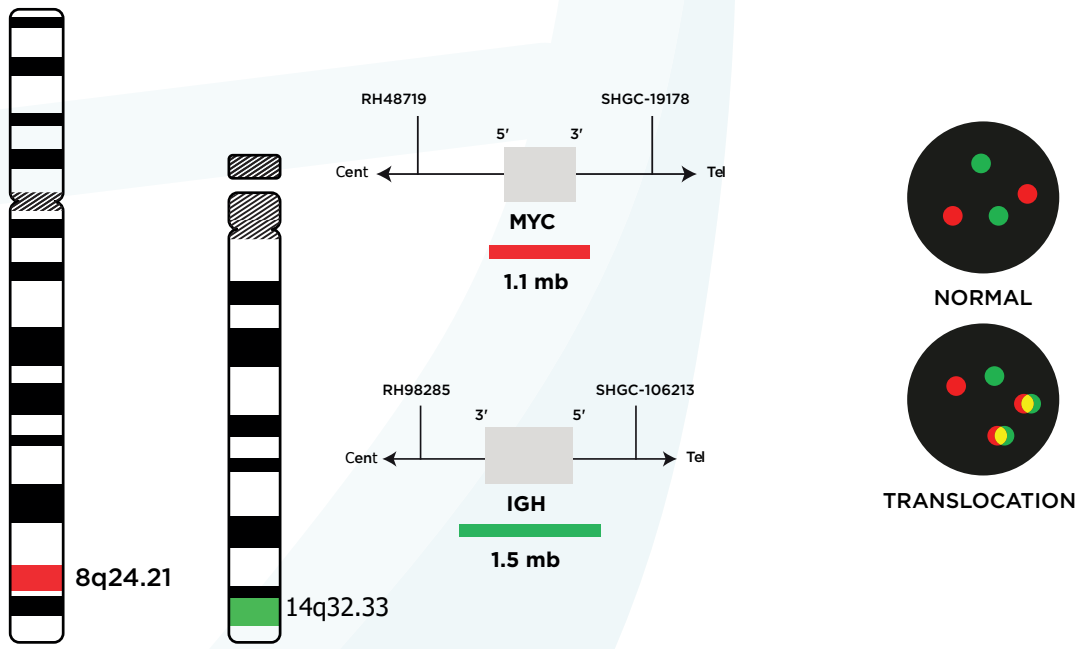

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17-077 IGH-CCNDl t(11;14)

The translocation moves the CCNDl gene (also known as cyclin D1; PRAD1 and BCL1) near the IGH (immunoglobulin heavy locus, also known as IGH) locus, resulting in constitutive overexpression of CCND1.The t(11;14)(q13;q32) rearrangement involving CCND1 and IGH is considered indicative of mantle cell lymphoma (MHL), whose presence can be used to aid in the differential diagnosis of CD5+ B-cell lymphoproliferative diseases.

The t(11;14)(q13.3;q32.3) translocation containing the CCND1 and IGH gene regions is detected in up to 95% of patients with mantle cell lymphomas (MCL) and is the genetic variant of this subtype of low-grade peripheral B-cell neoplasms considered to be an indicator. However, t(11;14) has also been detected in other lymphoproliferative disorders (LPDs) such as B-prolymphocytic leukemia (PLL) and less frequently in plasma celi myelomas, B-cell chronic lymphocytic leukemia, and villous lymphocyte splenic lymphomas (SLVL).

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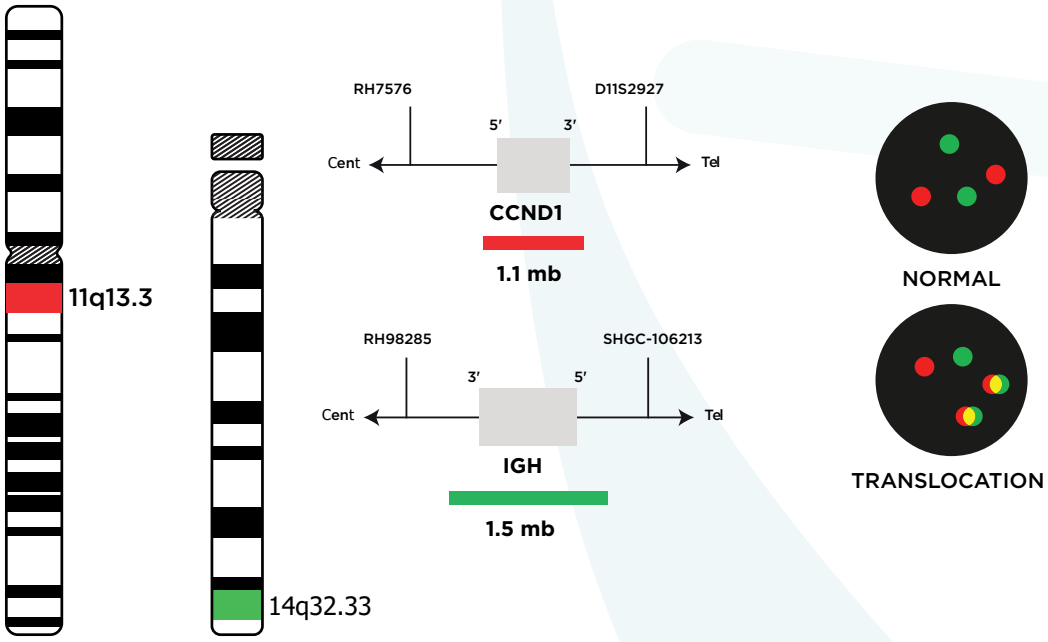

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HEMATOLOGY PANEL

17-093 IGH-MYEOV t(11;14)

Mantle cell lymphoma (MCL) is a B-cell non-Hodgkin lymphoma (NHL) with an aggressive clini cal course. it is genetically characterized by t(11;14)(q13;q32) found in ap-proximately 95% of MCL patients. Less frequently, t(11;14) can also be detected in B-cell prolymphocytic leukemia, my elomas, and chronic lymphocytic leukemia. The t(11;14)(q13;q32) translocation is the most common translocation in MM, occurring in approximately 15% of cases.

Unlike IGH rearrange ments in other neoplasms, those found in MM have IGH breakpoints predominantly in the C/J region, placing the MYEOV gene under the control of the 3′ Eal enhancer when in the MYEOV state. in contrast to CCND1 translocations, the Eμ enhancer controls CCND1 expression. MYEOV overexpression may be a possible prognostic factor in MM.

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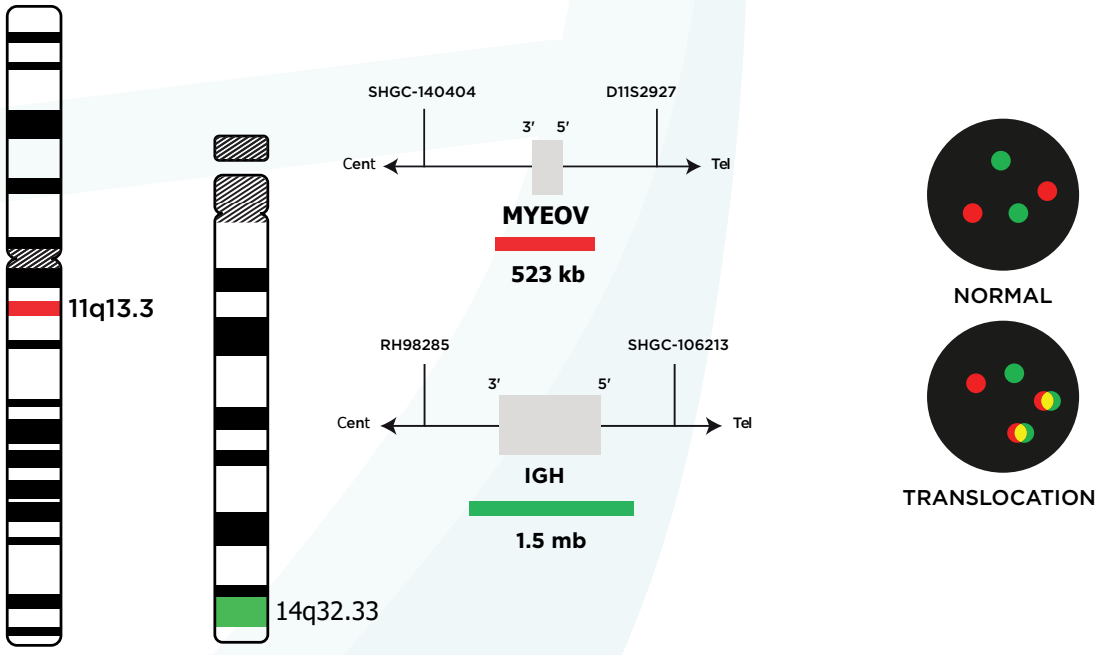

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17-011 IGH-MAF t(14;16)

The MAF (MAF bZIP transcription factor) gene is located in the IGH (immunoglobin heavy locus) at 16q23 and 14q32.3. Approximately 50-60% of multiple myeloma (MM) cases involve translocations involving IGH and one of several partners such as CCND1, NSD2 (WHSCl) and FGFR3, CCND3, MAF or MAFB. The t(14; 16) (q32.3; q23) translocation is a recurrent translocation seen in 2-10% of MM.

The t(14;16)(q32.3;q23) translocation is frequently found in multiple myeloma (MM). MM is a malignant post-germinal center tumor of somatic-mutated, isotype-transformed plasma cells that accumulate in the bone marrow.

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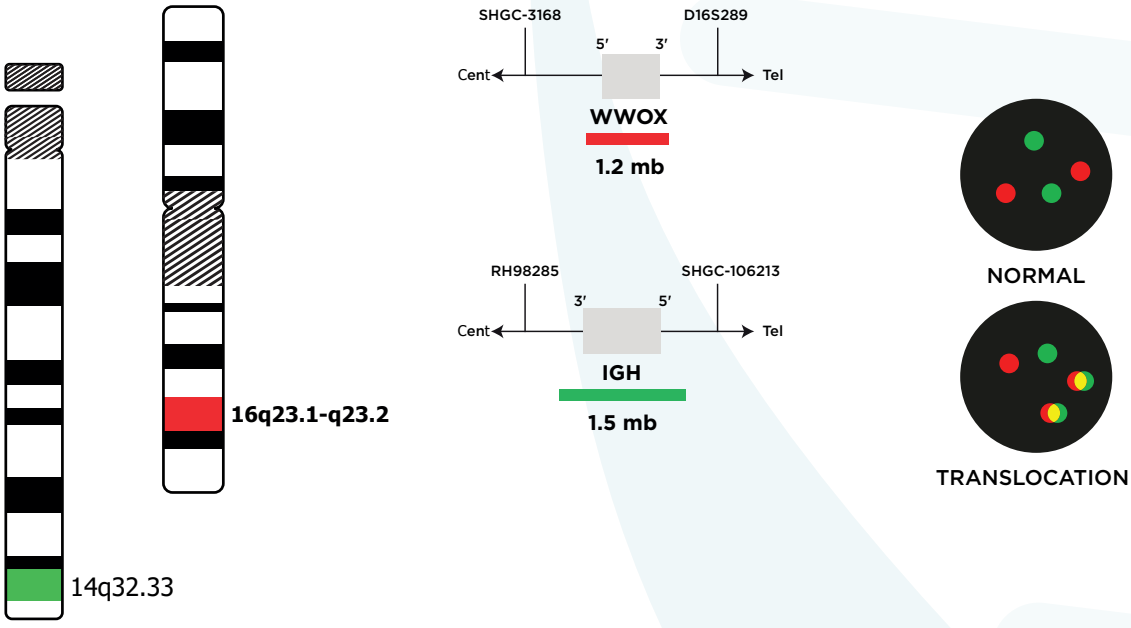

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HEMATOLOGY PANEL

17-058 IGH-BCL2 t(14;18)

Translocations involving the BCL2 (B-cell lymphoma 2) gene and the IGH (immunoglobulin heavy locus, also known as IGH) gene are considered cytogenetic markers of follicular lymphoma (FL). FL is one of the most common non-Hodgkin lymphomas (NHL). IGH-BCL2 rearrangements are observed in 70-95% of follicular lymphoma (FL) cases and in 20-30% of diffuse large B-cell lym phoma (YBBCL) cases. As a result of the rearrangement, the BCL2 gene at 18q21.33 is moved next to the IGH (immunoglobulin heavy chain) locus at 14q32.33, leading to overexpression of the anti-apoptotic protein BCL2.

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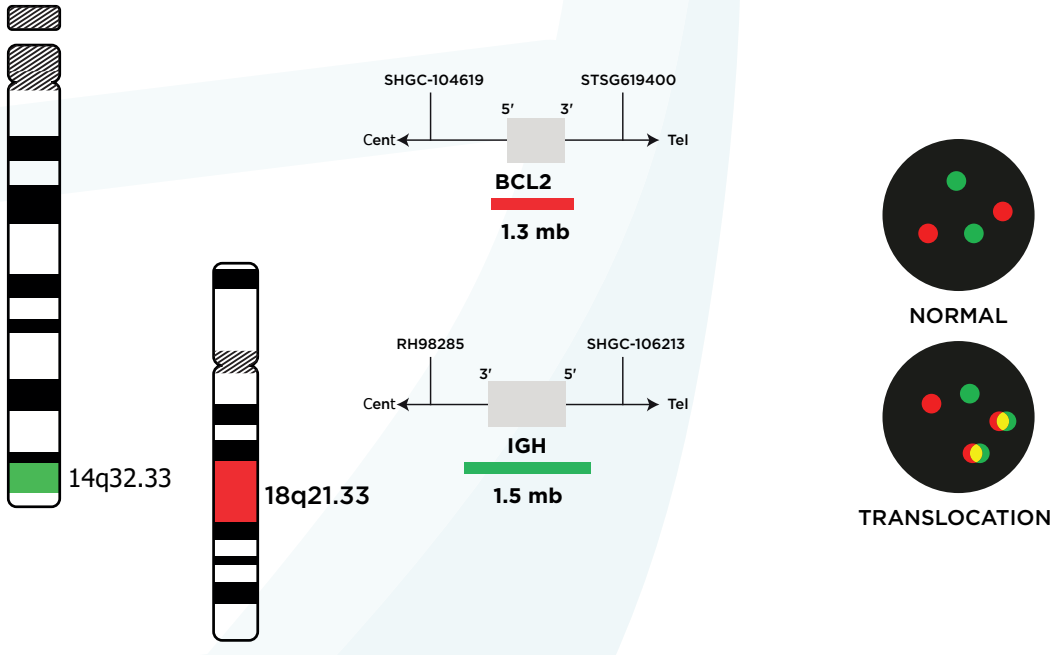

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17-086 IGH-MAFB t(14;20)

The t(14;20)(q32.33;q12) translocation is frequently found in multiple myeloma (MM). MM is a low-grade proliferative, malignant postgerminal center tumor of somatic-mutated, isotope-converted plasma cells that accumulate in the bone marrow. it is usually preceded by a premaline stage known as mono clonal gammopathy of unknown significance (MGUS). Five recurrent primary translocations involving the immunoglobulin heavy chain (IGH) locus were detected in 40% of MGUS and MM tumors. These are t(11;14)(q33;q32.3), t(6;14)(p2l.l;q32.3), which contain the CCND1, CCND3, FGFR3 and NSD2, MAF, and MAFB genes, respectively. (4;14)(p16.3;q32.33), t(14;16)(q32.33;q23), and t(14;20)(q32.33;q12) translocations. t(14;20) occurs in approximately 1-2% of MM patients and is associated with an unfavorable prognosis.

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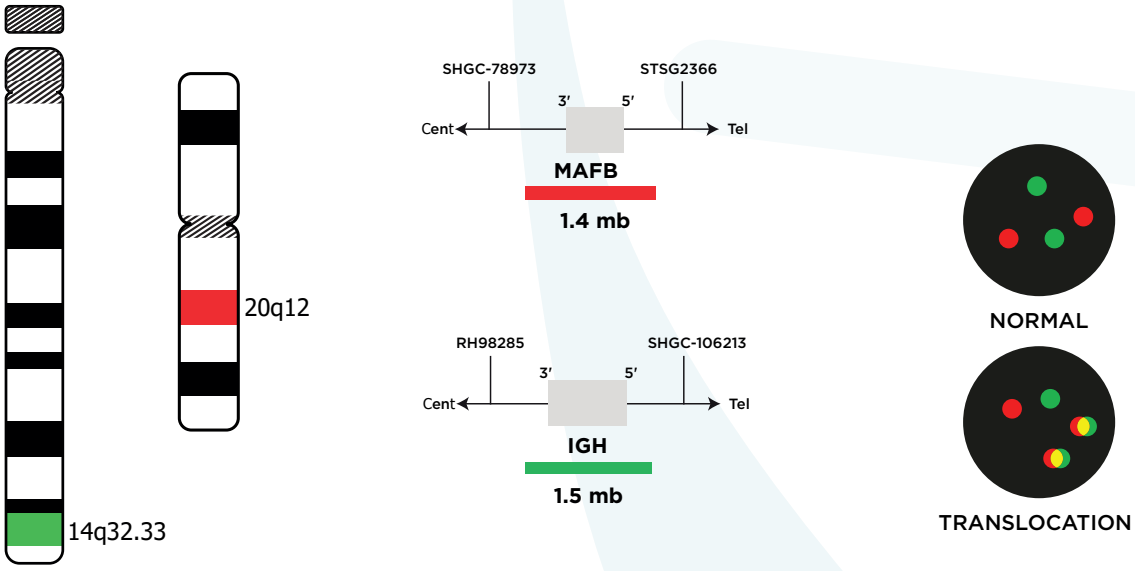

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Fonseca et al., Leukemia 2009;23(12):2210-2221
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HEMATOLOGY PANEL

17-005 MYB (6q23)

The MYB (MYB proto-oncogene, transcription factor) gene primarily codes for a transcription factor expressed in immature lymphoid and myeloid T-cells. The long arm of chromosome 6 (6q) is frequently associated with chromosomal abnormalities observed in various types of cancer, including hematological malignancies. 6q abnormalities are among the most common chromosomal changes found in different types of lymphoid neoplasms. Several major deletion regions have been identified in the long arm of chromosome 6, with 6q23 being one of them. It has been shown that 3-10% of chronic lymphocytic leukemia (CLL) cases carry structural abnormalities in the 6q chromosome region.

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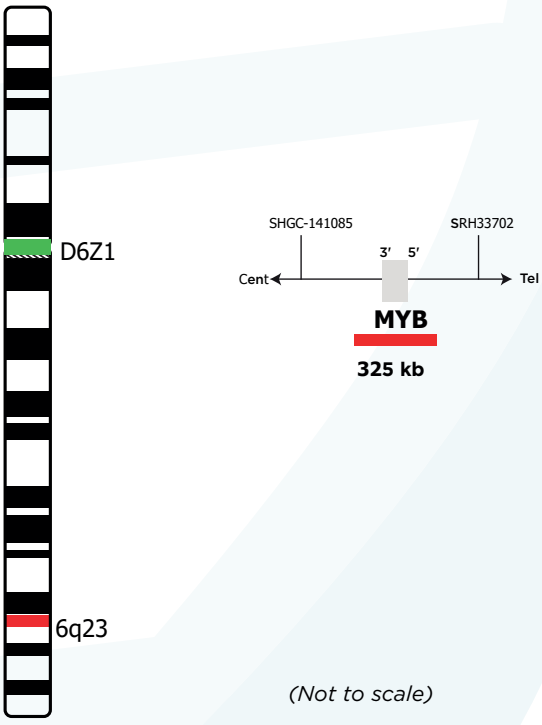

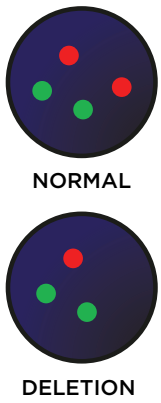

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Döhner H, et al. (1999) J Mol Med 77: 266-81.
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17-009 AFF1-MLL t(4;11)

Translocations involving the KMT2A gene are detected in approximately 5-6% of all acute myeloid leukemias (AML) and 5-10% of all acute lymphoblastic leukemias (ALL). The frequency of translocations involving the KMT2A gene is significantly higher in infants with AML (50%) and ALL (80%). Over 30 fusion partners have been documented for the KMT2A gene. The most common translocation involving the KMT2A gene in acute lymphoblastic leukemia (ALL) is the t(4;11)(q21;q23.3), which involves the KMT2A (lysine methyltransferase 2A) gene located at 11q23.3 and the AFF1 (AF4/FMR2 family member 1) gene located at 4q21.3.

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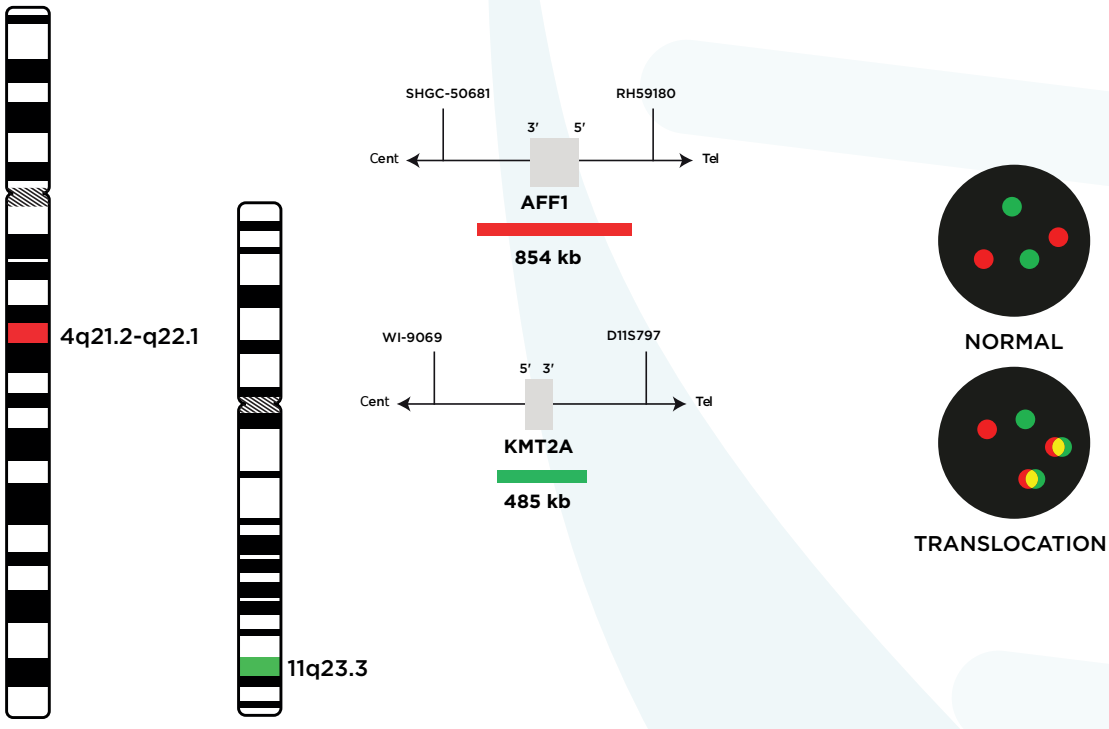

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Kumar et al., Leuk Res. 2011;35(3):305-9

HEMATOLOGY PANEL

17-133 MLL-MLLT3 t(9;11)

The KMT2A (MLL) gene located at 11q23 is rearranged in the majority of acute lymphoblastic leukemia (ALL) or acute myeloid leukemia (AML) patients, and in approximately 10% of all acute leukemia patients. In infants, the incidence of KMT2A rearrangements is around 70-80%. KMT2A is a nuclear protein with methyltransferase activity and is involved in the regulation of target genes necessary for early development and hematopoiesis as part of multiple protein complexes. It has been identified to have over 80 fusion partners. The most common translocation partners in KMT2A-associated leukemia are AFF1, MLLT3, MLLT1, MLLT10, ELL, and AFDN (MLLT4), respectively. KMT2A is involved in approximately 3-5% of adult de novo AML cases, and the most common deviation in this subgroup is the t(9;11)(p22;q23) involving the MLLT3 gene.

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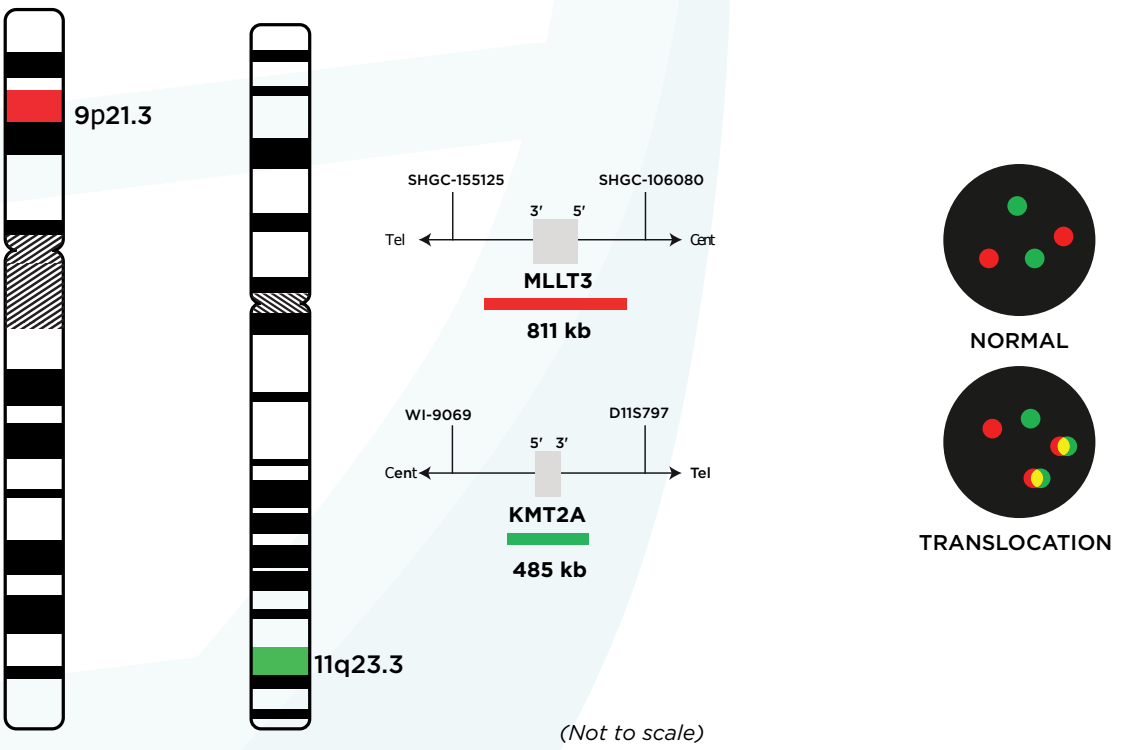

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17-134 MLL-MLLT4 t(6;11)

The KMT2A (MLL) gene located at 11q23 is rearranged in the majority of acute lymphoblastic leukemia (ALL) or acute myeloid leukemia (AML) patients, and in approximately 10% of all acute leukemia patients. In infants, the incidence of KMT2A rearrangements is around 70-80%. KMT2A is a nuclear protein with methyltransferase activity and is involved in the regulation of target genes necessary for early development and hematopoiesis as part of multiple protein complexes. KMT2A has been identified to have over 80 fusion partners. The most common translocation partners in KMT2A-associated leukemia are AFF1, MLLT3, MLLT1, MLLT10, ELL, and AFDN (MLLT4), respectively. The MLLT4 (AFDN) gene is located at 6q27. KMT2A-AFDN fusions result from translocations of the t(6;11)(q27;q23) type. The most frequent breakpoint is located in intron 9 of the KMT2A gene, leading to this translocation. A significant proportion of ALL patients have borderline values for the 1st or 2nd exon of the AFDN gene. T-cell ALL patients show a significantly higher percentage of KMT2A-AFDN and KMT2A-MLLT1 fusions compared to other subgroups of ALL patients.

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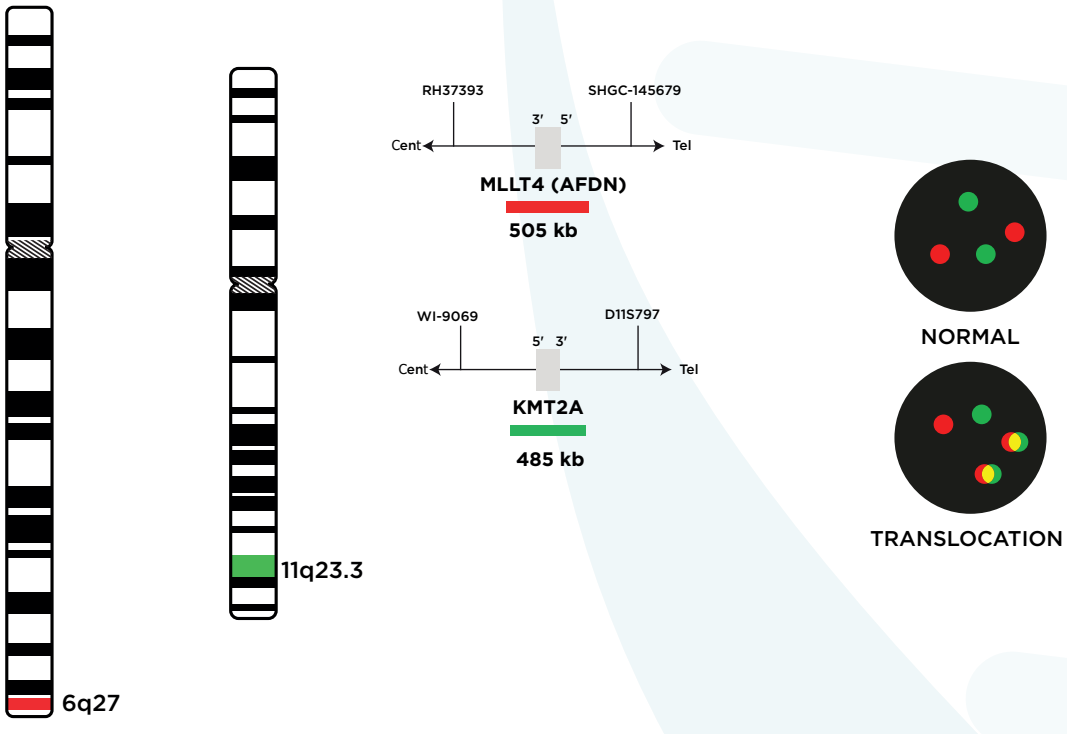

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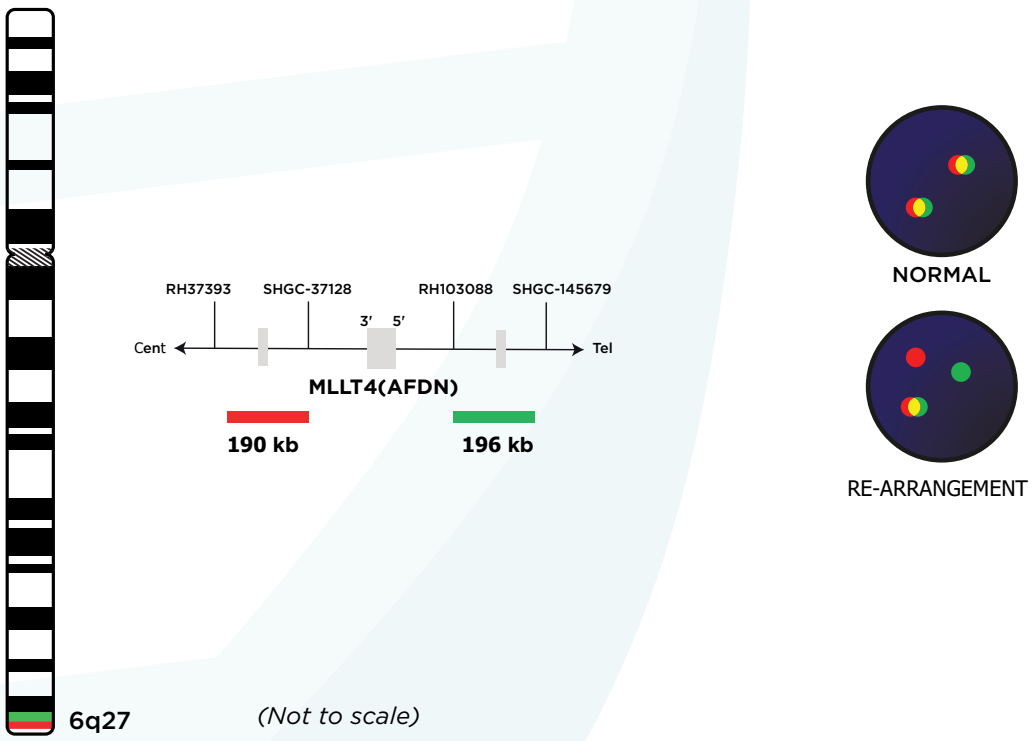
HEMATOLOGY PANEL

17-180 MLLT4 (6q26.27) Breakapart

The MLLT4 (AFDN) gene encodes a multidomain protein involved in cell adhesion signaling and organization during embryogenesis. It has also been identified as a fusion partner of the acute lymphoblastic leukemia-1 (ALL-1) gene in acute myeloid leukemias associated with the t(6;11)(q27;q23) translocation. Alternative spliced transcript variants that encode different isoforms of this gene have been identified, but not all of them have been fully characterized.

BREAKAPART



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17-017 RB1 (13q14)

The RB1 (RB transcriptional corepressor 1) gene is located at 13q14.2 and encodes a protein that plays a crucial role in cell cycle regulation and maintaining genome stability as a tumor suppressor. RB1 deletions are commonly found in retinoblastoma. However, monoallelic or biallelic deletions of RB1 are also prevalent in a wide range of solid tumors and hematological malignancies such as multiple myeloma (MM) and chronic lymphocytic leukemia (CLL). Deletions of 13q14 other than RB1 are associated with a more favorable prognosis in CLL patients, whereas deletions encompassing the RB1 locus at 13q14 (present in approximately 20% of all CLL cases) are associated with shorter overall survival.

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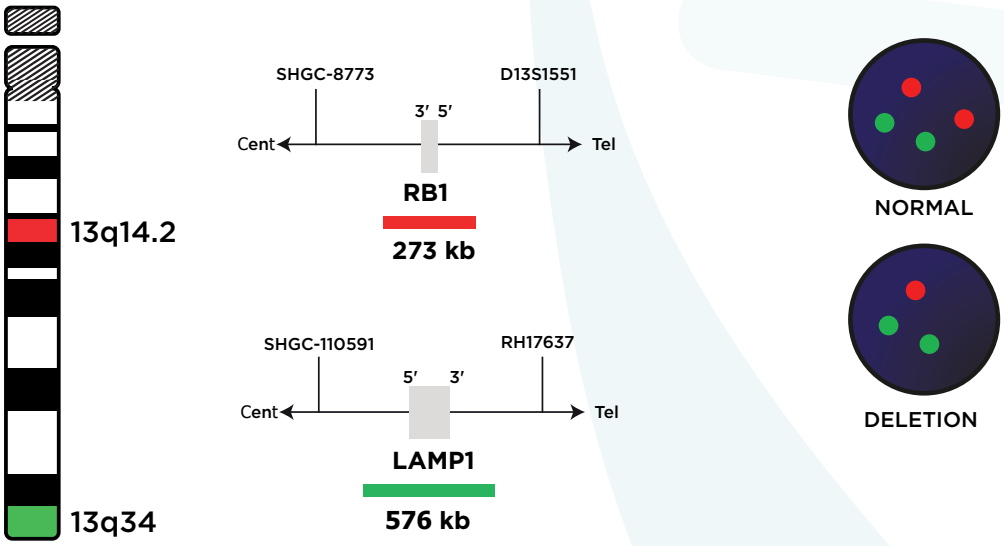

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HEMATOLOGY PANEL

17-042 ABL1 Breakapart

ABL1 gene rearrangements involving various fusion partners occur in various hematological malignancies, resulting in fusion of the ABL1 gene. The t(9;22)(q34.1;q11.2) translocation leads to the formation of the BCR/ABL1 fusion, which is observed in approximately 90% of patients with chronic myeloid leukemia (CML) and approximately 25% of adults with acute lymphoblastic leukemia (ALL). In 2017, the World Health Organization (WHO) recognized BCR-ABL1-like ALL as a distinct entity within the subtype of B-lymphoblastic leukemia/lymphoma. BCR-ABL1-like ALL, also known as Philadelphia chromosome (Ph)-like ALL, is found in approximately 10-20% of pediatric cases and 20-30% of all adult B-cell precursor ALL cases. BCR-ABL1-like ALL is characterized by a gene expression profile that significantly overlaps with Ph-positive (Ph+) ALL. Unlike Ph+ ALL, which is defined by the presence of the BCR-ABL1 fusion resulting from t(9;22)(q34;q11), BCR-ABL1-like cases involve various genomic alterations that enhance kinase and cytokine receptor signaling.

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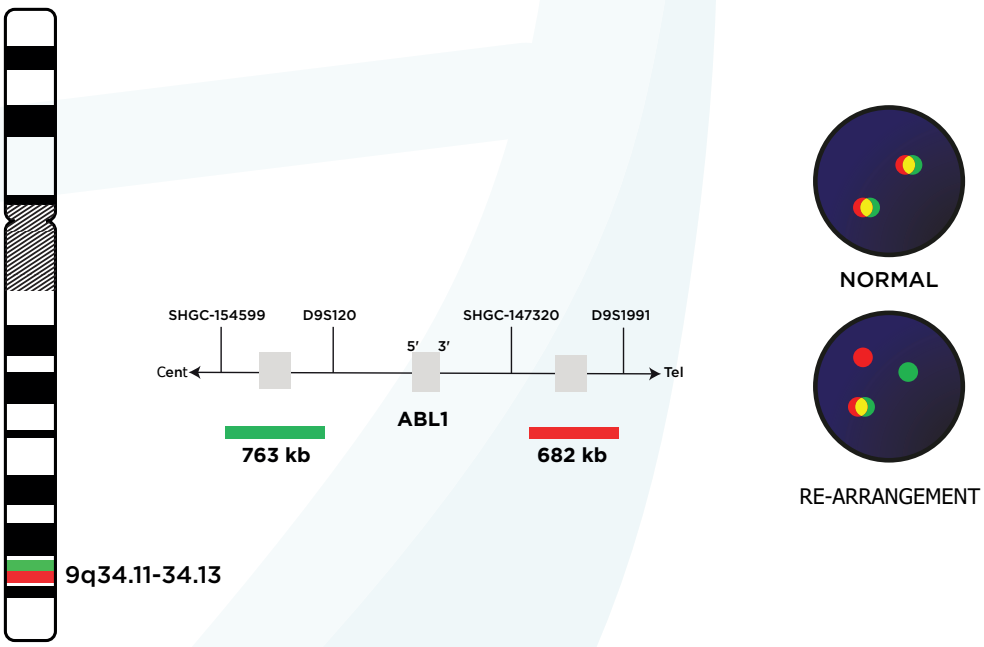

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17-044 RARA (17q21) Breakapart

RARA gene has been found to have various fusion partners, but in approximately 95% of acute promyelocytic leukemia (APL) cases, rearrangements involving the PML gene on 15q24.1 are detected. The RARA gene is located on chromosome 17q21.2. In the majority of APL cases, the fusion occurs between the RARA gene and the PML gene. However, in less than 5% of APL cases, the RARA gene is involved in fusion with different fusion partners.

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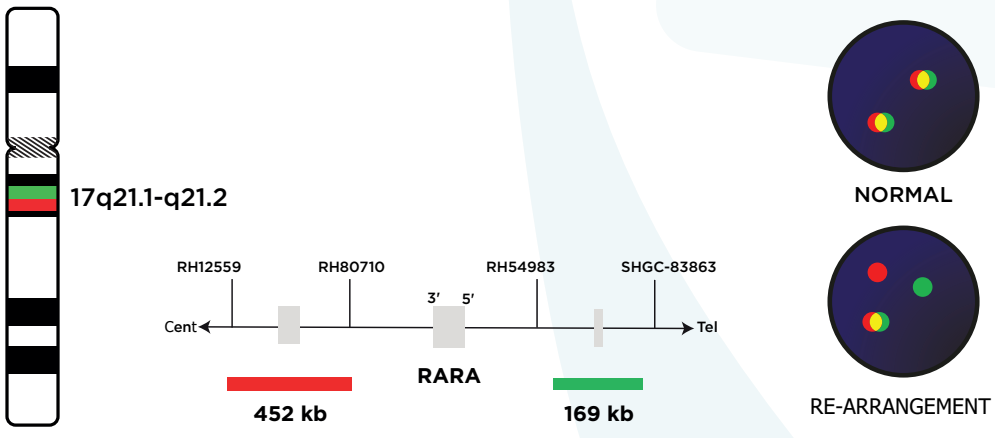

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HEMATOLOGY PANEL

17-075 CSF1R (5q33-34)

Deletion of the CSF1R gene at 5q32 is specifically observed in approximately 40% of patients with Myelodysplastic Syndrome (MDS). Studies have also shown that up to 58% of all breast carcinomas and 85% of invasive breast carcinomas express higher levels of CSF1R compared to normal breast tissue. Additionally, in cervical cancer, CSF1R expression has been demonstrated to be associated with a more aggressive and invasive disease.

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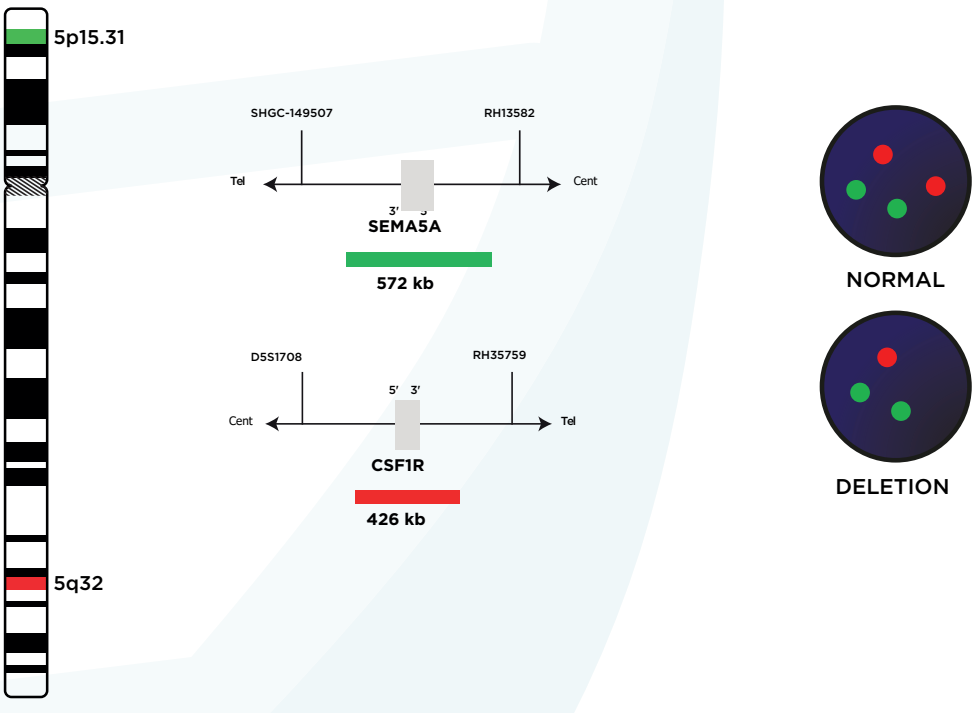

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17-142 PDGFRB (5q32) Breakapart

The PDGFRB (Platelet-Derived Growth Factor Receptor Beta) gene, located at 5q32-q33.1, encodes a transmembrane glycoprotein from the type III receptor tyrosine kinase family and plays an important role in various cellular processes. Translocations involving the PDGFRB gene are rare genetic disorders and are typically found in myelodysplastic/myeloproliferative neoplasms (MDS/MPNs), chronic myeloproliferative disorders (CMPDs), acute myeloid leukemia (AML), and atypical (BCR-ABL1-negative) chronic myeloid leukemia/chronic myelomonocytic leukemia (CML/CMML)-like diseases, often accompanied by eosinophilia and splenomegaly.

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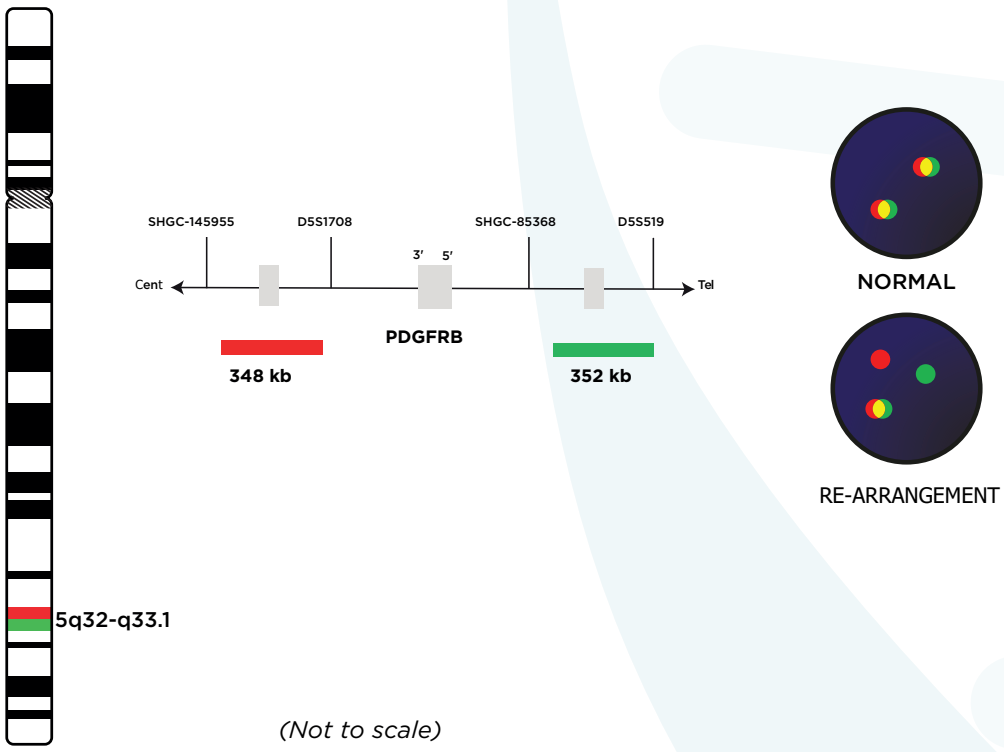

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HEMATOLOGY PANEL

17-207 DEK-NUP214 t(6;9)

Rearrangements of the NUP214 gene have been identified in several hematological malignancies, including T-cell acute lymphoblastic leukemia (T-ALL), acute myeloid leukemia (AML), and myelodysplastic syndrome (MDS). Several fusion partners have been identified for NUP214, with the most common ones being the chromatin-binding factor DEK, the histone chaperone SET, and the tyrosine kinase ABL1. The DEK-NUP214 fusion occurs as a result of the t(6;9)(p22.3;q34.1) translocation and constitutes a specific subset of AML according to the World Health Organization 2008 classification. The fusion resulting from the rearrangement between the DEK gene at 6p22.3 and the NUP214 gene at 9q34.12-q34.13, known as t(6;9)(p22;q34), accounts for 0.5% to 4% of acute myeloid leukemia (AML) cases and is associated with poor prognosis.

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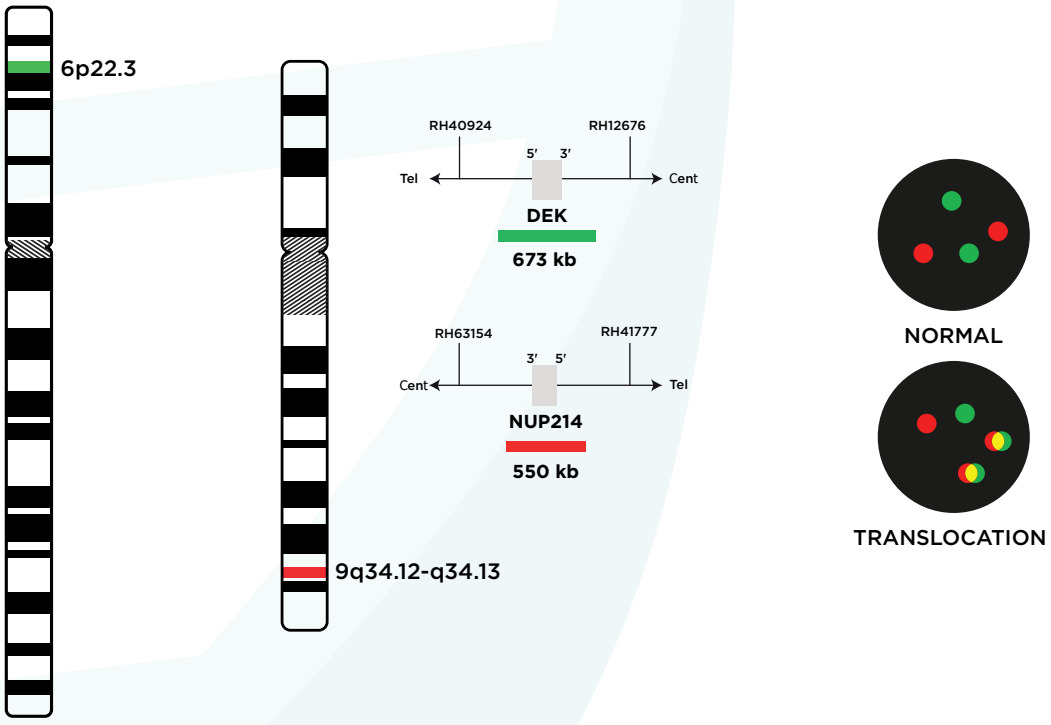

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17-001-B del (13q14) (D13S319) / LAMP1 (13q34)

Deletions involving the 13q14 region are frequently observed in a wide range of hematological disorders. Chromosome 13q deletions occur in 16% to 40% of multiple myeloma (MM) cases, with the majority being complete monosomy 13 (85%), while the remaining 15% represent deletions of 13q14. A case study in multiple myeloma patients has narrowed down the critical deleted region to 13q14. Historically, 13q deletions have been associated with poor prognosis in MM, but it is now believed that its prognostic relevance may be linked to other concurrent genetic lesions. Deletions on the long arm of chromosome 13 are also frequently detected in aggressive non-Hodgkin lymphoma (NHL) patients. Therefore, when combined with other biological markers, morphology, and clinical information, fluorescence in situ hybridization (FISH) is a valuable tool for predicting disease progression and overall survival in chronic lymphocytic leukemia (CLL) patients.

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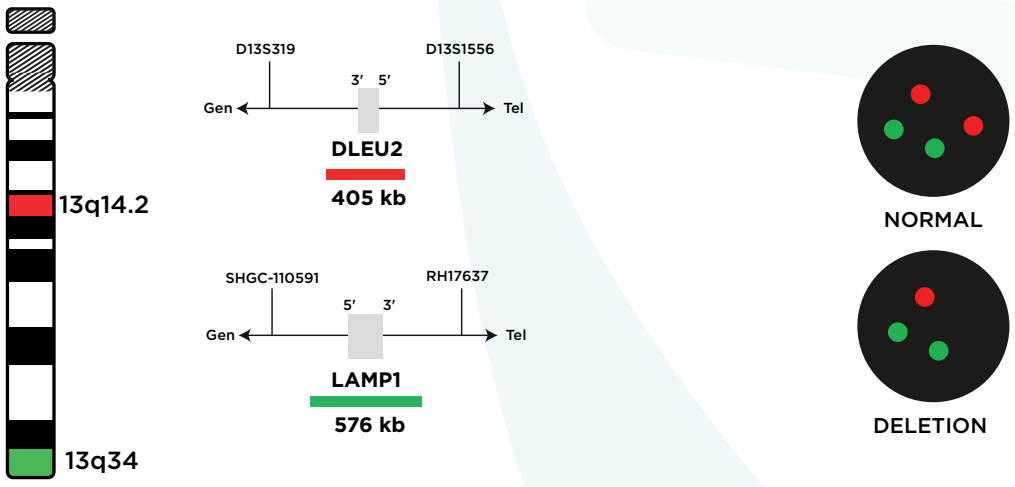

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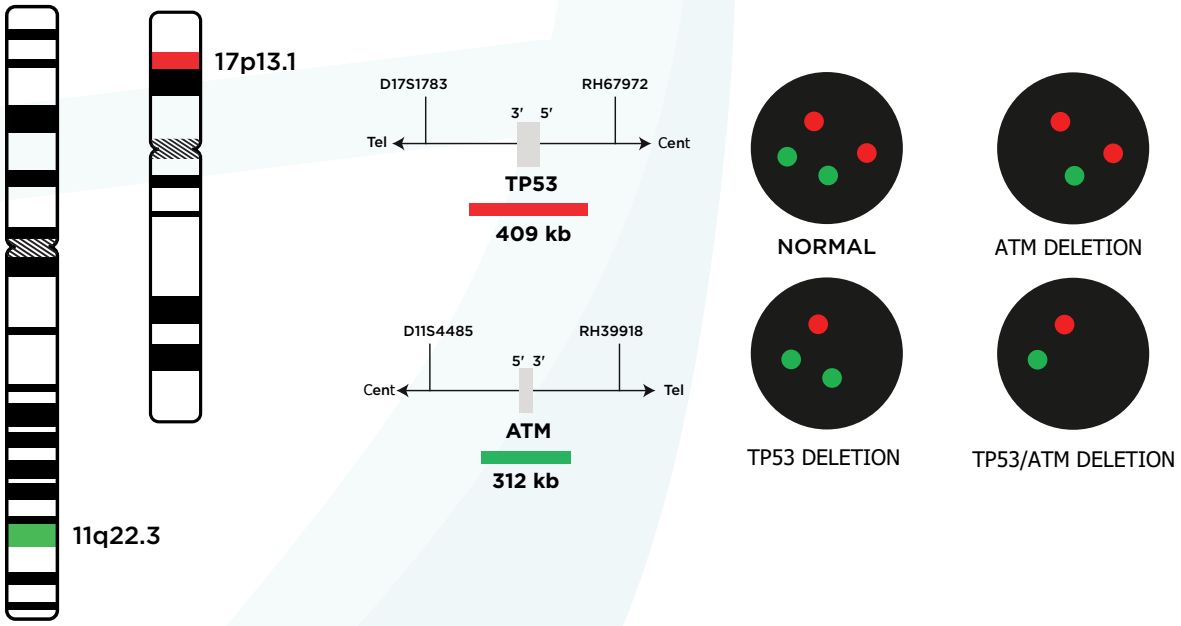
HEMATOLOGY PANEL

17-064 ATM / TP53

The tumor suppressor TP53 gene located in the 17p13.1 region and the protein kinase ATM gene located in the 11q22.3 region are frequently deleted in cases of chronic lymphocytic leukemia (CLL). TP53 (tumor protein 53; also known as p53) gene deletions have been detected in CLL, multiple myeloma (MM), and acute myeloid leukemia (AML) patients. Allelic loss of the short arm of chromosome 17 in CLL patients is associated with failure of treatment with alkylating agents and shorter survival times. The ATM (ataxia telangiectasia mutated) gene is located at 11q22.3 and encodes a protein kinase involved in cell cycle regulation, including TP53 activation. CLL patients with 11q deletion exhibit rapid disease progression and lower overall survival rates.

DELETION



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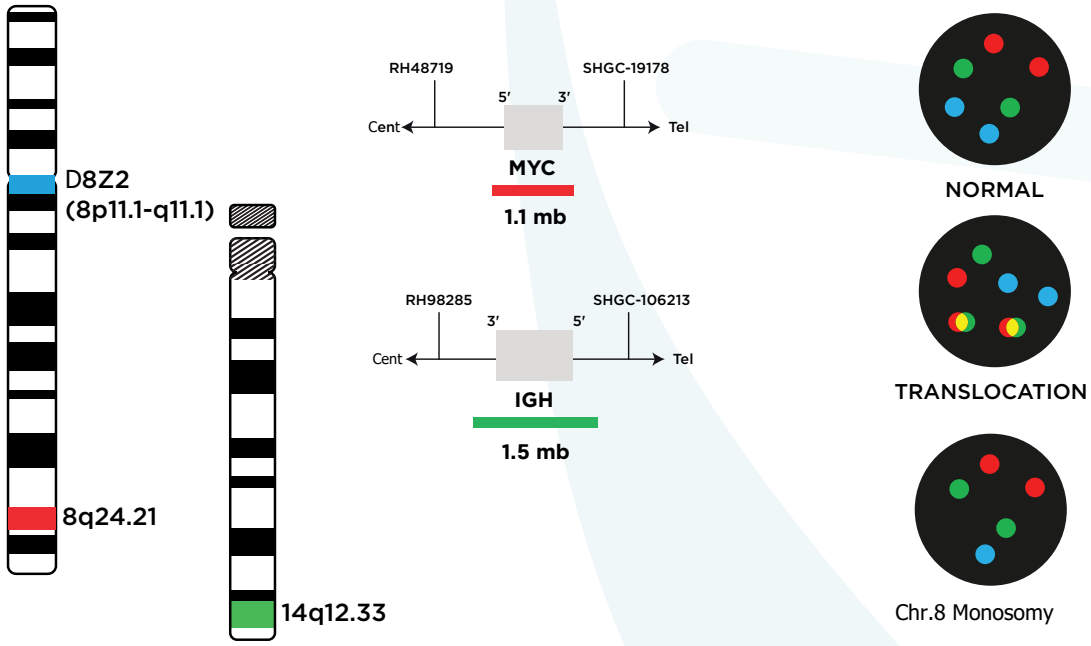
HEMATOLOGY PANEL

17-183 IGH-cMYC t(8;14)

The MYC proto-oncogene (MYC proto-oncogene, bHLH transcription factor) encodes a transcription factor that is essential for cell growth and proliferation, and it extensively participates in tumorigenesis. In Burkitt lymphoma, c-MYC/IGH translocation involving t(8;14)(q24;q32) and its variant forms t(2;8)(p13;q24) and t(8;22)(q24;q11) are observed, occurring in mature B cells or Burkitt-type Acute Lymphoblastic Leukemia (ALL). The most common translocation involving the MYC gene region is t(8;14)(q24.21;q32.3), which can be found in approximately 80% of Burkitt lymphoma cases, relocating the MYC gene next to the IgH (immunoglobulin heavy chain) locus. Other translocations affecting the MYC gene are t(8;22)(q24.21;q11.2) and t(2;8)(p11.2;q24.21), both of which involve one of the two immunoglobulin light chain loci.

TRI-COLOR TRANSLOCATION



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HEMATOLOGY PANEL

17-010 ATM (11q22)

The ATM gene is located in the 11q22.3 band region and encodes a protein kinase. The encoded kinase regulates responses to DNA double-strand breaks by triggering pathways that synchronize DNA repair and apoptosis during the cell cycle. Approximately 20% of Chronic Lymphocytic Leukemia (CLL) cases exhibit ATM deletions in the 11q22.3 region. Analyzing CLL cases using traditional banding techniques is challenging due to the low mitotic index of neoplastic cells. The introduction of fluorescence in situ hybridization (FISH) for interphase cytogenetics has greatly enhanced the sensitivity of cytogenetic analysis.

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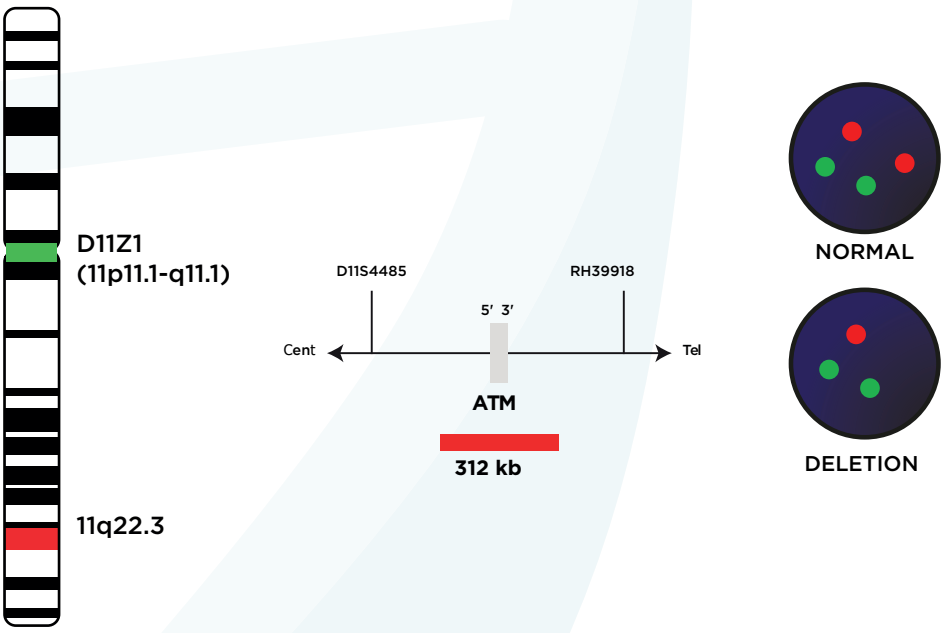

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17-003 TP53 (17p13)

The TP53 gene is located in the 17p13.1 band region and encodes a transcription factor. The encoded transcription factor protein functions as a tumor suppressor by activating the expression of genes that regulate cell proliferation and apoptosis, and inhibit cell growth. Deletion of the TP53 gene results in the loss of its tumor-suppressing activity. The presence of both mutation and deletion in TP53 has a significant negative impact on overall survival in hematological malignancies. In multiple myeloma, TP53 deletion is found in 33.8% of newly diagnosed patients, and even higher frequencies (54.5%) are observed during relapse. In acute myeloid leukemia (AML), TP53 alterations are observed in 13% of patients, with 5% having mutations and deletions, and 1% having deletions only. In myelodysplastic syndrome (MDS), TP53 alterations are found in 7% of cases, including 1% with mutations and deletions, and 1% with deletions only. In AML and MDS, TP53 alterations and 17p deletion are associated with complex karyotype, poor response to treatment, and decreased survival. In MDS, even TP53 deletion without mutation in the second allele has a significant negative impact on overall survival.

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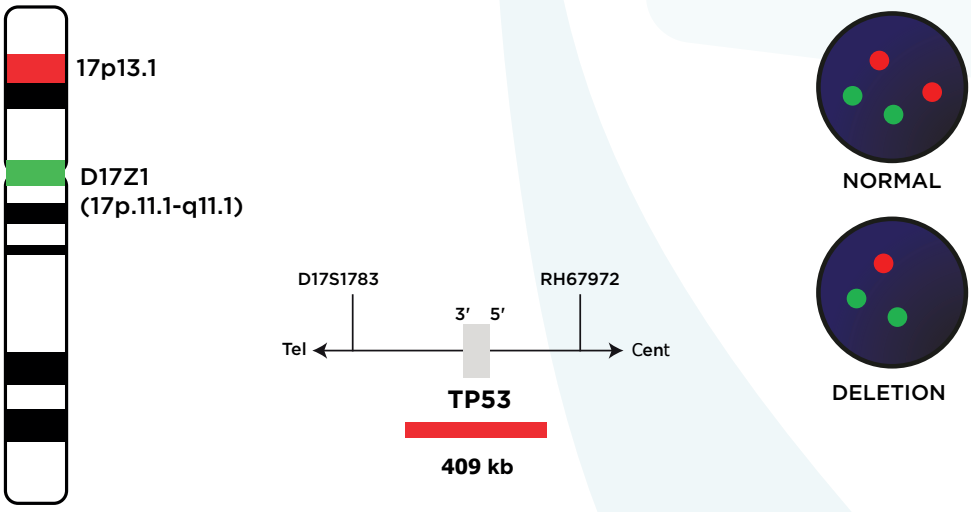

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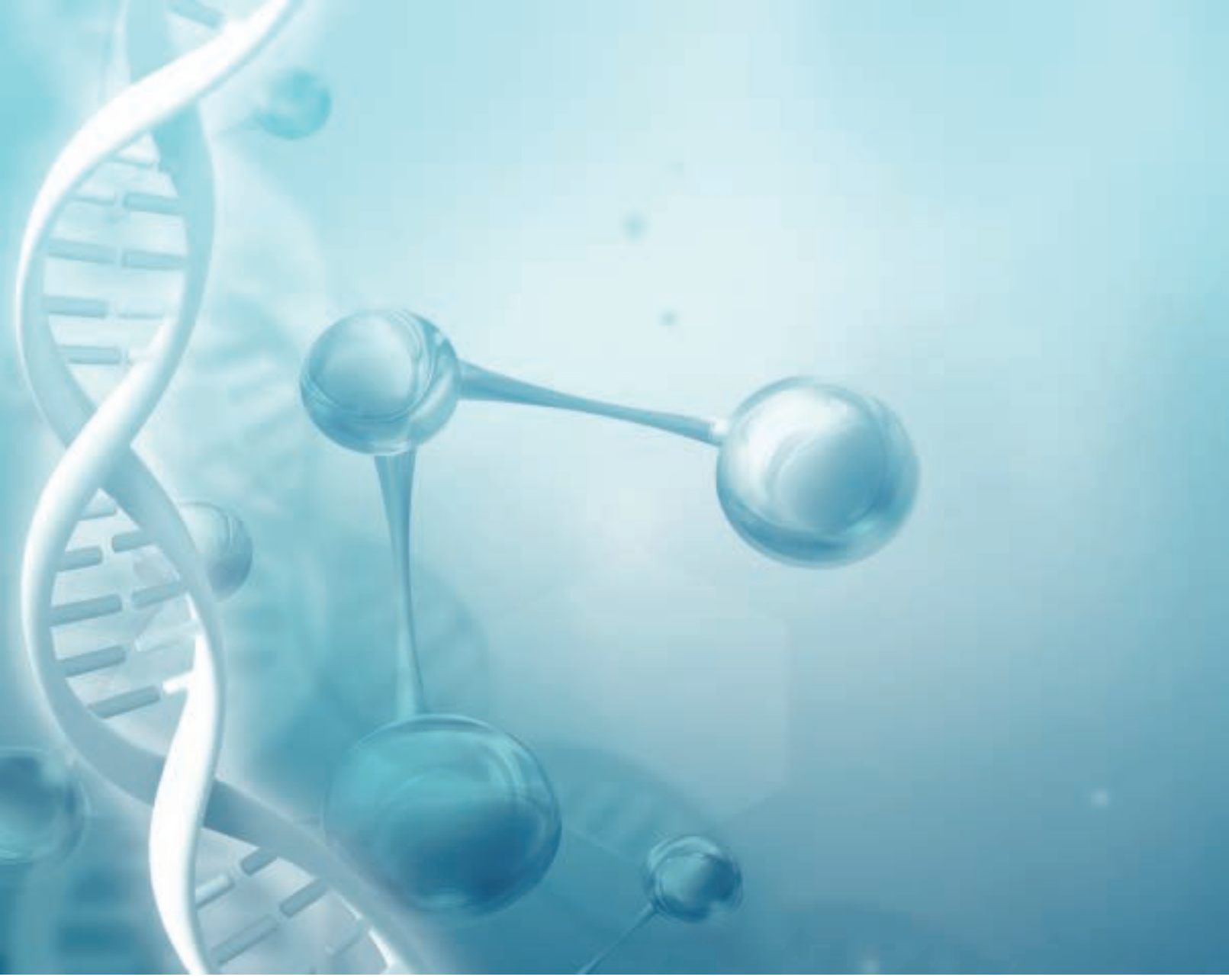

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