

Leukaemia Section

Mini Review

t(14;22)(q32;q11)

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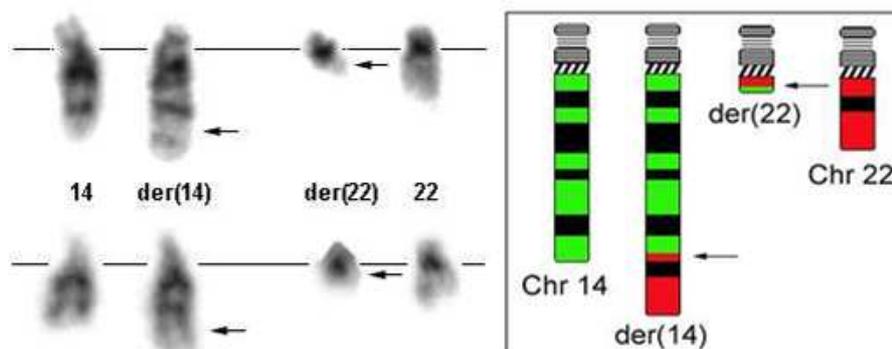
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Identity



t(14;22)(q32;q11) shown in ideograms and in G-banding. Both normal and rearranged chromosomes are shown. Arrows indicate the positions of the breakpoints.

Clinics and pathology

Disease

Lymphoid malignancies

Note

t(14;22)(q32;q11) analysed by G-banding has been reported in ALL, CLL/SLL, HCL, AML, NHL. Involvement of the genes IGH at 14q32 and IGL at 22q11 has been detected in one SLL and one DLBCL with t(14;22)(q32;q11).

Phenotype/cell stem origin

Small lymphocytic lymphoma (SLL): CD20+, CD23+, CD5+, CD10-, cyclinD1-.

Diffuse large B cell lymphoma (DLBCL): CD20+, BCL6+, CD10-, BCL2+.

Clinics

SLL: Cervical lymphadenopathy.

DLBCL: Generalized lymphadenopathy, night sweats, weight loss.

Pathology

SLL: The lymph node showed diffuse infiltration with small lymphocytic cells with typical coarse clumped nuclear chromatin. Proliferation centers with paraimmunoblasts were present.

DLBCL: Diffuse proliferation of large atypical lymphoid cells.

Cytogenetics

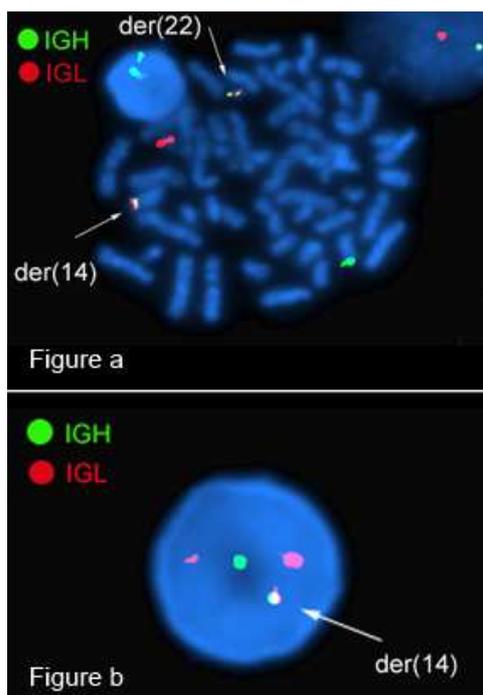
Cytogenetics morphological

The t(14;22)(q32;q11) was seen as the sole rearrangement in the SLL case. In the DLBCL case, there were several additional rearrangements. The complete karyotype of the latter was 52,XY,+Y,+der(3)t(3;9)(p11;p21),del(3)(q21),+7,+9,der(9)t(3;9)(q21;p21)x2,t(14;22)(q32;q11),der(15)t(1;15)(q21;p11),del(16)(p13),i(17)(q10),+18,+

mar. The apparently identical translocation by G-banding has been seen in chronic myeloid leukaemia as well. However, this has been shown to be a three-way variant translocation of the classical t(9;22)(q34;q11) involving the genes ABL (9q34) and BCR (22q11).

Cytogenetics molecular

Fluorescence in situ hybridization (FISH) analysis with locus-specific probes covering parts of IGH (PAC 998D24) and IGL (PAC 1019H10) showed fusion signals between the two probes. In the DLBCL case (figure to the left), two fusion signals were seen, indicating a reciprocal translocation between the two genes. In the SLL case (figure to the right), however, only the IGL probe was split and moved close to the IGH probe. The IGH probe remained seemingly intact on the der(14). To pinpoint more exact the breakpoint in IGL, three segments of the IGL probe were made using Long Range PCR. These segments were used as probes in further FISH analyses. In the SLL case, a split signal in the first segment probe was seen, locating the breakpoint between 12600bp and 37000bp from the centromeric end of the IGL probe.



The left image shows FISH analysis on an interphase nuclei from the SLL case and the right image shows FISH analysis on a metaphase spread from the DLBCL case. The arrows point to the fusion signals of the IGH (PAC 988D24, 14q32) and IGL (PAC 1019H10, 22q11) probes. In the DLBCL case, a reciprocal translocation was seen where both IGH and IGL probes were split and juxtaposed. In the SLL case, however, only the IGL probe was split and moved to der(14).

In the DLBCL case, a split signal in all the three segments was seen. One explanation might be that the IGL was duplicated and that one copy was moved to der(14). Another explanation might be that there was more than one breakpoint within IGL.

Genes involved and proteins

IGH

Location

14q32

DNA/RNA

IGH is composed of variable (IGHV), diversity (IGHD), joining (IGHJ), and constant (IGHC) segments.

Protein

IGH encodes the immunoglobulin heavy chains.

IGL

Location

22q11

DNA/RNA

IGL is composed of variable (IGLV), joining (IGLV), and constant segments (IGLC).

Protein

IGL encodes the immunoglobulin lambda chains.

Result of the chromosomal anomaly

Fusion protein

Note

Rearrangements of the three immunoglobulin genes IGK (2p12), IGH (14q32), and IGL (22q11) are often seen, especially in NHL, but it is uncommon that these genes are recombined with each other. None of these genes are known oncogenes, so how juxtaposition or fusion of the IGH and IGL in the t(14;22)(q32;q11) might act pathogenetically is completely unknown. In the SLL case, a gene dose effect of the IGL may be important if there really are two copies of the gene. However, how this may contribute to lymphoma development is not understood. In the DLBCL case, only the IGL probe was split and moved to der(14). There is a possibility that there is another, nearby gene that is involved and not the IGH. On the other hand, the breakpoint may be distal to our IGH probe and still be within the IGH gene.

References

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