

Leukaemia Section

Mini Review

t(9;14)(p13;q32)

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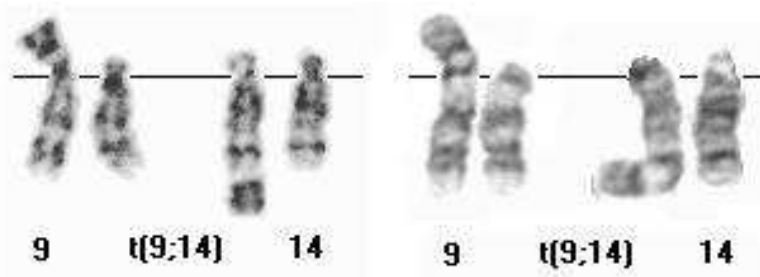
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Identity



t(9;14)(p13;q32) (G- banding) left: Courtesy Bruce Poppe, Pascale De Paepe, Frank Speleman, right: Courtesy Jean-Luc Lai.

Clinics and pathology

Disease

Rare recurrent chromosomal aberration, exclusively detected in B-cell lymphoproliferative disorders.

Phenotype/cell stem origin

B lymphocyte.

Epidemiology

Originally reported to be associated with a low-grade mature B-cell phenotype with plasmacytoid differentiation such as lymphoplasmacytic lymphoma, multiple myeloma/ plasma cell leukemia and chronic lymphocytic leukemia. However, the relatively frequent occurrence in diffuse large B-cell lymphoma, with or without a preceding phase of a low-grade lymphoma, suggests that this chromosomal aberration has a much wider clinical spectrum or is associated with disease progression. In addition, the t(9;14)(p13;q32) has been described occasionally in follicular lymphoma, mantle cell lymphoma and splenic marginal zone lymphoma.

Prognosis

No prognostic relevance has been attributed to the presence of the t(9;14)(p13;q32).

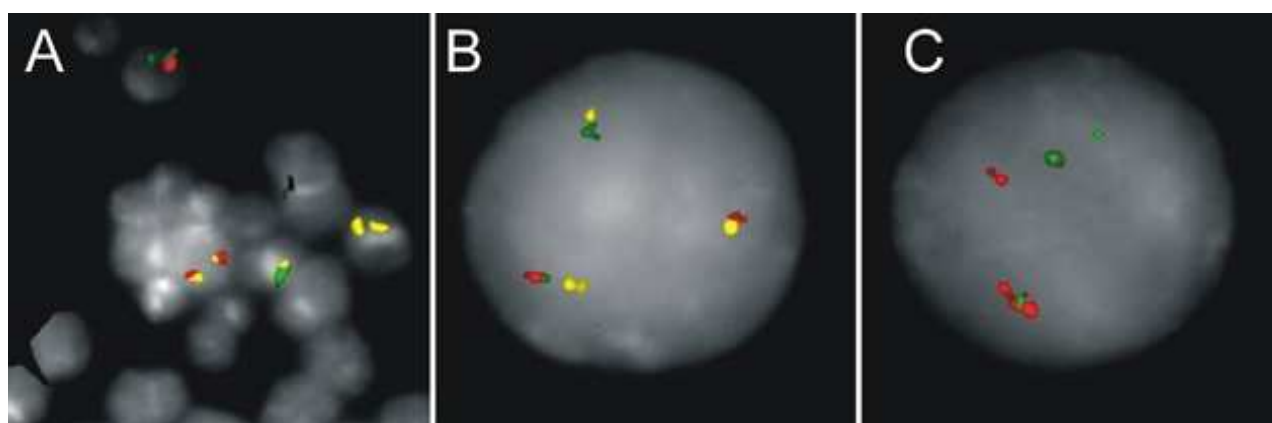
Cytogenetics

Cytogenetics morphological

The t(9;14)(p13;q32) is readily recognisable with G- as well as R-banding. The presence of complex chromosomal aberrations, however, can mask the presence of this rearrangement.

Probes

Probes used for detection of PAX5 rearrangements include PAX5 spanning probes (RP11-12P15, RP11-344B23 and RP11-297B17) and a probe extending approximately up to 200 kb upstream of PAX5, RP11-220I1. IgH rearrangements can be demonstrated using a commercially available dual colour probe, or IgH probes, RP11-47P23 and RP5-



Dual and triple colour hybridisations demonstrating the presence of a t(9;14)(p13;q32) resulting in PAX5/IGH rearrangement. A,B: partial metaphase and interphase nucleus cohybridized with PAX5 locus specific probes (yellow) and dual colour interphase cytogenetics using IgH flanking probes (red) and PAX5 locus specific probes.

998D24, mapping to the IgH constant and variable regions, respectively.

Additional anomalies

No recurrent additional aberrations have been described. However, the majority of t(9;14)(p13;q32) have been reported in addition to complex chromosomal aberrations.

Variants

In addition to the t(9;14)(p13;q32), other translocations presumably involving the immunoglobulin light chain genes and PAX5 have been reported, such as the t(2;9)(p12;p13) and the t(9;22)(p13;q11).

Genes involved and proteins

IgH

Location

14q32

PAX5

Location

9p13

DNA/RNA

The PAX5 coding region extends over a genomic interval of approximately 200 kb and comprises 10 exons. Two alternative transcripts have been identified, originating from alternative promoter usage, containing exon 1A or 1B. Full length mRNA is 3650 bp.

Protein

PAX5 belongs to the paired box family of transcription factors, involved in a multitude of developmental processes. PAX5 was originally identified as a B-cell specific transcription factor (hence its original name, BSAP). Recently it has been shown that PAX5 expression is continuously required in B cell lineage commitment during early B cell development.

Result of the chromosomal anomaly

Hybrid gene

Description

Translocation of the entire PAX5 gene to chromosome 14. The breakpoints at 9p13 are heterogeneous and can reside up to 200kb upstream (i.e. centromeric) of PAX5.

Detection

The variability of the chromosomal breakpoints at 9p13 as well as 14q32 precludes genomic PCR approaches for detection of IgH PAX5 juxtaposition. In addition, the expression pattern of PAX5 hampers RT-PCR methods for demonstrating elevated PAX5 expression in B-cell proliferations with suspected or proven PAX5 rearrangement. Currently, the only methods for detecting IgH PAX5 juxtaposition reliably include conventional and molecular cytogenetics.

Fusion protein

Description

In analogy to other 14q32 rearrangements, no fusion gene is created by the translocation. Rather, the genomic rearrangement leads to forced PAX5 expression.

Oncogenesis

In contrast to the novel insights in the role of PAX5 in B-cell lineage commitment, little is known on the role of PAX5 in the malignant transformation of B cells. The recent demonstration of PAX5 hypermutation in diffuse large-cell lymphomas, in addition to PAX5 overexpression associated with the t(9;14), suggest that PAX5 acts as a dominant oncogene.

References

Barberis A, Widenhorn K, Vitelli L, Busslinger M. A novel B-cell lineage-specific transcription factor present at early but not late stages of differentiation. *Genes Dev.* 1990 May;4(5):849-59

Offit K, Parsa NZ, Filippa D, Jhanwar SC, Chaganti RS. t(9;14)(p13;q32) denotes a subset of low-grade non-Hodgkin's lymphoma with plasmacytoid differentiation. *Blood.* 1992 Nov 15;80(10):2594-9

Busslinger M, Klix N, Pfeffer P, Graninger PG, Kozmik Z. Deregulation of PAX-5 by translocation of the Emu enhancer of the IgH locus adjacent to two alternative PAX-5 promoters in a diffuse large-cell lymphoma. *Proc Natl Acad Sci U S A.* 1996 Jun 11;93(12):6129-34

Iida S, Rao PH, Nallasivam P, Hibshoosh H, Butler M, Louie DC, Dyomin V, Ohno H, Chaganti RS, Dalla-Favera R. The t(9;14)(p13;q32) chromosomal translocation associated with lymphoplasmacytoid lymphoma involves the PAX-5 gene. *Blood.* 1996 Dec 1;88(11):4110-7

Avet-Loiseau H, Brigaudeau C, Morineau N, Talmant P, Lai JL, Daviet A, Li JY, Praloran V, Rapp MJ, Harousseau JL, Facon T, Bataille R. High incidence of cryptic translocations involving the Ig heavy chain gene in multiple myeloma, as shown by fluorescence in situ hybridization. *Genes Chromosomes Cancer.* 1999 Jan;24(1):9-15

Nutt SL, Heavey B, Rolink AG, Busslinger M. Commitment to the B-lymphoid lineage depends on the transcription factor Pax5. *Nature.* 1999 Oct 7;401(6753):556-62

Ohno H, Ueda C, Akasaka T. The t(9;14)(p13;q32) translocation in B-cell non-Hodgkin's lymphoma. *Leuk Lymphoma.* 2000 Feb;36(5-6):435-45

Pasqualucci L, Neumeister P, Goossens T, Nanjangud G, Chaganti RS, Küppers R, Dalla-Favera R. Hypermutation of multiple proto-oncogenes in B-cell diffuse large-cell lymphomas. *Nature.* 2001 Jul 19;412(6844):341-6

Poulsen TS, Silahtaroglu AN, Gisselø CG, Gaardsdal E, Rasmussen T, Tommerup N, Johnsen HE. Detection of illegitimate rearrangement within the immunoglobulin locus on 14q32.3 in B-cell malignancies using end-sequenced probes. *Genes Chromosomes Cancer.* 2001 Nov;32(3):265-74

Mikkola I, Heavey B, Horcher M, Busslinger M. Reversion of B cell commitment upon loss of Pax5 expression. *Science.* 2002 Jul 5;297(5578):110-3

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