Atlas of Genetics and Cytogenetics in Oncology and Haematology

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Leukaemia Section

Short Communication

t(8;13)(p12;q12)

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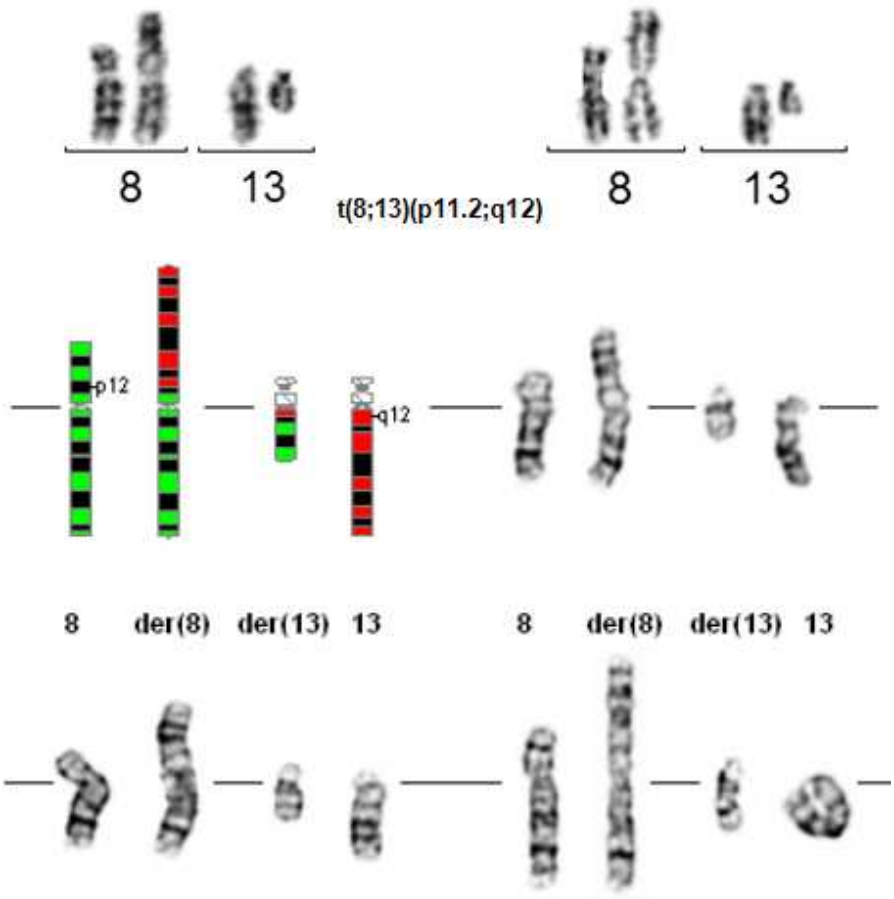


t(8;13)(p12;q12) G- banding - Top: Courtesy Melanie Zenger and Claudia Haferlach; Middle and bottom: Courtesy Charles Bangs and Patty Jones.

Clinics and pathology

Disease

A myeloproliferative disorder that is frequently associated with T cell, or less commonly, B-cell non Hodgkin lymphoma.

Phenotype/cell stem origin

May involve a stem cell involving both myeloid, T lineage, and B-cell lineage.

Epidemiology

14 cases are described; median age 43 yrs (range 18-68); sex ratio: 6M/8F.

Clinics

Aggressive disease; complex picture of myeloid hyperplasia progressing to myelodysplasia and Tor -B-cell lymphoma; enlarged lymph node; blood data: high WBC (median 40 X 10^9/l); myelemia; monocytosis and eosinophilia.

Evolution

The disease transforms to ANLL, or occasionally ALL, in a median of 6 months.

Prognosis

Median survival: 12 months.

Cytogenetics

Cytogenetics morphological

The same t(8;13) is found both in the bone marrow and in the lymph node, ruling out the hypothesis of a leukemoid reaction caused by a lymphoma; the multilineage involvement suggests the malignant transformation of a primitive hematopoietic stem cell.

Probes

Megac Yacs 770-c-2 (1390 kb) and 959-a-4 (1260kb), 856-b-6, 967; 899e2 - (CEPH); BAC 7M15; PAC RPCI 20-G12; FGFR1-specific cosmid 134.8;

Additional anomalies

Usually occurs as a single anomaly; duplication of the der(13) was found during disease progression, suggesting that the crucial event might lie on this derivative chromosome; +8, +21 are also recurrently found.

Genes involved and proteins

FGFR1

Location: 8p12

ZNF198 (also called FIM or ID_P)

Location: 13q12

Protein

zinc finger protein (ten repeats in the N-terminal region with the consensus sequence C-X2-C-X18-24-(F/Y)-C-X3-C that corresponds to a novel type of zing finger motifs), a hydrophobic repeat (proline-rich), and potentially two putative nuclear localisation signals.

Result of the chromosomal anomaly

Hybrid gene

Description

Breakpoint in FGFR1 intron 8.

Fusion protein

Description

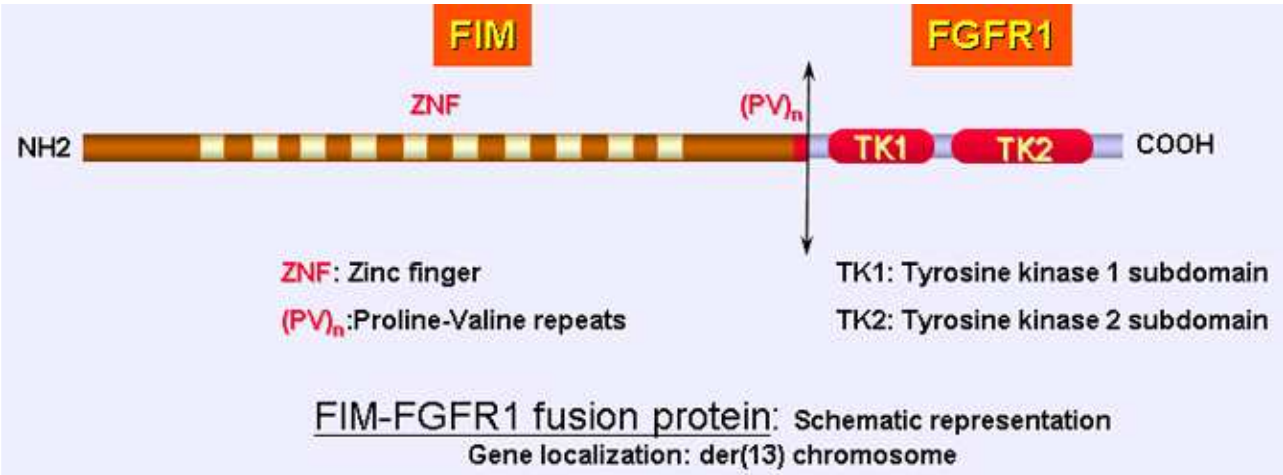
Aberrant tyrosine kinase composed of the N-term two-thirds of FIM (retaining the 10 putative zinc finger motifs), and the FGFR1 intracellular region minus the major part of the juxtamembrane domain (and deleting the N-term immunoglobulin-like and central transmembrane domains of FGFR1).

Expression / Localisation

Cytoplasmic.

Oncogenesis

Through constitutive activation of FGFR1 signal transduction pathways, possibly via dimerization capability mediated by the FIM N-term sequences of the fusion protein.



To be noted

Case Report

t(8;13)(p12;q12) in an atypical chronic myeloid leukaemia case.

References

Aguiar RC, Chase A, Coulthard S, Macdonald DH, Carapeti M, Reiter A, Sohal J, Lennard A, Goldman JM, Cross NC. Abnormalities of chromosome band 8p11 in leukemia: two clinical syndromes can be distinguished on the basis of MOZ involvement. Blood. 1997 Oct 15;90(8):3130-5

Popovici C, Adélaïde J, Ollendorff V, Chaffanet M, Guasch G, Jacrot M, Leroux D, Birnbaum D, Pébusque MJ. Fibroblast growth factor receptor 1 is fused to FIM in stem-cell myeloproliferative disorder with t(8;13). Proc Natl Acad Sci U S A. 1998 May 12;95(10):5712-7

Reiter A, Sohal J, Kulkarni S, Chase A, Macdonald DH, Aguiar RC, Gonçalves C, Hernandez JM, Jennings BA, Goldman JM, Cross NC. Consistent fusion of ZNF198 to the fibroblast growth factor receptor-1 in the t(8;13)(p11;q12) myeloproliferative syndrome. Blood. 1998 Sep 1;92(5):1735-42

Smedley D, Hamoudi R, Clark J, Warren W, Abdul-Rauf M, Somers G, Venter D, Fagan K, Cooper C, Shipley J. The t(8;13)(p11;q11-12) rearrangement associated with an atypical myeloproliferative disorder fuses the fibroblast growth factor receptor 1 gene to a novel gene RAMP. Hum Mol Genet. 1998 Apr;7(4):637-42

Xiao S, Nalabolu SR, Aster JC, Ma J, Abruzzo L, Jaffe ES, Stone R, Weissman SM, Hudson TJ, Fletcher JA. FGFR1 is fused with a novel zinc-finger gene, ZNF198, in the t(8;13) leukaemia/lymphoma syndrome. Nat Genet. 1998 Jan;18(1):84-7

Kulkarni S, Reiter A, Smedley D, Goldman JM, Cross NC. The genomic structure of ZNF198 and location of breakpoints in the t(8;13) myeloproliferative syndrome. Genomics. 1999 Jan 1;55(1):118-21

Ollendorff V, Guasch G, Isnardon D, Galindo R, Birnbaum D, Pébusque MJ. Characterization of FIM-FGFR1, the fusion product of the myeloproliferative disorder-associated t(8;13) translocation. J Biol Chem. 1999 Sep 17;274(38):26922-30

Smedley D, Demiroglu A, Abdul-Rauf M, Heath C, Cooper C, Shipley J, Cross NC. ZNF198-FGFR1 transforms Ba/F3 cells to growth factor independence and results in high level tyrosine phosphorylation of STATS 1 and 5. Neoplasia. 1999 Oct;1(4):349-55

Xiao S, McCarthy JG, Aster JC, Fletcher JA. ZNF198-FGFR1 transforming activity depends on a novel proline-rich ZNF198 oligomerization domain. Blood. 2000 Jul 15;96(2):699-704

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