

Leukaemia Section

Mini Review

t(8;9)(p12;q33)

Jacques Boyer

Laboratoire d'Hématologie, CH du MANS, France (JB)

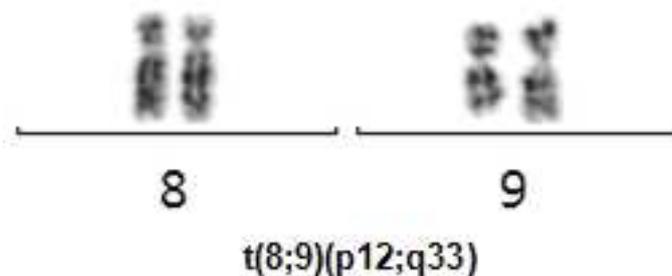
Published in Atlas Database: January 2004

Online updated version: <http://AtlasGeneticsOncology.org/Anomalies/t0809p12q33ID1129.html>

DOI: 10.4267/2042/38076

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Identity



t(8;9)(p12;q33) G- banding - Courtesy Melanie Zenger and Claudia Haferlach.

Note

8p12 myeloproliferative syndrome (EMS)/stem cell leukemia-lymphoma syndrome (SCLL) belongs to the tyrosine kinase fusion genes chronic myeloproliferative diseases. It is associated with recurrent translocations:

t(6;8)(q27;p12),
t(8;9)(p12;q33),
t(8;11)(p12;p15),
t(8;12)(p12;q15),
t(8;13)(p12;q12),
t(8;17)(p12;q25),
t(8;19)(p12;q13),
t(8;22)(p12;q11).

Clinics and pathology

Disease

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.

Epidemiology

9 cases are described; sex ratio : 6M/3F.

Clinics

Aggressive disease; myeloid hyperplasia progressing to myelodysplasia and T or B-cell lymphoma, splenomegaly, lymph node. High WBC with myeloid cells with frequently eosinophilia and sometimes monocytosis (near CMLL).

Evolution

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

Prognosis

Median survival: 12 months.

Cytogenetics

Cytogenetics morphological

This translocation is a variant of the t(8;13)(p12;q12).

Additional anomalies

+der(9), +21.

Genes involved and proteins

FGFR1

Location

8p12

CEP110

Location

9q33

DNA/RNA

DNA: 26kb-19 exons RNA: Three mains transcripts of approximatly 7.5, 4.5 and 1.5 kb. CEP transcripts are barely expressed in thymus and peripheral blood cells.

Protein

CEP110 gene codes for a 994-amino acid coiled-coil protein with 4 consensus leucine zippers (centrosome associated P110 protein).

Result of the chromosomal anomaly

Hybrid gene

Description

The t(8;9) breakpoint in the FGFR1 gene is localized in exon 8, 12 bp upstream of the exon 8/intron 8 junction. It is distinct from the breakpoints in the t(6;8) and t(8;13) but it preserves the same FGFR1 sequence in the chimeric protein.

The breakpoint in the CEP110 is localized in exon 15.

The translocation leads to the formation of the two reciprocal transcripts.

Fusion protein

Description

The CEP110-FGFR1 fusion protein encodes an aberrant tyrosine kinase of 150-kd wich retains most of CEP110 with the leucine zipper motif and the catalytic domain of FGFR1.

The CEP110-FGFR1 protein has a constitutive kinase activity and is located within the cell cytoplasm contrasting with the centrosome and membrane localizations of the wildtype respective proteins.

The FGFR1-CEP110 protein contains the FGFR1 N-terminal region with its ligand-binding and transmembrane domains and the CEP110 C-terminal region.

Oncogenesis

Activated aberrant tyrosine kinase are likely to promote leukemogenesis through contitutive activation of the FGFR1 kinase. This activation may be mediated by dimerisation of the portion of the fusion protein wich contains the leucine zippers.

This activation may interacts with the cell proliferation and the apoptose, additional anomalies may also play an important role in the evolution of the disease.

References

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This article should be referenced as such:

Boyer J. t(8;9)(p12;q33). *Atlas Genet Cytogenet Oncol Haematol*. 2004; 8(2):98-99.
