Atlas of Genetics and Cytogenetics in Oncology and Haematology

OPEN ACCESS JOURNAL AT INIST-CNRS

Leukaemia Section

Mini Review

t(5;12)(q31;p13) in MDS, AML and AEL

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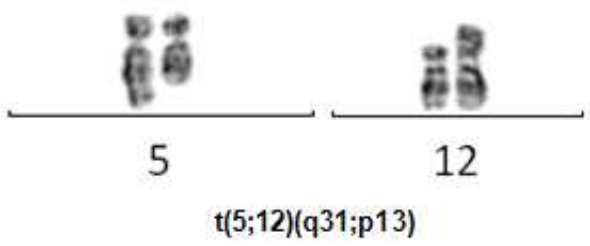
Published in Atlas Database: March 2007

Online updated version: http://AtlasGeneticsOncology.org/Anomalies/t0512q31p13ID1344.html
DOI: 10.4267/2042/38454

Identity



t(5;12)(q31;p13) G- banding - Courtesy Melanie Zenger and Claudia Haferlach.

Clinics and pathology

Disease

The t(5;12)(q31;p13) translocation involving ETV6 (12p13) and ACSL6 (5q31) was found in a patient with refractory anemia with excess blasts (RAEB) with basophilia, a patient with acute myelogenous leukemia (AML) with eosinophilia, and a patient with acute eosinophilic leukemia (AEL).

Phenotype / cell stem origin

Myeloid lineage.

Epidemiology

To date, one case with myelodysplastic syndrome (RAEB), one case with AML, one case with AEL, one case with atypical CML, and 2 cases with Polycythemia Vera (PV).
The t(5;12)(q31;p13) is a recurrent translocation in myeloid malignancies (at least 23 cases reported).

Prognosis

No prognostic value established.

Cytogenetics

Cytogenetics morphological

May be not easy to detect.

Cytogenetics molecular

The translocation can be detected by FISH with ETV6 probes. The ETV6 gene is rearranged, and the breakpoint is between exon 1 and exon 2 in all cases reported.

Additional anomalies

Disruption of the second ETV6 allele by t(12;19) was detected in the AML case by FISH analysis.

Variants

No variants.

Genes involved and Proteins

ETV6 (ETS Variant gene 6)

Location: 12p13
Note: The gene is known to be involved in a large number of chromosomal rearrangements associated with leukemia and congenital fibrosarcoma.

DNA / RNA

9 exons; alternate splicing

Protein

The gene encodes an ETS family transcription factor; the product of this gene contains a N-terminal pointed (PNT) domain that is involved in the protein-protein interactions, and a C-terminal ETS DNA-binding domain; wide expression; nuclear localization.

ACSL6 (Acyl-CoA Synthetase Long-chain family member 6)

Location: 5q31

Note: None of the resulting chimeric transcripts, except for the ACSL6/ETV6 transcript in the RAEB case, led to a fusion protein.

DNA / RNA

57,74 kb, 21 exons; alternate splicing.

Protein

Two splicing isoforms, a long and a short. The gene encodes an AMP binding enzyme; plays an important role in fatty acid metabolism in brain, responsible for activation of long-chain fatty acids in erythrocytes. Wide expression, expression low at earlier stages of erythroid development but very high in reticulocytes.

Results of the chromosomal anomaly

Hybrid gene

Description

A novel human gene, called ACS2 (acyl-CoA synthetase-2), was identified as an ETV6 fusion partner in a recurrent t(5;12)(q31;p13) translocation. Northern blot analysis detected high levels of ACS2 expression in brain, fetal liver, and bone marrow, and the gene was found to be highly conserved in man and rat. The ETV6/ACSL6 fusion transcripts showed an out-frame fusion of exon 1 of ETV6 to exon 1 of ACSL6 in the AEL patient, an out-frame fusion of exon 1 of ETV6 to exon 11 of ACSL6 in the AML patient, and a short in-frame fusion of exon 1 of ETV6 to the 3-prime untranslated region of ACSL6 in the patient with RAEB. Reciprocal ACSL6/ETV6 transcripts were identified in 2 of the cases. FISH with ETV6 cosmids on 12p13, and BACs and PIs on 5q31, demonstrated that the 5q31 breakpoints of the AML and AEL cases involved the 5-prime portion of the ACSL6 gene, and that the 5q31 breakpoint of the RAEB case involved the 3-prime portion of the ACSL6 gene. None of the resulting chimeric transcripts except for the ACSL6/ETV6 transcript in the RAEB case led to a fusion protein.

A case with a CML and a t(5;12)(q31;p13) was characterized, and 3 different ETV6/ACSL6 transcripts were detected. Moreover, as a consequence of the translocation IL-3/CSF2, located at 5q31, was ectopically expressed in the leukemic cells.

References

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This article should be referenced as such:
Odero MD. t(5;12)(q31;p13) in MDS, AML and AEL. Atlas Genet Cytogenet Oncol Haematol.2007;11(3):247-248.