Atlas of Genetics and Cytogenetics in Oncology and Haematology

OPEN ACCESS JOURNAL AT INIST-CNRS

Leukaemia Section
Mini Review

inv(8)(p11q13)

Jacques Boyer

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

Published in Atlas Database: December 2003

Online updated version: http://AtlasGeneticsOncology.org/Anomalies/inv8p11q13ID1189.html
DOI: 10.4267/2042/38072

Identity

Note
Two distinct clinical syndromes have been associated with the 8p11-12 region:
Stem-cell myeloproliferative disorder with FGFR1 rearrangement
AML M4 or M5 erythrophagocytosis-associated with MOZ rearrangement.
The inv(8)(p11q13) involves MOZ.
The partners of 8p11 are 8q13, 14q11, 16p13, 19q13, 22q13 and 3q27, 17q12 in a complexe translocation t(3;8;17)(q27;p11; q12).

Clinics and pathology

Disease

Acute myelomonocytic or monocytic leukaemia (M4, M5a, M5b FAB) with erythrophagocytosis by blasts.
Acute myeloblastic leukemia M0/M1 FAB (one case).

Epidemiology

Rare. Young age (6 patients, median: 23.5 years) and female sexe.

Cytology

Morphology feature observed in AML with t(8;16).

Prognosis

Probably poor.

Cytogenetics

Cytogenetics morphological

Inv(8) (p11q13) is a variant of t(8;16) (p11;p13)

Additional anomalies

In one case der(10)t(1;10)(q25;p15).

Genes involved and proteins

MOZ

Location
8p11

Note
MOZ contains a LAP (Leukemia associated protein) zinc finger domain, a HAT domain (Histone acetyltransferase) and a acidic domain. Detection by FISH: YAC 176C9.

Protein
ZNF220
Monocytic leukemia zinc finger protein.
2004 amino acids and 225 kDa nuclear protein, with 2 LAP/PHD-type zinc fingers.
MOZ is a histone acetyltransferase (HAT) and the founding member of the MYST family of HATs, a family that includes proteins involved in cell cycle regulation, chromatin remodeling and dosage compensation.
MOZ plays an important role during hematopoiesis with his transcriptional coregulator activity.

TIF2

Location
8q13

Note
Aliases: GRIP1, NCoA-2.
Nuclear receptors are ligand-inductible trans-cription factors with three structural domains : an activation function AF-1, a DNA-binding domain and a second activation function AF-2 that is mediated by nuclear coactivators (NRCoAs) : TIF2 was recently shown to be one such mediators of AF-2 function.
Detection by FISH: PAC clone 192D10.

Protein

The TIF-2 protein is homologous to other NRCoAs specically SRC-1 (alias NcoA-1). This protein has HAT activity and also interacts directly with CBP. It is likely that TIF-2 mediates transcriptional activation by a mechanism involving chromatin remodeling.

Result of the chromosomal anomaly

Hybrid gene

Description

The fusion gene produces a mRNA containing the 5' end of MOZ appended in translational frame to the 3' end of TIF2.

The inv(8) MOZ breakpoint is distinct from the breakpoint in the MOZ -CBP fusion. The fusion product retains the zinc fingers, the HAT domain of MOZ along with the HAT domains and CBP interacting domain of TIF2.

Fusion protein

Description

MOZ-TIF2

Oncogenesis

The ability of HATs to affect the chromatin structure and regulate gene expression is well appreciated. How the MOZ-TIF2 fusion protein is involved in acute leukemia is not known, but it probably affects the chromatin condensation. It may modulate or augment the transcriptional activity of genes normaly regulated by MOZ or it may serve as a bridge between MOZ and CBP. Recently, it was demonstrated that MOZ-TIF2 has transforming properties in vitro and causes AML. The C2HC nucleosome recognition motif of MOZ and MOZ-TIF2 interaction with CBP are essential for transformation.

To be noted

Case Report

inv(8)(p11.2q13) found in a patient with chronic myelomonocytic leukemia that progressed to acute myeloid leukemia

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This article should be referenced as such:

Boyer J. inv(8)(p11q13). Atlas Genet Cytogenet Oncol Haematol. 2004; 8(2):86-87.