t(1;3)(p36;q21) PSMD2/PRDM16 ???

Jean-Loup Huret

Medical Genetics, Dept Medical Information, University of Poitiers, CHU Poitiers Hospital, F-86021 Poitiers, France. jean-loup.huret@chu-poitiers.fr

Published in Atlas Database: September 2016
Online updated version : http://AtlasGeneticsOncology.org/Anomalies/t0103ID1002.html
Printable original version : http://documents.revuees.inist.fr/bitstream/handle/2042/68257/09-2016-t0103ID1002.pdf
DOI: 10.4267/2042/68257

This article is an update of:
Hess JL. t(1;3)(p36;q21). Atlas Genet Cytogenet Oncol Haematol 2002;6(3)
Huret JL. t(1;3)(p36;q21). Atlas Genet Cytogenet Oncol Haematol 1997;1(1)

This work is licensed under a Creative Commons Attribution-Noncommercial-No Derivative Works 2.0 France Licence. © 2017 Atlas of Genetics and Cytogenetics in Oncology and Haematology

Identity

This entity probably does not exist:
1- PSMD2 sits in 3q27, while the breakpoint is in 3q21;
2- PSMD2, a protein of the proteasome is well known by its alias, RPN1, while the true RPN1, a protein involved in N-glycosylation, sitting in 3q21, is better known by its full name: Ribophorin I.

The translocation is therefore likely to be t(1;3)(p36;q21) RPN1/PRDM16

Clinics and pathology

Disease

Myeloid lineage (MDS, AML, therapy related AML, CML, MPD); features similar to those of the 3q21q26 syndrome including normal or elevated platelet count at diagnosis, megakaryocytic hyperplasia and dysplasia. Very rarely in lymphoid lineage
Phenotype/cell stem origin

of 39 cases, there were: 22 myelodysplastic syndromes (MDS) (17/22 transformed into refractory acute myeloid leukemia (AML) of -M1 or -M4 type), 8 de novo AML, 3 therapy-related MDS, 2 polycythemia vera, 1 essential thrombocythemia, 1 chronic myelogenous leukemia (CML), 1 multiple myeloma, 1 waldenström's macroglobulinemia

Epidemiology

patients are aged: 30-80 yrs

Clinics

Roughly 50% of patients present with MDS, another 10% with therapy associated MDS, 25% with de novo AML, and the remainder with a range of other myeloproliferative disorders. The majority of MDS patients transform into AML with a short preleukemic phase.

Blood data: frequent thrombocytosis or normal platelet count

Cytology

frequently characterized by dysmegakaryocytopoiesis

Pathology

The pathology is typical of MDS, often with a prominent monocytic component. Trilineage dysplasia. Acute leukemias that evolve usually show the morphology of M4 AML.

Treatment

Patients are treated with conventional chemotherapy for AML.

Prognosis

Very poor so far: from 16 cases, median survival was 6 mths in AML, 20 mths in MDS

Cytogenetics

Note

Other rearrangements showing similar clinical features include inv(3)(q21q26), t(3;3)(q21;q26), t(3;5)(q21;q31), t(3;8)(q21;q24), and t(3;21)(q26;q22). The breakpoints in 3q21 cluster in a 50 kb region centromeric to the breakpoint in inv(3)(q21;q26) and the ribophorin gene (RPN1). The breakpoints at 1p36 are clustered in a 90 kb region at 1p36.3.

Additional anomalies

del (5q) in 5 of 20 cases (1/4)

Genes involved and proteins

Mechanisms of Oncogenesis: The available data suggest that transcription of MEL1 (MDS1/EVI1-like gene) is activated as a result of translocation bringing the gene just 3' to RPN1 gene at 3q21. MEL1 is a 1257 amino acid protein that is homologous (63% similar in amino acid sequence) to EVI. The mechanism of activation of MEL1 is similar to EVI1 that is activated by juxtaposition 3' to RPN1 in the (3;3)(q21;q26) and 5' to RPN1 in the inv(3)(q2126). It appears that MEL1 is normally expressed in uterus and kidney and not in normal hematopoietic cells or in leukemias that lack the t(1;3)(p36;q21). The MEL1 protein contains 2 DNA binding domains (7 C2H2 zinc finger repeats at the amino terminus and 3 zinc finger repeats at the carboxyl terminus). The amino terminal domain of MEL1 contains a PRD domain, a motif also found in the same location in the MDS1/EVI1 protein but not in MDS1). This is of interest because this domain is also found in RIZ, PRDI-BF1, and egl-43 and is homologous to the SET (Suvar3-9, Enhancer of zeste, Trithorax) domain that present in MLL. Inclusion of this domain in EVI1 appears to convert EVI1 from a transcriptional repressor to an activator. Therefore MEL1 may be a transcriptional activator. The target genes of MEL1 have not been identified.

References

Bitter MA, Neilly ME, Le Beau MM, Pearson MG, Rowley JD. Rearrangements of chromosome 3 involving bands 3q21 and 3q26 are associated with normal or elevated platelet counts in acute nonlymphocytic leukemia. Blood. 1985 Dec;66(6):1362-70


Marsden KA, Pearse AM, Collins GG, Ford DS, Heard S, Kimber RI. Acute leukemia with t(1;3)(p36;q21), evolution to t(1;3)(p36;q21), t(14;17)(q32;q21), and loss of red cell A and Le(b) antigens. Cancer Genet Cytogenet. 1992 Nov;64(1):80-5

Mochizuki N, Shimizu S, Nagasawa T, Tanaka H, Taniwaki M, Yokota J, Morishita K. A novel gene, MEL1, mapped to 1p36.3 is highly homologous to the MDS1/EVI1 gene and is transcriptionally activated in t(1;3)(p36;q21)-positive leukemia cells. Blood. 2000 Nov 1;96(9):3209-14

Atlas Genet Cytogenet Oncol Haematol. 2017; 21(6) 221


This article should be referenced as such: