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Short Communication

t(1;3)(p36;q21) RPN1/PRDM16

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Abstract

Review on t(1;3)(p36;q21) translocations, with data on clinics, and the genes involved.

Keywords
chromosome 1; chromosome3; t(1;3)(p36;q21); RPN1; PRDM16

Identity

A translocation t(1;3)(p36;q21), with the same breakpoints but involving PSMD2 and PRDM16 probably does not exist:
1- PSMD2 sits in 3q27, while the breakpoint is in 3q21;
2- PSMD2, a protein of the proteasome, is mainly known in PubMed by its alias: "RPN1", while the true RPN1, a protein involved in N-glycosylation and sitting in 3q21, is better known by its full name: "Ribophorin I".
Hence the confusion, found in a number of papers of the literature.

Clinics and pathology

Disease

Myelodysplastic syndromes and acute myeloid leukaemias

Note
A t(1;3)(p36;q21) RPN1/PRDM16 was found in 35 cases (Mochizuki et al., 2000; Shimizu et al., 2000: Xinh et al., 2003; Duhoux et al., 2012)

Phenotype/cell stem origin

There were 19 myeloproliferative/myelodysplastic syndromes: 1 chronic myeloid leukemia (CML), 3 refractory anaemia with ring sideroblasts (RARS); 6 refractory anemia with excess blasts (RAEB, RAEB2, RAEB-T), 6 chronic myelomonocytic leukaemia (CMML) and 3 myelodysplastic syndrome not otherwise specified (MDS-NOS); and 16, acute myeloid leukaemias; 7 apparently de novo (AML- M1, M2, M4, M5a, M6 and NOS), and 9 therapy-related or secondary AML.

Clinics

Median age was 66 years (range 29-92). Sex ratio was 21 male/14 female patients (3/5 male, 2/5 female).

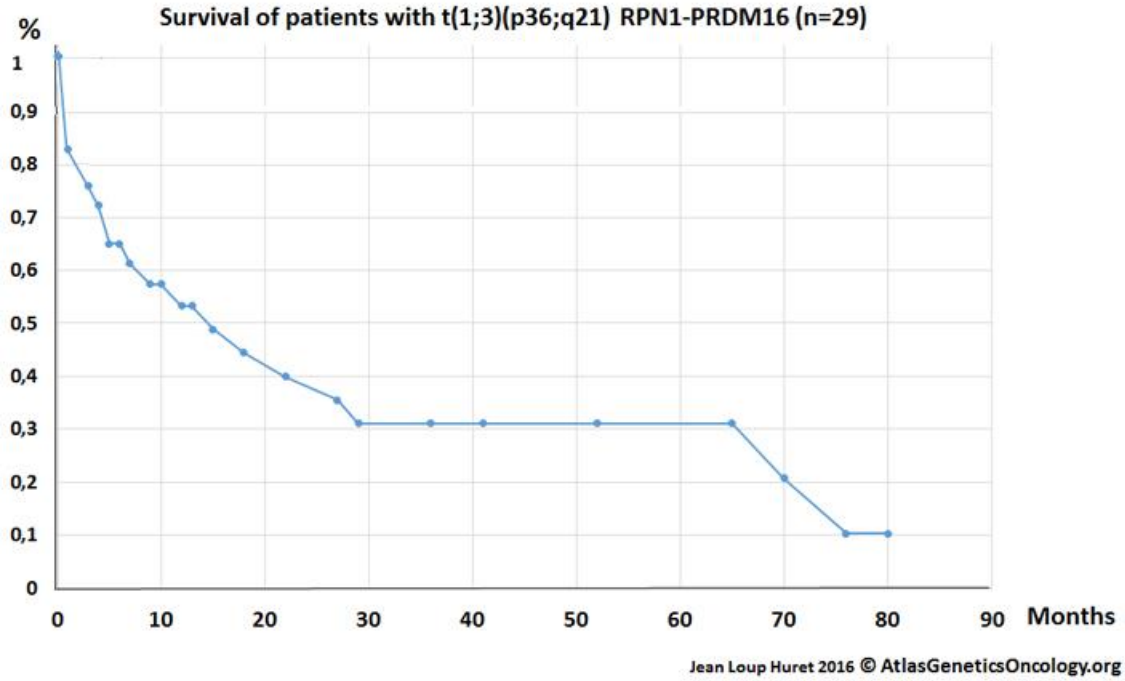
Prognosis

Median survival in 29 patients was 13-15 months; five patients died within a month after diagnosis, while 2 patients were long survivors (65 months + and 80 months+).

Cytogenetics

Cytogenetics morphological

The t(1;3)(p36;q21) was the sole abnormality in 26 of 35 cases, and accompanied with del(5q) at diagnosis in 5 cases. In 2 additional cases, the del(5q) occurred during course of the disease. There was one del(13q) and one del(20q), markers and a complex karyotype were found in two cases.



Genes involved and proteins

PRDM16 (PR domain containing 16)

Location
1p36.32

DNA/RNA
11 splice variants

Protein
1276 amino acids and smaller proteins. Contains a N-term PR domain; 7 Zinc fingers, a proline-rich domain, and 3 Zinc fingers in the C-term. Binds DNA.
Transcription activator; PRDM16 has an intrinsic histone methyltransferase activity.
PRDM16 forms a transcriptional complex with CEBPB. PRDM16 plays a downstream regulatory role in mediating TGFB signaling (Bjork et al., 2010).
PRDM16 induces brown fat determination and differentiation.
PRDM16 is expressed selectively in the earliest stem and progenitor hematopoietic cells, and is required for the maintenance of the hematopoietic stem cell pool during development. PRDM16 is also required for survival, cell-cycle regulation and self-renewal in neural stem cells (Chuikov et al., 2010; Kajimura et al., 2010; Aguilo et al., 2011; Chi and Cohen, 2016).

RPN1 (ribophorin I)

Location
3q21.3

Note
RPN1 (Ribophorin I) (3q21.3, starts at 128338813 and ends at 128369719 bp from pter) must not be confused with PSMD2 (proteasome 26S subunit, non-ATPase 2) (3q27.1; starts at 184018369 and ends at 184026842 bp from pter). PSMD2 aliases are: RPN1, P97, S2, TRAP2 (see above).

DNA/RNA
8 splice variants

Protein
607 amino acids. RPN1 comprised of a signal peptide (aa 1-23).RPN1 (Ribophorin I) is an endoplasmic reticulum transmembrane protein and a subunit of the oligosaccharyltransferase (OST) complex. RPN1 regulates the delivery of precursor proteins to the OST complex by presenting them to the catalytic core. RPN1 acts as a substrate-specific facilitator of N-glycosylation It may function as a chaperone that recognizes misfolded proteins, and plays a role in protein quality control in association with MLEC (malectin) (Wilson and High, 2007; Wilson et al., 2008; Takeda et al., 2014).

Result of the chromosomal anomaly

Hybrid gene

Description
5' RPN1 translocated to 3' PRDM16. The breakpoint in PRDM16 is located either in the ?rst intron, or 5' of exon 1. Transcriptional activation of can occur in some patients, and fusion transcripts have been generated in other patients.

Fusion protein

Oncogenesis

The 5' flanking regions of the rat RPN1 gene containes GC-rich elements and an octamer motif. It could serve as an enhancer, to activate transcription of PRDM16 (Mochizuki et al., 2000; Shimizu et al., 2000). Overexpression of PRDM16 (Duhoux et al., 2012).

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