Leukaemia Section
Short Communication

t(3;11)(p25;p15)

Jean-Loup Huret

Genetics, Dept Medical Information, University of Poitiers, CHU Poitiers Hospital, F-86021 Poitiers, France (JLH)

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Clinics and pathology

Disease

Myelodysplastic syndrome (MDS) and acute myeloid leukemia (AML)

Epidemiology

Two cases to date, with a possible identical rearrangement.

A 32-year-old man had a common acute lymphoblastic leukemia (c-ALL) with a del(9p). A bone marrow transplantation (BMT) was performed. The donor was his sister. Fifteen months later, a secondary AML with erythrophagocytosis developed. The karyotype was 46,XX (suggesting that the leukemic clone derived from the sibling bone marrow donor), with the following anomalies: a t(3;11)(p25;p15), but also the classical t(8;16)(p11;p13) with MYST3/REBBP rearrangement. The patient died a month later. NUP98 was not tested (Schmidt et al., 2004).

A 33-year-old woman with a refractory anemia with excess of blasts in transformation exhibited a t(3;5;11)(p24;q35;p15) with ANKRD28-NUP98 and NUP98-NSD1 rearrangements, Transformation to AML occurred 2 weeks later. In spite of a BMT, the patient died 7 months after diagnosis (Ishikawa et al., 2007).

Genes involved and proteins

ANKRD28

Location
3p25

Protein
1053 and 1086 amino acids isoforms.

Contains 30 ankyrin repeats (protein-protein interaction motifs). ANKRD28 forms a complex with BCAR1/p130Cas, CRK, and DOCK1 to enhance BCAR1 phosphorylation. ANKRD28 is required for cell migration (Kiyokawa and Matsuda, 2009).

PP6 is a multisubunit enzyme, comprising a catalytic subunit, a phosphatase-associated protein (SAPS) domain regulatory subunit and ankyrin repeat domain subunits. PP6 holoenzyme, comprising PPP6C catalytic, SAPS1-3 regulatory, and ANKRD28 and ANKRD44 subunits, is required for normal mitotic progression (Zeng et al., 2010).

NUP98

Location
11p15

Protein
Nucleoporin: associated with the nuclear pore complex. Role in nucleocytoplasmic transport processes.

Result of the chromosomal anomaly

Hybrid gene

Description
Two in-frame fusion transcripts 5' ANKRD28 - 3' NUP98 (exons 18 and 13 respectively), and 5' NUP98 - 3' NSD1 (exons 12 and 7 respectively) were produced in the case reported by Ishikawa et al. in 2007.

Fusion protein

Expression / Localisation
Although 5' NUP98 - 3' partner is the usual fusion transcript involved in leukemogenesis with 11p15 involvement, the present 5' ANKRD28 - 3' NUP98 fusion transcript may have played a role. ANKRD28-
NUP98 was localized in the nucleolus and cytoplasm and might have contributed to the leukemogenesis process. Cells transfected with ANKRD28-NUP98 formed more foci than cells transfected with the wild type ANKRD28 (Ishikawa et al., 2007).

References


Kiyokawa E, Matsuda M. Regulation of focal adhesion and cell migration by ANKRD28-DOCK180 interaction. Cell Adh Migr. 2009 Jul-Sep;3(3):281-4

Zeng K, Bastos RN, Barr FA, Gruneberg U. Protein phosphatase 6 regulates mitotic spindle formation by controlling the T-loop phosphorylation state of Aurora A bound to its activator TPX2. J Cell Biol. 2010 Dec 27;191(7):1315-32

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