t(5;14)(q35;q11) RANBP17 (or TLX3)/TRD

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Abstract

Review on t(5;14)(q35;q11), with data on clinics and the genes involved.

Keywords
Chromosome 5; chromosome 14; t(5;14)(q35;q11); RANBP17; TRD; TLX3; Acute lymphoblastic leukemia; Acute myeloid leukemia.

Clinics and pathology

Disease
Acute lymphoblastic leukemia (ALL)

Phenotype/cell stem origin
T- and B-ALL

Epidemiology
5 patients to date, 4 pediatric cases (14 months, 2, 10 and 12 years) (Whitlock JA et al., 1994; Hansen-Hagge TE et al., 2002), 1 case with no clinical information (Hansen-Hagge et al., 2002, case 2)

Clinics
One or more features of bulky disease.

Cytogenetics
Sole abnormality in one case of T-ALL and one case of B-ALL relapse, additional abnormalities in 2 cases [B-ALL with subclones with dup(1)(q32q21), add(X)(p22), der(11)(t(11:?))(?:?), and T-ALL with cytogenetically unrelated cell line with del(9)(p22) and trisomy 15 (t(11:11)], 2 cases not available.

Evolution
The 2 patients with B-ALL were in remission 19 and 22 months after diagnosis. One patient with T-ALL relapsed at 6 months and the second patient with T-ALL developed AML 17 months after diagnosis, with the t(5;14) being present in the myeloblasts.

Disease
Acute myeloid leukemia, FAB M5 (Welborn JL et al., 1993)

Note
Secondary abnormality.

Epidemiology
1 case to date, a 45-year-male.

Cytogenetics
The t(5;14)(q35;q11) was found in a follow-up specimen together with the primary abnormality, t(6;11)(q27;q23), identified in the sample obtained at diagnosis.

Genes
The genes involved in the translocation t(5;14) identified in this AML case have not been investigated and may be different from those of the t(5;14) found in the ALL cases.

Treatment
2 inductions with standard dose cytarabine - daunorubicin - 6-thioguanine.
Evolution

No response to treatment.

Genes involved and proteins

**RANBP17 (RAN binding protein 17)**

**Location** 5q35.1

**Note**

The 5q breakpoint was initially reported to be located at 5q34 (Hansen-Hagge et al., 2002), but the location of the gene potentially disrupted by the translocation is 5q35.1 in the hg38 assembly (UCSC Genome Browser, accessed Dec. 9th, 2016). However, Hansen-Hagge et al., 2002, mention that the 5q breakpoint is also in the vicinity of the TLX3 gene, which involvement was neither confirmed nor excluded. This gene has been involved in other ALL rearrangements and encodes a DNA-binding nuclear transcription factor (see Atlas t(5;7)(q35;q21), t(5;14)(q35;q32)).

**DNA/RNA**

The RANBP17 gene has 28 exons and spans 438 kb (hg38, UCSC Genome Browser, accessed Dec. 9th, 2016). Several transcripts have been identified, of 2.5, 4.5, 7.5 and 10 kb (Koch et al., 2000).

**Protein**

The Ran-binding protein 17 is 90-130 kD in size and contains an importin-β N-terminal domain. The RAN-binding protein-17 gene is a member of the importin-beta superfamily of nuclear transport receptors. Its protein is localized in the nucleus, with a restricted expression pattern in the testis (Koch P et al., 2000). It is a regulator of the E2A protein's action (Lee et al., 2010).

**TLX3 (T-cell leukemia, homeobox protein 3)**

**Location** 5q35.1

**TRD**

**Location** 14q11.2

Result of the chromosomal anomaly

**Hybrid gene**

**Description**

In one case, exon 24 of RANBP17 was found to be joined to TCR D62D83Iδ1 and containing the δ enhancer sequence located between the J61 and Cδ elements, while in a second case, data suggested an illegitimate recombination of TCR δ with sequences from chromosome 14 and 5, the 5q breakpoint being about 8 kb downstream of the last RANBP17 exon (and about 1KB upstream from TLX3). There was an increased RANBP17 expression in the leukemic cells (Hansen-Hagge et al., 2002).

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