t(11;14)(q24;q32) IGH/miR-125b-1

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Disease
B-cell precursor-acute lymphoblastic leukemia (BCP-ALL)

Epidemiology
Rare, only 5 cases published to date (Sonoki et al., 2005; Chapiro et al., 2010; Tassano et al., 2010; Enomoto et al., 2011).

Clinics
Sonoki et al. reported a 35-year-old woman with a leukemic recurrence as bilateral ovarian tumors 7 years after allogenic bone marrow transplantation for BCP-ALL.

Chapiro et al. reported two further adult cases: a female patient aged 45 years with an early-pre-B phenotype who died 21 months after diagnostic, and a male patient aged 33 years who were alive 4 months after diagnosis.

Tassano et al. described a 12-year-old girl who developed a dramatic macrophage activation and died during the induction phase of treatment.

Cytogenetics

Note
In the case reported by Sonoki et al., the t(11;14) was not detected by cytogenetic analyses: an insertion of miR-125b-1 sequence into the IGH locus was found by molecular analyses.

Cytogenetics morphological
In one of the cases described by Chapiro et al., only the derivated chromosome 14 of t(11;14) was present, associated with a t(1;3)(p?33;q2?7) and +21. In the other one, the t(11;14) was associated with a del(9)(p13) and dic(7;13)(q2?7;q10). In the pediatric case reported by Tassano et al., the t(11;14) was the sole abnormality.

Genes involved and proteins

IGH@
Location
14q32

miR-125b-1
Location
11q24

DNA/RNA
MicroRNAs are a family of small noncoding RNA (18-25 nucleotides) that play a key role in many fundamental processes, including differentiation, proliferation, and apoptosis, by regulating gene expression at the posttranscriptional level. MicroRNA miR-125b is the ortholog of lin-4 in Caenorhaditis elegans.

It is transcribed from two loci located on chromosomes 11q24 (miR-125b-1) and 21q21 (miR-125b-2). Mir-125b is involved in hematopoiesis: it enhances survival and proliferation of early hematopoietic progenitors and blocks their terminal differentiation (Shaham et al., 2012).

Mir-125b-1 and miR-125b-2 are both reported to be up-regulated in some solid cancers and hematological malignancies, including BCP-ALL, and AML/MDS.

In the latter, the over-expression of miR-125b-1 is the result of the rare translocation t(2;11)(p21;q23) (Bousquet et al., 2008).
Result of the chromosomal anomaly

**Hybrid gene**

Description
The translocation links sequences located 5 to 18 kb centromeric of miR-125b-1 on chromosome 11 to a JH segment on chromosome 14.

**Fusion protein**

Description
No fusion protein.

**Oncogenesis**

Transcriptional activation of miR-125b-1. Several murine models have been described, demonstrating that miR-125b is a leukemogenic oncogene. In bone marrow transplantation models, mice develop fatal hematological malignancies consisting of myeloproliferative neoplasms, B- and T-ALL (Bousquet et al., 2010; O’Connell et al., 2010). Transgenic mice mimicking the t(11;14)(Eµ/miR-125b) die from B-cell malignancies resistant to apoptosis (Enomoto et al., 2011). A recent study showed that miR-125b exerts its oncogenic function in progenitor B-cells by targeting ARID3a/Bright, a transcription factor implicated in the regulation of expression of the immunoglobulin heavy chain: miR-125b mediates ARID3a repression, thus leading to a blockage in differentiation, increased proliferation and inhibition of apoptosis (Puisségur et al., 2012).

**References**


This article should be referenced as such: