Leukaemia Section

Short Communication

**t(11;19)(q23;p13) KMT2A/MYO1F**

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**Abstract**

Review on t(11;19)(q23;p13), with data on clinics, and the genes involved.

**KEYWORDS**

Chromosome 11; Chromosome 19; KMT2A; MYO1F; Acute myeloid leukemia

**Clinics**

One patient was diagnosed at birth (Duhoux et al., 2011), and another one at 2 months of age (Taki et al., 2005).

**Prognosis**

Scarce data: one patient died 5 days after admission (Taki et al., 2005).

**Cytogenetics**

**Cytogenetics morphological**

The t(11;19)(q23:p13.3) was the sole abnormality in the case described by Duhoux et al., 2011, while the cases of Lo Nigro et al., 2002 and Taki et al., 2005 were complex translocations.

**Genes involved and proteins**

**KMT2A** (myeloid/lymphoid or mixed lineage leukemia)

**Location**

11q23.3

**DNA/RNA**

37 exons, spanning about 120 kb; 13-15 mRNA

**Protein**

3969 amino acids, 431 kDa; Transcriptional regulatory factor. MLL is known to be associated with more than 30 proteins, including the core components of the SWI/SNF chromatin remodeling
complex and the transcription complex TFII D. MLL
binds promoters of HOX genes through acetylation
and methylation of histones. MLL is a major
regulator of hematopoiesis and embryonic
development, through regulation of HOX genes
expression regulation (HOXA9 in particular).

**MYO1F**

**Location**
19p13.2

**DNA/RNA**
28 exons, 3297 nucleotides

**Protein**
1,098 amino acids; 124 KDa; Myosins are a large
family of ATP-driven mechanoenzymes. MYO1F
belong to myosin class I, which includes myosins
that are able to interact with actin filaments and lipid
membranes. Presence of three tail homology regions
(TH1, TH2 and a SH3 domain named TH3). These
"long-tailed" myosins (i.e. with additional TH2 and
TH3) are able to crosslink actin filaments via the
TH2 domain and generate mechanical activities
using the actin cytoskeleton as a tract. MYO1F
contains a myosin motor domain (amino acids 17
- 690); this motor domain contains an actin binding
site. It has an ATPase activity/cycle with
association/dissociation of myosin with actin. The
motor domain is followed by an IQ domain
(isoleucine/glutamine motifs, aa 693 - 722), and a
TH1 domain (Tail Homology domain, aa 728 - 917).
The TH1 domain is responsible for membrane
interaction and, within TH1, a pleckstrin homology
PH domain which is a negatively charged
phospholipids-binding motif. There are several
phosphosites located in the TH2 domain, required
for binding to microtubules and microfilaments.
TH2 is alanine and proline-rich (aa 941 - 1000). The
C-terminus is a SH3 domain (SRC Homology 3
domain, aa 1041 - 1098); it should mediate assembly
of specific protein complexes via binding to proline-
rich peptides. TLR4 activation induces
phosphorylation of MYO1F. MYO1F is a cytosolic
protein predominantly expressed in the immune
system (Wenzel et al., 2015; Walklate et al., 2016).

**Result of the chromosomal anomaly**

**Hybrid gene**

**Description**
KMT2A exon 9 was fused to MYO1F exon 2; the
breakpoint was thus located within MLL intron 9 in
the cases reported by Taki et al., 2005 and Duhoux
et al., 2011. The breakpoint in KMT2A was in intron
10 in cases studied by Meyer et al., 2013.

**Fusion protein**

KMT2A_MYO1F fusion protein, with AT hooks, zinc
fingers CXXC type from KMT2A in N-terminus, fused
to the entire MYO1F protein in C-terminus.

**References**

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