Leukaemia Section
Mini Review

**t(10;16)(q22;p13)**

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Published in Atlas Database: May 2006

Online updated version: http://AtlasGeneticsOncology.org/Anomalies/t1016q22p13ID1332.html

DOI: 10.4267/2042/38359

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**Identity**

![G-band analysis. Partial karyotype showing the t(10;16)(q22;p13). Arrows indicate breakpoints in both chromosomes.](image)

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**Clinics and pathology**

**Disease**
Acute myeloid leukaemia (AML) M4/M5a and therapy-related myelodysplastic syndromes (MDS).

**Epidemiology**
Very rare, only four cases described.

**Clinics**
There is no erythrophagocytosis associated

**Treatment**
Bad response to chemotherapy.

**Prognosis**
Poor.

**Cytogenetics**

**Additional anomalies**
First described in a 4-year-old girl with AML M5a with 47,XX,der(7)(7;10)(p13:p11),+8,der(10)t(7;10)(p13:p11)t(10;16)(q22;p13),der(16)t(10;16)(q22;p13)/46,XX. Later it was also described in an 84-year-old male without erythrophagocytosis and with this sole cytogenetic aberration. In addition, a variant breakpoint was described in a 52-year-old japanese woman with a therapy-related myelodysplastic syndrome (t-MDS) and also this sole translocation. Finally, another fusion variant was described in an AML-M4 female patient with the t(10;16) (q22;p13) and a t(11;17)(q23;q21).

**Variants**
There are no cytogenetic variants described, but there are molecular variants due to different breakpoints in the genes fused (see below).

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**Genes involved and Proteins**

**MYST4**

**Location:** 10q22.2

**Note:** This gene is also involved in rearrangements observed in uterine leiomyomata.

**DNA / RNA**

18 exons spanning 206.0 Kb. Transcription is from centromere to telomere. Up to 7 alternative transcripts.

**Protein**

Histone acetyltransferase MYST4 is located probably in the nucleous. And it is probably involved in both positive (N-terminus) and negative (C-terminus) regulation of transcription, maybe involved in cerebral cortex development, required for RUNX2-dependent transcriptional activation and ubiquitously expressed in adult human tissues.
CREBBP

Location: 16p13.3

Note: This gene is also involved in t(8;16)(p11;p13) with MYST3. CREBBP fusion observed in M4 ANLL and therapy related AML; t(11;16)(q23;p13) with MLL. CREBBP fusion observed also in therapy related. Mutations of CREBBP are associated with Rubinstein-Taybi syndrome.

DNA / RNA

Up to 32 exons spanning 154,14 Kb. Transcription is from centromere to telomere and up to 3 alternative transcripts between 8,0 and 8,7 Kb.

Protein

CREBBP is a wide expression histone acetyltransferase enzyme which locates in the nucleus. Function binds specifically to the DNA-binding protein CREB connecting it to the basal transcriptional machinery. Also acetylates non-histone proteins, like NCOA3 coactivator. It has an essential role in embryogenesis, cell differentiation, apoptosis, and proliferation and it is involved in the regulation of cell cycle during G1/S transition.

Results of the chromosomal anomaly

Hybrid gene

Description

Fusion in-frame between MYST4 exon 17 and CREBBP exon 3. Variants fusing MYST4 exon 16 and CREBBP exon 5; MYST4 exon 17 and CREBBP exon 7 have also been described.

Transcript

5’ MYST4 - CREBBP 3’

Detection protocol

CREBBP-MYST4 has been also detected.
Schematic representation of the fusion MYST4-CREBBP consequence of the t(10;16)(q22;p13). From up to down: MYST4 and CREBBP structures. H15 domain: domain in histone families 1 and 5; PHD zinc fingers: plant homeodomain (PHD) with a C4HC3-type motif, this domain is widely distributed in eukaryotes and it has been found in many chromatin regulatory factors; MOZ_SAS family region: this region has been suggested to be homologous to acetyltransferases but this similarity is not supported by sequence analysis; KIX domain: bind domain for CBP and P300, this domain also binds to transactivation domains of other nuclear factors including Myb and Jun.

**Fusion protein**

**Description**

In all cases published to date the breakpoints occur in the acidic domain of MYST4 but at different locations of the CREBBP protein: in the nuclear receptor-binding domain, in a C/H rich domain or between this domain and the KIX domain. The putative MYST4-CBP chimaeric protein retains the part of MYST4 that encodes the zinc fingers, two nuclear localization signals (NLS1 and NLS2), the HAT domain, and a portion of the acidic domain, and most of the CBP protein, including its HAT domain.

**Oncogenesis**

MYST4 has a 60% identity and 66% similarity to MYST3. All the fusions involving this genes result in several fusion proteins that target the acidic domain of MYST3 and MYST4. The partner fusion partners share also functional regions. All the fusion proteins are suspected to be leukaemogenic as a consequence of aberrant histone acetylation and transcription regulation, due probably but not exclusively, to the concomitant presence of two HAT domains coming from the different partners.

**References**


This article should be referenced as such: