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Gene Section
Mini Review

MYST4 (MYST histone acetyltransferase (monocytic leukemia) 4)

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Identity

Hugo: MYST4
Other names: qkf; MORF; MOZ2; FLJ90335; KIAA0383; querkopf; DKFZp313G1618; EC 2.3.1.-EC 2.3.1.48
Location: 10q22.2
Local order: ADK (adenosine kinase isoform a) is more centromeric. DUPD1 (dual specificity phosphatase and pro isomerase) is more telomeric.

DNA/RNA

Description

18 exons spanning 206.0 Kb on 10q22.2. Transcription is from centromere to telomere.

Transcription

1 transcript

Protein

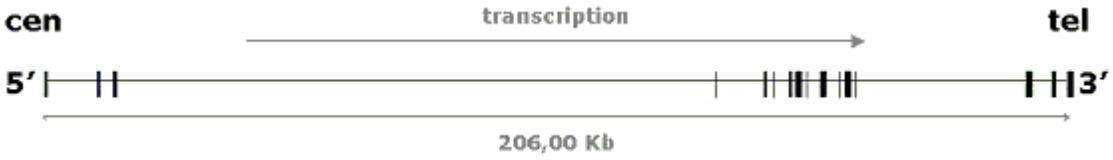
Note: MYST4_HUMAN; Histone acetyltransferase MYST4, MYST protein 4, MOZ, YBF2/SAS3, SAS2 and TIP60 protein 4, Histone acetyltransferase MOZ2, Monocytic leukemia zinc finger protein-related factor, or Histone acetyltransferase MORF.

Description

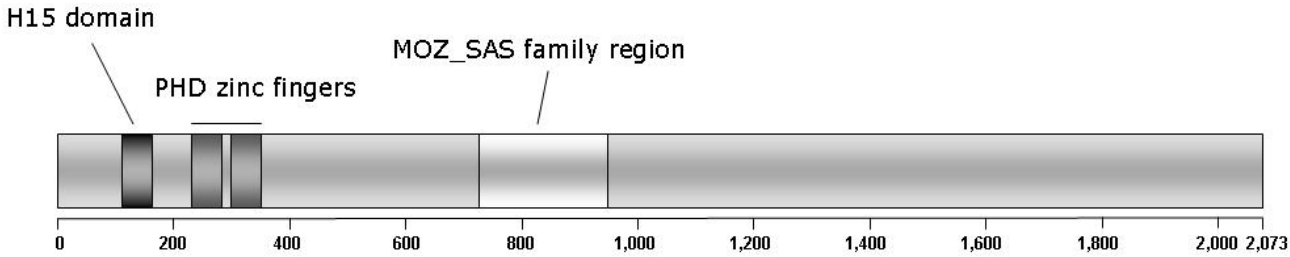
Histone acetyltransferase MYST4.

Localisation

Nucleous (probable).



Genomic structure of MYST4. Black boxes indicate exons.



Schematic representation of MYST4 protein. 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.

Function

It is a histone acetyltransferase 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.

Mutations

Somatic

MYST4 fusion genes in neoplasia t(10;16)(q22;p13) (see below) 5' MYST4 - CREBBP 3' (previously known as MORF-CBP, MORF- CREBBP, or MYST4-CBP) fusion was first described in a 4-year-old girl with AML M5a without signs of erythrophagocytosis and several chromosome abnormalities. It was also described in an 84-year-old male without erythrophagocytosis and with this sole cytogenetic aberration. This suggested that the recurrent fusion gene could contribute directly to the development of the AML. This fusion gene was also described with a variant breakpoint in a 52-year-old japanese woman with a therapy-related myelodysplastic syndrome (t-MDS) and this sole translocation. A novel fusion variant was also described in an AML-M4 female patient with the t(10;16)(q22;p13) and a t(11;17)(q23;q21).

t(10;17)(q22;q21-q24). It has been observed that 5% of chromosomally abnormal uterine leiomyomata had rearrangements of 10q22, most of them with balanced translocations with a variety of partners in chromosomes 4, 6, or 12 in leiomyomata and chromosomes 7, 11, 17, or 18 in leiomyosarcomas. Previously the t(10;17) had been reported as the sole cytogenetic abnormality in one leiomyosarcoma and as part of a complex karyotype in another leiomyosarcoma.

FISH analysis of four uterine leiomyomata has revealed a breakpoint in the third intron of MYST4 after the H15 domain and before the PHD zinc finger domain. This disruption of MYST4 seems to be more 5' to the breakpoints reported in hematopoietic malignancies. In addition, in three of the four uterine leiomyomata, the 10q22 rearrangement also involves a locus on 17q with probably the same breakpoint. This could suggest a cytogenetically distinct subgroup of uterine leiomyomata that could be also defined by a common phenotype.

Implicated in

t(10;16)(q22;p13)

Note: The t(10;16)(q22;p13) fusing MYST4 and CREBBP to generate a chimeric protein MYST4-CREBBP (previously known as MORF-CBP, MORF-CREBBP, or MYST4-CBP) is a very rare cytogenetic abnormality only described in 4 cases to date with AML M4/M5a and therapy-related MDS without signs of erythrophagocytosis; most of them with bad prognosis.

This translocation is related to t(8;16)(p11;p13) that fuses MYST3 to CREBBP (previously also known as MOZ-CREBBP or MOZ-CBP) also described in cases with AML/M4-M5 and therapy-related AML with a poor response to chemotherapy and frequently displaying erythrophagocytosis.

Disease

Described in two cases with AML M5, one case with AML M4 and one case with therapy-related MDS, all of them without signs of erythrophagocytosis (showed in the t(8;16), MYST3-CREBBP fusion).

Prognosis

Poor.

Cytogenetics

t(10;16)(q22;p13), rarely as sole anomaly.

Hybrid/Mutated Gene

5' MYST4 - CREBBP 3'

Abnormal Protein

MYST4-CREBBP The putative MYST4-CREBBP fusion protein retains the zinc fingers, two nuclear localization signals, the HAT domain, and a portion of the acidic domain from MYST4, and most of the CREBBP protein, including its HAT domain.

Rearrangements of 10q22 in uterine leiomyomata

Note: Some of the chromosomally abnormal uterine leiomyomata had rearrangements of 10q22, most of them with balanced translocations with a variety of partners in chromosomes 4, 6, or 12 in leiomyomata and chromosomes 7, 11, 17, or 18 in leiomyosarcomas. FISH analysis of some uterine leiomyomata has revealed a disruption of MYST4 between the H15 domain and the PHD zinc finger domain. In three cases the partner gene was a locus on 17q with probably the same breakpoint. This could delimit a distinct subgroup of uterine leiomyomata.

Prognosis

Unknown.

Cytogenetics

Rearrangements of 10q22, most of them with balanced translocations with chromosomes 4, 6, or 12 in leiomyomata and chromosomes 7, 11, 17, or 18 in leiomyosarcomas.

Hybrid/Mutated Gene

Several cases has shown disruption of MYST4, some of them with an unknown partner in 17q21-q24.

Abnormal Protein

Unknown.

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