

Gene Section

Mini Review

SEPT2 (septin 2)

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Identity

Hugo: SEPT2

Other names: KIAA0158; hNedd5; Pnut13

Location: 2q37.3

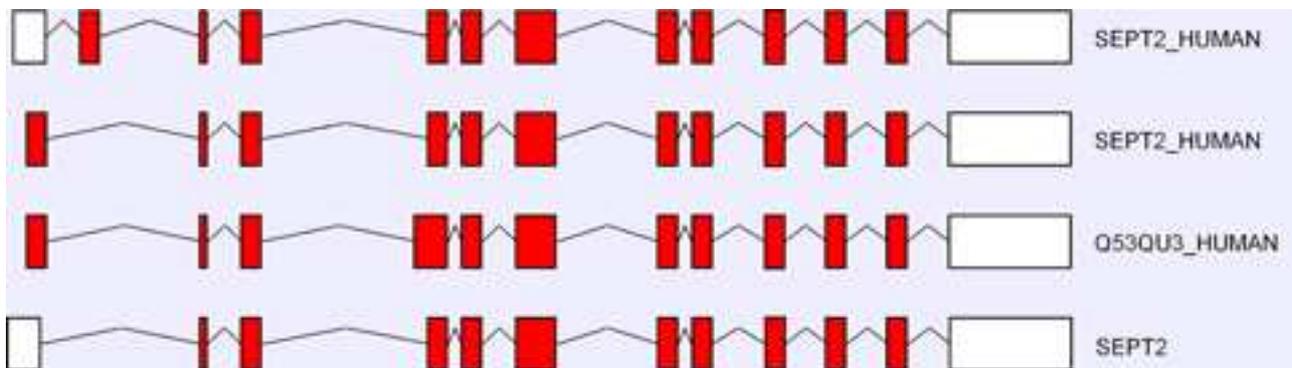
DNA/RNA

Description

The SEPT2 gene has 14 exons.

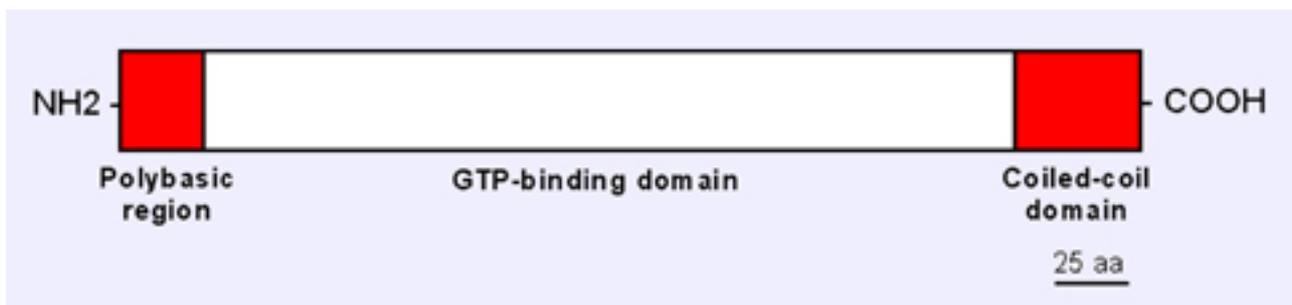
Transcription

SEPT2 has four types of transcripts with 3.6 kb, 3.5 kb, 3.4 kb and 3.3 kb encoding the same protein, as a result of alternative splicing.



Genomic structure of published SEPT2 alternatively spliced transcripts. Boxes indicate exons with coding regions in red. Exons are tentatively positioned in relative genomic order with overlapping exons indicating identical sequences.

Protein



The SEPT2 protein showing the localization of the three function-defining domains: a P loop-based GTP-binding domain flanked by a polybasic domain and the coiled-coil-region.

Description

SEPT2 belongs to an evolutionarily conserved family of genes that encode a P loop-based GTP-binding domain flanked by a polybasic domain and (usually) a coiled-coil region, and assemble into homo- and hetero-oligomers and filaments with key roles in cell division cytoskeletal dynamics and secretion. The SEPT2 gene codes for a protein with 361 amino acids and a molecular weight of 41.5 kDa.

Expression

SEPT2 was identified as a gene expressed in early embryonic mouse brain and down-regulated during development. It is ubiquitously expressed in cell lines and tissues with the highest protein levels found in brain tissue.

Localisation

The SEPT2 protein, like other septin family members, is thought to be cytoplasmic. SEPT2 co-localises with actin filaments in interphase cells, and in dividing cells concentrates at the cleavage furrow.

Function

SEPT2 is a multifunctional protein that was shown to be required for cytokinesis and to bind actin and associate with focal adhesions. Recent data support the idea that SEPT2 can have a role in chromosome congression and segregation. Additional functions have also been suggested; for instance, in rat brain lysates SEPT2 is part of a multi-septin complex that interacts with the exocyst complex, which plays a role in secretion and neurite outgrowth. SEPT2 has also been localised to senile plaques of brains in patients with Alzheimer's disease suggesting a role in neurodegeneration.

Homology

The SEPT2 protein belongs to an evolutionarily family of proteins with at least 14 members and shares a very high homology with septin 1, septin 4 and septin 5.

Implicated in

Acute myeloid leukemia

Disease

Therapy-related AML-M2 and AML-M4.

Prognosis

To date, the prognosis of acute leukaemia patients with the MLL-SEPT2 fusion is not known.

Cytogenetics

t(2;11)(q37;q23)

Hybrid/Mutated Gene

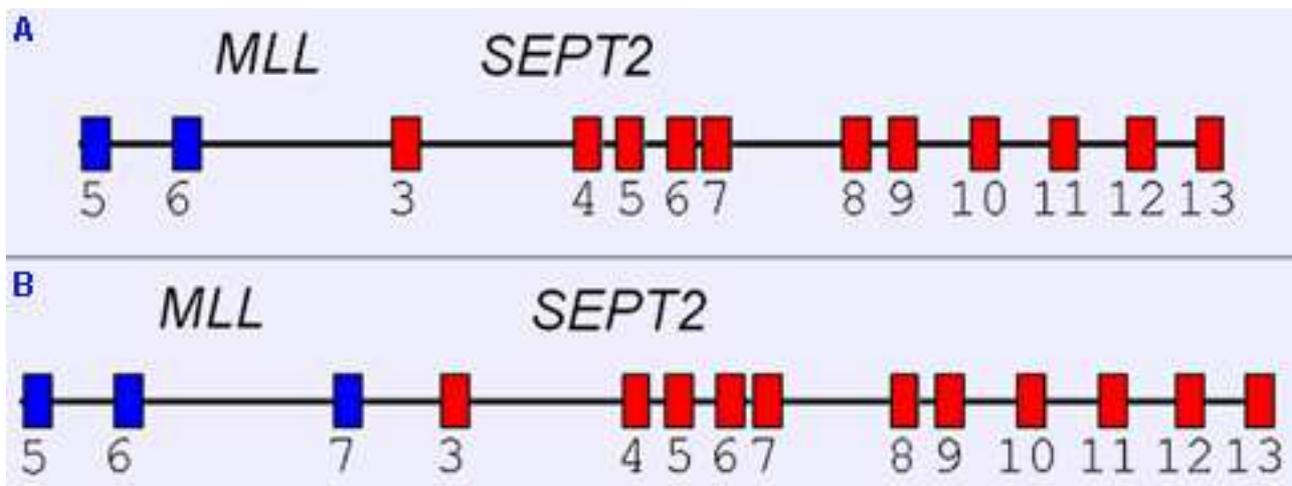
MLL-SEPT2. MLL exon 6 or 7 fused with SEPT2 exon 3.

Abnormal Protein

The N-terminal region of the MLL protein, including the AT hook, SNL-1, SNL-2 and DNA methyltransferase domains, is fused to almost the entire open-reading frame of SEPT2, containing all the three septin function-defining domains, except for the first three aminoacids. So far, no studies regarding the MLL-SEPT2 localization and function in the leukemic cell were performed.

Oncogenesis

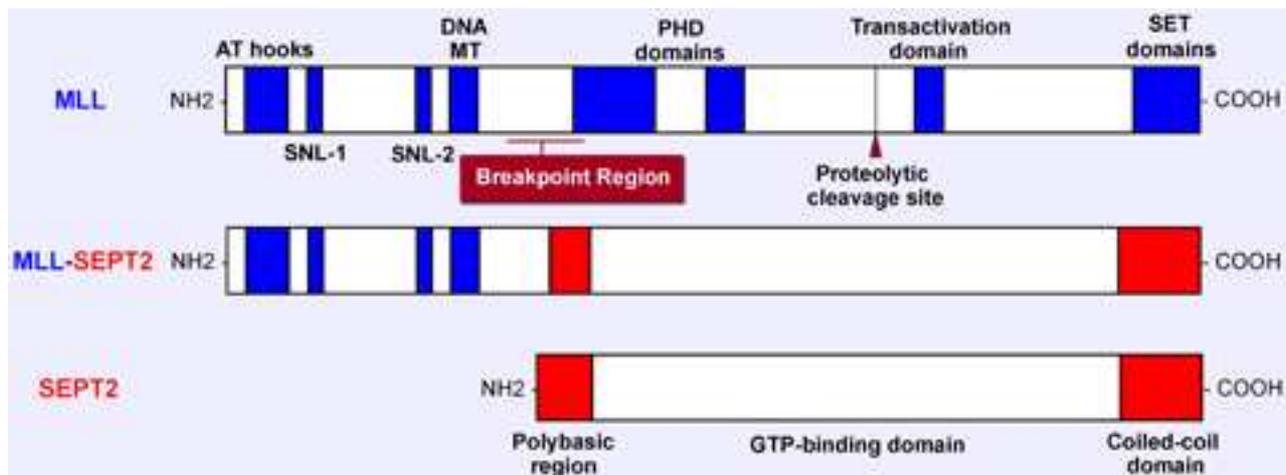
Although the presently available data suggest that the involvement of septins in MLL-related leukemia is only related to their capacity to oligomerize, there is some evidence that altered expression of SEPT2 may underlie the development of aneuploidy.



Schematic representation of the known MLL-SEPT6 genomic breakpoints as a result of the t(2;11)(q37;q23) translocation. To date, two different fusions between MLL and SEPT2 have been reported:

A: MLL intron 6 fused with SEPT2 intron 2, and

B: MLL intron 7 fused with SEPT2 intron 2.



Structure of the normal MLL and SEPT2 proteins and the resulting MLL-SEPT2 fusion protein.

References

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