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Gene Section
Short Communication

SETBP1 (SET binding protein 1)

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Identity

Other names: SEB

HGNC (Hugo): SETBP1

Location: 18q12.3

Local order: From centromere to telomere: SETBP1, SMAD2, SMAD4, BCL2.

DNA/RNA

Description

SETBP1 has two isoforms: transcript variant a spans 387,61 kb on the genomic DNA and has 6 exons; transcript variant b spans 197,24 kb on the genomic DNA and includes 4 exons.

Transcription

9899 bp mRNA (isoform a); 1804 bp mRNA (isoform b).

Protein

Description

Two isoforms: variant a (1596 amino acids); variant b (242 amino acids).

Expression

Expressed in numerous tissues.

Localisation

Predominantly in the nucleus (Minakuchi et al., 2001; Cristóbal et al., 2010).

Function

SETBP1 overexpression promotes leukemogenesis by enhancing full-length SET protein and then impairing the phosphatase activity of the tumor suppressor PP2A in acute myeloid leukaemia. In addition, defects in SETBP1 have been described as the cause of Schinzel-Giedion syndrome.

Homology

The protein contains a region homologous to the dimerization domain of the SKI oncoprotein, six PEST sequences, three AT-hook DNA binding domains, a SET-binding domain and three nuclear localization signals.

Mutations

Somatic

De novo mutations have been decribed in patients with Schinzel-Giedion syndrome: I871T (5 unrelated patients), D868N (4 unrelated patients), D868A (one case), G870D (one case) and G870S (three unrelated patients) (Hoischen et al., 2010; Suphapeetiporn et al., 2011).

Implicated in

Pediatric T-cell acute lymphoblastic leukemia (T-ALL) (Panagopoulos et al., 2007)

Cytogenetics

t(11;18)(p15;q12); only one case decribed so far.

Hybrid/Mutated gene
5' NUP98 - 3' SETBP1

Abnormal protein
The NUP98-SETBP1 fusion protein consists in the exon 12 of NUP98 fused in-frame with exon 5 of SETBP1.

Oncogenesis
SETBP1/NUP98 expression was not detected, suggesting that the NUP98/SETBP1 transcript is pathogenetically important.

Schinzel-Giedion syndrome

Prognosis
Defects in SETBP1 caused by the presence of the novo mutations have been described as the cause of Schinzel-Giedion midface retraction syndrome.

Cytogenetics
Normal karyotype.

Acute myeloid leukemia (AML)

Prognosis
SETBP1 overexpression associates with worse overall survival specially in the subgroup of elderly patients (older than 60 years).

Figure 1.

Cytogenetics
The presence of a t(12;18)(p13;q12) has been describe in one case with AML secondary to myelodysplastic syndrome (figure 1) (Cristóbal et al., 2010), and in one case with AML secondary to primary myelofibrosis (Albano et al., 2012).

Oncogenesis
SETBP1 overexpression promotes leukemogenesis by enhancing full-length SET protein and then impairing the phosphatase activity of the tumor suppressor PP2A through the formation of a SETBP1-SET-PP2A complex.

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