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Gene Section
Mini Review

SATB1 (SATB homeobox 1)

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Identity

HGNC (Hugo): SATB1

Location: 3p24.3

DNA/RNA

Description

The gene encompasses 93 kb of genomic DNA in mouse and 91 kb in humans both of which comprise 11 exons, 10 of which are coding.

Transcription

GenBank references two mRNA transcript variants in humans: #1 is 5423 bp in length and #2 is 3908 bp. They have identical 3' UTRs whereas variant #1 has a longer 5' UTR. GenBank references one mRNA transcript in mouse: 2922 bp in length.

Protein

Description

SATB1 is a 763 amino acid protein (~86 kDa molecular weight, migrates as 103 kDa on SDS gels) containing six described domains: nuclear localization signal (NLS), PDZ, BUR-binding domain, two Cut repeats (CUT1 and CUT2), and homeodomain (HD). The PDZ domain is a protein-protein interaction module found mostly in signaling proteins. The BUR (Base Unpairing Region) domain is the module responsible for specific recognition of the BURs as opposed to any AT-rich sequence motif. The CUT domain is a DNA-binding motif. The BUR-binding domain includes CUT1 and part of the CUT2 domain. Homeodomains are DNA-binding motifs typically found in transcription factors. Together with the BUR domain and the HD domain, SATB1 confers specific binding with high affinity to the core unwinding elements of BURs. SATB1 is highly conserved between vertebrates.

Expression

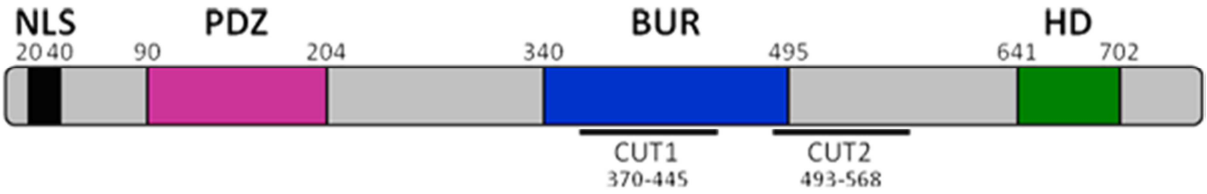
SATB1 mRNA is expressed abundantly in thymocytes. It is also detected in multiple other progenitor cells and brain neurons.

Localisation

Nuclear.

Function

SATB1 was identified by virtue of its high affinity and specificity to a DNA probe containing a nucleation site for base-unpairing, a phenomena whereby these sites become continuously unpaired under negative helical strain. Evidence suggests these base unpairing regions (BURs) mark the genome as essential components of chromosomes for tissue-specific gene expression and chromatin accessibility. SATB1 localization is nuclear exhibiting a cage- or honeycomb-like network distribution in thymocytes that is partially resistant to high-salt extraction and is excluded from the heterochromatin compartment. SATB1 tethers its target genes onto the SATB1 network via BURs which reside within the gene loci, and assembles them with chromatin remodeling and histone modification enzymes which SATB1 recruits. In this manner, SATB1 establishes a region-specific epigenetic status and proper nucleosomal positioning at the SATB1 target gene loci.



SATB1 is essential for T-cell activation by controlling chromatin looping events, thus bringing remote cytokine genes together for simultaneous induction of these genes. SATB1 has been reported to interact with: CtBP1, SUMO-1, PIAS, Ubc9, PML, HDAC1, p300, RPB11, SNF2H (ISWI), Mi-2, MTA-2, and ACF1.

Homology

SATB1 has 59.5% identity to SATB2 (mouse protein sequence; 46.6% for the human protein sequence).

Mutations

Note
None identified.

Implicated in

Breast cancer

Prognosis
In breast cancer SATB1 protein expression levels have high prognostic significance independent of lymph node status.

Oncogenesis
In aggressive human breast cancer cell lines and in tissue samples from patients with aggressive breast tumors SATB1 protein is highly expressed. Ectopic expression of SATB1 in non-aggressive breast cancer cells induces metastasis, whereas depletion of SATB1 in highly-aggressive breast cancer cells reverses their metastatic capabilities and other tumorigenic characteristics.

Acute myeloid leukemia (AML), and lymphoma

Oncogenesis
SATB1 positively regulates the PU.1 gene by binding to its distal enhancer. PU.1 is a transcription factor important for B-cell and myeloid development. A single mutation in the distal enhancer dramatically reduces binding by SATB1. SATB1 was found to be an important factor of Xist (X-inactivation specific transcript) silencing in thymic lymphoma cells, potentially by stabilizing Xist transcripts.

Breakpoints

Note
None known.

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