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Gene Section
Mini Review

MYBBP1A (MYB binding protein (P160) 1a)

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Identity

Other names: FLJ37886; P160; PAP2

HGNC (Hugo): MYBBP1A

Location: 17p13.2

DNA/RNA

Note

Total gene length 16491 bp, mRNA length 4122 bp, telomeric to SPNS2 and centromeric to GGT6. Two variants described. MYBBP1A gene is composed by 26 exones and 28 introns.

Description

The human MYBBP1A gene is located on chromosome 17p13.3 (Keough et al., 1999).

Transcription

The complete MYBBP1A cDNA is 4518 bp, including 25 bp of 5' UTR and 506 bp of 3' UTR up to the polyA tail.

Protein

Description

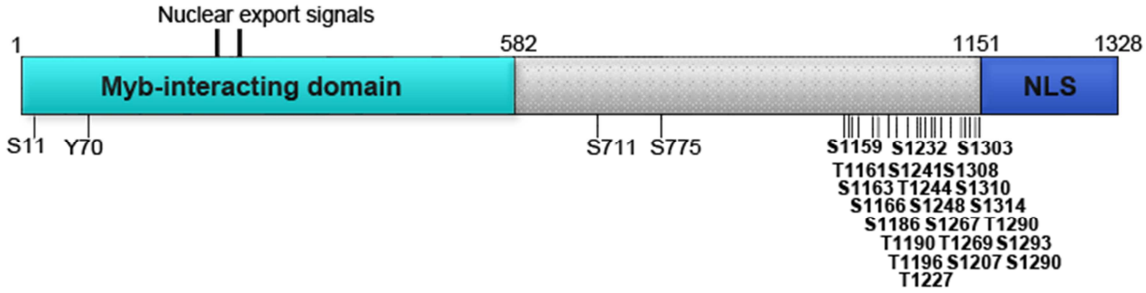
Human MYBBP1A is a 1328 aa long protein. Murine MYBBP1A was originally identified as a protein interacting with the leucine zipper of c-Myb (Favier et al., 1994). Subsequently, in 1998, the human gene homologue of MYBBP1A was cloned and its chromosomal location mapped to 17p13.3 (Keough et al., 1999).

Expression

MYBBP1A is ubiquitously expressed (Tavner et al., 1998).

Localisation

MYBBP1A is a nuclear protein, predominantly localized in the nucleolus (Keough et al., 2003). MYBBP1A has been confirmed as a resident protein of the nucleolus by three large-scale proteomic studies that have established a protein inventory of this sub-nuclear compartment



Schematic representation of Mybbp1A protein. aa 1-582 is the domain reported to interact in vitro with Myb. NLS: Nuclear and nucleolar localisation signal. The indicated S, T and Y are phosphorylated residues identified in several phospho-proteomic studies.

(Andersen et al., 2002; Scherl et al., 2002; Andersen et al., 2005). The nuclear/nucleolar localization signals are present in the C-terminal tail of MYBBP1A.

Function

MYBBP1A functions have not yet been completely clarified. It was originally identified as a protein able to interact with the negative regulatory domain (NRD) of c-Myb; however, it was later shown to lack any significant effect in a Myb-dependent transcription reporter assay (Favier et al., 1994). MYBBP1A has been found to interact with and regulate several transcription factors: it binds and represses both Prep1-Pbx1, involved in development and organogenesis, and also PGC-1a, a key regulator of metabolic processes such as mitochondrial biogenesis and respiration and gluconeogenesis in liver (Fan et al., 2004; Diaz et al., 2007). MYBBP1A acts as a co-repressor for RelA/p65, a member of the NFkB family, by competing with the co-activator p300 histone acetyltrasferase for interaction with the transcription activation domain (TAD) of RelA/p65. It is also a co-repressor on the Period2 promoter, repressing the expression of Per2, an essential gene in the regulation of the circadian clock (Owen et al., 2007; Hara et al., 2009). Conversely, MYBBP1A is a positive regulator of the aromatic hydrocarbon receptor (AhR) which mediates transcriptional responses to certain hydrophobic ligands, such as dioxin, by enhancing the ability of AhR to activate transcription (Jones et al., 2002).

MYBBP1A has also been reported to be a component of macromolecular complexes such as the B-WICH complex, a 3 MDa assembly made of proteins and RNAs, formed during active transcription (Cavellan et al., 2006) or part of large interactomes such as the SMN interactome (Fuller et al., 2010).

MYBBP1A can be post-translationally processed in some type of cells to generate an amino-terminal fragments of 67 kDa (p67). Ribosomal stress induced by Actinomycin D (an inhibitor of ribosome biogenesis) treatment causes MYBBP1A processing and translocation from the nucleolus to the nucloplasm (Diaz et al., 2007; Yamauchi et al., 2008), indicating a possible MYBBP1A role in ribosome biogenesis.

Several post-translational modifications have been described for MYBBP1A, even if their biological significance is not yet clarified. MYBBP1A is reported to be a heavily phosphorylated protein in cells, according to several large-scale mass spectrometry-based phosphoproteomic studies (Beausoleil et al., 2004; Beausoleil et al., 2006; Nousiainen et al., 2006; Olsen et al., 2006; Cantin et al., 2008; Daub et al., 2008; Dephoure et al., 2008; Imami et al., 2008). The majority of the phosphosites mapped in MYBBP1A in these studies (18 out of a total of 21) reside within the ~200 amino-acid long C-terminal portion of the protein, which has been shown to be relevant for its nuclear and nucleolar localization (Keough et al., 2003). Notably, MYBBP1A was also found to be also a component of the proteome as well as the phospho-proteome of the human mitotic spindle. MYBBP1A contains several consensus motifs for several kinases, but until now, only Ser1303 has been proven in vitro and in HeLa cells to be indeed phosphorylated by Aurora B kinase (Perrera et al., 2010). In this work, it has been shown that MYBBP1A depletion by RNAi causes a delay in progression through mitosis and defects in mitotic spindle assembly and stability, indicating that, like other nucleolar proteins, MYBBP1A may have a role in insuring correct mitotic progression (Perrera et al., 2010).

MYBBP1A has been reported to be also sumoylated upon MG132 treatment (Matafora et al., 2009).

Homology

Orthologous genes for MYBBP1A sharing a high degree of similarity are present in rat and mice. Protein homologues have also been recognized in dog, bovine, and chicken and a MYBBP1A-like protein spanning 1269 residues and showing a 60% similarity to the human protein has been identified in zebrafish, suggesting that MYBBP1A is significantly conserved across vertebrate species (Amsterdam et al., 2004). MYBBP1A shares some homology to a yeast protein called POL5, reported to be an essential DNA polymerase in Saccharomyces cerevisiae (Yang et al., 2003).

Implicated in

Various cancers

Disease

MYBBP1A maps at 17p13.3, a region frequently lost in many solid and haematological tumors, such as breast and ovarian cancer, medulloblastoma, astrocytoma, leukemias, etc. This indicates that this chromosomal band contains one or more tumor suppressor genes. However, MYBBP1A is unlikely a candidate for being a tumor suppressor gene, as it lies centromeric to the regions of LOH described (Keough et al., 1999).

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