PRKAB1 (protein kinase, AMP-activated, beta 1 non-catalytic subunit)

Monserrat Sanchez-Cespedes

Molecular Pathology Program, Spanish National Cancer Center (CNIO), Melchor Fernandez Almagro, 3, 28029 Madrid, Spain

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Identity

Hugo: PRKAB1
Other names: AMPK; AMPKb; AMPK beta; AMPKbeta1; HAMPKb; MGC17785; NM_006253
Location: 12q24.1
Local order: Centromere-H11-BC040553-PRKAB1-CIT-RAB35-telomere.

DNA/RNA

Description

The PRKAB1 gene, with a total genomic size of 13639 bp, is composed of 7 coding exons of varying lengths.

Transcription

The human PRKAB1 transcript has approximately 2500-bp and contains an open reading frame of 813 bases, resulting in a predicted protein of 270 amino acid residues. PRKAB mRNA is detected in most tissues.

Protein

Description

PRKAB1 has a molecular mass of 30382 Da; This protein constitutes a regulatory subunit of the AMP-activated protein kinase (AMPK).
AMPK is an heterotrimer of an alpha catalytic, a beta and a gamma non-catalytic regulatory subunits, each encoded by two or three distinct genes (AMPKalpha1 – AMPKalpha2; AMPKbeta1 - AMPKbeta2; AMPKgamma1 - AMPKgamma2 - AMPKgamma3) which have varying tissue and subcellular expression. Post-translational modifications of PRKAB1 include myristoylation and phosphorylation in vivo at Ser24/25, Ser108 and Ser182. Phosphorylation at Ser108 is required for the activation of the AMPK enzyme, whereas phosphorylation at Ser24/25 and Ser182 affects the localization of the complex.

Expression

AMPKbeta1 protein expression is highest in the liver, and testis and low in kidney and skeletal muscle. In contrast, expression of PRKAB2, encoded by a different gene, is higher in skeletal muscle. This indicates a tissue specific pattern of expression of these two regulatory beta subunits.

Localisation

AMPKbeta1 localises in the cytoplasm. However nuclear translocation is possible because mutations of Ser24/25 and Ser182 to alanine lead to the redistribution of PRKAB1 to the nucleus.

Function

AMPKbeta1, may act as a positive regulator of AMPK activity and it may serve as an adaptor molecule for the catalytic subunit. It has also been reported that AMPKbeta1 contains a glycogen-binding domain (GBD) that may target the heterotrimer to glycogen storage sites.
The heterotrimeric protein AMPK senses low intracellular energy levels upon increased in the AMP/ATP ratio. Binding of AMP results in allostERIC activation, inducing phosphorylation on Thr-172 of the AMPKa regulatory subunit (PRKA) by LKB1 in complex with STE20-related adapter-alpha (STRAD alpha). AMPK activation leads to the modulation of the activity of multiple downstream targets to normalize ATP levels. Among these substrates is the tuberin protein, the product of the tuberous sclerosis complex 2 gene (TSC2) that upon activation by AMPK represses the activity of the mammalian target of rapamycin, mTOR. It has been reported that PRKAB1 and PRKAB2 contain a glycogen binding domain that targets AMPK to glycogen. Moreover, it has been shown that expression of PRKAB1 and PRKAB2 genes, in human cells, may be mediated by p53.

Homology

There is a AMPKbeta1 isoform, designated AMPKbeta2, encoded by the PRKAB2 gene. The N-terminal region of beta2 differs significantly from that of AMPKbeta1 isoform, suggesting that this region could play a role in isoform-specific AMPK activity. The AMPKbeta subunit is the mammalian homolog of the S. cerevisiae Sip1p/Sip2p/Gal83p family of proteins that interact with the AMPKa homolog, Snf1p, and are involved in glucose regulation of gene expression.

Mutations

Note: No germ-line or somatic mutations have been reported in the PRKAB1 gene.

To be noted

Note: Although PRKAB1 itself does not seem to be directly implicated in human disease, there is an indirect relationship between AMPKbeta and heart disease and cancer due to the implication of other subunits of the AMPK complex or to the implication of other related kinases:
- AMPK in heart disease:
  Mutations at the PRAAG2 (encoding the gamma2 subunit of AMP-activated protein kinase) causes glycogen overload, Wolff-Parkinson-White syndrome, arrhythmias, and heart failure.
- AMPK in cancer:
  LKB1 is a serine/threonin kinase that phosphorylates and activates AMPK. Germ-line mutations at LKB1 lead to the cancer-prone syndrome Peutz-Jeghers syndrome whereas somatic mutations are implicated in the development of non-small cell lung cancer.

References


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