

Gene Section

Mini Review

PPP1R13L (protein phosphatase 1, regulatory (inhibitor) subunit 13 like)

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Identity

Hugo: PPP1R13L

Other names: RAI (relA associated inhibitor); IASPP (Inhibitor of ASPP protein)

Location: 19q13.32

DNA/RNA

Description

26,674 bp 13 exons.

Transcription

3,076 bps.

Protein

Description

828 amino acids.

Function

PPP1R13L was originally named RAI, an acronym for RelA associated inhibitor. It was originally identified by yeast two-hybrid screening using RelA as bait. PPP1R13L was shown to associate specifically with relA and inhibit relA mediated NF-kappaB activated transcription when NF-kappaB specific transcription was activated by TNF. Yang et al. found no interaction with p53. The mRNA expression was examined in several tissues and was found to be high in heart, placenta, prostate tissues and detectable in lung, kidney, pancreas, spleen thymus, ovary, small intestine and colon. Bergamaschi et al found that PPP1R13L interacts with p53. Antisense RNA or RNAi mediated down regulation of PPP1R13L expression and induced apoptosis. Increased expression of PPP1R13L lead to

increased resistance towards cisplatin and UV-induced apoptosis. This indicates that RAI inhibits apoptosis.

Several studies provide evidence that PPP1R13L expression is increased in tumor tissue. In a study of colorectal adenomas and colorectal cancers, PPP1R13L expression was found to be substantially higher in lesions than in the normal tissue from the same patient. PPP1R13L expression has also been found to be increased in breast carcinomas and in blood cells in patients with acute leukemia.

In a prospective study of lung cancer among 265 lung cancer cases and 272 controls nested within the population based 'Diet, Cancer and Health study', PPP1R13L expression in mononuclear blood cells (isolated by buffy coat) was not associated with risk of lung cancer. mRNA levels were found to be 41% higher in women than in men.

Mutations

Note: Genetic Epidemiology:

The most frequently studied polymorphism in PPP1R13L is PPP1R13L IVS1 A4364G (rs1970764). Carriers of the variant allele have been shown to be at decreased risk of basal cell carcinoma among younger persons (<50 years), breast cancer (<55 years) and lung cancer (<56 years).

The polymorphism is part of a haplotype, which has a stronger association with risk of cancer than the polymorphism itself. Homozygous carriers of the haplotype ERCC1 Asn118AsnA, ASE-1 G-21AG, PPP1R13L IVS1 A4364GA have been shown to be at increased risk of breast cancer and lung cancer. Thus, women who were homozygous carriers of the haplotype ERCC1 Asn118AsnA, ASE-1 G-21AG, RAI IVS1 A4364GA, had a 9.5-fold higher risk of breast

cancer before 55 years of age than women who were not homozygous carriers of the haplotype. Older women and heterozygous carriers were not at an increased risk of breast cancer. Homozygous carriers of the haplotype were found to be at 4.9-fold increased risk of lung cancer in the age interval 50-55 years. The association was stronger among women than among men, although the difference was not statistically significant. In subsequent study including more cases and a larger comparison group, a statistically significant difference between genders was found. Furthermore, it was found that the haplotype interacts with smoking intensity. Thus, among women, who were carriers of the haplotype, additional smoking at high smoking intensity (>20 cigarettes/day) was associated with increased lung cancer risk. This was not seen among women who were not homozygous carriers of the haplotype or among men. The haplotype was not associated with risk of testis cancer or with risk of colorectal adenomas or colorectal cancer. Furthermore, the haplotype was not associated with risk of basal cell carcinoma among older persons (>60 years).

These results indicate that the haplotype may be associated with risk of cancer primarily among young and middle aged persons and that it may be specific for women.

Implicated in

General increased cancer risk

Note: No human disease has been linked to inactivation of PPP1R13L. However, polymorphisms in PPP1R13L may be associated with increased cancer risk (see above).

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