Atlas of Genetics and Cytogenetics in Oncology and Haematology

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Gene Section
Mini Review

PTTG1IP (pituitary tumor-transforming 1 interacting protein)

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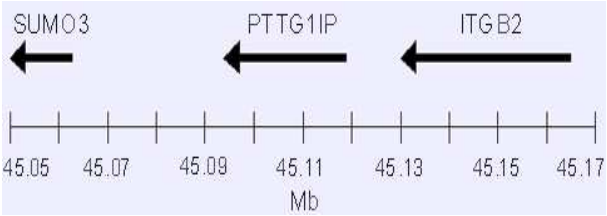
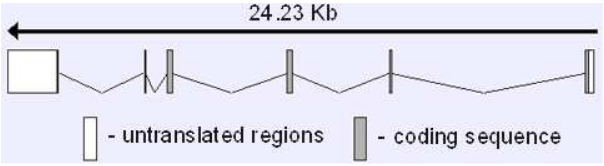
Identity

Hugo: PTTG1IP
Other names: C21orf1; C21orf3; PBF
Location: 21q22.3



DNA/RNA



Description

The PTTG1IP gene consists of 6 exons and spans 24.23 kb of genomic sequence on chromosome 21 (from position 45,093,941 bp to 45,118,169 bp in the reverse strand orientation).

Transcription

The mRNA transcribed from this gene is 2,736 nucleotides long.

Pseudogene

No pseudogene has been described.

Protein

Description

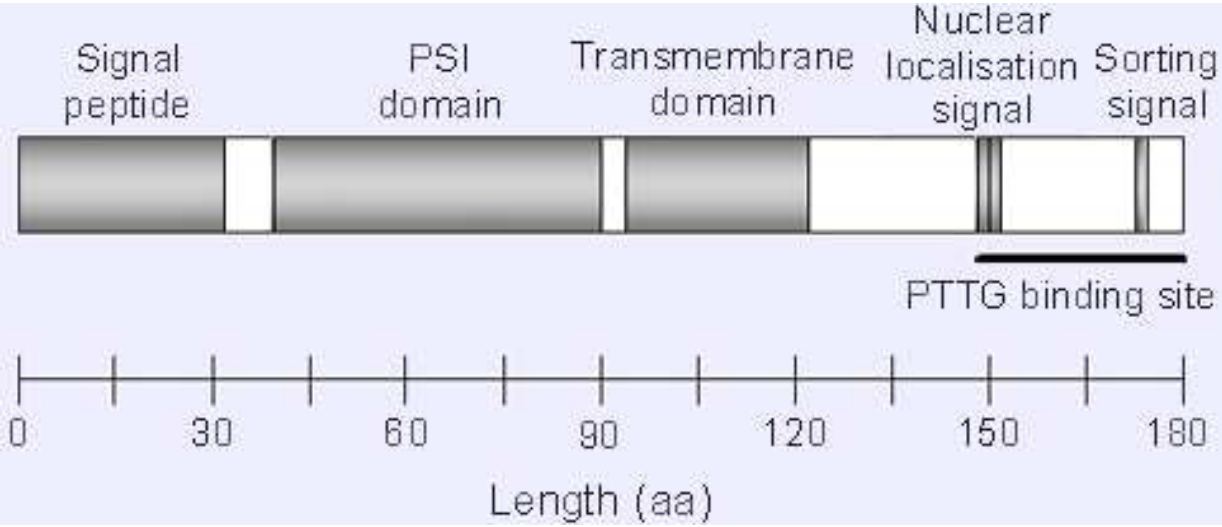
Identified through its interaction with pituitary tumor transforming 1 (PTTG), the PTTG1IP protein is 180 amino acids long with a molecular mass of approximately 25 kDa.
A putative signal peptide exists at the N-terminus (1-32). A domain of unknown function common to plexins, semaphorins and integrins (PSI) is located between residues 39-92. Adjacent to this is a putative transmembrane domain (95-122). A bipartite nuclear localisation signal (NLS) is located between amino acids 149 and 166. The C-terminal 30 amino acids of PTTG1IP contain the PTTG binding domain and a putative tyrosine-based sorting signal.
Potential post-translational modifications include putative phosphorlyation sites for cAMP- and cGMP-dependent kinase, protein kinase C and casein kinase II and five glycosylation sites for N-linked and O-linked oligosaccharides.

Expression

PTTG1IP is widely expressed and has been identified in all tissues examined including spleen, thymus, prostate, testis, ovary, small intestine, colon, leukocytes, spinal cord, thyroid, pituitary, lymph node, trachea, adrenal gland and bone marrow.

Localisation

A tagged PTTG1IP protein was located predominantly in the nucleus with partial expression also in the cytoplasm. Mutation of the NLS shifted PTTG1IP expression to a perinuclear and cytoplasm location. Other reports suggest that PTTG1IP is located predominantly in the cytoplasm.



Function

PTTG expression is predominantly nuclear in the presence of PTTG1IP. However, in the absence of PTTG1IP or with the NLS mutant of PTTG1IP, PTTG is mainly cytoplasmic. Hence, PTTG1IP is thought to facilitate the translocation of PTTG into the nucleus.

Itself upregulated by PTTG, PTTG1IP is required for the ability of PTTG to transactivate basic fibroblast growth factor (FGF2).

PTTG1IP has a described role in repressing iodide uptake into thyroid cells via transcriptional regulation of the sodium iodide symporter.

In MC3T3-El cells, PTTG1IP is regulated by the transcription factor Runx2, implying a role in osteoblast differentiation.

Mutations

Note: PTTG1IP has been sequenced in a series of thyroid tumours, but no mutations were evident. No mutations have been reported to date in any other studies.

Implicated in

Thyroid tumours

Disease

Overexpression is observed in thyroid tumours compared to normal thyroid tissue.

Prognosis

PTTG1IP overexpression was significantly associated with early thyroid tumour recurrence.

PTTG1IP can repress the expression of the sodium iodide transporter (NIS) and inhibit iodide uptake in in vitro models of the thyroid. NIS mRNA expression was inhibited by PTTG1IP via the NIS upstream enhancer (NUE). A poorer prognosis in thyroid tumours with increased PTTG1IP expression might be inferred, therefore, as a significant reduction of iodide uptake would reduce the efficacy of ablative radioiodine therapy.

Oncogenesis

PTTG1IP transforms cells in vitro and is tumourigenic in vivo.

Pituitary tumours

Disease

PTTG1IP is overexpressed in pituitary tumours compared with normal pituitary tissue.

References

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