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Gene Section
Mini Review

TAC1 (tachykinin, precursor 1)

Philip K Lim, Shyam A Patel, Pranela Rameshwar

University of Medicine and Dentistry of New Jersey - New Jersey Medical School,Newark, New Jersey, USA (PKL, SAP, PR)

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Identity

Other names: NK2; NKA; NKNA; NPK; PPT; TAC2

HGNC (Hugo): TAC1

Location: 7q21.3

DNA/RNA

Description

The TAC1 gene maps (Homo sapiens) to NC_000007.12 in the region between 97199311 and 97207720 on the plus strand and spans 8410 bp.

Transcription

4 transcript variants:
alpha (1134 bp); open reading frame from bp 247-582
-lacks exon 6
-encodes substance P on exon 3
beta (1188 bp); open reading frame from bp 247-636
-encodes the full-length version of Tac1
-encodes substance P, neurokinin A, neuopeptide K
delta (1089 bp); open reading frame from bp 247-537
-lacks exons 4 and 6
-encodes substance P on exon 3
gamma (1143 bp); open reading frame from bp 247-591
-lacks exon 4
-encodes substance P, neurokinin A

Protein

Note
The TAC1 gene encodes multiple transcripts through post-translational modifications. Each encodes peptides belonging to the tachykinin family of peptides. The major peptides produced from the TAC1 transcripts are substance P and neurokinin A. Others include neuropeptide K, and neuropeptide gamma. The tachykinins exert multiples functions such as neurotransmission, immune modulation and hematopoietic regulation. TAC1 encodes peptides that target nerve receptors, immune cells, stem cells, hematopoietic cells and smooth muscle cells. They function in vasodilatory responses; act as secretagogues and can induce behavioral responses.

Description

4 peptides:
alpha: 111 aa
-comprises substance P
beta: 129 aa
-comprises substance P, neurokinin A, neuropeptide K
delta: 96 aa
-comprises substance P
gamma: 114 aa
-comprises neuropeptide gamma, substance P, neurokinin A.

Expression

Expressed by various immune and neuronal cells.
TAC1 expression in the setting of osteoarthritis can be induced by mechanical stimulation (Howard et al., 2008).
TAC1 expression is also regulated by microRNAs in neurons derived from human mesenchymal stem cells (Greco et al., 2007). This occurs by binding of miRNA-13-a, miRNA206 and miRNA302a to the Tac1 3'UTR.
HIV1 infection resulted in increase production of TAC1 peptide (substance P). The source of substance P has been identified as monocytes-derived macrophages from placenta cord blood and adult peripheral blood. The production of substance P correlates with HIV 1 infection (Douglas et al., 2002).

Localisation

Secreted peptide.

Function

TAC1 peptides function in both pathologic and physiologic processes. These include hematopoiesis, gastrointestinal secretory processes, respiratory patterns, calcium signaling, neuropeptide signaling, pain, synaptic transmission, insemination (Murthy et al., 2008; David et al., 2009); inflammatory response, autism, and pulmonary infection (Marui et al., 2007; Grissell et al., 2007). In normal respiratory development, TAC1 appears to be a crucial gene, exerting plasticity during development (Berner et al., 2007).

TAC1 is involved in hematopoietic regulation. The mRNA is targeted by RNA-binding protein that confers translational control, which could be negatively regulated by cytokines with hematopoietic stimulator properties (Murthy et al., 2008). TAC1 has been implicated in macrophage and monocyte functions (Chernova et al., 2009).

Homology

Homo sapiens TAC1 shares sequence homology with mouse and rat sequences.

Implicated in

Breast cancer

Note

A gene expression signature for breast cancer has been shown to involve TAC1 (Ellsworth et al., 2009).

Prognosis

TAC1 expression occurs in breast cancer and is directly proportional to aggressiveness of the cancer and thus, TAC1 may also be a prognostic factor in breast cancer (Ellsworth et al., 2009; Reddy et al., 2009).

Oncogenesis

TAC1 expression favors breast cancer cell entry into the bone marrow during stage IV disease (Reddy et al., 2009). TAC1 regulates the interaction between CXCL12 and its receptor, CXCR4 in the interaction between breast cancer and mesenchymal stem cells (Corcoran et al., 2008).

The TAC1 gene products, substance P and neurokinin A, and neurokinin receptor antagonists have been shown to have anti-proliferative effects on breast cancer cells (Rameswhar et al., 1996; Singh et al., 2000).

Colon cancer

Note

Substance P, the major peptide encoded by the TAC1 gene, is mitogenic to colon cancer. Its action on the cancer cells appears to be autocrine since NK1 antagonist has been shown to mediate anti-tumor activity (Rosso et al., 2008). On the other hand, Substance P also enhances the expansion of lymphokine-activated killer cells against colon cancer cells (Flageole et al., 1992). These two properties of substance P appear paradoxical. Thus, targeted therapy will need to balance the immune-enhancing effects with the tumor promoting functions of substance.

Prognosis

In Dukes stage A/B cancers, TAC1 methylation levels were significantly higher than in Dukes stage C/D cancers (Mori et al., 2006).

Oncogenesis

TAC1 was found to be silenced via promoter methylation in primary colon cancer and may lead to early stage carcinogenesis by aiding tumor cells to escape immune surveillance and autocrine growth-inhibitory signaling (Mori et al., 2006).

Esophageal cancer

Prognosis

Promoter hypermethylation of TAC1 confers poor prognosis in esophageal cancer (Jin et al., 2007).

Oncogenesis

TAC1 promoter hypermethylation has been suggested to be a putative marker for esophageal carcinoma (Jin et al., 2007).

Gastric adenocarcinoma

Oncogenesis

Promoter hypermethylation of TAC1 has also been found in gastric adenocarcinoma (David et al., 2009).

Multiple sclerosis

Note

The genetic region surrounding TAC1 may be unstable and has been associated with increased susceptibility to multiple sclerosis (Vandenbroeck et al., 2002).

Narcolepsy

Note

TAC1 and other related peptides have been associated with narcolepsy. Stimulation by amphetamines promotes increased TAC1 expression (Lindberg et al., 2007).

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