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Gene Section

Mini Review

WISP2 (Wnt-1-inducible signaling parthway protein-2)

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Identity

Other names: CCN5; rCop-1; CT58; CTGF-L

HGNC (Hugo): WISP2

Location: 20q12-13

Note: WISP-2 is a member of the connective tissue growth factor/cysteine-rich 61/nephroblastoma overexpressed (nov) (CCN) family and is upregulated in the mouse mammary epithelial cell line C57MG transformed by Wnt-1 and in several non-invasive human breast tumor cell lines.

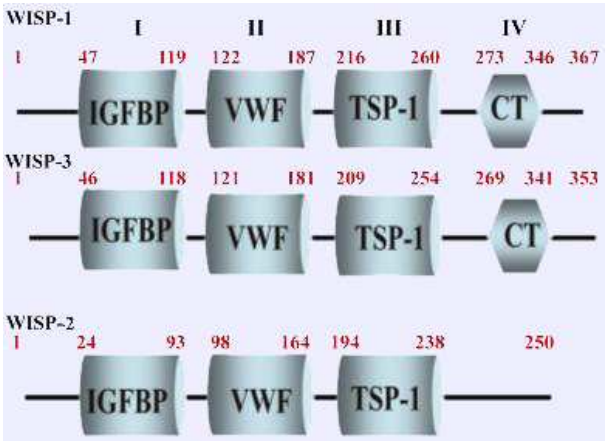
WISP-2 is a serum and PMA (phorbol 12-myristate 13-acetate)-induced early responsive gene. Blocking the expression of this gene by WISP-2 antisense oligos or siRNA drastically reduce serum or PMA-induced cell proliferation in MCF-7 cells. Therefore, these studies suggest that WISP-2 signaling may be essential for mitogen-induced breast tumor cell proliferation.

WISP-2 expression is enhanced by important modulators of human breast cancer cell proliferation such as estrogen, progesterone and epidermal growth factor (EGF) in MCF-7 cells. These effects, inhibited by appropriate antagonists, indicate that steroids and growth factor-induced upregulation of WISP-2 may be mediated through receptors.

The expression profile of WISP-2 gene in breast tumor biopsy tissue specimens are similar with that of in vitro studies and suggest that WISP-2 mRNA and protein levels are significantly higher in tumor samples as compared to the normal breast samples, and this expression is significantly correlated with the expression of estrogen receptor protein. However, within the tumor specimens, expression was predominant in the non-invasive carcinoma lesions as well as benign hyperplastic areas adjacent to the invasive tumors. Together, these findings suggest that bi-phasic regulation of WISP-2 signaling may be critical for initial events of growth, survivability and invasion of breast tumor cells.

WISP-2 also acts as a negative regulator in some cells including vascular smooth muscle cells.

DNA/RNA



Modular structure of individual genes of WISP sub-family of CCN family. Module shown with color boxes are the predicted primary translational.

Note

Until now, three genes have been identified and isolated as members of WISP sub-family. WISP-1/CCN4, WISP-2/CCN5 and WISP-3/CCN6 genes were localized in human chromosomes 8q24.1-q24.3, 20q12-q13 and 6q22-23, respectively and exhibit tissue

specific patterns of expression. Nucleotide and protein sequence alignment studies have demonstrated a 30-40% sequence homology within WISP genes and their modular architecture is similar except in their C-terminal domains, which is absent in the WISP-2 gene.

Protein

Description

The translation products of most of the CCN family members are secreted proteins of 35-40 kDa and have been shown to contain four distinct structural modules: 1) an IGF-binding protein type (IGFBP) domain, 2) a Von Willebrand type C (VWC) domain; 3) a Thrombospondin-1 (TSP-1) domain and 4) a C-terminal Cysteine-knot (CT) domain (10).
Although the functional roles of these multiple modules are unclear, they raise interesting questions as to the contribution of each individual module to the biological properties of the full-length proteins.

Expression

Epithelial cells and vascular smooth muscle cells.

Localisation

Adrenal gland, breast, colon, pancreas, uterus and ovary.

Function

Positive regulator of epithelial cells and negative regulator of vascular smooth muscle cells.

Mutations

Somatic

Amplified in breast tumor cells.

Implicated in

Disease

Breast cancer.

Disease

Colon cancer.

Disease

Macronodular adrenal hyperplasia.

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