**GPC3 (glypican 3)**

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**Identity**

Other names: Glypican-3 (GPC3); MXR7; OCI-5; GTR2-2

HGNC (Hugo): GPC3

Location: Xq26.1

**DNA/RNA**

**Description**

The gene spans more than 500 kb of DNA consisting of 8 exons.

**Transcription**

2.2 kb mRNA; 1740 bp open reading frame.

**Protein**

**Description**

580 amino acids; 65 kDa protein. GPC3 is a heparan sulfate proteoglycan (HSPG) that is attached to the cell surface via a glycosyl-phosphatidylinositol (GPI) anchor.

**Expression**

GPC3 is highly expressed in embryonal tissues such as the developing intestine and the mesoderm-derived tissues, and its expression is downregulated in most adult tissue.

**Localisation**

Attached to the membrane by a GPI anchor.

**Function**

The biochemical function of GPC3 has yet to be established. HSPG may be involved in the suppression/modulation of growth in the predominantly mesodermal tissues and organs; may play a role in the modulation of IGF-II interactions with its receptor and thereby modulate its function; can have a potential role as a regulator of growth and tumor predisposition. Therefore it is likely that GPC3 is able not only to bind more than one growth factor, but also to functionally affect the signalling of different growth factors. A role for GPC3 in the regulation of insulin-like growth (IGF) factors has been proposed. IGF-II is a growth factor that can act as a survival factor in the early stages of tumorigenesis. The co-expression of GPC3 and IGF-II has been observed in embryonal tumors as well as in mouse foetal tissues; GPC3 expression is able to induce apoptosis in a cell-specific manner, but this effect could be reversed by the addition of IGF peptides; IGFs could be needed to prevent GPC3-induced apoptosis in any cell, allowing cellular responses to other factors to take place and be mediated, enhanced or inhibited by GPC3; GPC3 mutations lead to SGBS (see below), a syndrome that shares significant similarities with the Beckwith-Wiedemann syndrome that is an overgrowth syndrome that is thought to be associated with increased expression of IGF2.

**Homology**

Belongs to the glypican family; six members, glypican-1 to 6, have been identified in mammalians; the protein core of glypicans are 20-50% identical; The glypican family is represented by at least two known members in Drosophila, dally and dally-like.

**Mutations**

**Germinal**

Most known mutations are deletions involving different exons of GPC3; missense, nonsense as well as splicing site mutations.
**Somatic**

The expression of GPC3 is altered in cancer cells. GPC3 is upregulated in hepatocellular carcinoma, in Wilms' tumor and in metastatic colorectal malignancy. With regard to tumors with neuronal phenotype, GPC3 was detected at variable levels in a neurofibrosarcoma and in most neuroblastomas, but was absent from medullloblastomas. These findings suggest that GPC3 expression is differentially regulated in the various cell lineages giving rise to pediatric tumours of the peripheral and central nervous systems. On the other hand, GPC3 is frequently silenced in mesotheliomas, in ovarian cancer cell lines and in breast cancer, often due to hypermethylation of the GPC3 promoter.

**Implicated in**

**Simpson-Golabi-Behmel Syndrome (SGBS)**

**Disease**

X-linked disease characterized by a wide variety of clinical manifestations, including pre- and post-natal overgrowth, tissue dysplasia, in particular of the kidneys, and cardiac anomalies; associated with a greater risk of developing embryonal cancers; caused by loss-of-function mutation in the GPC3 gene; the abnormalities found in SGBS patients suggest that GPC3 might be involved in the regulation of growth and/or apoptosis during development.

**To be noted**

**Note**

The ability of GPC3 to bind various growth factors or morphogens, including IGF-II, fibroblast growth factor 2 as well as the tissue factor pathway inhibitor, is supported by evidence from other members of the glypicans and HSPGs in general. HSPGs of the cell surface are highly interactive macromolecules playing various roles in cell migration, proliferation, differentiation and adhesion, and participating in many developmental and pathological processes. HSPGs consist of two major families: syndecans and glypicans. Syndecans are attached to the cell membrane by a transmembrane domain while glypicans are attached through a GPI anchor. To date six members of the glypican family, glypican-1 to 6, have been identified in mammals; the glypican family is represented by at least two known members in Drosophila, dally and dally-like. Dally is now known to act as a co-receptor that controls signalling by morphogens and growth factors such as decapentaplegic (dpp) and wingless. Although GPC3 cannot as yet be thought of as the strict orthologue of dally, this information strengthens the notion that it may have growth factor binding and regulatory properties.

**References**


Xiang YY, Ladeda V, Filmus J. Glycan-3 expression is silenced in human breast cancer. Oncogene. 2001 Nov 1;20(50):7408-12

This article should be referenced as such: