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Gene Section
Short Communication

GALNT6 (UDP-N-acetyl-alpha-D-galactosamine: polypeptide N-acetylgalactosaminyltransferase 6 (GalNAc-T6))

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Abstract

Review on GALNT6, with data on DNA/RNA, on the protein encoded and where the gene is implicated.

Identity

Other names: GALNAC-T6, GalNAcT6

HGNC (Hugo): GALNT6

Location: 12q13.13

DNA/RNA

Note

GALNT6 is highly expressed in many types of cancer, but expression of GALNT6 is hardly detectable in human normal tissues (Park et al., 2010).

Description

Human GALNT6 gene is located on 12 chromosome at q13.13 location. The GALNT6 gene is composed of 12 exons and ORF (open reading frame) is 1869 bp.

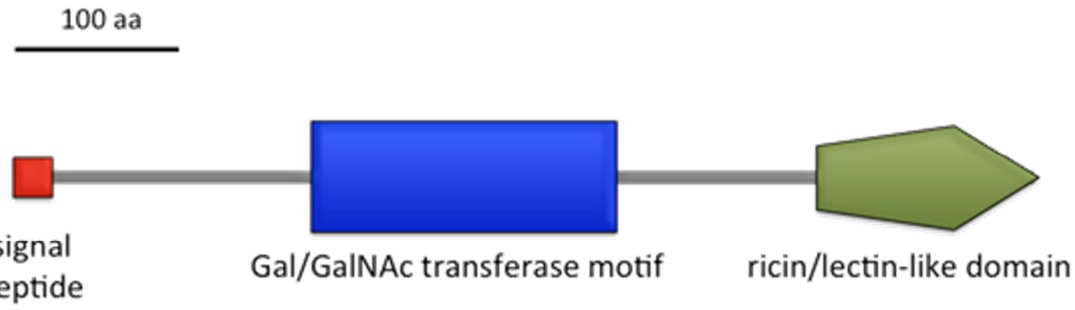
Protein

Note

Human GALNT6 gene encodes 622 amino acids of 71159 Da.

The protein is involved in the first step of O-type glycosylation by transferring UDP-GalNAc to Ser/Thr site of substrate protein. GALNT6 was firstly identified as a glycosyltransferase with high sequence similarity to GALNT3 (Bennett et al., 1999).

GALNT6 has similar kinetic properties with other GALNTs but preferentially glycosylated fibronectin peptide in vitro. Because of expression in WI38 fibroblast cells, GALNT6 was regarded as a candidate for synthesis of the oncofetal fibronectin (Bennett et al., 1999). GALNT6 has two possible N-type glycosylation sites at N476 and N611.



Functional domain of GALNT6. The protein contains signal peptide (1-34 aa), Gal/GalNAc transferase motif (180-370 aa), and ricin/lectin-like domain (496-622 aa).

Description

The mucin-type O-glycosylation is initiated by GALNT family members that transfer N-acetyl-alpha-D-galactosamine (GalNAc) to serine or threonine residues on the target protein (Ten Hagen et al., 2003). This modification occurs in the Golgi complex and is presumably controlled by the expressions and distributions of GALNT proteins (Brooks et al., 2007). Interestingly, structural alterations of these glycan chains are often detected in cancer cells, especially in breast cancer. For instances, the O-glycans were often truncated (core 1-based type) in breast carcinoma cells, whereas they were extended its chain (core 2-based type) in normal breast cells (Burchell et al., 2001). O-type glycosylation is one of common modifications that have multiple functions related to the folding, stability, and targeting of various glycoproteins (Carraway et al., 2007). Accumulating evidences have suggested that the GALNT family members are involved in several cellular functions by catalyzing substrates specific to each member. For instances, glycosylation by GALNT3 prevents proteolytic processing of FGF23 (fibroblast growth factor 23) and that by GALNT14 promotes ligand-stimulated clustering of death receptors (Wagner et al., 2007; Ichikawa et al., 2009).

Expression

GALNT6 is highly expressed in many types of cancer including breast, gastric, kidney, oral, and pancreatic cancer (Berois et al., 2006; Gomes et al., 2009; Kitada et al., 2013; Wandall et al., 2007; Li et al., 2011). However, in human normal tissues, GALNT6 is merely expressed in normal tissues and vital organs including lung, heart, liver, and kidney (Park et al., 2010). A specific expression of GALNT6 was also reported in the nonkeratinized epithelium of ocular cicatricial pemphigoid (OCP) patients (Argüeso et al., 2003).

Localisation

Similarly to other isoforms in the GALNT family, GALNT6 is localized in the Golgi complex as shown by double immunofluorescence staining with anti-GALNT6 mAb and anti-Golgi-58k mAb (Park et al., 2010).

Function

GALNT6 is involved in the first step of O-type glycosylation, and thereby may influence on folding, stability, and subcellular localization of target proteins. GALNT6 was reported to stabilize MUC1 protein throughout O-glycosylation and subsequently the accumulated MUC1 protein promoted breast cancer cell proliferation and induced anti-adhesive effects (Park et al., 2010). By O-glycosylation of fibronectin protein, GALNT6 showed transformational potentials through disruptive acinar morphogenesis and cellular changes similar to EMT (epithelial-to-mesenchymal transition) in normal mammary epithelial cell (Park et al., 2011).

The GALNT6-mediated O-glycosylation of fibronectin was also reported in the TGF-β-induced EMT process in human prostate cells (Freire-de-Lima et al., 2011).

Homology

GALNT6 has 30~63% of amino acid homology with other family members, with the highest homology to GALNT3 (63%). In crystal structure analysis of murine GALNT isoforms, GALNT1 was reported to be more similar to GALNT6 according to the electrostatic surface potential models (Fritz et al., 2004).

Implicated in

Breast cancer

Note

High expression of GALNT6 was frequently observed in human breast cancers (Berois et al., 2006; Freire et al., 2006; Patani et al., 2008; Park et al., 2010). In particular, strong expression of GALNT6 was reported in most of DCIS (ductal carcinoma in situ) indicating that GALNT6 should play important roles in early human breast carcinogenesis (Berois et al., 2006).

On the other hand, a study of metastatic breast cancer showed that GALNT6 expression was frequently detected in bone marrow biopsy samples and therefore suggested that GALNT6 would be a good target for detection of disseminated breast cancer cells (Freire et al., 2006).

Prognosis

Disease free survival was elongated in breast cancer patients who showed negative expression of GALNT6 from bone marrow biopsy (Freire et al., 2006).

Gastric cancer

Note

High expression of GALNT6 was reported in human gastric cancers. A heterogeneous expression and staining pattern of GALNT6 was observed in 79% of gastric carcinomas, and its expression level was associated with the presence of venous invasion (Gomes et al., 2009).

Oral cancer

Note

GALNT6 was expressed in the oral squamous carcinoma cells, but not expressed in normal stromal fibroblasts (Wandall et al., 2007).

Pancreatic cancer

Note

GALNT6 was highly expressed in pancreatic cancer, but not expressed in normal ductal epithelium. A close relationship was noted between GALNT6-positive expression and pathological well/moderate

differentiated type, small tumor size, and absence of vascular invasion (Li et al., 2011).

Prognosis

In contrast to other reports, the outcome of the patients who had GALNT6-positive expression was significantly better than that with GALNT6-negative expression, especially in the early period after surgery (Li et al., 2011).

Renal cell carcinoma

Note

GALNT6 was weakly expressed in 64 out of 254 renal cell carcinomas (Kitada et al., 2013).

Prognosis

GALNT6-positive patients showed poor prognosis with lower disease-specific survival rate (Kitada et al., 2013).

Ocular cicatricial pemphigoid (OCP)

Note

OCP is one of the subsets of mucous membrane pemphigoid, which may be caused by aberrant synthesis of mucin O-glycans and thus by alteration of the physicochemical properties of mucins. GALNT6 was expressed in the apical stratified epithelia, but specific expression of GALNT6 was detected in nonkeratinized epithelium of OCP patients, without expression in keratinized epithelium nor normal subjects (Argüeso et al., 2003).

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