

Gene Section

Review

SULF1 (sulfatase 1)

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Identity

Other names: HSULF-1, SULF-1

HGNC (Hugo): SULF1

Location: 8q13.2

- Homo sapiens sulfatase 1 (SULF1), transcript variant 3, mRNA, 5710 bp

Accession: NM_015170.2 GI: 189571635

- Homo sapiens sulfatase 1 (SULF1), transcript variant 4, mRNA, 5548 bp

Accession: NM_001128204.1 GI: 189571637

DNA/RNA

Note

The sulfation pattern of heparan sulfate chains influences signaling events mediated by heparan sulfate proteoglycans located on cell surface. SULF1 is an endosulfatase able to cleave specific 6-O sulfate groups within the heparan chains.

This action can modulate signaling processes, modulating the effects of heparan sulfate by altering binding sites for signaling molecules.

Description

Size: 5551 bp.

Transcription

4 isoforms:

- Homo sapiens sulfatase 1 (SULF1), transcript variant 1, mRNA, 5716 bp

Accession: NM_001128205.1 GI: 189571640

- Homo sapiens sulfatase 1 (SULF1), transcript variant 2, mRNA, 5554 bp

Accession: NM_001128206.1 GI: 189571642

Protein

Note

Sulfs are sulfatases that edit the sulfation status of heparan sulfate proteoglycans on the outside of cells and regulate a number of critical signaling pathways.

The Sulfs are dysregulated in many cancers.

The Sulfs are synthesized as pre-proproteins.

The signal sequence is removed and the pro-protein is cleaved by a furin-type proteinase.

Sulfs mature proteins are secreted as well as retained on the cell surface.

Description

871 amino acids; 101027 Da.

Expression

Expressed at highest levels in testis, stomach, skeletal muscle, lung, kidney, pancreas, small intestine and colon.

It is also detected in normal ovarian surface epithelial cells.



Adapted from Genecards.

Localisation

Sulf1 mature proteins are secreted as well as retained on the cell surface.

Function

The Sulf1s are endoglucosamine-6-sulfatases. They liberate 6-O-S mainly from trisulfated disaccharide units within the S-domains of heparin/HS chains. The Sulf1s have been shown to modulate the interaction of a number of protein ligands with heparin or heparan sulfate.

Homology

SULF1 shares about 64% identity with SULF2.

Implicated in

Ovarian cancer

Oncogenesis

Sulf1 expression was found to be absent or significantly downregulated in ovarian cancer resulting in highly sulfated heparin sulfate proteoglycans.

It has been observed that this down-regulation results in increased sulfation of heparin sulfate chains and could produce the stabilization of ternary receptor complexes, leading to an increased in GF signaling, as described for heparin-binding epidermal growth factor-like growth factor (HB-EGF), fibroblast growth factor 2 (FGF2) or amphiregulin in ovarian cancer.

This modulation of GF effects can affect major events including proliferation of tumor cells. Epigenetic silencing by methylation is associated with ovarian cancer cells and primary ovarian cancer tissues lacking Sulf1 expression.

Cisplatin-induced apoptosis of the ovarian cancer cell line, OV207, requires Sulf1 activity.

Breast cancer

Oncogenesis

Sulf1 expression was first described to be significantly downregulated in breast cancer. Recent analysis using microarray data demonstrated a significant upregulation of Sulf1 in breast cancer compared to normal counterpart.

It has been observed that this down-regulation results in increased sulfation of heparin sulfate chains and could produce the stabilization of ternary receptor complexes, leading to an increased in growth factors signaling, as described for heparin-binding epidermal growth factor-like growth factor (HB-EGF), fibroblast growth factor 2 (FGF2) or amphiregulin in breast cancer.

This modulation of GF effects can affect major events including proliferation of tumor cells.

A marked reduction of the growth of myeloma or breast cancer cell lines was observed in severe combined immunodeficient mice when injected cell lines were transfected with SULF1 cDNA. It was found

an aberrant hypermethylation of the Sulf1 promoter in breast cancer cell lines and patient samples, leading to a reduction of Sulf1 expression.

Hepatocellular carcinoma

Oncogenesis

Sulf1 expression was also found to be significantly downregulated in hepatocellular carcinoma.

It has also been observed that this down-regulation results in increased sulfation of heparin sulfate chains and could produce the stabilization of ternary receptor complexes, leading to an increased in growth factors signaling.

Forced expression of SULF1 also significantly delayed the growth of hepatocellular carcinoma cell lines xenografts in nude mice.

Sulf1 enhances acetylation of histone H4 by inhibiting HDAC, which subsequently decreased hepatocellular carcinoma cell tumorigenesis in mouse model.

Pancreatic cancer

Oncogenesis

Hsulf-1-mediated desulphation of HSPGs reduces the growth ability of pancreatic cancer cells, but increases the basal invasiveness of these cells and chemoresistance, suggesting an important role of this enzyme in pancreatic cancer progression. Recent analysis using microarray data demonstrated a significant upregulation of Sulf1 in pancreatic adenocarcinoma compared to normal counterpart.

Head and neck squamous cell carcinoma

Oncogenesis

Sulf1 expression was also found to be significantly downregulated in head and neck squamous cell carcinoma cell lines.

It has also been observed that this down-regulation results in increased sulfation of heparin sulfate chains and could produce the stabilization of ternary receptor complexes, leading to an increased in growth factors signaling in head and neck squamous cell carcinoma cell lines.

Hepatocyte growth factor (HGF)-mediated motility and invasion were attenuated in neck squamous cell carcinoma cell lines displaying an overexpression of this sulfatase.

However, recent analysis using microarray data demonstrated a significant upregulation of Sulf1 in head and neck squamous cell carcinoma compared to normal counterpart.

Leukemia

Oncogenesis

Recent analysis using microarray data demonstrated a significant upregulation of Sulf1 in leukemia compared to normal counterpart.

Gastric cancer

Oncogenesis

Promoter hypermethylation is correlated with the HSulf-1 silencing in gastric cancer.

The restoration of the expression of HSulf-1 inhibited cell proliferation, motility, and invasion of the MKN28 cell line in vitro, as well as in a xenograft mouse model.

No noticeable changes in proliferation and motility were observed following restoration of HSulf-1 in another gastric cancer cell line AGS.

HSulf-1 function as a negative regulator of proliferation and invasion in MKN28 gastric cancer cell line by suppressing Wnt/ β -catenin signaling. However, as for others cancers, recent analysis using microarray data demonstrated a significant upregulation of Sulf1 in leukemia compared to normal counterpart.

Colon cancer

Oncogenesis

Recent analysis using microarray data demonstrated a significant upregulation of Sulf1 in colon cancer compared to normal counterpart.

Adrenal cancer

Oncogenesis

Recent analysis using microarray data demonstrated a significant upregulation of Sulf1 in adrenal cancer compared to normal counterpart.

Esophageal cancer

Oncogenesis

Recent analysis using microarray data demonstrated a significant upregulation of Sulf1 in esophageal cancer compared to normal counterpart.

Lung cancer

Prognosis

In a cohort of 127 patients with lung adenocarcinoma, it was described that high expression of Sulf1 is associated with a bad prognosis compared to patients with low Sulf1 expression.

Oncogenesis

Recent analysis using microarray data demonstrated a significant upregulation of Sulf1 in esophageal cancer compared to normal counterpart.

Mesothelioma

Oncogenesis

Recent analysis using microarray data demonstrated a significant upregulation of Sulf1 in mesothelioma compared to normal counterpart.

Furthermore, a review of transcriptome studies identified Sulf1 as a mesothelioma gene that could represent a new biomarker or therapeutic target in mesothelioma.

Renal carcinoma

Oncogenesis

Recent analysis using microarray data demonstrated a significant upregulation of Sulf1 in renal carcinoma compared to normal counterpart.

Sarcoma

Oncogenesis

Recent analysis using microarray data demonstrated a significant upregulation of Sulf1 in sarcoma compared to normal counterpart.

Melanoma

Oncogenesis

Recent analysis using microarray data demonstrated a significant upregulation of Sulf1 in cutaneous melanoma compared to normal skin.

Testicular cancer

Oncogenesis

Recent analysis using microarray data demonstrated a significant upregulation of Sulf1 in testicular cancer compared to normal counterpart.

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