**SDC1 (syndecan 1)**

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### Identity

**Other names:** CD138; SDC; SYND1; Syndecan 1

**HGNC (Hugo):** SDC1

**Location:** 2p24.1

**Local order:** Human syndecan1 gene is localized to 2p23-24, just centromeric to the N-myc gene at 2p24.1.

**Note:** Syndecan 1, a cell surface heparan sulfate proteo-glycan, is one of the four members of the syndecan family.

### DNA/RNA

<table>
<thead>
<tr>
<th>Transcript Variant</th>
<th>Exons</th>
<th>Transcript Length (bp)</th>
<th>Translation Length (residues)</th>
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<tbody>
<tr>
<td>NM_001006946</td>
<td>6</td>
<td>3309</td>
<td>310</td>
</tr>
<tr>
<td>NM_002997</td>
<td>5</td>
<td>3217</td>
<td>310</td>
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</tbody>
</table>

Genomic structure of the two alternative transcript variants of SDC1. Black boxes indicate exons and red boxes indicate untranslated exons.

### Description

The SDC1 gene contains 9 exons and spans 24,636 bases (start 20,264,039 bp from pter to end 20,288,675) oriented at the minus strand.

**Transcription**

While several transcript variants may exist for this gene, the full-length natures of only two have been described to date. These two represent the major variants of this gene and encode the same protein. Variant 1 (NM_001006946) represents the longer transcript and variant 2 (NM_002997) differs in the 5' UTR compared to variant 1.

Variant 1: exons-6; transcript length-3309 bp and translation length -310 residues.

**Pseudogene**

None

### Protein

**Description**

310 amino acids; 32477 Da; charge -19.5; iso-electric point 4.2618.

The core protein contains 3 domains, an ectodomain (extracellular domain), transmembrane domain and cytoplasmic domain. The ectodomain contains a cleavable amino terminal single peptide and the glycosaminoglycan attachment sites. There are 3 highly conserved serine-glycine sites for heparan sulfate attachment (amino acids 37, 45 and 47) near the N terminal of the core protein and 2 highly conserved serine-glycine sites for chondroitin sulfate attachment (amino acids 210 and 220), adjacent to the cell membrane. Shedding of the ectodomain occurs via protease sensitive sites near the plasma membrane. The transmembrane domain, which is highly conserved among the syndecan family members, contains an unusual motif of glycine/alanine that aligns on one face of the domain in the outer membrane leaflet. The non-catalytic COOH-terminal, cytoplasmic domain, which is relatively short (30 amino acids) contains 2 highly conserved regions (C1 and C2) which are identical in each of the 4 syndecan family members (the exception being a conservative substitution of arginine for lysine in syndecan 2). These flank a central variable region (V) that is distant for each family member.
The sequence for variable domain (V) for SDC1 is SLEEPKQANGGAYQKPTKQE. The cytoplasmic domain of SDC1 is required for linking the molecule to the cytoskeleton and this interaction is dependent on a tyrosine residue that is conserved among all known syndecan family sequences. The cytoplasmic V region plays critical role in lamellipodial spreading, actin bundling and cell migration.

**Expression**

SDC1 is expressed predominantly on epithelial cells but is also found on distinct stages of differentiation of normal lymphoid cells (pre-B), mesenchymal cells during development and in mature plasma cells.

**Localisation**

Membrane; Single-pass type I membrane protein.

**Function**

The syndecan-1 proteoglycan regulates cell proliferation, cell migration, cell signaling, cytoskeletal organization and mediates both cell-cell and cell-extracellular matrix interactions. Additionally, via its heparan sulfate chains, it binds a wide range of bioactive molecules (e.g., growth factors, chemokines) that regulate cell behaviors in normal and pathological processes. For example, it can function as trans HIV receptors via binding of HIV-1 gp120 to the syndecan heparan sulfate chains and also serves as a primary receptor for natural HPV infection of keratinocytes. SDC1 is required for Wnt-1-induced mammary tumorigenesis and can function as either tumor suppressor or tumor promoter depending on tumor type and specific location of the proteoglycan (either cell surface or shed into the microenvironment). Core proteins also have functions independent of the heparan sulfate chains. The cytoplasmic domains can transmit signals and they also bind to anchoring molecules including PDZ family members. The extracellular domains bear the attached heparan sulfate chains but also interact with, and regulate, other cell adhesion molecules and cell surface receptors independent of their heparan sulfate chains. It was recently demonstrated that a domain within the syndecan-1 core protein is required for activation of alphaV/beta3 and alphaV/beta5 integrins and mutational analysis of SDC1 has identified a stretch of 5 hydrophobic amino acids, AVAAV (amino acids 222-226), which are critical for the SDC1 mediated inhibition of tumor cell invasion.

**Homology**

Belongs to the syndecan family; four members, syndecan-1, syndecan-2, syndecan-3 and syndecan-4, have been identified in mammalians. SDC1 orthologs are found in mouse, rat, dog, chimpanzee, guinea pig, Chinese hamster, Hedgehog, cat, Pika, Platypus, Bushbaby, Tree Shrew, and chicken. The extracellular domains of human and mouse SDC1 show 70% sequence identity while the trans-membrane domain and cytoplasmic domain show 96% and 100% identity respectively (see MapViewer).

**Mutations**

Note

No mutations in the SDC1 gene have been reported.

**Implicated in**

**Multiple Myelomas**

Note

Syndecan-1 (CD138) is the dominant heparan sulfate proteoglycan expressed on the surface of myeloma cells both in bone marrow and in peripheral blood, and is used as a standard marker by many labs for identification and purification of myeloma cells. On normal cells, syndecan-1 is not expressed on mature B lymphocytes but becomes present at the onset of plasma cell differentiation.

**Disease**

Myeloma resides predominantly within the bone and is marked by fatigue, intractable bone pain, renal failure and recurrent infections. These effects result from high tumor burden with accompanying cytokine dysregulation, osteolytic bone disease and from the deposition in some patients of high levels of immunoglobulin light chain. Cell surface SDC1 mediates adhesion of myeloma cells to collagen, inhibits invasion through collagen gels and also can mediate myeloma cell-cell adhesion. In contrast, shed syndecan-1 actively promotes myeloma tumor growth and metastasis.
Prognosis
Shedding of syndecan-1 from the myeloma cell surface occurs actively via proteolytic sheddases and a high level of syndecan-1 in the serum is an independent predictor of poor prognosis in myeloma. Patients with high serum SDC1 had a median survival of 20 months, whereas those with a low serum SDC1 had a median survival of 44 months.

Haematological malignancies
Note
SDC1 (CD138) is detectable on B-cell chronic lymphocytic leukemia (B-CLL) cells, acute lymphoblastic leukemia (ALL) cells and acute myeloblastic leukemia (AML) cells.

Disease
The serum levels of syndecan-1 were elevated in patients with B-cell chronic lymphocytic leukemia (CLL) and Hodgkin disease (HL).

Prognosis
Serum CD138 level is higher in early stage B-CLL patients than in healthy controls, correlates negatively with peripheral blood lymphocyte count, and is higher in patients with more indolent disease course. Serum CD138 levels increase in early stage B-CLL patients and may have a positive prognostic value as to the dynamics of the disease. The serum levels of syndecan-1 were elevated in patients with HL but did not correlate with markers of tumor burden and prognosis, including serum interleukin-10 and soluble CD30.

Breast tumors
Note
Syndecan-1 is expressed at high levels in a significant percentage of breast carcinomas and is related to an aggressive phenotype and poor prognosis. High syndecan-1 expression contributes to the identification of a patient population at particularly high risk of relapse and death.

Disease
High syndecan-1 expression in breast tumors is associated with an aggressive phenotype characterized by larger tumor size, higher tumor grade, higher mitotic count, negative steroid status, and over expression of c-erbB-2 and p53.

Prognosis
In breast cancer, increased expression of SDC1 correlates with an unfavorable prognosis and poor response to chemotherapy.

Pancreatic cancer
Note
Syndecan-1 is upregulated in the stroma of pancreatic cancer. Pancreatic cancer tissues express significantly higher levels of syndecan-1 mRNA and protein. SDC1 over expression is an early event in pancreatic carcinogenesis.

Disease
Carcinoma of the pancreas is the 4th leading cause of cancer death in Western countries, with a very short patient survival after diagnosis. Pancreatic cancers over-express a variety of mitogenic growth factors and their receptors and they exhibit tumor-suppressor gene mutations such as p53, p16 and Smad4 and proto-oncogene mutations such as k-ras.

Prognosis
Patients with stromal syndecan-1-positive pancreatic cancer had a worse outcome than patients with stromal syndecan-1 negative tumors. Stromal expression of syndecan-1 seems to be an independent prognostic factor in pancreatic cancer.

Gastric cancer
Note
Stromal syndecan-1 expression correlates with deep tumor penetration and larger tumor size. Positive stromal syndecan-1 immunoreactivity correlated with decreased epithelial syndecan-1 expression.

Disease
Risk factors for gastric cancer include: Helicobacter pylori gastric infection, advanced age, male gender, diet including dry salted foods, atrophic gastritis, pernicious anemia, cigarette smoking, Menetrier's disease, and familial polyposis. The prognosis of patients with gastric cancer is related to tumor extent and includes both nodal involvement and direct tumor extension beyond the gastric wall.

Prognosis
High expression of syndecan-1 in the stroma in gastric carcinoma is a tumor characteristic associated with a poor prognosis independent of tumor size. Patients with low epithelial syndecan-1 expression in cancer cells had worse overall survival than patients with strong epithelial syndecan-1 staining. Stromal syndecan-1-positive patients had a worse outcome than patients with syndecan-1 negative stroma.

Prostate cancer
Note
Expression of syndecan-1 is associated with established features of biologically aggressive prostate cancer including high PSA levels and lymph node metastases.

Disease
Prostate cancer is the most common noncutaneous malignancy affecting males in the USA. The disease course is variable and about a third of patients eventually fail treatment, as evidenced by a detectable and rising PSA levels.

Prognosis
Patients with features of aggressive progression were more likely to exhibit increased syndecan-1 expression compared with those with features of non aggressive progression.
Endometrial Cancer

Note
Stromal syndecan-1 expression is elevated in high-grade endometrial cancer.

Disease
Endometrial cancer is the most common disease among gynecological malignancies and remains a major health concern worldwide.

Prognosis
Loss of epithelial syndecan-1 expression and induction of stromal syndecan-1 expression are associated with reduced survival outcomes in patients with endometrial cancer. Stromal syndecan-1 expression serves as an indicator of poor prognosis in patients with endometrial cancer.

Ovary carcinoma

Note
Syndecan-1 is present in the epithelial cells, cancer cells, and stromal cells of benign, borderline, and malignant ovarian tumor sections. Stromal syndecan-1 expression is observed in the most invasive areas of ovarian cancer.

Disease
Epithelial carcinoma of the ovary is one of the most common gynecologic malignancies. The most important risk factor for ovarian cancer is a family history of a first-degree relative (mother, daughter, or sister) with the disease.

Prognosis
Stromal syndecan-1 expression is associated with decreased survival in patients with ovarian carcinoma.

Lung cancers

Note
Serum syndecan-1 is a powerful prognostic factor in lung cancer. Lung cancer patients have high serum syndecan 1. High levels of circulating syndecan-1 also in part reflect the presence of a large tumor mass and are associated with advanced cancer.

Disease
Lung cancers are neuroendocrine lung tumors (small cell lung carcinomas, carcinoids, large cell neuroendocrine carcinomas) or non neuroendocrine lung tumors (squamous carcinomas, adenocarcinoma, large cell carcinomas).

Prognosis
High serum syndecan-1 levels at diagnosis are associated with an advanced stage and poor outcome in lung cancer.

References


This article should be referenced as such: