S100P (S100 calcium binding protein P)

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Identity

Other names: MIG9; S100E
HGNC (Hugo): S100P
Location: 4p16.1

DNA/RNA

Description
S100P gene contains two exons and one intron. Genomic size of 3,332 bases.

Transcription
1279 bases mRNA; 288 bases coding sequences. The transcript is on Chromosome 4 at location 6,745,697-6,749,797.

Pseudogene
None identified.

Protein

Description
S100P protein consists of 95 amino acids with a molecular weight of 10.4 kDa. S100P is a Ca\(^{2+}\) binding protein that belongs to S100 family ("Soluble in 100% saturated solution with ammonium sulfate") which was first isolated from human placenta and is therefore designated as "P". S100 family includes at least 26 members, which are thought to be expressed only in vertebrates and are present in a tissue and cell-specific manner. S100 proteins are characterized by common structural motifs including 2 EF-hands (helix-loop-helix calcium binding domains) with different affinities for calcium ions, a central hinge region and the C-terminal extension. The N-terminal half of the protein contains an unconventional EF hand that binds calcium with lower affinity, while the C-terminal is canonical and binds calcium with high affinity. The connecting hinge region and the C-terminal extension are the most variable regions and thus determine the functional specificity of S100 family members, including S100P. In addition to Ca\(^{2+}\), S100P also binds Zn\(^{2+}\) and Mg\(^{2+}\) and can form homo- and heterodimers.

Expression
S100P is expressed in various normal tissues including placenta, lung, heart, kidney, bladder, skeletal muscle, bone marrow, spleen, mammary epithelium, epidermis, prostate gland, gastric and intestinal mucosa, and malignant tissues such as pancreatic ductal adenocarcinoma, pancreatic intraductal papillary mucinous neoplasm, non-small-cell lung cancer, melanoma, gastric adenocarcinoma, ovarian, breast, colon and prostate carcinoma as well as in the body fluids such as tear, pancreatic juice, blood and urine.

Localisation
Cytoplasm, nucleus, also secreted in the culture media.

Function
S100P is involved in diverse biological functions but the exact role or mechanism of its action is still largely unknown. Upon binding of calcium ions S100P undergoes a conformational change that results in an exposure of a hydrophobic surface which allows the interaction with specific target proteins. To date, several S100P interacting partners have been identified including S100P binding protein S100PBP, EZR, S100A1, ECD, CacyBP, RAGE, S100Z and S100A6, but the consequences of their interactions are not fully understood.
**Homology**

S100P shares 50% sequence identity with human S100A1 and 44% identity with S100B.

**Mutations**

**Note**

Mutations have not been reported.

**Implicated in**

**Cancers**

**Disease**

S100P has been associated with the progression of several types of cancer including pancreatic, prostate, non-small cell lung, breast, and colorectal cancer.

**Oncogenesis**

S100P has been implicated in migration, invasion, proliferation and survival of cancer cells in vitro and increased tumour growth in vivo. In fibroblasts, S100P has been shown to function as an autocrine growth and survival factor that enhanced cell proliferation and survival by activating RAGE receptor through MAPK and NF-kB signaling.

**Pancreatic cancer**

**Oncogenesis**

The up-regulation of S100P is an early event in the development of pancreatic cancer and its expression increases throughout the progression of pancreatic intraepithelial neoplasia (PanINs) to invasive pancreatic ductal adenocarcinoma. S100P plays a critical role in the maintenance of the structural organization of intermediate filaments (cytokeratins 8, 18 and 19) and actin cytoskeleton, and its over-expression changes the phosphorylation status of the actin regulatory protein cofilin. Over-expression of S100P also increases the expression of S100A6 and cathepsin D, both of which are involved in cellular invasion. As S100P is expressed early in pancreatic ductal adenocarcinoma and is secreted into body fluids, it can serve as a useful diagnostic marker.

**Prostate cancer**

**Oncogenesis**

In prostate cancer over-expression of S100P increases cell growth both in vitro and in vivo. S100P over-expression also up-regulates androgen receptor that leads to prostate cancer progression. Its expression has also been associated with poor clinical prognosis of patients with this malignancy.

**Non-small-cell lung cancer**

**Oncogenesis**

Higher levels of S100P have been correlated with progression to metastasis and decreased survival in patients with lung cancer. This may also serve as a predictor of distant metastasis and poor survival in non-small cell lung carcinomas.

**Colorectal cancer**

**Oncogenesis**

In colon cancer, expression of S100P correlates with resistance to chemotherapy and has also been associated with doxorubicin resistance in colon cancer cell lines.

**Breast cancer**

**Oncogenesis**

S100P has been associated with immortalization of breast cancer cells in vitro and tumour progression in vivo. Higher level of S100P expression has also been correlated with decreased survival in patients with breast cancer.

**Other cancer types**

**Note**

S100P is also expressed at higher levels in gastric, ovarian and cervical carcinomas.

**References**


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