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in Oncology and Haematology

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Gene Section
Short Communication

S100PBP (S100P binding protein)

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Identity

Other names: S100PBPR

HGNC (Hugo): S100PBP

Location: 1p35.1

DNA/RNA

Description

There are two different transcript variants of S100PBP. Variant 1 is 4317 base pairs and contains 7 exons. Variant 2 is 1483 base pairs and also contains 7 exons.
This is shown in the below alignment. The coding sequence for each isoform is indicated in red, with the non-coding sequence in grey.
Unmatched base pairs between the two isoforms are highlighted in green and the position of a missing CAG codon in isoform B is circled. The end of the isoform B sequence is indicated by a bold line.

Protein

Description

S100PBP isoform A codes for a 45 kDa protein and isoform B for 37 kDa protein.
Secondary structure analysis of the S100PBP protein sequence was performed using the secondary structure consensus prediction tool (NPS@, Lyon, France). Based on three different methods: DSC (Discrimination of protein Secondary structure Class), MLRC (Multivariate Linear Regression Combination) and PHD neural network system, S100PBP was shown to be largely unstructured and unfolded, as seen below ("h" represents a helix, "c" a coil and "e" an extended strand).

Expression

S100PBP is expressed in various normal tissues including prostate and lung and in both the endocrine and exocrine pancreas.
S100PBP is also expressed in malignant tissues such as liver hepatocellular carcinoma and thyroid carcinoma (Lines et al., 2012).
In pancreas, S100PBP is expressed in decreasing levels as cancer develops and progresses, which is an inverse pattern of expression of its binding partner, S100P.
This is shown on picture below (a= acinar cells, d= ducts; PanIN= pancreatic intraepithelial neoplasia, a precursor lesion to pancreatic cancer, black arrows= PanIN-1, red arrows= PanIN-2; PDAC= pancreatic cancer).

Localisation

Predominantly nuclear.

Function

The exact functions of S100PBP are currently unknown, however it has been shown that S100PBP can bind to the metastasis related protein S100P (Dowen et al., 2005).

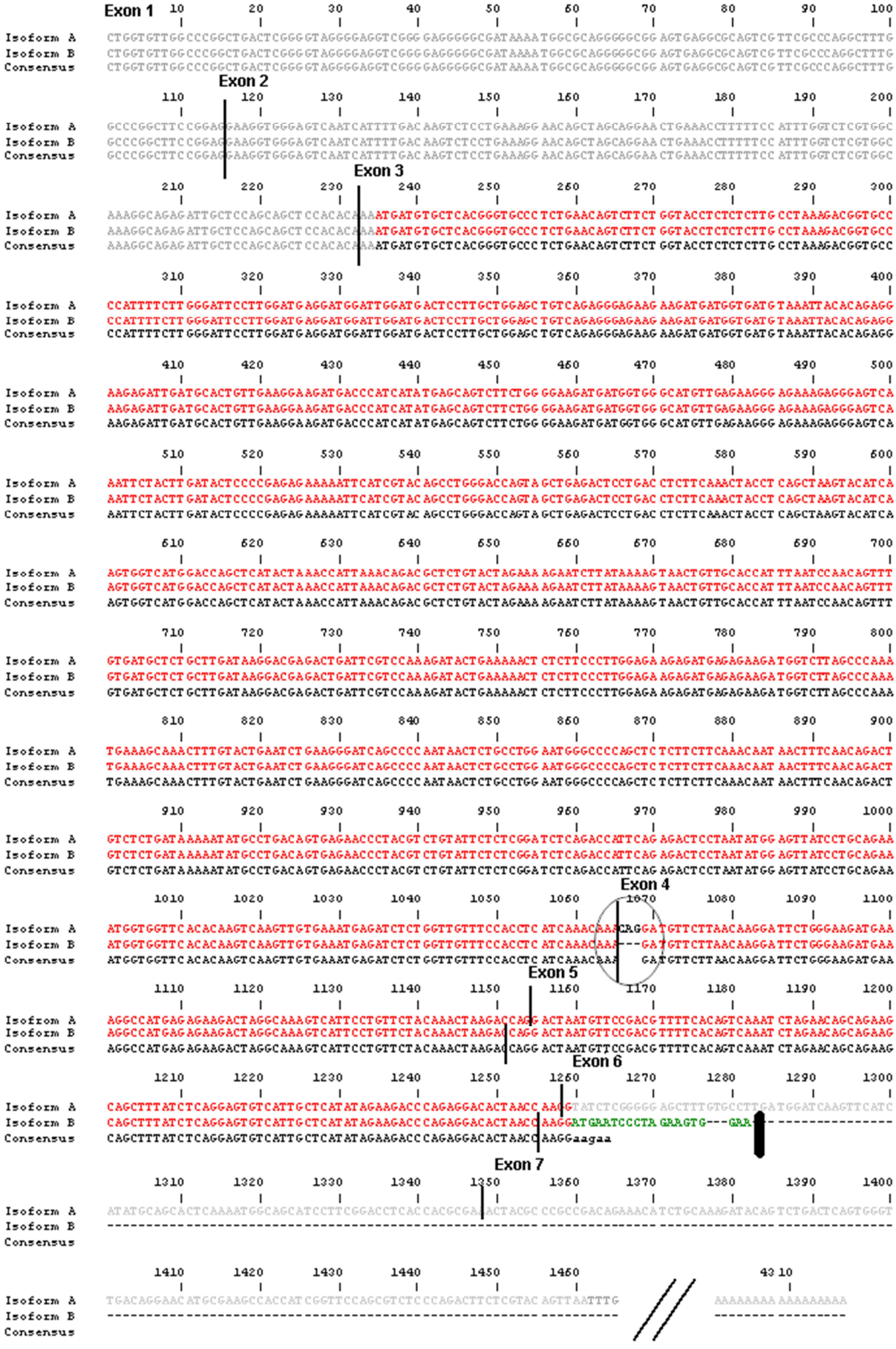
Homology

No homology to any currently described protein is seen.

Mutations

Note

No mutations have yet been reported.


Exon 1
Exon 2
Exon 3
Exon 4
Exon 5
Exon 6
Exon 7
Isoform A
Isoform B
Consensus

```
                    10        20        30        40        50        60        70
                    |         |         |         |         |         |         |
UNK_148480 MMCSRVPSEQSSGTSLLPKDGAPFSWDSLDEDGLDDSLLELSEGEEDDGDVNYTEEEIDALLKEDDPSYE
DSC        ccccccccccccccccccccceeecccccchhhhhhhhhccccccccccccchhhhhhhhhccccccc
MLRC       ccccccccccccceeecccccceecccccchhhhhhhhhhccccccccccccchhhhhhhhhccccccc
PHD        ccccccccccccccccccccccccccccchhhhhhhhhccccccccccccchhhhhhhhhccccccc
Sec.Cons.  ccccccccccccccccccccccceecccccchhhhhhhhhccccccccccccchhhhhhhhhccccccc

                    80        90        100       110       120       130       140
                    |         |         |         |         |         |         |
UNK_148480 QSSGEDDGGHVEKGERGSQILLDTPREKNSSYSLGPVAETPDLFKLPQLSTSSGHGPAHTKPLNRRSVLE
DSC        ccccccccccccccccccccccccccccccccccccccccccccccccccccchhhhhhhhh
MLRC       ccccccccccccccccceeecccccccccceecccccccccccccccccccccchhhhhh
PHD        ccccccccccccccccccccccccccccccccccccccccccccccccccccchhhh
Sec.Cons.  ccccccccccccccccccccccccccccccccccccccccccccccccccccchhhhhh

                    150       160       170       180       190       200       210
                    |         |         |         |         |         |         |
UNK_148480 KNLIKVTVAPFNPTVCDALLDKDETDSSKDTEKLSSLGEEMREDGLSPNESKLCTESEGISPNNSAWNGP
DSC        hccccccccccccccccccccccccccchhhhhhhccccccccccccccccccccc
MLRC       hchaaaaaccccccccccccccccccchhhhhhhhhhhhhhccccccccccccccccccccc
PHD        hccccaaaccccccccccccccccccccccccccccccccccccccccccccccccccccc
Sec.Cons.  hccccaaaccccccccccccccccccccccchhhhhhhccccccccccccccccccccc

                    220       230       240       250       260       270       280
                    |         |         |         |         |         |         |
UNK_148480 QLSSSNNNFQQTVSDKNMPDSENPTSVFSRISDHSETPNMELSCRNGGSHKSSCEMRSLVVSTSSNKQDV
DSC        ccccccccaaaaccccccccccccccaaaaaccccccccccccccccccccaaaaaaaaccccccc
MLRC       ccccccccaaaccccccccccccccccaaaaaccccccccccccccccccccaaaaaaaaccccccc
PHD        ccccccccccccccccccccccccccccccccccccccccccccccccccccaaaaaaaaccccccc
Sec.Cons.  ccccccccaaaccccccccccccccccaaaaaccccccccccccccccccccaaaaaaaaccccccc

                    290       300       310       320       330       340       350
                    |         |         |         |         |         |         |
UNK_148480 LNKDSGKMKGHERRLGKVIPVLQTKTRTNVPTFSQSNLEQQKQLYLRSVIAHIEDPEDTNQGISGELCAL
DSC        eccccccccccchhccccaaaaccccccccccccchhhhhhhhhhhhhaaaaccccccccccchhhhh
MLRC       eccccccccchhhhhccaaaaaaccccccccccccchhhhhhhhhhhhhhhccccccccccchhhhhhhh
PHD        ccccccccccccccccccaaaaaaccccccccccccchhhhhccaaaaaaaaaccccccccccchhhhc
Sec.Cons.  eccccccccccchhccaaaaaaccccccccccccchhhhhhhhhhhhhaaaaccccccccccchhhhh

                    360       370       380       390       400
                    |         |         |         |         |
UNK_148480 MDQVHHMQHSKWQHPSDLTTRNYARRQKHLQRYSLTQWVDRNMRSHHRFQRLPDFSYS
DSC        hhhhhhccccccccccchhhhhccchhhhhccchhhhhhhhhhccccccccccccccc
MLRC       hhhhhhhhccccccccccchhhhhhhhhhhhhhhhhhhhhhccccccccccccccc
PHD        ccccccccccccccccchhhhhhhhhhccccccccehhhccccccccccccccccc
Sec.Cons.  hhhhhhccccccccccchhhhhhhhhhhhhccchhhhhhccccccccccccccc
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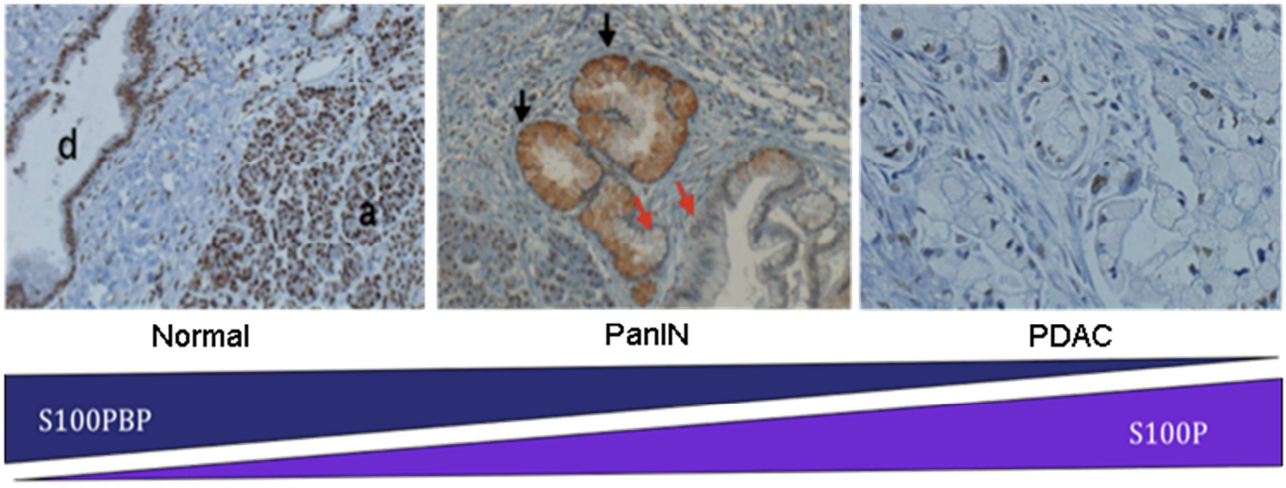
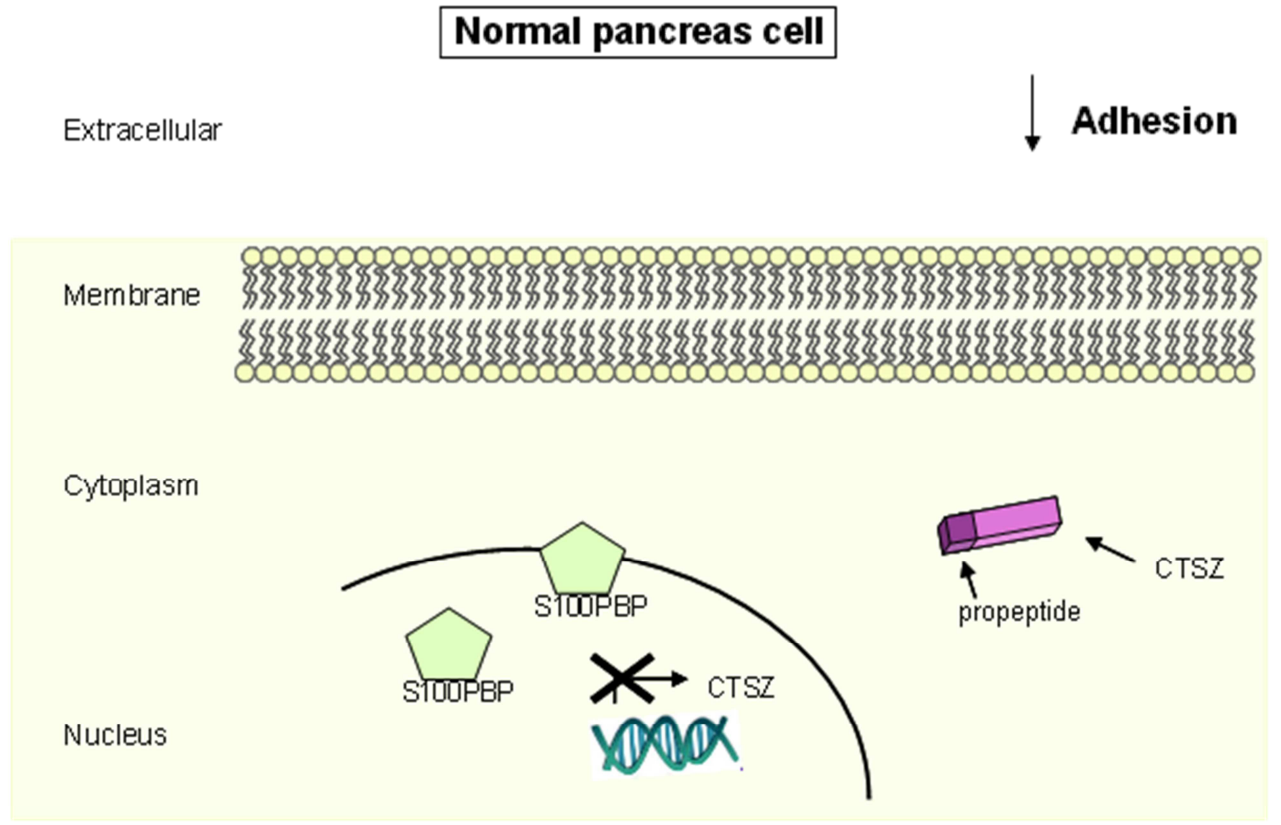
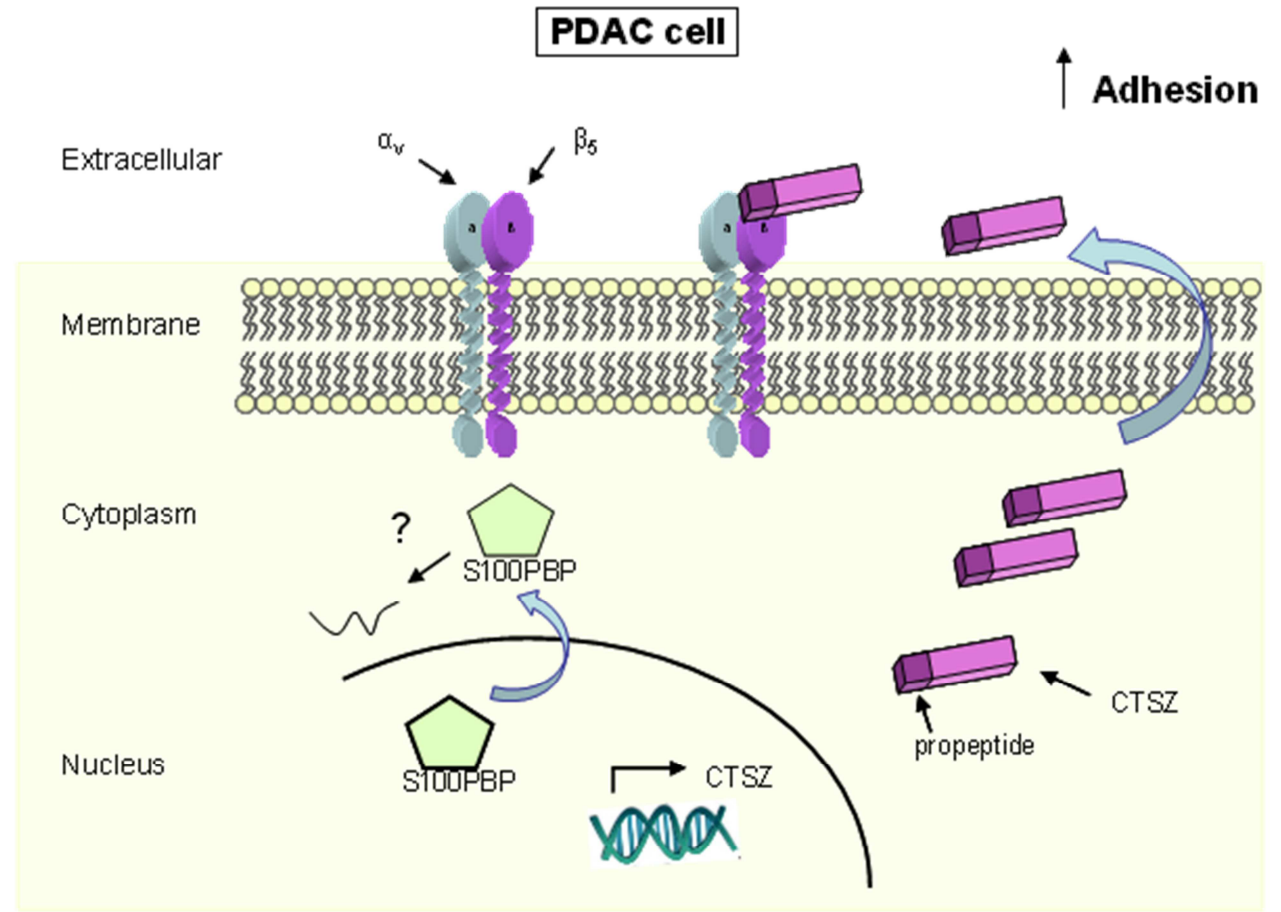



Normal pancreas cell
Extracellular
Adhesion
Membrane
Cytoplasm
S100PBP
S100PBP
CTSZ
propeptide
CTSZ
Nucleus


PDAC cell
Adhesion
Extracellular
α_v
β_5
Membrane
Cytoplasm
?
S100PBP
S100PBP
CTSZ
propeptide
CTSZ
Nucleus

Implicated in

Pancreatic ductal adenocarcinoma (PDAC)

Note

Overexpression of S100PBP in FA6 pancreatic cancer cells that show low levels of endogenous
S100PBP expression and silencing of S100PBP in MiaPaCa2 cells (high levels of endogenous S100PBP) showed no effect on proliferation or wound healing.
While cell migration was not affected in majority of tested pancreatic cancer cell lines after modulation of S100PBP expression, significant changes in invasion (increase in MiaPaCa2 and Panc1 cells after S100PBP silencing and decrease in RwP1 cells after overexpression) were seen. However, the most affected cellular function after modulation of S100PBP expression was adhesion. Loss of S100PBP causes an increase in pancreatic cancer cell adhesion to extracellular matrix proteins which was mediated by cysteine protease Cathepsin Z (CTSZ) and the integrin αvβ5 (Lines et al., 2012).
Schematic and simplified diagram of the putative mechanism behind S100PBP mediated changes in pancreatic cell adhesion is shown below: in normal cells where S100PBP is highly expressed, low levels of CTSZ are present; no or very little αvβ5 is seen on the cellular surface. In cancer cells (PDAC), S100PBP levels decrease, which results in an increase in CTSZ expression; CTSZ is then secreted and can interact with αvβ5, promoting thus the adhesion.

Disease

Pancreatic cancer.

References

Dowen SE, Crnogorac-Jurcevic T, Gangeswaran R, Hansen M, Eloranta JJ, Bhakta V, Brentnall TA, Lüttges J, Klöppel G, Lemoine NR. Expression of S100P and its novel binding partner S100PBPR in early pancreatic cancer. Am J Pathol. 2005 Jan;166(1):81-92

Lines KE, Chelala C, Dmitrovic B, Wijesuriya N, Kocher HM, Marshall JF, Crnogorac-Jurcevic T. S100P-binding protein, S100PBP, mediates adhesion through regulation of cathepsin Z in pancreatic cancer cells. Am J Pathol. 2012 Apr;180(4):1485-94

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