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Gene Section
Review

MMP15 (matrix metallopeptidase 15 (membrane-inserted))

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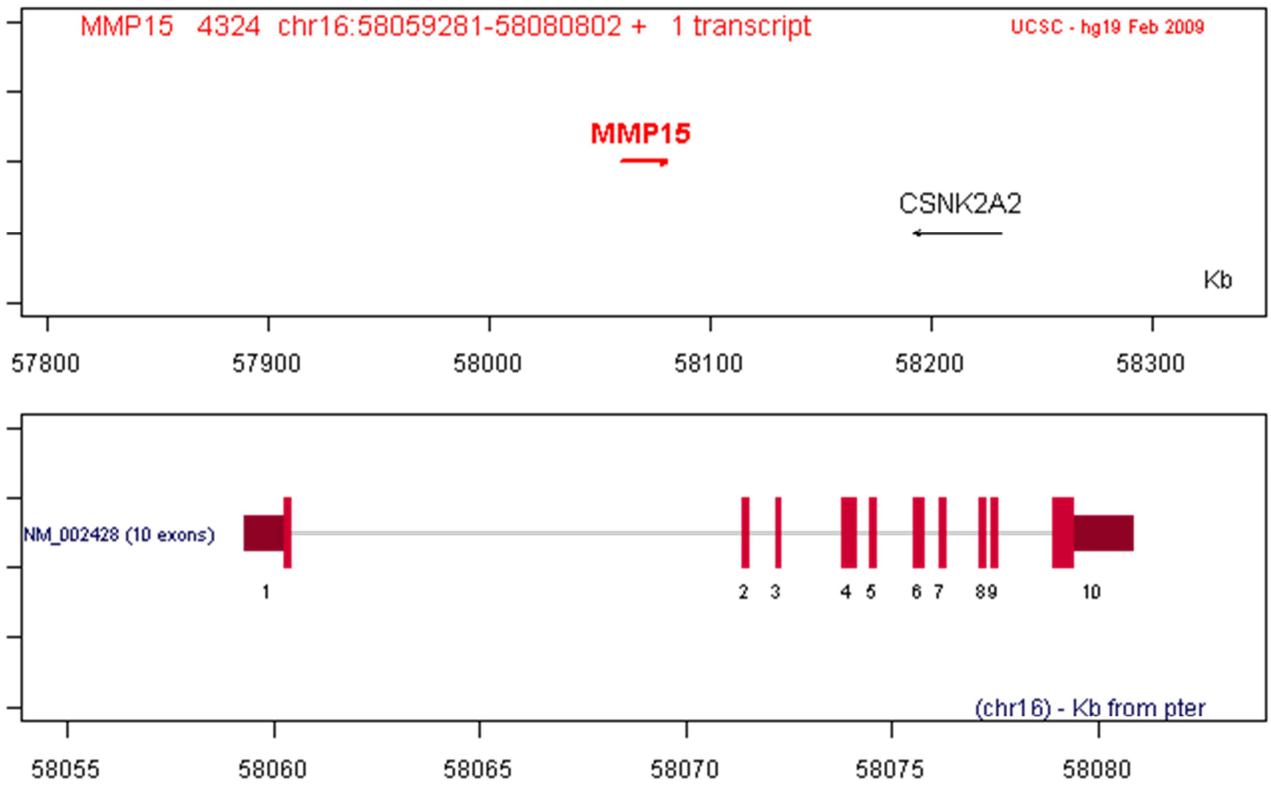
Identity

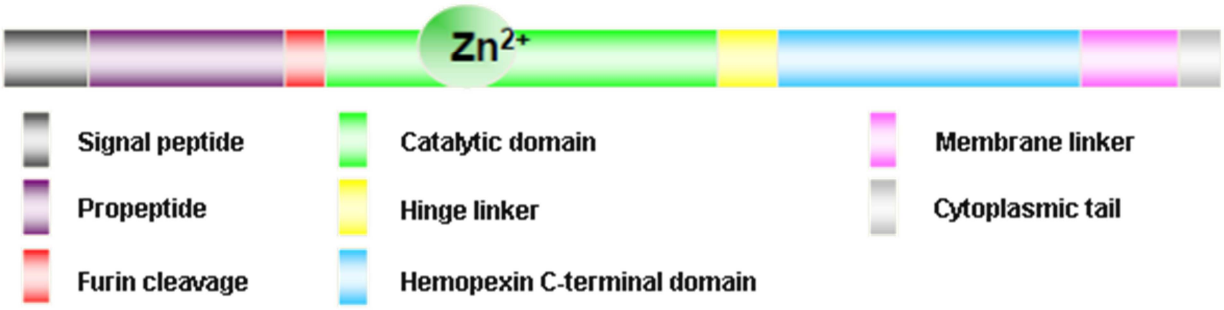
Other names: MT2-MMP, MTMMP2, SMCP-2
HGNC (Hugo): MMP15
Location: 16q21

DNA/RNA

Description

This gene can be found on chromosome16 at location: 58028573-58163296.





Transcription

The DNA sequence contains 10 exons and the transcript length: 3530 bp translated to a 699 residues protein.

Protein

Description

MT2-MMP belongs to which consist a gene family over 25 different members in humans (refer to MT1-MMP).

Expression

Expression of MT2-MMP has been reported in many cancers, such as glioblastomas, ovarian, urothelial, and breast. In addition, MT2-MMP is involved in endothelial tubulogenesis, malignant conversion of keratinocytes, and is an antiapoptotic factor.

Both MT2-MMP and MT3-MMP were detected predominantly at the interface between the epithelium and substantia propia in mice intracornea infected with Pseudomonas aeruginosa. On the other hand, MT1-MMP was mainly expressed at epithelium in the same tissue (Dong et al., 2000). During pregnancy, MT2-MMP is expressed in the invaded cytotrophoblasts where both MT1-MMP and gelatinase A are extensively colocalized (Bjørn et al., 2000).

Over all, MT2-MMP may plays an important and distinct role from MT1-MMP in normal physiological processes.

Localisation

Plasma membrane.

Function

In a previous study with a cell line established from MT1-MMP gene knocked-out mice, MT2-MMP has been suggested to contribute alternatively to cell invasion through fibrin rich matrices (Hotary et al., 2002).

Like as MT1-MMP, MT2-MMP may also play some role in MMP-2 activation in microenvironment with TIMP-2 involvement (Morrison et al., 2001; Morrison and Overall, 2006).

In corporation with the enzymatic action of MT1-MMP, MT2-MMP can contribute to remodel basement membrane (Hotary et al., 2000; Hotary et al., 2006).

Development

1) Branching morphogenesis

MT2-MMP has been shown to be induced to the epithelia in migration, thereby speculated to be involved in branching morphogenesis of salivery gland (Harunaga et al., 2011), and submandibular gland (Rebustini et al., 2009).

2) Cardia valve development in endocardial cushion

Cardiac valve is constituted by tissue-specific fibroblasts originated from endocardial cushion through EMT. It has been demonstrated that MT2-MMP, which may play a key role in the valve formation, is likely expressed at the period of EMT by Snail1-related signal (Tao et al., 2011).

3) Placenta development (chorionic villus)

It has been demonstrated by separate research groups that MT2-MMP may play a important role in placental labyrinth formation at the period of embryogenesis or in menstrual cycle (Szabova et al., 2010; Plaisier et al., 2006). During the placenta development, MT2-MMP is induced at trophoblasts under TNF alpha-related signal.

Homology

MT2-MMP is supposed to be 72 kDa in molecular weight with overall similarity to MT1-MMP by 73,9%.

Implicated in

Cancer progression

Note

Both MT1-MMP and MT2-MMP have potential to play important role in cancer either for proliferation or transmigration through extracellular matrix (ECM). Ota and his colleagues have suggested that membrane-localized proteolytic enzyme such as MT1/2-MMP can be induced and recruited towards the tumor cell surface during epithelial-mesenchymal transition (EMT) mediated by Snail1-related signal (Ota et al., 2009). Other group has indicated that cancer cells, such as PANC-1, induce MT2-MMP under hypoxia in a HIF-1 dependent manner (Zhu et al., 2011). These data suggest MT2-MMP may play some role in cancer progression against the physiological stress. It has not been clarified, however, that MT2-MMP can entirely substitute the function of MT1-MMP and vice versa.

Several IHS analyses with clinical samples suggested

that MT2-MMP is expressed in several tumor types which include esophageal (Chen et al., 2010), bladder (Mohammad et al., 2010), colorectal (Lyall et al., 2006), and urothelial carcinoma (Kitagawa et al., 1998). In such reports for the colorectal and bladder cancer, the expression of MT2-MMP was shown to be associated with disease prognosis (Lyall et al., 2006; Mohammad et al., 2010).

Idiopathic pulmonary fibrosis (IPF)

Note

IPF is a disease characterized by fibroblast expansion and ECM accumulation in lung. A previous report suggests MT1-MMP as well as MT2-MMP, was expressed in alveolar epithelial cells, and active MMP-2 was increased in bronchoalveolar lavage (BAL) fluids in IPF tissue. These MMPs possibly play roles in the pathogeny (García-Alvarez et al., 2006).

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