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Gene Section
Short Communication

CLDN9 (claudin 9)

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Identity

HGNC (Hugo): CLDN9

Location: 16p13.3

DNA/RNA

Description

2050 base-pairs DNA linear, starts at 30624573 and ends at 3064506 bp from pter with plus strand orientation. This gene contains 1 exon.

Transcription

The transcription produces 1 spliced mRNA variant (NM_020982), 2139 bp.

Pseudogene

Not found.

Protein

Description

The transcription of this gene gives 1 spliced mRNA that encodes 1 protein isoform with 217 aa and 22848 Da of molecular weight.

Expression

Pituitary gland (71,08%), lung (14,44%), intestine (6,87%), eye (6,56%), and brain (1,05%).

Localisation

This is a multi-pass membrane protein localized in the tight junction, cell membrane, cytoplasm and nucleus.

Sequence:

```
MASTGLELLG MTLAVLGWLG TLVSCALPLW KVTAFIGNSI VVAQVVWEGL WMSCVVQSTG
QMQCKVYDSL LALPQDLQAA RALCVIALLL ALLGLLVAIT GAQCTTCVED EGAKARIVLT
AGVILLLAGI LVLIPVCWTA HAIIQDFYNP LVAEALKREL GASLYLGWAA AALLMLGGGL
LCCTCPPPQV ERPRGPRLGY SIPSRSGASG LDKRDYV
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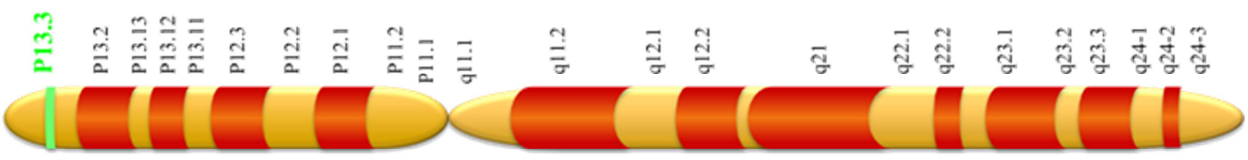
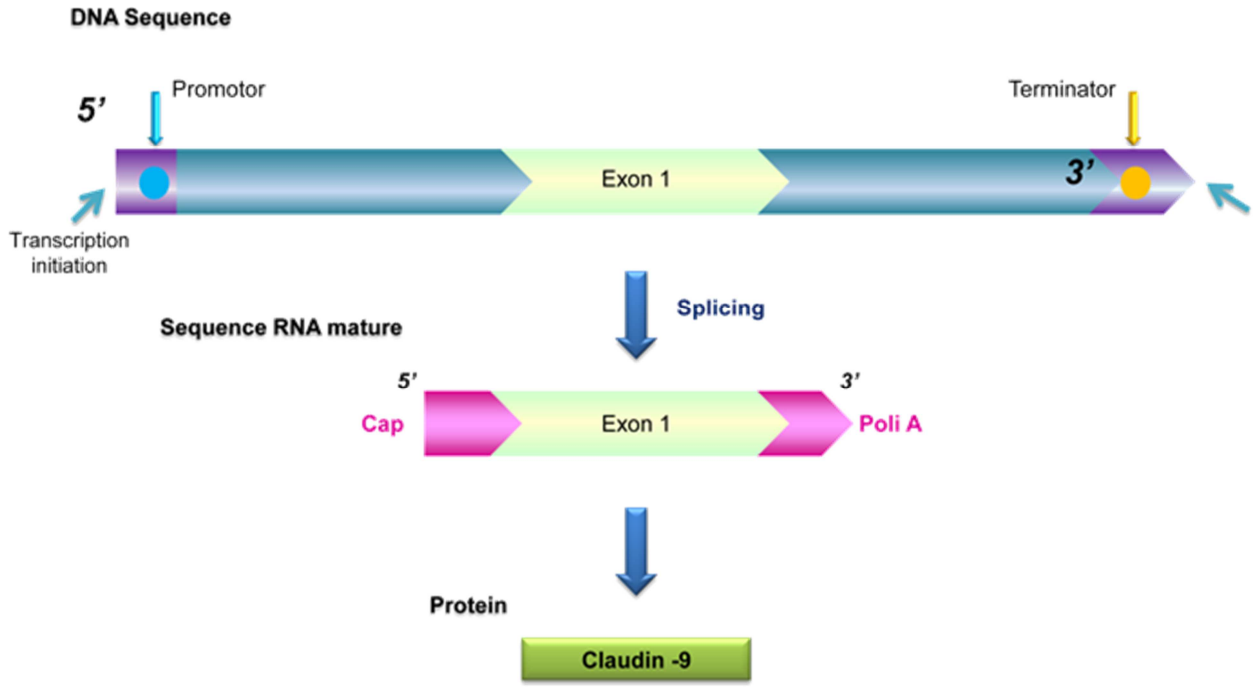


Gene: Claudin-9

Location: 3,062,457-3,064,506 bp

Lenght: 2050 bases

Claudin-9 Chr 16 p13.3



Function

Claudin-9 belongs to the claudin family. Claudins constitute integral membrane proteins responsible for solute and electrolyte permeability of the tight junction that serve as a physical barrier to prevent solutes and water from passing freely through the paracellular space between epithelial or endothelial cell sheets. Tight junctions also play a critical role in maintaining cell polarity and signal transductions. Claudin-9 creates charge specific channels in the paracellular space, plays a major role in tight junction-specific obliteration of the intercellular space, through calcium-independent cell-adhesion activity, is required to preserve sensory cells in the hearing organ because claudin-9-defective tight junctions fail to shield the basolateral side of hair cells from the K+-rich endolymph. Its ion barrier function is essential in the cochlea, but appears to be dispensable in other organs. Is one of the entry cofactors for hepatitis C virus; it enables HCV entry into target cells just as efficiently as CLDN1.

Homology

The CLDN9 gene is conserved in chimpanzee, dog, cow, mouse, rat, dog, opossum, lizard and zebrafish.

Implicated in

Gastric adenocarcinoma

Note

Abnormal claudin expression has been documented in several malignancies. Strong claudin-9 expression was associated with higher mortality rate (66%) in the diffuse- vs the intestinal-type (25%) gastric adenocarcinoma after a 2-year follow-up (Rendón-Huerta et al., 2010).

Claudin-9 expression is closely related to gastric carcinogenesis, and their detection is a useful prognostic marker in gastric adenocarcinoma.

Claudin-9 overexpression in AGS cells enhanced their invasive potential (1,6-fold), cell migration and proliferation rate (13,3%); it also increased claudin-1 and zonula occludens-1 levels (Zavala et al., 2011).

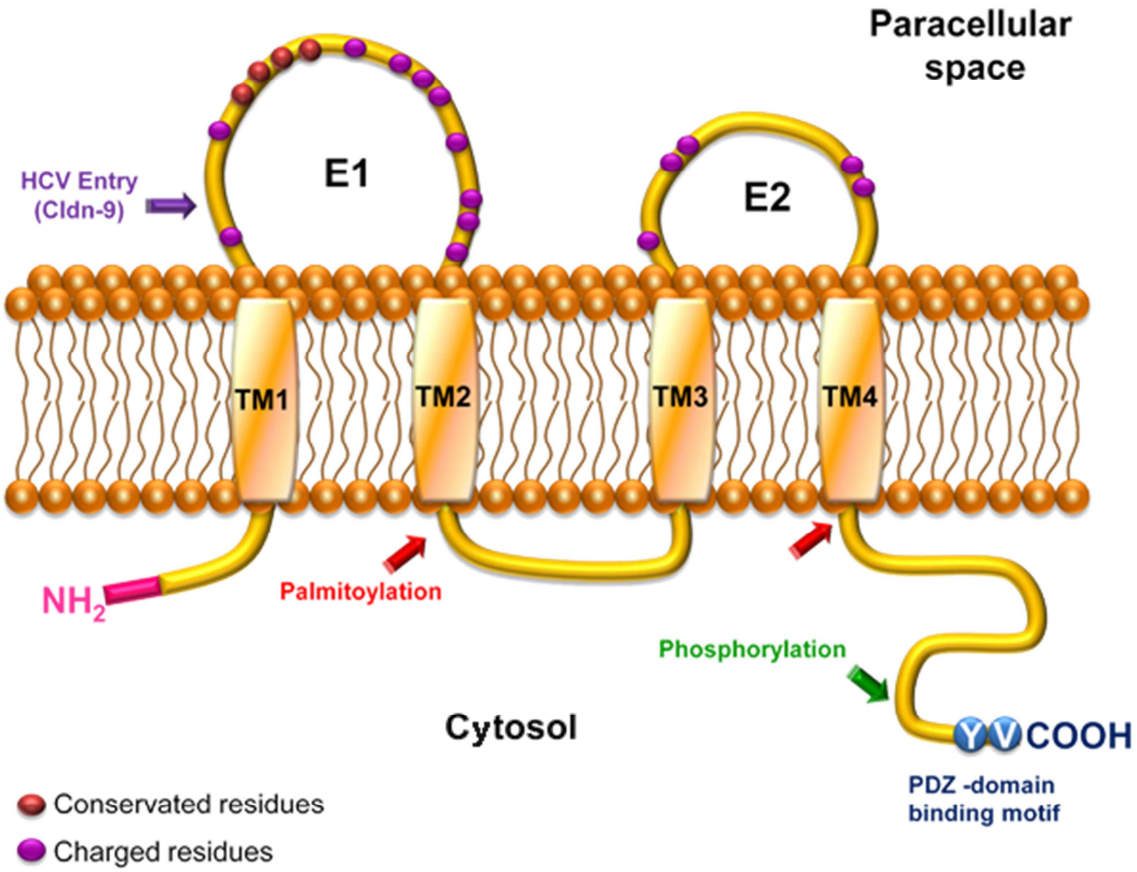
Increased expression of claudin-9 is sufficient to enhance tumorigenic properties of a gastric adenocarcinoma cell line.

Hepatitis C virus infection

Note

Claudin-9 mediates the entry of HCV into target cells. CLDN9 is expressed in the liver, the primary site of HCV replication, and peripheral blood mononuclear cells, an additional site of HCV replication. Sequence comparison and mutagenesis studies, showed that residues N38 and V45 in the first extracellular loop of CLDN9 are necessary for HCV entry (Zheng et al., 2007).

Claudin-9 expressed in CD81+ (tetraspanin) cells also enables the entry of HCV pseudoparticles. Claudin -1 and -9 function equally well as entry cofactors in endothelial cells but claudin-1 is more efficient in hepatoma cells (Meertens et al., 2008). This suggests that additional cellular factors modulate the ability of claudins to function as HCV entry cofactors.



Hearing

Note

Claudin-9 is required for the preservation of sensory cells in the hearing organ because its absence in a specific subdomain underneath more apical tight-junction strands formed by other claudins, fails to shield the basolateral side of hair cells from the K+-rich endolymph (Nakano et al., 2009). Claudin-9 mutant mice have shown that even the deeper (subapical) tight-junction strands have biologically important ion barrier function.

Cornea

Note

Epigenetic regulators such as TSA, 5-aza, and DMSO significantly enhance the expression of claudin-9 in corneal cells, changing transcriptional signals by demethylating CpG islands (Nishikiori et al., 2008); additionally, the epigenetic regulators increase transendothelial electrical resistance and suppress fluxes of corneal cells, thus enhancing the corneal barrier function, in murine experimental corneal trauma.

Neonatal development

Note

Claudins are the gatekeepers of the paracellular pathway, and claudin isoform expression determines the permeability characteristics of the paracellular pathway. Claudin-9 is not expressed or barely detectable in the adult mouse but it is expressed in the neonatal mouse kidney. Claudin-9 mRNA is present in 1-day-old proximal convoluted tubules (Abuazza et al., 2006). Expression of claudin-9 results in an increased transepithelial resistance, decreased chloride permeability, and decreased P(Na)/P(Cl) and P(HCO3)/P(Cl) (Sas et al. 2008). Claudin-9 may play a role in the maturational changes in kidney paracellular permeability.

Pathway signalling

Note

Transmembrane proteins of the claudin family are critical determinants of TJ permeability but little is known about the signaling pathways that control their expression.

In mammary epithelial cells SP600125 (an inhibitor of Jun N-terminal kinase) increased claudin-9 expression whereas PD169316 (a p38 MAPK inhibitor) did not modify claudin-9 expression (Carrozzino et al., 2009). Claudin-9 expression is associated with cellular stress.

References

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