

## Gene Section

### Mini Review

# TSPAN8 (tetraspanin 8)

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### Identity

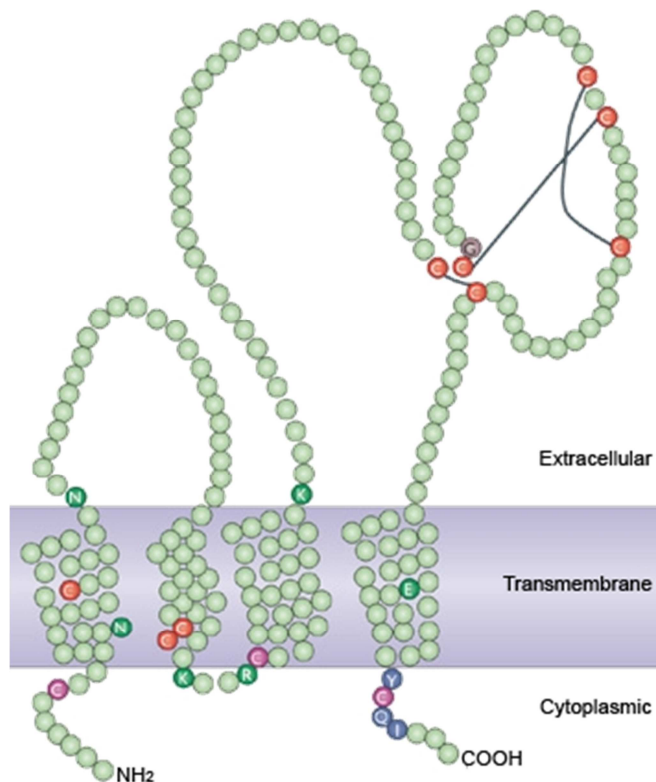
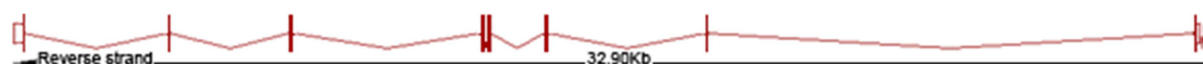
**Other names:** CO-029; TM4SF3; Tspan-8

**HGNC (Hugo):** TSPAN8

**Location:** 12q21.1

### DNA/RNA

The human Tspan8 gene contains 9 exons and 8 introns and was predicted to span over 32,9 kb approximately of the genomic DNA. Transcript length: 1130 bps, translation length: 237 residues.



Tetraspanin 8 has a short amino- and carboxy-terminal tail, a small intracellular loop between transmembrane region 2 (TM2) and TM3, a small extracellular loop (ECL1) between TM1 and TM2 and a large extracellular loop (ECL2) between TM3 and TM4. Extracellular loop 2 contains six conserved cysteine residues (red) including the CCG motif; disulphide bonds are indicated. The transmembrane regions 1 and 4 have polar amino acids (green), the cytoplasmic domains contain palmitoylation sites (pink) and the carboxy-terminal domain contains a sorting motif (blue).

## Protein

### Description

Tspan8 is a member of the transmembrane 4 superfamily, also known as the tetraspanin family.

### Expression

Tetraspanin 8 is expressed in squamous epithelial cells (not epidermis), capillary endothelial cells, nerves, smooth and striated muscle cells, and subpopulations of hematopoietic progenitor cells.

### Function

Like other tetraspanins, Tspan8 act as a "molecular facilitator" by forming a web in glycolipid-enriched membrane microdomains, called TEM (tetraspanin enriched membrane domains). Tspan8 associates with additional tetraspanins, integrins, preferentially CD49c, CD104, but also CD49d. It is directly associated with EWI-F, CD13 and intersectin 2. Via its associated molecules Tspan8 becomes involved in cell adhesion and motility as well as signal transduction. Motility promotion mostly proceeds via its association with CD104 and is in line with pronounced metastatic spread of Tspan8 overexpressing tumors as described for hepatocellular cancer. Similar to other tetraspanins, Tspan8 is abundantly present in exosomes, where it accounts via its association with CD49d for endothelial cell and endothelial cell progenitor targeting with the consequence of endothelial cell activation and endothelial cell progenitor maturation. Regulates cell motility and survival and is involved in the promotion of angiogenesis.

## Mutations

### Note

Not known in Homo sapiens.

## Implicated in

### Tumors of the gastrointestinal tract

#### Note

CO-029 is associated with tumor progression and is supposed to promote metastasis formation. It has been described as a marker of several types of carcinomas and sarcomas. In gastrointestinal tumors the expression of CO-029 has been associated with a poor prognosis.

#### Disease

Gastric tumors, colorectal tumors, pancreatic tumors and liver tumors.

## Hepatocellular carcinoma (HCC)

### Note

Tetraspanin CO-029 was found to be frequently and significantly overexpressed in HCC. CO-029 was overexpressed in poorly differentiated HCCs compared with well to moderately differentiated tumors, and in HCCs showing intrahepatic spreading compared with those without spreading.

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