IGSF8 (immunoglobulin superfamily, member 8)

Yanhui H Zhang, Mekel M Richardson, Xin A Zhang

Vascular Biology and Cancer Centers and Departments of Medicine and Molecular Science, University of Tennessee Health Science Center, Memphis, USA (YHZ, MMR, XAZ)

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**Identity**

**Other names:** CD316, CD81P3, EW1-2, EW12, KCT-4, LIR-D1, PGRL

**HGNC (Hugo):** IGSF8

**Location:** 1q23.2

**Local order:** Centromere -- PIGM - KCNJ10 - LOC100287448 - KCNJ9 - CD316/IGSF8 - ATP1A2 - ATP1A4 - CASQ1 - PEA15 -- Telomere (NCBI Map Viewer).

**DNA/RNA**

**Description**

Gene type: protein coding.

Gene size: 7604 bp, 7 exons.

**Transcription**

mRNA 2366 bp (length may vary for alternative splicing forms).
The CD316/IGSF8 gene typically contains 7 exons. The green bars represent the non-coding exons while the blue bars represent the coding ones. The length of each intron is indicated above and the size of each exon is indicated below (information sourced from Ensembl (ENSG00000162729)).

There are 5 transcripts (Ensembl).

<table>
<thead>
<tr>
<th>Name</th>
<th>Transcript ID</th>
<th>Length (bp)</th>
<th>Protein ID</th>
<th>Length (aa)</th>
<th>Exon</th>
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<tbody>
<tr>
<td>IGSF8-001</td>
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<td>ENSP00000316664</td>
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<td>ENST00000460351</td>
<td>876</td>
<td>No protein product</td>
<td>-</td>
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</tbody>
</table>

There are 7 putative alternative splicing forms (AceView).

<table>
<thead>
<tr>
<th>IGSF8 alternative variant</th>
<th>mRNA size (bp)</th>
<th>Exons</th>
<th>NCBI 36, March 2006 genome (kb)</th>
<th>Aa</th>
<th>Protein size (kDa)</th>
<th>pI</th>
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<td>7.36</td>
<td>674</td>
<td>71.8</td>
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<td>311</td>
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<td>eApr07-unspliced</td>
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<td>1</td>
<td>6.18</td>
<td>166</td>
<td>18.1</td>
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<td>fApr07 (partial mRNA)</td>
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<td>4.71</td>
<td>165</td>
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<tr>
<td>variant gApr07-unspliced</td>
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<td>0.58</td>
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<td>9.6</td>
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</table>

**Pseudogene**

IGSF8-004, an alternative splicing form of IGSF8/CD316, is predicted to have no protein product (Ensembl).

**Protein**

**Description**

613 amino acids, molecular weight is 65034 Da. Basal isoelectric point: 8.23 (PhosphoSitePlus).

**Expression**

CD316 mRNA is ubiquitously expressed in human tissues, with high expression in brain, kidney, testis, liver and placenta, with low expression in peripheral blood cells, lung, and skeletal muscle.

CD316 protein is highly expressed in human brain (cortex, white matter, hippocampus and cerebellum), astrocytes, hepatocytes and lymphoid cells (majority of B-cells, T-cells and natural killer cells, but not on monocytes, polymorphonuclear cells and platelets). CD316 is constitutively expressed on plasmacytoid dendritic cells and on cord blood-derived Langerhans-like cells. Upon stimulation, CD316 is expressed on monocytes, monocytes derived dendritic cells and myeloid dendritic cells.

**Localisation**

Plasma membrane, cell-cell contacts, microvilli.

**Function**

1. Suppresses cell movement and cell aggregation.
2. Regulates integrin alpha3beta1- and alpha4beta1-dependent cell morphology and cell spreading.
3. May participate in the regulation of neurite outgrowth and maintenance of the neural network in the adult brain.
4. Interacts with its ligand, HSPA8, and may influence the behavior of dendritic cells and control adaptive immune response.
5. Links tetraspanin web to the actin cytoskeleton through direct associations with ezrin-radixin-moesin proteins.
6. Inhibits glioblastoma growth in vitro and in vivo.
7. EWI-2 wint inhibits hepatitis C virus entry.
8. May play a role in fertilization. Lack of CD316 present at the cell surface of CD9-null oocytes may contribute to the loss of ability of CD9-null oocytes to fuse with sperm.

CD316 typically inhibits cell migration and negatively regulates cell proliferation. It associates with tetraspanins CD9, CD81, and CD82 and likely contributes to various functions of these associated tetraspanins. It also regulates the functions of alpha3beta1 and alpha4beta1 integrins, probably through its associated tetraspanins (Clark et al., 2001; Stipp et al., 2001; Stipp et al., 2003; Zhang et al., 2003; Kolesnikova et al., 2004; Kolesnikova et al., 2009; Sala-Valdés et al., 2006).

**Mutations**

**Note**
Currently there is no known disease-related or biologically significant mutation (see HGMD).

**Implicated in**

**Glioma or glioblastoma**

**Note**
CD316 inhibits glioblastoma growth in vitro and in vivo. Loss of CD316 expression correlates with a shorter survival time in human glioma patients (Kolesnikova et al., 2009).

**Hepatitis and liver cancer**

**Note**
Hepatitis C virus (HCV)-infected population has higher risk of developing liver cancer. Ectopic expression of EWI-2wint, i.e., EWI-2 without its N-terminus, can inhibit HCV entry and reduce HCV infection (Rocha-Perugini et al., 2008).

**Autoimmune diseases**

**Note**
It was reported that CD316 is an inducible receptor of HSPA8 on human dendritic cells, it may control the adaptive immune response through its influence on the behavior of dendritic cells. Therefore it maybe utilized in the treatment of antoimmune diseases such as rheumatoid arthritis (Kettner et al., 2007).

**Infertility**

**Note**
CD316 plays a role in fertilization. Oocytes from CD9 null mice cannot fuse with sperm. The level of CD316 proteins on the CD9-null oocyte surface is less than 10% of that on the wild-type one. The loss of CD316 on the CD9-null oocyte surface may be responsible for the loss of fusion ability (He et al., 2009; Glazar et al., 2009).

**Type 2 diabetes mellitus**

**Note**
CD316 is a candidate for human disorders on 1q22-q23, including type 2 diabetes mellitus (Murdoch et al., 2003).

**To be noted**

EWI-2wint, a cleavage product of EWI-2 in which the first Ig-domain of the 4 extracellular Ig-domains is cleaved off.

**References**

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