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Gene Section
Mini Review

IGSF8 (immunoglobulin superfamily, member 8)

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Identity

Other names: CD316, CD81P3, EWI-2, EWI2, 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).

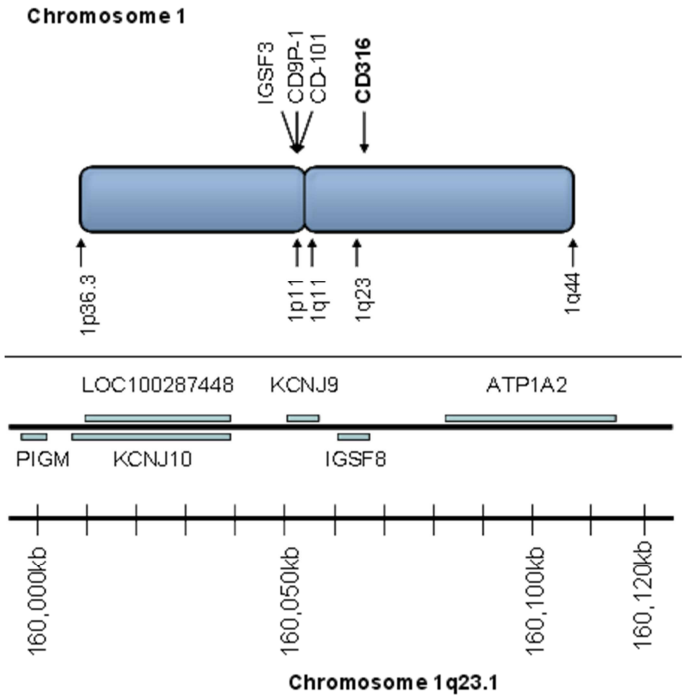
DNA/RNA

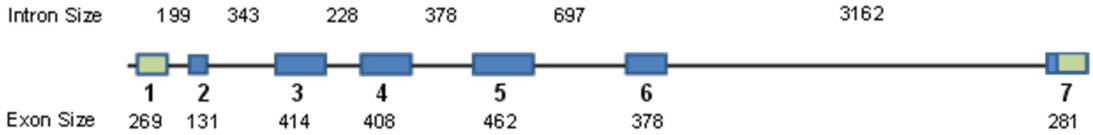
Description

Gene type: protein coding.
Gene size: 7604 bp, 7 exons.

Transcription

mRNA 2366 bp (length may vary for alternative splicing forms).





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).

Name	Transcript ID	Length (bp)	Protein ID	Length (aa)	Exon
IGSF8-001	ENST00000314485	2343	ENSP00000316664	613	7
IGSF8-002	ENST00000448417	1059	ENSP00000397464	301	4
IGSF8-003	ENST00000368086	2366	ENSP00000357065	613	7
IGSF8-201	ENST00000358475	2004	ENSP00000351261	526	8
IGSF8-004	ENST00000460351	876	No protein product	-	2

There are 7 putative alternative splicing forms (AceView).

IGSF8 alternative variant	mRNA size (bp)	Exons	NCBI 36, March 2006 genome (kb)	Aa	Protein size (kDa)	pI
aApr07	2352	7	7.36	674	71.8	8.2
bApr07	2304	8	7.60	664	70.4	8.3
cApr07	1995	4	2.92	311	32.7	8.2
dApr07	1005	4	5.58	283	30.5	6.7
eApr07-unspliced	6184	1	6.18	166	18.1	6.7
fApr07 (partial mRNA)	571	4	4.71	165	17.9	7.3
variant gApr07-unspliced (partial mRNA)	581	1	0.58 Appear non coding	91 Appear non coding	9.6 Appear non coding	11.5 Appear non coding

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, polynuclear 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.

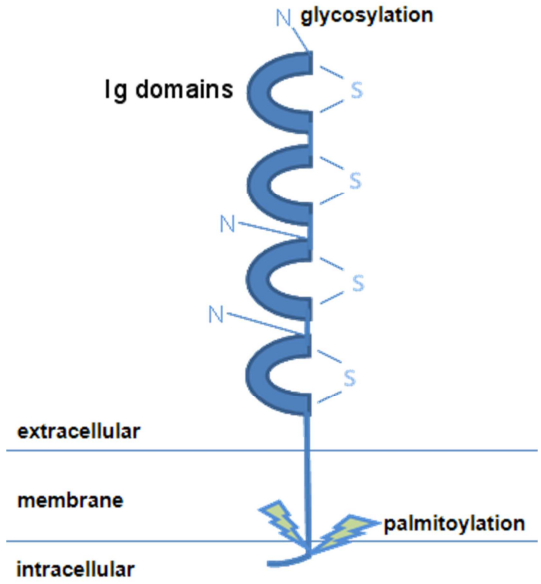
Localisation

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 sperms.
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).



Type I transmembrane protein CD316 contains an ectodomain that consists largely of four immunoglobulin domains, a transmembrane region, and a positively charged, 10-amino acid residue cytoplasmic tail. Glycosylation sites are found in the ectodomain and palmitoylation sites in the cytoplasmic domain. CD316 is constitutively palmitoylated and linked to actin cytoskeleton through direct association of its cytoplasmic domain with ezrin-radixin-moesin proteins. CD316 associates with tetraspanins such as CD9, CD81, and CD82.

Homology

CD316 protein is conserved in chimpanzee, cow, mouse, rat, and zebrafish and belongs to the EWI subfamily of Ig superfamily. Other human EWI subfamily proteins include FPRP/CD9P-1, IGSF3, and CD101.

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

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

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