

Gene Section

Mini Review

CAV1 (caveolin 1, caveolae protein, 22kDa)

Cristiana Tanase

"Victor Babes" National Institute of Pathology, 99-101, Splaiul Independentei, Sector 5, Bucharest, Romania (CT)

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Identity

Other names: CAV; VIP21; MSTP085

HGNC (Hugo): CAV1

Location: 7q31.2

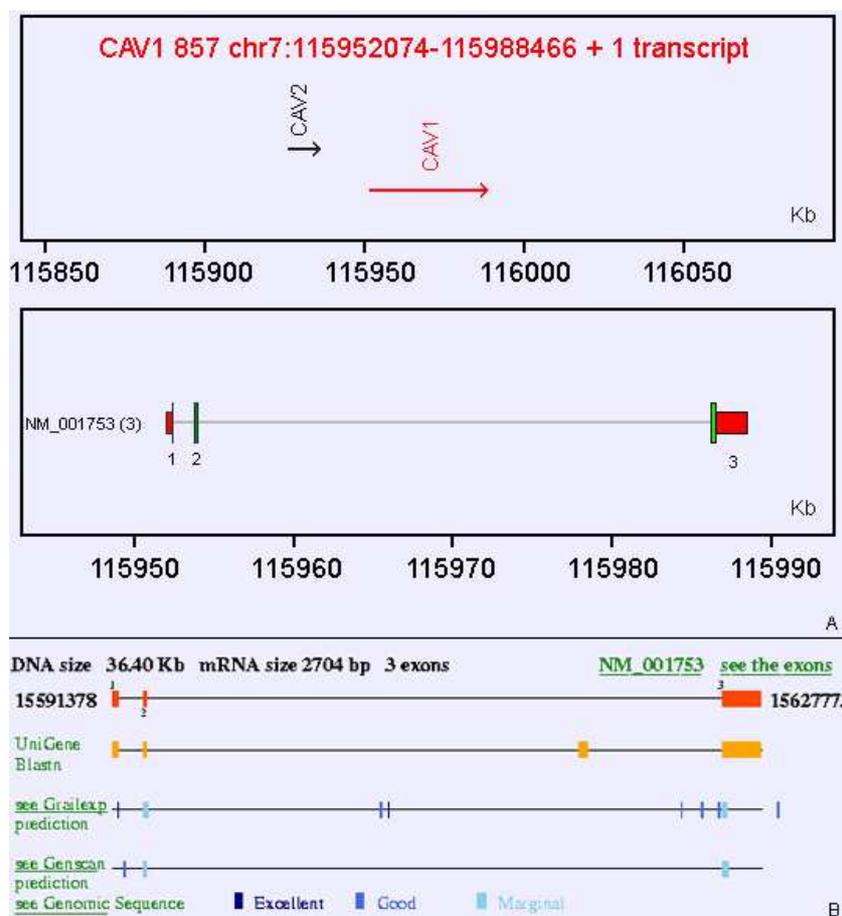
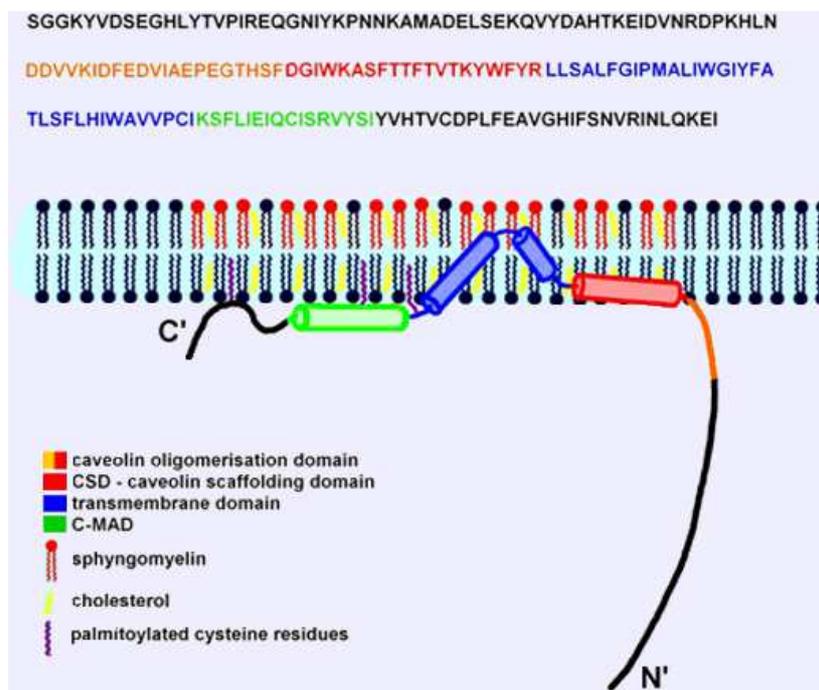


Figure A.

Figure B. present in the contig : [NT_079596](#) of Genbank.



Structure of caveolin-1. Primary structure of caveolin (upper part of the image) with aminoacids colored to illustrate classic domains considered within its molecule. Tertiary structure of caveolin depicted in the lower part of the image shows: 4 alpha-helices, one corresponding to CSD partially embedded in the membrane, 2 alpha-helices corresponding to the transmembrane domain and an alpha helix in C-terminal end with variable length according to different authors. A beta-sheet organized region is also thought to exist in the oligomerisation domain of CAV1.

DNA/RNA

Description

The gene consists of 3 exons (respectively 30, 165 and 342 bp long) separated by two introns of 1.5 kb and 32 kb. Two isoforms have been identified: caveolin-1alpha (corresponding to the 2-178 sequence) and caveolin-1beta (corresponding to the 32-178 sequence). The two isoforms are generated by alternative splicing of the CAV1 gene (Kogo et al., 2000) and by alternative initiation of the same mRNA translation (Shatz et al., 2008).

Protein

Description

CAV1 (21-24 kDa) is an integral membrane protein, expressing two isoforms (alpha and beta) of different length and distinct potential in caveolae formation. The full length CAV1 (isoform alpha, 178 aminoacids) has a hairpin-like structure spanning the plasmatic membrane, both C- and N-termini facing the cytosol. The beta isoform is 31 aminoacids shorter and is translated from the same mRNA as the longer form, but at divergent translation initiation sites. Both isoforms have two hydrophilic domains at the C- and N-termini, that flank a hydrophobic central domain. Several functional domains were defined. The membrane attachment domains are located at the N- and C-

termini and are designated as N-MAD (residues 82-101) and C-MAD (residues 135-150). CAV1 contains palmitoylation sites on Cys 133, 143 and 156, involved in membrane anchorage. The central region (residues 102-134) (TMD) was first suggested to be the transmembrane domain, but, after predicting its beta-sheet rather than alpha-helix conformation, it was suggested that it is involved in hetero-oligomerization of CAV1 with caveolin-2 and in specific interactions with other proteins. The caveolin scaffolding domain (CSD), located at the N-terminus (aminoacids 82-101), is involved in the binding and inhibition of proteins containing a defined caveolin binding motif, such as ω xxxx ω xx ω or ω x ω xxxx ω - where ω is an aromatic aminoacid (Trp, Phe or Tyr). The oligomerization domain (aminoacids 61-101) contains CSD and directs the formation of homooligomers (14-16 CAV1 molecules), which interact with cholesterol and signaling molecules.

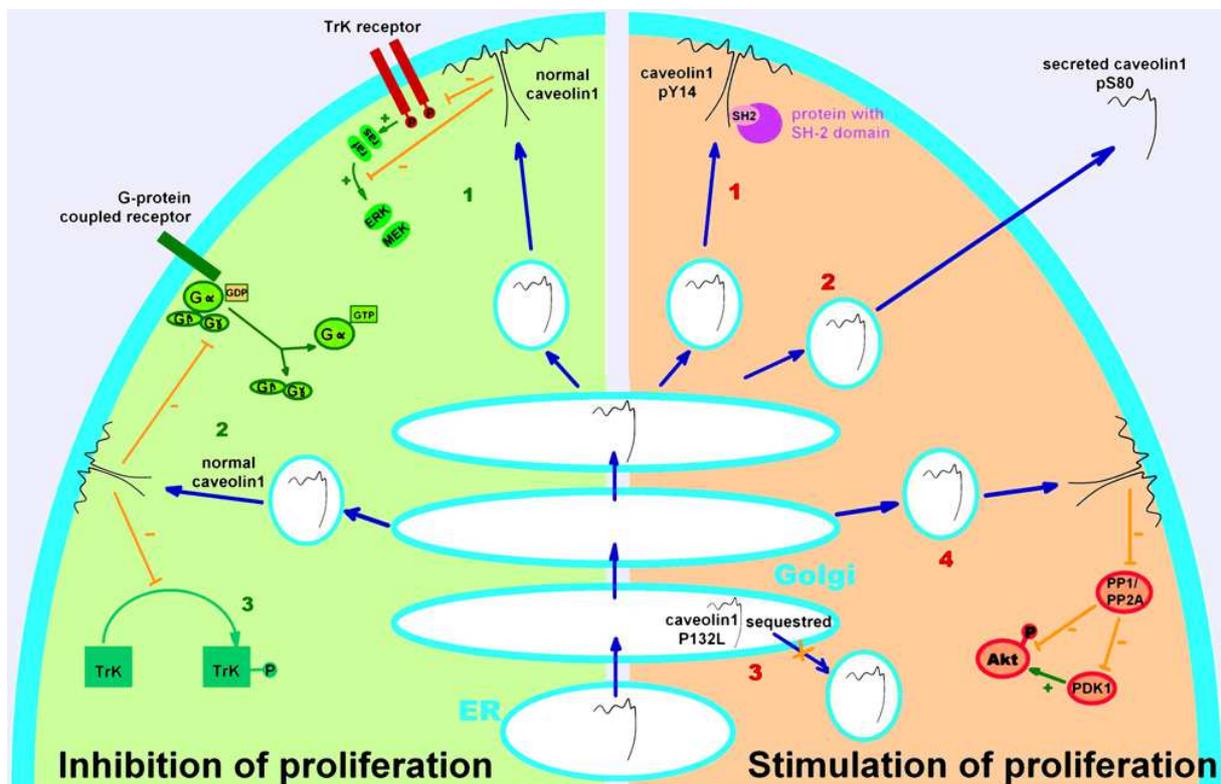
The structure of CAV1 underlies two separate important functions of the protein: membrane attachment and protein-protein interaction. CAV1 is reported to be involved in various cellular functions, like vesicular transport and regulation of signal transduction in cellular adhesion, growth, and survival.

Expression

The table below shows the expression of CAV1 in different organs and tissues.

Systems	Organs	Expression
Cardiovascular	heart	moderate
Vessel	-	predominant
Digestive	esophagus	high
Lymphoid/Immune	spleen	high
Reproductive	uterus	moderate
Respiratory	lung	moderate
Skin/Tegument	-	high

Tissue	Type	Expression
Connective	adipose	high
Muscular	smooth	-



Localisation

CAV1 is localized in the cytoplasmic side of the peripheral membrane of the cell in caveolae and in the Golgi apparatus membrane. Membrane protein of caveolae. Potential hairpin-like structure in the membrane.

Function

- Transforming suppressor activity in T cell leukemia.
- Playing a functional role in a novel post-Golgi trafficking pathway.
- Playing a crucial role in the mechanisms that

coordinate lipid metabolism with the proliferative response occurring in the liver after cellular injury.

- Being essential for liver regeneration.
- Regulating the trafficking of SLC1A1 on and off the plasma membrane.
- As an important regulator of downstream signaling and membrane targeting of EPHB1.
- CAV1 represents a key switch between tumor suppression and metastases promotion.

Homology

The table below shows the homology of CAV1 with different organisms.

Organism	Gene	Description	Human Similarity	NCBI accessions
Dog (<i>Canis familiaris</i>)	Cav1	caveolin 1, caveolae protein, 22kDa	93.97 (n), 96.61 (a)	403980 NM_001003296.1 NP_001003296.1
Chimpanzee (<i>Pan troglodytes</i>)	Cav1	caveolin 1, caveolae protein, 22kDa	100 (n), 100 (a)	463670 XM_519325.2 XP_519325.2
Cow (<i>Bos taurus</i>)	Cav1	caveolin 1, caveolae protein, 22kDa	93.63(n), 96.07 (a)	281040 NM_174004.3 NP_776429.1
Rat (<i>Rattus norvegicus</i>)	Cav1	caveolin, caveolae protein 1	92.51 (n), 94.38 (a)	25404 NM_031556.1 NP_031642.1
Mouse (<i>Mus musculus</i>)	Cav1	caveolin, caveolae protein 1	92.32 (n), 94.94 (a)	12389 NM_007616.3 NP_031642.1 AB029929 AB029930
Chicken (<i>Gallus gallus</i>)	Cav1	caveolin 1, caveolae protein, 22kDa	82.84 (n), 86.39 (a)	373996 XM_001234147.1 XP_001234148.1
Zebrafish (<i>Danio rerio</i>)	Dr.25966	Transcribed sequence with strong similarity to protein	94.48 (n)	CD590363.1
African clawed frog (<i>Xenopus laevis</i>)	MGC68815	Hypothetical protein MGC68815	78.12 (n)	BC061678.1
Tropical Clawed frog (<i>Silurana tropicalis</i>)	Str.8474	Transcribed sequence with moderate similarity to protein	82.38 (n)	CF345371.1

Mutations

Somatic

Converting proline-132 to leucine is a dominant-negative mutation of caveolin-1 that occurs in 16% of primary human breast cancer. Also identified six novel CAV1 mutations associated with ERalpha-positive breast cancers (W128Stop, Y118H, S136R, I141T, Y148H, and Y148S) (Li et al., 2006). This point mutation in the membrane spanning domain leads to mislocalization and intracellular retention of endogenous caveolin-1 and causes morphological transformation in NIH3T3 cells (Hayashi et al., 2001; Lee et al., 2002).

Converting isoleucine-141 to phenylalanine is a missense mutation of caveolin-1 found in human oral squamous cell carcinoma (Han et al., 2004).

Implicated in

Note

Clinical studies accordingly validated high caveolin-1 expression as a negative prognostic factor for the overall and/or disease-free survival in patients with tumors of gastrointestinal (GI) tract (esophagus and oral cavity, pancreas, kidney), prostate, breast, lung, and brain (meningioma). For other entities, including the GI-tract (stomach, colon, liver), bladder, thyroid, brain (glioma) and Ewing's sarcoma, increased caveolin-1 expression compared to matched normal tissue was validated by several independent detection methods (immunohistochemistry, pPCR, cDNAarray), however correlation with clinical outcome is pending (Burgermeister et al., 2008).

Pancreatic cancer

Prognosis

CAV1 expression is increased in pancreatic adenocarcinoma relative to peritumoral tissue. CAV1 expression correlates with tumor size, histological grade, conventional tissue marker for tumor progression and with reduced survival time after tumor resection. Increased CAV1 expression is an independent unfavorable prognostic factor following surgical resection (Tanase, 2008; Suzuoki et al., 2002).

Prostate cancer

Prognosis

CAV1 expression is increased in metastatic human prostate cancer and that CAV1 cellular protein expression is predictive of recurrence of the disease after radical prostatectomy. Recently, we reported that CAV1 is secreted by androgen-insensitive prostate cancer cells, and we detected, by Western blotting, CAV1 in the high-density lipoprotein(3) fraction of serum specimens from patients with prostate cancer (Tahir et al., 2003).

Lung cancer

Prognosis

Overexpression of caveolin-1 is significantly correlated with a poor prognosis in patients with pleomorphic carcinoma of the lung (PCL) and that it is a marker for predicting prognosis in PCL (Moon et al., 2005).

Tyroid papillary carcinoma

Prognosis

Studies investigated caveolin-1 expression in thyroid neoplasms by means of immuno-histochemistry.

Normal follicular cells did not express caveolin-1. In papillary carcinoma, caveolin-1 expression was observed in high incidence, and especially in microcancer (Ito et al., 2002).

Brain tumors

Prognosis

All studied astrocytomas of any grade (from II to IV) were CAV1 positive, displaying staining patterns and intensity specifically associated to the different tumor grades. In glioblastomas and gliosarcomas, CAV1 staining is extremely intense, typically localized at the cell membrane and recognized a variable percentage of cells, including the majority of spindle cells and palisade-oriented perinecrotic cells. In contrast oligodendrogliomas lacks CAV1 immunoreactivity. A well structured membrane pattern of CAV1 associates with tumor progression, suggesting a neoplastic shift towards a mesenchymal phenotype (Cassoni et al., 2007).

Mammary carcinoma

Prognosis

No Caveolin-1 expression was observed in epithelial cells of normal breast tissue, benign breast disease and ductal carcinoma in situ. However, Caveolin-1 expression was found in 32 of 109 cases of invasive breast carcinomas (29.4%). Caveolin-1 expression in invasive breast cancer could neither be correlated with survival parameters such as overall or disease-free survival nor with established clinical and pathological markers (Liedtke et al., 2007).

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