

Gene Section

Mini Review

TRPV6 (transient receptor potential cation channel, subfamily V, member 6)

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Identity

Other names: CaT1; ECaC2; CATL; ABP/ZF; LP6728; ZFAB

HGNC (Hugo): TRPV6

Location: 7q34

Local order: Colocalized with another Ca²⁺-selective epithelial channel gene, TRPV5.

DNA/RNA

Description

TRPV6 gene consists of 15 exons and 14 introns including a coding, and a 5'-/3'- non-coding region.

The regions encoding the ankyrin repeats, 6 transmembrane domains and a pore region are indicated. Several VDREs (vitamin D responsive element) have been identified in its promoter region.

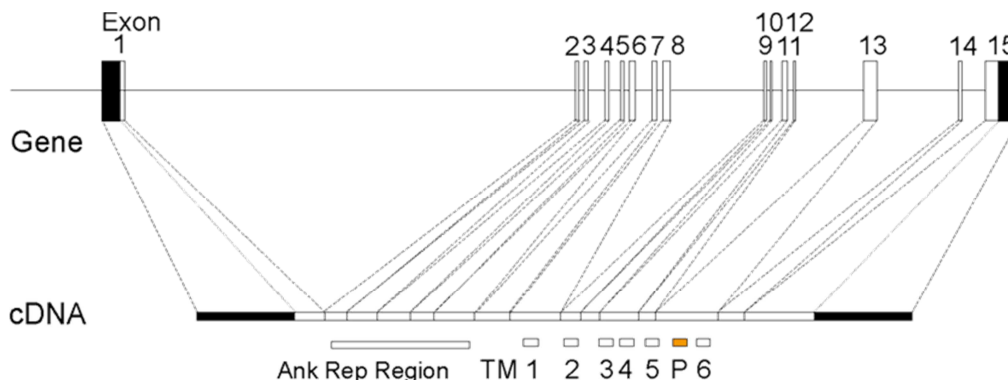
A haplotype containing 3 non-synonymous polymorphisms (C157R+M378V+M681T) represent a recent positive selection in human evolution. The same haplotype seems to be associated with renal calcium stone formation.

Transcription

There is an alternative splice variant which missed 25-192 (a.a.). In EST database, there seems to be at least one more variant using different exon 1 (V2) and a variant starting from another site (P3) just upstream of exon 2 (V3).

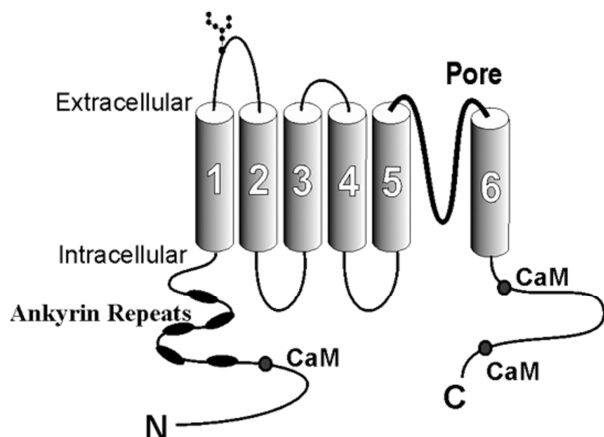


Schematic representation of human TRPV6 gene and neighbouring genes.



Genomic structure of human TRPV6. The coding region is shown by open bars. The non-translated regions are shown by filled bars.

Protein



Schematic representation of TRPV6 protein. Four subunits makes one channel pore. Several ankyrin repeats, one N-glycosylation site and several calmodulin binding sites (CaM) are indicated.

Description

Glycosylated membrane protein (725 a.a., MW ~70 kDa) with 6 transmembrane regions and a pore-forming loop. N- and C-terminal tails are in cytoplasmic side. This protein forms a Ca^{2+} -selective ion channel in the plasma membrane. TRPV6 interacts with calmodulin which contribute to the intracellular Ca^{2+} -dependent inactivation to avoid an increase of free Ca^{2+} concentration. The ankyrin repeats may play a role in the interaction between subunits. TRPV6 can form a homo-tetramer as well as a hetero-tetramer with TRPV5, which exhibits distinct channel properties.

Expression

Highly expressed in placenta, moderately expressed in exocrine pancreas, mammary gland and salivary gland. Highly induced in small intestine under low calcium conditions or by 1,25-dihydroxyvitamin D3 treatment. Highly induced in prostate, breast and other cancer tissues during tumor progression.

Localisation

Plasma membrane. Localized in the apical membrane of the epithelial cells in the duodenum, and syncytiotrophoblasts in placenta.

Function

Apical Ca^{2+} entry pathway for total body calcium homeostasis in the small intestine under the control of 1,25-dihydroxyvitamin D3. TRPV6 likely also be involved in the placental Ca^{2+} transport from mother to fetus to maintain fetal bone mineralization. TRPV6 may play a role in the Ca^{2+} entry pathway essential for keratinocyte differentiation. Although its exact function in cancer cells and tumor progression is still under investigation, TRPV6 is involved in an

increase in proliferation and apoptotic resistance in cancer cells.

Homology

73% identity with human TRPV5. 89% identity with mouse TRPV6.

Implicated in

Prostate cancer

Oncogenesis

Expression of TRPV6 may be a predictor for prostate cancer progression since TRPV6 mRNA and protein levels are elevated in prostatic carcinoma compared to benign prostatic hyperplasia and positively correlated with Gleason grade/score in prostatic carcinoma. TRPV6 is involved in an increase in proliferation and apoptotic resistance in cancer cells, suggesting that TRPV6 could be a new therapeutic target for the treatment for advanced prostate cancer.

Breast cancer

Oncogenesis

TRPV6 mRNA was also found to be increased in breast cancer tissues compared to normal breast tissues. TRPV6 could be a prognostic marker for breast cancer and therapeutic target for breast cancer treatment.

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