**Transient receptor potential cation channel, subfamily C, member 2**, also known as **TRPC2**, is a [protein](https://en.wikipedia.org/wiki/Protein) that in humans is encoded by the *TRPC2*[pseudogene](https://en.wikipedia.org/wiki/Pseudogene). This protein is not expressed in humans but is in certain other species such as mouse.

Thought to form a receptor-activated calcium permeant cation channel. Probably is operated by a phosphatidylinositol second messenger system activated by receptor tyrosine kinases or G-protein coupled receptors. Is not activated by intracellular calcium store depletion.

<https://www.ncbi.nlm.nih.gov/gene/7221>

transient receptor potential cation channel subfamily C member 2 (pseudogene)

Biased expression in bone marrow (RPKM 1.0), lung (RPKM 0.4) and 11 other tissues

<https://www.ncbi.nlm.nih.gov/pubmed/17217050>

TRPC (canonical transient receptor potential) channels are the closest mammalian homologs of Drosophila TRP and TRP-like channels. TRPCs are rather nonselective Ca2+ permeable cation channels and affect cell functions through their ability to mediate Ca2+ entry into cells and their action to collapse the plasma membrane potentials. In neurons the latter function leads to action potentials. The mammalian genome codes for seven TRPCs of which TRPC2 is the largest with the most restricted pattern of expression and has several alternatively spliced variants. Expressed in model cells, TRPC2 mediates both receptor- and store depletion-triggered Ca2+ entry. TRPC2 is unique among TRPCs in that its complete gene has been lost from the Old World monkey and human genomes, in which its remnants constitute a pseudogene. Physiological roles for TRPC2 have been studied in mature sperm and the vomeronasal sensory system. In sperm, TRPC2 is activated by the sperm's interaction with the oocyte's zona pellucida, leading to entry of Ca2+ and activation of the acrosome reaction. In the vomeronasal sensory organ (VNO), TRPC2 was found to constitute the transduction channel activated through signaling cascade initiated by the interaction of pheromones with V1R and V2R G protein-coupled receptors on the dendrites of the sensory neurons. V1Rs and V2Rs, the latter working in conjunction with class I MHC molecules, activate G(i)- and G(o)-type G proteins which in turn trigger activation of TRPC2, initiating an axon potential that travels to the axonal terminals. The signal is then projected to the glomeruli of the auxiliary olfactory bulb from where it is carried first to the amygdala and then to higher cortical cognition centers. Immunocytochemistry and gene deletion studies have shown that (1) the V2R-G(o)-MHCIb-beta2m pathway mediates male aggressive behavior in response to pheromones; (2) the V1R-G(i2) pathway mediates mating partner recognition, and (3) these differences have an anatomical correlate in that these functional components are located in anatomically distinct compartments of the VNO. Interestingly, these anatomically segregated signaling pathways use a common transduction channel, TRPC2.

<https://www.ncbi.nlm.nih.gov/pubmed/17517433>

Receptor-activated Ca(2+) influx is mediated largely by store-operated channels (SOCs). TRPC channels mediate a significant portion of the receptor-activated Ca(2+) influx. However, whether any of the TRPC channels function as a SOC remains controversial. Our understanding of the regulation of TRPC channels and their function as SOCs is being reshaped with the discovery of the role of STIM1 in the regulation of Ca(2+) influx channels. The findings that STIM1 is an ER resident Ca(2+) binding protein that regulates SOCs allow an expanded and molecular definition of SOCs. SOCs can be considered as channels that are regulated by STIM1 and require the clustering of STIM1 in response to depletion of the ER Ca(2+) stores and its translocation towards the plasma membrane. TRPC1 and other TRPC channels fulfill these criteria. STIM1 binds to TRPC1, TRPC2, TRPC4 and TRPC5 but not to TRPC3, TRPC6 and TRPC7, and STIM1 regulates TRPC1 channel activity. Structure-function analysis reveals that the C-terminus of STIM1 contains the binding and gating function of STIM1. The ERM domain of STIM1 binds to TRPC channels and a lysine-rich region participates in the gating of SOCs and TRPC1. Knock-down of STIM1 by siRNA and prevention of its translocation to the plasma membrane inhibit the activity of native SOCs and TRPC1. These findings support the conclusion that TRPC1 is a SOC. Similar studies with other TRPC channels demonstrate their regulation by STIM1 and indicate that all TRPC channels, except TRPC7, function as SOCs.

**Pseudogenes** are segments of DNA that are related to real [genes](https://en.wikipedia.org/wiki/Gene). Pseudogenes have lost at least some functionality, relative to the complete gene, in [cellular](https://en.wikipedia.org/wiki/Cell_(biology)) [gene expression](https://en.wikipedia.org/wiki/Gene_expression) or [protein](https://en.wikipedia.org/wiki/Protein)-coding ability.[[3]](https://en.wikipedia.org/wiki/Pseudogene#cite_note-Biomed10.1186-3)Pseudogenes often result from the accumulation of multiple [mutations](https://en.wikipedia.org/wiki/Mutation) within a gene whose product is not required for the survival of the organism, but can also be caused by genomic [copy number variation (CNV)](https://en.wikipedia.org/wiki/Copy-number_variation) where segments of 1+ kb are duplicated or deleted.[[4]](https://en.wikipedia.org/wiki/Pseudogene#cite_note-4) Although not *fully* functional, pseudogenes may be functional, similar to other kinds of [noncoding DNA](https://en.wikipedia.org/wiki/Noncoding_DNA), which can perform [regulatory functions](https://en.wikipedia.org/wiki/Regulation_of_gene_expression). The "pseudo" in "pseudogene" implies a variation in sequence relative to the parent coding gene, but does not necessarily indicate pseudo-function. Despite being non-coding, many pseudogenes have important roles in normal physiology and abnormal pathology.[[5]](https://en.wikipedia.org/wiki/Pseudogene#cite_note-pmid25391452-5)

Although some pseudogenes do not have [introns](https://en.wikipedia.org/wiki/Intron) or [promoters](https://en.wikipedia.org/wiki/Promoter_(genetics)) (such pseudogenes are copied from [messenger RNA](https://en.wikipedia.org/wiki/Messenger_RNA) and incorporated into the [chromosome](https://en.wikipedia.org/wiki/Chromosome), and are called "processed pseudogenes"),[[6]](https://en.wikipedia.org/wiki/Pseudogene#cite_note-6) others have some gene-like features such as promoters, [CpG islands](https://en.wikipedia.org/wiki/CpG_island), and [splice sites](https://en.wikipedia.org/wiki/RNA_splicing). They are different from normal genes due to either a lack of protein-coding ability resulting from a variety of disabling mutations (e.g. premature [stop codons](https://en.wikipedia.org/wiki/Stop_codon) or [frameshifts](https://en.wikipedia.org/wiki/Frameshift)), a lack of [transcription](https://en.wikipedia.org/wiki/Transcription_(genetics)), or their inability to encode RNA (such as with [ribosomal RNA](https://en.wikipedia.org/wiki/Ribosomal_RNA) pseudogenes). The term "pseudogene" was coined in 1977 by Jacq *et al.*[[7]](https://en.wikipedia.org/wiki/Pseudogene#cite_note-pmid561661-7)

Because pseudogenes were initially thought of as the last stop for genomic material that could be removed from the genome,[[8]](https://en.wikipedia.org/wiki/Pseudogene#cite_note-Zheng-8) they were often labeled as [junk DNA](https://en.wikipedia.org/wiki/Junk_DNA). Nonetheless, pseudogenes contain biological and [evolutionary](https://en.wikipedia.org/wiki/Evolution) histories within their sequences. This is due to a pseudogene's shared ancestry with a functional gene: in the same way that [Darwin](https://en.wikipedia.org/wiki/Charles_Darwin) thought of two species as possibly having a shared [common ancestry](https://en.wikipedia.org/wiki/Common_descent)followed by [millions of years of evolutionary divergence](https://en.wikipedia.org/wiki/Speciation), a pseudogene and its associated functional gene also share a common ancestor and have diverged as separate genetic entities over millions of years.

<http://www.uniprot.org/uniprot/Q3C1U7>

[calcium channel activity](https://www.ebi.ac.uk/QuickGO/term/GO:0005262)

<https://www.ncbi.nlm.nih.gov/pubmed/27099524>

| **Gene** | **CL** | **SNP** | **BPs** | **A1** | **FM** | **FC** | **A2** | ***χ*2** | **OR** | ***P*-value** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| *TRPC2* | 11 | rs7108612 | 3,628,856 | T | 0.1923 | 0.06667 | G | 4.509 | 3.333 | 0.03372 |
| *TRPC2* | 11 | rs6578398 | 3,616,831 | A | 0.3462 | 0.1833 | G | 4.506 | 2.358 | 0.03378 |

| **Gene** | **CL** | **SNP** | **Genotype** | **ME/CFS, n (%)** | **Unfatigued controls, n (%)** | ***χ*2** | **OR** | ***P*-value** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| *TRPC2* | 11 | rs7108612 | GT | 15 (78.9) | 4 (21.1) | 5.37 | 4.06 | 0.021 |

**Notes:** Genotypes from 39 ME/CFS patients and 30 unfatigued controls. Data presented all *P*<0.05; *df*=1 for basic allelic test.