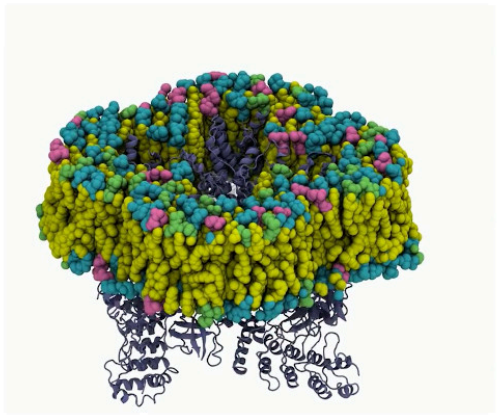
UAB DIVULGA
BARCELONA RECERCA I INNOVACIÓ

23/04/2024

TRPV2 ion channel paves the way to more effective therapies for hypertension



Researchers at the UAB have carried out two revealing studies on TRPV2, a key ion channel in several cellular functions, which points to it as a possible new therapeutic target in the treatment of hypertension. They have discovered the vessel-dilating effects of its activation and have identified a molecule capable of activating it in a more potent way than the drugs known to date.

TRPV2 ion channel is formed by proteins that can be found in the membrane of some cells. When activated, they allow the entry of positive ions from the extracellular environment, changing the state of the cell and temporarily modifying aspects such as its ability to replicate, to contract (in the case of muscle cells) or even causing its death.

TRPV2 are important in cardiac and neuromuscular function, immunity and metabolism; and they are associated with pathologies such as muscular dystrophy and cancer. However, their ability to interact with other molecules is still largely unknown. For this reason, in two studies conducted by members of the Department of Pharmacology, Therapeutics, and Toxicology, the Department of Biochemistry and Molecular Biology, and the Institut de Neurociències at the UAB, these proteins were studied in depth.

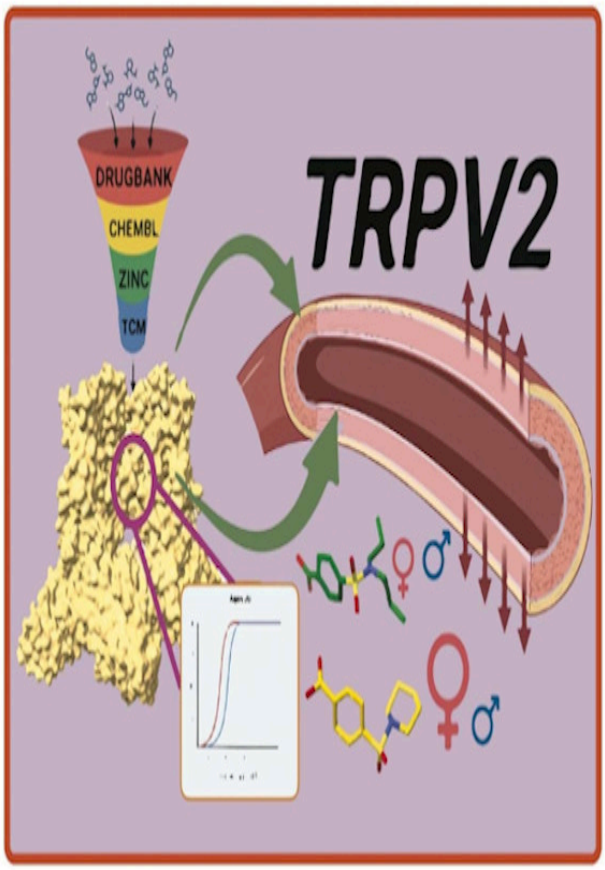
In the first study, coordinated by Dr. Francesc Jiménez-Altayó and published in th
Life Sciences, we analyzed in male mice the mechanisms involved in the contrac

relaxation of blood vessels due to TRPV2 activation. We saw that TRPV2 produces multiple effects in the different layers of the blood vessel, resulting in vasodilation.

This is important because it is the first time that the processes triggered by the activation of TRPV2 in blood vessels have been identified and have been described as leading to their dilation. This study represents a very important starting point for using TRPV2 activation as a therapeutic strategy against diseases that cause excessive vasoconstriction, such as hypertension.

In a second study coordinated by Dr. Álex Perálvarez-Marín, published in the Computational and Structural Biotechnology Journal, we used computer techniques (*in silico* analysis) to identify a set of 270 molecules that, due to their physical and chemical characteristics, could interact with TRPV2. We grouped them into families based on how each of these molecules would bind to TRPV2 and, by expressing the TRPV2 protein in yeast, we designed a screening system to test their effects. This allowed us to find a molecule (4-piperidin-1-sulfonyl-benzoic acid) capable of activating this protein more powerfully than the only drug known to do so until now: probenecid.

Therefore, the activation of TRPV2 produced by the new molecule identified in this study has a very interesting vasodilator effect that suggests it might be a good candidate for antihypertensive therapy. Furthermore, an effect linked to the sex of the mice has been observed, which opens the door to a therapy adjusted and personalized to each patient, especially due to the sex bias in drug prescription. However, further studies will have to determine the possible viability and commercialization of this molecule as a medicine.



Graphical summary of the structure and function of the TRPV2 ion channel.

Alex Perálvarez-Marín
Department of Biochemistry and Molecular Biology
Area of Biochemistry and Molecular Biology
Alex.Perálvarez@uab.cat

Francesc Jiménez Altayó
Department of Pharmacology, Therapeutics and Toxicology
Pharmacology Area
Francesc.Jiménez@uab.cat

References

1. Catalina-Hernández È, López-Martín M, Masnou-Sánchez D, Martins M, Lorenz-Fonfria VA, Jiménez-Altayó F, Hellmich UA, Inada H, Alcaraz A, Furutani Y, Nonell-Canals A, Vázquez-Ibar JL, Domene C, Gaudet R, Perálvarez-Marín A. **Experimental and computational biophysics to identify vasodilator drugs targeted at TRPV2 using agonists based on the probenecid scaffold.** *Comput Struct Biotechnol J*. 2023 Dec 29;23:473-482. doi: 10.1016/j.csbj.2023.12.028. PMID: 38261868; PMCID: PMC10796807.

2. Perálvarez-Marín A, Solé M, Serrano J, Taddeucci A, Pérez B, Penas C, Manich G, Jiménez M, D'Ocon P, Jiménez-Altayó F. **Evidence for the involvement of TRPV2 channels in the modulation of vascular tone in the mouse aorta**. *Life Sci.* 2024 Jan 1;336:122286. doi: 10.1016/j.lfs.2023.122286. Epub 2023 Nov 24. PMID: 38007144.

View low-bandwidth version