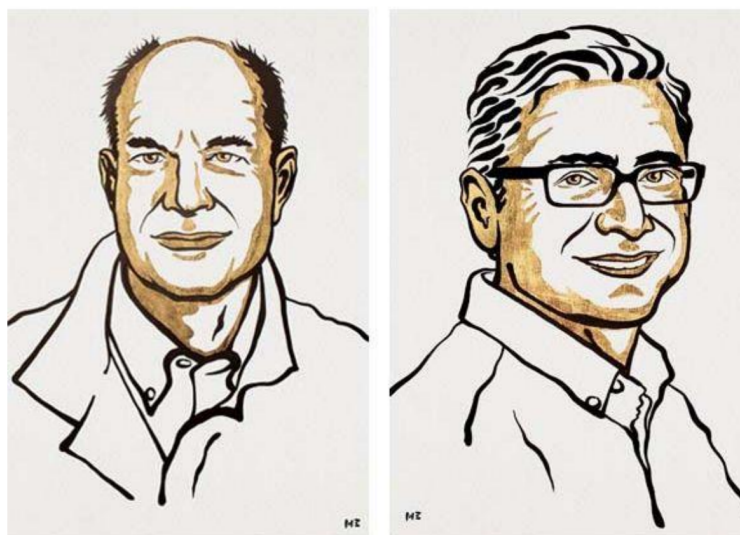




Nobel Prize 2021: Physiology/Medicine

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The 2021 Nobel Prize in Physiology or Medicine was awarded jointly to David Julius and Ardem Patapoutian “for their discoveries of receptors for temperature and touch” on Monday, 4 October 2021 by the Nobel Assembly at Karolinska Institutet. Independently of one another, both David Julius and Ardem Patapoutian used the chemical substance menthol to identify TRPM8, a receptor that was shown to be activated by cold.

Ardem Patapoutian is an American molecular biologist age 54 years and born to an Armenian family in Beirut, Lebanon. His father, known by the pen name Sarkis Vahakn, is a poet and an accountant. His mother, Haykuhi Achemian, was the principal of an Armenian school in Beirut. He has a brother and a sister. He enrolled at the American University of Beirut for a year before immigrating to the United States in 1986. His academic career can be summarised as follows:

- B.S. degree in cell and developmental biology from the University of California, Los Angeles in 1990;
- Ph.D. degree in biology from the California Institute of Technology in 1996, guided by Barbara Wold;
- Post doctorate at the University of California, San Francisco guided by Louis F. Reichardt Assistant professor at the Scripps Research Institute in 2000;
- Additional research position for the Novartis Research Foundation from 2000 to 2014;
- Investigator for the Howard Hughes Medical Institute (HHMI) since 2014.

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He and his co-workers found a cell line that gave off a measurable electric signal when individual cells were poked with a micropipette. Then they identified a single gene which upon gene silencing turned the cells insensitive to poking with the micropipette. Through further investigations two entirely unknown mechanosensitive ion channels Piezo1 and Piezo2 were discovered. Just like when poked with a micropipette, they are activated by the exertion of pressure on cell membranes. Piezo2 ion channel is essential for the sense of touch, play a role in proprioception (sensing of body position and motion). Both Piezo1 and Piezo2 channels have been shown to regulate physiological processes like blood pressure, respiration and urinary bladder control.

Two of his most important publications in this field were:

- (i) Kim, Sung Eun; Coste, Bertrand; Chadha, Abhishek; Cook, Boaz; Patapoutian, Ardem (February 19, 2012). "The role of Drosophila Piezo in mechanical nociception", *Nature* **483** (7388) 209–212; doi:10.1038/nature10801
- (ii) Ranade, Sanjeev S.; Woo, Seung-Hyun; Dubin, Adrienne E.; Moshourab, Rabih A.; Wetzel, Christiane; Petrus, Matt; Mathur, Jayanti; Bégay, Valérie; Coste, Bertrand; Mainquist, James; Wilson, A. J. (December 2014). "Piezo2 is the major transducer of mechanical forces for touch sensation in mice", doi:10.1038/nature13980

David Jay Julius is an American physiologist aged 66 and born to a family with Russian descent in New York, USA. His father was an electrical engineer and mother an elementary school teacher. He has two brothers. His academic career can be summarised as follows:

- Undergraduate degree from Massachusetts Institute of Technology in 1977;
- Ph.D. degree at the University of California, Berkeley in 1984, under joint supervision of Jeremy Thorner and Randy Schekman;
- Post doctorate at Columbia University in 1989, under the supervision of Richard Axel.

Julius was interested in serotonin receptors and its relation with psilocybin mushrooms, which questioned him how things from nature interact with human receptors. He and his co-workers created a library which included a DNA fragment encoding the protein capable of reacting to capsaicin. After individual genes were expressed in cultured cells, a single gene was identified that was able to make cells capsaicin sensitive. Further investigations revealed that this new gene encoded a novel ion channel protein with ability to respond to heat. The newly discovered capsaicin receptor was named TRPV1.

Three of his most important publications in this field were:

- (i) Bautista, Diana M.; Siemens, Jan; Glazer, Joshua M.; Tsuruda, Pamela R.; Basbaum, Allan I.; Stucky, Cheryl L.; Jordt, Sven-Eric; Julius, David (July 12, 2007). "The menthol receptor TRPM8 is the principal detector of environmental cold", *Nature* **448** (7150): 204–208, doi:10.1038/nature05910. ISSN 1476-4687.
- (ii) Jordt, Sven-Eric; Bautista, Diana M.; Chuang, Huai-Hu; McKemy, David D.; Zygmunt, Peter M.; Högestätt, Edward D.; Meng, Ian D.; Julius, David (January 15, 2004). "Mustard oils and cannabinoids excite sensory nerve fibres through the TRP channel ANKTM1", *Nature* **427** (6971): 260–265, doi:10.1038/nature02282.
- (iii) Liao, Maofu; Cao, Erhu; Julius, David; Cheng, Yifan (December 5, 2013). "Structure of the TRPV1 ion channel determined by electron cryo-microscopy", *Nature* **504** (7478): 107–112, doi:10.1038/nature12822.

Reference: <https://www.nobelprize.org/prizes/medicine/2021/press-release/>