

# EXPLAINED

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A challenge overcome: David Julius and Ardem Patapoutian honoured for discoveries of receptors for temperature and touch. | Photo Credit: [AFP](#)

**The story so far:** The [2021 Nobel Prize in Physiology or Medicine](#) was jointly awarded to David Julius, 66, at the University of California, San Francisco, and Ardem Patapoutian, 54, at Scripps Research, La Jolla, California, “for their discoveries of receptors for temperature and touch”.

Editorial | [Sensing heat: On 2021 Nobel Prize in Physiology or Medicine](#)

The two researchers discovered the molecular mechanism by which our body senses temperature and touch. Being able to do this opens the field for a lot of practical chemistry whereby individual cells and pathways can be tweaked, suppressed or activated to quell pain or sensation. How the body senses external stimuli is among the oldest excursions of natural philosophy. Entire schools of philosophy were based on speculating how the senses influenced the nature of the reality we perceive. Only when physiology developed as an independent discipline and anatomy came into its own did it become widely accepted that specific sensations were the result of different categories of nerves getting stimulated. Thus, a caress or a punch induces cells in our bodies to react differently and convert into specific patterns of electrical stimulation that is then conveyed via the nerves to the central nervous system. Since the Nobel Prizes came to be, at least three of them were for establishing key principles for how sensations travelled along skin and muscle sensory nerve fibres. Much like the length, thickness, material and incident force on their strings elicit specific tones out of a guitar or a piano, there are specific nerve fibre types that in tandem create a response to touch, heat and proprioception, or the sense of our body’s movement and position in space. However, the prominence of molecular biology means that physiology wanted to go a level deeper and find out what specific proteins and which genes are responsible in this symphony of the nerves.

Capsaicin (8-methyl-N-vanillyl-6-nonenamide), the active component of chili peppers, generates the burning sensation when eating spicy food. Studies on capsaicin showed that when it acted on sensory nerves it induced ionic currents, or the gush of charged particles along a membrane. In the late 1990s, Professor Julius pursued a project to identify a nerve receptor for capsaicin. He thought that understanding the action of capsaicin could provide insights into how the body sensed pain. He and his team went about this by looking for a gene that could induce a response to capsaicin in cells that usually wouldn’t react to it. They found one in a novel ion channel protein, later called TRPV1, where TRP stands for transient receptor potential, and VR1 is vanilloid receptor1. They were part of a super family of TRP and it was found that TRPV1 was activated when temperatures were greater than 40 degrees Celsius, which is close to the body’s pain threshold. Several other TRP channels were found, and this ion channel could be activated by various chemical substances, as well as by cold and heat in a way that differs between mammalian species.

Growing up in Beirut as an Armenian, during the Lebanese Civil War, Patapoutian has related stories of being captured by militants at university, before he moved to the United States. Patapoutian and his colleagues were working on how pressure and force affected cells. Following an approach similar to that of Professor Julius, they identified 72 potential genes that could encode an ion channel receptor and trigger sensitivity to mechanical force, and it emerged that one of them coded for a novel ion channel protein, called Piezo1. Via Piezo1, a second gene was discovered and named Piezo2. Sensory neurons were found to express high levels of

Piezo2 and further studies firmly established that Piezo1 and Piezo2 are ion channels that are directly activated by the exertion of pressure on cell membranes. The breakthrough by Professor Patapoutian led to a series of papers from his and other groups, demonstrating that the Piezo2 ion channel is essential for the sense of touch. Moreover, Piezo2 was shown to play a key role in proprioception as well as regulate blood pressure, respiration and urinary bladder control. Independently of one another, Professor Julius and Professor Patapoutian used the chemical substance menthol to identify TRPM8, a receptor activated by cold.

Along with the discoveries of specific genes, proteins and pathways, the scientists pioneered experimental methods that allow insight into the structure of these pain and temperature sensors. The challenge for pain relieving drugs is to precisely target regions without causing imbalance in other necessary functions. These scientists' work, the Nobel Prize committee said, significantly helped towards reaching that goal.

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Going by past experience, the FDA might greenlight the vaccine for young children in a matter of weeks. The company expects to submit data of children 2–4 years and 6 months to 1 year by the end of the year.

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