MEDICINE NOBEL FOR DUO WHO DISCOVERED BIOLOGY OF SENSES

David Julius and Ardem Patapoutian share award for uncovering how cells sense temperature and touch.

By Heidi Ledford & Ewen Callaway

Two researchers who discovered the molecular basis for our ability to sense temperature and touch have won this year's Nobel Prize in Physiology or Medicine.

Physiologist David Julius at the University of California, San Francisco, used capsaicin — the compound that gives chilli peppers their gustatory kick — to track down a protein called TRPV1 that responds to painful heat. Molecular neurobiologist Ardem Patapoutian at Scripps Research in La Jolla, California, identified receptors in skin and other organs that respond to mechanical forces, such as those generated by touch and pressure.

In addition to explaining the basic biology of such senses, the findings have potential medical applications: to combat chronic pain, researchers are looking for compounds that target some of the proteins Julius and Patapoutian discovered.

Making sense of senses

The pair's work provided crucial links between external stimuli — such as temperature or touch — and the electrical signals that drive nervous-system responses.

Capsaicin, for example, was known to trigger pain responses, but it was unclear how. In the 1990s, Julius and his colleagues searched through the genes that are switched on in response to pain, heat and touch to find one that would react to capsaicin. Their search led them to a gene that codes for TRPV1, a protein that forms a channel in cell membranes that, when activated, allows ions to pass through[1].

Patapoutian and his collaborators, meanwhile, were looking for molecules that became activated by mechanical forces. The team identified cells that emitted an electrical signal when prodded, and then hunted for genes that might control this response. This led to the discovery of two more ion channels, named Piezo1 and Piezo2, which are activated by pressure[2].

Julius and Patapoutian also independently used menthol — a compound that creates a cooling sensation — to study how cells respond to cold. This led to the discovery of another ion channel, called TRPM8, that is activated by cold[3].

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Ardem Patapoutian (L) and David Julius (R), recipients of the 2021 medicine Nobel prize.

"Both David and Ardem have really changed our understanding of sensory biology. I think it's a fantastic decision to have awarded this," says Michael Caterina, a neuroscientist at the Johns Hopkins University School of Medicine in Baltimore, Maryland, who was part of the team that identified the capsaicin-sensing TRPV1 channel in Julius's laboratory.

The identification of TRPV1 and other related pain-sensing proteins has helped researchers to understand the molecular basis of pain — and seek out new treatments. "We knew it had a chance of being medically important if it could explain some aspects of pain," says Caterina.

"It's a well-deserved award for Ardem and David, and very exciting to me," says Bailong Xiao, a biochemist at Tsinghua University in Beijing and a former postdoctoral researcher in Patapoutian's lab. Patapoutian's discovery of Piezo1 and Piezo2 was especially significant, Xiao says, because the molecules had little in common with other known ion channels, opening up fresh avenues of research for labs worldwide.

"There are a lot of medical problems involving pain and [these] receptors will, for sure, be targets for drug development in the future," medicine Nobel committee chair Nils-Göran Larsson said at the announcement ceremony.

Additional reporting by Tosin Thompson.

1. Caterina, M. *et al. Nature* **389**, 816–824 (1997).
2. Coste, B. *et al. Science* **330**, 55–60 (2010).
3. McKemy, D. D., Neuhausser, W. M. & Julius, D. *Nature* **416**, 52–58 (2002).

CLIMATE MODELLERS AND SYSTEMS THEORIST SHARE PHYSICS NOBEL

Syukuro Manabe, Klaus Hasselmann and Giorgio Parisi split the award for work on complex systems.

By Davide Castelvecchi & Nisha Gaind

Three researchers have won the 2021 Nobel Prize in Physics for their work on describing complex physical systems — including foundational research that created a pioneering mathematical model of Earth's climate and predicted that increasing levels of carbon dioxide in Earth's atmosphere would raise global temperatures.

Syukuro Manabe and Klaus Hasselmann share half of the prize for this modelling. Theoretical physicist Giorgio Parisi at the Sapienza University of Rome receives the other half for his contributions to the theory of complex systems. His work has affected many areas, from neuroscience to how granular materials pack, the Nobel committee said.

"These are two different prizes, but there is the common theme that has to do with this order, these fluctuations together that can give rise to something that we can understand and predict," said Thors Hans Hansson, chair of the physics Nobel committee. "We can predict what is happening with the climate in the future if we know how to code the chaotic weather."

Climate models

Manabe, now at Princeton University in New Jersey, showed in the 1960s how increased levels of carbon dioxide in Earth's atmosphere lead to increased temperatures at the surface, and developed early mathematical models of the planet's climate. Around a decade later, Hasselmann, at the Max Planck Institute for