Acceptance speech
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David Julius, awardee in the Biology and Biomedicine category (13th edition)

Pain is a critical protective sensation that warns us against harm from infection, cancer, and environmental forces. In doing so, it overrides other sensory and cognitive systems to urgently focus our attention on real or impending danger. But pain can outlive its usefulness as an acute and beneficial warning system and, instead, become persistent and debilitating, distracting us from life's daily pleasures and activities and significantly diminishing our quality of life. Indeed, chronic pain remains a major unmet medical need and widespread public health issue affecting millions of people throughout the world. The societal toll is further compounded by the over-dependence on morphine and other opiate analgesics with their attendant side effects and potential for abuse.

Pain is a complex physiological and behavioral response that engages the nervous system at many levels, from sensory nerve endings in the skin to emotional centers deep within the brain. Better strategies for assessing and treating pain require a deeper understanding of the basic biological mechanisms underlying the detection, transmission, and processing of pain signals at each stage along this pathway. This is a shared goal of scientists and clinicians throughout the world, including many friends and colleagues here in Spain. My own group has focused largely the first step in pain sensation whereby noxious signals from our bodies or the environment are initially detected by sensory nerve endings in the skin or other tissues, including muscle, bones, or the gut. What types of molecules enable nerve fibers to respond to physical factors, such as heat and cold, or to chemical irritants, such as acid? And if such molecules exist, how are their properties altered following physiological insults, such as inflammation or nerve damage, that promote chronic pain?

Answers to these questions emerged, in part, from my own long-term fascination with what one might call 'chemical neuroethology', or the study of how evolution and behavior converge to enable the discovery and use of natural products for culinary, spiritual, or medicinal purposes. Of course, exploiting natural products to uncover new molecules and signaling pathways is not unique to our work, and this approach has already played an outsized role in the pain world by yielding two of the most widely used classes of analgesic drugs, namely morphine from opium poppies and salicylate (aspirin) from willow bark. Taking inspiration from these examples, and from classic physiologic studies of Janscó Gábor in Hungary and Hensel and Zotterman in Sweden, we asked two simple questions: (i) what specific molecular mechanisms enable us to appreciate the pungent 'heat' of chili peppers or the refreshing 'coolness' of mint, and (ii) how do such mechanisms relate to our normal sensations of temperature and pain? Answers to these questions led to the discovery of heat- and cold-activated ion channels (TRPV1 and TRPM8, respectively), providing a unique molecular toehold into deciphering the neural logic of thermosensation, nociception and pain, while validating the sensory nerve fiber as a rational and selective target for novel analgesics.

This exciting journey of discovery, with its unanticipated forays into new territory (chemical, structural, physiological, and behavioral) has been traveled in partnership with many exceptional trainees and collaborators who brought their own unique talents, insights, and creativity to the group dynamic. Watching students and fellows develop their scientific persona and then move on to forge their independent careers has been a thrill all its own, and a daily reminder of the guidance and support that I received from my own mentors along the way. In fact, heading an academic research group is something of a Shangri-La existence in which the continuous matriculation of energetic trainees keeps an aging mentor like myself intellectually youthful, curious, and ready for new challenges. I am enormously grateful to members of my lab - past and present – for this amazing gift, and for their contributions to all that we have accomplished together.

The other great engine of discovery has been public financing of research, which in my case has come from the US National Institutes of Health and the University of California. Bedrock support from these institutions, together with contributions from dedicated philanthropies, has allowed us to follow our dreams and curiosity, even when there was no guarantee of a practical outcome. But as we have seen time and again, this is how so many of the most impactful and unanticipated scientific breakthroughs are made. I am proud to be associated with institutions such as these that support intellectual freedom and creativity in pursuit of fact-based thinking, discovery, and decision making.

In closing, I would like to thank the BBVA Foundation and the selection committee for recognizing somatosensation and pain as a significant and prizeworthy area of research. I am pleased to share this award with Ardem Patapoutian, whose beautiful work on mechanosensation has provided complementary and critical insight into the biology of touch and pain sensation. Beyond our groups, I am indebted to the many friends and colleagues around the world who share their insights, ideas, reagents, and passion for research with the hope that our collective discoveries will help alleviate suffering from chronic pain and other debilitating disorders.