

## Salience

SALT IS AN INTRIGUING OBJECT OF SCIENTIFIC RESEARCH. Alchemists considered it an elementary principle from which all other substances were to be made. That belief, though misplaced, speaks to salt's ubiquity in the natural world and to its essential role in the biochemical processes that support all life.

Within the past two decades, scientists have come to understand how water and salts move in and out of cells through protein channels in the cell membrane. This research, notably by 2003 Nobel laureates Roderick MacKinnon, an HHMI investigator at The Rockefeller University, and Peter Agre, then at Johns Hopkins University, provides an atom-level view of how our kidneys function and how the heart pumps. It may also lead, in time, to new drug targets and therapies.

Now, scientists are hunting for the receptors that enable the taste of salt to register on the tongue—whether that salt pours from the iconic blue and yellow Morton salt container or comes in pearlescent flakes from the coast of France. HHMI investigator Charles Zuker at the University of California, San Diego, has spent years teasing apart the sensory network that allows mammals to experience taste. Zuker and his collaborators, including Nicholas Ryba of the National Institutes of Health, have identified receptors for four of the five basic qualities of taste: sweet, bitter, umami or savory, and sour. The salt receptor remains elusive.

This issue of the *HHMI Bulletin* highlights Zuker's research and that of other HHMI scientists whose work connects the convergent senses of taste and smell. They include HHMI investigators like Richard Axel and Linda Buck—who shared the Nobel Prize in Physiology or Medicine in 2004—who have systematically mapped the molecular, genetic, and cellular systems that generate our perception of the external world through the sense of smell. They also include Catherine Dulac, an HHMI investigator at Harvard University, whose research probes the power of pheromones, tantalizing chemical signals that influence animal (and perhaps human) behavior. The discoveries made by these scientists generate new questions: How is sensory information mapped in the brain? How is the map used to generate an appropriate response? How does information generated by odor receptors in the nose and taste receptors in the tongue shape behavior?

What connects these scientists, in addition to a shared interest in the sensory world, is the freedom to explore new areas of research, freedom given to them as HHMI investigators. We are committed to the Institute's long-standing philosophy of picking people not projects—that is, of identifying creative scientists and then freeing them to pursue challenging questions. It takes our scientists—like Bruce Walker of the Massachusetts General Hospital—as far as the bedside of a patient in South Africa in a quest to understand how the AIDS virus exhausts the immune system. It allows Craig Mello of the University of Massachusetts Medical School to make connec-



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tions between interrelated research interests—RNA interference and embryonic development. It fosters bold thinking.

We are poised to add a dash of salt—in this case, two competitions for new HHMI investigators—to sharpen the Institute's flagship research program and ensure its characteristic liveliness. Late last year, we announced a focused competition for physician-scientists who bridge the gap between clinical medicine and basic science, and we hope to name 15 researchers by fall 2007. A second, general competition will be announced this spring with the expectation that another 50 investigators will be selected in 2008. In both competitions—and for the first time in HHMI's history—we will accept direct applications from scientists at eligible institutions across the nation. Institutional vetting of nominees generated excellent candidates in prior competitions, but we believe this open approach will generate an even richer, broader pool of potential investigators.

This infusion of fresh scientific talent—and potentially new fields of inquiry unrepresented among our current cadre of investigators—offers HHMI an extraordinary opportunity to refresh our commitment to original and creative biomedical research. Our support can also be a career-defining opportunity for scientists at a critical stage in their careers, at a moment when they hunger for flexible funding, recognition, and access to great colleagues. Like salt, when added in the right proportions, it can make all the difference.

*Thomas R. Cech*