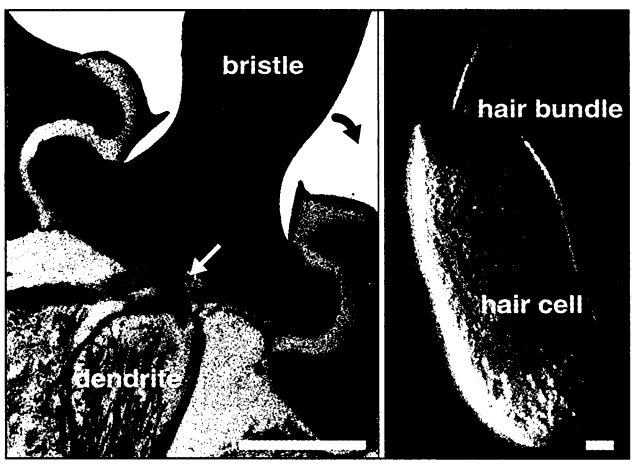
Hair-cell physiologists have long wanted to see what the hair-cell channel looks like, because their experiments had shown that it has fascinating biophysical properties. By studying the electrical currents passing through the membranes of hair cells as they are stimulated, they learned that hair-cell channels are stunningly fast, opening up within microseconds, compared to the milliseconds needed by biochemically activated channels. They are also exquisitely sensitive to the slightest movement and to direction; they open when the tip of the cell's cilia bundle is deflected by a mere atom's width—akin to bending the tip of the Eiffel Tower by the width of your thumb. If the cilia bundle moves one way, the channel opens; the other way and it shuts. The channels are also able to register tiny cilia movements on top of a larger constant deflection—a trait that lets us discern meaningful sounds from background noise.



Nonidentical twins. Both this insect sensory bristle *(left)* and this hair cell from the inner ear of a frog *(right)* have ion channels that respond to the deflections shown by the black arrows.

CREDITS: (TOP TO BOTTOM) PHOTOGRAPHS COURTESY OF THOMAS KEIL [*MICROSC. RES. TECH.* **39**, 506 (1997)]; R. A. JACOBS, AND A. J. HUDSPETH; ZUKER LAB/HOWARD HUGHES MEDICAL INSTITUTE

Efforts to isolate the channels have been stymied, however, primarily because hair cells are so sparse and contain relatively few channel molecules. So Zuker decided to apply the power of fruit fly genetics to the problem, on the hunch that the flies' bristles might contain channels similar to those in hair cells. In the first phase of the work, begun about 7 years ago, Zuker and then-postdoc Maurice Kernan, now at the State University of New York, Stony Brook, created mutant flies and screened them for those that were defective in their sense of touch. Some of those flies, they reasoned, would have mutations in genes specific to the touch response—including the gene for the touch-sensitive channel itself.

In a separate phase of the work, postdoc Richard Walker, who arrived in Zuker's lab in 1996, examined whether the bristle system would be a good model for hair cells. It was. Using electrophysiological methods similar to those employed to study hair cells, Walker found that when the fly neurons respond to touch, they share key characteristics of hair cells: fast responses to even the tiniest movements, directional sensitivity, and adaptability to new bristle positions. Hair-cell researcher David Corey of Massachusetts General Hospital in Boston calls the comparison "beautiful." Walker "repeated the last 20 years of human hair-cell physiology on this bristle system," he says, "and everything looks the same."

Walker then applied the same methods to the bristle neurons of the mutant flies to search for those in which the mutations caused defects in the channel's function—a good indication that the affected gene encodes the channel. He found that a gene called *nompC* (for no mechanoreceptor potential C) seemed to fit the bill. Mutations in *nompC* either blocked the opening of the channel in response to bristle movement or in one case altered the channel so it opened but let through less current than normal. To Bargmann, this is the "most convincing" evidence that the NOMPC protein is the mechanically sensitive bristle channel.

The sequence of the *nompC* gene supports that view, as it encodes a protein with the general structural features of proteins that form ion channels. The gene sequence also contains a clue to how mechanically sensitive ion channels open. To be tugged open, a channel must be anchored so that pulling on it changes its shape. NOMPC appears to have "a great way of anchoring the channel" to the cell's skeleton, says Corey. This is a set of 29 so-called ankyrin repeats—short amino acid sequences that link up to other proteins.

Although all these data constitute strong evidence that NOMPC is a mechanically sensitive channel, definitive proof would require putting it into cultured cells and showing that it renders them responsive to touch. That is a tough experiment, because other specialized proteins are likely required for NOMPC function. And even if NOMPC does turn out to be a mechanically sensitive channel in flies, that doesn't necessarily mean that it will be related to the elusive hair-cell channel in vertebrates.

So far, opinion on that issue is mixed. Neuroscientist Denis Baylor of Stanford Medical School is cautious. "The anatomy [of bristles and hair cells] is so different that I wouldn't be surprised if [the hair-cell channel] is a completely different molecule, not even a relative," he says. But Corey and fellow hair-cell researcher James Hudspeth of The Rockefeller University in New York City come down on the other side. Given the similarities that Walker found between the hair-cell responses and those of the bristle neurons, "chances are very good" that the two are related, Hudspeth says.

To find out, his team is now using the Zuker group's cloned gene to look for expression of a similar gene in hair cells from chickens. Researchers will also want to determine, Hudspeth suggests, whether a human version of *nompC* might turn out to be mutated in any of the many forms of hereditary deafness for which genes have not yet been identified. If either of these searches is successful, then the similarity of bristles to hair cells will indeed have paid off.

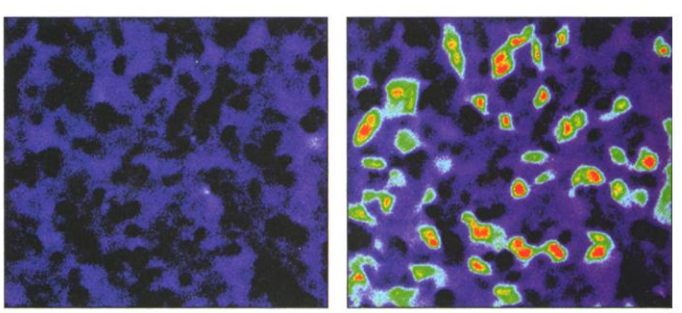
–MARCIA BARINAGA

NEUROSCIENCE

Family of Bitter Taste Receptors Found

Our ability to savor the sweetness of a fig or the sour tang of a lemon may seem more like a pleasure than a necessity, but the sense of taste is actually honed for survival. Sweetness, for example, means that a food has high caloric value, while bitterness tells us that it may be poison. For neuroscientists, however, bitter has been a perplexing flavor, because a wide range of unrelated chemicals all taste similarly bitter even though their diverse structures suggest that they must trigger different receptor molecules. The solution to that puzzle may now be at hand—along with other insights into the phenomenon of taste.

A team led by Nicholas Ryba of the National Institute of Dental and Craniofacial Research and Charles Zuker of the University of California, San Diego, reports in the current issue of *Cell* that it has identified a



Bitter match. Cultured cells containing a bitter receptor fluoresce in response to cycloheximide *(right)*, but not to three other bitter-tasting chemicals *(left)*.

huge family of receptors, each of which seems to respond to different bitter-tasting compounds. The researchers have also discovered how those various signals are apparently combined to send just one bitter message to the brain. "This is clearly a major breakthrough for taste research," says Gary Beauchamp, director of the Monell Chemical Senses Center in Philadelphia. "It all fits together in a very nice story. My only regret is that I didn't make the discovery."

For years researchers have struggled to identify receptors for the five different tastes—sweet, bitter, sour, salty, and umami (MSG)—that the taste cells in our taste buds detect. The stumbling block has been a lack of starting material; there is no way to grow taste-bud cells in the lab. So with the exception of a recent discovery of a possible receptor for umami, receptors for the different tastes in vertebrates have not been identified.

Taking a new tack, Ryba and Zuker (whose team this week also reports the discovery of a receptor for touch sensation; see previous story), decided to let genetics lead the way. Taste researchers have long known that some people can taste a bitter compound known as PROP, while others can't. Last year, Danielle Reed at the University of Pennsylvania and Linda Bartoshuk at Yale narrowed down the chromosomal location of the gene responsible for that difference. Zuker grad student Ken Mueller suspected that this gene might encode a bitter taste receptor and set out to find it.

Mueller had one clue to guide him. Bitter receptors are known to interact with so-called G proteins, which are involved in intracellular signaling in taste and other responses. So Mueller looked in the vicinity of the PROP-tasting mutation for genes that might encode receptors with the ability to interact with G proteins. He found one, and together with Elliot Adler, a postdoc in Ryba's lab, discovered that it is part of a family of at least 50 genes that cluster at several locations along the human chromosomes. The large number of genes was encouraging, says Zuker, because the team had suspected that many bitter receptors would be required to recognize all the different chemicals that taste bitter. What's more, in mice as in humans, the genes turned out to reside in chromosomal areas known to be involved in bitter perception.

Next, Mark Hoon, a postdoc in Ryba's lab, isolated the mouse counterparts of the human genes and investigated which taste cells in mice express them. He discovered that taste cells that respond to bitter flavors generally express not just one or two of the receptor genes, but most of them. As a result, each individual cell should be able to detect a wide variety of bitter-tasting compounds. This may explain why the brain can't distinguish among bitter chemicals, because no matter which receptor type is activated, the cell will send the same signal to the brain. As a result, the brain receives "a single channel of information" with the simple message that this food is to be avoided, says Robert Margolskee, a taste researcher at the Mount Sinai School of Medicine in New York City. In addition, Hoon found that the receptors are made in the same taste cells as gustducin, a G protein necessary for the perception of bitter tastes. To Margolskee, whose lab discovered gustducin, that essential association nearly cinched the case.

But definitive proof that the family of genes does in fact encode the bitter receptors came when Jayaram Chandrashekar, a postdoc in Zuker's lab, showed directly that the receptors are activated by bitter-tasting compounds. He did this by separately putting each of 11 receptor genes into cultured cells that were engineered so that triggering the receptor would activate a dye. Chandrashekar then exposed the cells one at a time to several bitter compounds. He found that three receptors responded, each to different compounds. What's more, in a different test, the team showed that the activated receptors bind to gustducin, the first step in sending their bitter signal to the brain. The team was able to go even further to show that a mutation in the receptor molecule that recognizes the bitter chemical cycloheximide makes mice less able to taste that compound.

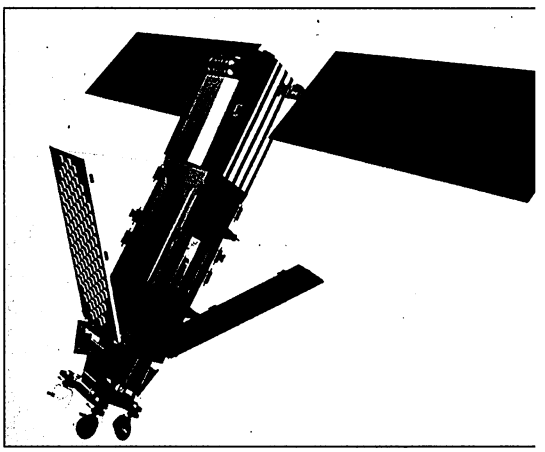
These results led Margolskee to conclude that the molecules are "unqualified taste receptors, as opposed to 'candidate' receptors." Those bona fide bitter receptors represent "an extremely powerful tool," says Catherine Dulac, who studies the chemical senses at Harvard University. They will enable researchers not only to learn more about how the brain encodes taste, but also to develop antidotes for bitter flavors in medicines and foods. And for kids who hate brussels sprouts or taking their medicine, that would be a sweet outcome indeed. **–MARCIA BARINAGA**

COMMUNICATIONS SATELLITES

Iridium's Loss Is Astronomers' Gain

A spectacular business flop is evoking sweet sorrow among radio astronomers. The once high-flying Iridium mobile phone company last week pulled the plug on its $5 billion satellite fleet and will eventually send the 68 orbiting craft into fiery death dives in Earth's atmosphere. That means an end to electronic smog that clouded sensitive telescopes. "I'm not going to say Iridium deserved it, but they certainly were not good neighbors," says Willem Baan, director of Holland's Westerbork Observatory. The experience has also steeled astronomers' resolve to protect important frequencies.

Iridium's globe-girdling constellation was supposed to be the next big thing in communications when it went live in late 1998 (*Science*, 2 October 1998, p. 34). But radio astronomers weren't thrilled, because the satellites produced static that interfered with the faint cosmic signals they study. In particular, Iridium threatened a 1612-megahertz signal produced by hydroxyl masers, blasts of laser-like radio waves that provide important insights into stellar evolution. After 6 years of tense negotiations, the company agreed to provide some unobstructed listening hours each day to radio telescopes in Europe, the United States, and India, and to fix the problem in newer satellites. That deal is now moot, however, as technical glitches and Iridium's high prices—the phones cost $3000 and calls up to $7 a minute—forced the company to shut down on 17 March.



Going down. Iridium's bankruptcy dooms 68 satellites that have irritated researchers.

CREDIT: IRIDIUM

The Iridium episode has prompted astronomers "to become much more vigilant" about the interference threat from the growing communications industry, says Baan. In the United States, for instance, a recent government proposal to loosen standards on satellite radio emissions drew angry replies from 50 concerned astronomers, an unprecedented response. And researchers are organizing to protect key bandwidths at an international spectrum-allocation conference to be held in Istanbul in May.

Meanwhile, Iridium's demise will also lighten the load on some optical astronomers. Solar panels on the satellites produce flashes that amateur sky watchers occasionally mistake for new celestial bodies, says Daniel Green of the Harvard-Smithsonian Center for Astrophysics in Cambridge, Massachusetts. "At least we won't be getting these weekly reports from people saying they've discovered another naked-eye supernova," he says. **–DAVID MALAKOFF**