

Teasing Out a Tongue's Taste Receptors

Of the five senses, taste has remained in some ways the most mysterious. Scientists have found that people recognize five main tastes—sweet, sour, bitter, salty, and umami (the taste associated with mono-sodium glutamate, or MSG)—but they've had a devil of a time identifying the cell-surface proteins on the tongue that detect these tastes.

Now, a research team has identified two new proteins that seem to fill the bill. "They may be key to unlocking taste. They have the hallmarks of taste receptors, but we have to actually show they function as such," says Nicholas J.P. Ryba of the National Institute of Dental and Craniofacial Research in Bethesda, Md. His research group, in collaboration with one led by Charles S. Zuker of the Howard Hughes Medical Institute at the University of California, San Diego, describes the putative taste receptors in the Feb. 19 CELL.

Identifying taste receptors is no easy task. Cells with taste receptors concentrate in small clusters known as taste buds, which are scattered like small islands on the tongue. "Taste tissue is really hard to work with. . . . The tongue has many fewer receptor cells than the nose," notes Sue C. Kinnamon of Colorado State University in Fort Collins.

Until now, the only known taste receptor was one discovered in 1996 that senses the meaty taste of umami. Researchers found this MSG receptor only because they assumed that it would resemble other cellular proteins known to bind to the amino acid glutamate.

"If you're looking for a sweet or bitter receptor, you really don't know what strategy to use," says Kinnamon.

Zuker's and Ryba's groups analyzed genetic activity in cells from the front of the tongue, where taste buds abound, and in cells from an area at the back of the tongue not involved in tasting. By sifting through the hundreds of extra genes active in the taste cells, they found one, named *TR1*, that encodes a cell-surface protein somewhat resembling receptors for glutamate and pheromones, the odorless molecules that many mammals sense with their noses (SN: 3/14/98, p. 164). Using the DNA sequence of *TR1* to search genetic databases, the scientists then identified a similar gene, which they call *TR2*.

Further studies showed that *TR1* and *TR2* are active only in taste cells and that their proteins cluster at taste pores, the cell-surface sites where molecules are thought to be actually tasted. Although a few cells made both proteins, each protein studded largely its own distinct areas

Mark A. Hoon et al./CELL



The protein encoded by the gene *TR1* (green) clusters on taste-sensitive regions of this section of rat tongue.

of the tongue.

Surprisingly, the two putative receptors covered a wide swath of the tongue, suggesting there's a small number of different taste receptors overall. "One-third of all cells in taste buds contain either one or the other receptor," says Ryba.

Ryba and his colleagues must still confirm that the proteins encoded by *TR1* and *TR2* mediate taste. They plan to create mice that lack the proteins and to study the animals' taste preferences. They're also trying to slip the genes into laboratory-grown cells and determine what substances the receptors recognize. From the distribution of the two proteins on the tongue, Ryba speculates that *TR1* may encode a sweet receptor and *TR2* a bitter receptor.

"I don't think they can really come out and say what [the receptors'] functions are yet in terms of what substances bind to them," says Kinnamon.

Once the tongue's full roster of taste receptors is revealed, scientists might develop compounds that better fool the mouth into thinking something tastes sweet, says Alan R. Hirsch of the Smell and Taste Treatment and Research Foundation in Chicago. Such compounds could help people undergoing chemotherapy, who develop a constant bitter taste, or mask the harsh taste of coffee without sugar, for example.—J. Travis

Red-yeast product is no drug, court says

In a setback for the Food and Drug Administration, a federal district court ruled last week that the agency had unlawfully attempted to restrict an herbal supplement as a prescription drug.

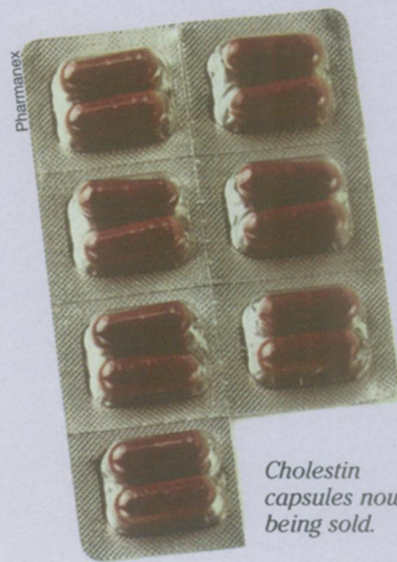
Pharmanex of Simi Valley, Calif., began marketing capsules of rice fermented with a red yeast in November 1996. Almost immediately, FDA ordered the company to stop selling the cholesterol-lowering product, sold as Cholestin, charging that it is a drug. Studies had shown that the fermented rice contains a natural compound that is chemically indistinguishable from lovastatin, the active ingredient in a cholesterol-lowering prescription drug (SN: 11/14/98, p. 311).

Pharmanex fought the drug designation for its over-the-counter product, however, citing a 1994 law known as the Dietary Supplement Health and Education Act (DSHEA). When FDA countered by ordering the company to stop importing its bulk fermented rice from China, Pharmanex sued in what became the first legal test of DSHEA.

Last June, pending a thorough study of the case, Judge Dale A. Kimball of the Federal District Court in Salt Lake City restrained FDA from imposing its ban on the Chinese rice. Kimball's final decision now decrees that Cholestin indeed is a food as defined by DSHEA.

The judge noted that Congress, in explaining a clause in the legislation, had acknowledged, "On occasion, a substance that is properly included as a dietary ingredient in a dietary supplement (food) product may also function as an active ingredient in a drug." That's the case here, Kimball said.

For now, FDA is "reviewing the court's decision and evaluating what steps we might take," says Brad Stone, a spokesman in Rockville, Md. —J. Raloff



Cholestin capsules now being sold.