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Cells in the Lungs Use Taste Receptors to Detect Bitter Compounds

Image Title: Cilia on the surface of epitheial cells in the human airway can both detect bitter compounds and help expel them. - Louisa Howard / Photo Researchers, Inc

When it comes to matters of taste, the lungs have a thing or two in common with the tongue—specifically taste receptors that detect bitter substances then cause them to be rejected.

Bitter compounds are often toxic, and the body generally tries to keep them out. In the mouth, bitter taste receptors are found on taste cells in the tongue. When those cells activate neurons, they alert the brain that they have detected a bitter compound, the brain quickly returns a “reject” message and the offending substance is expelled.

Now researchers have shown that the epithelial cells that line the airways in the lungs use the same type of sensory receptors, but they have cut out the nervous system as the middle man. In the airways, tiny, hair-like projections called cilia both sense the bitter material and help expel it by speeding up the

rate at which they push the offending substance along the airway. The research suggests that the lungs have evolved their own mechanisms for detecting and expelling potentially dangerous substances.

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> **- Michael J. Welsh**

This means that cilia can multitask better than scientists thought, says Howard Hughes Medical Institute investigator Michael J. Welsh, who led the research, which was published online July 23, 2009 in *Science Express*.

There are two general types of cilia that protrude from the surface of cells in the bodies of humans and other vertebrates -- primary and motile cilia. Primary cilia are structures that collect information about the cell's environment -- such as which smells are arriving at olfactory neurons in the nose, when light strikes photoreceptor cells in the eye, or how fast fluids are flowing past cells in the kidney. Motile cilia beat back and forth in coordinated waves that exert a mechanical force that can move substances, such as mucus.

"There's been a bit of a dichotomy," says Welsh, who is at the University of Iowa Carver College of Medicine. "We know that primary cilia are sensory organelles, whereas motile cilia do the work of moving material. What we found was that classical motile cilia can also be sensory. These results suggest a new mechanism for detecting threats to the lung," Welsh says.

"The research stemmed from previous work indicating that primary and motile cilia evolved together, and they share many of the same molecular components," Welsh says. "Those things led us to ask the question: Could they share another property—and both be sensory receptors?"

To find out, Welsh and his colleagues at the University of Iowa searched for sensory-related genes that were active in human airway epithelial cells. The team identified genes for four members of the family of bitter taste receptors found in the tongue, known as T2R. In airway epithelia, those genes were active only in the cells that had cilia.

Welsh points out that cilia are ideally positioned to act as sentries for potential toxins entering the lungs. "Cilia are almost like a little antenna; they would be well positioned to detect anything that comes in with the air or

anything in that thin layer of liquid covering airway epithelial cells." he says.

To test whether the taste receptors were active, the researchers applied bitter compounds to the cells. They found that the compounds increased the concentration of

calcium ions within the epithelial cells. Calcium is known to be important in stimulating ciliary beating, the synchronized undulations that can move fluid or other substances, Welsh says. Indeed, the cilia beat 25 percent faster than normal when the bitter compound was present.

"The cells have the receptor and in that same cell you initiate increased ciliary beating, which would serve to help eliminate the offending substance," he explains.

Such offending substances could include irritants like cigarette smoke, or molecules that activate bitter receptors such as those that are generated, for instance, by the infectious microorganism *Pseudomonas aeruginosa*.

The research also revealed that cells in the lungs and the tongue rely on the same signaling molecules to transform the detection of a bitter compound into a response – either the beating of the motile cilia in the lungs or the generation of a nerve impulse in the tongue. "So far as we've looked, the signaling cascade looks to be similar," Welsh says, suggesting that evolution used the same trick twice.