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The Right Snuff

By Tina Hesman Of the Post-Dispatch
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Heavy metal smells.

While it may sound like music criticism, the conclusion is actually a new scientific model that may explain for the first time how humans and other mammals detect odors.

Scientists at the University of Illinois have discovered that odor-sensing proteins, called olfactory receptors, may owe much of their stink-detecting capabilities to heavy metals such as zinc or copper.

The discovery is based on simple knowledge that inorganic chemists have had for a long time, but biologists have largely overlooked - things that bind to metals smell strongly and badly.

"Inorganic chemistry stinks," said Kenneth S. Suslick, a chemist at the University of Illinois at Champaign-Urbana who led the work on smell. The results of the study appear today in the Proceedings of the National Academies of Science.

The primary function of the olfactory system - the scientific name for the part of the body responsible for the sense of smell - is to help mammals avoid spoiled food, Suslick said. Bacteria often give off malodorous chemicals that stick strongly to metals, he said. Those metals - zinc, copper, iron, magnesium and others - may come from food and water.

The Illinois researchers have used this bit of wisdom to develop an artificial nose that could help detect noxious chemicals. Metal-binding dyes in the artificial nose change colors when certain odors latch onto the metals. The scientists began to wonder if the human nose worked the same way, Suslick said.

Robert Crabtree, an inorganic chemist at Yale University, thought it might. The idea came to Crabtree 25 years ago when a colleague broke a bottle of vile-smelling chemicals on the floor. The chemist knew that stinky stuff, such as the hydrogen sulfide that give rotten eggs their smell, or amines, which are responsible for fishy odors, stick to metals well. And people can smell rank odors better than pleasant ones, so Crabtree hypothesized that smell-receptor proteins probably contain metals. The Yale chemist wrote a paper outlining his idea that day and later published it in a scientific journal.

That seemed to be the end of the story - except for good-natured ribbing from Crabtree's wife, who has never let him forget that his paper was never cited by other researchers.

"In science, you don't get many points for a proposal. ... You've got to have proof," Crabtree said. "It took a long time before the proposal was testable."

To find out if metals play a role in smell, the Illinois researchers examined DNA sequences of the olfactory receptors. The sequences weren't hard to come by, Suslick said. Mammals have about 1,000 genes for olfactory receptors. That's about 3 percent of the human genome.

The scientists found a small portion of protein in about 75 percent of the receptors that looked as if it could bind to metals. The researchers produced that portion of the receptor in the laboratory and found that it could hold onto metals.

Olfactory receptors look like many other receptor proteins in that they have seven regions that cross a cell's membrane. Most of these receptor proteins are tightly stitched into the membrane, with only small loops of protein connecting the membrane-spanning regions, Suslick said. But olfactory receptors have one large, floppy loop that hangs outside the cell like a snag on a sweater.

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That loop contains the metal-binding part of the protein. When metal ions bind to the protein, the floppy loop changes into a corkscrew-shaped helix that slides into the cell membrane. That action pushes a loop of protein inside the cell out the membrane, just as when a strand of yarn is pulled from the underside of a sweater to hide a snag. The protein is now primed to detect smells.

When a smelly chemical sticks to the metal ion, the loop pops back out of the membrane. That "shuttlecock" motion sends a signal to the smell-detecting cell that an odor is present, the researchers say.

Some smell receptors don't have metal-binding regions but may work in much the same way, Suslick said. Chemical bonds within the protein could mimic the action of the metal ions, he said.

Those receptors that do not bind metals - only a quarter of the smell-detecting proteins - may sniff out pleasant-smelling chemicals, Crabtree speculates. Aromatic chemicals such as esters, which give flowers their scent, don't stick well to metals, he said.

The model still needs more testing, Suslick said. But the researchers have other clues that they may have sniffed out a winning theory. The first symptom of zinc deficiencies is the loss of the sense of smell, Suslick said.

But taking zinc supplements may not improve the sense of smell, he said.

"Most people get all the zinc they need from their diet," Suslick said, "and excess zinc won't buy you anything."

Crabtree, who proclaimed the Illinois researchers' model "a beautiful mechanism," said the study provided validation for his idea. That could mean that his wife will have to find something else to tease him about.

"Now I've got the upper hand!" Crabtree crowed.

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