

Sensitivity of smell cilia depends on location and length in nasal cavity

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Olfactory sensory neurons with longer cilia and higher sensitivity are situated in highly stimulated regions of the nose. Credit: Rosemary Challis, Kai Zhao, and Minghong Ma, Perelman School of Medicine, University of Pennsylvania; Current Biology

Like the hairs they resemble, cilia come in all lengths, from short to long. But unlike the hair on our heads, the length of sensory cilia on nerve cells in our noses is of far more than merely cosmetic significance. A team of researchers from the Perelman School of Medicine at the University of Pennsylvania found a location-dependent pattern in cilia length in the mouse nasal cavity that affects sensitivity to odors. The discovery may also have important implications for the study of sight and touch. Their work was published this week online in *Current Biology* ahead of print.

Although the research team, led by Minghong Ma, PhD, an associate professor of Neuroscience, has been studying the olfactory system for years, this new discovery was a happy accident. The team was investigating the potential role of a particular gene in the maturation of olfactory sensory neurons (OSNs) in mice. Because the growth of OSN cilia is a milestone in determining cell maturity, Ma and her colleagues were already studying cilia length in the mouse <u>nasal cavity</u>.

"We unexpectedly discovered a striking gradient in cilia length, in which cells in the front of the nose have much longer cilia than those in the back," Ma said. "The discovery that these longer, more sensitive olfactory cilia are located in regions of the nasal cavity where they can detect more molecules may lead to important clues about how such cells operate in other sensory systems. Many other cell types use cilia to detect external stimulation, such as photoreceptors in the eye and epithelial cells in the kidney. We hope that our work will build on the



work of others to better understand how cells use their 'antenna' to detect stimuli and ultimately shed light on diseases with impaired cilia."

As the researchers investigated the OSNs in more detail, they were excited to find that the spatial organization of cells in the nasal cavity matched cell sensitivity to incoming odors - such as the clove oil chemical they used—and shared many similarities with other sensory systems. While cilia are part of almost all mammalian cells, many of the details of how they work, such as how their individual shapes relate to function, remain unknown.

Using an array of microscopic, computational, physiological, and genetic methods, the team delved further into what factors create the patterns they observed. Cilia on OSNs of the nasal cavity underside had no significant length gradient, as opposed to the marked location-dependent length difference seen in the upper nasal cavity.

The team asked whether the length differences might be due to the amount of stimulation each OSN receives at a particular location. They found that longer cilia definitely appear to be located in areas that receive more odorant molecules and that longer cilia are more sensitive. But while external stimulation does affect length, the overall pattern throughout the nasal cavity is inherent and established at birth, independent of external factors.

"Our study suggests that if you deprive one nostril of airflow and odorants, then the cilia grow longer in all regions of that nostril," Ma explained. "Interestingly, however, the cilia length gradient remains intact, albeit with longer cilia overall. These data suggest that stimulation can modulate cilia length, but is not required to establish the pattern."

Since the intracellular signaling molecule cyclic AMP (cAMP) can regulate cilia length in various cells, including OSNs, the researchers



studied the effects of eliminating a key enzyme, ACIII (type III adenylyl cyclase) in the pathway. Mice lacking ACIII showed a significant disruption in the cilia length pattern, with markedly shortened or absent cilia. Meanwhile, normal, control mice had higher expression of the Adcy3 gene, which correlates with the cilia length distribution pattern.

"We know that ACIII, and likely downstream cAMP signaling, plays an integral role in establishing and maintaining the cilia pattern," Ma notes. "How these molecules are causing location-dependent differences in cilia length, however, is not yet understood." The team plans to look into that question, along with how the brain integrates information from OSNs with different <u>cilia</u> lengths and sensitivities.

Provided by University of Pennsylvania School of Medicine

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