Sweet taste receptors are primary sentinels in defense against bacterial infections in the upper airway, study finds

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(Medical Xpress)—The body uses mucus as a protective barrier to defend against pathogens, toxins, and allergens in the upper respiratory tract that can lead to such conditions as chronic sinusitis. Aiding in this defense are antimicrobial peptides (AMPs), a diverse group of small proteins found in mucus that kill bacteria, viruses, and fungi. In addition to these known defensive systems, researchers have recently surmised that taste receptors serve "double duty" by also acting as first line sentinels against infection in the upper airway.

Now, scientists from the Perelman School of Medicine at the University of Pennsylvania reveal that the release of AMPs is partially controlled by bitter taste receptors in the upper airway on a cell previously identified in animals and only recently in humans known as solitary chemosensory cells (SCCs). What's more, the action of the bitter receptors is blocked when sweet taste receptors are stimulated by sugars such as glucose. This study, published online ahead of print in the *Journal of Clinical Investigation*, suggests that sweet taste receptors expressed on SCCs in the upper airway sense bacterial overgrowth and, in turn, control the release of AMPs.

In previous work, Penn researchers found that bitter taste receptors in the human airway play a role in detecting bacterial communication molecules and launching a defensive response to combat bacteria. The new study complements the prior findings by revealing another

defensive response mediated by taste receptors.

"Chronic rhinosinusitis is a common upper respiratory infectious and inflammatory disorder that impacts nearly 35 million Americans, with related health care costs exceeding $6 billion annually," said senior study author Noam Cohen, MD, PhD, associate professor of Otorhinolaryngology: Head and Neck Surgery at Penn and staff surgeon at the Philadelphia VAMC. "Despite how widespread this condition is, we still struggle to understand exactly how to best fight it. We're just now starting to discover how taste receptors in the upper respiratory tract are used to regulate the immune system against these infections, so defining the underlying mechanisms at play is critical to understanding these illnesses and developing new treatments."

Cohen said that the current study is the first to elucidate a functional role for sweet receptors in the human airway. "This could have critically important clinical consequences, as we found that patients with chronic sinusitis have elevated glucose concentrations in their nasal secretions compared with control individuals, which likely impairs their respiratory immunity. Because prior studies have shown that hyperglycemic patients also exhibit elevated nasal glucose levels, it is likely that the sweet taste receptor function we demonstrate here may also contribute to the predisposition of diabetic patients to airway infections."

Sweet Vs. Bitter

To study the role of sweet taste receptors, Cohen and lead study author Robert J. Lee, PhD, a post doctoral researcher in his lab, partnered with colleagues from the Children's Hospital of Philadelphia and the Monell Chemical Senses Center to analyze cultures and tissue samples from the upper respiratory tract of patients who were undergoing sinonasal surgery for a variety of conditions.

The research team, using multiple approaches including live-cell imaging techniques, demonstrated that activation of bitter taste receptors (T2Rs) on SCCs engages a signal to surrounding cells, which stimulates release of high concentrations of AMPs capable of killing a variety of pathogens, including antibiotic-resistant bacteria. While previous research in the last year has shown that SCCs exist in humans as well as animals, the current study was the first to reveal a function for SCC's in the human airway.

The team also found that compounds that activate the sweet taste receptor (T1R2/3) suppressed the release of the AMPs produced by bitter taste receptors, indicating that these receptors have complimentary roles in regulating the innate immune pathway. They hypothesize that this system may control microbial overgrowth in the airway to maintain a colonized state within the upper airway without infection.

"We believe that the complimentary roles of the bitter and sweet taste receptors in these SCCs keeps upper airway colonizing bacteria at optimal levels during periods of relative health," Cohen says. "But as the bacteria multiply, they consume more glucose, removing the sweet taste receptor 'brake' and allowing for release of AMPs by the bitter taste receptors."

Cohen says that in the future, clinicians may be able to use certain compounds, such as sweet-receptor blockers, to activate the solitary chemosensory cell innate defense pathway, even in the presence of pathologically high glucose concentrations, to help regulate bacterial growth and prevent harmful infections and chronic inflammation.

More information: "Bitter and sweet taste receptors regulate human upper respiratory innate immunity." Robert J. Lee, Jennifer M. Kofonow, Philip L. Rosen, Adam P. Siebert, Bei Chen, Laurel Doghramji, Guoxiang Xiong, Nithin D. Adappa, James N. Palmer,

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