Bitter taste receptors regulate the upper respiratory defense system, research shows

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A new study from a team of researchers at the Perelman School of Medicine at the University of Pennsylvania, the Monell Chemical Senses Center, and the Philadelphia VA Medical Center, reveals that a person's ability to taste certain bitter flavors is directly related to their ability to fight off upper respiratory tract infections, specifically chronic sinus infections. The new research is published in the latest edition of the *Journal of Clinical Investigation*.

Most humans experience five types of tastes: sweet, salty, sour, bitter, and savory. The sense of taste is mediated by taste receptor cells which are bundled in our taste buds. "Sour" and "bitter" taste sensations alert the body to harmful foods that have spoiled or are toxic. But based on genetics, up to 25 percent of the population cannot detect certain bitter flavors (non-tasters), 25 percent can detect exceedingly small quantities (super-tasters), and the rest of us fall somewhere between these two extremes.

So what exactly does drinking a cup of bitter coffee have to do with chronic sinus infections, which account for approximately 18-22 million physician visits in the U.S. each year? Recent investigations have shown that these taste receptors (known as T2Rs) are also found in both upper and lower human respiratory tissue, likely signaling a connection between activation of bitter tastes and the need to launch an immune response in these areas when they are exposed to potentially harmful bacteria and viruses.

"With this information in mind, we wanted to better understand the exact role that bitter taste receptors play in the upper airway, especially between these super and non-tasters," says Noam Cohen, MD, PhD, assistant professor of Otorhinolaryngology: Head and Neck Surgery, staff physician at the Philadelphia VAMC, and senior author of the new study.

Cohen and his colleagues formulated the following hypotheses around the connection: (1) bitter taste receptors are functional in the nose (upper respiratory tract), and each receptor detects a specific type of bacteria; (2) upon activation by a specific bacterial product, the bitter taste receptor initiates a local defensive response to combat the attacking bacteria; and (3) genetic variability of the bitter taste receptors alters the vigorousness of the response, thus leaving certain individuals with very strong defenses and others with weak defenses against a specific bacteria.

To test these hypotheses, the team grew cell cultures from sinus and nasal tissue samples collected during sinus surgical procedures. These cultures develop cilia, produce mucus, and reflect many of the defensive workings found inside the nose and sinuses.

They found that one of the bitter taste receptors that functions in upper airway cells, known as T2R38, acts as a type of "security guard" for the upper airway by detecting molecules that a certain class of bacteria secretes. "These molecules instruct other bacteria to form a biofilm, which helps harbor the bacteria. From previous work, we know that these biofilms spur the immune system to mount an over-exuberant inflammatory response that can lead to sinusitis symptoms. When the T2R38 receptor detects these molecules, it activates local defensive maneuvers to increase mucus clearance and kill the invading bacteria. It's really like modern warfare – intercept the enemies' early communications to thwart their plans and win the battle," Cohen said.

Through the cultures, the research team demonstrated that super-tasters detect very small concentrations of the offending molecules, while non-tasters and the middle-ground individuals require 100 times more of the molecule for detection. The research team also examined the patients that the original sinus tissue samples were collected from. They found that none of the super tasters were infected with the specific type of bacteria that are detected by the T2R38 receptor, known as a gram-negative bacteria.

"Based on these findings, we believe that other bitter taste receptors in the airway perform the same "guard duty" function for early detection of attack by different types of bacteria, and we hope to translate these findings into personalized diagnostics for patients with chronic rhinosinusitis," Cohen says.

The research team is also using the results of the current study to develop a simple "taste-test" protocol to be conducted during clinic visits. "We're optimistic that a test of this nature will help us predict who is at risk to develop biofilms based on their ability to taste various bitter compounds. Additionally, we are looking at therapeutic outcomes, both surgical and medical, based on the taster/non-taster genetic status to determine whether knowing this status will stratify patients to either surgical or medical interventions."

More information: T2R38 taste receptor polymorphisms underlie susceptibility to upper respiratory infection, *Journal of Clinical Investigation*, 2012.

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