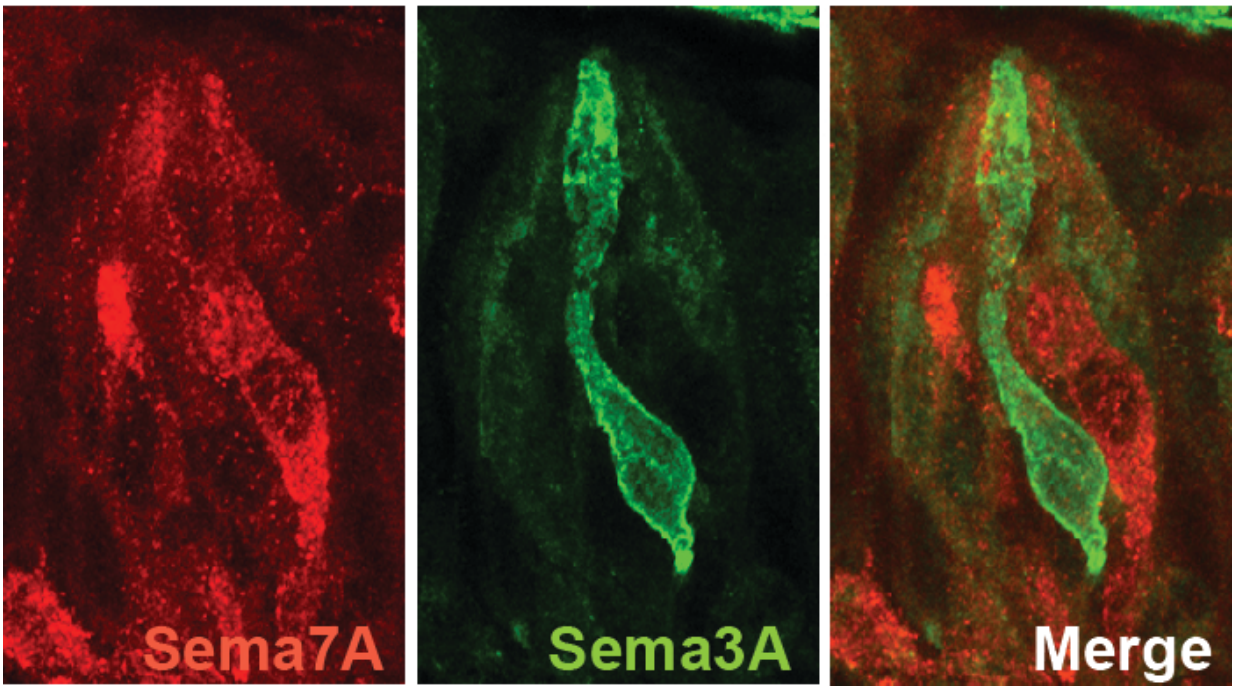
MedicalXpress

Rewired taste system reveals how flavors move from tongue to brain

August 9 2017



In cells in the mouse taste bud, the protein Semaphorin 3A (green) helps bitter-sensing taste receptor cells attract the correct neural target. The protein Semaphorin 7A (red) marks sweet-sensing cells. Credit: Lee et al./*Nature* 2017

By tangling up bitter- and sweet-sensing cells on the tongues of mice, researchers have teased apart how the taste system wires itself. The results, from Howard Hughes Medical Institute (HHMI) Investigator Charles Zuker at Columbia University and colleagues, reveal how cells

constantly reconnect to keep taste abilities running smoothly, allowing flavor information to flow from tongue to brain.

The ability to sense sweet, bitter, salty, sour, and savory (also called umami) is innate, says Hojoon Lee, a postdoctoral researcher in Zuker's lab who led the study, which is published August 9 in the journal *Nature*. "We are born to be averse to sour or bitter tastes and attracted to sweet things," he says.

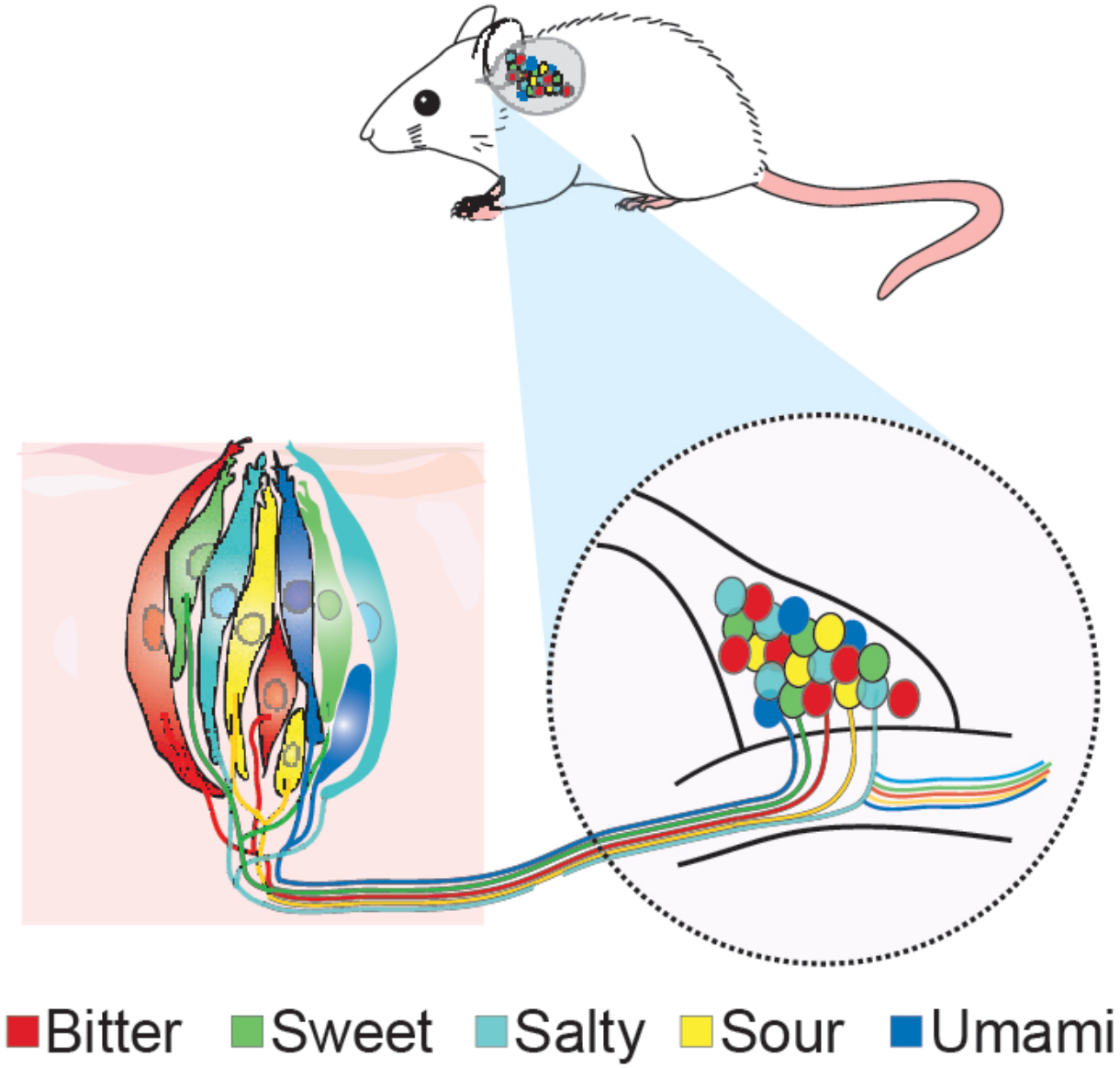
Although it may seem like taste is merely a matter of pleasure (or mild disgust), those responses can be key to survival, especially for other animals. Sweet tastes can signal nutrient-dense fare, whereas bitter tastes can mark a deadly poison.

For such an important job, the taste system has remarkably high turnover. Like a string of fritzy Christmas lights, the cells on the tongue that detect tastes are constantly dying and being replaced. These cells, called taste receptor cells, are nestled on the taste buds and live for only about two weeks—which means that stem cells need to churn out new taste receptor cells continually.

The short life span of taste cells created a conundrum, Zuker says: Amid such high turnover, how does the taste system do its job reliably? Connections between cells in the taste buds and neurons must be re-wired correctly each time for the taste system to work. "If you don't connect properly, you're going to be triggering the wrong behavioral responses," Zuker says. But just how the taste system pulled off this feat was a mystery.

"Essentially, very little was known about the wiring of the taste system," Lee says. Using sophisticated genetics and single-cell functional imaging, Zuker, Lee, and colleagues created genetically modified mice with mixed-up taste systems. Then, the researchres watched how the

miswiring linked bitter taste receptor cells to sweet neurons or sweet receptor cells to bitter neurons.



Mouse taste buds (left inset) host a collection of taste receptor cells, each one tuned to a particular flavor. When key proteins in these cells are swapped, taste sensations get scrambled as they move to geniculate ganglion neurons (right inset), and then on to the brain. Credit: Lee et al./*Nature* 2017

Each taste receptor cell is tuned to detect one of the five flavors. When the cell recognizes a chemical taste, it jumps into action. This activity is picked up by a bundle of nerves originating in ganglion neurons located just behind the mice's ears. These neurons send taste messages from the tongue to the brain.

To figure out how ganglion neurons find and reconnect to the correct newly-born taste receptor cells, Zuker, Lee and colleagues focused on bitter and sweet. Using a method called RNA-seq, they found two molecules that may function as critical signals. Bitter-sensing taste receptor cells produced a molecule called Semaphorin 3A, while sweet-sensing taste receptor cells had an abundance of different one, Semaphorin 7A. Both molecules are known to help neural circuits wire up correctly.

Next, the researchers tested mutant mice with bitter-sensing taste receptor cells that lacked Semaphorin 3A. Most ganglion neurons usually hook up with receptor cells that all sense the same flavor. But without Semaphorin 3A, previously bitter ganglion neurons expanded their repertoire and reached out to other kinds of taste receptor cells. Nearly half of these ganglion cells also responded to sweet, umami and salty flavors, the researchers found.

More mix-ups followed. When mice were genetically engineered to produce the bitter signal, Semaphorin 3A, in sweet and umami taste receptor cells (rather than in the expected bitter taste receptor cells), the neurons that normally respond to bitter now responded to sweet tastes, too. The mice's behavior reflected this confusion. They had trouble distinguishing between plain water and water laced with the bitter chemical quinine.

Similar results came from experiments in which Semaphorin 7A, the sweet signal, was produced in bitter-sensing taste receptor cells. Ganglion cells that usually respond to sweet flavors now began detecting bitter ones, too.

The results confirm the idea that specific chemical signals in newborn taste receptor cells can pull the right nerve cell connections toward them, creating cellular links that lead to proper taste sensation. "As new taste cells are born, they provide the right instructions to establish the right connection," Zuker says.

The experiments were done in mice, but because of the strong similarities between human and mice taste systems, Lee suspects the results may apply to humans too. And by revealing how the taste system continually remakes itself, the work may lead to a deeper understanding of how the senses are assembled and wired, and how their signals make their way to the brain.

More information: Hojoon Lee et al, Rewiring the taste system, *Nature* (2017). DOI: 10.1038/nature23299

Provided by Howard Hughes Medical Institute