Medical Xpress

Discovering the epigenetic mechanism that causes bitter taste distortion

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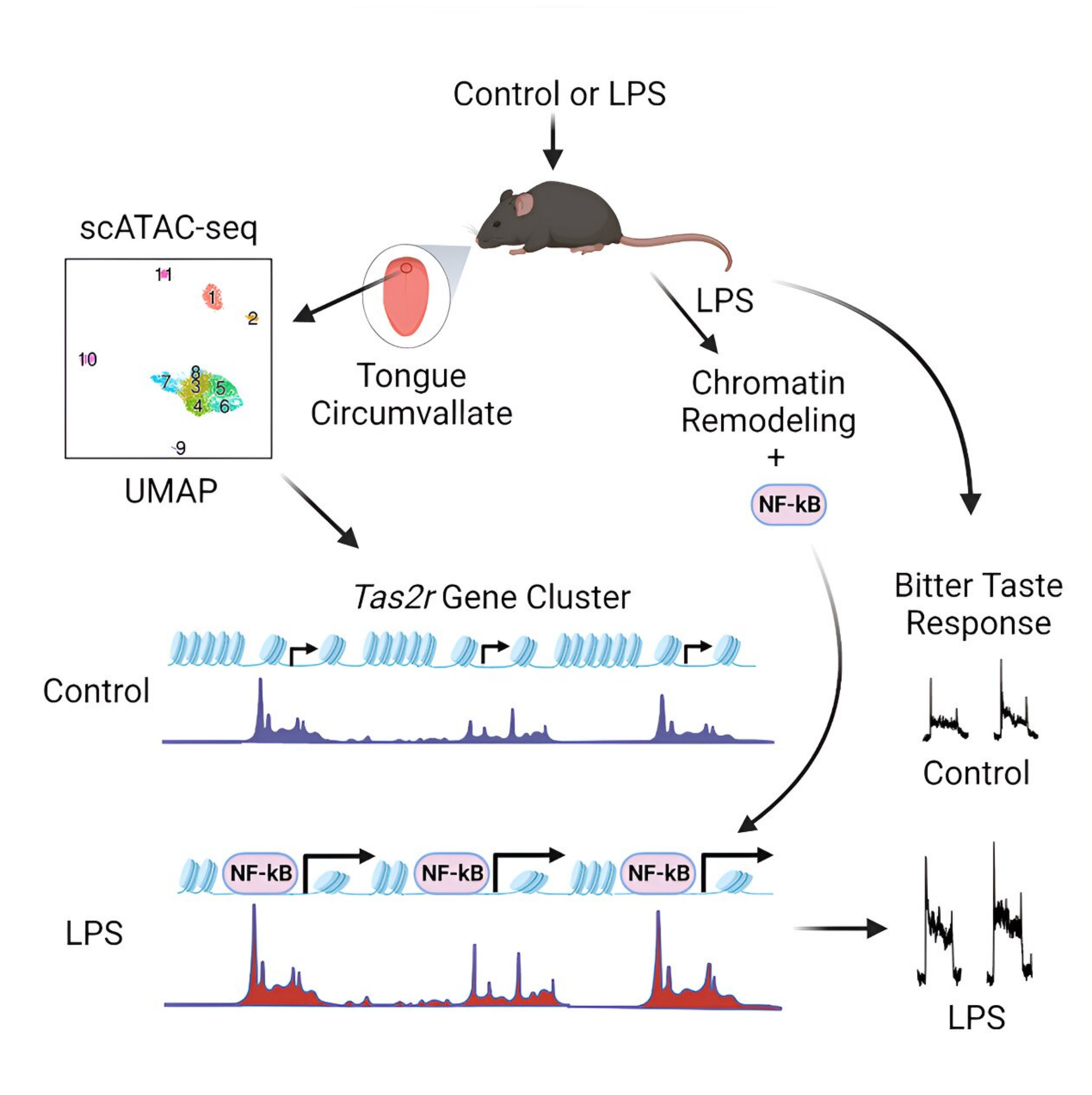

Graphical Abstract. Credit: *iScience* (2023). DOI: 10.1016/j.isci.2023.106920

A bitter taste in the mouth is often a symptom or side effect of illness, which may be the result of how the body reacts to pathogens. A new study published in *iScience*, by Hong Wang, Ph.D., an Associate Member at the Monell Chemical Sense Center, and colleagues sheds light on the mechanisms involved in the complex interplay between taste perception and immune function.

Their work also highlights the potential of a sequencing tool for investigating epigenetic mechanisms that affect taste-cell gene expression. Epigenetics is the study of how and when genes are expressed rather than alteration of the genetic code itself.

In addition to being unpleasant, a bitter taste in the mouth or from food can contribute to a loss of appetite, an effect associated with ailments from the common cold to cancer. Bitter taste can also affect patients' willingness to take certain medications, especially when they are young children. Bitter receptors are encoded by Tas2r genes, which also provide an important defense against bacteria and parasites in the mouth and gut. However, this process is not well understood.

For this study, the team explored how inducing inflammation would affect gene regulation of these taste receptors. Using lipopolysaccharide (LPS), a compound that induces inflammation similar to that caused by bacterial infections, they found that mice showed a distinct elevated aversion to bitter tastes. The team used nerve-recording experiments to confirm that this aversion originates in the taste buds of mice, rather than in their brains.

"Our study had very clear data showing this is actually a change at the peripheral level, not deep in the brain," said Wang, confirming that genes in taste cells govern bitter taste distortion to this type of inflammation.

This finding has interesting clinical implications for the study of behavioral aspects of illness, such as a loss of appetite. When people are sick they often do not feel like eating. This can affect even humans' love for sugary treats, as other studies have noted. Mice also have a decreased preference for sweet tastes during illness and forced intake of sugar can make them sicker. These results potentially indicate a protective behavior with a biological or evolutionary basis.

To investigate the underlying gene expression mechanisms of the bitterness response, the team used several methods of analysis. Real-time quantitative reverse-transcription polymerase chain reaction (qRT-PCR) revealed a significantly increased response across the majority of the Tas2r taste-receptor genes, with peak gene expression ranging from three to five days during the sickness period.

The researchers also used single-cell sequencing assay for transposase-accessible chromatin (scATAC-seq) to explore the expression of Tas2r genes in response to LPS—the first reported instance of this method to study taste receptor gene expression. LPS markedly increased the accessibility of many Tas2r genes, indicating that the bitter taste distortion in this experiment is caused by an epigenetic mechanism, similar to how disease-causing bacteria can affect those genes.

Finally, the study showed that LPS-induced inflammation globally affected gene expression in taste stem cells, suggesting a "remodeling" of the cells' genome. This may leave an epigenetic memory, enabling the cells to respond faster to future infections, but may also contribute to long-lasting effects on taste responses. This finding sheds light on why cancer treatment and certain chronic illnesses can cause a lingering bitter taste in the mouth or alter the taste perception of certain foods.

This diverse response across taste receptors has potential implications for research on how to make more effective bitter blockers for medications and other edible health and wellness products. "The spectrum of the bitter taste receptor expression is not uniform," Wang said. "If we want to look at a bitter blocker for an individual taste receptor, we may want to take these factors into consideration, such as whether it's for after a sickness, during a sickness, or which of the taste receptor genes is most prominently expressed."

More information: Cailu Lin et al, Lipopolysaccharide increases bitter taste sensitivity via epigenetic changes in Tas2r gene clusters, *iScience* (2023). DOI: 10.1016/j.isci.2023.106920

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