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Researchers find the pathway responsible for taste changes among chemotherapy patients

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Many patients undergoing chemotherapy experience severe taste disruptions that make eating a challenge at a time when maintaining good nutrition is extremely important. Because the type of chemotherapy drugs used varies among cancer types, numerous theories exist about how and why certain medications interfere with taste perception. Now researchers at the University of Michigan have identified the pathway responsible for taste changes among users of chemotherapy drugs that treat basal cell carcinoma (BCC), a skin cancer that is among the most commonly diagnosed in the US.

The life span of a taste bud ranges from three to 30 days. Throughout their lifecycle, taste buds are extremely susceptible to environmental, metabolic and pharmacologic factors. Previous research has shown that taste cell differentiation, turnover and maintenance are regulated by the Hedgehog (HH) signaling pathway, which is active within and around the taste buds in the taste system. However, in contrast to the highly regulated normal functions of HH signaling, uncontrolled HH signaling drives the development of BCC tumors. Non-surgical therapy to treat advanced BCC involves drugs that block the HH pathway. While these drugs can lead to regression of cancer, side effects related to taste perception can be severe. The majority of patients taking these HH pathway inhibitors (HPIs) complain of taste disturbances and many discontinue treatment because of these taste-related side effects.

In this study, the research team explored the novel idea that taste disturbances in BCC patients result from HPI drug interference with HH

signaling in taste organs. Using a mouse model to simulate the effect of HPI-treated patients, the researchers observed that blocking the HH signaling pathway led to "profound alterations in taste bud structure and function." While these changes affected taste responses from the chorda tympani nerve, they surprisingly did not affect tactile or temperature sensation.

"Our study establishes an essential and modality-specific requirement for HH signaling in maintaining neurophysiological taste sensation in mice, underlying the likely cause of taste disruption in HPI-treated patients," the authors wrote. "We propose that taste disturbances in HPI-treated patients derive from HH-dependent loss of taste papilla integrity and taste buds, with a specific, concomitant reduction of peripheral nerve taste responses that transmit taste sensation centrally."

More information: "Hedgehog pathway blockade with the cancer drug LDE225 disrupts taste organs and taste sensation." *Journal of Neurophysiology* 1 February 2015 Vol. 113: 1034-1040 DOI: 10.1152/jn.00822.2014

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