Unraveling the enigma of salty taste detection

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Molecular biologist Sunil Sukumaran, Ph.D. (left) and neuroscientist Brian Lewandowkski, Ph.D. are unraveling the enigma of salty taste detection. Credit: Monell Center

Public health efforts to reduce dietary sodium intake have been hindered by an incomplete understanding of the complex process by which humans and other mammals detect salty taste.

Now, a multidisciplinary team from the Monell Center has further characterized the identity and functionality of salt-responding taste cells on the tongue. The knowledge may lead to novel approaches to develop salt replacers or enhancers that can help reduce the sodium content of food.

"Understanding more about the mechanisms involved in detecting salt taste moves us closer to developing strategies to reduce the amount of salt in our food while still retaining the salty taste that people enjoy," said the study's lead author Brian Lewandowski, PhD, a neurophysiologist at Monell.

'Salt' is a chemical term that describes a compound made of positively and negatively charged ions; the most well-known example is sodium chloride (NaCl). The primary process by which mammals detect NaCl, common table salt, is well understood, and occurs via a sodium receptor known as ENaC (epithelial sodium channel). The ENaC receptor responds almost exclusively to sodium (Na+) salts and is not influenced by the salt's negative ion (eg, Cl-).

However, scientists know that a second salt-sensing receptor also exists, but much about this receptor, including its identity, remains unknown. Like ENaC, the second receptor detects sodium salts, but it also is sensitive to non-sodium salts such as potassium chloride (KCl), which is frequently used to replace sodium in foods.

Unlike the ENaC receptor, this second receptor for salt taste is affected by the size of the salt's negative ion such that salts with smaller negative ions taste more salty. For this reason, sodium chloride, a salt with a small

negative ion, tastes saltier than sodium gluconate (Na(C6H11O7)), which has a very large negative ion.

In the current study, published in the *Journal of Neuroscience*, Monell researchers identified the taste cells involved in this second salt taste mechanism and increased understanding of how they function.

To identify and study the cells involved in the second salt pathway, the Monell researchers first needed to address several challenges related to taste physiology. Taste cells, including those that contain the various types of taste receptors, are tightly grouped together in structures known as taste buds. This clustering enables the cells to communicate with one another, but also makes it difficult for scientists to distinguish between a given cell's direct response and one indirectly caused by a message from a neighboring cell.

In addition, the tight junctions that hold taste cells together form a nearly impenetrable barrier that restricts the movement of larger ions, making it difficult to directly compare how different sized ions affect taste cell function.

To eliminate cell-to-cell communication and the tight junctions, the Monell scientists used a rodent model and applied sophisticated neurophysiological techniques to isolate single living taste cells. They then measured the isolated taste cells' responses to different salts to classify the cells and identify those involved in the second salt pathway.

The isolated second pathway cells were found to be a subset of what are known as Type III taste cells, which are also thought be involved in detecting sour taste.

Subsequent experiments with the isolated second pathway cells revealed that negative ions still influenced the cells' response to a given salt, with

the effect of the negative ion remaining dependent on the ion's size.

Since the scientists had eliminated the tight junctions between cells, they concluded that this result was not an indirect effect of the ion's size (as a previous theory had suggested), but instead indicated a direct interaction between the taste cell and the negative ion.

Thus, unlike the ENaC pathway, both positive and negative ions directly interact with cells involved in the second salt pathway to influence how these cells respond to salts.

By knowing which cells to study and more about how they interact with salts, the team can now focus on determining the identity of the second salt receptor.

"Now that we have isolated and better understand the cells involved in the second salt taste pathway, we can begin to study them in more detail," said study author Alexander Bachmanov, PhD, DVM, a behavioral geneticist at Monell. "We now will analyze these cells to determine which genes and proteins are expressed and which are important for sensing salty taste. This should help us pinpoint the specific receptor mechanism."

The new findings provide an important step toward a more complete understanding of salty taste and how it is detected. After more pieces of the system are decoded, scientists may be able to identify alternative approaches to activate salty taste and alleviate the negative health consequences of sodium overconsumption.

More information: B. C. Lewandowski et al. Amiloride-Insensitive Salt Taste Is Mediated by Two Populations of Type III Taste Cells with Distinct Transduction Mechanisms, *Journal of Neuroscience* (2016). DOI: 10.1523/JNEUROSCI.2947-15.2016

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