Shape changes in aroma-producing molecules determine the fragrances we detect

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Shakespeare wrote "a rose by any other name would smell as sweet." But would it if the molecules that generate its fragrance were to change their shape?

That's what Dr. Kevin Ryan, Assistant Professor of Chemistry at The City College of New York (CCNY) and collaborators in the laboratory of Dr. Stuart Firestein, Professor of Biology at Columbia University, set out to investigate. Their findings, reported today in the journal "Chemistry & Biology," shed new insight into how our sense of smell works and have potential applications in the design of flavors and fragrances.

When odor-producing molecules, known as odorants, pass through the nose, they trigger intracellular changes in a subset of the approximately 400 different varieties olfactory sensory neurons (OSN) housed in the nose's internal membrane tissue, Professor Ryan explained. The unique reaction pattern produced, known as the olfactory code, is sent as a signal to the brain, which leads to perception of odors.

Professor Ryan and his team wanted to learn how these receptor cells respond when odorants change their shape. They studied the odorant octanal, an eight-carbon aldehyde that occurs in many flowers and citrus fruits. Octanal is a structurally flexible molecule that can adapt to many different shapes by rotating its chemical bonds.

The researchers designed and synthesized eight-carbon aldehydes that resembled octanal, but had their carbon chains locked by adding one additional bond. These molecules were tested on genetically engineered OSNs known to respond to octanal. This work was done in Professor Firestein's laboratory at Columbia.

The aldehyde molecules that could stretch to their greatest length triggered strong activity in the OSNs. However, those molecules whose carbon chains were constrained into a U shape blocked the receptor and left the cell unable to sense octanal.

"Conformationally constrained odorants were more selective in the number of OSNs they activated," Professor Ryan noted. "The results indicate that these odorant molecules might be able to alter fragrance mixture odors in two ways: by muting the activity of flexible odorants present in a mixture and by activating a smaller subset of OSNs than chemically related flexible odorants. This would produce a different olfactory code signature."

Olfactory receptors belong to the G-protein coupled receptor (GPCR) class of proteins, a family of molecules found in cell membranes throughout the body. Professor Ryan pointed out that half of all commercial pharmaceuticals work by interaction with proteins within this family. Thus, the findings could also have applications to GPCR drug design, as well.

Source: City College of New York