Bitter taste perception is not just about flavors, geneticists show

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Long the bane of picky eaters everywhere, broccoli's taste is not just a matter of having a cultured palate; some people can easily taste a bitter compound in the vegetable that others have difficulty detecting. Now a team of Penn researchers has helped uncover the evolutionary history of one of the genes responsible for this trait. Beyond showing the ancient origins of the gene, the researchers discovered something unexpected: something other than taste must have driven its evolution.

The team was led by Penn researchers Sarah Tishkoff, a Penn Integrates Knowledge professor with appointments in the genetics department in Penn's Perelman School of Medicine and the biology department in the School of Arts and Sciences, and Michael C. Campbell, a postdoctoral fellow in the genetics department at the medical school, and included undergraduate and postdoctoral researchers from both the genetics and biology departments. The team included their collaborator Paul Breslin from the Monell Chemical Senses Center in Philadelphia and Rutgers University and researchers from the Musée de L'Homme in France, the National Institutes of Health and several African universities and research institutes.

Their research was published in the journal *Molecular Biology and Evolution*.

The researchers were interested in the gene TAS2R38, which codes for a bitter taste receptor protein with the same name. People with a certain version of that gene can taste a compound, phenylthiocarbamide, or

PTC, which is chemically similar to naturally occurring bitter compounds, called glucosinolates, present in many foods, including cruciferous vegetables like broccoli and Brussels sprouts. These "tasters" find such foods to have a bitter taste that people with a different version can't detect. As a result, "nontasters" have been shown to consume fewer cruciferous vegetables.

Modern humans originated in Africa, and populations from that region have the highest levels of genetic diversity globally. Previous studies had looked at variations in the PTC-sensitivity gene, but none had ever studied a large sample of diverse African populations with different cultures, ethnicities or diets.

"Because there is more genetic variation in African populations, you're likely to see unique variants you may not see elsewhere," Tishkoff said. "Our study of variation at the TAS2R38 gene in Africa and correlations with taste perception and diet gives us a clue about the evolutionary history of the gene and how natural selection might be influencing the pattern of variation."

Genes that influence perception are of particular interest to geneticists because those genes are under strong evolutionary pressure; organisms with senses that are well adapted to their environment have better chances to survive and reproduce. PTC-sensitivity's potential impact on nutrition, or the ability to detect bitter-tasting toxins, would therefore make it an obvious target for natural selection.

By looking at the TAS2R38 gene in 611 Africans from 57 diverse ethnic populations with distinct diets (for example, Pygmy hunter-gatherers and Maasai pastoralists), as well as in 132 non-Africans, the researchers showed that Africans had more variation than non-Africans, including several never-before-seen rare mutations.

The researchers also tested the correlation between genetic variation at this gene and levels of PTC tasting ability in 463 Africans, another first-of-its-kind study. In an experiment that was challenging to carry out across a wide swath of the African continent, participants sampled successively concentrated solutions of PTC and water until they were able to detect the bitter taste. When correlated with the participants' genetic data, the study revealed that Africans have a broader range of PTC taste sensitivity than typically seen outside of Africa, and that relatively new rare mutations also decrease an individual's ability to taste PTC.

Comparing different African populations confirmed that the PTC-sensitivity gene is millions of years old, meaning it predates the evolution of modern humans and likely existed in the common ancestor of modern humans and Neanderthals.

The study also revealed something surprising: local diet did not have an effect on the evolution of any of the PTC-sensitivity gene variants.

"Although we typically see a lot of genetic variation among diverse African populations, the frequency of TAS2R38 variants is fairly similar across different ethnicities, cultures and diets," Campbell said. "This is suggestive that variation at this gene serves some other function beyond oral sensory perception."

This counter-intuitive discovery is in line with other recent studies, which found receptors similar to TAS2R38 in the lungs, upper airways and gut. If the variations of the TAS2R38 gene have had a heretofore-undiscovered impact on breathing or digesting, alongside tasting, the former traits might be the true focus of natural selection.

"Why are we 'tasting' in our guts or in our lungs? There must be something else," Tishkoff said, "that these taste receptors are doing, and it must be a pretty important physiological process, otherwise these variants wouldn't be maintained."

"We now believe the chemical senses play key sentinel roles at points of entry to the body like the mouth, airways and gastro-intestinal tract," Breslin said. "It is possible that, in addition to detecting bitter-tasting thyroid toxins, products of this gene help to defend against ubiquitous pan-African threats, such as inhaling injurious compounds or growing undesirable bacteria in airway mucus or intestines."

Provided by University of Pennsylvania

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