

The finer points of taste

As more receptors are defined, researchers will further unlock the mechanics of taste. How the mind perceives these sensory signals is another matter.

BY BIJAL P. TRIVEDI

Take a sip of milk, look in the mirror and stick out your tongue. The tiny pink bumps emerging from the creamy film coating your tongue are the mushroom-shaped, or fungiform, papillae that conceal many of your taste buds. These are the gateway to detecting the sweetness of a cake, the saltiness of a potato crisp, the meatiness of a steak, the bitterness of beer, and the sourness of a lemon.

The four types of papillae that speckle the tongue (see 'Taste discovery') give it a rough surface that helps move the food around as we chew. The filiform papillae simply detect texture, whereas the other three — fungiform, foliate and circumvallate — contain onion-shaped taste buds. Each taste bud is packed with taste cells, which are capped with sensors for the five basic tastes (although we may be able to detect other taste qualities too). Contrary to popular belief, every part of the tongue is sensitive to all five taste qualities — the once common 'tongue map' depicting specific regions for each taste was based on a misunderstanding in the early 1900s and is wrong.

In 1931, Arthur Fox, a chemist at US chemical giant DuPont, made a remarkable discovery after accidentally releasing a cloud of fine phenylthiocarbamide (PTC) crystals while transferring the powder to a bottle. A colleague commented that the compound tasted bitter, but Fox, in the midst of the powder cloud, tasted nothing. After testing friends, family and colleagues, Fox found that people are either 'tasters' or 'non-tasters' of PTC (ref. 1). Geneticist L. H. Snyder confirmed Fox's work and found that non-tasting is a recessive Mendelian trait. Later work uncovered a range of PTC sensitivity, suggesting the involvement of more than one gene in perceiving this bitter compound².

TASTE TRANSDUCER

It took almost seven decades to pinpoint the genes that encode taste receptors. It was widely believed that each taste cell carried sensors for several, if not all, of the five tastes, with the signals being decoded in the brain. But this made no sense to neuroscientist Charles Zuker, a

Howard Hughes Medical Investigator now at Columbia University in New York. He couldn't understand why a cell could carry sensors for both sweet, signalling an energy-rich food, and bitter, which could warn of spoiled or toxic food — a mix-up could be lethal.

Zuker rejected this 'broad tuning' and assumed that the difference between a sweet and a bitter taste cell, for example, was the collection of receptors on its surface. He joined forces with geneticist Nicholas Ryba of the National Institute of Dental and Craniofacial Research in Bethesda, Maryland, and over the next 12 years they sought to discover the sensors for all five tastes (see 'Taste discovery').

In 2000, using the first draft of the human genome, Zuker and Ryba's team identified the first taste sensors: a family of G-protein-coupled receptors (GPCRs)³ on chromosome

More than five teams were competing to find the sweet receptor.

5. These so-called Taste-2 receptors (T2Rs) can detect bitter tastes from a wide range of different chemical compounds, requiring a collection of sensors.

Some T2Rs can detect only one bitter compound, but some can respond to more than 50 natural and synthetic bitter chemicals.

Each bitter taste cell carries from 4–11 T2Rs — this variety, along with underlying genetic variation, is thought to account for an individual's tolerance of bitter tastes. For example, variation in the gene encoding T2R38 modifies sensitivity to PTC, which correlates with sensitivity to bitter compounds in cabbage or Brussels sprouts⁴.

The race was on to find the remaining taste receptors. In 2001, more than five teams were competing to find the sweet receptor and narrowed the candidates to a different family of GPCRs. These T1R receptors have a different structure from the T2Rs, including a bulky extracellular region that interacts with sweet molecules. Zuker and Ryba provided the decisive evidence by transforming a sweet-insensitive mouse into a sugar-loving one, showing that T1R2 and T1R3 combine to detect natural and artificial sweeteners⁵. Barely a year later, they also found that the combination of T1R1 and T1R3 receptors can detect all 20 amino acids found in nature⁶, sensing a taste described as umami or savoury (for example, in meat or

cheese) that can be chemically distilled into the common food additive monosodium glutamate. The receptors for sweet, bitter and umami all use essentially the same signalling molecules to convey nutrient sensing to the brain.

SOUP SUCCESS

In 2006, Zuker and Ryba discovered the PKD2L1 receptor⁷, which detects sourness — a high concentration of hydrogen ions, or acidity, found both unripe and spoiled foods. Sour taste cells also host the Car4 receptor⁸, which senses carbon dioxide — block this receptor and a carbonated beverage will taste flat (even though it might still feel bubbly). Finally, in 2010, Zuker and Ryba found that the epithelial sodium channel (ENaC) detects sodium salt⁹ (other salts, such as potassium chloride, probably have other receptors). Instead of GPCRs, salt and sour detection uses ion channels — proteins that shuttle sodium and hydrogen ions in and out of cells.

Five basic tastes are generally recognized but there may be others, and the hunt for receptors continues. In 2003, neuroscientist Robert Margolskee, then at the Mount Sinai School of Medicine in New York, showed that mice lacking the T1R3 receptor couldn't taste artificial sweeteners but still had an affinity for sugars, especially glucose, and could also perceive umami¹⁰. "It said very clearly to us there are two different sweet mechanisms," he says.

But receptors don't tell the whole taste story. Zuker and Ryba are using the taste sensors already discovered to figure out, as Zuker says, "how the brain transforms detection into perception". ■

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TASTE DISCOVERY

Study of the basic tastes, and how these are detected by the tongue, is an evolving field.

ORGAN

The tongue contains four types of papillae. Circumvallate, fungiform and foliate papillae contain taste buds, whereas filiform papillae detect only the texture of food.

1901

D. Hänig publishes a paper containing data on taste sensitivity in different regions of the tongue. The data are later misinterpreted, giving rise to the myth of the 'tongue map'.



350 BC

Aristotle writes about the basic tastes, sweet and bitter, which can be modified, he says, by salty and acidic.



350 BC

1900

1910

1908

Fifth basic taste discovered: savoriness, described as umami, which is conferred by glutamate.

1920

1931–1932

Geneticists confirm findings about sensitivity to bitter tasting PTC and discover non-tasting is a recessive genetic trait^{2,11}.

1931

Bitter taste sensitivity found to vary among humans¹.

1930

1940

1939

Geneticists show that chimpanzees, like humans, vary in their ability to perceive the bitterness of PTC (see 'The lost appetites', page S16).



1950

1960

1970

1992

Discovery of gustducin, a taste cell-specific G-protein, in the taste buds. Gustducin is later shown to mark bitter, umami and sweet cells¹³.

1980

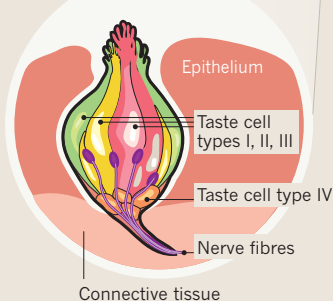
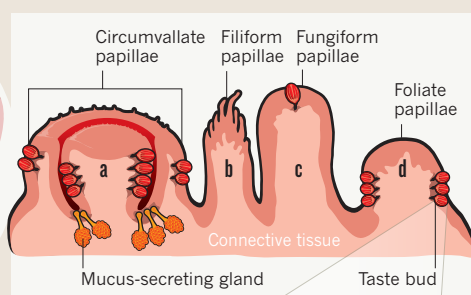
1990

2000

2010

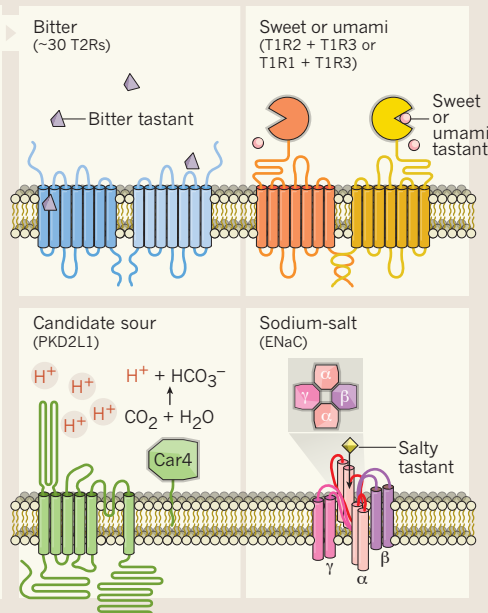
CELLS

Each taste bud is an onion-like structure packed with 50 to 100 taste cells, anatomically classified into four types. Type II cells contain receptors for sweet, bitter, umami and possibly salty tastes; type III for sour; type I are probably supporting cells. Type IV are suspected to be stem cells that supply new taste cells every two weeks.



RECEPTORS

Sweet, umami and bitter receptors belong to the superfamily of G-protein coupled receptors. ENaC, the receptor for sodium-salt taste, is an ion channel. Less is known about PKD2L1, but taste cells expressing it respond to the presence of protons (H^+), a breakdown product from acids.



2000 / BITTER

First taste sensors, the T2R bitter receptors, discovered³.

2001 / SWEET

The sweet receptor is discovered⁵: a combination of T1R2 + T1R3.

2002 / UMAMI

Amino acid detector, T1R1 + T1R3, identified⁶.

2006 / SOUR

Cells for sour taste discovered, identified by PKD2L1 (refs 4–7).

2010 / SALTY

ENaC identified as the sodium-salt taste receptor⁹.

2002

Bitter taste receptors found¹⁴ in the gastrointestinal tract.

2005

Sweet taste receptor found¹⁵ in the gastrointestinal tract.

2009

The Car4 receptor, which senses the carbon dioxide in fizzy drinks, is found on sour cells⁸.

