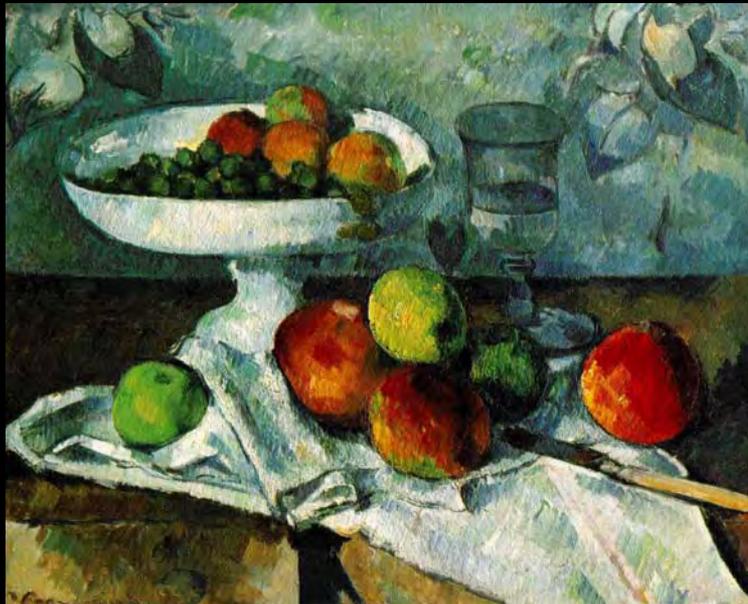


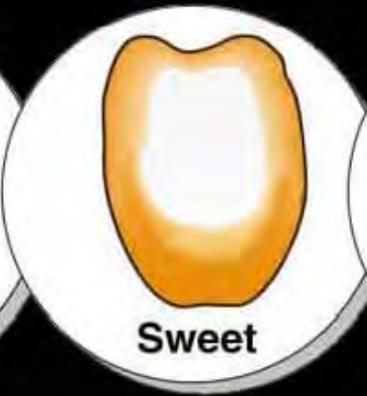
Taste: from detection to perception

- demystifying medicine?
- most “taste” problems in fact have an olfactory basis
- close inter-relation of these two chemical senses

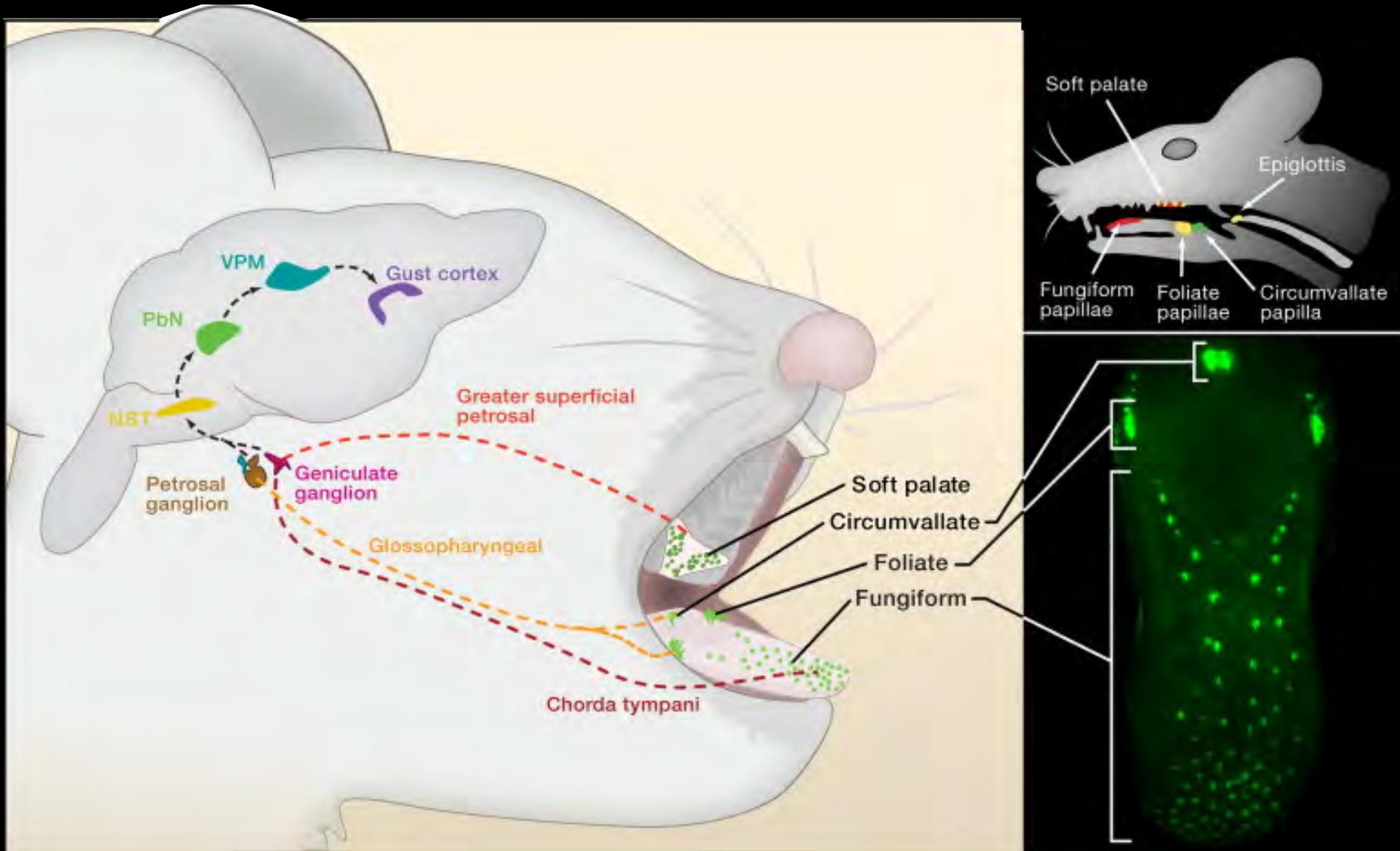


Taste evolved as an arbiter for consumption

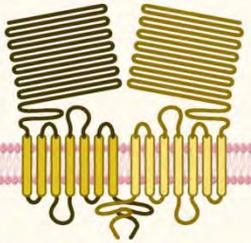
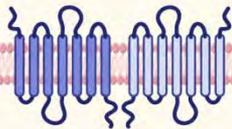
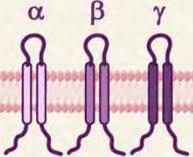
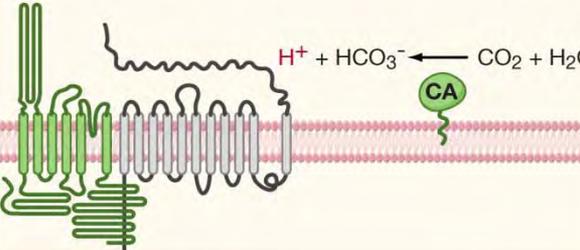




The anatomy and pathways of taste perception



Mammalian Taste Receptors

| Umami | Sweet | Bitter | Sodium | Sour and carbonation cells | |
|--|--|---|---|---|---|
|  |  |  |  |  | |
| <p>T1R1+T1R3</p> <p>L-glutamate L-amino acids glycine L-AP4</p> <p>Nucleotide enhancers IMP, GMP, AMP</p> | <p>T1R2+T1R3</p> <p>Sugars Sucrose, fructose, glucose</p> <p>Artificial sweeteners saccharin, acesulfame K aspartame, cyclamate</p> <p>D-amino acids D-alanine, D-serine, D-phenylalanine</p> <p>Glycine</p> <p>Sweet proteins Monellin, thaumatin</p> | <p>~30 T2Rs</p> <p>Cycloheximide (mT2R5)</p> <p>Denatonium (mT2R8, hT2R4)</p> <p>Salicin (hT2R16)</p> <p>PTC (hT2R38)</p> <p>Saccharin (hT2R43, hT2R44)</p> <p>Quinine strychnine atropine</p> | <p>ENaC</p> <p>Low NaCl Sodium salts</p> | <p>PKD2L1</p> <p>Acids Citric acid Tartaric acid HCl</p> | <p>CA IV</p> <p>Carbonated drinks</p> |

necessary and sufficient for detection

reflect the evolutionary pressure on an organism

responsible for differential responses within and across species

provide a logic for the encoding of taste quality

necessary and sufficient for detection

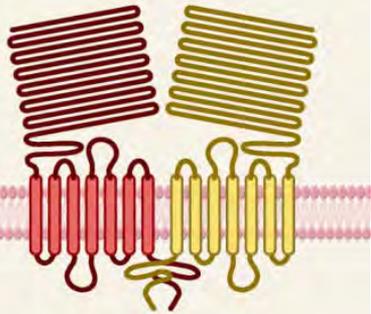
reflect the evolutionary pressure on an organism

responsible for differential responses within and across species

provide a logic for the encoding of taste quality

Sweet taste depends on T1R2 and T1R3

Sweet



T1R2+T1R3

Sugars

Sucrose, fructose, glucose

Artificial sweeteners

saccharin, acesulfame K, aspartame, cyclamate

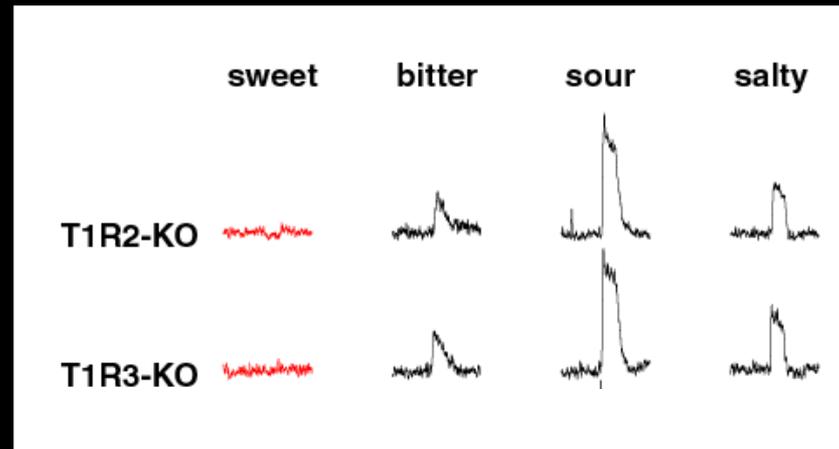
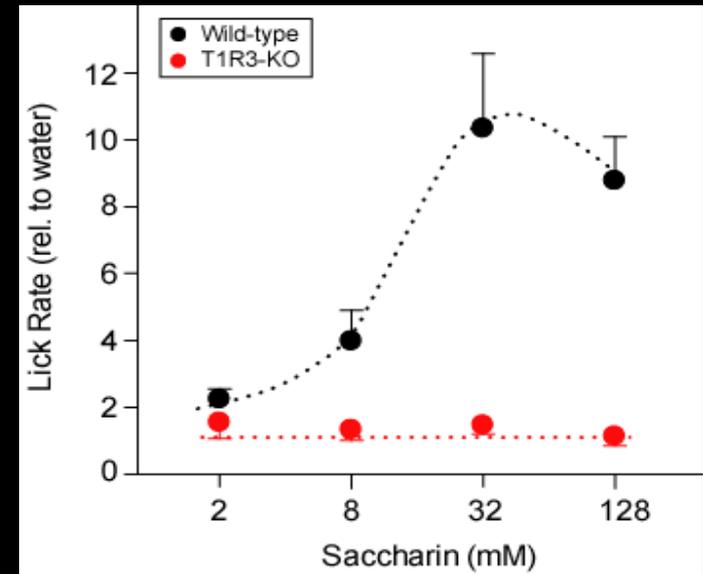
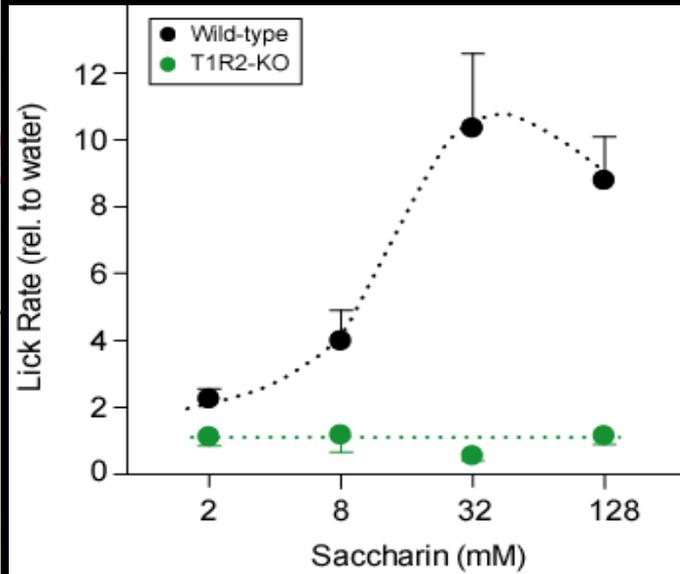
D-amino acids

D-alanine, D-serine, D-phenylalanine

Glycine

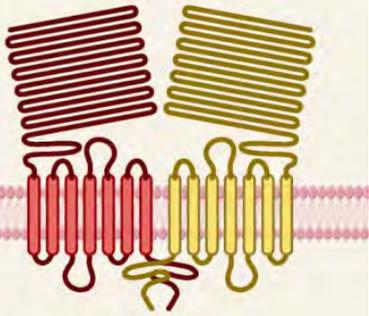
Sweet proteins

Monellin, thaumatin



Sweet-spectrum is determined by T1Rs

Sweet



T1R2+T1R3

Sugars

Sucrose, fructose, glucose

Artificial sweeteners

saccharin, acesulfame K, aspartame, cyclamate

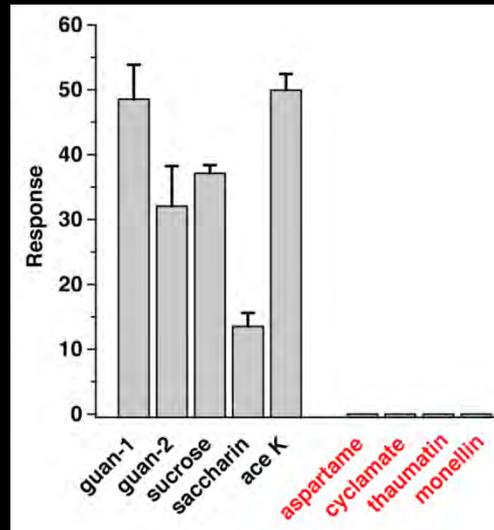
D-amino acids

D-alanine, D-serine, D-phenylalanine

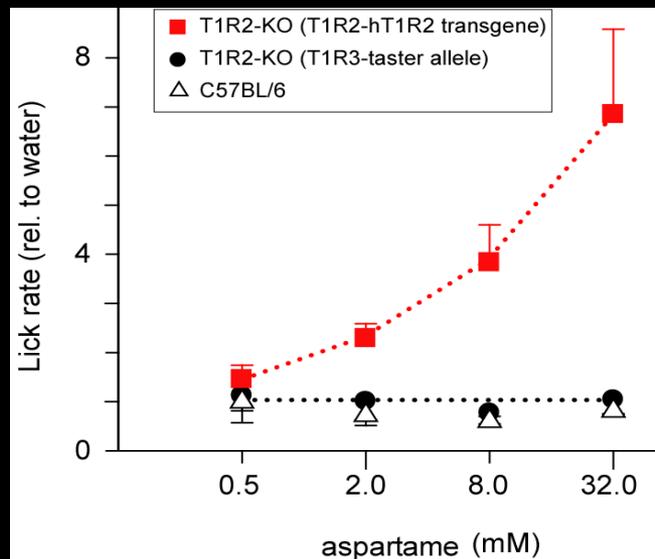
Glycine

Sweet proteins

Monellin, thaumatin

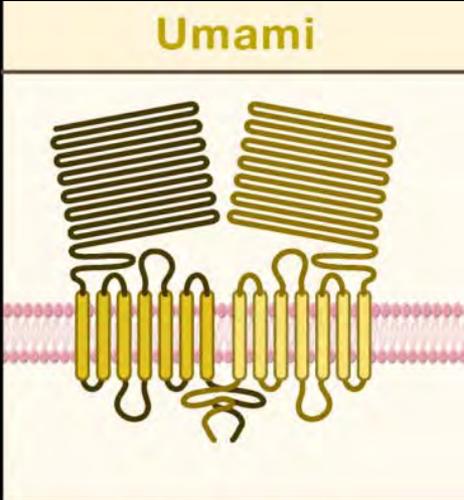


Neither mice nor mouse receptors normally detect a range of artificial sweeteners



Transgenic expression of hT1R2 “humanizes” the sweet preference of mice

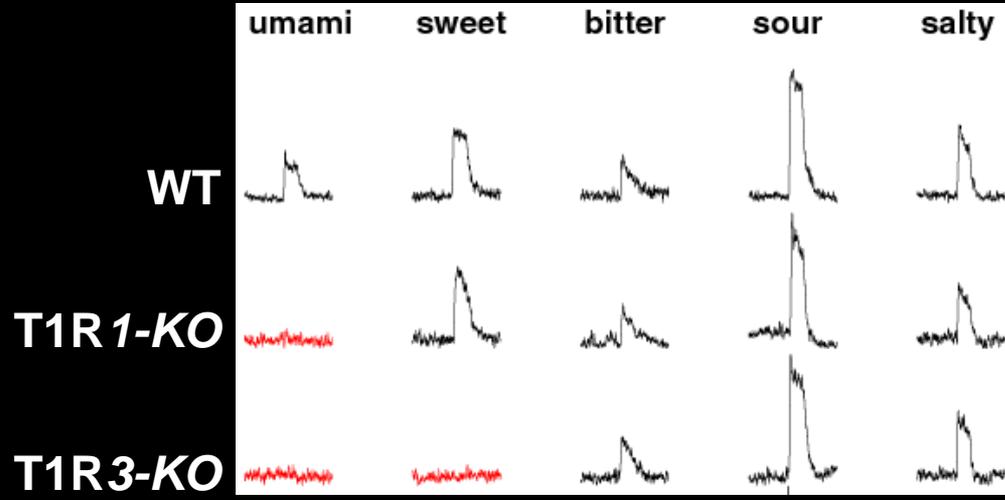
The savory taste umami provides a taste for protein



T1R1+T1R3

L-glutamate
 L-amino acids
 glycine
 L-AP4

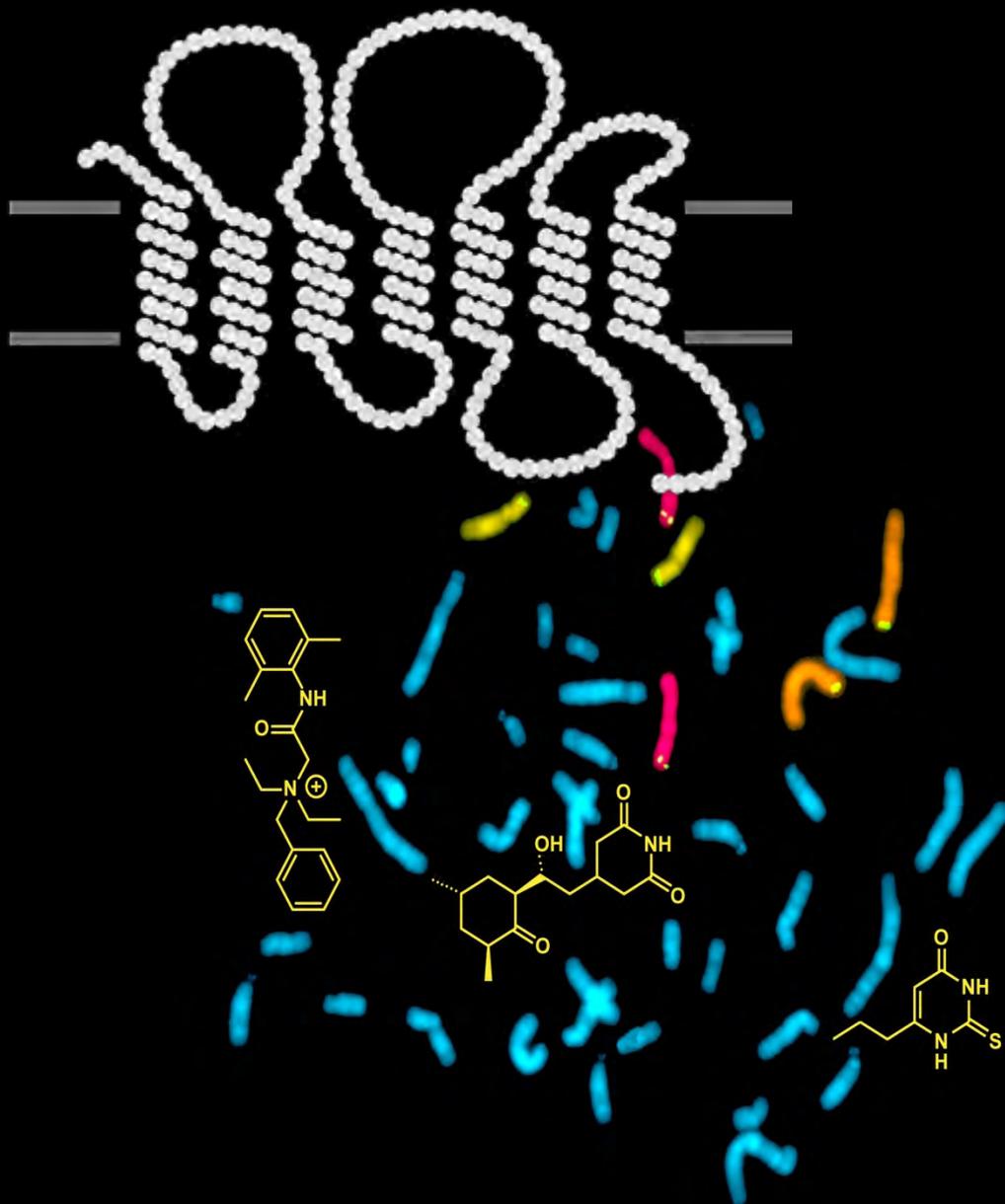
Nucleotide enhancers
 IMP, GMP, AMP



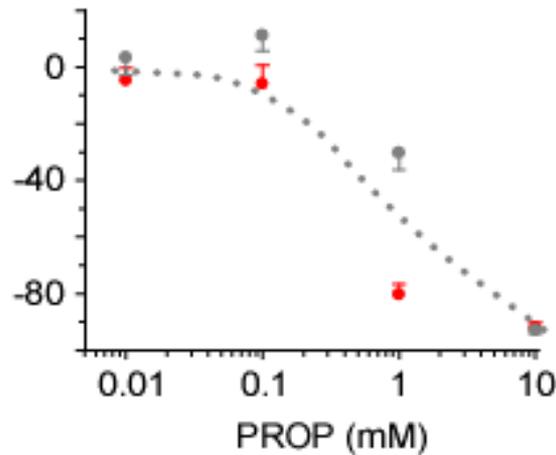
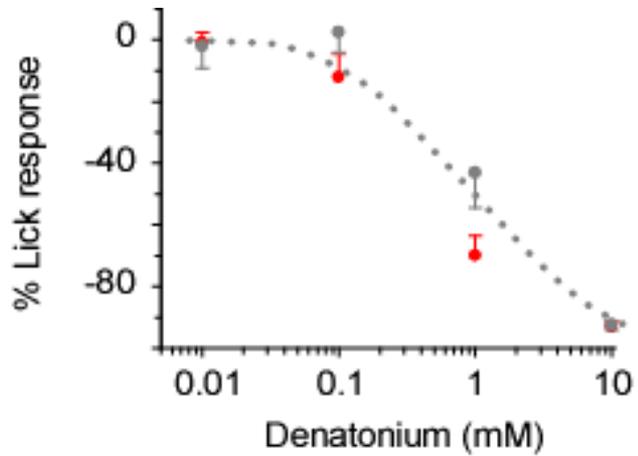
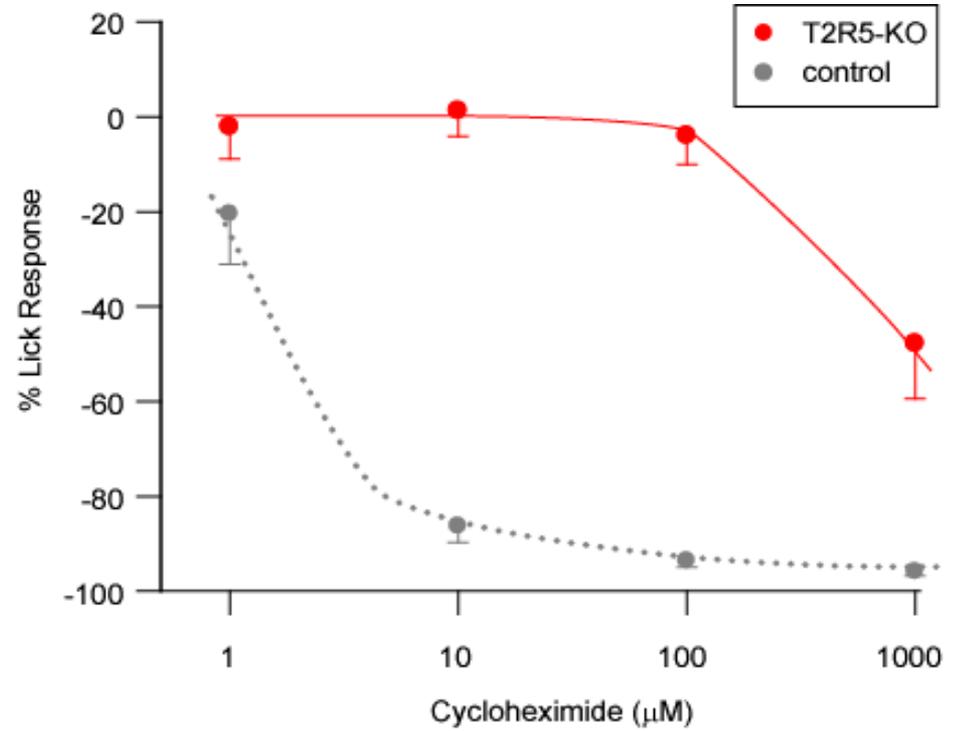
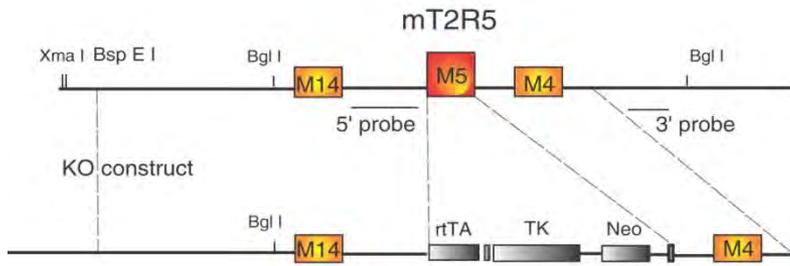
Human and mouse T1R1+3 have very different selectivity

Giant pandas lost T1R1-activity when they switch diet

T2Rs- a very diverse family of about 30 receptors



genes all map to bitter taste loci
selectively expressed in TRCs



Ken Mueller
Mark Hoon

How is taste coded at the periphery?

Probe:

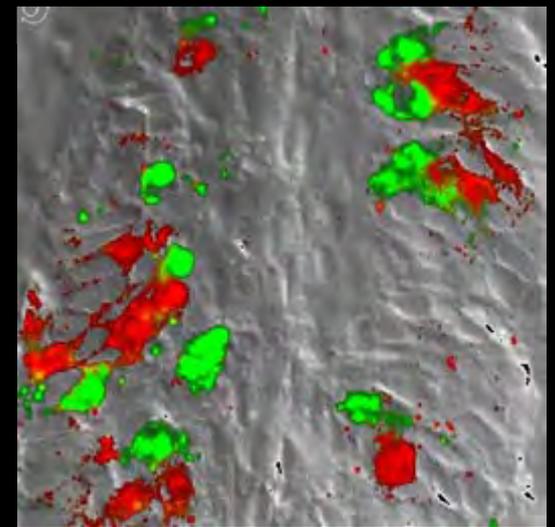
T2R7



mix of 10 T2Rs

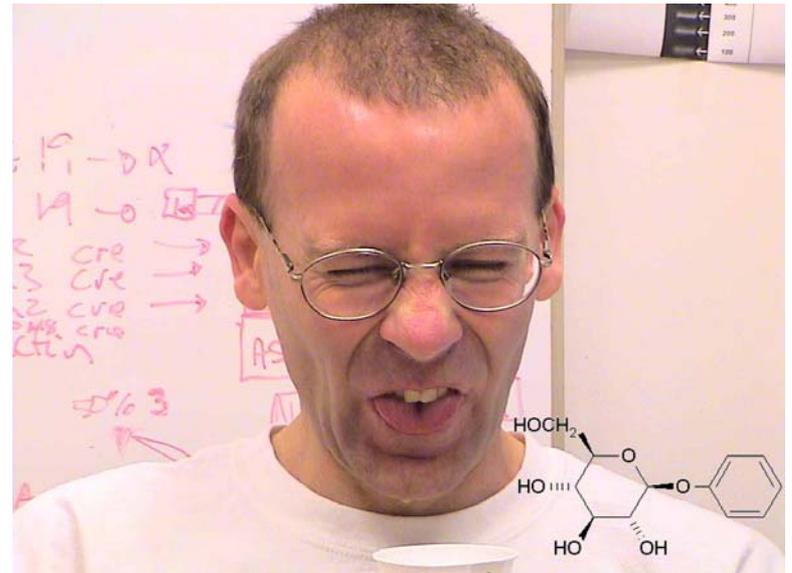
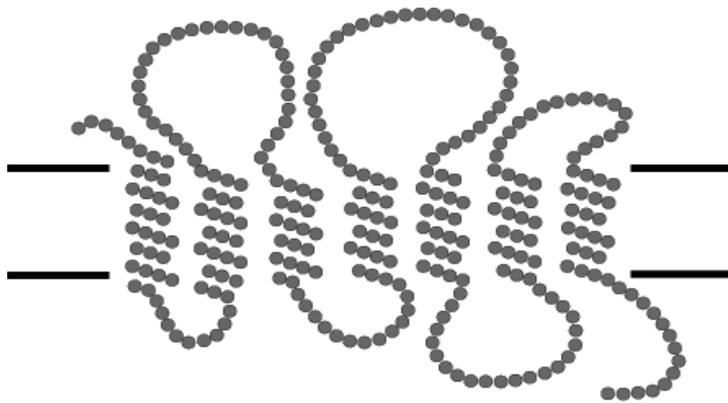


T2Rs + T1Rs



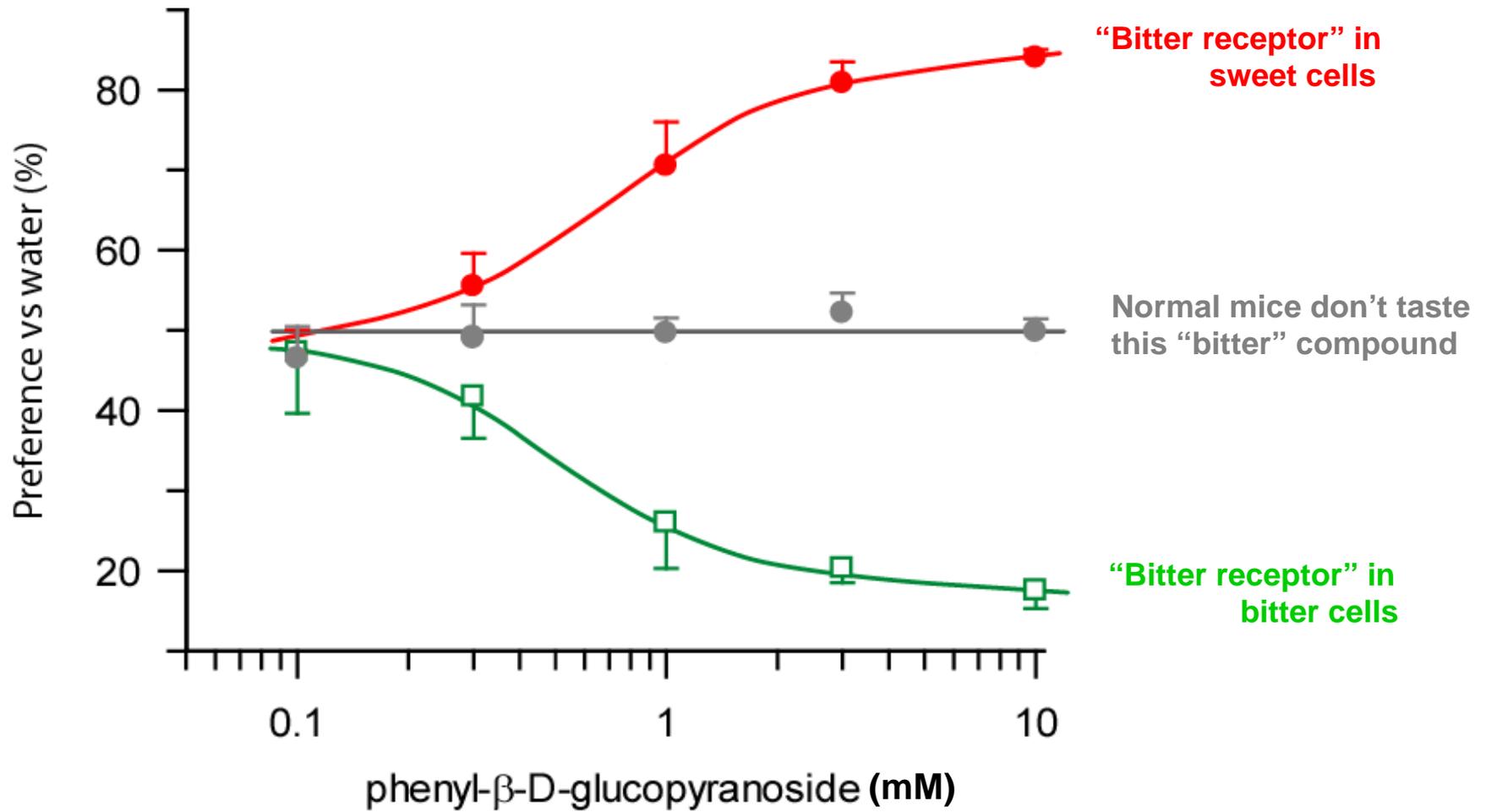
suggests cells are responsible for encoding taste quality

Attractive (sweet) and aversive (bitter) taste behaviors are mediated by dedicated cells hardwired to trigger stereotypic responses

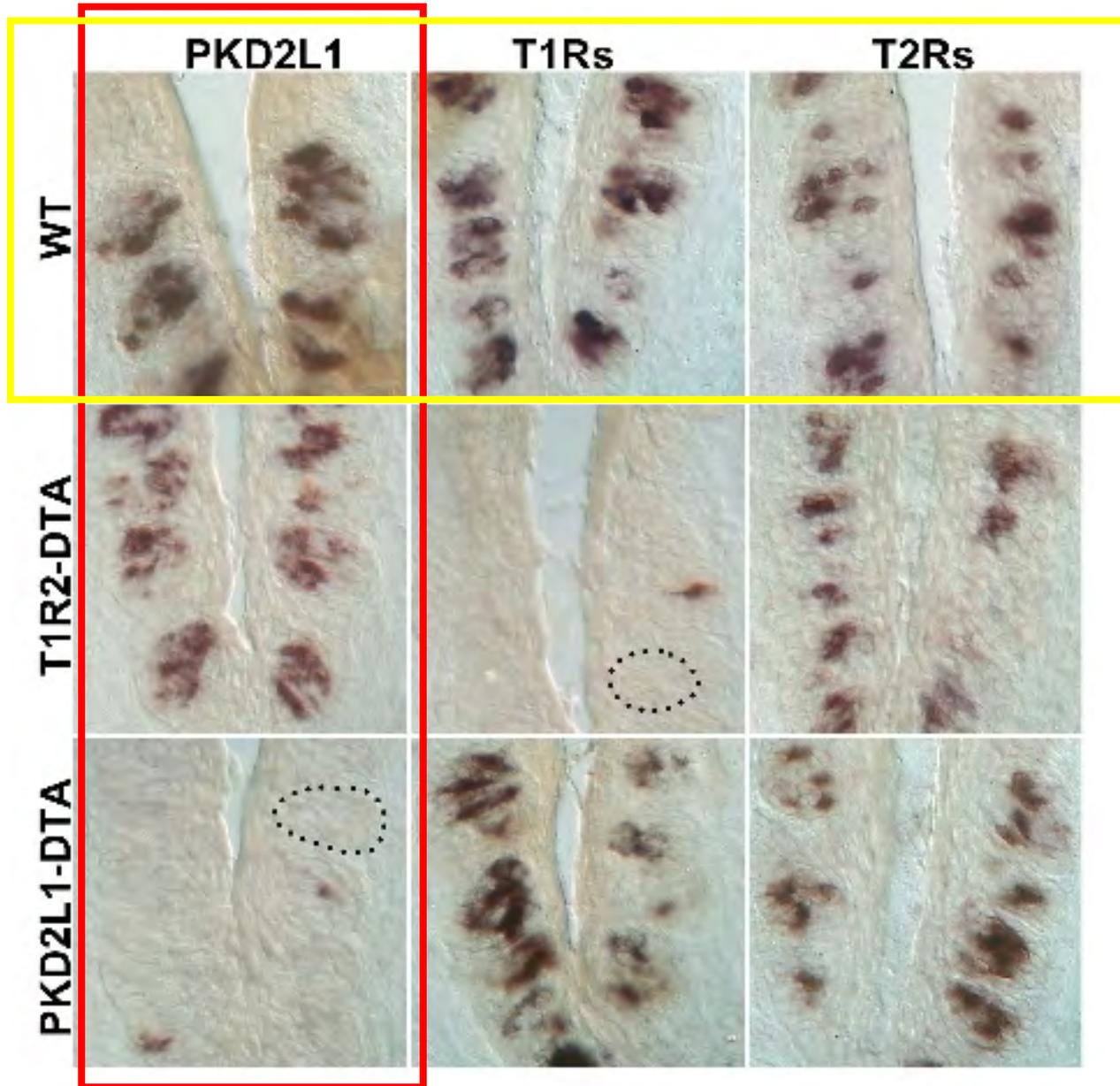


hT2R16 stimulated by phenyl β-D-glucopyranoside, which tastes very bitter to a human

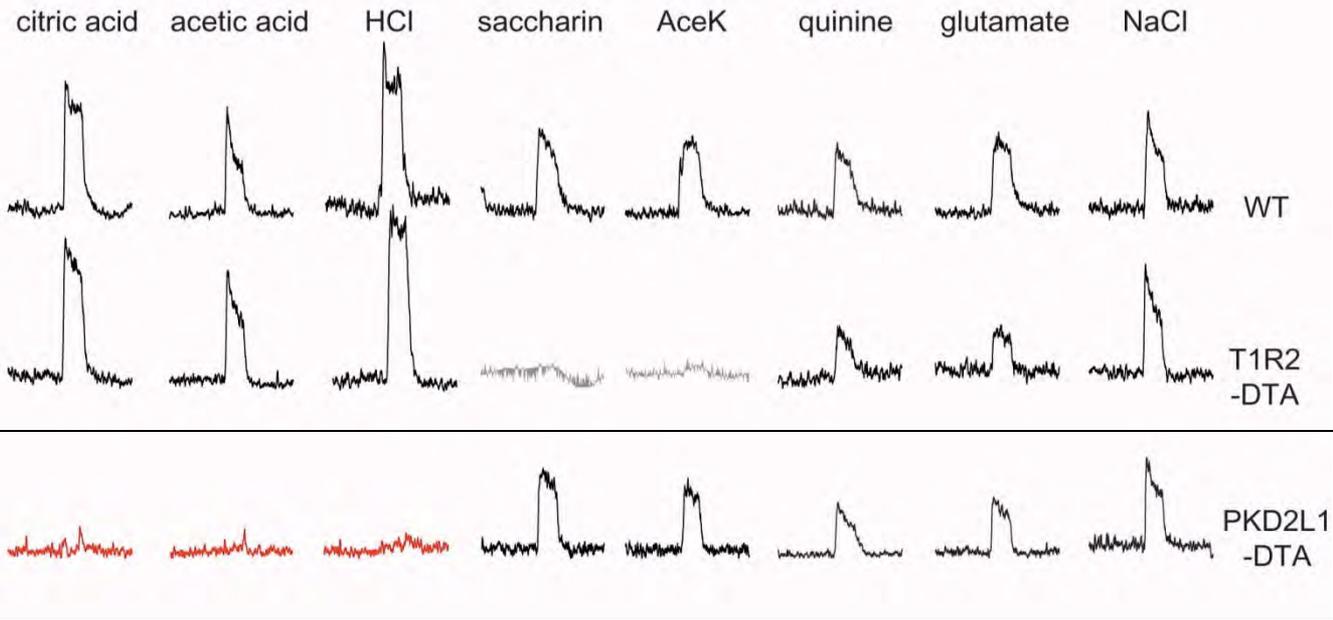
BUT ...



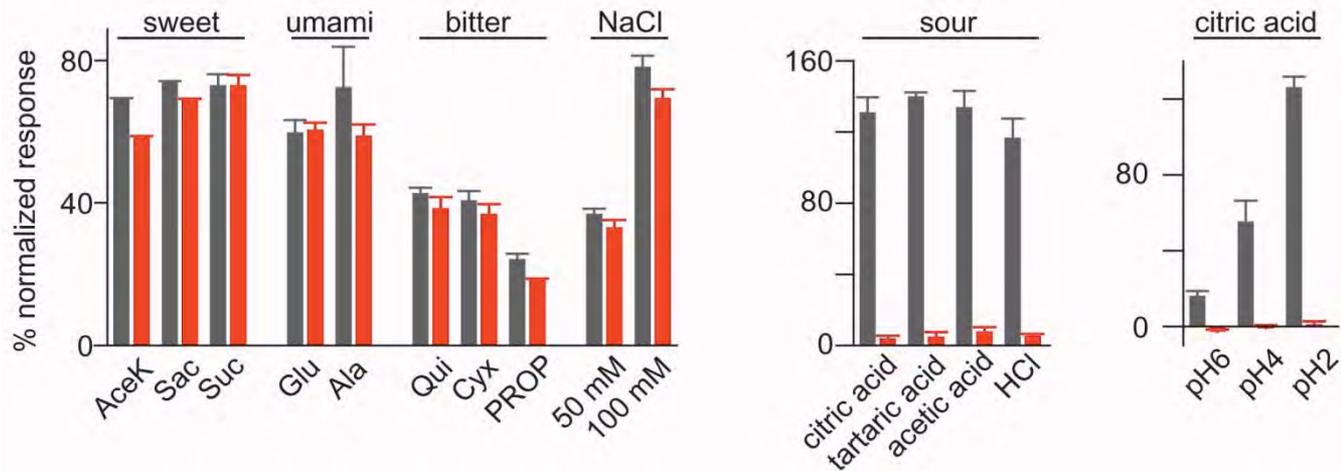
Targeted genetic ablation of TRCs (diphtheria toxin)



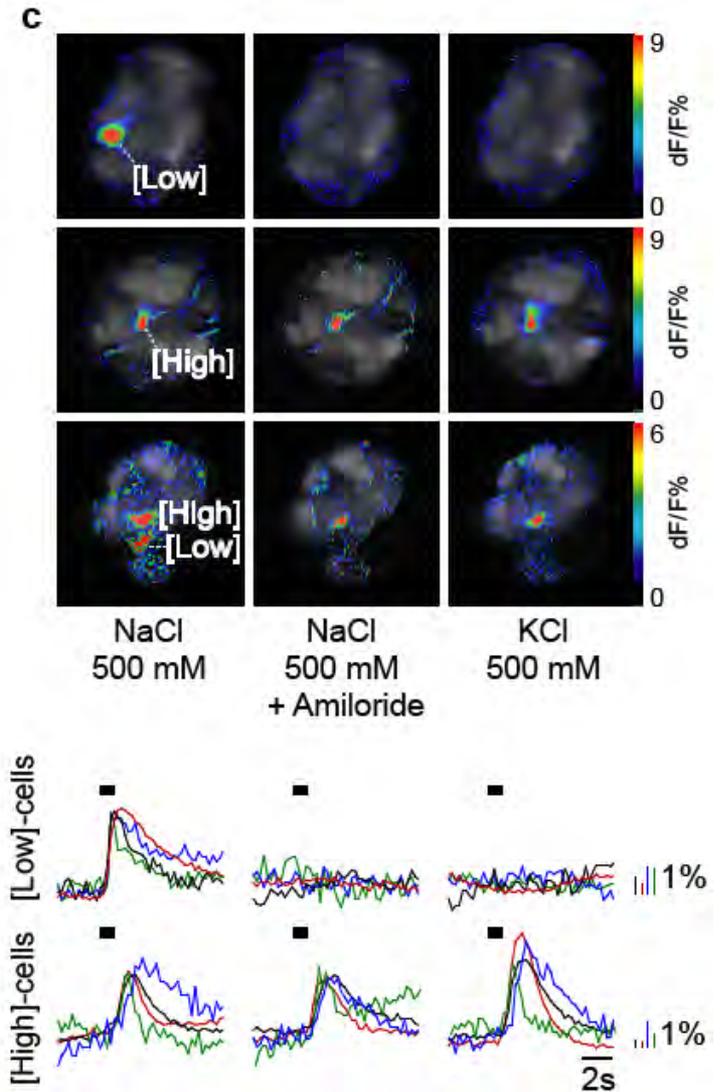
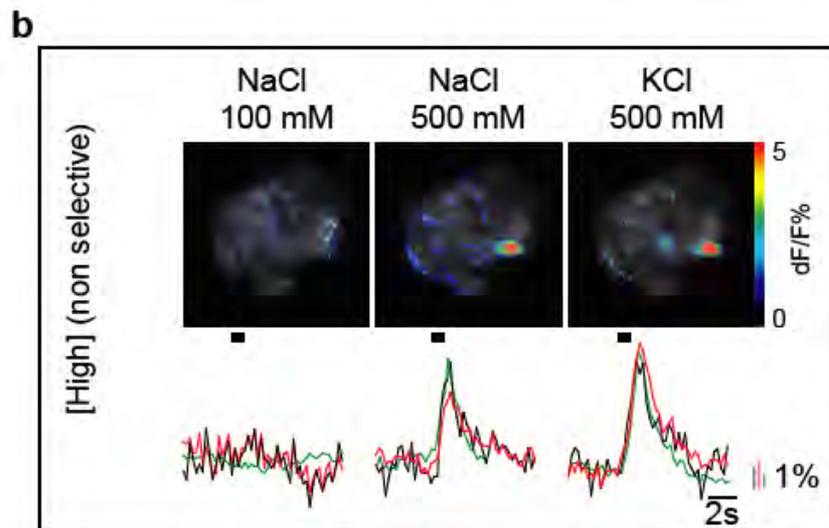
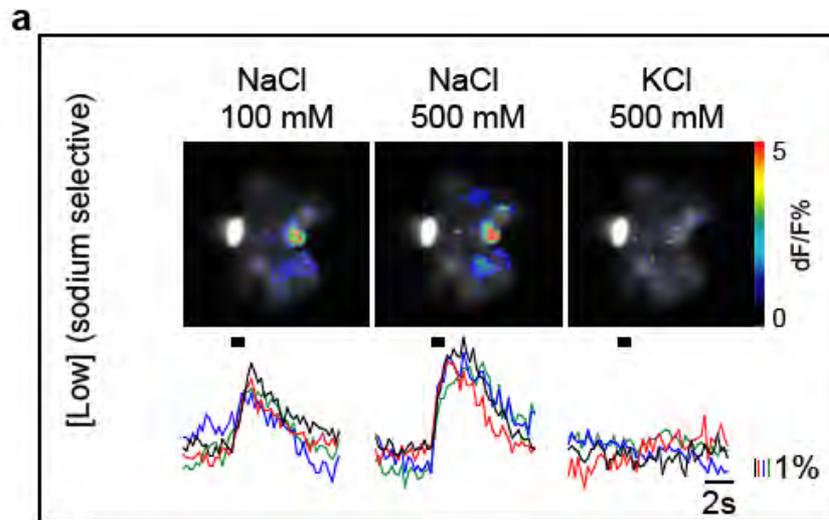
PKD2L1-expressing cells are the Sour Sensors



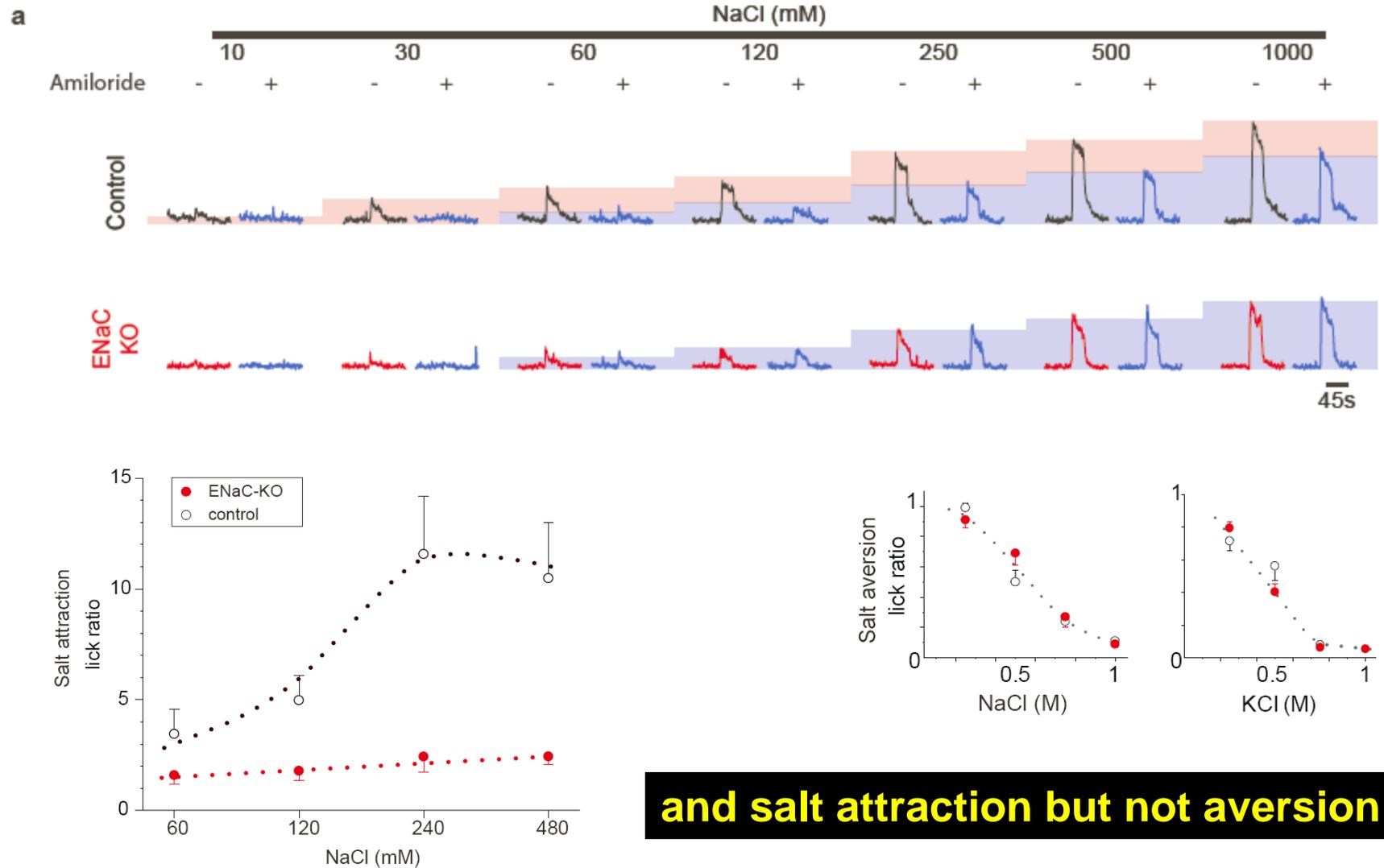
b



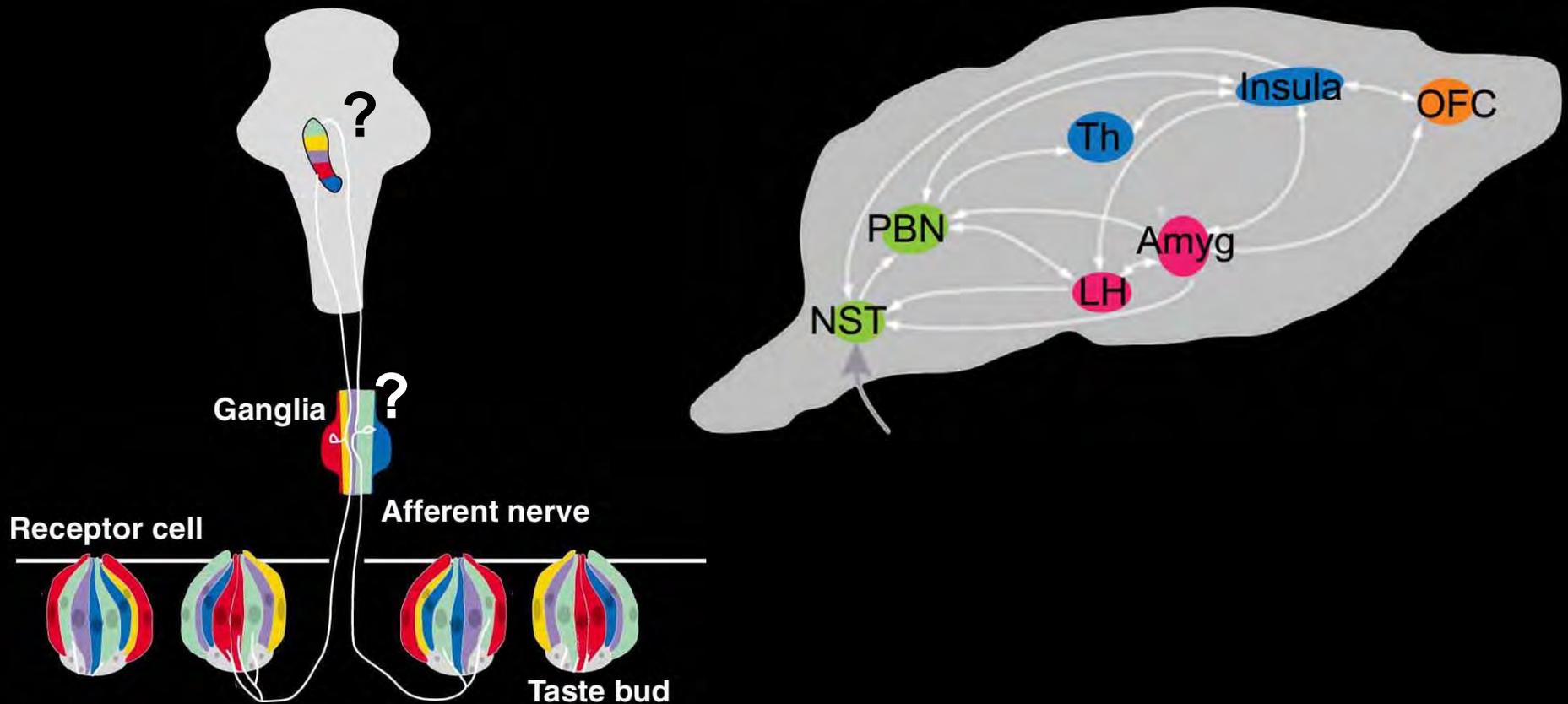
Salt taste is mediated by multiple mechanisms and cell types



Taste cell KO of ENaC abolishes sodium selective taste responses

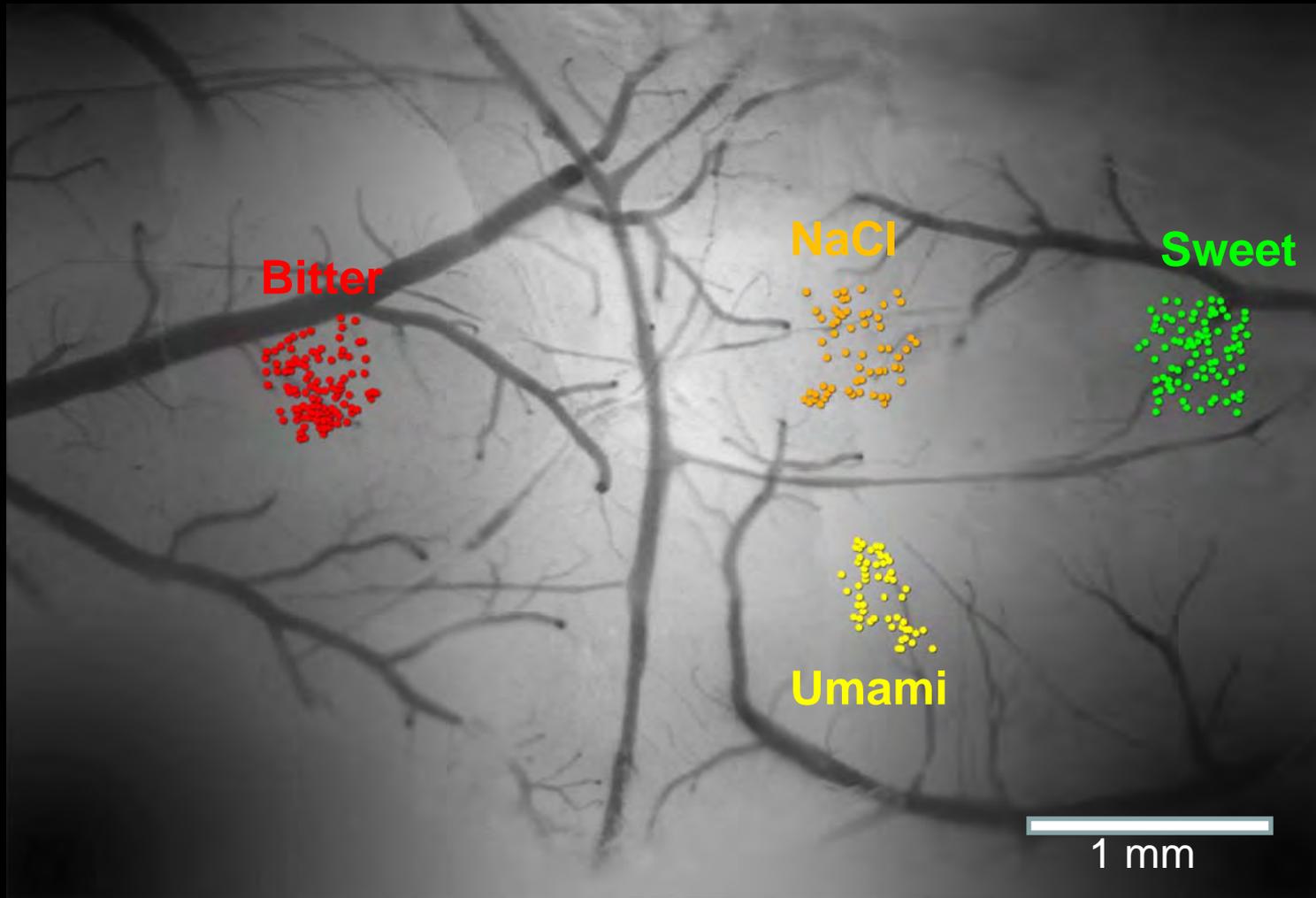


How is taste quality represented in the brain?



Peripheral coding of taste characterized by elegant simplicity

A substrate for taste quality in the brain



stereotyped spatially distinct fields for the primary tastes in insula