nature REVIEWS
NEUROSCIENCE
April 2004 Vol 5 No 4
REVIEWS

Nature Reviews Neuroscience **5**, 263 -278 (2004); doi:10.1038/nrn1365

GENES AND LIGANDS FOR ODORANT, VOMERONASAL AND TASTE RECEPTORS

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Abstract

The chemical senses (smell and taste) have evolved complex repertoires of chemosensory receptors — G-protein coupled receptors with a seven-transmembrane domain structure. In the mouse, ~1,000 odorant receptors are dedicated to the conventional sense of smell, ~300 vomeronasal receptors mediate the detection of chemical stimuli (such as pheromones) by the vomeronasal organ, and ~40 taste receptors are implicated in bitter, sweet and umami taste. Nearly all receptor genes have now been identified as the result of genome sequencing, but few receptor–ligand interactions have been characterized. Targeted expression of the green fluorescent protein in chemosensory cells is a promising approach to achieve this objective.

Summary

- Chemosensation — the detection of chemicals in the external environment — is essential for the survival of the individual and of the species. The chemical senses (smell and taste) detect molecules of immense chemical variety, and this requires a massive array of receptors to match the diversity in chemical structures.
- Olfactory signals are transduced by odorant receptors or ORs — a family of G-protein-coupled receptors (GPCRs). Axons of olfactory sensory neurons (OSNs) that express the same OR recognize each other and coalesce into discrete glomeruli in the olfactory bulb. The idea that each OSN expresses a single OR gene is widely accepted, but has not been proved.
- Most mammals possess a second olfactory system — the accessory olfactory system or vomeronasal system. The mammalian vomeronasal organ (VNO) is generally considered to specialize in pheromone detection, although it does not have a monopoly in this regard. It also seems to detect 'common odorants' that are not typically regarded as pheromones. The vomeronasal receptors represent two superfamilies of GPCRs that are distinct from the OR superfamily.
- The sensation of taste initiates at taste papillae that are distributed in and around the oral cavity. Each papilla contains one or more taste buds, each of which consists of around 100 cells, including taste receptor cells. Taste receptor genes, which code for another family of GPCRs, were the last mammalian chemosensory receptor genes to be identified.

- Several assays have been developed to match odorants to ORs, and vice versa. The first unambiguous OR–ligand pair to be reported was the rat I7 receptor and octanal. This was identified using a system in which I7 was co-expressed with green fluorescent protein in OSNs. A heterologous expression system has also been developed in human embryonic kidney cells (HEK293), but its success has been limited, because expression of ORs on the cell surface is often poor.
- For around 300 vomeronasal receptors in mice and rats, only one receptor–ligand interaction has been described to date. Seven T2R taste receptors have been functionally characterized, six in HEK293 heterologous expression systems and one by positional cloning in humans.
- The identification of receptor–ligand interactions is not merely a descriptive exercise, but is directed towards understanding how chemical structure relates to chemosensory quality. For example, why does acetophenone smell like almond? This Holy Grail of olfaction is within sight, but there is still a long way to go.

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