

Quick guide

Cephalopod chemotactile sensation

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What is a chemotactile sense?

Chemical senses are ancient, diverse, and specially adapted to the lifestyle and ecological niche of every organism. Familiar examples include sensory modalities such as olfaction (smell) that evolved to detect chemicals associated with often distant resources such as prey, predators, or mates. Contact-dependent chemosensory systems, or chemotactile senses, represent the extreme opposite of this spectrum. Chemotactile sensation is specialized for the detection of chemical cues at close range and, therefore, typically requires probing an interface such as a physical surface. Accordingly, chemotactile systems are often tuned for detection of chemicals not readily dispersed in an organism's environment: those which are not volatile in the air of terrestrial environments, or soluble in the water of aquatic environments. In many organisms, taste represents a common chemotactile sense, but some organisms possess additional and highly specialized chemotactile sensory organs that reflect their adaptive strategy. For example, octopuses possess one of the most prominent and specialized chemotactile systems.

What do octopuses use their chemotactile sense for? Octopuses are voracious benthic predators that use their long flexible arms to find prey within crevices of the seafloor that are inaccessible to conventional sense organs like their eyes. The chemotactile system is part of an elaborated distributed nervous system that mediates sophisticated behaviors, which rival vertebrates in terms of complexity. Perhaps the most conspicuous adaption in octopuses is their body plan consisting of flexible

arms that are lined with specialized suction cups (suckers) used for adhering to surfaces of their prey, predators, and environment. While suckers have long been hypothesized to represent chemotactile sensory organs, the molecular and cellular basis for this ability has only recently begun to be revealed. Chemotactile sensation appears to have originated from synergistic adaptations across levels of biological organization, including the evolution of new tissues and organs (arms, suckers), but has also involved molecular innovations in the form of novel sensory receptors called chemotactile receptors, or CRs (Figure 1).

What are CRs? CRs are a recently discovered family of sensory receptor ion channels in the 'Cys-loop' superfamily, most closely related to nicotinic acetylcholine receptors. CRs are the most derived lineage of acetylcholine-like receptors within mollusks and represent an early cephalopod-specific innovation. In terms of genomic structure, different CR genes are organized in tight clusters of tandem arrays on the same chromosome, suggesting this receptor family arose through gene duplication and neo-functionalization. In octopus, CRs appear to have undergone an

especially massive expansion in number relative to other cephalopods, which may reflect their broad behavioral repertoire. For example, *Octopus bimaculoides* possess over twenty different CR genes that enable its elaborated 'taste by touch' exploration of the sea floor.

Importantly, CRs do not function as individual proteins, and must instead combine to form five-membered pentameric ligand-gated ion channels. Individual CR subunits can form homopentameric receptors with five of the same CR, or they can heteromerize with other CR subunits, thereby giving rise to diverse ion channels with distinct biophysical properties. Therefore, CRs have the theoretical capacity to form an immense variety of multimeric receptor ion channels, which likely contribute to signal detection and filtering required for complex behaviors. This organization represents a departure from how many sensory receptors function. For example, in the vertebrate olfactory system, each olfactory receptor neuron expresses one receptor and signals to specific locations in the central nervous system for downstream processing and behavior. In contrast, the octopus chemotactile system could use combinatorially assembled CRs to directly encode the identity of diverse



Figure 1. Chemotactile sense in cephalopods.

(Left) Diverse cephalopods use their chemotactile sense to probe their environment. (Right) Suckers are chemotactile organs that use novel chemotactile sensory receptors (CRs) to detect poorly soluble molecules for 'taste by touch' behavior. (Artwork by Lily Soucy.)



stimuli without relying on a labeled line organization. Such a system would be well suited for local signal processing by the octopus' distributed nervous system. Thus, the octopus chemotactile sense has enormous potential to mediate complex sensation and signal transduction, but the molecular logic of this system is only beginning to be studied.

Do squid and cuttlefish use CRs?

Although in fewer numbers compared with octopus, Decapodiformes or 'ten-limbed' cephalopods such as squid and cuttlefish also possess CRs. Whereas octopus have eight arms, decapods like squid and cuttlefish possess two additional catch-tentacles that can be rapidly projected to capture prey. Interestingly, squid and cuttlefish exhibit a unique repertoire of early-diverging CRs that are functionally distinct from octopus CRs. Indeed, CRs appear organized into three major groups, including a lineage unique to octopus, a lineage unique to decapods, and a lineage which is represented in both taxa.

How do CRs mediate behavior?

CRs appear to mediate sensation of diverse chemical cues, including terpenes produced by plants, bacteria, and fungi, hormones, and bile acids. CRs are therefore likely to mediate various behaviors, including predation, exploration, and reproduction, and these roles may be tuned to facilitate the lifestyle of different species. Indeed, decapodiforme-specific CRs exhibit robust sensitivity to bitter compounds to control acceptance or rejection of captured prey, suggesting decapod chemotactile sensation may be functionally analogous to vertebrate taste, as opposed to functioning in exploration as observed in octopus (Figure 1).

While the circuits that transduce these signals to the nervous system are unresolved, CR agonists elicit robust responses in behaving animals and, remarkably, in isolated arms and tentacles. Therefore, CRs are likely part of a sensory-motor circuit that induces discrete behaviors driven by local circuits within cephalopod appendages, which function even in the absence of the central brain. Furthermore, CRs likely mediate

sensation in concert with the mechanosensitive ion channel NompC, which is also expressed in sucker sensory cells. How the peripheral and central nervous systems integrate and process sensory information to produce appropriate behavioral responses to chemotactile cues is a fascinating open question.

Is 'taste by touch' in cephalopods the same as taste in other animals?

While a useful analogy, taste by touch sensation in cephalopods is distinct in terms of the cells, molecules, and neural pathways involved in vertebrate taste or invertebrate gustation, which are mediated by a host of non-homologous sensory ion channels and G-protein-coupled receptors. Accordingly, CRs are not found outside of coleoid cephalopod lineages, such as octopus, squid, and cuttlefish, and are even absent in more ancient cephalopods, such as the nautilus.

How did CRs evolve?

CRs represent a clear example of proteins which recently transitioned functional roles to mediate novel organismal traits. The CR family diverged from ancestral acetylcholine-like receptors, which facilitate neurotransmission, including at the neuromuscular junction. Remarkably, all CR genes are intronless, implying they arose as retrocopies of 'jumping genes'. These genes are DNA sequences that move from one location to another, yet retrotransposed genes like the CRs are particularly special among jumping genes as they go through an intermediate RNA in order to transpose. That is, a mature mRNA is reverse transcribed in a complementary DNA copy devoid of introns and then randomly inserted back into the genome. Since retrogenes insert randomly, they usually lose their regulatory sequences and mostly decay into pseudogenes. However, rather than decaying into gene fossils, the CRs have undergone dramatic neofunctionalization, evolving new biological functions as sensory receptors via the adaptive accumulation of coding substitutions. Indeed, despite the global conservation of receptor architecture between acetylcholine receptors and CRs, the CR ligand binding site shows

signatures of rapid adaptive evolution. Thus, CRs represent a striking case of how jumping genes contribute to the evolution of novelty, organismal diversity, and adaptation.

Why study chemotactile sensation in cephalopods?

Cephalopods are a unique model system for understanding the evolution of biological novelty. Compared with complex vertebrates like humans, cephalopods are distantly related invertebrates that have independently evolved elaborate nervous systems, complex body plans, and sophisticated behaviors. Chemotactile sensation is a salient and tractable feature of these organisms that provides a powerful perspective to functionally investigate the molecular evolution and origins of their distinctive nervous systems and morphological traits.

Where can I find out more?

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Van Giesen, L., Kilian, P.B., Allard, C.A.H., and Bellono, N.W. (2020). Molecular basis of chemotactile sensation in octopus. *Cell* 183, 594–604. <https://doi.org/10.1016/j.cell.2020.09.008>.

DECLARATION OF INTERESTS

The authors declare no competing interests.

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