

# Brief overview of the structure, function, and distribution of solitary chemosensory cells (SCCs) in vertebrates

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## SUMMARY

Chemosensation is the biological process by which organisms detect chemical stimuli forming the basis for taste and smell perception. While vertebrate chemosensory systems traditionally center around olfactory and gustatory pathways, recent research has uncovered an auxiliary mechanism involving solitary chemosensory cells (SCCs). These specialized cells are dispersed throughout the various epithelial tissues, particularly near the taste buds and the olfactory epithelium, as well as extending into the respiratory and gastrointestinal tracts.

SCCs exhibit remarkable structural and functional diversity across taxa. In the aquatic vertebrates, chemosensory cells are found both internally and externally, enabling detection of various waterborne molecules. Originally identified in fish, SCCs have since been observed in a wide range of species including rodents, amphibians, reptiles, bovines and humans. In mammals, they play a pivotal role in sensing irritants and triggering protective reflexes such as coughing and sneezing while also contributing to immune responses and appetite regulation.

This review synthesizes current insights into the morphology, distribution and physiological roles of SCCs, highlighting their significance in chemosensory perception and their broader impact on homeostasis and adaptive behavior.

**Key words:** Solitary chemosensory cells – Taste receptor cells – Teleost fish – Taste buds – Taste

## INTRODUCTION

Chemosensation is the physiological process by which organisms detect chemical stimuli within their environment. From the perception of taste and smell to perceiving differences in oxygen, carbon dioxide and even pH levels, chemosensory mechanisms are vast and widely distributed across taxa, exhibiting remarkable diversity in structure, function, and localization. Aquatic vertebrates, such as fish and amphibians, possess chemosensory cells not only in the oral cavity but also externally on the skin, allowing them to sense a wide variety of waterborne molecules (Kotrschal, 1996; Lee and Cohen, 2014). In nematode *Caenorhabditis elegans*, CO<sub>2</sub> can be detected via BAG chemosensory neurons, and it is thought that similar receptors in other animals also me-

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diate the CO<sub>2</sub> effects on behavior and the neural circuits (Smith et al., 2013).

In vertebrates, in addition to the olfactory and the gustatory pathways, which primarily detect the sense of smell and taste, these animals possess an auxiliary chemosensory mechanism mediated by SCCs. These cells are scattered throughout various epithelia, most of the time in proximity to taste buds and the olfactory epithelium; they are also present in the respiratory and digestive tracts. SCCs share some morphological similarities with taste bud cells and olfactory epithelial cells, such as the presence of the microvilli in both the taste buds and the SCCs and the connection to the trigeminal, afferent or the olfactory nerve that all of these cells share; however, SCCs typically appear as isolated single cells that function as multifunctional sensory interfaces (Fig. 1). Other than morphological similarities, SCCs also share molecular features with taste cells, such as the expression of  $\alpha$ -gustducin, phospholipase C $\beta$ 2 (PLC $\beta$ 2), and transient receptor potential cation channel, subfamily M member 5 (TRPM5) (Zheng et al., 2019; Kotrschal et al., 1998; Banerjee et al., 2018; Sell et al., 2023). These were first discovered in fish as isolated cells in the epithelia. They have a particular morphology, different from that of taste buds: they are elongated cells with heavy neural innervation (Kotrschal et al., 1998) (Fig. 1A). Recently, cells similar to this morphology have been found in rats, mice, amphibians, alligators, bovines and now humans (Lee and Cohen, 2014; Lee and Reyno, 2021).

Mammalian SCCs, in particular, play a crucial role in detecting irritants and triggering protective reflexes, such as coughing or sneezing; they are also involved in immune modulation and ap-

petite regulation (Sell et al., 2023; Zheng et al., 2019; Lee and Reyno, 2021; Yang et al., 2024). Their strategic placement and molecular versatility underscore their importance in maintaining homeostasis and facilitating adaptive behaviors across species. In this review, we will focus on the current knowledge of the structure, patterning and localization of SCCs. We will further explore their functional role in chemosensory perception and their importance in the animal body.

## MORPHOLOGY

SCCs exhibit a polymorphic morphology, meaning they can take on various shapes depending on their location and function within different tissues. Even though these cells share similar functions across taxa and have some interesting morphological similarities, the typical structure is found to be spindle-shaped, with a wider basal end and narrow apical end, which projects microvilli to the free epithelial surface (Kotrschal et al., 1998; Finger et al., 2003; Sbarbati and Osculati, 2005) (Fig. 1A). These brush-like rigid microvilli resemble taste receptor cells, and hence are often referred to as “brush cells” due to this distinctive feature. Some SCCs contain secretory exocrine granules, while others show endocrine differentiation, suggesting diverse functional roles (Kotrschal et al., 1998; Banerjee et al., 2018). SCCs are frequently innervated by trigeminal nerve fibers, particularly in the upper respiratory tract, where they are contacted by sensory endings that are immunoreactive for Substance P and calcitonin gene-related peptide (CGRP) (Kotrschal et al., 1998; Finger et al., 2003). The cytoplasm of a SCC is often filled with vesicles of varying size and shape.

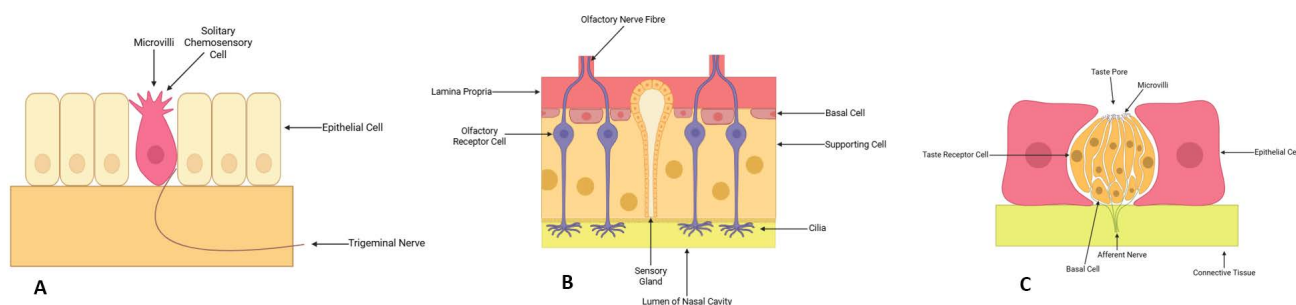


Fig. 1.- Schematic diagrams of vertebrate sensory structures: (A) A chemosensory cell, (B) The olfactory epithelium containing sensory receptor cells, and (C) A taste bud.

First observed in fish, in a study by Kotrschal et al. (1998), these spindle-shaped cells are quite small, being only 25-30 microm long and about 10 microm wide, with the basal end being the widest and the apical end terminating in microvilli protrusions that stem out to be 2-5 microm above the epithelial surface. The distal part of the cell contains distinguishing vesicles, elongated mitochondrion and intermediate filaments in longitudinal strands, which help in intracellular transport and locomotion. In their basal ends, these specialized cells contain an abundance of endoplasmic reticulum, both smooth and rough, and a large Golgi apparatus as well as free polyosomes.

SCCs of the rockling fish specifically are connected to the cranial nerves of the fish, with more than one active synaptic site (Kotrschal et al., 1998). The nucleus is smooth and oval in shape, as well as less electron-dense compared to neighboring epidermal cells; they also lack a proper nucleolus, but the actual cell contains more cytoplasmic content than other gustatory cells. SCCs are arranged in parallel to one another and perpendicular to the epidermis. These cells are separated by a sheet-like layer of epidermal cells, with the basal of the epidermis containing a nerve plexus that includes the dendritic sites of the facial nerves. They can form spurs that can project into the membrane invaginations at the synaptic sites of a nerve cell, or form synapses with a group of neighboring nerve fibers (Kotrschal et al., 1998). On occasion, nerve fibers can be seen penetrating into the basal lamina, with the dendritic swelling reaching up to 3  $\mu\text{m}$  in diameter, to receive the synapsis. Synapses can be identified due to distinct structural features at the point of contact, where the membranes line up parallel to each other, thicker on the postsynaptic (nerve terminal) end than on the presynaptic (SCC) end. The cytoplasm of the postsynaptic nerve is lighter or less dense under the microscope and might carry mitochondria and dense-cored vesicles. The synapses between these two cells resemble those found in teleost tastebuds in size, and also in the lack of presynaptic vesicles (Kotrschal et al., 1998). Both the lack of presynaptic vesicles and the electronlucent postsynaptic vesicles indicate

that SCCs might not use the usual fast communication, but a slow, more diffuse type of chemical communication. The study done on the rockling fish indicated that their sample size was too small to determine the SCC to nerve cell ratio (Kotrschal et al., 1998). More research needs to be conducted in order to understand whether a given SCC can form multiple synapses with one nerve fiber, or if one nerve fiber can receive information from more than one SCC.

SCCs are a very rare cell type especially in the upper vertebrates. As seen within the human fungiform papillae, biopsies marked with TRPM5 probes were shown to be in the minority cell population within the human nasal epithelium (Chen et al., 2019). In the same study it was also indicated that individual cells rarely express more than one SCC marker, further supporting data claims that they are a rare cell type (Chen et al., 2019). Interestingly, a study showed that there is direct contact between unmyelinated fibers of a mature neuron and the basolateral surface of a neighboring SCC derived tuft cell. Terminal axons even contained electron-dense synaptic vesicles, but no evidence of a synapse was observed. Banerjee et al. (2018), alluded to the fact that communication might still occur without the need for a synapse. Still, even within humans this is an uncommon sighting. Out of 300 human biopsy specimens, only one was observed to have their tuft cells associated with the nerve endings (Banerjee et al., 2018). Only six tuft cells were definitively identified, and due to their scarcity, it remains challenging to determine the functional significance of tuft cell-nerve contacts. It is currently unclear whether these interactions play a critical role in tuft cell activity or represent incidental, non-essential occurrences. In a separate study examining intestinal SCCs, these cells were found to be spatially associated with nearby nerve fibers, suggesting a potential neuroepithelial communication pathway (Wei et al., 2023).

In mammals, these cells are primarily endoderm-derived epithelial cells, characterized by a brush of rigid apical microvilli with long rootlets that project into the lumen of the hollow of visceral organs (Sbarbati and Osculati, 2005). These cells are known as brush cells, tuft cells, fibrillovesicu-

lar cells, multivesicular cells and caveolated cells (O'Leary et al., 2019). In rats, the nasopharyngeal SCCs have a distinct morphology. For instance, some are shaped in a barrel-like manner, while others are slender, all having protrusions laterally in the epithelial layer, attaching to the neighboring ciliated epithelial cells. These shapes indicate a role in intracellular communication (Yamamoto et al., 2021). Even in mice, similar morphology is found, an apical process that extends into the lumen and a connection to the nervous system (Finger et al., 2003).

## LOCATION

SCCs have often been associated with taste buds due to their similar morphology and in one study, Berning et al. (2023) alluded to the fact that in fish specifically, in the Mexican Tetra cavefish, SCCs might have been mistaken for taste buds and counted as such, inflating their actual number. But as of now no concrete evidence is present of their actual location though. SCCs in other teleost fish such as the 'Sea Robin', the 'Rockling' and others from amongst the Gadidae family, are found in various locations on the body, such as gills, fins, as well as the surface epithelium of the organism (Sbarbati et al., 2003; Peters et al., 1991; Kotrschal, 1996). These cells function by perceiving the odors around them (Kotrschal, 1996). Wilkens and Strecker (2017) have also found that all taste organs, whether taste buds or SCCs, develop inside the mouth cavity, as well as on the upper jaw and the lower jaw, with the highest density being present on the labial margin surrounding the mouth opening. This information remains to be seen in the Mexican tetra cavefish. In the rockling fish, however, the highest density is found around the specialized dorsal fin, with the numbers reaching around 5 million SCCs (Kotrschal, 1996). It is also found that in many ostariophysan fishes, SCCs are generally evenly distributed along the surface of the body, with higher densities along the head, and may even be found in clusters surrounding free neuromast cells (Kotrschal, 1996).

In mammals, SCCs are often found in hollow organs like the crypts and villi of the small and the large intestine, the thymus, stomach, tracheae, urethra and the nasal cavity (Pan et al., 2020;

Rane et al., 2019; Wei et al., 2023; Sell et al., 2023; Yang et al., 2024). In humans specifically, SCCs are also found in the sinonasal mucosa and the extra-hepatic peribiliary gland epithelia (Barham et al., 2013; Chen et al., 2019). Specifically in the pancreaticobiliary system, these cells reside in the pancreaticobiliary duct, as well as in the intra- and interlobular duct, but are absent from the acinar cells and the main pancreatic duct (Wei et al., 2023). It is also thought that they would be present in higher quantities in areas of airflow and sites exposed to inhaled substances like the septum and the turbinate structures (Chen et al., 2019). A bitter taste receptor, T2R, expressed by SCCs and other chemosensing cells, has been found in the brain, gastrointestinal tract, bronchi, testes and the upper airway (Lee and Cohen, 2014). It currently remains to be seen what chemosensory cell is expressing this receptor at these sites.

Within amphibians, SCCs or SCC-adjacent cells are found only on the ranid tadpoles of *Rana temporaria*, scattered within the epidermis (Kotrschal, 1996). The lack of SCCs found on other amphibians could be due to the thick keratinous layer found on top of the SCCs in these animals rather than a total absence of these cells (Kotrschal, 1996). Research done on SCCs in amphibians is few, and more studies need to be conducted in order to understand their role within the ranid tadpoles and whether SCC or SCC-adjacent cells appear in other amphibians.

One of the defining features of SCCs is their conserved morphological homology across taxa. As an instance, these cells possess a receptive apical end, often characterized by microvilli, which facilitates the detection of chemical stimuli. Sensory signals received at the apical surface are transmitted across the cell to associated sensory nerve fibers for further processing. The cell membranes of SCCs consistently express receptors such as taste receptors that exhibit conserved functional homology, highlighting their chemosensory role. In terms of localization, SCCs are invariably scattered throughout barrier epithelia, including the skin, respiratory tract, and gastrointestinal lining, placing them in direct contact with the external environment. In aquatic vertebrates, their positioning on the external skin is crucial for de-

tecting waterborne cues, whereas in terrestrial vertebrates, SCCs are typically found internally (e.g., within the nasal, tracheal, and gut epithelia) to monitor airborne or ingested stimuli.

## FUNCTIONS

In recent years, researchers have been trying to figure out the function and role of the SCCs in different organisms, and in different organs. Between different animals and organs, these cells provide a variety of functions, but currently no general function has been established.

### Predation and Cover

SCCs, especially in fish are assumed to aid in predator detection and avoidance (Kotrschal et al., 1998). Rockling fish use them to sample upstream water to detect potential predators, competitors or even conspecifics (Kotrschal, 1996). The rockling's SCCs are highly sensitive to chemical cues that originate from other animals like body mucus or bile, which results in a response of arousal or vigilance, dashing or even zig-zagging (Kotrschal, 1996). Previously, this behaviour was thought as predator avoidance, or predator distraction, but new evidence has shown that this behavior could also serve to sample the water further, activating the SCCs on the anterior dorsal fin, giving the fish a more clear picture of what is around it (Kotrschal, 1996). Even in zebrafish, water sampling to avoid predators is observed (Berning et al., 2024). Though predator avoidance seems to be a big function of SCCs in the rockling, zebrafish, and possibly other fish as well, there does not seem to be any correlation between SCCs density and the fish most susceptible to predation, such as small or juvenile fish (Kotrschal, 1996).

### Food Hunting

In contrast to rocklings, whose SCCs are innervated by cranial nerves, sea robins exhibit an opposing pattern, with their SCCs receiving innervation from spinal nerves. The rockling uses its SCCs as predator detection and the sea robins use theirs to respond to food-related stimuli (Kotrschal, 1996). Specifically, they use the rays of the pectoral fins, whereas other fish use their extraoral taste systems to localize food in their en-

vironment (Finger, 2000).

TRPM5, a receptor of the SCCs, expressed in both mammals and fish, is required for the sweet, bitter and umami, as well as possibly for fat perception within these organisms to protect them from harmful substances as well as aid in food search (Vennekens et al., 2017). SCCs along with taste receptor cells in catfish carry a common taste receptor for the amino acid arginine (Finger et al., 2003). Similarities like this are also found within rodents and other mammals, which use several different taste receptor molecules within their SCCs (Finger et al., 2003).

### Immune Responses

In humans and other mammals, SCCs have been linked to many different immune responses. Succinate, a signal of cellular distress, can be released extracellularly at times of metabolic stress or inflammation (Sell et al, 2023). SCCs express a succinate receptor: SUCNR1, which in the presence of succinate will trigger type 2 immune response through a canonical taste transduction pathway that utilizes T2R receptors, as well as downstream taste signaling elements like PLC $\beta$ 2, TRPM5 and G protein subunit  $\alpha$ -gustducin (GNAT3) to fight off pathogens, chemical and other irritants including parasites specifically in the small intestine as well as monitor the airway surface liquid (ASL) (Sell et al, 2023; Wei et al., 2023; Zheng et al., 2019; Chen et al., 2019). They are also an important source of both interleukin-25 and cysteinyl leukotrienes, being a very crucial part of the upper airway innate immunity, often acting as early signals (Sell et al, 2023).

### Disease Control

Variances in individuals experiencing different levels of diseases can be explained via a hypothesis that looks into the polymorphisms in the gene coding for a T2R receptor. T2R receptors expressed in both SCCs and ciliated cells have a great amount of genetic variance which contributes to variance in taste preferences in humans; they can also contribute to how an individual SCC generally works and recognizes a pathogen or a bacterial infection (Lee and Cohen, 2014). In other words, they can reduce the functionality of an individual

SCC and make the body more or less susceptible to different infections. Preliminary studies have shown that the polymorphisms in the gene coding for one T2R receptor, T2R38, in ciliated cells has reduced functionality, making it more vulnerable to certain infections (Lee and Cohen, 2014). More research needs to be conducted in order to understand the polymorphism of T2R receptors in SCCs and their larger impact on the body.

However, in chronic diseases like chronic rhinosinusitis (CRS) or asthma, upregulation in inflammation (type 2 immune response) has been observed as a response to succinate. This is proven by the increased quantity of SCCs in the nasal epithelium of humans (Sell et al., 2023; Chen et al., 2019). Succinate along with higher levels of denatonium can even activate the formation of new SCCs from p63-expressing lineage-negative progenitors in lungs after an influenza attack (Rane et al., 2019). This development of SCCs in post influenza lungs means that they might be central to dysplastic remodeling in different organs (Rane et al., 2019). However, in other regions of the body, the mere presence of SCCs does not constitute definitive evidence of pathology.

Interestingly, this pattern is also observed in the pancreas, an organ not typically associated with the presence of such specialized chemosensory cells. Tuft cells have been identified in precursor lesions of pancreatic cancer in both human and murine models. Notably, one study reported that tuft cell formation occurs in approximately 27% cases of human pancreatitis, suggesting a potential role in disease pathogenesis (Wei et al., 2023). Inflammation or a mutation in the Kirsten Rat Sarcoma Viral Oncogene Homolog (KRAS) gene can induce tuft cell formation from acinar cells in the pancreas (Wei et al., 2023). Prostaglandin D (PDG), a substance excreted by these cells at the site of injury, is believed to play a tumor suppressor role in the development of Pancreatic Ductal Adenocarcinoma (PDAC) (Wei et al., 2023). Though SCCs can be seen to play a variety of roles within the body, their full function or the extent of their role in specifically pancreatic cancer is not fully understood yet.

### **Epithelium Regeneration**

Chemosensory organs require mucus to help trap the present stimuli and present it to the chemosensory receptor cells. Taste buds use the mucus produced by surrounding cells, while SCCs are known to generate their own mucus environment (Kotrschal et al., 1998). In the rockling fish, SCCs have a high secretory environment, which not only serves to capture and present the chemical stimuli but also helps to replenish the membrane (Kotrschal et al., 1998).

Tuft cells in mammals have also been linked to regeneration of the epithelium, specifically the pancreatic, intestinal and colonic epithelium (Wei et al., 2023). Tuft-cell-derived acetylcholine (ACh) has been known to participate in maintaining homeostasis, and modulating airway remodeling, amongst other things (Pan et al., 2020). Non-neuronal ACh plays a substantial role in the repair of intestinal epithelium. The interaction of ACh with M3R activates the Wnt-signaling pathway, which is known to play a critical role in the regeneration of the epithelium (Pan et al., 2020). In response to injury, SCCs will also secrete mucin and PGD<sub>2</sub>, as well as reduce amylase. In mice, reduced amylase expression has been detected in tuft cells after an injury than in the mice strain without injury (Wei et al., 2023). Although they have proven to regulate regeneration and homeostasis, there is still a lack of knowledge as to exactly how they contribute to the epithelial maintenance. They support regeneration, but they are not stem cells.

### **Tasting the other Tastants besides bitter compounds**

In different studies, it has been noted that in the human airway epithelia or the human sinonasal cavity, the SCCs express different taste receptors (Chen et al., 2019). Specifically, in the sinonasal cavity, 25 different bitter taste receptors are observed, as well as the sweet/ umami receptor subunit TAS1R3, which is a G-protein coupled receptor made up of the T1R2 and T1R3 isoforms. (Chen et al., 2019; Lee and Cohen, 2014). Different taste signaling effectors have also been found to be expressed within the sinonasal tissue (Chen et al., 2019). In the human airway epithelia, both the multi-ciliated cells and the SCCs express the different taste receptors, which is in contrast to

a study found in rodents where only the SCCs express taste receptor genes (Chen et al., 2019). It has also been studied that the human nose is capable of detecting bitter, sweet and umami compounds indicating the presence of SCCs beyond the vomeronasal organ (Lee and Cohen, 2014). A very interesting feature of the SCCs is that they co-express TAS1R sweet/umami taste receptor and TAS2R bitter taste receptor, which is in contrast to taste buds that can either express TAS1RS or TAS2RS receptors, but not both (Zheng et al., 2019).

## SCCs SUBSETS

### Tuft Cells

Tuft cells are increasingly recognized as a specialized derived subset of SCCs, particularly within mucosal tissues. Both cell types share a core sensory function, detecting chemical stimuli through taste-related receptors such as TAS1RS, TAS2RS, SUCNR1, FFAR3, and other GPCRs (Yang et al., 2024). These receptors initiate a conserved signal transduction cascade involving GNAT3, PLC $\beta$ 2, IP3R2, AND TRPM5, which is characteristic of SCCs (Yang et al., 2024). Structurally, tuft cells resemble SCCs through their apical microvilli that interface with the lumen, and their cytoskeleton is composed largely of intermediate actin filaments, supporting both sensory and structural roles (Yang et al., 2024). Like SCCs, tuft cells engage in neuroepithelial communication, evidenced by cytoplasmic spinules that extend into adjacent nuclei, potentially facilitating molecular exchange. The presence of ACh and interleukin-25 (IL-25) within tuft cell vesicles suggests a paracrine signaling role similar to SCC-mediated neuroimmune interactions (Yang et al., 2024). Recent research has identified two tuft cell subtypes, Tuft-1 and Tuft-2, mirroring the functional diversity seen in SCC populations. Tuft-1 is associated with neuronal development, while Tuft-2 is linked to immune responses, each marked by distinct molecular signatures (Yang et al., 2024). Furthermore, tuft cells contribute to the non-neuronal cholinergic system by producing ACh, which regulates reflexes, promotes muscle constriction, modulates inflammation, and influences tissue

remodeling (Pan et al., 2020). These shared features highlight the close relationship between tuft cells and SCCs, positioning tuft cells as organ-specific, multifunctional extensions of the solitary chemosensory cell lineage.

### Oligovillous Cells

Oligovillous cells found on lamprey skin exhibit several defining characteristics that align them with SCCs, suggesting that they are part of a homologous vertebrate cell line, a class of sensory cells distributed across aquatic vertebrates (Kotrschal, 1996). These cells possess prominent apical villi that project from the epidermal surface, a structural feature consistent with SCCs' role in environmental chemical detection (Whitear and Lane, 1983). Their distribution varies across developmental stages located under the roof of the oral cavity in larvae and on papillae near the dorsal fin, gill vents, and male genital papilla in adults, suggesting a functional adaptation to different sensory needs throughout the lamprey's life cycle. Although these cells are associated with nerve fibers, they notably lack typical synaptic vesicles; instead, they contain irregular vesicular or canalicular structures adjacent to neurite spurs, indicating a potentially unique mode of neuroepithelial communication (Whitear and Lane, 1983). This deviation from classical synaptic architecture may reflect an alternative mechanism for signal transmission, similar to the paracrine or juxtacrine signaling observed in other SCCs. Beyond lampreys, such cells are widely distributed across aquatic vertebrate lineages including paleonisciforms, sarcopterygians, teleost actinopterygians, and elasmobranchs, highlighting their evolutionary conservation and functional importance in aquatic sensory biology (Kotrschal, 1996). These features collectively support the classification of these lamprey epidermal cells as SCCs, specialized for detecting environmental cues and facilitating localized sensory responses in aquatic habitats.

## CONCLUSION

SCCs represent a versatile and evolutionarily conserved component of the vertebrate chemosensory system. SCCs exhibit remarkable

**Table 1.** Literature on solitary chemosensory cells

| Taxa         | Species   | Histology/<br>Morphology   | Location  | Function  | Tasting Anything But<br>Bitter Compounds | SCC Subsets                                     |
|--------------|---|--|---|---|--|---|
| Jawless fish | Lamprey<br>( <i>Petromyzon marinus</i> )                |  |   |   |  | Kotrschal,<br>1996<br>Whitear and<br>Lane, 1983 |
| Teleost Fish |   |  | Kotrschal,<br>1996<br>Sbarbati et al.,<br>2003<br>Wilkens and<br>Strecker, 2017                                       | Kotrschal et al.,<br>1998<br>Vennekens et al.,<br>2017  |  |   |
|              | Rockling Fish<br>( <i>Ciliata mustela</i> ,<br>Gadidae) | Kotrschal et<br>al., 1998  | Kotrschal,<br>1996<br>Kotrschal et<br>al., 1998<br>Peters et al.,<br>1991   | Kotrschal, 1996<br>Kotrschal et al.,<br>1998  |  |   |
|              | Zebrafish<br>( <i>Danio rerio</i> )                     |  | Berning et al.,<br>2024   | Berning et al.,<br>2024<br>Kotrschal, 1996  |  |   |
|              | Sea Robin<br>( <i>Prionotus carolinus</i> )             |  |   | Finger, 2000  |  |   |
|              | Catfish<br>( <i>Siluriformes</i> )                      |  |   | Finger et al.,<br>2003  |  |   |
| Amphibians   | Ranid Tadpoles<br>( <i>Rana temporaria</i> )            |  | Kotrschal,<br>1996  |   |  |   |
| Mammals      |   | O'Leary et al.,<br>2019<br>Sbarbati and<br>Osculati, 2005              | Wei et al.,<br>2023   | Lee and Reyno,<br>2021<br>Vennekens et al.,<br>2017<br>Wei et al., 2023   |  |   |
|              | Rats<br>( <i>Rattus</i> )                               | Yamamoto et<br>al., 2021   |   |   |  | Banerjee et al.,<br>2018<br>Pan et al.,<br>2020 |
|              | Mice<br>( <i>Mus musculus</i> )                         | Finger et al.,<br>2003<br>Rane et al.,<br>2019<br>Yang et al.,<br>2024 | Rane et al.,<br>2019<br>Yang et al.,<br>2024  | Rane et al., 2019<br>Wei et al., 2023<br>Yang et al., 2024<br>Zheng et al., 2019  |  | Pan et al.,<br>2020<br>Yang et al.,<br>2024     |
|              | Humans<br>( <i>Homo sapiens</i> )                       | Chen et al.,<br>2019   | Barham et al.,<br>2013<br>Chen et al.,<br>2019<br>Pan et al.,<br>2020<br>Rane et al.,<br>2019<br>Sell et al.,<br>2023 | Banerjee et al.,<br>2018<br>Chen et al., 2019<br>Lee and Cohen,<br>2014<br>Pan et al., 2020<br>Rane et al., 2019<br>Sell et al., 2023<br>Wei et al., 2023 | Chen et al., 2019<br>Lee and Cohen, 2014 | Pan et al.,<br>2020                             |

structural and functional diversity across taxa. The discovery of tuft cell subtypes (Tuft-1 and Tuft-2) further expands our understanding of SCC specialization, linking them to both neuronal development and immune responses. Their involvement in cholinergic pathways, immune modulation, and epithelial homeostasis positions SCCs as key players in maintaining physiological balance and responding to environmental challenges. As research continues to uncover the molecular intricacies and functional roles of SCCs across species, these cells emerge not merely as auxiliary detectors but as central nodes in the sensory and regulatory networks of the vertebrate body. Future studies will be essential to fully elucidate their mechanisms of action, developmental origins, and potential therapeutic relevance in health and disease.

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