The Sensory Receptor System of the Caenorhabditis Elegans

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Abstract: Sensory system, as the initiation of neural activities, allows animals to detect and update dynamic information of the external world. Losing any sensation can threaten survival. Due to the complexity of higher animals' sensory systems, neuroscientists usually use simple animals for basic studies, such as the *Caenorhabditis elegans*. Two sensations, mechanosensation and chemosensation, allow nematode to detect mechanical (e.g., gentle touch, harsh touch) and chemical stimulations (e.g., odors, salts, oxygen), respectively. Both sensations are felt by related sensory neurons and translate to action potentials which downstream neurons can read. These translational processes were known as mechanotransduction and chemotransduction. This revived introduced *C. elegans'* sensory system to explain how each transduction is achieved by revealing underlaying molecular mechanisms. Mechanotransduction of *C. elegans* is functioned by the gating of ion channels on the mechanoreceptor neurons (MRNs). Different mechanical stimulation regarding its force can activate distinct neurons, in addition, to different ion channels. For example, gentle touches are sensed by the DEG/ENaC channels, expressed on the touch receptor neurons (TRNs). Harsh touches are detected by the TRP channels, which are expressed on the harsh touch neurons. Two putative models of mechanotransduction proposed that channels are either tethering with both intracellular microtubules and extracellular matrix or only tethering with microtubules to directly regulate channel gating. Chemotransduction of *C. elegans* is unitarily mediated by G-protein coupled receptors (GPCRs). Like mechanosensation, different chemosensory neurons are responsible for probing different chemicals. This differentiation is represented by the downstream signalling pathways of initially activated GPCRs. Currently, there are two pathways: the OSM-9/OCR-2 TRPV channel mediated signalling pathway and the cGMP-gated channel mediated signalling pathway.

1. Introduction

The mammalian sensory system often includes auditory, olfactory, somatosensory, gustatory and vision. A complete sensory circuit involves three steps: detecting stimulation and converting it to electric signals (sensory receptor neurons), transporting it to the brain (neural pathways) and sensory processing (brain). Dysfunction of any part of the circuit can lead to a crash of the whole system. Even damages to the latter two are untreatable due to the complexity of the cortical neural system and lack of a method to target. Curing sensory receptor neuron dysfunction of sensory organs is theoretically achievable. Several approaches such as drug modulations [1] and stem cell medicated regeneration [2, 3] have been implicated in sensory system regulation. Therefore, understanding sensory receptor neurons and underlaying mechanisms are required to establish effective therapeutic strategies and drugs. However, studying human and mammalian sensory systems is limited by existing biological approaches and economic reasons (e.g., cost and time). Even modern understating in the field of the mammalian sensory systems has been profoundly promoted, we still rely on the studies on the simple model organisms such as drosophila, worms, and rats to reveal the mechanism underlaying the behaviors for multiple scientific and real-world reasons. For instance, completed gene sequencing and neuron identification can advance studies of sensory neurons. Hence, selecting simple animals known as the model organisms can avoid such difficulties. The nematode

Caenorhabditis elegans, as one of the simplest organisms, only has 302 neurons whose functions were almost identified [4]. Also, the complete gene sequencings were identified as well [5]. Therefore, knowing the sensory receptor neurons of this model animal can be beneficial for promoting our understandings of sensory mechanism as a whole, thus, implicating mammals. This review concentrated on the two main types of the sensory system of *C. elegans*, which are mechanosensation and chemosensation. Neural correlate components and neurons were introduced with each sensation involved molecular mechanism.

2. Mechanosensation in the C. elegans

Mechanosensation refers to the perception of mechanical forces generated either by colliding with external objects (e.g., soil and other animals) or by sensing the internal colliding while moving (e.g., stretching). Mechanosensation is highly dependent on mechanotransduction, which is the process of converting mechanical forces to electrical signals. Numerous studies have found 30 mechanosensation correlated neurons in hermaphrodites and 52 additional neurons in males [6] by using cell abortion and genetic methods. These neurons are known as the mechanoreceptor neurons (MRNs). Since mechanotransduction is a rapid process that second-messenger signaling pathways or hormonal regulations cannot medicate, therefore, it is inferred to rely on ion channels, which are directly gated by mechanical forces [7]. Therefore, MRNs are so unique by containing mechano-electrical transduction (MeT) channels on their lipid bilayers, which are believed to drive the mechanotransduction by evoking the rapidly activating mechanoreceptor currents (MRCs). Genetical and electrophysiological methods have characterized several MeTs in *C. elegans,* such as transient receptor potential (TRP) [8] and degerin/epithelial Na+ channel (DEG/ENaC) channel [9]. However, no study has suggested that recently discovered Piezo channels that mediate the mechanosensation in mammals [10] are involved in the *C. elegans* touch circuits.

2.1 Mechanoreceptor neurons (MRNs) of the C. elegans

Even all MRNs in *C. elegans* are responsible for mechanotransduction. However, their functions and sensitivities vary among families. Some MRNs detect external forces, while others only respond to internally generated stimuli. The latter often refers to the interneurons, which do not directly respond to the external forces, but they are indispensable for postural sensation and locomotion. In addition, the sensory dendrites of MRNs can be either ciliated or nonciliated. Ciliated MRNs can be exposed to external environments. More importantly, different MRNs can have different ranges of the threshold of the action potential. This threshold specificity allows *C. elegans* to distinguish a gentle touch and prodding with a nail. For instance, PVD neurons were found mediating the strong stimuli (greater than ~100μN) only, while touch receptor neurons only respond to ~10μN touches (Iris Chin, M.B.G., and Marty Chalfie, unpublished).

2.2 Touch receptor neurons

2.2.1 Gentle touch sensation depends on multiple touch receptor neurons

Gentle touch, as known as weak mechanical stimuli, would activate nonciliated touch receptor neurons (TRNs), a member of MRNs in *C. elegans*. Gentle touches were usually induced by hitting the worm with soft hair. These weak mechanical stimuli were found able to activate escape behaviors. Touches to the anterior half of the *C. elegans* led to a backward movement while stimulating the posterior half (tail) made worms accelerate forward [11]. It is because that touch sensation is dependent on multiple neurons along the worm body which their receptive fields and signaling pathways are different due to distinct motor outputs. Chalfie and his team later found that there were six nonciliated touch receptor neurons, including the anterior located bilaterally symmetric pair of neurons (ALML, ALMR), the posterior located bilaterally symmetric pair of neurons (PLML, PLMR), mid anterior located AVM neuron and mid posterior PVM neuron [11, 12]. Each touch receptor neuron innervates about one-half of the worm's body length. Hence, an intact three-dimensional receptive field is established. Cooperation among touch receptor neurons

facilitates backwards and forward escape reflex. Moreover, touch stimuli to the *C. elegans* noses also evoked avoidance responses which are directly detected by the other three neurons: ASH, FLP, and OLQ [13]. Mutant worms and laser-induced worms which lack those neurons lost avoidance responses when inducing the gentle touches [13].

AVM and the pair of ALM neurons (ALML and ALMR) respond to anterior touches (backward movement). In contrast, the pair of PLM neurons (PLMR and PLML) are responsible for posterior touches (forward movement) [12]. The function of PVM neurons remined controversial. Some studies suggested that PVM neurons would receive a response to gentle posterior touches but are not involved in the activation of escape behaviors [14]. However, others suggested that PVM neurons alone are insensitive to a touch stimulus, but their synaptic structures suggested that PVM neurons may play roles in anterior touch sensation [12].

2.2.2 The DEG/ENaC channel complex mediated mechanotransduction of TRNs

The convincing evidence had reported that mechanotransduction of TRNs in *C. elegans* was mediated by the DEG/ENaC channels, a voltage-independent, amiloride-sensitive (Na+ channel blocker) Na+ channel [9]. In the experiment, *in vivo* recordings of MRCs in mutant *C. elegans* had revealed certain characteristics and molecular components of this type of ion channel. *MEC-4* and *MEC-10* are two channel pore-forming subunits, also as known as the degenerins, which gain-of-function mutations can cause neural degenerations [15]. Two other channel complex proteins are *MEC-2* and *MEC-6*, form the membrane-anchored complex, which interacts with *MEC-4* and *MEC-10* to compose a whole channel complex. DEG/ENaC channel complex was found punctate distributed in the TRNs by anti-*MEC-2* antibody induced visualisation [16]. Moreover, these channels only respond to transit physical force changes (both positive and negative) but are insensitive to sustained tensions which like the mammalian Pacinian corpuscles. Additional proteins include extracellular matrix (ECM) apparatus (*MEC-1, MEC-9,* and *MEC-5*) and tubulins (*MEC-7* and *MEC-12*) are also involved. Tubulins form large-dimeter microtubules (because other cells only contain 11-p microtubules) or 15-protofilament microtubules in TRNs, which the molecular role remained unclear. Recent studies have found that the 15-p microtubule disruptions could cause touch insensitivities in *C. elegans* whose channel complexes were maintained [17], suggesting the 15-p microtubule might be important for transporting signals which contributing to the mechanosensation of touch.

2.2.3 Non-DEG/ENaC channel medicated neurons also respond to touch

A very recent study has reported that the *C. elegans* outer labial lateral (OLL) sensory neurons also respond to touch sensation and cold [18]. They found that OLL neuron mediated mechanotransduction was insensitive to amiloride but largely relied on the extracellular Na+ level. By inducing different mechanotransduction-related candidate channel mutants (e.g., DEG/ENaC, TRP-4, TMC, and Piezo channel), Fan and his team have concluded that OLL neurons contained a new molecular pathway of mechanosensation which was mediated by a novel Na+ sensitive channel [18]. This study realized that more neurons could be involved in the mechanosensation, and the whole system of mechanosensation could be more complex than current understandings.

2.2.4 Two models of mechanosensation of TRNs

According to channel structures, neuroscientists proposed two putative models for mechanosensation of TRNs. The first model is called the 'dual-tether model' [19]. In this model, the mechanoreceptor channel complex is located between 15-p microtubules and ECM proteins and directly interacts with both-side components. The two pore-forming subunits *MEC-10* and MEC-4, are tethered in the ECM; therefore, physical forces would act on the microtubule thus to pull or push the channels via MEC-2-microtubules interactions hence to gate channels (Fig. 1). This model is like mammalian auditory-electrical transduction. However, recent studies have reported that null mutation of *mec-7* and *mec-12* genes would not affect touch sensation, suggesting that intracellular 15-p microtubule tethering might not be necessary for channel gating. Hence, scientists proposed the second model, the 'single tether model' [20]. In this model, microtubule tether in the lipid bilayer membrane rather than channel complex and channels is only tethered in ECM. External forces would

initially act on the membrane for up-down movement and either stretch or compress the channels like a trampoline (Fig. 1).

2.3 Harsh touch neurons

2.3.1 Distinct responses after gentle and harsh touch

C. elegans can distinguish two types of touch stimuli: gentle touch and harsh touch. Differing from gentle touch, harsh touch refers to a strong unpleasant or painful stimulation (100-200μN). In the behavior studies, gentle touches and harsh touches resulted in different responses in *C. elegans*. Although both stimulations would trigger the backward movement, the travelled distances (measured by head swings) of gentle-touch stimulated worms were less than harsh-touch stimulated worms [21]. This behavioral difference between harsh touch and gentle touch facilitated further investigations by quantifying the responses.

2.3.2 Harsh touch sensation depends on multiple harsh touch neurons

The sensation of harsh touch is also different from the TRNs-mediated gentle touch circuits. The dysfunction of TRNs caused by mutating the *mec-4* gene [22] only eliminated gentle touch sensitivities but not harsh touches [23]. Laser ablation of certain neurons facilitated us to investigate neural correlates of harsh touches sensation. Like gentle touch neurons, receptor fields polarize between anterior and posterior body segments. BDU, SDQR, FLP, ADE and AQR are responsible for sensing the anterior harsh touch, in which PVD and PDE are responsible for harsh posterior touch. Like the TRNs, ADE and AQR are nose-specific neuros for sensing the stimuli near noses since their dendrites project into the nose tips [24]. The FLP neurons are also located at the noses. However, their dendrites project to the whole anterior body [24]. Ablation of either PVD or PDE neurons could lead to severe defects of posterior sensation but not completely abolish it. Ablation of both neurons led to a total loss of posterior sensation but did not affect anterior sensation [21]. Therefore, it is suggested that PVD and PDE neurons are required for harsh posterior sensation.

2.3.3 The TRP channel regulates harsh touch sensations

Since the worms lacking the *mec-4* genes still represented a functional harsh touch sensation [23], other putative type(s) of channels should be involved. TRP superfamily channels have been revealed which are involved in the mechanosensation in *C. elegans* [8]. The *C. elegans* exhibit 7 sub-branches of TRP channel proteins, which are encoded by 17 canonical genes in the *C. elegans* genome [8, 25]. Patch-clamp recordings of harsh touch neurons in different TRP channel complex related mutants have facilitated scientists to understand how TRP channels participate in harsh touch sensation. Inspiring by the mammalian TRPA1 channels proteins, TRPA channels have been implicated in the mechanosensation in *C. elegans* by mutating *trpa-1* genes, the ortholog of mouse *Trpa1* [26]. TRPA1 channels have been found in PVD and PDE neurons [26]. The *trpa-1(-) C. elegans* which lack TRPA1 channels, did not show any defects on harsh touch sensation, suggesting that PVD/PDE located TRPA channels are dispensable for harsh touch sensation [21]. Moreover, the TRP-4 channel as the TRPN channel subfamily member has been found to involve the harsh touch sensation in PVD neurons since the *trp-4(-)* mutants lost avoidance responses posteriorly [21].

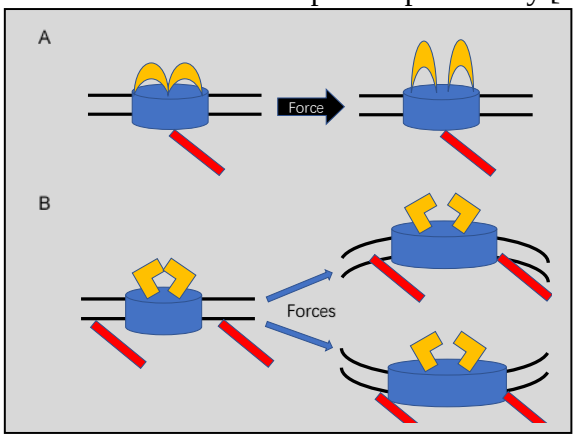

Figure 1. Two models of mechanotransduction of TRNs

A. The dual-tether model, channel complex is tethered in both ECM and microtubules. B. In the single-tether model, the channel complex is tether only to microtubules. Blue: channel complex. Yellow: gating complex. Red: microtubules. Black line: cell membrane.

2.3.4 PVD neurons may be regulated by a novel ENaC channel, not the TRP channel

Interestingly, PVD neuron mediated currents may also depend on ENaC channels like TRNs. For example, Chatzigeorgiou's team found that *mec-10(-) C. elegans* exhibited no Ca2+ transmission in response to harsh stimulations, and MEC-10 requires another protein, DEGT-1, a second ENaC subunit for harsh touch sensation in PVD neurons [27], suggesting that ENaC channels rather than TRP channels might dominate PVD neuron sensation.

2.3.5 The MEC-10 involved composite model may explain touch differentiation

ALM neurons were used to establish a new putative model which may explain the correlation between molecular properties and touch differentiation. Since ALM can detect both gentle and harsh touches by cross mutating MEC-4, MEC-10 and DEGT-1, they proposed a new model that gentle touch sensation requires MEC-4 and MEC-10 complex, in which harsh touch sensation requires MEC-10 and DEGT-1 complex [27]. This new model promoted our understandings of the field of exploring the molecular bases of touch sensation differentiation.

2.4 Bacterial sensing neurons

The third group of neurons is dopaminergic (DA) neurons which function to sense the bacteria. The four CEP, two ADE, and two PDE neurons, as the member of MRNs, are the only class of DA neurons in the *C. elegans'* nervous system [28]. They are all ciliated neurons in which CEP neurons are located at the mouth, the ADE and PDE neurons are located at the bi-lateral midlines under the cuticle. Again, this division of receptor field is like the other MRNs. When worms collide with a lawn of bacteria (the food of *C. elegans*), they would slow down forward movement and crawl on the bacteria lawn [29]. This locomotory rate decrease response mediated by the mechanosensation of CEP, ADE, and PDE neurons via DA regulation was called basal slowing response [29]. Mutating any DA synthesis-related genes (*cat-2, cat-4, and bas-1*) would result in a loss of basal slowing response [29]. Additionally, this response is independent of the existence of bacteria since the basal slowing responses were observed in a three-dimensional matrix of sterile Sephadex G-200 beads (to mimic the shape of bacteria without other sensory cues) [30]. Even the mechanism and ion channel involved in this sensation remained unclear. Several studies have provided some hints for future research. For instance, the bacterial sensing neurons have been found activating the touch receptor neurons on the cuticle of worms by releasing DA [30]. Additionally, the TRPN1 channels, the member of TRP-4 channels, had been found in those neurons which are required for mechanosensation [31].

However, this basal slowing response was only found in well-fed worms since food-deprived worms would represent the enhanced slowing responses, a more pronounced slowing response [29]. The bacterial sensing neurons do not mediate this response since mutating the DA synthesis related genes did not affect the enhanced slowing responses [29]. The enhanced slowing responses were found mediated by the serotonergic neurons in worms, but the mechanism remained unknown [29].

3. Chemosensation in the C. elegans

The law of diffusion realized us that chemicals could spread in an environment. Hence, sensing surrounding substances can be essential for living, which is known as chemosensation. Chemosensation allows worms to detect different olfactory and gustatory cues (e.g., salt, odor, and ions) released from foods and other animals in the environment. Unlike mechanosensation, all chemosensation-related neurons are ciliated neurons that facilitate direct or indirect chemicals detection. Eleven bilaterally symmetric pairs of chemosensory neurons consisted of amphid chemosensory organ of *C. elegans* are responsible for eliciting chemotaxis, avoidance behaviors and regulation of locomotion. Each chemosensory neuron can detect a set of attractants and repellents depending on the receptors expressed on the surface of neurons (Table 1). The chemo-electro

transduction largely relies on those receptors identified as the G protein-coupled receptors (GPCRs) by inducing specific mutations. Following the activation of GPCRs, downstream messages would act on either cGMP-gated channels or TRPV channels to regulate action potentials and neurotransmitter releases in the nervous system.

Table 1. Main chemosensory neurons and their functions and related GPCRs. The table displays GPCRs of several different chemosensory neurons. Others are not shown. The data is adapted from WormBook [32].

Table.1. Main chemosensory neurons and their functions and related GPCRs

Neuron	Function	GPCRs
ASE	Water-soluble chemotaxis	*gpa-3*
AWC	Volatile chemotaxis	*odr-3, gpa-3, gpa-2, gpa-5, gpa-13*
AWA	Volatile chemotaxis,	*odr-3, gpa-3, gpa-5; gpa-13; gpa-6*
AWB	Volatile avoidance	*odr-3*
ASH	Nose touch avoidance, Chemical avoidance	*odr-3, gpa-3, gpa-11, gpa-1, gpa-13, gpa-14, gpa-15*
URX, AQR, PQR	Oxygen	Soluble guanylate cyclase (*gcy-35, gcy-36); gpa-8*

3.1 ASE neurons detect water-soluble attractants and metal ion repellents

Cell ablation of ASE neuron pairing has led to reduced chemotaxis towards the water-soluble attractants such as Na+, Cl-, cAMP and serotonin [33]. This water-soluble substance sensation seems unique since ablating all other chemosensory neurons did not affect the sensation of water-soluble attractants. Even the anatomy of two ASE neurons, ASEL (left) and ASER (right), is symmetric. However, the function and gene expressed in each cell are distinct. The ASER neurons are more sensitive to chloride and potassium ions, while the ASEL neurons preferentially sense sodium [34]. This functional asymmetry is caused by asymmetric expression of the *lim-6* genes, as the human *LMX1* genes. In which only ASEL expresses *lim-6* [34]. In addition, ASE neurons also display an ON-OFF asymmetry when the concentration of NaCl changes. It is demonstrated by measuring the calcium transmission in ASE neurons, in which ASEL neurons were activated when NaCl concentration increases, so called- ON-cell. In contrast, ASER neurons were activated by decreasing NaCl concentration, so called OFF-cell [35].

Similar studies in searching the repellents have reported that ASE neurons are responsible for sensing Cd2+ and Cu2+ ions and elicit avoidance behaviors [36]. Mutants (*che-2(-)* and *osm-3(-)*) which had the structural defects in neurons and worms with laser-ablated neurons, lost avoidance behavior from Cd2+ and Cu2+ [36]. The whole neural pathway also includes ADL and ASH neurons but is dominated by ASE neurons [36].

3.2 Volatile odors sensing neurons

The *C. elegans* can sense the water-soluble molecules and detect volatile odors released by bacteria and other animals. Odors can reach the sensory neurons either by being transported across the sheath to the sensory nerve endings or by directly diffusing through the cuticle. AWC, AWB and AWA neurons medicate this sensation. In which AWC neuron pairing (AWCL and AWCR) can detect attractive odors including benzaldehyde, butanone, isoamyl alcohol, 2,3-pentanedione, and 2,4,5-trimethylthiazole [32]. AWA neurons pairing (AWAL and AWAR) can detect attractive odors, including diacetyl, pyrazine, and 2,4,5-trimethylthiazole [32]. Differing from AWC and AWA neurons, AWB neuron paring (AWBL and AWBR) can detect repellents including 2-nonanone, 1-octanol and trigger avoidance responses [37]. Although the mechanism underlaying the differentiating repellents and attractants remained unknown. By inserting *ODR-10* genes (AWA neuron excusive gene for detecting attractive odor diacetyl) into AWB neurons, worms acted to move away from diacetyl [37], suggesting this differentiation might be determined the receptor expression.

3.3 Oxygen sensing neurons

The *C. elegans*, as aerobic animals, require oxygen for living. In addition, oxygen level also determines the enrichment of bacteria since their metabolic system also relies on oxygen. Both hyperoxia and hypoxia can cause DNA damages and tissue death. In this case, *C. elegans* should hold a radar like system to avoid such environments since it has been reported that worms like 5-12% oxygen levels. Certain neurons of worms are sensitive to oxygen, including URX, AQR and PQR neurons [38]. AQR and PQR are body fluid exposed ciliated neurons, URX is nose-tip projected non-ciliated neurons [32].

The mechanism underlaying the oxygen sensation has not been fully understood. However, several studies have provided certain evidence which may explain this process. The oxygen sensor, *GCY-35* (soluble guanylate cyclase), have been found in oxygen sensing neurons, including URX, AQR and PQR, which mediated the hyperoxia evoked avoidance responses [38]. It is because that *GCY-35* can interact with oxygen via heme iron like the mammalian hemoglobin proteins. Worms with *gcy-35* mutations exhibited defective responses when encountered to hyperoxia conditions [38]. The mechanism of how hypoxia evokes responses remained unknown.

3.4 GPCRs mediated chemotransduction

Heterotrimeric G proteins are consisted of alpha, beta, and gamma subunits. Genome studies have revealed that at least 1300 genes are encoded for GPCRs in *C. elegans* [39]. There are at least 20 α subunits, 2 β subunits and 2 γ subunits in the worms' GPCR family [32]. For instance, *odr-3* gene, the ortholog of human *GNAI1* (G protein subunit alpha i1, Gi1), has been identified in the chemosensory neurons. Mutating *odr-3* gene led to defects of sensation functions of neurons, including AWA, AWB, AWC and ASH neurons [40]. Once GPCRs detect chemosensory stimuli, downstream signaling pathways initiate. In AWC neurons, a putative GPCR signaling pathway requires components including GPCRs, receptor guanylate cyclase, cGMP-gated channel and phosphodiesterase [32]. Odorants activated GPCRs will lead to ODR-3 disassociation from the complex hence to regulated cGMP level, thus, to gate the cGMP-gated channels. This regulation might occur at both phosphodiesterase and receptor guanylate cyclase by converting cGMP to GMP and GTP to cGMP, respectively [32]. GPCRs mediated signaling pathways also facilitate *GCY-35* mediated oxygen sensation [32].

3.5 The OSM-9/OCR-2 TRPV channel mediated signaling pathway

Downstream of GPCRs activation, the TRPV channel mediated signaling pathway has been found in AWA and ASH. Mutating *osm-9* and *ocr-2* would cause dysfunction of AWA and ASH neurons and their related sensations and behaviors. In this signaling pathway, instead of cGMP, lipid mobilization is involved between *ODR-3* and ion channels. Although the complete molecular signaling flow remained unclear. Kahn-Kirby and his team found that worm mutants that could not synthesise long-chain polyunsaturated fatty acids (PUAFs) normally displayed defects in producing chemotaxis responses [41]. Suggesting that PUAFs might play a transduction role between GPCRs and TRPV channels. However, the mechanism by which GPCRs recruit PUAFs remained unknown.

4. Conclusion

In this review, we introduced that the mechanosensation is divided into gentle touch and harsh touch, in which different neurons detect each stimulation. However, some neurons like ALM can detect both stimuli. The ion channels responsible for converting weak touch mechanical forces into electric signals are ENaC channels, which TRNs hold. TRP superfamily channels mediate harsh touch sensation. Single neurons studies have realized us that PVD neurons (harsh touch neurons) may hold ENaC channels. Together with the study of ALM neurons, more complex and integrated molecular mechanisms have been revealed. In which sensation differentiation between gentle and harsh touches may be determined by the combination of channel subunits. In addition, the discovery

of the OLL neuron extended our understandings of the neural system of *C. elegans*. A complete map of the neuronal function of worms is created.

The chemosensory neurons, like mechanosensory neurons, perform one's own tasks in the whole system. However, the chemosensory system is believed to be complex because worms can detect numerous chemicals and odors. The mechanism of chemosensation seems to be unitary. In which this process largely relies on the GPCRs activation. However, the downstream signaling pathways are still mazy. We are not sure whether there are more signaling streams excluding the PUAFs and cGMP mediated pathways.

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