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C. elegans phototransduction requires a G protein–dependent cGMP pathway and a taste receptor homolog

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The eyeless animal *C. elegans* is able to sense light and engages in phototaxis behavior that is mediated by photoreceptor cells. However, the molecular and cellular mechanisms underlying phototransduction in *C. elegans* remain largely unclear. By recording the photoreceptor neuron ASJ in wild-type and various mutant worms, we found that phototransduction in ASJ is a G protein–mediated process and requires membrane-associated guanylate cyclases, but not typical phosphodiesterases. In addition, we found that *C. elegans* phototransduction requires LITE-1, a candidate photoreceptor protein known to be a member of the invertebrate taste receptor family. Our genetic, pharmacological and electrophysiological data suggest a model in which LITE-1 transduces light signals in ASJ via G protein signaling, which leads to upregulation of the second messenger cGMP, followed by opening of cGMP-sensitive CNG channels and stimulation of photoreceptor cells. Our results identify a phototransduction cascade in *C. elegans* and implicate the function of a 'taste receptor' in phototransduction.

Being able to sense light is essential for the survival of most organisms. In animals, photoreceptor cells in the eye detect light and transduce it into electrical responses through a process called phototransduction. Among the best-characterized photoreceptor cells are vertebrate rods and cones, a group of ciliated sensory neurons in the retina. In these photoreceptor cells, light is absorbed by the rhodopsin family of GPCRs, which activate the G protein transducin[1]. Light-activated transducin then turns on phosphodiesterases (PDEs) to cleave the second messenger cGMP, resulting in a decrease in cGMP level and hence closure of CNG channels[1]. In vertebrate parietal eye photoreceptor cells, however, light-activated G proteins can inhibit PDEs, leading to an increase in cGMP level and opening of CNG channels[2]. In both cases, membrane-associated guanylate cyclases that produce cGMP in these photoreceptor cells are constitutively active in the dark and therefore have a passive role in phototransduction by providing substrates to PDEs[1]. In addition to this canonical phototransduction pathway, recent studies have found that photosensitive retinal ganglion cells, which mediate non–image forming visual functions, may employ a distinct pathway for phototransduction[3]; nevertheless, the exact mechanisms remain unclear.

The nematode *C. elegans* has been widely used as a model for the study of sensory transduction. Among the three major sensory stimuli are chemicals, mechanical forces and light. Worms rely on olfactory neurons (for example, AWA and AWC) and gustatory neurons (for example, ASE) to respond to chemical stimuli[4], while reacting to mechanical forces via touch receptor neurons (for example, ALM, AVM and PLM) and proprioceptor neurons (for example, DVA)[5,6]. However, worms were long thought to lack the sense of light, as they do not have eyes and live in dark soil.

Recent work from us and others has shown that, despite lacking eyes, the soil-dwelling *C. elegans* is able to sense light and engages in negative phototaxis behavior that allows it to avoid lethal doses of light[7,8]. We suggested that this behavior may also provide a potential mechanism for retaining worms in the dark soil[7]. We also reported that worms sense light through a group of photoreceptor cells, some of which respond to light by opening cGMP-sensitive CNG channels[7]. These channels also mediate temperature-evoked currents in the thermosensory neuron AFD[9]. In addition, a genetic screen identified *lite-1*, a taste receptor-like gene that is important for phototaxis behavior and has been suggested to encode a light-sensing molecule[8]; however, it is not clear whether this gene is involved in phototransduction in photoreceptor cells.

Nevertheless, numerous unanswered questions remain. In particular, the phototransduction cascade in worm photoreceptor cells has not been elucidated. First, phototaxis behavior appears to persist in some G protein–signaling mutants (G_q and G_s signaling)[8]. Does this indicate that *C. elegans* phototransduction is independent of G protein signaling? Second, do *C. elegans* photoreceptor cells also employ PDEs rather than guanylate cyclases for phototransduction? Third, is the *lite-1* gene involved in phototransduction in photoreceptor cells?

We conducted a comprehensive dissection of the phototransduction cascade in *C. elegans* using a combination of electrophysiological, pharmacological and genetic approaches. We found that phototransduction

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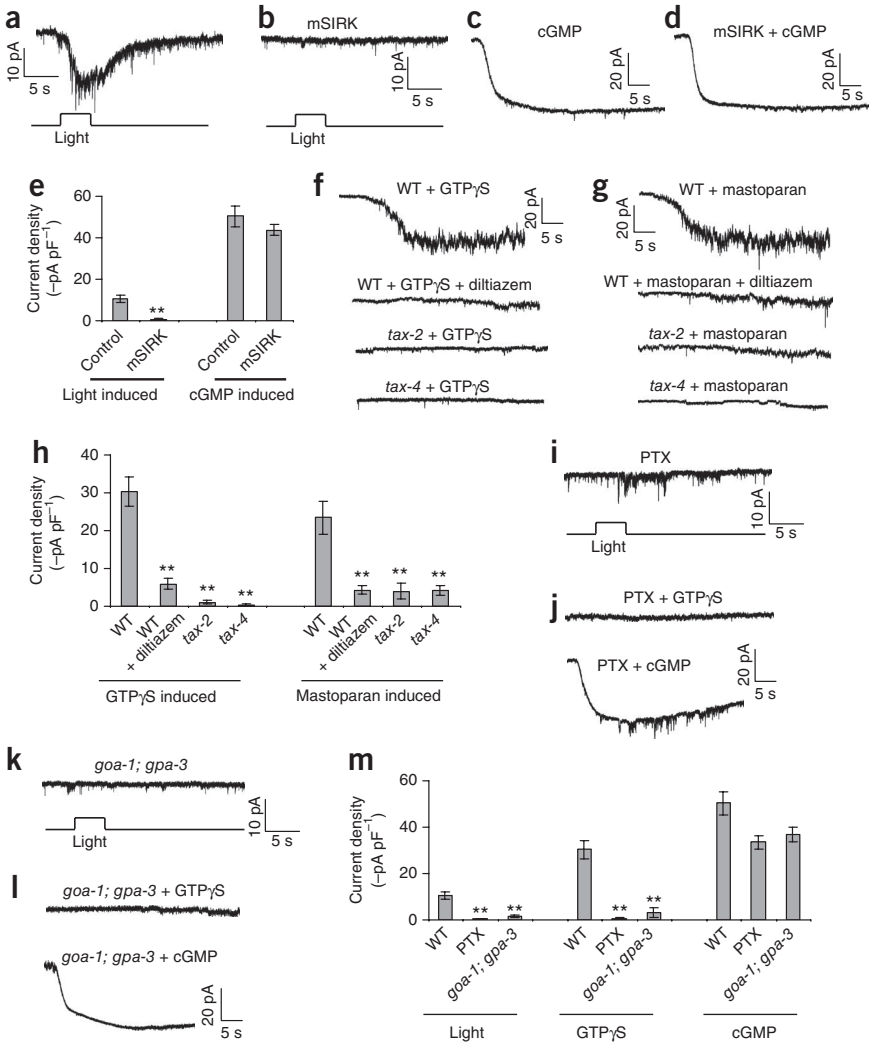

Figure 1 Phototransduction in ASJ is a G protein–mediated process. (**a**) Light-induced conductance in ASJ (clamping voltage, −70 mV; light stimulus, 350 ± 25 nm, 5 s, −1.75 log I/I_0). Worm photoreceptor cells are most sensitive to UV-A light[7]. The downward spikes in this trace and in other figures are typical for many worm neurons that are very small (~1 pF, ~2 μm in diameter) and exhibit high input resistance[46]. (**b**) Blocking G protein signaling blocked phototransduction. mSIRK (50 μM) is membrane permeable. (**c**,**d**) cGMP-evoked currents were not affected by mSIRK (1 mM cGMP). (**e**) Bar graph summarizing the data in **a**–**d** ($n \geq 6$, photocurrents; $n \geq 4$, cGMP-induced currents). Error bars represent ± s.e.m. $^{**}P < 0.002$ (*t* test). (**f**) Activation of G proteins opened CNG channels in the dark (100 μM GTPγS). We used the *tax-2* allele *p671* and the *tax-4* allele *p678*. WT, wild type. (**g**) Activation of $G_{i/o}$ opened CNG channels in the dark (5 μM mastoparon). (**h**) Bar graph summarizing the data in **f** and **g** ($n \geq 6$). $^{**}P < 0.0003$ (ANOVA with Dunnett test). (**i**) Blocking $G_{i/o}$ blocked phototransduction. PTX was expressed as a transgene in ASJ. (**j**) PTX blocked GTPγS-induced (top), but not cGMP-induced (bottom), current. (**k**) The *goa-1(n1134); gpa-3(pk35)* double mutant lacked photocurrents. See **Supplementary Figure 1** for single mutant data. (**l**) Mutations in *goa-1* and *gpa-3* blocked GTPγS-induced (top), but not cGMP-induced (bottom), current. (**m**) Bar graph summarizing the data in **i**–**l** ($n \geq 5$). Error bars represent ± s.e.m. $^{**}P < 0.005$ (ANOVA with Dunnett test).

in the photoreceptor cell ASJ required a G protein–dependent cGMP pathway and the taste receptor homolog LITE-1.

RESULTS

Phototransduction in ASJ requires G protein signaling

We first asked whether phototransduction in *C. elegans* photoreceptor cells requires G protein signaling. We focused on ASJ, the best characterized photoreceptor cell[7], and recorded its activity in response to light by perforated whole-cell recording[7]. Classic whole-cell recording protocols are incapable of detecting light-induced currents (photocurrents) in this neuron[7], probably because some components that are important for phototransduction are dialyzed out by the recording pipette. A similar phenomenon has been observed in recording vertebrate photoreceptor cells[2].

To test whether G protein signaling is required for phototransduction in ASJ, we examined the effect of mSIRK, a membrane-permeable peptide that dissociates G_α from $G_{\beta\gamma}$ without affecting its GTPase activity and thereby exerting an inhibitory effect on GPCR-mediated activation of G_α[10]. mSIRK blocked the light-evoked conductance in ASJ (**Fig. 1a**,**b**). As a control, the cGMP-induced currents were not affected in ASJ (**Fig. 1c**–**e**). Thus, blocking G protein signaling can inhibit phototransduction in ASJ, suggesting that G protein signaling is required for phototransduction in *C. elegans* photoreceptor cells.

If G protein signaling mediates phototransduction, then stimulating G protein signaling should stimulate photoreceptor cells. To test this, we perfused GTPγS, a non–hydrolyzable GTP analog that activates G proteins, into ASJ through the recording pipette. GTPγS stimulated ASJ by evoking an inward current in the dark (**Fig. 1f**). This current was apparently carried by CNG channels, as it can be blocked by the CNG channel–specific inhibitor L-*cis*-diltiazem and was absent in the CNG channel mutants *tax-2* and *tax-4* (**Fig. 1f**)[11–13]. Therefore, stimulating G protein signaling can stimulate photoreceptor cells, suggesting that phototransduction in ASJ is a G protein–mediated process. These results also suggest that CNG channels act downstream of G proteins.

We next asked which type of G protein mediates phototransduction in *C. elegans* photoreceptor cells. Phototransduction in vertebrate rods and cones requires transducin, a G_α protein that belongs to the $G_{i/o}$ family[1]. We tested the effect of mastoparan, a peptide that can activate $G_{i/o}$ proteins[14]. Perfusion of mastoparan into ASJ elicited an inward current (**Fig. 1g**,**h**). Similarly, this current appeared to be carried by CNG channels, as we were able to block it with L-*cis*-diltiazem and mutations in *tax-2* and *tax-4* (**Fig. 1g**,**h**). Thus, activation of $G_{i/o}$ can lead to the opening of CNG channels.

To provide additional evidence, we sought to block the function of $G_{i/o}$. The worm genome encodes 21 G_α proteins, at least three of which belong to the $G_{i/o}$ family[15]; in addition, many others are closely related to $G_{i/o}$[16]. We first tested the effect of pertussis toxin (PTX), which inhibits $G_{i/o}$ function[17]. PTX blocked the photoresponse in ASJ, suggesting that $G_{i/o}$ proteins are required for phototransduction in ASJ (**Fig. 1i**). As expected, PTX also blocked the ability of GTPγS to stimulate CNG channels in ASJ (**Fig. 1j**). As a control, direct application of cGMP was still able to efficiently activate CNG channels in ASJ (**Fig. 1j**), consistent with the view that CNG channels act downstream

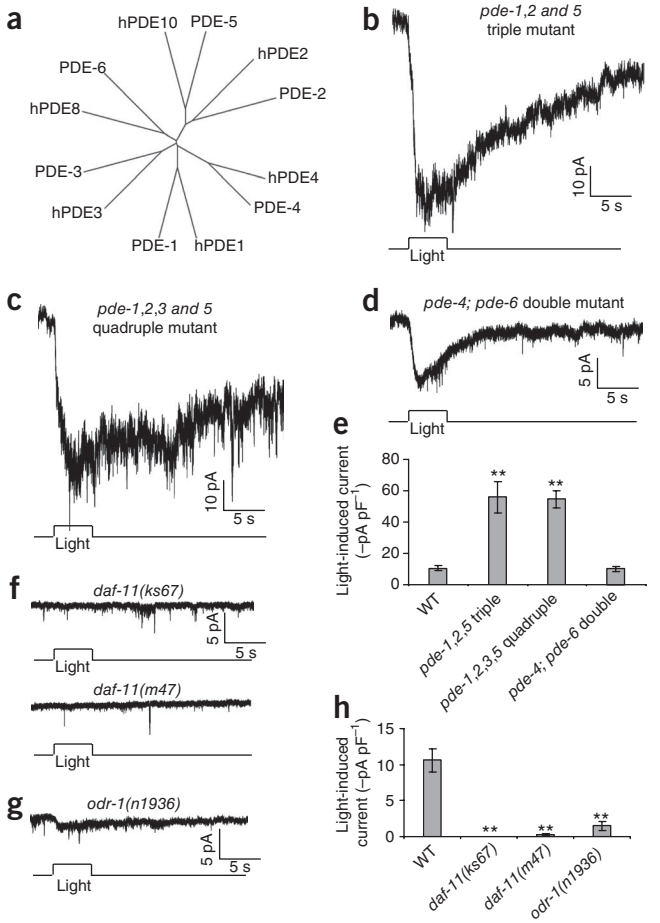

Figure 2 Phototransduction in ASJ requires membrane-associated guanylate cyclases. (**a**) Dendrogram of *C. elegans* and human PDEs (hPDEs). (**b**) The light-induced current was greatly potentiated in the *pde-1*, *2* and *5* triple mutant *pde-1(nj57)pde-5(nj49); pde-2(nj58)*. (**c**) The light-induced current was greatly potentiated in the *pde-1*, *2*, *4* and *5* quadruple mutant *pde-1(nj57)pde-5(nj49); pde-3(nj59); pde-2(nj58)*. A similar result (51.7 ± 3.28 pA pF^{-1}, $n = 5$) was obtained with another quadruple mutant strain, *pde-1(nj57)pde-5(nj49); pde-3(nj59); pde-2(tm3098)*. (**d**) The light-induced current was normal in the *pde-4(nj60); pde-6(ok3410)* double mutant. (**e**) Bar graphs summarizing the data in **b**–**d** ($n \geq 7$). Error bars represent ± s.e.m. $^{**}P < 0.0001$ (ANOVA with Dunnett test, compared with wild type). (**f**) No light-induced current was detected in the guanylate cyclase mutants *daf-11(ks67)* and *daf-11(m47)*. (**g**) The light-induced current in the guanylate cyclase mutant *odr-1(n1936)* was greatly reduced. (**h**) Bar graph summarizing the data in **f**–**g**. *daf-11(ks67)* is temperature sensitive[47] and all recordings involving this allele were carried out at 25 °C. All other recordings were performed at 20 °C. The photocurrent density in wild-type recorded at 25 °C was similar to that at 20 °C (data not shown; $n \geq 7$). Error bars represent ± s.e.m. $^{**}P < 0.0005$ (ANOVA with Dunnett test, compared with wild type).

of G proteins. These results strongly suggest that phototransduction in ASJ is mediated by the $G_{i/o}$ family of G proteins.

At least five *C. elegans* G_α genes are targets for PTX[18]. Among them, *goa-1*, *gpa-1* and *gpa-3* are known to be expressed in ASJ[19]. Although photocurrents appeared to be normal in *goa-1*, *gpa-1* and *gpa-3* single mutants (**Supplementary Fig. 1**), the *goa-1; gpa-3* double mutant had a severe defect in phototransduction in ASJ (**Fig. 1k**). In addition, GTPγS could no longer stimulate CNG channels in *goa-1; gpa-3* mutant worms (**Fig. 1l**,**m**). As a control, cGMP could still efficiently activate CNG channels in these mutant worms, indicating that the mutations did not affect the general health of the neuron (**Fig. 1l**,**m**). Thus, *goa-1* and *gpa-3* have a redundant role in mediating phototransduction in ASJ. Nevertheless, as the known expression patterns for G_α genes could be incomplete, it is possible that other G_α genes may be involved in phototransduction in ASJ. It is also possible that other photoreceptor cells may depend on different sets of G_α genes for phototransduction.

Phototransduction in ASJ does not require typical PDEs

How does G protein activation lead to the opening of CNG channels? In vertebrate photoreceptor cells, light-activated G proteins either inhibit PDEs (for example, parietal eye photoreceptor cells) or stimulate PDEs (for example, rods and cones), resulting in an increase or reduction in cGMP level and thus the opening or closing of CNG channels, respectively[1,2]. Mice lacking the retina PDE (PDE-6) are blind[20]. If *C. elegans* photoreceptor cells use such a mechanism, it would be similar to that in vertebrate parietal eye photoreceptor cells; namely, G proteins upregulate cGMP by inhibiting PDEs, thereby opening CNG channels. Thus, we examined the role of PDEs in worm phototransduction.

The *C. elegans* genome encodes six PDEs, PDE-1–6, each of which has a closely related human homolog (**Fig. 2a**). PDE-4 and PDE-6 are highly homologous to human PDE-4 and PDE-8, respectively, both of which are cAMP specific[21]. The other four PDEs (PDE-1, 2, 3 and 5) may cleave cGMP and could therefore be involved in phototransduction. We isolated mutant alleles of all these four *pde* genes and generated mutant strains lacking multiple PDEs. In the *pde-1*, *2* and *5* triple mutant, the photocurrent was not only present in ASJ, but also markedly potentiated, with a current density about fivefold greater than that in wild-type worms (**Fig. 2b**–**e**). The same phenomenon was observed in quadruple mutant strains devoid of all four PDEs (**Fig. 2c**,**e**). We also generated a *pde-4; pde-6* double mutant strain lacking the two putative cAMP-specific PDEs and found that these worms had normal photocurrents (**Fig. 2d**,**e**).

The photocurrent in the *pde-1*, *2*, *3* and *5* quadruple mutant exhibited very slow or no recovery after cessation of the light stimulus, consistent with a role for PDEs in downregulating cGMP (**Fig. 2c**). Notably, the input resistance in ASJ of the *pde* quadruple mutant (4.43 ± 0.66 GΩ, $n = 4$) was similar to that in the wild type (4.30 ± 0.60 GΩ, $n = 6$). This indicates that a loss of PDE function did not lead to the opening of additional channels in the dark, the opposite of which has been observed in vertebrate parietal eye photoreceptor cells[2]. This also suggests that guanylate cyclases have very low activity in the dark in ASJ, a feature that is distinct from that observed in vertebrate photoreceptor cells. Taken together, these results suggest that PDEs may not be required for phototransduction, but are instead involved in modulation of phototransduction in ASJ. It should be noted that, although we examined all of the predicted *pde* genes, we cannot rule out the possibility that some unknown type of PDEs, which do not show homology to known PDEs, may act in phototransduction.

Phototransduction in ASJ requires guanylate cyclases

Alternatively, stimulation of guanylate cyclases in principle may also upregulate cGMP, leading to activation of CNG channels. There are two major types of guanylate cyclases: soluble guanylate cyclases and membrane-associated guanylate cyclases[22,23]. In *C. elegans*, soluble guanylate cyclases are sensitive to O_2 and are required for social feeding, whereas membrane-associated guanylate cyclases are essential for chemotaxis and thermotaxis[24–27]. Notably, two membrane-associated guanylate cyclases (*daf-11* and *odr-1*) are expressed in *C. elegans* photoreceptor cells, including ASJ, ASK and AWB[26,28].

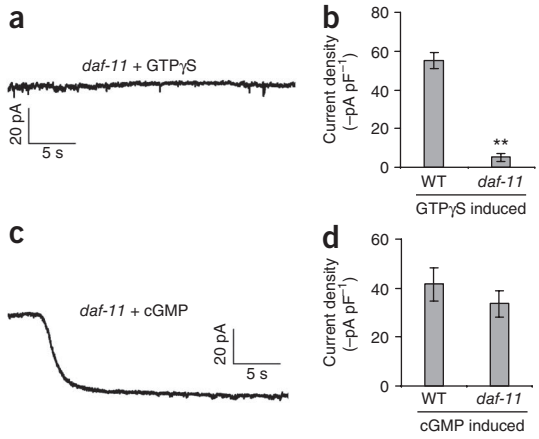

Figure 3 Guanylate cyclases act downstream of G proteins and upstream of CNG channels to mediate phototransduction. (**a**,**b**) Guanylate cyclase/DAF-11 acted downstream of G proteins. The *Ks67* mutation in *daf-11* blocked the ability of GTPγS in stimulating ASJ. A sample trace is shown in **a** ($n \geq 5$). Error bars represent ± s.e.m. $^{**}P < 0.00001$ (*t* test). (**c**,**d**) Guanylate cyclase/DAF-11 acted upstream of CNG channels. cGMP efficiently opened CNG channels in ASJ of *daf-11* (*Ks67*) mutant worms. A sample trace is shown in **c** ($n \geq 5$). Error bars represent ± s.e.m.

We examined *daf-11* and *odr-1* mutants. There were no photocurrents in ASJ from *ks67* and *m47* mutants, which are two independent alleles of *daf-11* (**Fig. 2f**). *odr-1(n1936)* mutant worms also had a severe reduction in the density of photocurrents (**Fig. 2g**,**h** and **Supplementary Fig. 2**). These results indicate that membrane-associated guanylate cyclases are required for phototransduction in ASJ. Supplementing *daf-11* mutant worms with non–saturating levels of cGMP did not restore photosensitivity in ASJ (**Supplementary Fig. 3**). This indicates that cGMP does not simply have a permissive role in phototransduction, providing additional evidence that cGMP is a second messenger for phototransduction in ASJ.

Guanylate cyclase act downstream of G proteins

These results suggest a model in which G protein activation leads to upregulation of cGMP level, which in turn causes CNG channel activation. In other words, guanylate cyclases act downstream of G proteins, but upstream of CNG channels. If this is true, activation of G proteins should no longer be able to stimulate CNG channels in guanylate cyclase mutant worms, but cGMP should still be able to open these channels.

To test this model, we examined the effects of GTPγS and cGMP on CNG channels in *daf-11* mutant worms. Indeed, GTPγS failed to stimulate CNG channels in ASJ of *daf-11* mutant worms (**Fig. 3a**,**b**), whereas cGMP was still able to efficiently activate CNG channels in this mutant (**Fig. 3c**,**d**). This observation suggests that guanylate cyclases act downstream of G proteins, but upstream of CNG channels, to mediate phototransduction in ASJ.

pde mutants allow further testing of the proposed model

In wild-type worms, we were able to detect light-induced currents under the perforated, but not classic, whole-cell configuration. As a result of this technical constraint, we can only test the effect of membrane-permeable chemicals on photocurrents by including them in the bath solution. Unlike classic whole-cell configuration, perforated patch does not allow for dialyzing most membrane-impermeable chemicals into photoreceptor cells through the recording pipette. We were surprised to find that we were able to detect photocurrents in *pde* mutant worms under classic whole-cell configuration (**Fig. 4a**). The exact mechanism underlying this observation is not known, but it is probably because the loss of PDEs potentiated cGMP level under light stimulation, which may offset the negative effect of the washout by the recording pipette of some phototransduction-promoting factors. This offers us a unique opportunity to gather further evidence supporting the proposed phototransduction model.

We first examined the effects of GDPβS (membrane impermeable), one of the most commonly used G protein–signaling blockers. Dialysis of GDPβS into ASJ of *pde* mutant worms through the recording pipette abolished photocurrents, indicating that phototransduction requires G protein signaling (**Fig. 4b**). In another experiment, we first activated CNG channels in ASJ of *pde* mutants by dialyzing GTPγS or cGMP (both membrane impermeable) into ASJ and then stimulated ASJ with light (**Fig. 4c**,**d**). Light could not further induce an inward current under these conditions, suggesting that light, GTPγS and cGMP all act on the same type of CNG channels and stimulate the same signaling cascade (**Fig. 4c**–**e**). This is also consistent with our phototransduction model in which G protein signaling upregulates cGMP levels, leading to CNG channel activation.

Phototransduction in photoreceptor cells require LITE-1

The *C. elegans* genome does not encode any closely related homologs for opsins[29], a group of GPCRs that represent the most common photoreceptor proteins in metazoan photoreceptor cells. This suggests that *C. elegans* photoreceptor cells may adopt an opsin-independent mechanism for phototransduction. We carried out a forward genetic screen for mutants defective in phototaxis in hopes of identifying candidate photoreceptor genes. Three mutants (*xu7*, *xu8* and *xu10*) had

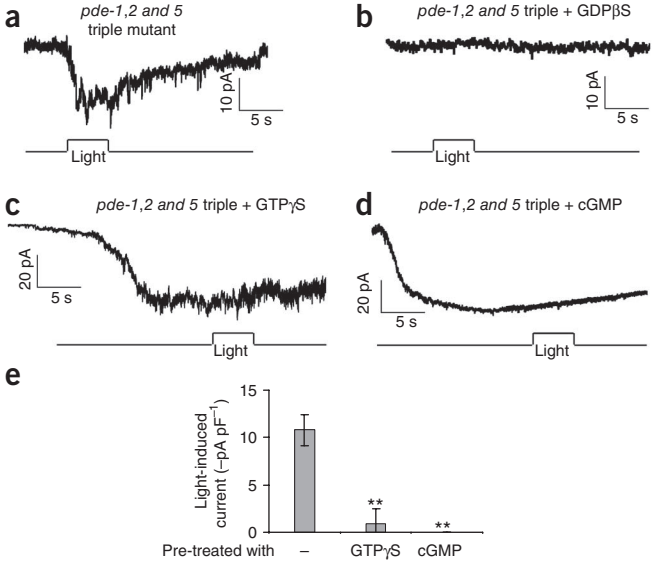

Figure 4 Light, GTPγS and cGMP activate the same type of CNG channels in photoreceptor cells. (**a**) Light evoked an inward current in the *pde-1*, *2* and *5* triple mutant under the classic whole-cell mode. (**b**) GDPβS blocked phototransduction. GDPβS (100 μM) was dialyzed into ASJ through the recording pipette. (**c**) Light and GTPγS acted on the same type of CNG channels. In the *pde* triple mutant, once CNG channels were activated by GTPγS, light did not further induce an inward current. (**d**) Light and cGMP activated the same type of CNG channels. In the *pde* triple mutant, once CNG channels were activated by cGMP, light did not further induce an inward current. (**e**) Bar graph summarizing the data in **a**–**d** ($n \geq 6$). Error bars represent ± s.e.m. $^{**}P < 0.0001$ (ANOVA with Dunnett test).

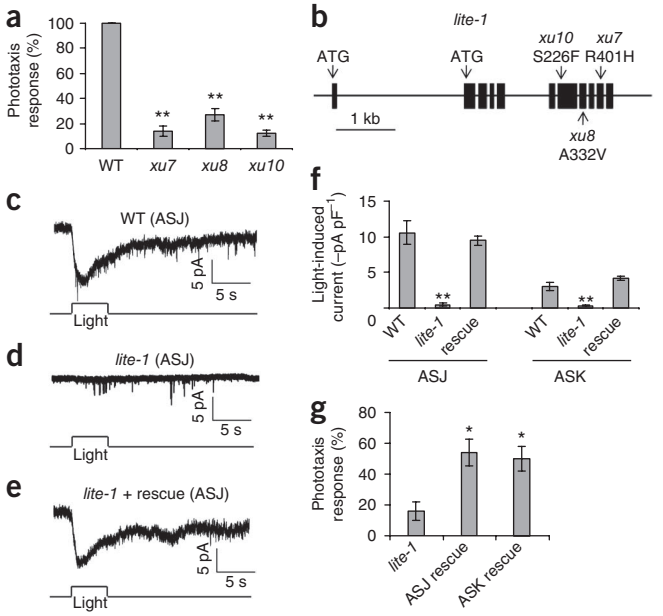

Figure 5 LITE-1 is required for phototransduction in photoreceptor cells. (**a**) Three mutants had a strong defect in phototaxis behavior. Head avoidance response to UV-A light (2 s, −1.43 log I/I_0) was scored as previously described[7,48]. The response rate in *xu7* and *xu10* was similar to that of a no-light control and likely resulted from spontaneous reversals ($n \geq 10$). Error bars represent ± s.e.m. $^{**}P < 0.00001$ (ANOVA with Dunnett test, compared with wild type). (**b**) *lite-1* genomic structure and mutations identified in *lite-1*. We identified two *lite-1* isoforms. There is an SL1 sequence before the ATG in the second exon, indicating that there is a short form of *lite-1*, which we used here. (**c**–**e**) LITE-1 was required for phototransduction in ASJ. Shown are sample traces of ASJ in wild type (**c**), *lite-1(xu7)* (**d**) and *lite-1(xu7)* expressing a wild-type *lite-1* transgene specifically in ASJ under the *trx-1* promoter[49] (**e**). See **Supplementary Figure 5** for ASK traces. (**f**) Bar graph summarizing the data in **c**–**e**. Error bars represent ± s.e.m. ($n \geq 7$). $^{**}P < 0.00002$ (ANOVA with Dunnett test, compared with wild type). (**g**) Expression of a wild-type *lite-1* transgene specifically in ASJ or ASK had a rescuing effect on the phototaxis behavioral defect in *lite-1(xu7)* mutant worms. The *trx-1* and *srg-8* promoters were used to drive expression of the transgene in ASJ and ASK, respectively[49,50]. Error bars represent ± s.e.m. ($n \geq 10$). $^{*}P < 0.05$ (ANOVA with Bonferroni test, compared with *lite-1*).

a strong defect in phototaxis behavior and failed to complement each other, suggesting that the mutations occur in the same gene (**Fig. 5a** and data not shown). Using SNP (single nucleotide polymorphism) mapping, we found that these mutations were in the close proximity to *lite-1* and sequencing analysis revealed that they all were alleles for *lite-1* (**Fig. 5b**)[8]. *lite-1* encodes a seven transmembrane domain receptor–like protein and is a member of the invertebrate taste receptor family (**Supplementary Fig. 4**)[8]. This family was first identified in *Drosophila*[30,31]. The *C. elegans* genome encodes a total of five such taste receptor genes (**Supplementary Fig. 4**).

The *lite-1* gene has been reported to be located in a large, complex operon, and GFP transgenic approaches appear to be unsuccessful at revealing its full expression pattern[8]. Although *lite-1* mutant worms have a strong defect in phototaxis behavior, it is not clear whether *lite-1* has a role in phototransduction in photoreceptor cells. Mutations in *lite-1* may simply disrupt synaptic transmission in motor circuits or the function of interneurons and/or motor neurons that act downstream of photoreceptor cells to induce phototaxis behavior. Indeed, many mutants that affect synaptic transmission disrupt phototaxis behavior in a nonspecific manner (A.W., D.M. and X.Z.S.X., unpublished observations).

To determine whether LITE-1 participates in phototransduction in photoreceptor cells, we recorded the photoresponse in ASJ of *lite-1* mutant worms. Light failed to elicit an inward current in mutant neurons, indicating that LITE-1 is required for phototransduction in ASJ (**Fig. 5c**,**d**). Expression of wild-type LITE-1 specifically in ASJ fully rescued the photoresponse in ASJ (**Fig. 5e**,**f**). The same transgene also rescued *lite-1* phototaxis defect (**Fig. 5g**). These results suggest that LITE-1 functions in ASJ to mediate phototransduction.

We also recorded another putative photoreceptor cell, ASK, which expresses the same set of CNG channels and membrane-associated guanylate cyclases as ASJ[12,13,26,28]. Light stimulation evoked an inward current in ASK of wild-type worms (**Fig. 5f** and **Supplementary Fig. 5**). This photoresponse required CNG channels and membrane-associated guanylate cyclases, but not PDEs (**Supplementary Fig. 6**). Notably, although *pde* mutants retained photocurrents in ASK, the current density in these mutants was not higher than that in wild type (**Supplementary Fig. 6**). This is different from the case with ASJ, indicating that PDEs have a modulatory role in some, but not all, photoreceptor cells. Mutations in *lite-1* eliminated ASK photocurrents, and expression of wild-type LITE-1 specifically in ASK fully rescued this defect (**Fig. 5f** and **Supplementary Fig. 5**). The same transgene also rescued the phototaxis defect of *lite-1* mutants (**Fig. 5g**). Nevertheless, given the smaller amplitude and slower kinetics of ASK photocurrents compared with those recorded in ASJ (**Supplementary Fig. 5**), it remains possible that the recorded photocurrents in ASK may indirectly result from ASJ (ASJ synapses onto ASK) or other photoreceptor cells.

LITE-1 acts upstream of G proteins in phototransduction

We next sought to place LITE-1 in the phototransduction cascade. We reasoned that if LITE-1 functions upstream of G proteins, we would expect that both GTPγS- and cGMP-elicited currents in *lite-1* mutants are similar to those in wild type. This is indeed the case. In *lite-1* mutant worms, both GTPγS and cGMP can efficiently stimulate CNG channels in ASJ, indicating that LITE-1 acts upstream of G proteins (**Fig. 6a**–**c**). These results suggest that LITE-1 may be part of the photoreceptor complex or required for the function of this complex.

If LITE-1 is part of the photoreceptor complex, it should also function upstream of guanylate cyclases and CNG channels. Mutations in the membrane-associated guanylate cyclase DAF-11 and CNG channel subunit TAX-4 abrogated the photoresponse in ASJ and ASK, but these mutants did not exhibit a strong phenotype in phototaxis behavior (**Fig. 2e** and unpublished observations from A.W. and X.Z.S.X.). This can be explained by the fact that some other photoreceptor cells (for example, ASH and ADL) do not express these genes and perhaps utilize distinct phototransduction mechanisms. Nonetheless, expression of wild-type LITE-1 in guanylate cyclases/CNG channel–expressing photoreceptor cells, such as ASJ, ASK and AWB, was sufficient to rescue the phototaxis defect in *lite-1* mutant worms (**Fig. 6d**). Notably, mutations in *daf-11* and *tax-4* can suppress the effect of the *lite-1* transgene on rescuing *lite-1* phototaxis defect (**Fig. 6d**). These results provide additional evidence that guanylate cyclases and CNG channels function downstream of LITE-1 in phototransduction.

ChR2 restores photosensitivity in *lite-1* mutant worms

Expression of the light-gated ion channel channelrhodopsin-2 (ChR2) specifically in ASJ of *lite-1* mutant worms rendered ASJ photosensitive (**Supplementary Fig. 7**). The same ChR2 transgene

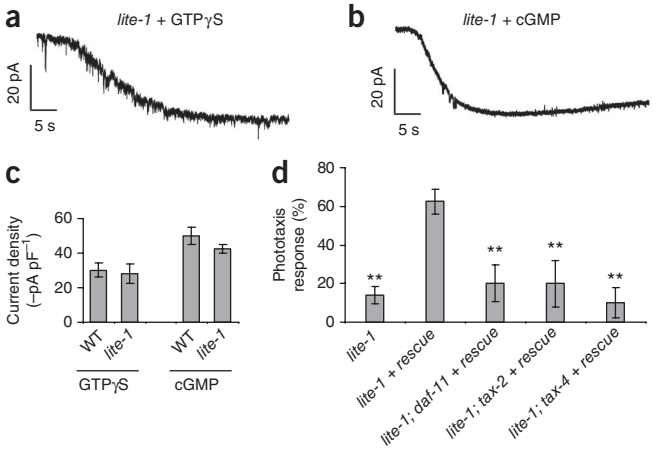

Figure 6 LITE-1 functions upstream of G proteins. (**a**,**b**) LITE-1 acted upstream of G proteins. GTPγS (**a**) and cGMP (**b**) induced an inward current in ASJ of *lite-1(xu7)* mutant worms. (**c**) Bar graph summarizing the data in **a** and **b**. The densities of GTPγS- and cGMP-induced currents in ASJ of *lite-1(xu7)* mutant worms were similar to those in wild type ($n \geq 6$). Error bars represent ± s.e.m. (**d**) LITE-1 acted upstream of guanylate cyclases and CNG channels. Wild-type *lite-1* was expressed as a transgene under the *tax-2*Δ promoter in the photoreceptor cells ASJ, ASK and AWB. This transgene rescued the phototaxis defect in *lite-1(xu7)* mutant worms. This rescuing effect required the guanylate cyclase DAF-11 and CNG channels TAX-2 and TAX-4. $^{**}P < 0.001$ (ANOVA with Dunnett test, compared with the rescue). Error bars represent ± s.e.m. ($n \geq 10$).

also restored photosensitivity in ASJ of *daf-11*, *tax-2* and *tax-4* mutant worms (**Supplementary Fig. 7**). These results indicate that these mutations did not affect the general health of the neuron. Consistent with the idea that ChR2 is an ion channel that is directly gated by light independently of second messengers[32,33], the ChR2-dependent photocurrents in ASJ developed virtually instantaneously on light stimulation, without a detectable latency, and also exhibited rapid activation kinetics (activation time constant $\tau_{act} = 8.95 \pm 0.03$ ms under 2 mW mm^{-2} of blue light; **Supplementary Fig. 7**). These features are in sharp contrast with those of the LITE-1–dependent intrinsic photocurrents in ASJ, which exhibited a latency of hundreds of milliseconds and slow activation kinetics (latency = 356 ± 37 ms in ref. 7, τ_{act} = 566 ± 2.6 ms). Such a long latency and slow activation kinetics are typical for a process requiring second messengers. This is consistent with a model in which LITE-1 acts as a receptor protein that requires G protein signaling and the second messenger cGMP to transduce light signals in ASJ. This is also consistent with the fact that the LITE-1–dependent intrinsic photocurrents in ASJ are carried by downstream CNG channels.

We also tested whether reactive oxygen species (ROS) can activate LITE-1. Perfusion of hydrogen peroxide evoked a small inward current in ASJ. However, this current persisted in *lite-1* mutant worms (**Supplementary Fig. 8**). Although it is unclear what mediates this ROS-induced current in ASJ, it apparently does not occur through the activation of LITE-1. This result suggests that the trace amount of ROS produced by light illumination, if any, cannot fully account for the activation of LITE-1.

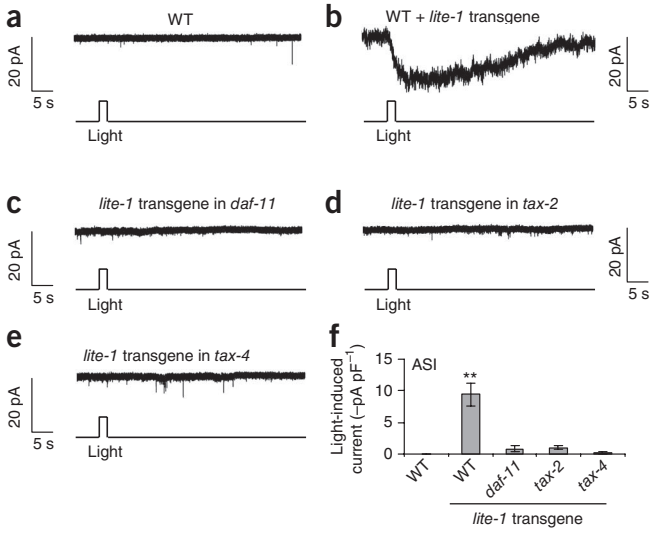

Figure 7 Transgenic expression of LITE-1 can confer photo-sensitivity to the photo-insensitive neuron ASI. (**a**) The ASI neuron was photo-insensitive. No photocurrent could be detected in ASI. (**b**) Expression of LITE-1 in ASI made it photo-sensitive. LITE-1 was expressed as a transgene in ASI under the *sra-6* promoter, which labels both ASI and ASH in the head[50]. ASI recordings performed in ASH-ablated worms and non-ablated worms yielded similar results (9.1 ± 1.3 pA pF^{-1} versus 9.4 ± 1.8 pA pF^{-1}, $n = 5$). (**c**–**e**) The function of LITE-1 in ASI also required *daf-11*, *tax-2* and *tax-4*, as mutations in these genes blocked LITE-1–dependent photocurrents in ASI. (**f**) Bar graph summarizing the data in **a**–**e** ($n \geq 5$). Error bars represent ± s.e.m. $^{**}P < 0.00001$ (ANOVA with Dunnett test, all compared with wild type without transgene).

LITE-1 confers photosensitivity to photo-insensitive cells

We sought to test the function of LITE-1 in heterologous systems. However, all of our attempts to functionally express LITE-1 in cultured cell lines were unsuccessful (L.K. and X.Z.S.X., unpublished observations). LITE-1 has been ectopically expressed in worm muscles and found to induce muscle contraction[8]. However, we only detected a tiny, if any, photocurrent in muscle cells expressing *lite-1* transgenes by whole-cell recording (0.46 ± 0.1 pA pF^{-1}, $n = 15$). This may be caused by the fact that muscle cells lack some standard components in the phototransduction machinery, such as CNG channels and guanylate cyclases.

We thus expressed LITE-1 as a transgene in the ASI neuron that also expresses the guanylate cyclase DAF-11 and the CNG channels TAX-2 and TAX-4 (refs. 12,13,28). No photocurrent could be detected in ASI of wild-type worms, indicating that this neuron is photo-insensitive (**Fig. 7a**). Notably, expression of LITE-1 as a transgene in ASI rendered this neuron photosensitive (**Fig. 7b**). The LITE-1–dependent photocurrent in ASI also showed a latency of hundreds of milliseconds and slow activation kinetics (latency = 432 ± 66 ms, τ_{act} = 908 ± 3.4 ms), suggesting that second-messenger signaling was involved. Indeed, as was the case with ASJ and ASK, the LITE-1–dependent photocurrent in ASI also required the guanylate cyclase DAF-11 and the CNG channels TAX-2 and TAX-4 (**Fig. 7c**–**f**). These results provide electrophysiological evidence that LITE-1 expression is sufficient to confer photosensitivity to photo-insensitive cells.

DISCUSSION

Despite many similarities between *C. elegans* and vertebrate photoreceptor cells (both are ciliated neurons and depend on G protein signaling, the second messenger cGMP and CNG channels for phototransduction), there are clear differences between the two (a model for *C. elegans* phototransduction cascade is summarized in **Supplementary Fig. 9**). For example, they likely use distinct types

of photoreceptor proteins (**Supplementary Fig. 9**). In addition, *C. elegans* phototransduction in ASJ requires membrane-associated guanylate cyclases, but not typical PDEs (**Supplementary Fig. 9**). Membrane-associated guanylate cyclases are known to be activated by peptide ligands and calmodulin-like guanylate cyclase–activating proteins[22]. Our results raise the possibility that G protein signaling may modulate membrane-associated guanylate cyclases, suggesting an unusual mechanism for regulating cGMP-sensitive CNG channels. It is unclear whether G protein directly or indirectly modulates guanylate cyclases. Notably, it has been suggested that a similar mechanism may also function in some marine species to regulate K^+ channels[34,35]; however, the molecular and genetic evidence supporting its presence in organisms other than *C. elegans* has been lacking.

Chemotaxis to some odorants and thermosensation in AFD neurons in *C. elegans* also require membrane-associated guanylate cyclases[26–28], but it is not known whether PDEs are involved in these processes. Thus, it is unclear whether chemosensation and thermosensation signal through guanylate cyclases or PDEs in *C. elegans*[4], as guanylate cyclases might have a passive role by supplying substrates to PDEs for cleavage, just as they do in vertebrate phototransduction. In fact, knockout mice lacking either membrane-associated guanylate cyclases or PDE are blind[1], indicating that a requirement at the genetic level does not provide adequate information to assess the role of these genes in the transduction pathway. Thus, the transduction mechanisms underlying chemosensation and thermosensation in *C. elegans* remain to be determined.

Worm photoreceptor cells do not seem to utilize opsins, but instead require LITE-1, a taste receptor–like protein, for phototransduction. LITE-1 acts upstream of G proteins and ectopic expression of LITE-1 in photo-insensitive cells can endow them with photosensitivity. These data suggest that LITE-1 may be part of the photoreceptor in worm photoreceptor cells. Unlike light-gated ion channels, such as ChR2, LITE-1 most likely functions as a receptor protein that requires downstream signaling events (for example, G protein signaling) to transduce light signals. Despite this view, we do not exclude the possibility that LITE-1 might possess a very small ion channel activity that is beyond the sensitivity of our detection method; however, such activity, if any, does not have a noticeable contribution to the photocurrent in ASJ. As LITE-1 shows no strong homology to known GPCRs and may adopt a reversed membrane topology[36], our results suggest the intriguing possibility that LITE-1 may represent a previously unknown type of GPCR. Nevertheless, it remains possible that LITE-1 may be indirectly coupled to G protein signaling.

LITE-1 may function on its own or form a complex with other proteins, similar to many membrane receptors. The observation that ROS-induced dark currents in ASJ did not depend on LITE-1 argues against a role for a light irradiation–induced byproduct in LITE-1 activation. However, it should be noted that such a possibility cannot be completely ruled out and a definitive role for LITE-1 as a photoreceptor requires biochemical validation.

LITE-1 is a member of the invertebrate taste receptor family that was first identified in *Drosophila*. Currently, it is not known how *Drosophila* taste receptors function *in vivo* and these receptors have not been functionally expressed in heterologous systems. Whole-cell recording of taste neurons in *Drosophila* has not been reported, which makes it challenging to directly interrogate the transduction mechanisms *in vivo*. Notwithstanding these technical challenges, genetic and behavioral studies have implicated G protein signaling in *Drosophila* taste transduction[37–39]. However, this view has recently been questioned. As taste receptors are related to odorant receptors in insects, it has been suggested that these taste receptors may function as ion channels and that G protein signaling may not be directly involved in the transduction pathway in taste neurons[40]. Nonetheless, more recent work has found that insect taste receptors and olfactory receptors have evolved along distinct paths during evolution and may employ distinct mechanisms for ligand recognition and signal transduction[41]. In light of this notion and the fact that LITE-1 and insect taste receptors belong to the same gene family, our results support the view that some *Drosophila* taste receptors may recruit G protein signaling in the transduction pathway.

LITE-1 is probably not the only member in the invertebrate taste receptor family that has a role in phototransduction. Ectopic expression of GUR-3, another *C. elegans* member of this family, can also confer photosensitivity to photo-insensitive cells (A.W. and X.Z.S.X., unpublished observations). Over sixty taste receptor genes have been identified in *Drosophila*[42–44]. Clearly, many of them function as taste receptors and are required for taste transduction[42–44]. Notably, some *Drosophila* taste receptor genes are expressed in many non–chemosensory neurons, suggesting that these receptors may adopt a distinct function in these neurons[45]. It will be interesting to determine whether some of them have a role in photo-sensation.

METHODS

Methods and any associated references are available in the online version of the paper at http://www.nature.com/natureneuroscience/.

Note: Supplementary information is available on the Nature Neuroscience website.

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AUTHOR CONTRIBUTIONS

J.L. performed most of the electrophysiological recordings and analyzed the data. A.W. carried out most of the molecular biology, genetic and behavioral experiments and analyzed the data. J.G. and Z.X. performed some of the molecular biology, genetic and behavioral experiments. Y.D. and L.K. carried out some of the recordings. N.N., H.I. and I.M. isolated *pde* mutants. A.W. and D.M. isolated *lite-1* mutants. A.W., Y.Y. and T.X. mapped *lite-1* mutants. X.Z.S.X. supervised the project and wrote the paper with help from all of the other authors.

COMPETING FINANCIAL INTERESTS

The authors declare no competing financial interests.

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ONLINE METHODS

Behavioral analysis. Phototaxis behavior was analyzed exactly as described previously[7]. Briefly, day 1 adult worms were tested for head avoidance response to UV-A light on NGM plates freshly seeded with a thin layer of OP50 bacteria. Each worm was tested five times and a percentage score was tabulated. Light pulses (350 ± 25 nm, 2 s, –1.43 log I/I_o) from an Arc lamp (EXFO) were delivered to the head of a worm that was slowly moving forward through a 10× objective under a fluorescence dissection stereoscope (Zeiss Discovery). To do so, we manually moved the testing plate such that only the head and a small portion of the anterior worm body appeared in the view field. Ultraviolet light is most efficient for triggering phototaxis responses[7]. Background light was filtered into red. I_o was set as 20 mW mm^{-2} in all cases. Light intensity was measured with a radiometric ultraviolet-specific sensor head (268S, UDT Instruments) coupled to an optometer (S471, UDT Instruments). A positive response was scored if the animal stopped forward movement within 3 s of the cessation of light illumination and initiated backward movement that lasted at least half a head swing. Under the no-light condition, we typically observed a basal level of response (10–20%) in most genotypes, which apparently resulted from spontaneous reversals. The whole event was recorded by a digital camera (Cohu 7800) at 16 Hz. A laboratory-developed software package was used to control the light source and the camera and for image processing[6,48].

Electrophysiology. Photocurrents were recorded in most cases by perforated whole-cell patch clamp, a configuration that does not allow for dialysis of chemicals (with the exception of monovalent ions) into the recorded cell through the recording pipette. All other types of currents were recorded by classic whole-cell recording protocols that permit perfusion of chemicals into the patched cell through the recording pipette. Recordings were performed on an upright Olympus microscope (BX51WI) with an EPC-10 amplifier (HEKA), a micromanipulator (Sutter) and the Patchmaster (HEKA) software as previously described[7]. Worms were glued on the surface of a sylgard-coated cover glass. A small piece of cuticle in the worm head was cut open and pinned down to the cover glass to expose the neurons of interest for recording. Background light was filtered into red. Light flashes were delivered to neurons from an Arc lamp (EXFO) controlled by a mechanical shutter (Sutter) triggered by the amplifier. The bath solution consisted of 145 mM NaCl, 5 mM KCl, 1 mM $CaCl_2$, 5 mM $MgCl_2$, 11 mM dextrose and 5 mM HEPES (330 mOsm, pH adjusted to 7.3). The pipette solution consisted of 115 mM potassium gluconate, 15 mM KCl, 5 mM $MgCl_2$, 10 mM HEPES, 0.25 mM $CaCl_2$, 20 mM sucrose, 5 mM EGTA and 50 μg ml^{-1} nystatin (315 mOsm, pH adjusted to 7.2). Neurons were identified for recording by a mCherry fluorescence marker expressed as a transgene[7]. During classic whole-cell recordings, we included 5 mM ATP and 0.25 mM GTP in the pipette solution. Recording pipettes (~10 MΩ) were pulled from borosilicate glass. Voltages were clamped at –70 mV. Series resistance and membrane capacitance were both compensated during recording.

Genetics and molecular biology. *lite-1* mutants (*xu7*, *xu8* and *xu10*) were isolated in an F1 clonal EMS mutagenesis screen for mutants defective in phototaxis behavior. Standard SNP mapping protocols were used to position *xu7* near the SNP marker uCE6-981 (−4.03 cM) on the X chromosome, which is very close to *lite-1*. The three alleles failed to complement each other and *ce314*. Molecular lesions in the *lite-1* gene in all three alleles were identified by sequencing PCR products amplified from genomic DNA. Mutants were extensively outcrossed (for example, six times for *xu7*) to N2 before behavioral and electrophysiological analysis.

Most *pde* deletion mutants were isolated by TMP/ultraviolet-based mutagenesis screens and were extensively outcrossed before behavioral and electrophysiological analysis. Some *pde* strains were directly obtained from knockout consortiums. Primers used in deletion screens and the deleted segments are listed below.

pde-1(nj57): CCA CCT GAA ATC GCA GAA CT (forward), TTC AAG GAT AAA TTT GCC GC (reverse), with a deletion in exon 5 and 6 causing a frame shift.

pde-2(tm3098): GTT CAA CCC GCA ACA ATG TAC (forward), GCT GAG TTT TCG AAC AAT CGG (reverse), with a deletion of part of exon 3 causing a frame shift.

pde-2(nj58): TCG TTG TCG TTG TCG TCT TC (forward), GAT AAT GAC GTG GCA ATG AGG (reverse), with a deletion of exon 1.

pde-3(nj59): CAC CAC AAT TGA CGG ACA AC (forward), ACT TCA CGG GAA ACA AAT GC (reverse), with a deletion in exon 3 and 4 causing a frame shift.

pde-4(nj60): GGG ATA TCA CGT GGC TTT GGA G (forward), CCT TGA CGC TAA CAC CGA ACA C (reverse), with a deletion of exon 4 (isoform a) causing a frame shift.

pde-5(nj49): CGG ATC TAT CAA TGA AGC GGA G (forward), CCA ATT GTG GTA GGC AAC TCG G (reverse), with a deletion spanning exon 4–9.

pde-6(ok3410): CAA CTT AAA GAT CTC GGC CAC C (forward), GCT GAC ACA ATC CCC ACT CTC (reverse), with a deletion in exon 8 encoding most of the catalytic domain.

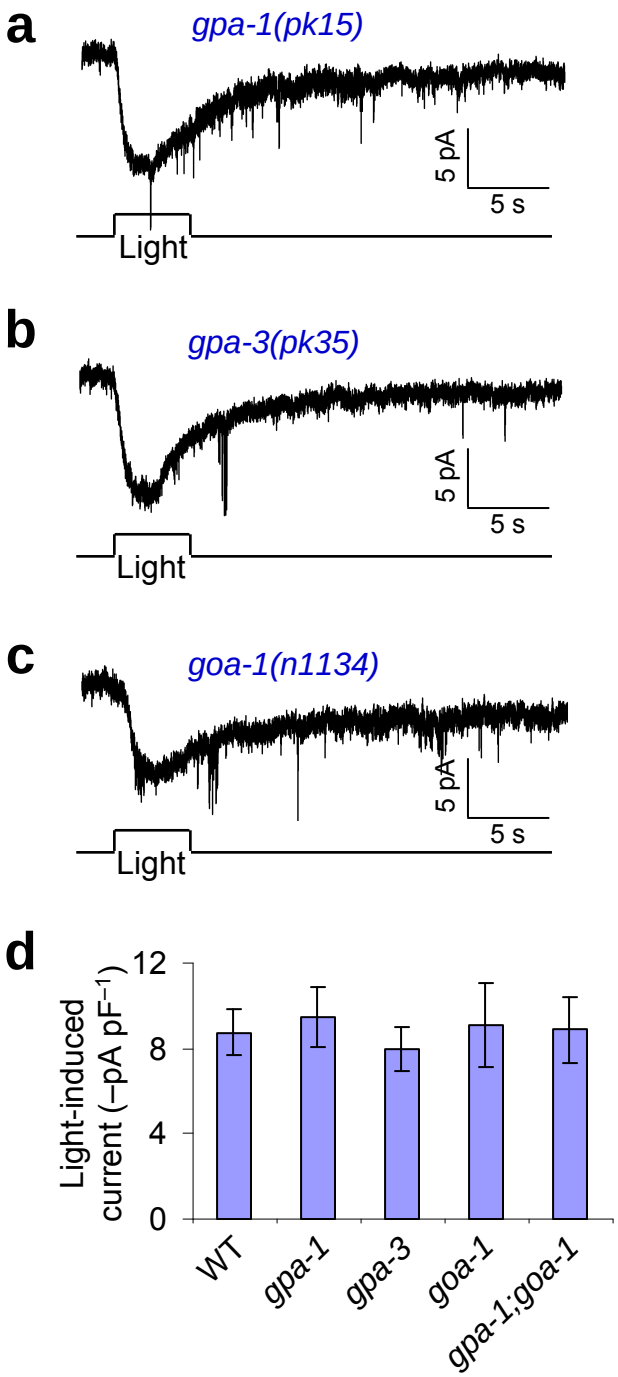
Standard protocols were used to generate transgenic lines. The *myo-3* promoter was used to express *lite-1* cDNA in muscle cells. The *trx-1* and *srg-8* promoters were used to express *lite-1* cDNA in the ASJ and ASK neurons, respectively, to rescue mutant phenotypes[49,50]. A fragment of the *tax-2* promoter (*tax-2*Δ) was also used to express *lite-1* cDNA in a subset of CNG neurons, including the photoreceptor cells ASJ, ASK and AWB, to rescue the behavioral phenotype of *lite-1* (ref. 12).

Statistical analysis. Statistical analysis was performed using KaleidaGraph (Synergy Software) or Statistica (StatSoft). *P* values were generated by ANOVA followed by a *post hoc* test. $P < 0.05$ was considered to be significant.

C. elegans phototransduction requires a G protein-mediated cGMP pathway and a taste receptor homolog

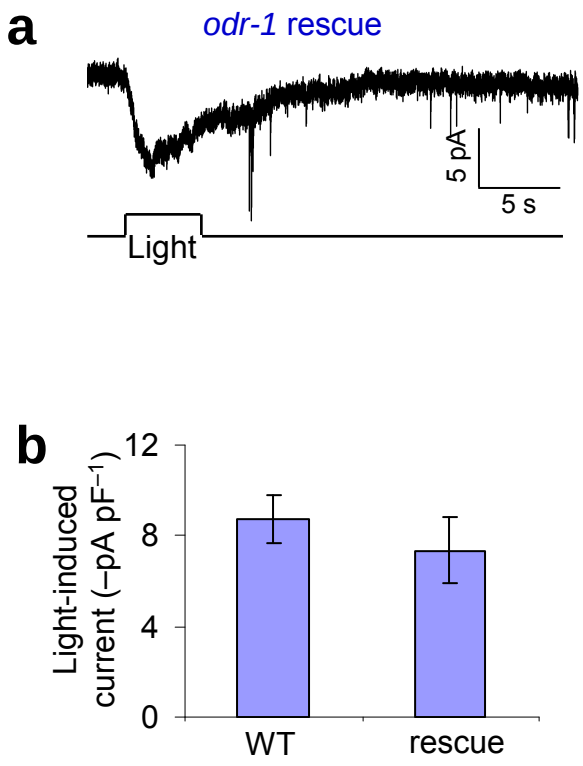
Jie Liu, Alex Ward, Jingwei Gao, Yongming Dong, Nana Nishio, Hitoshi Inada, Lijun Kang, Yong Yu, Di Ma, Tao Xu, Ikue Mori, Zhixiong Xie, and X. Z. Shawn Xu

Figure S1



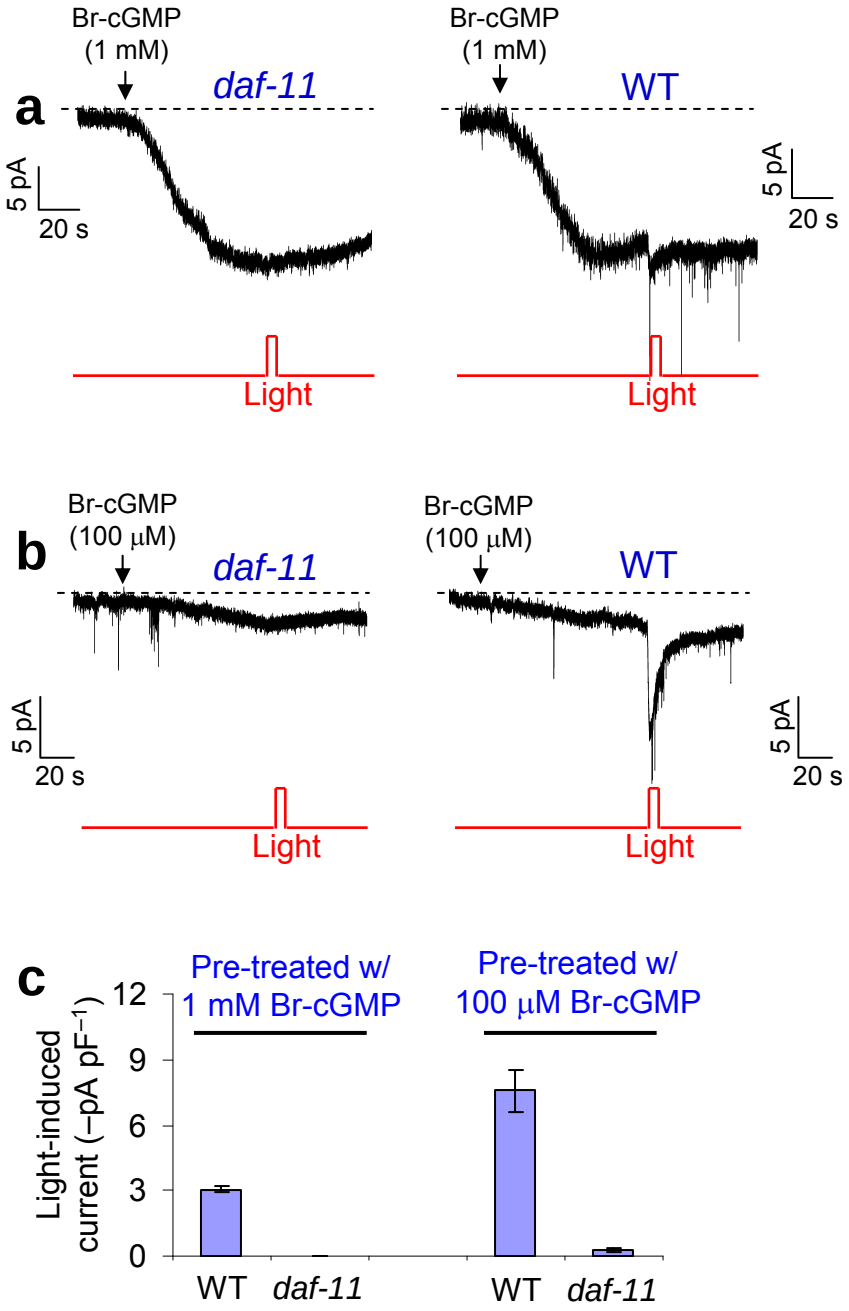
Supplementary figure 1. *gpa-1, gpa-3* and *goa-1* single mutants do not show a noticeable defect in phototransduction in ASJ. (a–c) Sample traces recorded from *gpa-1, gpa-3* and *goa-1* mutants. (d) Bar graph. $n \geq 5$. Error bars: SEM.

Figure S2



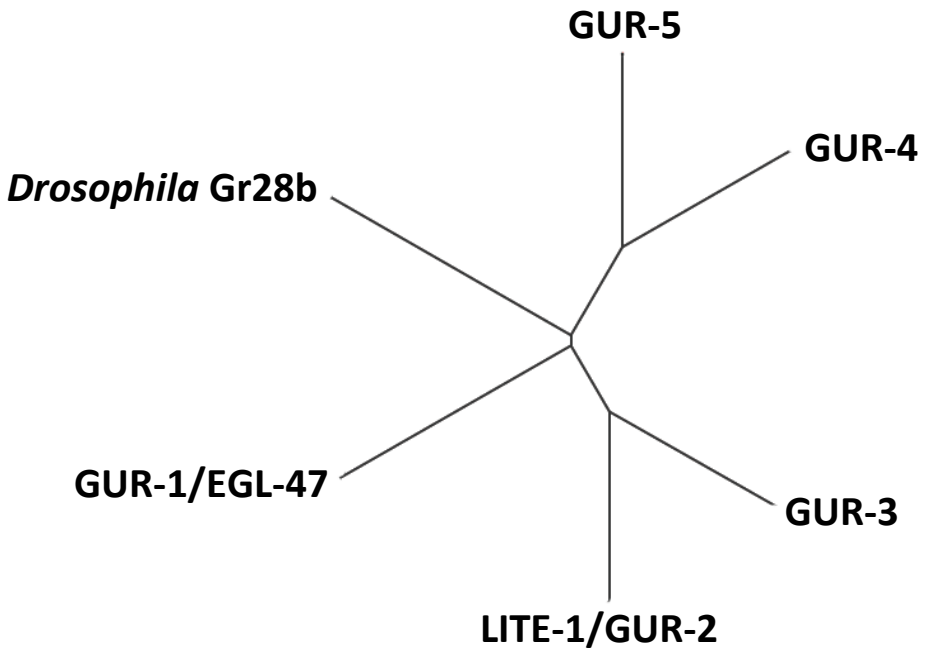
Supplementary figure 2. Rescue of *odr-1* phototransduction defect. As we only analyzed one *odr-1* allele (only one allele is available at CGC), we rescued the mutant phenotype. Expression of wild-type *odr-1* gene under its own promoter restored photocurrents in ASJ (n = 14). *odr-1* is expressed in a subset of photoreceptor cells, including ASJ, ASK and AWB (ref 26). Error bars: SEM.

Figure S3



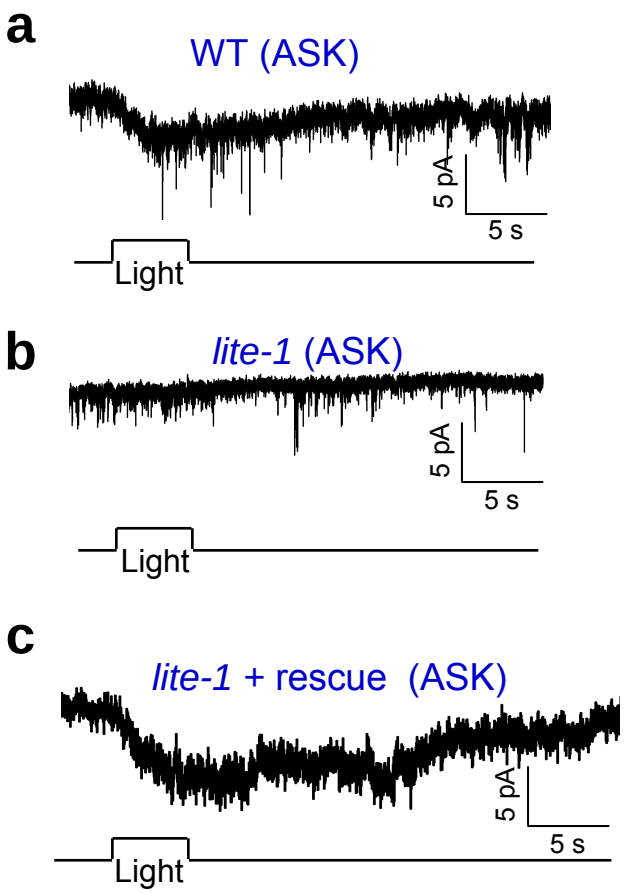
Supplementary figure 3. Supplement of cGMP does not restore photosensitivity in ASJ of *daf-11* mutant worms. ASJ was first perfused with the membrane-permeable Br-cGMP at non-saturating levels to evoke a small inward dark current with an amplitude of ~5 pA (100 μM Br-cGMP) shown in (b) and ~20 pA (1mM Br-cGMP) shown in (a). Complete activation of CNG channels by cGMP would lead to a dark current of ~40 pA (fig. 3c,d). Subsequently, ASJ was stimulated with light. While wild-type worms showed photocurrents in ASJ under both Br-cGMP conditions, *daf-11(m47)* mutant worms did not. This shows that cGMP does not simply play a permissive role in phototransduction, providing further support for its role as a second messenger for phototransduction.

Figure S4



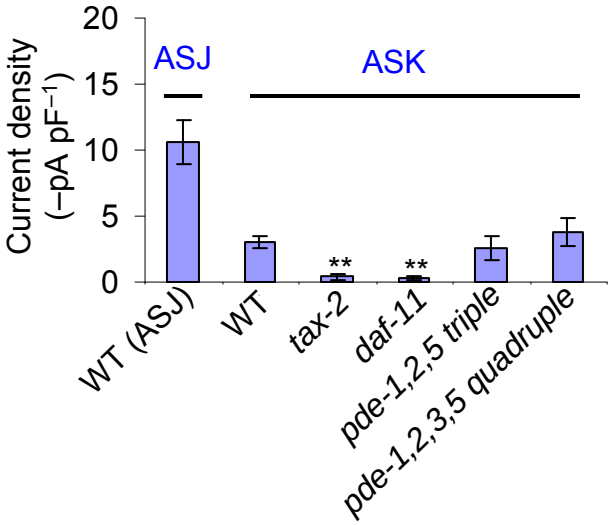
Supplementary figure 4. Dendrogram of *C. elegans* taste receptors. Five gustatory receptor (GUR) genes are encoded by the *C. elegans* genome (www.wormbase.org). The closely-related *Drosophila* gustatory receptor Gr28b is also included for analysis.

Figure S5



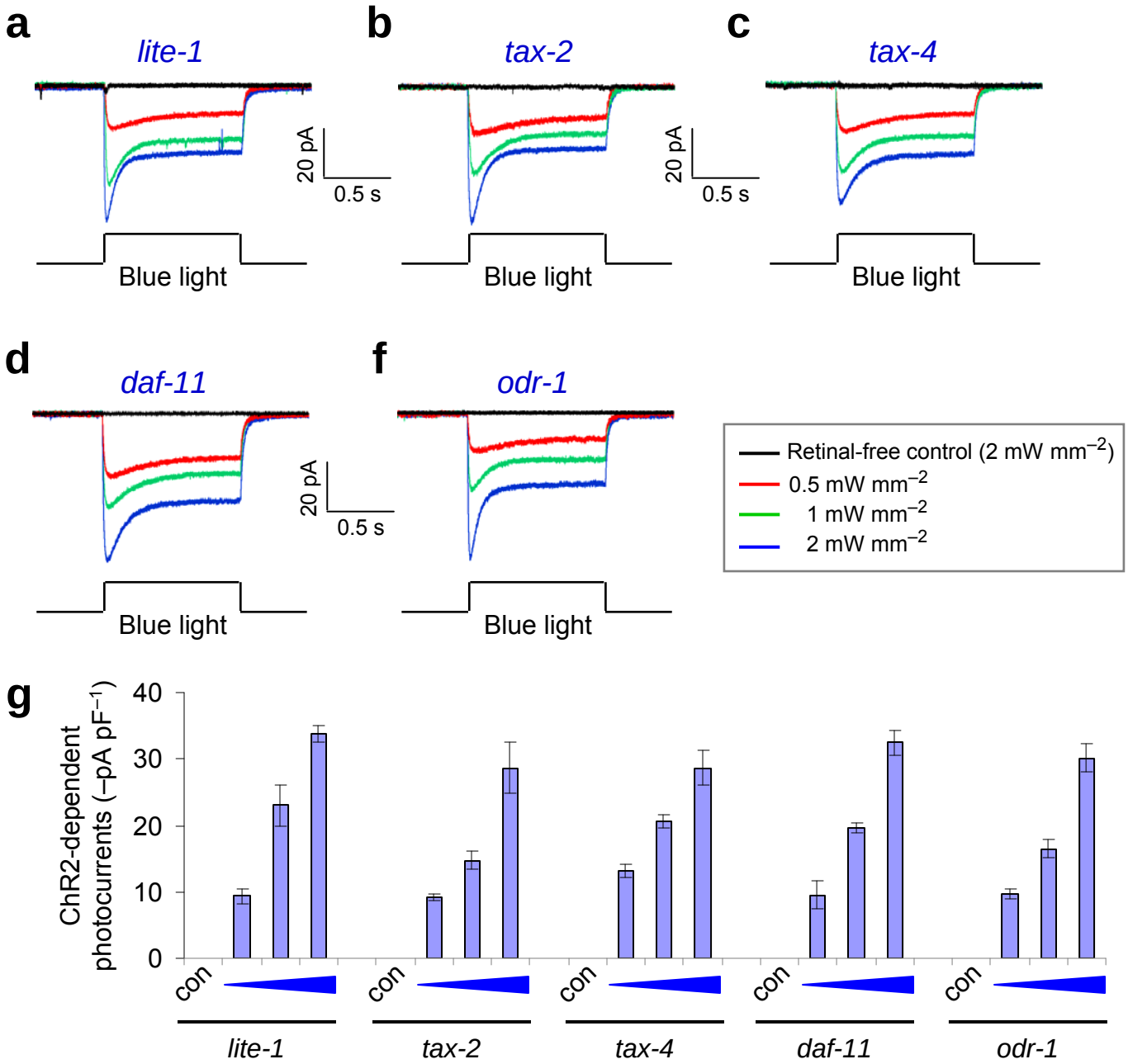
Supplementary figure 5. LITE-1 is also required for phototransduction in the photoreceptor cell ASK. Shown are sample ASK traces for figure 5f. (a) light-induced current in ASK of wild-type. (b) *lite-1(xu7)*. (c) *lite-1(xu7)* expressing a wild-type *lite-1* transgene under the control of the ASK-specific promoter *srg-8*.

Figure S6



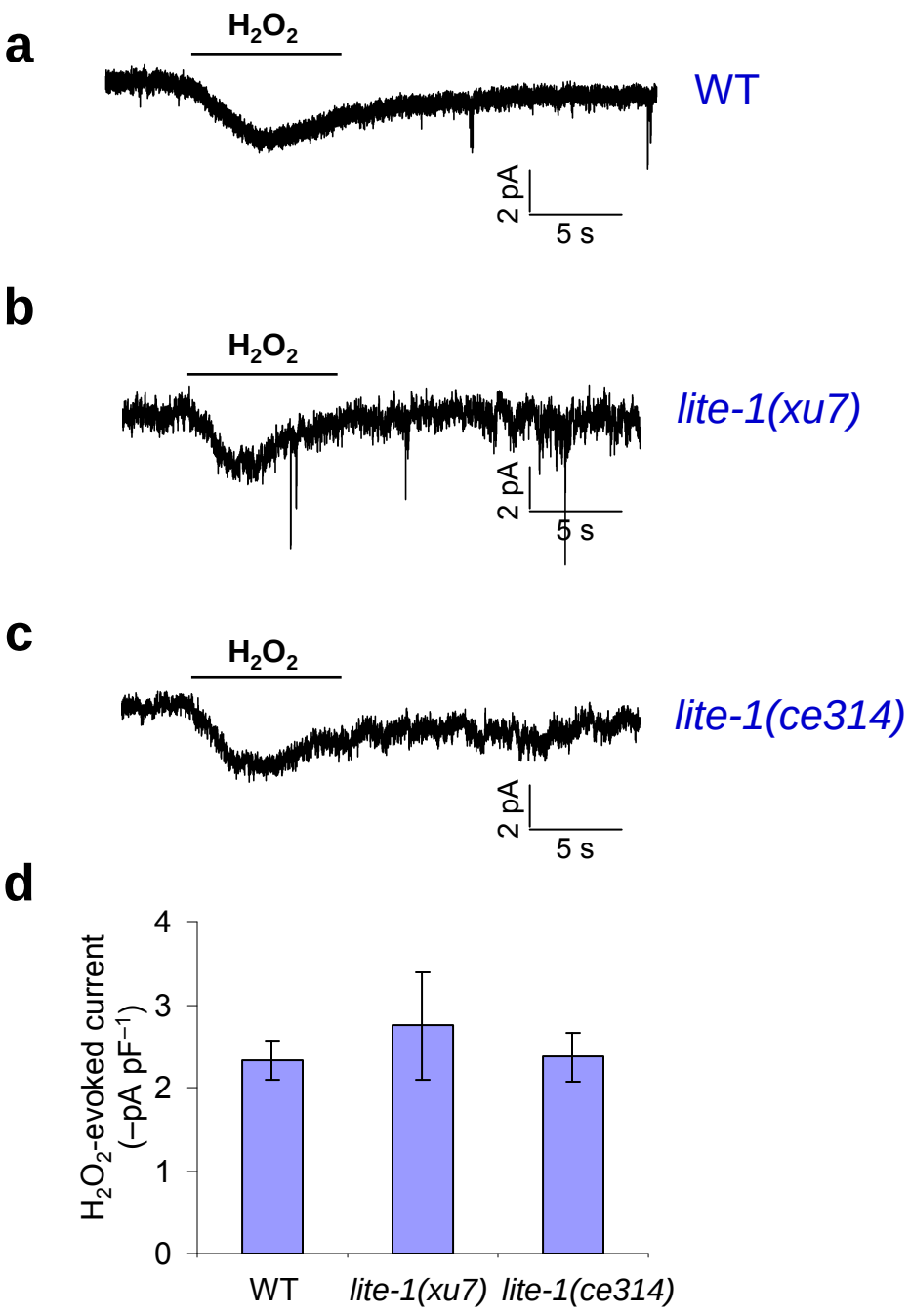
Supplementary figure 6. The photoreceptor cell ASK requires CNG channels and membrane-associated GCs but not PDEs for phototransduction. Though ASK exhibits a relatively smaller photocurrent than ASJ, it requires a similar set of genes for phototransduction. Mutations in the CNG channel TAX-2 and the membrane associated GC DAF-11 block the photoresponse in ASK. In contrast, the photocurrent density in the *pde* triple and quadruple mutants is similar to that in wild-type, suggesting that PDEs may not play a modulatory role in ASK. $^{**}P < 0.005$ (ANOVA with Dunnett test to ASK WT). $n \geq 5$. Error bars: SEM.

Figure S7



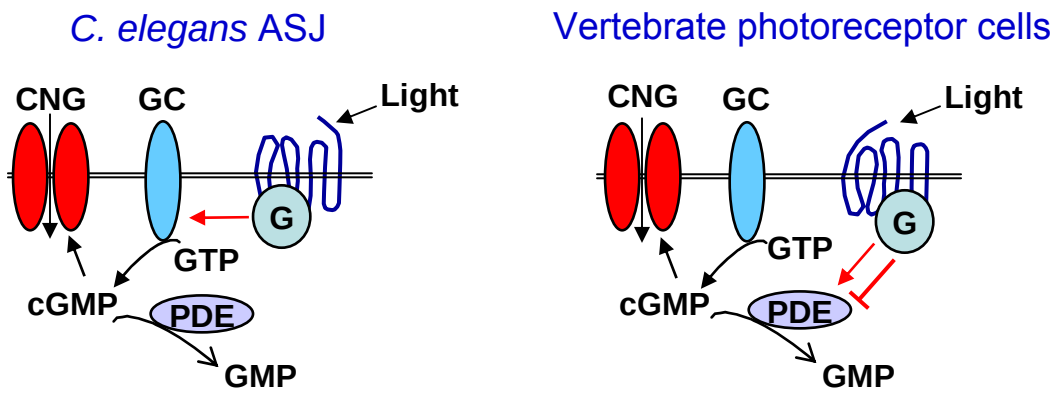
Supplementary figure 7. The light-gated channel channelrhodopsin-2 (ChR2) is functional in *lite-1, daf-11, odr-1, tax-2* and *tax-4* mutant worms. (a-f) sample traces. (g) bar graph. Three different intensities (0.5, 1, and 2 mW mm^{-2}) of blue light were used to stimulate ChR2 expressed as a transgene specifically in ASJ under the *trx-1* promoter. Photocurrents developed virtually instantaneously without detectable latency, indicating that no second messenger is involved. The ChR2-dependent photocurrents also showed fast activation kinetics (activation time constant τ = 8.95 ± 0.03 ms under 2 mW mm^{-2}). This is consistent with the fact that ChR2 is directly gated by light. These features are in sharp contrast to those of the intrinsic photocurrents in ASJ that depend on *lite-1*, GCs and CNG channels, which show a very long latency and slow activation kinetics 356 ± 37 ms in ref[7]; activation time constant τ = 566 ± 2.6 ms). Long latency and slow kinetics of the intrinsic photocurrents in ASJ are consistent with the requirement of the second messenger cGMP.

Figure S8



Supplementary figure 8. Reactive oxygen species (ROS) evoke an inward current in ASJ independently of LITE-1. Perfusion of 1 mM hydrogen peroxide (H_2O_2) towards ASJ evoked an inward current in wild-type worms (a), but this current persisted in *lite-1* mutant worms (b–d). These data do not support the possibility that the trace amount of ROS induced by photo-oxidation, if any, fully accounts for the activation of LITE-1. $n \geq 5$. Error bars: SEM.

Figure S9



Supplementary figure 9. A model for *C. elegans* phototransduction cascade in the photoreceptor cell ASJ. The phototransduction cascade in vertebrate photoreceptor cells is shown for comparison. In vertebrate photoreceptor cells, G-proteins may stimulate PDE (rods and cones) or inhibit PDE (parietal eye photoreceptor cells), leading to down- or up-regulation of cGMP followed by closure or opening of CNG channels, respectively. In the *C. elegans* ASJ neuron, G-proteins (GOA-1 and GPA-3) may be coupled to the guanylate cylcases (GC) DAF-11/ODR-1, leading to up-regulation of cGMP and opening of the CNG channel TAX-2/TAX-4. Note that other *C. elegans* photoreceptor cells may employ different sets of signaling genes or even adopt different transduction mechanisms.