NEUROSCIENCE

Eyeless worms detect color

Roundworms discriminate color of toxic food despite a lack of eyes and opsin photoreceptor genes

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Animals use color vision to explore their environment, recognize mates, avoid predators, and guide feeding decisions. Color vision across the tree of life relies on specialized retinal photoreceptor cells and light-sensitive opsins with different spectral sensitivities. *Caenorhabditis elegans* are eyeless roundworms that dwell in rotting vegetation and compost heaps, feeding on a rich diversity of microbes (*1*). In its natural environment, *C. elegans* must traverse a complex microbial terrain while determining which food is safe for consumption. Some bacteria produce colorful toxins (*2*), making color discrimination a potentially life-or-death decision for the worm. On page 1059 of this issue, Ghosh *et al.* (*3*) demonstrate that *C. elegans*, despite lacking eyes and opsin genes, can discriminate between colors to guide foraging decisions. They identify two conserved stress-response genes that are required for color discrimination, revealing a new biology of color vision.

An estimated 80% of the bacteria naturally found in the *C. elegans* environment are beneficial to the organism, but the worm can encounter potentially harmful microorganisms while foraging for food (*1*). Pyocyanin, a blue-pigmented toxin secreted by the bacterium *Pseudomonas aeruginosa*, is known to generate tissue-damaging reactive oxygen species. This pigment is a major cause of pathogenicity because mutant *P. aeruginosa* that do not produce pyocyanin are less pathogenic to humans (*2*). When *C. elegans* encounters this colorful and toxic microbe, how does it recognize and avoid it?

Previous work demonstrated that *C. elegans* is sensitive to visible and ultraviolet light. *lite-1* (high-energy light unresponsive protein 1) and *gur-3* (gustatory receptor family protein 3) were identified as two components of a non-opsin phototransduction pathway that contributes to light-avoidance behavior (*4*–*7*). Ghosh *et al.* demonstrated that avoidance of toxic blue *P. aeruginosa* bacterial lawns by *C. elegans* on a Petri dish is enhanced in the presence of white light and requires the *lite-1*–*gur-3* pathway. Adding pyocyanin to a culture of beneficial bacteria triggered repulsion by *C. elegans* in white light, yet solely illuminating beneficial bacteria with blue light in the absence of pyocyanin did not. The authors triggered avoidance of beneficial bacteria by adding a colorless chemical that produces reactive oxygen species and illuminating the environment with precise blue-amber wavelengths to mimic the color of pyocyanin. Moreover, this blue-amber light enhanced avoidance of nonpathogenic bacteria scented with an odor that worms find repellent. Therefore, pathogen avoidance is a multisensory experience that relies on both visual and chemical cues.

Ghosh *et al.* uncovered pronounced behavioral variation under blue or amber illumination in 59 wild strains of *C. elegans*. Some strains avoided pathogens only in blue light, and others were sensitive only to amber light. Several strains avoided these colors even without a repellent odor—a compelling demonstration that *C. elegans* detects and discriminates colors. The authors identified two genes that together strongly influenced color-dependent foraging, *jkk-1* (dual specificity mitogen-activated protein kinase kinase) and *lec-3* (32-kDa β-galactoside-binding lectin). Both are conserved in mammals and function as a kinase activator and a sugar-binding protein, respectively, but how they contribute to color discrimination is unknown.

"...bacteria produce colorful toxins, making color discrimination a... life-or-death decision..."

The work of Ghosh *et al.* suggests that *C. elegans* integrate multiple chemosensory and visual inputs to create a "view" of their environment, allowing them to identify toxic bacteria by both their spectral and chemical properties. *P. aeruginosa* advertises its presence not only with pyocyanin, the bifunctional toxin that induces the generation of reactive oxygen species and is blue, but also with a characteristic smell. It was previously shown that *C. elegans* can learn to avoid *P. aeruginosa* by pairing this bacterial odor with the aversive memories associated with encountering the pathogen (*8*, *9*). It is possible that all three types of sensory cues are integrated to trigger an avoidance response. Although high concentrations of pyocyanin are naturally toxic to *C. elegans* and are avoided in the absence of light, at lower pyocyanin concentrations, blue light illumination seemingly intensifies the behavioral response, providing sensory circuits in the worm with additional input to influence their movement away from the potentially toxic food source. Where in the *C. elegans* nervous system these disparate sensory cues are integrated remains an important topic for future investigation (*10*).

The discovery that *C. elegans* can detect and discriminate different wavelengths of light raises many additional questions. How *jkk-1* and *lec-3* participate in color vision is unknown: These proteins might directly detect light or indirectly transduce a signal from unidentified non-opsin photoreceptors. It is possible that the *jkk-1*–*lec-3* pathway interacts with the previously described *lite-1*–*gur-3* pathway, or it may function independently. It is also unknown what cells are required for the detection of colorful toxins: Are there dedicated sensory structures, or is worm color vision distributed across many cells and tissues?

The work by Ghosh *et al.* additionally raises the question of what evolutionary path led to *C. elegans* color discrimination. The development of colorful toxins could enhance the survival of a bacterial species and may serve as a warning to potential predators. It would be highly advantageous for roundworms to discriminate pathogenic and nonpathogenic bacteria by color. Indeed, Ghosh *et al.* reported that color discrimination varies widely in natural populations, suggesting that genetic variation of pigmented toxins in the local microbial community may coevolve with noncanonical *C. elegans* color vision. How ambient light filtered through decomposing vegetation in the local microenvironment enables color discrimination by *C. elegans* would also be interesting to understand. This study will inspire the search for unconventional mechanisms of color vision in other eyeless invertebrates, as well as the evolution of the *jkk-1* and *lec-3* pathway as a mediator of color discrimination across species. ■

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