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Eyeless Worms Can Run Away from Dangerous Blues

Caenorhabditis elegans without conventional eyes are equipped with a color-detecting system that helps in avoiding blue pathogenic bacteria.

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The roundworm *Caenorhabditis elegans* is one of the most important model organisms for genetic research. Various environmental stimuli, including dietary cues and changes in ambient temperatures, affect the behavior and physiology of *C. elegans* (Goodman and Sengupta, 2019; Jeong et al., 2012). Interestingly, despite the lack of conventional eyes, *C. elegans* can perceive light via a signal transduction mechanism mediated by seven transmembrane receptors, including LITE-1 (high-energy LIghT unrEsponsive protein 1) (Gong et al., 2016; Iliff and Xu, 2020). Nevertheless, whether *C. elegans* can distinguish any color in the visible light, which was almost an unimaginable possibility, remained unknown.

Surprisingly, a recent study has reported that *C. elegans* can discriminate colors (Ghosh et al., 2021). They first tested whether *C. elegans* avoided harmful bacteria by detecting colored microbial pigments. *Pseudomonas aeruginosa*, a gram-negative opportunistic pathogenic bacterium in humans, is a popular model pathogen used for studying immunity and behavior of *C. elegans* (Park et al., 2017). *P. aeruginosa* secretes pyocyanin, a blue toxin that generates reactive oxygen species (ROS) (Mahajan-Miklos et al., 1999). *C. elegans* feeds on microbes enriched with potential pathogens in nature (Meisel and Kim, 2014; Schulenburg and Félix, 2017) and utilizes multiple sensory systems to avoid harmful bacteria (Meisel and Kim, 2014; Liu and Sun, 2021). Interestingly, Ghosh et al. (2021) demonstrated that *C. elegans* avoided *P. aeruginosa* better under white light than in the dark (Fig. 1). When exposed to a mutant *P. aeruginosa* strain that cannot synthesize pyocyanin, white light did not affect the avoidance behavior of *C. elegans*. In addition, *C. elegans* exhibited an increased avoidance to paraquat, a colorless ROS-generating toxin, only with blue dye or blue light, but did not avoid either paraquat or blue dye alone under white light. These data indicate that *C. elegans* avoids pyocyanin by perceiving both ROS and the blue color of the toxin (Fig. 1).

Can *C. elegans* discriminate among different colors to better avoid other adverse stimuli? The authors exposed *C. elegans* to the odor of 1-octanol, an aversive odorant, under different color combinations of blue-to-amber light. They found that colors ranging from blue to amber differentially affected its avoidance to 1-octanol, whereas exposure to pure blue or amber light had no effect on its avoidance to 1-octanol. Thus, *C. elegans* discriminates different colors of light to avoid aversive stimuli better.

Wild *C. elegans* lives in diverse natural habitats, including rotten fruits and soil, and encounters toxic microbes with various colors (Schulenburg and Félix, 2017). Thus, the authors tested whether *C. elegans* strains from various environmental niches responded differently to color combinations during foraging. Interestingly, several *C. elegans* strains displayed

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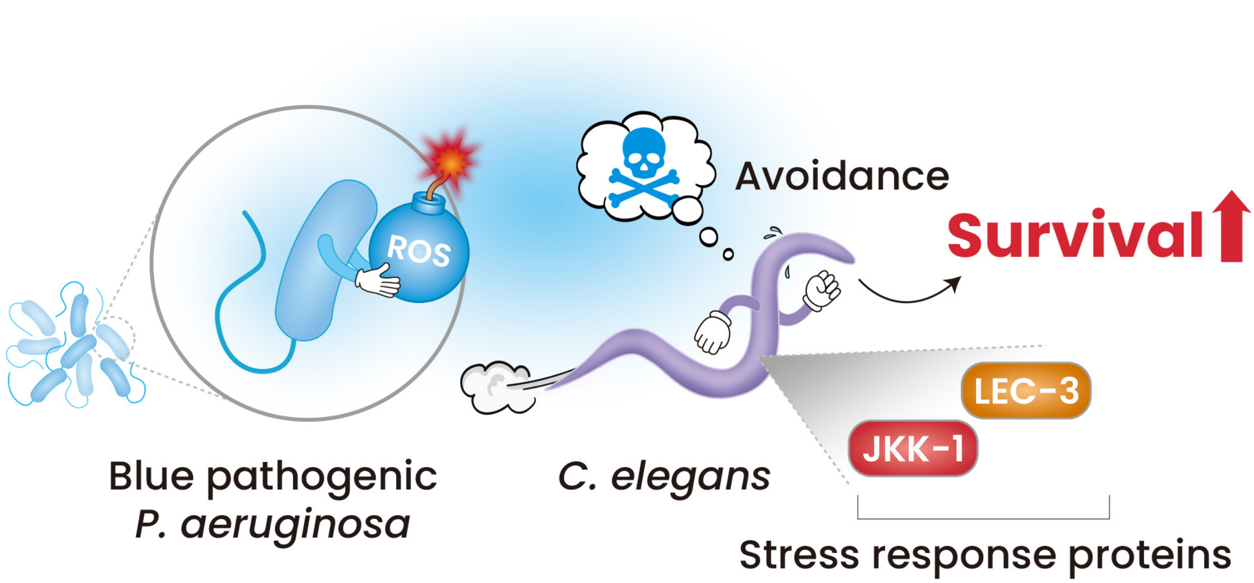

Fig. 1. *C. elegans* avoids toxic bacteria better by detecting blue color. *P. aeruginosa*, a pathogenic bacterium, synthesizes pyocyanin, a blue toxin that generates reactive oxygen species (ROS). *C. elegans* avoids blue color with ROS. JKK-1 (c-Jun N-terminal kinase kinase 1) and LEC-3 (galectin-3), which are cellular stress response proteins, mediate the blue color-dependent avoidance of wild-type *C. elegans*. This color detection system of *C. elegans* may help avoid pathogens and enhance its survival in nature.

avoidance to colored light even without aversive stimuli. These results suggest that spectral sensitivity varies among wild *C. elegans* strains that live in different natural habitats.

To identify genetic factors responsible for variations in the color-dependent avoidance behaviors of *C. elegans*, the authors analyzed the genomes of 59 wild *C. elegans* strains. They found that single nucleotide variations in two cellular stress response genes of *C. elegans*, *jkk-1* (*c-Jun N-terminal kinase kinase 1*) and *lec-3* (*galectin 3*), were highly variable among the strains. The authors then showed that the genetic inhibition of *jkk-1* or *lec-3* in laboratory wild-type strains suppressed their color-dependent avoidance to 1-octanol. Overall, these results indicate that JKK-1 and LEC-3 are the key factors responsible for the color-dependent avoidance response of *C. elegans* (Fig. 1).

In summary, the authors showed that *C. elegans*, which do not have conventional eyes or color-detecting opsin receptors, can discriminate colors, and this trait is crucial for avoiding potentially harmful stimuli. They demonstrated that *C. elegans* that lives in various natural environments responds differently to colors and harmful odorants. This is the first report showing that *C. elegans* can distinguish among different colors of light by utilizing a newly discovered color-detecting system.

This ground-breaking work conducted by Ghosh et al. (2021) raises exciting possibilities regarding the evolution of color perception. *C. elegans* have been known to avoid ultraviolet light, and this study demonstrated that *C. elegans* avoids toxic bacteria via color perception. Many new questions arise from this study, as is the case for almost all the important discoveries. The color-detecting system in *C. elegans* may have evolutionarily emerged to avoid harmful stimuli for survival. If so, do *C. elegans* strains from different environmental niches avoid certain colors to enhance their survival in their own habitats? Do colors help *C. elegans* detect beneficial food sources as well? How do JKK-1 and LEC-3, which potentially play roles in cellular stress responses, mediate the color perception of *C. elegans*? In which neural circuits and molecular signaling pathways do JKK-1 and LEC-3 act? Do color-perceiving systems exist in other eyeless species, including mammals? Some mammals probably retain ancient color-detecting systems that may be utilized when their conventional visions are compromised. Addressing all these questions will help understand and devise novel biological systems that perceive colors without "seeing" them.

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AUTHOR CONTRIBUTIONS
G.Y.L. and S.J.V.L. wrote the paper.

CONFLICT OF INTEREST
The authors have no potential conflicts of interest to disclose.

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REFERENCES

Ghosh, D.D., Lee, D., Jin, X., Horvitz, H.R., and Nitabach, M.N. (2021). *C. elegans* discriminates colors to guide foraging. Science *371*, 1059-1063.

Gong, J., Yuan, Y., Ward, A., Kang, L., Zhang, B., Wu, Z., Peng, J., Feng, Z., Liu, J., and Xu, X.Z.S. (2016). The *C. elegans* taste receptor homolog LITE-1 is a photoreceptor. Cell *167*, 1252-1263.e10.

Goodman, M.B. and Sengupta, P. (2019). How *Caenorhabditis elegans* senses mechanical stress, temperature, and other physical stimuli. Genetics *212*, 25-51.

Iliff, A.J. and Xu, X.Z.S. (2020). *C. elegans*: a sensible model for sensory biology. J. Neurogenet. *34*, 347-350.

Jeong, D.E., Artan, M., Seo, K., and Lee, S.J. (2012). Regulation of lifespan by chemosensory and thermosensory systems: findings in invertebrates and their implications in mammalian aging. Front. Genet. *3*, 218.

Liu, Y. and Sun, J. (2021). Detection of pathogens and regulation of immunity by the *Caenorhabditis elegans* nervous system. mBio *12*, e02301-20.

Mahajan-Miklos, S., Tan, M.W., Rahme, L.G., and Ausubel, F.M. (1999). Molecular mechanisms of bacterial virulence elucidated using a *Pseudomonas aeruginosa-Caenorhabditis elegans* pathogenesis model. Cell *96*, 47-56.

Meisel, J.D. and Kim, D.H. (2014). Behavioral avoidance of pathogenic bacteria by *Caenorhabditis elegans*. Trends Immunol. *35*, 465-470.

Park, H.H., Jung, Y., and Lee, S.V. (2017). Survival assays using *Caenorhabditis elegans*. Mol. Cells *40*, 90-99.

Schulenburg, H. and Félix, M.A. (2017). The natural biotic environment of *Caenorhabditis elegans*. Genetics *206*, 55-86.