Scientists discover a mechanism for memory transfer between individuals in C. elegans

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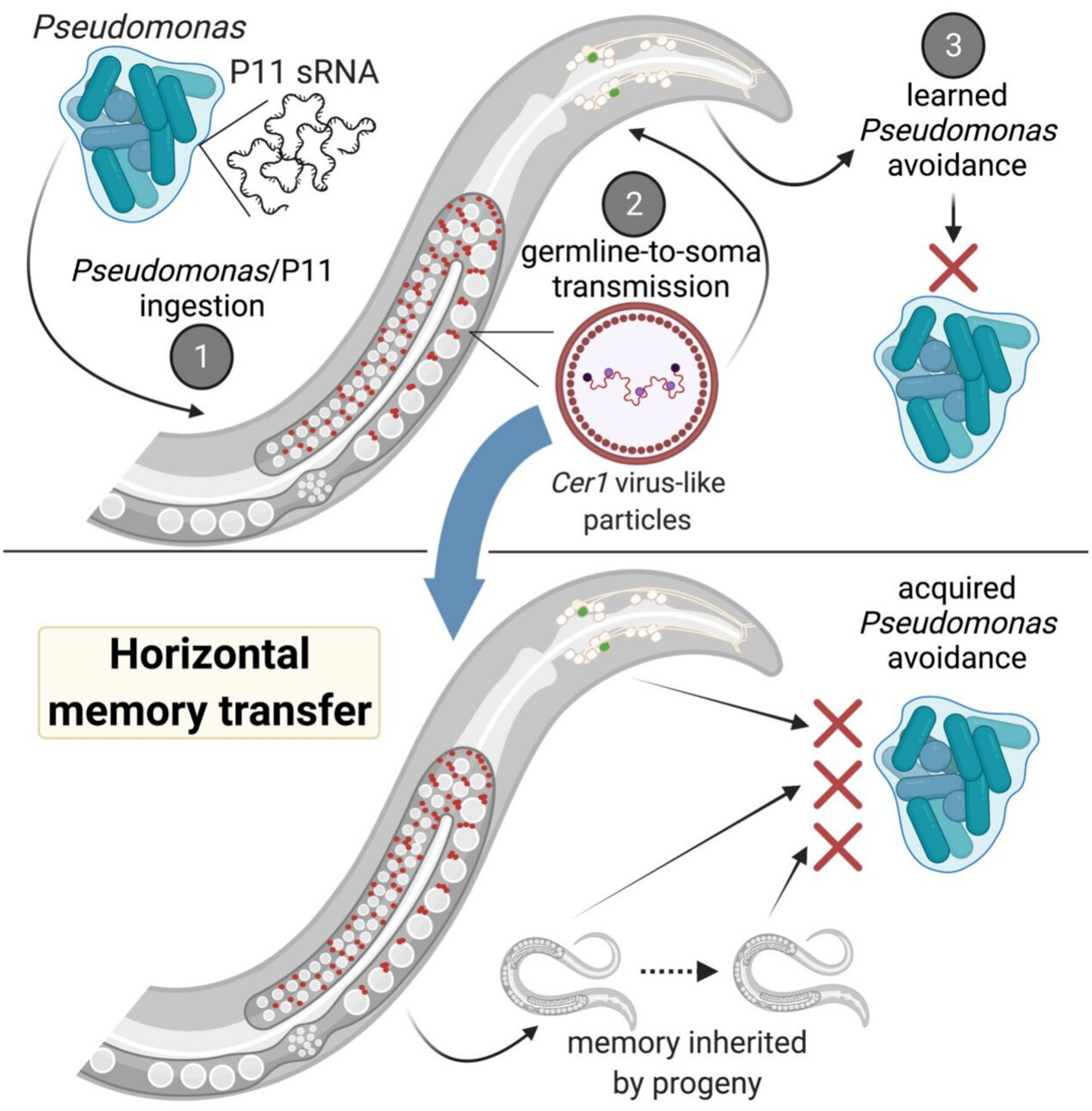

Researchers in Coleen Murphy’s lab at Princeton University found that mother worms who encounter pathogenic Pseudomonas aeruginosa in their environment learn to avoid the bacterium via a mechanism involving the retrotransposon Cer1. Cer1 is also needed for inheritance of avoidance behavior by the worms’ offspring, and its release into the environment can transfer avoidance behavior to naïve worms. Image courtesy of Murphy lab. Credit: Murphy lab

When an organism encounters a threat in its environment, it is to the species' advantage to warn others of the peril. The microscopic roundworm *C. elegans* regularly encounters dangers in its environment such as the pathogenic bacterium *P. aeruginosa*, which seems like an appealing food source but can sicken worms if eaten. *C. elegans* isn't equipped to shout out warnings as a human would, but new work by researchers from Princeton researcher Coleen Murphy's laboratory shows that worms who encounter *P. aeruginosa* can help others avoid the danger, and identifies a crucial part of the mechanism by which this is done.

In earlier work, Murphy's lab discovered that mother worms who are sickened by *P. aeruginosa* learn to avoid the bacterium, and that they can impress this avoidance behavior upon their offspring for the next four generations. Mother worms who've eaten *P. aeruginosa* absorb a bacterial small RNA called P11 through their intestines, which touches off a signal in the worm's germ line reproductive cells that is then transmitted to a neuron that controls behavior. Afterwards, the new behavior is conveyed to future progeny via changes made to germ line cells. In their new paper, co-first authors Rebecca Moore, Rachel Kaletsky, and Chen Lesnik, and colleagues show that avoidance behavior can also be conveyed from trained worms to other, naïve adult worms.

"We found that one worm can learn to avoid this pathogenic bacterium and if we grind up that worm, or even just use the media the worms are swimming in, and give that media or the crushed-worm lysate to naive worms, those worms now 'learn' to avoid the pathogen as well," explains Murphy.

This finding suggests that worms secrete some signal that, when picked up by other worms, can modify their behavior. Interestingly, the progeny of worms "educated" by receipt of this signal also avoid pathogenic *P. aeruginosa* for the following four generations. This suggests that the secreted signal touches off the same learning pathway in recipient worms as in those directly exposed to the pathogen. Murphy's group sought to identify the secreted signal.

"What we discovered is that a retrotransposon called Cer1 that forms viral-like particles seems to carry a memory not only between tissues (from the worm's germline to its neurons) but also between individuals," says Murphy.

A retrotransposon is a genetic element, similar to a virus, that has inserted itself into a host animal's DNA. The researchers found that Cer1 is present in the DNA of the worms' germ line cells, and that mother worms in whom the retrotransposon was knocked down by RNA interference could not learn avoidance of *P. aeruginosa* via exposure to P11, convey avoidance behavior to offspring, or educate nearby worms. In addition, adult recipient worms needed *Cer1* to be present in their genome in order to learn to avoid the pathogen. The authors found that two wild worm strains that naturally lack *Cer1* are incapable of doing these things, suggesting that in these strains, Cer1 is needed to establish, transmit and receive this avoidance behavior.

"We think that *Cer1* may give worms an advantage in their battle with pathogens, even though acquiring *Cer1* in its genome can be deleterious for the worm under non-pathogenic conditions," says Murphy.

"The findings by Murphy et al. are provocative," says Craig Mello, a professor of molecular medicine at the University of Massachusetts and co-discoverer of RNA interference. "This is another intriguing episode in a growing number of studies that have implicated systemic RNA signals in influencing behavior transgenerationally, and if this study is correct, now even horizontally."

Although other studies have shown that animals such as the sea slug Aplysia are capable of transferring memories between individuals, the work by Moore, Kaletsky, Lesnik and colleagues is the first to suggest a mechanism by which such transfer can occur in nature. However, this study also raises a number of urgent questions. For example, as Mello points out, it's now well established that worms use RNA signals to pass information to offspring, but it is currently unclear what Cer1 contributes to this pathway.

"Why would the animal need the virus to pass signals to offspring?" Mello asks. "What exactly is being transferred?"

To demonstrate an evolved relationship between the worms and the Cer1 retro-element, says Mello, it will be important to fill in these gaps in understanding. This is precisely what Murphy's group is now working to do.

More information: Rebecca S. Moore et al, The role of the Cer1 transposon in horizontal transfer of transgenerational memory, *Cell* (2021). DOI: 10.1016/j.cell.2021.07.022

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