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How behavior can transcend generations

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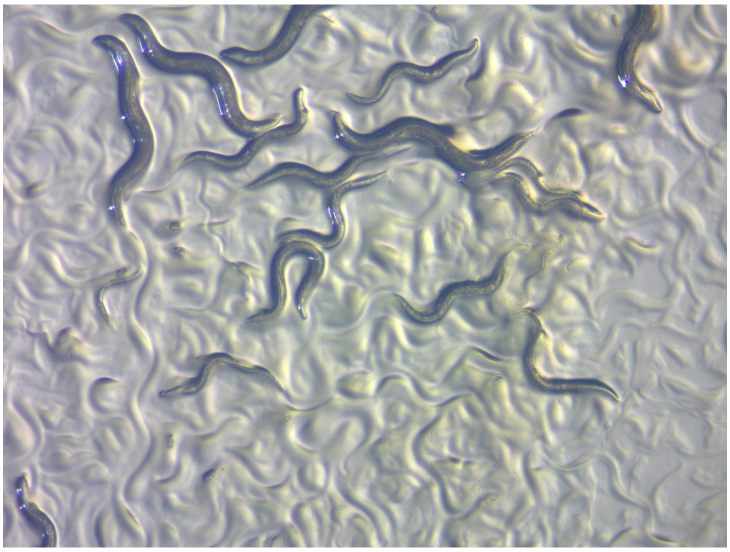
ABSTRACT
Classical genetics dictates that chromosomal DNA stores all the heritable information. However, the DNA sequence is not the only piece of information that one generation passes down to the next. We here present a compelling case where the ability of roundworm to efficiently find food is passed on to its future generation by the production of small molecules, known as small RNAs.



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The brain is a specialized organ that interprets information about the surroundings and translates it into behavior, allowing animals to cope with their dynamic environments. Ever since antiquity, thinkers (and helpless parents) have suggested that the activity of one's brain could somehow impact the fate of the next generation. If perception of the environment, or even acquired knowledge and memories stored in the brain, could produce heritable information that would influence the behavior of descendants, it could have far-reaching consequences on the survival of species and on the course of evolution.

Despite its appeal, this idea is highly controversial, mainly because no known mechanism could explain such a form of heredity. Moreover, a major theory articulated by the prominent 19th century biologist August Weismann, stated that heritable genetic information is stored solely in germ cells (oocytes and sperm), and is fully isolated from the influence of other tissues in the body. Therefore, the "Weismann barrier" rules out the possibility for information to transit from the brain to the germ cells and on to the offspring.

The emergence of molecular biology in the heart of the 20th century lead to the understanding that chromosomal DNA stores genetic information that is passed on to future generations. DNA encodes the information required for life, in the form of a sequence that consists of only a few components. In recent years, however, accumulating evidence from various organisms demonstrates that the DNA sequence is not the only piece of information that one generation passes down to the next. Additional layers of information, grouped under the term "epigenetics", can be inherited and affect how cells interpret the information stored in DNA to perform their functions.

Small RNAs are molecules produced in many organisms (such as bacteria, plants and animals) that regulate the use of genetic information encoded in DNA. The research that deciphered the mode of action of small RNAs was distinguished with a Nobel Prize in 2006. It was observed that these molecules operate similarly across the tree of life, including humans. Most importantly, these epigenetic agents don't care much about the "Weismann barrier". When artificially supplied to roundworms in their food, small RNAs can move from the intestine to the germ cells and pass to the offspring, affecting the way DNA is interpreted in their descendants for multiple generations.

Small RNAs are produced naturally in many tissues, including the brain. Yet, how small RNAs in the brain can influence behavior is unknown. For the purpose of our investigation, we engineered mutant roundworms that had lost the ability to produce a subset of small RNAs and restored this ability only in brain cells, also known as neurons. This allowed us to monitor the effect of small RNAs generated in neurons specifically. With this approach, we found that neuronal small RNAs affect gene expression not only in the brain, but also in germ cells and in the offspring.

We also discovered that under an elevated temperature which is stressful to roundworms, the production of small RNAs in neurons is necessary for them to efficiently perform a critical task: detecting and moving towards odors associated with food (a behavior termed ***chemotaxis***). Finally, we found that the production of neuronal small RNAs improved the chemotaxis performance also in the roundworms' descendants, for at least three generations.

Together, our experiments demonstrate that the activity of the brain can impact behavior for multiple generations, thanks to the production of small RNAs that can affect the way information encoded in the DNA is used. Further investigation will be needed to determine whether the brain can generate heritable small RNAs in response to specific environmental triggers, and by doing so, transmit information that could potentially help the progeny to better adapt to their habitat.

Another question, one that worm researchers find rather provocative, would be: "what about humans"? Straightly put, it is not known if these phenomena also apply to humans. Yet, similar mechanisms of epigenetic inheritance were found to take place in various organisms. Also, while most complex human diseases have inherited components, extensive studies aiming to explain them using principles of classical genetics have not always been successful. Therefore, a better understanding of unconventional forms of inheritance could potentially be practical also for human biology and better understanding of human diseases.