**Neuronal activity (of worms) regulates also the behavior of the next generations**.

*Small RNAs are molecules that regulate genes and were found in worms to be inherited to the progeny, thereby breaking rules defined by classical genetics. We found that the production of small RNAs in neurons is important for proper behavior of worms and that its effects are maintained for at least three generations*.

The nervous system is a specialized organ that interprets information about the surroundings and translates it into behavior, to allow animals to cope with their dynamic environments. Ever since antiquity, thinkers (and helpless parents) have suggested that the activity of the brain could somehow generate heritable changes that would have an impact on the fate of the progeny. If perception of the environment, or even acquired knowledge and memories stored in the nervous system, 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 there is no known mechanism that could explain such 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 nervous system to the germ cells and the progeny.

The emergence of molecular biology in the heart of the 20th century lead to the realization that genetic information is embodied in the DNA sequence, and also that DNA genetics are remarkably obedient to Weismann’s rule. Nevertheless, in recent years, accumulating evidence from various organisms demonstrates that additional layers of information, other than the DNA sequence itself, can be maintained across cell divisions, and sometimes be transmitted from parents to offspring. These other forms of information transfer are grouped under the term ***Epigenetics***. Epigenetic processes have profound consequences on gene expression, (that is, the way genetic information is interpreted by a cell to execute its specific physiological functions), and therefore on the development of healthy tissues and of harmful diseases.

***Small RNAs*** are molecules produced in many organisms (such as bacteria, plants and animals), that regulate the expression of genes and that have emerged as major players in epigenetic mechanisms. The research that deciphered the mode of action of small RNAs was distinguished with a Nobel prize in 2006, rapidly after it was discovered that these molecules operate in a similar fashion across the tree of life, including in humans. Most importantly, these epigenetic agents don’t care much about the “Weismann barrier”: when artificially supplied to worms in their food, small RNAs can move from the intestine to the germ cells and pass to the progeny, affecting gene expression in descendants for multiple generations.

Small RNAs are produced naturally in many tissues, including the nervous system. Yet, the function of natural neuronal small RNAs in behavior and in the regulation of other tissues is not known. For the purpose of our investigation, we engineered mutant worms that had lost the ability to produce a subset of small RNAs, and restored this ability only in their nervous system. This allowed us to specifically monitor the effect of small RNAs generated in neurons. With this approach, we found that neuronal small RNAs affect gene expression not only in the nervous system, but also in germ cells and in the progeny.

We also discovered that under an elevated temperature (which is stressful to worms), the production of small RNAs in neurons is required for worms 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 worms’ descendants, for at least three generations.

Together, our experiments demonstrate that the activity of the nervous system can impact behavior for multiple generations, thanks to the production of small RNAs that affect the expression of specific genes in the germ cells and the progeny. Further investigation will be needed to determine whether the nervous system 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 nematode investigators find rather provocative, would be: “what about humans”? Straightly put, it is not known if these phenomena also apply to humans. Yet, epigenetic inheritance was found to take place in various organisms, and some human diseases might have an epigenetically inherited component. Therefore, a better understanding of unconventional forms of inheritance could potentially be practical also for the study of human biology.