Researchers discover stress in early life extends lifespan

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Caenorhabditis elegans. Credit: Wikipedia

Some stress at a young age could actually lead to a longer life, new research shows.

University of Michigan researchers have discovered that oxidative stress experienced early in life increases subsequent stress resistance later in life.

Oxidative stress happens when cells produce more oxidants and free radicals than they can deal with. It's part of the aging process, but can also arise from stressful conditions such as exercise and calorie restriction.

Examining a type of roundworm called *C. elegans*, U-M scientists Ursula Jakob and Daphne Bazopoulou found that worms that produced more oxidants during development lived longer than worms that produced fewer oxidants. Their results are published in the journal *Nature*.

Researchers have long wondered what determines variability in lifespan, says Jakob, a professor of molecular, cellular and developmental biology. One part of that is genetics: If your parents are long-lived, you have a good chance for living longer as well. Environment is another part.

That other stochastic—or random—factors might be involved becomes clear in the case of *C. elegans*. These short-lived organisms are a popular model system among aging researchers in part because every hermaphroditic mother produces hundreds of genetically identical offspring. However, even if kept in the same environment, the lifespan of these offspring varies to a surprising extent, Jakob says.

"If lifespan was determined solely by genes and environment, we would expect that genetically identical worms grown on the same petri dish would all drop dead at about the same time, but this is not at all what happens. Some worms live only three days while others are still happily moving around after 20 days," Jakob said. "The question then is, what is it, apart from genetics and environment, that is causing this big difference in lifespan?"

Jakob and Bazopoulou, a postdoctoral researcher and lead author of the paper, found one part of the answer when they discovered that during development, *C. elegans* worms varied substantially in the amount of reactive oxygen species they produce.

Reactive oxygen species, or ROS, are oxidants that every air-breathing organism produces. ROS are closely associated with aging: the oxidative damage they elicit are what many anti-aging creams claim to combat. Bazopoulou and Jakob discovered that instead of having a shorter lifespan, worms that produced more ROS during development actually lived longer.

"Experiencing stress at this early point in life may make you better able to fight stress you might encounter later in life," Bazopoulou said.

When the researchers exposed the whole population of juvenile worms to external ROS during development, the average lifespan of the entire population increased. Though the researchers don't know yet what triggers the oxidative stress event during development, they were able to determine what processes enhanced the lifespan of these worms.

To do this, Bazopoulou sorted thousands of *C. elegans* larvae according to the oxidative stress levels they have during development. By separating worms that produced large amounts of ROS from those that produced little amounts of ROS, she showed that the main difference between the two groups was a histone modifier, whose activity is sensitive to oxidative stress conditions.

The researchers found that the temporary production of ROS during development caused changes in the histone modifier early in the worm's life. How these changes persist throughout life and how they ultimately affect and extend lifespan is still unknown. What is known, however, is that this specific histone modifier is also sensitive to oxidative stress

sensitive in mammalian cells. Additionally, early-life interventions have been shown to extend lifespans in mammalian model systems such as mice.

"The general idea that early life events have such profound, positive effects later in life is truly fascinating. Given the strong connection between stress, aging and age-related diseases, it is possible that early events in life might also affect the predisposition for age-associated diseases, such as dementia and Alzheimer's disease," Jakob said.

Next, the researchers want to figure out what key changes are triggered by these early-life events. Understanding this might allow scientists to develop lifespan-extending interventions that work at later stages in life.

More information: Developmental ROS Individualizes Organismal Stress Resistance and Lifespan, *Nature* (2019). DOI: 10.1038/s41586-019-1814-y , nature.com/articles/s41586-019-1814-y

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