MEDICAL

Anti-aging study boosts worm lifespans with glucose

By Nick Lavars
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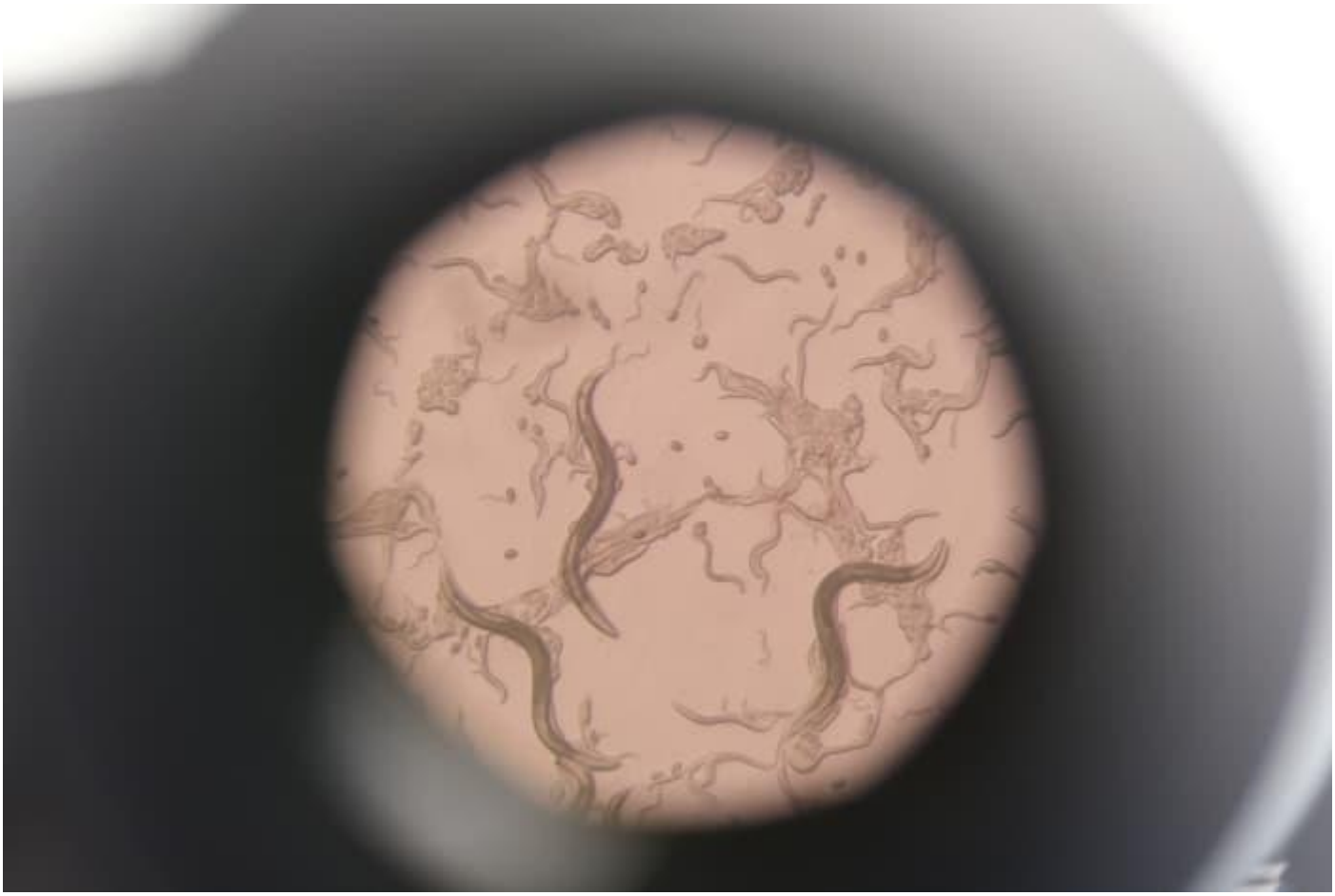

New research on aging in roundworms has thrown up some intriguing results, with scientists at Nanyang Technological University (NTU), Singapore finding they could increase the animals' lifespan by feeding them a high-sugar diet. Far from suggesting people adopt this lifestyle intervention, the authors say the breakthrough highlights a new mechanism underlying the aging process, and paves the way for new therapies to tackle age-related disease.

“Aging is a critical risk factor for a variety of human pathologies, from metabolic diseases such as diabetes to cancer and neurodegenerative diseases,” said cell biologist at NTU and study lead Associate Professor Guillaume Thibault. “From a public health perspective, determining the cellular pathways that underpin the aging process could take us one step closer to developing novel therapeutic strategies to treat age-related disorders.”

The study zeroed in on a stress response that takes place when there is an accumulation of unfolded proteins inside a cell. This could be caused by an excess of glucose or through natural aging, as our cellular machinery responsible for generating healthy proteins deteriorates. Known as the unfolded

protein response, the mechanism monitors these things with stress sensors, and kicks into action as needed, clearing away the unfolded proteins to maintain balance in the cell.

The study authors sought to explore the role the unfolded protein response plays in aging, turning to the roundworm *C. elegans* for help. These worms serve as popular models in aging research, as they share a similar genome and many cellular pathways with humans, but live for just three or four weeks, which makes changes to their lifespan relatively easy to measure.

A group of worms were fed a high-glucose diet at a post-reproductive age (at day five when they were no longer fertile), while a group of young worms at the start of adulthood (one day old), were fed the same diet. The older worms lived almost twice as long, seeing out 24 days, while the younger worms lived for just 13. A control group of worms on a normal diet lived for 20 days. Compared to these control animals, the aged worms on a high-fat diet were more agile and featured more energy storage cells, which the researchers say is indicative of healthier aging.

As the scientists were feeding the worms their sugary diets, they closely monitored the activity of stress sensors linked to the unfolded protein response, and found one that was highly active in the young worms compared to their older counterparts. Called IRE1, the scientists then removed the gene coding for this stress sensor, in effect switching off the cellular pathway for the stress response.

Interestingly, this led the young worms to live for an impressive 25 days, despite their high-sugar diet, almost twice as long as the young worms with the IRE1 stress sensor in place. This indicates that the perpetual activation of the stress response throughout the worms' lives was effectively shortening their lifespan.

"We believe that the high-glucose diet fed to the aged worms stimulated their otherwise sluggish unfolded protein response and switched on certain cellular pathways, tackling not just the stress caused by excess glucose but also other aging-related stress, restoring cellular stability," said Thibault. "In contrast, young worms subjected to a high-glucose diet provoked unresolved stress in the cells due to an overactivated IRE1. This prolonged activation led the cells to initiate cell death instead."

The authors say this is the first research to link this particular stress response to aging. Much more work is needed to properly understand the mechanics at play, including how the mechanism influences the processes of other cells. But an ability to safely manipulate this stress response could lead to therapeutics that extend lifespans and slow down cellular aging.

"While our study found that a high-glucose diet could be useful to slow down aging and promote longevity in aged worms, we are not recommending that the aged population should now turn to a high-sugar diet," said Thibault. "What this study does show is that triggering certain stress responses in cells may translate to longevity, and that activating this stress response with a drug might be critical to decelerate cellular aging."

The research was published in the journal *Nature Communications*.