



Science 19 OCT 2022 8:01 PM AEDT

Share

Manipulating stress response in cells could help slow down aging, reveals NTU Singapore study

Nanyang Technological University

Scientists at Nanyang Technological University, Singapore (NTU Singapore) have found that a stress response in cells, when 'switched on' at a post-reproductive age, could be the key to slow down ageing and promote longevity.

In lab experiments on a type of roundworm that shares similarities with humans, the NTU Singapore team found that switching on this stress response in aged worms by feeding them a high-glucose diet extended their lifespan as compared to worms fed a normal diet.

This is the first time a link between this stress response and ageing has been uncovered, said the NTU team of their findings published on 19 October in *Nature Communications*.

While further studies are needed to gain a deeper understanding of this link, the scientists said their findings open the door to the development of therapies that could delay the onset or even tackle age-related disorders such as cancer, dementia, and stroke.

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

"While our study found that a high-glucose diet could be useful to slow down ageing and promote longevity in aged worms, we are not recommending that the aged population should now turn to a high-sugar diet. 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 ageing."

Aside from showing that the effect of manipulating this stress response in aged worms, the NTU scientists also showed that the same response, when 'switched off' in young worms fed a high-glucose diet, helped them to live longer than worms on a normal diet.

Commenting as an independent expert, Professor Rong Li, Director of the Mechanobiology Institute at the National University of Singapore said: "Metabolic diseases have serious consequences in the elderly if left untreated. This work is impactful because the scientists identified a cellular pathway, called the unfolded protein response, which affects lifespan in animals fed a high glucose diet. They found that inhibiting this pathway dramatically extended the lifespan of these animals. They therefore propose that targeting this pathway may extend lifespan in humans with metabolic disorder."

This study is aligned with the research pillar of the University's NTU2025 five-year strategic plan, which focuses on health and society as one area with potential for significant intellectual and societal impact.

How the cell's stress response is activated

Cells produce a stress response when stressors (such as an excess of glucose) cause a build-up of problematic 'unfolded' proteins in the cell. The stress response, called the unfolded protein response, works to clear up these problematic proteins to restore balance in the cell.

Ageing could also lead to an accumulation of unfolded proteins due a natural decline in the ability of the cell's machinery to produce healthy proteins, triggering the same stress response.

The molecular machinery in the cell tackles this build-up through its 'stress sensors', which initiate a series of molecular mechanisms to rescue the cell from this stress. If the overload of unfolded proteins is not resolved, the prolonged unfolded protein response induces cell death instead.

Unfolded protein response in aged worms led to healthier ageing

To investigate how the unfolded protein response affects longevity in animals, the scientists induced this response in adult roundworms (*Caenorhabditis elegans*) using glucose. While *C. elegans* is significantly anatomically simpler than a human, it relies on many of the same genes that humans do to control the division of cells and to programme faulty cells to die.

The scientists fed some of the worms a high-glucose diet at two different life stages: young i.e. at the start of their adulthood (Day 1), and at a post-reproductive age (Day 5), when the worms are aged and no longer fertile. A control group of worms were fed a normal diet throughout.

The scientists found that the aged worms given a high-glucose diet lived for 24 days – almost twice the lifespan of the young worms given the same diet (13 days). Worms on a normal diet lived for 20 days.

Aside from living longer, the aged worms on a high-glucose diet were more agile and had more energy storage cells as compared to worms given a normal diet, suggesting healthier ageing.

Prolonged stress response in young worms led to cell death

A day after feeding the worms a high-glucose diet, the NTU scientists monitored the activity of the three stress sensors that are each responsible for a cellular pathway in the unfolded protein response.

They found that that one of the stress sensors, IRE1, was significantly more active in young worms compared to aged worms.

When the scientists removed the gene coding for IRE1 in worms to 'switch off' the cellular pathway the stress sensor initiates, they found that young worms fed a high-glucose diet from Day 1 lived for 25 days – twice as long as when the IRE1 gene was intact.

This suggests that the increased activity of stress sensor IRE1 seen in young worms fed a high-glucose diet from Day 1 – what the scientists say is a prolonged unfolded protein response – was responsible for shortening their lifespan.

Assoc Prof Thibault said: "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 ageing-related stress, restoring cellular stability.

"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 findings suggest that a drug that reduces the activity of IRE1 while increasing the activity of the other two stress sensors could potentially be developed to decelerate cellular ageing and consequently extend lifespans, he added.

More studies and findings will need to be conducted in the roundworms to further dissect the complex mechanism behind the lifespan extension induced by a high-glucose diet, as well as how this mechanism interacts with other processes in cells.

Other authors of the study are research fellow Dr Cenk Celik and research assistant Aishah Tul-Firdaus Abdul Khalid from NTU; former NTU researchers Caroline Beaudoin-Chabot, Wang Lei, Subhash Thalappilly, Xu Shiyi; and NTU graduates Koh Jhee Hong, Venus Lim Wen Xuan, and Low Ann Don.

/Public Release. This material from the originating organization/author(s) may be of a point-in-time nature, edited for clarity, style and length. The views and opinions expressed are those of the author(s).View in full [here](#).



Why?

Tags: biological, communications, energy storage, longevity, Nanyang Technological University, National University of Singapore, Nature Communications, pathways, population, Professor, public health, research fellow, Scientists, Singapore, university, venus

You might also like



Tokyo Tech Academy for Leadership holds Leadership Symposium with Dr. Haim ...



Researchers Develop Electrokinetic Mining Technology for Rare Earth...



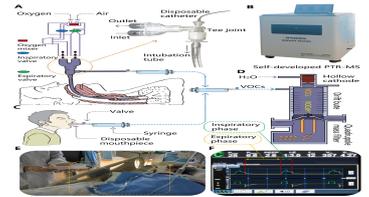
Research partnership to help prepare for future infectious disease threats officially...



Goodbye boarding passes, hello biometric facial recognition



Harvest Rock kickstarts SA's multi-million-dollar festival season



Scientists Screen for Ventilator Associated Pneumonia Infection...

Timeline

Protect your business from potential disaster

4:23 PM AEDT

Committee to hear from Parliamentary Clerks on privilege and corruption investigations

4:22 PM AEDT

Police responding to serious traffic crash at Macgregor

4:19 PM AEDT

Environmental DNA successfully captures marine biodiversity

4:19 PM AEDT

Research yields clues to why Alzheimer's damages certain parts of brain

4:18 PM AEDT

Selective nodal radiation may be more effective approach in

cancer treatment

4:18 PM AEDT

Lung infections caused by soil fungi are problem nationwide

4:16 PM AEDT

Glenfield Road Animal Shelter Open Day

4:14 PM AEDT

Nesting has begun for Little Terns

4:10 PM AEDT

St George pilots: put Control back into flying at non-controlled aerodromes

4:08 PM AEDT

High-power electrostatic actuators to realize artificial muscles

4:07 PM AEDT

Affordable Care Act linked to reduced smoking among US adults with mental health and substance use disorders

4:06 PM AEDT

Student-based contact-tracing program prevented Covid exposures and infections among university students and staff

4:06 PM AEDT

GeneSight mental health monitor finds gap on front line of mental health care

4:06 PM AEDT

MidCoast businesses excel in tourism industry awards

4:05 PM AEDT

Vast phytoplankton blooms may be lurking beneath Antarctic ice

4:04 PM AEDT

Migrant Workers Call for Compensation for Abuses: FIFA/Qatar

4:04 PM AEDT

Research suggests need for improved support for transgender and non-binary young people after hospitalization

4:04 PM AEDT

Research reveals no need for concerns about behavioral issues

4:04 PM AEDT

Investigation raises concerns about poor FDA oversight of clinical trials

4:04 PM AEDT

Studies provide latest 'real world' evidence on effectiveness of Covid treatments

4:03 PM AEDT

Deaths among mothers almost four times higher in Slovakia and UK than in Norway and Denmark

4:03 PM AEDT

Rising housing cost to income ratio strongly linked to poor health, death, suicide

4:02 PM AEDT

Air Force wows Illawarra air show crowds

4:02 PM AEDT

Price of puppies to surge under NSW Labor

3:59 PM AEDT

AGL's new board must deliver on climate: Health workers

3:59 PM AEDT

Auckland businessman arrested in Customs illegal tobacco case

3:58 PM AEDT

Local students create amazing art

3:52 PM AEDT

[Show More](#)

Popular Topics

- Australia Government university
- community police Australian
- research Victoria NSW Professor
- Minister environment health
- covid-19 Queensland business
- council UK local council
- New South Wales industry
- Investment education infrastructure
- investigation technology AusPol
- project crime Emergency
- United States QLD UK Government
- New Zealand sustainable future
- Sydney President Scientists
- Impact court Internet
- climate change resources
- coronavirus

All trademarks and rights are owned by their respective owners.

All content is used for news reporting purposes. For news reporting purposes, we rely on fair use (fair dealing) ^[1] ^[2] for textual and media content to keep the public informed of the latest developments. If you are a person mentioned in the story or you are a copyright holder and believe that any content should be removed, revised or taken down, please contact us. See [our disclaimer page](#).