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Singapore researchers shed light on tackling Alzheimer's

Yale-NUS College's Assistant Professor Jan Gruber and research fellow Emelyne Teo with a magnified image of the tiny worm called Caenorhabditis elegans. The researchers worked with the worms, which share many similarities with humans at the molecular level, to find a way to fight Alzheimer's disease. ST PHOTO: KELVIN CHNG

Key to fighting such age-related diseases may lie in targeting ageing process itself, they find

Timothy Goh

Singapore researchers have taken the first steps in developing new methods to tackle Alzheimer's disease, which affects one in 10 people over the age of 60 here.

They have discovered that the key to fighting the disease may lie in tackling ageing itself.

In their study, scientists from the National University of Singapore (NUS), Yale-NUS College, Duke-NUS Medical School, SingHealth Geriatric Medicine Residency Programme, the National University Health System Centre for Healthy Ageing and two overseas institutions mimicked the disease in worms and attempted to treat them.

The results of the study were published in the scientific journal eLife earlier this month.

Yale-NUS College's Assistant Professor Jan Gruber, the study's principal investigator, said: "There's some evidence that people who get diagnosed with Alzheimer's have some defects around eight years before (the diagnosis).

"We tend to excuse these things because we just think of this as normal ageing... but if you want to intervene, then that's the time to intervene – early, before brain cells die."

He and his team worked with *Caenorhabditis elegans*, tiny worms which share many similarities with humans at the molecular level.

The worms were genetically modified to produce fragments of a protein called amyloid beta in their neurons.

It was previously thought that an accumulation of this protein in human brains, known as plaques, was the primary cause of Alzheimer's, and a lot of research has focused on eliminating these plaques, said Prof Gruber.

He said: "Billions of dollars have been spent on clinical trials for drugs and antibodies that can remove the amyloid beta plaques, and it doesn't help with the disease. There's nothing you can really do to block it once it's diagnosed.

"You can slow down the symptoms a bit, you can improve the quality of life, but there's nothing disease-modifying at all."

As expected, the worms that were modified to produce the protein developed issues similar to those faced by humans with Alzheimer's. They got lost trying to find food and their sense of smell was weakened. Their lifespan was shorter too.

But the team noticed that the worms also showed the same metabolic defects seen in the brains of patients with Alzheimer's.

These defects occurred before tissue death and the accumulation of proteins, and might even contribute to the formation of plaques as the body lacks energy to get rid of excess "junk" proteins, said Prof Gruber.

Metabolic dysfunction is also a feature of other age-related diseases. The team decided to tackle this by targeting the ageing process itself.

"Age-dependent diseases (such as Alzheimer's) are late manifestations of the process of ageing. So if you understand early events, you can intervene early on and prevent the disease from occurring in the first place," said Prof Gruber.

They did this by treating the worms with metformin, a drug that tricks the body into thinking it lacks nutrition, making it take better care of itself. It also increases the body's metabolism.

The team found that the treated worms not only recovered from their Alzheimer's-like symptoms, but also lived longer than healthy worms that were not treated.

Prof Gruber emphasised that the point of the discovery was not that people should start taking metformin or similar drugs, but that there should be a paradigm shift in the treatment of age-related diseases such as Alzheimer's.

In future, the team plans to expand its research to work with different organisms and delve deeper into researching the mechanisms behind Alzheimer's.

Prof Gruber said: "There's a long way to go from here, but what's clear is that if you want to prevent age-dependent diseases, targeting ageing is a better strategy than targeting the individual diseases."

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