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New worm strain to facilitate study of Alzheimer's disease

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Researchers from Yale-NUS College have partnered with researchers from the National University of Singapore (NUS) and SingHealth Group to develop a novel *Caenorhabditis elegans* (*C. elegans*) worm strain which expresses an amyloid beta protein fragment involved in the development of human Alzheimer's Disease (AD). This strain will serve as a tool for the testing of interventions against AD and to help researchers understand the disease better.

Alzheimer's Disease is a progressive neurological disorder characterised by the deposition of amyloid beta plaques in the brain. In this project, the researchers have managed to create a novel nematode strain producing amyloid beta in their nerve cells. Worms from this strain display neuromuscular defects, impairing metabolic function and age-dependent behavioural dysfunction resembling those seen in human AD. In contrast to previous models, this strain was designed specifically to accumulate amyloid beta slowly with the aim of investigating events that occur early in AD. Their findings have shown that mitochondrial bioenergetic deficit or biochemical 'energy crisis' is an early event (characterised by the deterioration of certain functions) in AD, preceding the onset of global metabolic failure. These results are consistent with an emerging view that AD may be a metabolic neurodegenerative disease.

The work was published online in *Scientific Reports*.

Research was carried out by a multidisciplinary team spearheaded by

Emelyne Teo, a NUS PhD student, and Fong Sheng, a (then) medical student from Duke-NUS Medical School, both working in Yale-NUS College Assistant Professor of Science, Jan Gruber's laboratory. The team also involved a Yale-NUS undergraduate student, Sau Yee Tsoi, who gained early exposure in advanced research methodology and made important contributions to the project by detecting and quantifying olfactory and behavioural deficits in the AD model strain. Ms Tsoi's contribution was recognised through authorship credit on the publication. Dr Gruber said that as a scientist working in a teaching-intensive undergraduate college, it was very rewarding for him to be able to create such research opportunities for undergraduate students, and nurture them to become future scientists.

Ms Tsoi said: "Besides learning more advanced molecular biology techniques in this research project, the opportunity to work closely with Dr Gruber has also given me a better understanding of the processes involved in research and inspired me to pursue a career in the biomedical sciences. I am glad for the many research opportunities offered by Yale-NUS College to its undergraduates."

On the significance of the findings, senior author of the research paper, Dr Gruber, said: "Given that we are starting to realise that mitochondrial dysfunction plays an important and early role in the pathogenesis of AD, interventions such as those involving mitochondrial-targeted therapeutics could prove a promising intervention strategy to prevent or delay the progression of AD."

More information: Sheng Fong et al, Energy crisis precedes global metabolic failure in a novel Caenorhabditis elegans Alzheimer Disease model, *Scientific Reports* (2016). DOI: 10.1038/srep33781