

## **NEWS RELEASE**

**Singapore, 9 April 2026**

### **Fat-producing enzyme may amplify damage in Parkinson’s disease, finds NTU Singapore study**

*Targeting the enzyme may offer a new strategy for treating the neurodegenerative disease*

A fat-producing enzyme in brain cells may play a key role in driving damage in Parkinson’s disease and could offer a new target for treatment, scientists at **Nanyang Technological University, Singapore (NTU Singapore)** have found.

Scientists from NTU Singapore’s **Lee Kong Chian School of Medicine (LKCMedicine)** found that this enzyme, called **glycerol-3-phosphate acyltransferase (GPAT)**, can amplify the harmful effects of  $\alpha$ -synuclein – a protein that accumulates in the brains of people with Parkinson’s disease – by altering how brain cells process fats.

Through laboratory experiments, the scientists reduced the activity of GPAT and observed less brain cell damage in fruit flies and mouse brain cells grown in the lab.

Inside brain cells, structures called mitochondria act as “power stations” that keep cells running. The study found that GPAT contributes to cellular damage that can impair these power stations, reducing the cells’ ability to generate energy. At the same time, it increases the toxicity of  $\alpha$ -synuclein. Together, these effects deliver a “double hit” to brain cells.

The findings reveal how fat metabolism in brain cells influences  $\alpha$ -synuclein toxicity and point to new possibilities for treating Parkinson’s disease, which currently has no cure, said **Professor Lim Kah Leong, Lead Investigator and Director of the Neuroscience & Mental Health Programme at NTU LKCMedicine.**

**Professor Lim, who is also NTU’s Associate Vice President for Research (Biomedical and Life Sciences),** said: “Just like mechanics who know how to repair cars because they understand how the vehicle’s engine system works, understanding how  $\alpha$ -synuclein disrupts the brain’s cellular energy powerhouses provides us with

insight into how we can possibly fix this problem and find a treatment for Parkinson's disease along the way.”

Parkinson's disease is the second most common neurodegenerative disorder worldwide, affecting more than 11 million people globally<sup>1</sup>. In Singapore, about three in every 1,000 individuals aged 50 years and above suffer from the disease<sup>2</sup>. This number is expected to rise as the country becomes a super-aged society, underscoring the urgent need for new treatments.

Commenting as an independent expert, **Professor Tan Eng King, Deputy Chief Executive Officer and Senior Consultant in Neurology at the National Neuroscience Institute**, said: “This study sheds novel insights into the interplay between metabolic dysregulation and brain dysfunction, suggesting that targeting metabolic pathways may be a relevant strategy to consider for brain disorders. The clinical implications are important as we currently lack effective disease-modifying therapies for Parkinson's disease, largely because of our limited understanding of the molecular events underlying its pathogenesis.”

The study was published in January in *Nature Communications*.

### **How fat metabolism amplifies damage in Parkinson's disease**

To investigate the biological mechanisms underlying Parkinson's disease, the NTU team conducted experiments using fruit flies engineered to produce excess human  $\alpha$ -synuclein, a well-established model used to study the disease.

As the flies aged, they developed Parkinson's-like symptoms – including impaired movement and loss of brain cells – mirroring key aspects of disease progression seen in humans.

Using large-scale genetic screening made possible by the fruit fly model, the researchers systematically identified genes involved in  $\alpha$ -synuclein-induced toxicity. Among these, the gene *mino* stood out for its strong effects on disease-related symptoms, leading the team to investigate its role further. This gene codes for the enzyme GPAT and plays a key role in regulating fat metabolism in cells.

When the scientists reduced the activity of the *mino* gene, the flies experienced less loss of brain cells, improved movement, and healthier activity patterns. In contrast, increasing the gene's activity worsened the flies' symptoms.

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<sup>1</sup> Dorsey, E. R. & Bloem, B. R. The Parkinson Pandemic-A Call to Action. *JAMA Neurol* 75, 9-10, doi:10.1001/jamaneurol.2017.3299 (2018).

<sup>2</sup> Tan, L. C. et al. Prevalence of Parkinson disease in Singapore: Chinese vs Malays vs Indians. *Neurology* 62, 1999-2004, doi:10.1212/01.wnl.0000128090.79756.10 (2004).

## Targeting GPAT activity

The researchers then explored whether blocking GPAT could help counter these toxic effects. They tested a compound called FSG67, which blocks the activity of GPAT and has previously been studied in laboratory settings for obesity-related and metabolic disorders.

When the flies were treated with FSG67, the harmful effects of  $\alpha$ -synuclein – including protein clumping and fat damage – were reduced. The scientists observed similar protective effects in mouse brain cells grown in the laboratory.

**Dr Ren Mengda, Co-Investigator and Senior Research Fellow at LKC Medicine,** said, “We found that excessive fat damage in brain cells makes  $\alpha$ -synuclein far more toxic. By inhibiting GPAT using FSG67, we were able to reduce these harmful effects in both fruit flies and mouse brain cells.”

Going forward, the scientists will focus on further validating these findings and exploring the possibility of developing GPAT inhibitors as a new class of drugs for Parkinson’s disease.

This research could deepen scientists’ understanding of the neurodegenerative processes underlying Parkinson’s disease and help identify new therapeutic strategies.

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### **Note to Editor:**

Paper titled “[Glycerol 3-phosphate acyltransferase exacerbates  \$\alpha\$ -synuclein-induced toxicity by increasing lipid peroxidation](https://doi.org/10.1038/s41467-026-68325-3)” published online in *Nature Communications* **17**, 1618 (2026). <https://doi.org/10.1038/s41467-026-68325-3>

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***About Nanyang Technological University, Singapore***

A research-intensive public university, Nanyang Technological University, Singapore (NTU Singapore) has 40,000 undergraduate and postgraduate students in the Business, Computing & Data Science, Engineering, Humanities, Arts, & Social Sciences, Medicine, Science, and Graduate colleges.

NTU is also home to world-renowned autonomous institutes – the National Institute of Education and the S Rajaratnam School of International Studies – and various leading research centres such as the Earth Observatory of Singapore, Nanyang Environment & Water Research Institute, Energy Research Institute @ NTU (ERI@N), and the Singapore Centre for Environmental Life Sciences Engineering.

Under the NTU Smart Campus vision, the University harnesses the power of digital technology and tech-enabled solutions to support better learning and living experiences, the discovery of new knowledge, and the sustainability of resources.

Ranked amongst the world's top universities, the University's main campus is also frequently listed among the world's most beautiful. Known for its sustainability, NTU has achieved 100% Green Mark Platinum certification for all its eligible building projects. Apart from its main campus, NTU also has a medical campus in Novena, Singapore's healthcare district.

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