PRESS RELEASE

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A molecule our bodies produce may help defend against Alzheimer's disease: NUS Medicine study

Singapore, 29 December, 2025 – Singapore has one of the highest life expectancies in the world, yet many individuals spend almost a decade in poor health toward the end of life. Scientists from the Yong Loo Lin School of Medicine, National University of Singapore (NUS Medicine) are working to understand how ageing itself can be modified to prevent age-related diseases, including Alzheimer's disease.

Published in Aging Cell, a new study led by Professor Brian K Kennedy, Department of Biochemistry, Chair of the Healthy Longevity Translational Research Programme (TRP), NUS Medicine, has discovered that calcium alpha-ketoglutarate (CaAKG), a safe, naturally occurring metabolite commonly studied for healthy ageing, can restore key memory-related brain functions that have been disrupted in Alzheimer's disease. The main aim of the study was to evaluate whether CaAKG could also enhance synaptic plasticity in the Alzheimer's brain, restore memory-related signalling, protect neurons from early degenerative changes, and contribute to healthier cognitive ageing. For healthcare and medicine, this shift opens the door to geroprotective strategies—treatments that target ageing biology itself rather than individual disease symptoms.

"Our findings reveal the exciting potential of longevity compounds in addressing Alzheimer's disease," said Prof Kennedy. "The research suggests that safe, natural compounds like CaAKG may one day complement existing approaches to protect the brain and slow memory loss. Because AKG is already present in our bodies, targeting these pathways may offer fewer risks and broader accessibility. Thanks to that, we may have a powerful new strategy to delay cognitive decline and support healthy brain ageing."

The study shows that CaAKG helps brain cells communicate better in Alzheimer's disease models. It not only repairs the weakened signals between neurons, but also restores associative memory, one of the early abilities lost in Alzheimer's. Because AKG levels naturally fall as we age, replenishing this molecule could be a promising way to support healthier brain ageing and lower the risk of neurodegenerative diseases.

To understand how CaAKG helps the brain, the researchers measured long-term potentiation (LTP), which is the process that allows neurons to strengthen their connections. LTP is

essential for learning and forming lasting memories, but in Alzheimer's disease it becomes severely impaired. The team found that CaAKG brought this signal-strengthening process back to normal. CaAKG also boosted autophagy, the brain's built-in "clean-up" system that removes damaged proteins and keeps neurons healthy. The molecule worked through a newly identified pathway, helping neurons become more flexible by activating L-type calcium channels and calcium-permeable AMPA receptors, while avoiding NMDA receptors, which are often disrupted by amyloid buildup. Importantly, CaAKG restored synaptic tagging and capture, a key mechanism that allows the brain to link events and form associative memories. This suggests CaAKG may support not just basic memory function, but also more complex learning abilities that decline early in Alzheimer's disease.

"Our goal was to determine whether a compound originally explored for extending healthy lifespan could be helpful for Alzheimer's disease," said Dr Sheeja Navakkode, first author of the study, and research scientist at Healthy Longevity TRP, NUS Medicine. "Understanding the cellular mechanisms of how CaAKG improves synaptic plasticity sheds light on new ways to protect memory and slow brain ageing."

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Our multidisciplinary and real-world approach to education, research and entrepreneurship enables us to work closely with industry, governments, and academia to address crucial and complex issues relevant to Asia and the world. Researchers in our faculties, research centres of excellence, corporate labs and more than 30 university-level research institutes focus on themes that include energy; environmental and urban sustainability; treatment and prevention of diseases; active ageing; advanced materials; risk management and resilience of financial systems; Asian studies; and Smart Nation capabilities such as artificial intelligence, data science, operations research, and cybersecurity.

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Through a dynamic and future-oriented five-year curriculum that is inter-disciplinary and inter-professional in nature, our students undergo a holistic learning experience that exposes them to multiple facets of healthcare and prepares them to become visionary leaders and compassionate doctors and nurses of tomorrow. Since the School's founding in 1905, more than 12,000 graduates have passed through our doors.

In our pursuit of health for all, our strategic research programmes focus on innovative, cutting-edge biomedical research with collaborators around the world to deliver high impact solutions to benefit human lives.

The School is the oldest institution of higher learning in the National University of Singapore and a founding institutional member of the National University Health System. It is one of the leading medical schools in Asia and ranks among the best in the world (Times Higher Education World University Rankings 2025 by subject and the Quacquarelli Symonds (QS) World University Rankings by subject 2025).

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