

PRESS RELEASE

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Novel gene therapy offers hope for epilepsy patients

Singapore, 9 October 2024—Researchers from the **Yong Loo Lin School of Medicine, National University of Singapore (NUS Medicine)** are working on a therapy that holds potential in treating patients with epilepsy, a neurological disorder defined by recurring seizures due to abnormal brain activity.

Led by **Research Assistant Professor Huang Hua from the Department of Physiology and Electrophysiology Core Facility at NUS Medicine**, they have trialled a novel gene therapy approach for a rare genetic form of epilepsy linked to a mutation in the *KCNA2* gene in the human brain, which is associated with recurring seizures. A specialised treatment called a Gapmer antisense oligonucleotide (ASO) is designed to specifically target and break down faulty ribonucleic acids (RNA) while keeping normal gene function intact. Using this RNA therapy led to a notable decrease in a problematic potassium channel protein encoded in the *KCNA2* gene, which helped restore normal potassium flow and reduce excessive neuron activity linked to epilepsy.

Asst Prof Huang said, “Epilepsy is associated with hyper-excitability neurons, and potassium helps dampen the excitability levels. The potassium channel encoded by *KCNA2* is like a door that controls the potassium ion flow on the surface of the cells—when the gene is mutated, the door fails to work and potassium cannot be released to control neuron activity, which results in epilepsy. Our therapy targets the faulty RNA in the gene and ‘fixes the door’, so that potassium can flow and regulate the neuron activity levels.” Asst Prof Huang is also from the Healthy Longevity Translational Research Programme at NUS Medicine.

Published in *Molecular Therapeutics Nucleic Acids*, a top journal in the field of nucleic-acid-based therapeutics, the research study was conducted on *in vitro* cell samples. The research work began in 2021, when the team was approached by the family of an infant who suffered from multiple generalised seizures that were resistant to multiple medications and conventional treatments. While the research work is in early stages and will need to undergo further testing in laboratory models before moving to clinical trials, the remarkable results from the research offer hope that the therapy can be delivered to patients suffering from severe epilepsy caused by channelopathies—genetic disorders caused by abnormalities in the ion channels of cells—within the next 10 to 20 years.

The new Gapmer technology being worked on by the research team could also be adapted to target other mutations in the same gene or other ion channel genes—opening the possibility of creating personalised treatments for different *KCNA2*-related issues, potentially offering hopeful outcomes for patients with rare forms of epilepsy that are unresponsive to standard medications.

Professor Soong Tuck Wah from the Department of Physiology and Electrophysiology Core Facility at NUS Medicine, a co-author of the study, said, “Our research seeks not only to address the unique challenges posed by this specific mutation, but also stems from our team’s desire to improve the quality of life for patients. Since the therapy has shown promise in targeting a specific gene mutation causing epilepsy, we hope to eventually pioneer new treatment options for patients suffering from this condition, and other similar gene mutations.” Prof Soong is also from the Healthy Longevity Translational Research Programme at NUS Medicine.

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About National University of Singapore (NUS)

The National University of Singapore (NUS) is Singapore's flagship university, which offers a global approach to education, research and entrepreneurship, with a focus on Asian perspectives and expertise. We have 16 colleges, faculties and schools across three campuses in Singapore, with more than 40,000 students from 100 countries enriching our vibrant and diverse campus community. We have also established more than 20 NUS Overseas Colleges entrepreneurial hubs around the world.

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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About the NUS Yong Loo Lin School of Medicine (NUS Medicine)

The NUS Yong Loo Lin School of Medicine is Singapore's first and largest medical school. Our enduring mission centres on nurturing highly competent, values-driven and inspired healthcare professionals to transform the practice of medicine and improve health around the world.

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 2024 by subject and the Quacquarelli Symonds (QS) World University Rankings by subject 2023).

For more information about NUS Medicine, please visit <https://medicine.nus.edu.sg/>