

International study discovers three potential new targets for treating epilepsy

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A major international study has uncovered three molecules that have the potential to be developed into new drugs to treat epilepsy. The findings



are an important step towards discovering new drugs for people with epilepsy whose seizures cannot be controlled with current treatments.

The study was led by researchers at FutureNeuro, the SFI Research Centre for Chronic and Rare Neurological Diseases and RCSI University of Medicine and Health Sciences. It is the result of seven years of research, involving contributions from 35 scientists, based in eight different European countries, across the fields of neuroscience, genetics, computer science and synthetic chemistry. The research is published in the current issue of *Proceedings of the National Academy of Sciences* (*PNAS*).

In one of the largest sequencing projects of its kind, researchers identified and measured levels of over a billion strands of microRNAs, <u>small molecules</u> that control gene activity in the brain, to investigate if they were changed in <u>epilepsy</u>. They discovered a small set of microRNAs which were always elevated in epilepsy and designed druglike <u>molecules</u>, synthesized by chemists from the group, to target these. Three of the synthetic molecules were found to stop seizures in preclinical tests.

Computer simulations demonstrated how the potential treatments influenced molecule networks inside <u>brain cells</u> by changing the inflammatory response, part of the brain's immune system which is thought to contribute to seizures.

"Our approach to drug discovery has led us to new types of molecules that can be targeted to prevent seizures with hopefully fewer side effects." said Dr. Cristina Reschke, FutureNeuro Research Fellow and Honorary Lecturer at RCSI, and Co-Lead Author. "Currently, most drugs used to treat epilepsy work by blocking the signals brain cells use to communicate. This results in many of the side effects experienced by people with epilepsy."



Epilepsy is one of the most common chronic brain diseases, affecting over 40,000 people in Ireland and 65 million people worldwide. People with epilepsy are prone to repeated seizures, but for the majority of people, these can be well controlled. There are more than 20 medicines available to prevent seizures in people with epilepsy, but progress has slowed in recent years and new treatments offer little benefit over those that have been around for decades.

"By characterising and targeting an entire new class of molecules in epilepsy, we hope to develop novel and innovative treatment strategies for <u>temporal lobe epilepsy</u>." said Dr. Gareth Morris, Marie Sklodowska-Curie Actions Fellow at FutureNeuro and Co-Lead Author of the paper. "This is an important step closer to fulfilling the urgent and unmet clinical needs for the one third of people whose seizures are resistant to currently available drugs."

Senior author on the study, Professor David Henshall, Director of FutureNeuro and Professor of Molecular Physiology and Neuroscience at RCSI said: "The project is a great example of team science, where groups with different areas of expertise combine to create innovative solutions that keep people with epilepsy as the central focus. The discoveries here may be just the tip of the iceberg for new strategies in the treatment of epilepsy. I'm optimistic this can be translated to the clinic."

The work began under EpimiRNA, an RCSI-led pan-European project, funded through the EU 7th Framework Programme and concluded in FutureNeuro which is funded by Science Foundation Ireland.

More information: Morten T. Venø et al. A systems approach delivers a functional microRNA catalog and expanded targets for seizure suppression in temporal lobe epilepsy, *Proceedings of the National Academy of Sciences* (2020). DOI: 10.1073/pnas.1919313117



Provided by RCSI University of Medicine and Health Sciences

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