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Researchers identify new genetic cause of epilepsy

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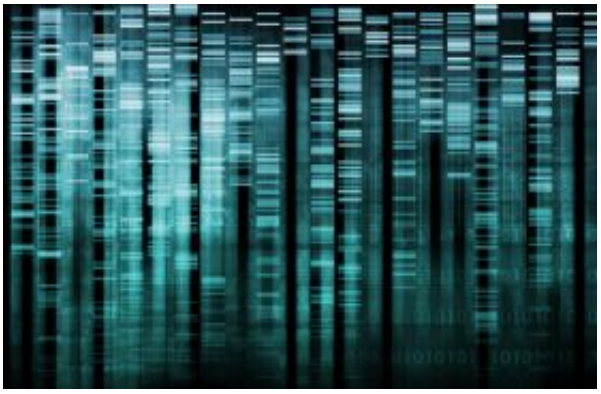

A research team led by scientists at the Scripps Translational Science Institute (STSI) has used whole genome sequencing to identify a new genetic cause of a severe, rare and complex form of epilepsy that becomes evident in early childhood and can lead to early death.

The researchers found a mutation in the KCNB1 gene after mapping the DNA of a 10-year-old girl who suffers from epileptic encephalopathy. The findings were reported in the October edition of the peer-reviewed medical journal *Annals of Neurology*.

The KCNB1 gene encodes the Kv2.1 voltage-gated potassium channel, which regulates the flow of potassium ions through neurons, affecting

how the cells communicate with one another. The voltage-gated potassium channel also regulates potassium flow in the kidney, which affects potassium excretion and fluid balance.

The link between the KCNB1 mutation and epileptic encephalopathy has opened new treatment options for the young patient, said Robert Bjork, M.D., her physician and a member of the Scripps Memorial Hospital La Jolla staff.

Earlier this year, "her prognosis was grim and appeared hopeless when she was experiencing many convulsive seizures, could barely eat or drink, and had 'drop attacks' where she would abruptly drop to the floor up to 25 times a day," he said.

Given continued close medical monitoring, an expanded medical treatment team, a uniquely designed home-school program and avoidance of dehydration, Dr. Bjork is optimistic that she can be kept out of harm's way and her status will improve over time.

Case part of IDIOM Study

The research was part of STSI's IDIOM Study, an ongoing project that uses whole genome sequencing to help determine the causes and treatments of idiopathic diseases - those serious, rare and perplexing health conditions that defy a diagnosis and standard treatment.

"We are continuing to learn the impressive power of whole genome sequencing for making a difficult - and heretofore impossible—diagnosis," said Eric Topol, M.D., who is the director of STSI and chief academic officer of Scripps Health.

STSI is a National Institutes of Health sponsored consortium led by Scripps Health in collaboration with The Scripps Research Institute

(TSRI). Through this innovative partnership, Scripps is leading the effort to translate genetic and wireless medical technologies into high-quality, cost-effective treatments and diagnostics for patients.

To validate their findings, STSI researchers teamed with colleagues at Northwestern University Feinberg School of Medicine in Chicago, who had previously looked at similar KCNB1 mutations. The Northwestern colleagues were listed as co-authors of the journal report, along with contributors from the University of California, San Diego; Kennedy Krieger Institute; Johns Hopkins University; and Vanderbilt University.

Potential benefits of discovery

The benefits of discovering the role of KCNB1 mutations in epileptic encephalopathy reach far beyond the STSI research case, said Ali Torkamani, director of genome informatics at STSI and an assistant professor of integrative, structural and computational biology at TSRI.

"These findings can serve as a model on how to treat this particular form of epilepsy in other patients," he said. "The KCNB1 mutations also might have a role as a diagnostic biomarker for this condition, and they could help to direct the discovery and testing of new drugs to treat epilepsy."

Provided by The Scripps Research Institute