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# Genome study offers new hope for children with rare diseases

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An international team involving University of Queensland researchers has used advanced genome sequencing to diagnose 30 patients with unresolved rare diseases.

The patients were among 70 people with disorders of the brain's white matter and were examined using whole exome sequencing (WES)—a method that looks at all the genes in a person's genetic code at once.

White matter disorders, which affect one in 7000 children born each year, damage the nerves that connect different brain regions to each other and the spinal cord, causing impaired brain function.

The team was led by Children's National Health System's Myelin Disorders Program Director Dr Adeline Vanderver, and included Illumina Director of Scientific Research Dr Ryan Taft, and the UQ Institute for Molecular Bioscience's Dr Cas Simons.

Dr Simons, from the UQ IMB Centre for Rare Diseases Research, said white matter disorders could have a devastating impact on patients and families.

"Access to a timely and accurate diagnosis is critical to inform many healthcare decisions and improve quality of life for patients," he said

The diagnoses led to refinements in some patients' clinical care, with families carrying certain mutations referred to specialised clinics for

monitoring for cancer.

Dr Vanderver said the term 'rare' genetic disease was somewhat misleading, with up to 350 million people across the world affected by rare disorders.

"Our study found that next-generation sequencing could shine a diagnostic light on an especially challenging group of genetic disorders that impact the brain's white matter," she said.

Dr Taft, a UQ alumnus who retains a part-time research position at IMB, said he was were delighted by the power of this approach., "."

"In this study, use of next-generation sequencing-based WES dramatically increased the diagnostic yield and reduced the time to diagnosis," he said

Dr Taft said more than 100 genetic disorders are linked to white matter abnormalities in the central nervous system but standard approaches to diagnose white matter disorders, such as MRI, fail nearly 50 per cent of these children, complicating their care and exacting a substantial psychological toll on families.

The researchers concluded that adding whole-exome sequencing to the diagnostic tools at clinicians' disposal could decrease the number of patients with unsolved genetic white matter disorders from 50 per cent of white matter disorder patients to less than 30 per cent.

The team is now investigating the use of whole genome sequencing, which looks at the entire genome at a single point in time and could further increase the chances of diagnosis when used in combination with MRI and whole genome sequencing.

**More information:** Adeline Vanderver et al. Whole exome sequencing in patients with white matter abnormalities, *Annals of Neurology* (2016). DOI: 10.1002/ana.24650