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Gene that causes intellectual disability when mutated finally identified

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At least half of those with an intellectual disability across the world do not have a formal diagnosis. However, thanks to new DNA sequencing technology, along with the expertise and perseverance of University of Adelaide researchers over 45 years, dozens of Australians with intellectual disability now have a name for their condition.

The research was published this month in the *American Journal of Human Genetics*.

Dr Raman Sharma, from the University of Adelaide's Robinson Research Institute, discovered a novel gene, which when mutated, causes intellectual disability that affects 1 in 50 individuals.

"Protein coded by the THOC2 gene is part of a large protein complex that is fundamental for all living human cells and essential for normal development and function," says Dr Sharma, lead author on the paper.

"In collaboration with European researchers, we have identified four mutations in the THOC2 gene in four families. The defected gene is found in males who have an intellectual disability – females in the families are carriers of the gene mutation but are not affected by the condition.

"As well as identifying the gene, we also discovered that it is partial loss of function of the THOC2 gene that leads to the altered brain function and specific facial characteristics associated with this intellectual

disability," he says.

Dr Sharma says hundreds of defected genes have been identified in the quest to learn more about neurological disorders but the team at the University of Adelaide is taking the next step – looking at why certain mutations cause what they cause.

"Advanced genetic technologies have accelerated the discovery of genes responsible for diseases like epilepsy, autism, intellectual disability and other neurological disorders," says Dr Sharma. "But the number of genetic conditions in which we have functional understanding of the mutated genes can be counted on two hands.

"For many reasons it's important to know about familial gene mutations but that's just the first step.

"Before we can develop a treatment for a condition, we first need to understand what is going on in the body and discover how a specific defected gene causes a particular disease," he says.

"Our lab is one of the few in the world looking at the molecular and cellular pathways altered by the gene variants. Our research is an upcoming field of genetics, which we hope will lead to the discovery of treatments for debilitating intellectual disabilities," he says.

More information: "THOC2 Mutations Implicate mRNA-Export Pathway in X-Linked Intellectual Disability." *Am J Hum Genet*. 2015 Jul 8. pii: S0002-9297(15)00235-9. DOI: 10.1016/j.ajhg.2015.05.021

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