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New form of intellectual disability discovered

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Researchers at the Centre for Addiction and Mental Health (CAMH) led a study discovering a gene for a new form of intellectual disability, as well as how it likely affects cognitive development by disrupting neuron functioning.

CAMH Senior Scientist Dr. John Vincent and his team found a mutation in the gene NSUN2 among three sisters with intellectual disability, a finding to be published in the May issue of the American Journal of Human Genetics.

The discovery was made after mapping genes in a Pakistani family, in which three of seven siblings had intellectual disability as well as muscle weakness and walking difficulties, says Dr. Vincent, who heads the Molecular Neuropsychiatry and Development Laboratory in the Campbell Family Mental Health Research Institute at CAMH.

Intellectual disability is a condition in which individuals have limitations in their mental abilities and in functioning in daily life. It affects one to three per cent of the population, and is often caused by genetic mutations.

Another study in the same journal, submitted together with the CAMH-led research, also identified NSUN2 gene mutations in Iranian and Kurdish families with intellectual disability. As with the Pakistani family, first cousin marriages in these families carrying the mutations increased the likelihood of intellectual disability among their children, and enabled researchers to focus on areas to map genes.

"The combined results from these two studies mean that NSUN2 is among the most common causes of intellectual disability resulting from recessive genes," says Dr. Vincent.

As a recessive disorder, a child must inherit one defective NSUN2 gene from each parent to develop intellectual disability. This gene, located on chromosome 5p, encodes a type of protein called an RNA methyltransferase.

At the cellular level, the researchers found that the mutated protein was prevented from reaching its target area within the nucleus of a cell. As a result, it was unable to perform its normal role in cell division and/or RNA methylation.

Collaborators from the Wellcome Trust Centre for Stem Cell Research in Cambridge, U.K., showed which type of brain cells were likely to be most affected by this mutation. They are called Purkinje cells, a type of neuron that responds to the neurotransmitter GABA. Purkinje cells also control motor coordination, which were affected in the Pakistani family.

"We speculate that the muscle effects may result from the accumulation of the NSUN2 protein outside its target area in the nucleus," says Dr. Vincent.

To date, Dr. Vincent's lab has identified five genes causing different forms of recessive intellectual disability.

Provided by Centre for Addiction and Mental Health