Gene identified as cause of some forms of intellectual disability

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A gene involved in some forms of intellectual disability has been identified by scientists at the Centre for Addiction and Mental Health (CAMH), as published this month in The *American Journal of Human Genetics*. The gene is called TRAPPC9.

In the same journal two other international research teams independently confirm the findings of Dr. John B. Vincent, a scientist at CAMH, and his team. "This spotlights the intense interest that genetics is bringing to types of inherited intellectual disability that, to date, have been poorly understood," says Dr. Vincent.

"Now that we have identified TRAPPC9 as a gene that may be associated with hundreds of thousands of cases of intellectual disability world-wide, we can build on that knowledge with research to help individuals and their families," says Dr. Vincent.

May account for many cases of intellectual disability

Unlike intellectual disabilities that are part of a syndrome with other medical conditions or physical abnormalities, TRAPPC9 is associated with non-syndromic types of intellectual disability; these cause up to 50 per cent of intellectual disability worldwide. "The discovery announced today sheds light on a gene for intellectual disability on one of the non-sex chromosomes," says Dr. Vincent, "just the seventh such gene that we know of." The mutation in the TRAPPC9 gene identified by Dr. Vincent's team causes the production of a truncated version of a protein

and results in faulty cell function.

Findings in two families

Because there are no highly recognizable physical differences that are associated with the non-syndromic intellectual disabilities, it is more difficult to tease out the genetic mutations that may cause them. But researchers and families themselves have long suspected an inherited factor, based on patterns observed in extended families. Families with many affected individuals, and particular families from cultures where cousin-cousin marriages are common, have become invaluable in the search for such genes, and with recent advances in technology it is now possible to map disease-causing genes in a single family.

Dr. Vincent's team first identified and mapped out the TRAPPC9 gene in a large family from Pakistan that had at least seven members with non-syndromic intellectual disability. "To date, most such genes have only been found responsible for disease in a single family," he adds.

But Dr. Vincent's team also found a mutation in the same gene in a family from Iran, confirming the gene's importance. "This additional finding gives us a very strong reason to continue to explore the gene and its possible mutations," he says.

Normal brain function

Future research may include studying how the gene is involved in normal brain function, as well as studying genes with similar functions as candidate genes for intellectual disability, and devising potential therapeutic strategies. Dr. Vincent's team aims to provide scientists more clues to understand, diagnose, prevent, and treat intellectual disabilities.

Intellectual disabilities, also known as developmental delay or mental

retardation, are a group of disorders defined by diminished cognitive and adaptive development. Affecting more males than females, they are diagnosed in between one and three percent of the population.

Provided by Centre for Addiction and Mental Health