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Two new genes linked to intellectual disability

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Researchers at the Centre for Addiction and Mental Health have discovered two new genes linked to intellectual disability, according to two research studies published concurrently this month in the journals *Human Genetics* and *Human Molecular Genetics*.

"Both studies give clues to the different pathways involved in normal neurodevelopment," says CAMH Senior Scientist Dr. John Vincent, who heads the MiND (Molecular Neuropsychiatry and Development) Laboratory in the Campbell Family Mental Health Research Institute at CAMH. "We are building up a body of knowledge that is informing us which kinds of genes are important to, and involved in, intellectual disabilities."

In the first study, Dr. Vincent and his team used microarray genotyping to map the genes of a large Pakistani family which had intermarriage. Five members of the youngest generation were affected with mild to moderate intellectual disability. Dr. Vincent identified a truncation in the FBXO31 gene, which plays a role in the way that proteins are processed during development of neurons, particularly in the cerebellar cortex.

In the second study, using the same techniques, Dr. Vincent and his team analyzed the genes of two families with intermarriage, one Austrian and one Pakistani, and identified a disruption in the METTL23 gene linked to mild recessive intellectual disability. The METTL23 gene is involved in methylation—a process important to brain development and function.

About one per cent of children worldwide are affected by non-syndromic (i.e., the absence of any other clinical features) intellectual disability, a condition characterized by an impaired capacity to learn and process new or complex information, leading to decreased cognitive functioning and social adjustment. Although trauma, infection and external damage to the unborn fetus can lead to an intellectual disability, genetic defects are a principal cause.

These studies were part of an ongoing study of affected families in Pakistan, where the cultural tradition of large families and consanguineous (inter-) marriages among first cousins increases the likelihood of inherited intellectual disability in offspring.

"Although it is easier to find and track genes in consanguineous families, these genes are certainly not limited to them," Dr. Vincent points out. A recent study estimated that 13

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