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Scientists discover gene behind rare disorders

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Scientists at the Montreal Neurological Institute and Hospital – The Neuro, McGill University working with a team at Oxford University have uncovered the genetic defect underlying a group of rare genetic disorders.

Using a new technique that has revolutionized genetic studies, the teams determined that mutations in the RMND1 gene were responsible for severe neurodegenerative disorders, in two infants, ultimately leading to their early death. Although the teams' investigations dealt with an infant, their discovery also has implications for understanding the causes of later-onset neurological diseases.

The RMND1 gene encodes a protein that is an important component of the machinery in mitochondria which generates the chemical energy that all cells need to function. Mutations in genes affecting mitochondrial function are common causes of neurological and neuromuscular disorders in adults and children. It is estimated that one newborn baby out of 5000 is at risk for developing one of these disorders. Mortality among such cases is very high.

"Mitochondria are becoming a focus of research because it's clear they're involved in neurodegenerative disorders in a fairly big way," says Dr. Eric Shoubridge, an internationally recognized specialist on mitochondrial diseases at The Neuro and lead author of the paper published in *The* American Journal of Human Genetics. "For instance, we're finding that dysfunctional mitochondria may be at the heart of adult-onset disorders like Parkinson's and Alzheimer's disease."

Discovery of the mutations in the RMND1 gene involved using whole-exome sequencing at the McGill University and Genome Québec Innovation Centre. This technique allows all of the genes in the body that code for proteins to be sequenced and analyzed in a single experiment. At a cost of about $1000, whole-exome sequencing is much more economical than previous techniques in which lists of candidate genes had to be screened in the search for mutations. The technique is poised to change the face of genetic diagnosis, making testing more efficient and available.

"Parents who have had a child with a mitochondrial disorder and who are hesitating to have another child now have the possibility to know the cause of the disease. With genetic information, they have reproductive options like in vitro fertilization," says Dr. Shoubridge. The discovery of the RMND1 gene's role sheds light on disorders of mitochondrial energy metabolism, but therapies to alleviate or cure such disorders remain elusive. Dr. Shoubridge is hopeful that the discovery will encourage pharmaceutical interest. "Drug companies are starting to be interested in rare diseases and metabolic disorders like this. They're picking some genes as potential drug candidates."

Provided by McGill University