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Researchers discover gene behind devastating vitamin B12-related disorder

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Swiss, British and Canadian researchers have identified the gene responsible for a rare but serious genetic disorder and have simultaneously provided more clues as to how vitamin B12 works in the body. Their results will be published April 3 in the *New England Journal of Medicine*.

Scientists at the University Children's Hospitals of Basel and Zurich in Switzerland, Brunel University in West London, England and McGill University and the McGill University Health Centre (MUHC) in Montreal, Canada, have discovered the MMADHC gene, the role it plays in the metabolism of vitamin B12, and its relationship to the vitamin B12-related disorder, isolated and combined homocystinuria and methylmalonic aciduria (MMA) of the cblD variety..

Authors of the study include Dr. David Coelho, Dr. Terttu Suormala and Dr. Brian Fowler of the University Children's Hospital, Basel, Dr. David Rosenblatt and his graduate student Jordan Lerner-Ellis of McGill and the MUHC and colleagues at the University Children's Hospital, Zurich, the University of Zurich and Brunel University. In 2005, Dr. Rosenblatt and his McGill and MUHC colleagues made a related breakthrough involving another gene, called MMACHC.

Isolated and combined homocystinuria and MMA of the cblD variety is a rare genetic inability to process vitamin B12, which is usually diagnosed in infancy or childhood. Patients may suffer from a range of debilitating health problems, including serious developmental delay,

psychosis and anemia. Despite the variety of symptoms presented by the disorder, this research shows all of them are caused by mutations in different parts of the same gene.

Vitamin B12 is an essential water-soluble vitamin found in animal-based foods -- including dairy, eggs, meat, poultry, fish and shellfish -- but not in plants. It is vital for the synthesis of red blood cells and the healthy maintenance of the nervous system, and also helps control homocysteine levels.. Excess homocysteine is associated with increased risk of heart disease, stroke and dementia.

“Most patients with B12 problems have difficulty absorbing the vitamin, or may be vegans who don’t get it in their diet,” said Dr. Rosenblatt, Chair of McGill’s Department Human Genetics, Director of Medical Genetics in Medicine at the MUHC, and Chief of Medical Genetics at the Jewish General Hospital. “However, this select group of patients becomes extremely sick because their bodies cannot transform the vitamin into its active forms.”

The research relied heavily on the expertise developed at McGill and Basel as world referral centres for the diagnosis of B12-related genetic diseases, Dr. Rosenblatt said. The study was funded in part by the Canadian Institutes of Health Research (CIHR).

“This important paper - published in the world's highest impact medical journal - is on-going testimony to the international leadership of Dr. Rosenblatt and his colleagues at McGill in their studies of vitamin B12 and the genetic diseases that disrupt the ability of the body to use vitamin B12,” said Dr. Roderick McInnes, Scientific Director of CIHR's Institute of Genetics. “This research also exemplifies the outstanding genetics research done by Canadian scientists.”

“This discovery offers earlier diagnosis and treatment options for this

serious disease, and also helps explain the mechanism of how vitamin B12 works in everyone," said Dr. Rosenblatt.

Source: McGill University