Vitamin B12 deficiency: Tracking the genetic causes

August 26 2012

Vitamin B12 is essential to human health. However, some people have inherited conditions that leave them unable to process vitamin B12. As a result they are prone to serious health problems, including developmental delay, psychosis, stroke and dementia. An international research team recently discovered a new genetic disease related to vitamin B12 deficiency by identifying a gene that is vital to the transport of vitamin into the cells of the body. This discovery will help doctors better diagnose this rare genetic disorder and open the door to new treatments. The findings are published in the journal *Nature Genetics*.

"We found that a second transport protein was involved in the uptake of the vitamin into the cells, thus providing evidence of another cause of hereditary vitamin B12 deficiency", said Dr. David Rosenblatt, one of the study's co-authors, scientist in medical genetics and genomics at the Research Institute of the McGill University Health Centre (RI MUHC) and Dodd Q. Chu and Family Chair in Medical Genetics and the Chair of the Department of Human Genetics at McGill University. "It is also the first description of a new genetic disease associated with how vitamin B12 is handled by the body".

These results build on previous research by the same team from the RI MUHC and McGill University, with their colleagues in Switzerland, Germany and the United States. In previous work, the researchers discovered that vitamin B12 enters our cells with help from of a specific transport protein. In this study, they were working independently with two patients showing symptoms of the cblF gene defect of vitamin B12

metabolism but without an actual defect in this gene. Their work led to the discovery of a new gene, ABCD4, associated with the transport of B12 and responsible for a new disease called cblJ combined homocystinuria and methylmalonic aciduria (cblJ-Hcy-MMA).

Using next generation sequencing of the patients' genetic information, the scientists identified two mutations in the same ABCD4 gene, in both patients. "We were also able to compensate for the genetic mutation by adding an intact ABCD4 protein to the patients' cells, thus allowing the vitamin to be properly integrated into the cells," explained Dr. Matthias Baumgartner, senior author of the study and a Professor of metabolic diseases at Zurich's University Children's Hospital.

Vitamin B12, or cobalamin, is essential for healthy functioning of the human nervous system and red blood cell synthesis. Unable to produce the vitamin itself, the human body has to obtain it from animal-based foods such as milk products, eggs, red meat, chicken, fish, and shellfish – or vitamin supplements. Vitamin B12 is not found in vegetables.

"This discovery will lead to the early diagnosis of this serious genetic disorder and has given us new paths to explore treatment options. It also helps explain how vitamin B12 functions in the body, even for those without the disorder," said Dr. Rosenblatt who is the director of one of only two referral laboratories in the world for patients suspected of having this genetic inability to absorb vitamin B12. Dr. Rosenblatt points out that the study of patients with rare diseases is essential to the advancement of our knowledge of human biology.

Provided by McGill University Health Centre