Dysfunction of cellular powerplant shakes B-vitamin metabolism and causes genetic damage

March 4 2016

The recent Finnish study clarified a mechanism underlying a severe progressive children's brain disease and adult's muscle disease. The results indicate for the first time that the energy-metabolic defect in a cell can shake its B-vitamin balance and lead to genetic changes.

The study was led by MSc Joni Nikkanen in the research group of Professor Anu Suomalainen-Wartiovaara, University of Helsinki, and the results were published in a distinguished science journal, *Cell Metabolism*.

Mitochondria are the cellular powerplant, but their functions in conjunction with B-vitamins are only starting to be revealed. When nutrient status is good, vitamin B9, folate, turns mitochondria to cellular builders. Through folate, mitochondria produce substances to make ingredients for genome replication and repair, cell membrane renewal and synthesis of antioxidants. The mechanism also inlcudes other B-vitamins.

The researchers showed that a progressive mitochondrial myopathy, PEO-disease, and infantile spinocerebellar ataxia, both caused by mitochondrial dysfunction, lead to shaken folate-metabolism, irrespective of nutrient intake. This leads to the imbalance of ingredients required for DNA synthesis, and consequently to genetic damage and/or reduction of mitochondrial genome amount.

"These results indicate for the first time that the energy-metabolic defect in a cell can shake its B-vitamin balance and lead to genetic changes. This information opens new routes in search for treatment, especially concerning specific forms of B-vitamins as specific modifiers of metabolic routes", Professor Anu Suomalainen-Wartiovaara states.

Linus Pauling, who was twice awarded with Nobel prize, suggested in his late career stage that metabolic imbalance in a cell can cause a vitamin metabolic imbalance, irrespective of nutrient intake, and contribute to disease progression. "The hypothesis was heavily criticized at the time. The current results of our study support Pauling's original idea", Wartiovaara-Suomalainen says.

More information: Joni Nikkanen et al. Mitochondrial DNA Replication Defects Disturb Cellular dNTP Pools and Remodel One-Carbon Metabolism, *Cell Metabolism* (2016). DOI: 10.1016/j.cmet.2016.01.019

Provided by University of Helsinki