Medical Xpress

# New inherited neurometabolic disorder discovered

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Researchers at the Swedish medical university Karolinska Institutet have discovered a new inherited disorder that causes severe mental retardation and liver dysfunction. The disease, adenosine kinase deficiency, is caused by mutations in the ADK gene, which codes for the enzyme adenosine kinase.

The findings, which are presented in the American Journal of Human Genetics, were made possible through the detailed biochemical examination of a Swedish family in which two children suffered from progressive brain damage and abnormal liver function that could not be traced to known mechanisms. One symptom displayed by the children was the impaired metabolism of the amino acid methionine.

By sequencing all protein-coding gene sequences in the family - a process known as whole-exome sequencing - the team was able to identify a gene the function of which matched the biochemical abnormality. Whole-exome analyses were conducted at the Science for Life Laboratory (SciLifeLab) in Stockholm. Two additional unrelated families could then be identified with the same clinical profile and mutations in the same disease gene.

The findings illustrate the strength of combining the detailed biochemical examination of patients with the large-scale methods of analysing our genetic makeup that have recently become available, in order to expose new mechanisms behind congenital diseases. Modern tools of genetic analysis make it considerably easier to identify the

damage responsible for hereditary diseases, which is essential if the affected families are to receive correct information about their disease. It is also a critical first step towards the development of new therapies.

The newly discovered disease, adenosine kinase deficiency, sheds light on an unexpected functional link between two known metabolic processes: the methionine cycle and adenosine/AMP metabolism, thus revealing a previously unknown pathogenetic mechanism. The study was led by Dr. Anna Wedell, Professor at the Department of Molecular Medicine and Surgery, Karolinska Institutet. Dr Wedell is also affiliated to Centre for Inherited Metabolic Diseases at the Karolinska University Hospital, the Center for Molecular Medicine (CMM), and the SciLifeLab in Stockholm.

**More information:** Magnus K. Bjursell, et al., Adenosine Kinase Deficiency Disrupts the Methionine Cycle Causing Hypermethioninemia, Encephalopathy and Abnormal Liver Function, Am J Hum Genet, online 29 September 2011

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