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Genetic disorder causing strokes and vascular inflammation in children has been discovered

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Academy research fellows from University of Turku (Finland), Andrey and Anton Zavialov, and a team of researches from the National Institutes of Health (NIH), USA, discovered that inherited mutations in a blood enzyme called ADA2 cause a syndrome of sporadic fevers, skin rashes and recurring strokes, beginning early in childhood. The novel genetic disorder was called deficiency of ADA2, or DADA2.

The disease has a broad range of symptoms and its severity varies significantly, which represent a problem for making an accurate diagnosis. Since the cause of the disease is now known, it will be possible to confirm DADA2 by gene sequencing or measuring the enzymatic activity of ADA2. The group of Dr. Andrey Zavialov is now working on development of novel DADA2 diagnostics. "The screening for mutations in ADA2 or its activity in blood of patients will show how common the disease is and will likely provide explanation to some other poorly understood disorders" Dr Andrey Zavialov said.

The discovery of the molecular basis of DADA2 has treatment implications. Since ADA2 circulates in the blood stream, the researches are evaluating a way to replace ADA2 that is missing in the bloodstreams of those affected by DADA2. For example, freshly frozen plasma from healthy donors could be used to restore ADA2 functionality for treated patients. The groups of Drs Anton and Andrey Zavialov will also work on developing artificial forms of the protein. "We have an excellent

experience and wealth of structural information for engineering therapeutic ADA2" said Dr. Anton Zavialov, who recently determined an atomic resolution 3D structure of the protein.

The study has been published in the top medical journal, *New England Journal of Medicine*.

More information: www.nejm.org/doi/full/10.1056/NEJMoa1307361

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