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One specific gene explains many diseases

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Genetic differences in the FADS1 gene determine the risk for many different diseases. The ability to produce polyunsaturated fats like omega-3 and omega-6 differs between individuals and this affects the risk for disturbed metabolism, inflammatory diseases and several types of cancer. Scientists at Uppsala University/SciLifeLab in Sweden have clarified this in detail and the work is published in the journal *Nucleic Acids Research*.

"After detailed experiments we now know exactly which mutation in the region that is functional and directly involved in FADS1 regulation," says Gang Pan at the Department of Immunology, Genetics and Pathology, Uppsala University and one of the authors of the article.

In this new study the scientists show that the gene region which controls FADS1 appeared 6 million years ago and is present in human and chimpanzee but not in other species. Since increased production of omega-3 and omega-6 is favourable to brain development this event may have contributed to human evolution. A mutation happened 300 000 years ago which further increased the capacity of the gene to produce both omega-3 and omega-6 fatty acids. This mutation constituted an evolutionary advantage that has led to the more active variant of FADS1 being the common one in major parts of the world.

In historical times people ate equal amounts of omega-3, coming from fish and vegetables, and omega-6 coming from meat and egg.

"Since we now live longer and have changed our diet radically - modern

food in the Western world has drastic excess of omega-6 - what was an advantage in historical times may have turned against us and become an increased risk for many diseases," says Gang Pan.

The genetic difference at FADS1 affects levels of LDL- and HDL-cholesterol, several other important fats, blood sugar and the metabolic syndrome, as well as how well we respond to treatment to control blood fat. It affects the risk for allergies and inflammatory diseases like rheumatism and inflammatory bowel disease. In addition it influences the risk for colon cancer and other types of cancer, as well as the heart rate.

"Polyunsaturated fats are involved in a surprising number of processes and the hope is that the new knowledge will make it possible to treat some of these diseases in a targeted way," says Claes Wadelius, Professor in Medical Genetics at Uppsala University and SciLifeLab, Sweden, and the main author of the study.

More information: Gang Pan, Adam Ameur, Stefan Enroth, Madhusudhan Bysani, Helena Nord, Marco Cavalli, Magnus Essand, Ulf Gyllensten and Claes Wadelius*, PATZ1 down-regulates FADS1 by binding to rs174557 and is opposed by SP1/SREBP1c, *Nucleic Acids Research*, 2016 1-15, DOI: 10.1093/nar/gkw1186

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