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Large Finnish genetic study uncovers potential new treatments for inflammatory diseases

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Researchers from the Research Centre of Applied and Preventive Cardiovascular Medicine at the University of Turku, Finland, have studied over ten million DNA variations and found new links between the human genome and inflammation tracers. The study uncovered new possibilities for treatment of diseases such as multiple sclerosis, Crohn's disease and coeliac disease.

Cytokines and growth factors, which circulate in the bloodstream, are important proteins for regulating inflammation reactions. Changes in their mode of operation have been linked with many inflammatory diseases, such as Crohn's disease, multiple sclerosis, atherosclerosis, ulcerative colitis and many types of cancer.

In this latest study, based on population data and coordinated by the University of Turku's Research Centre of Applied and Preventive Cardiovascular Medicine, an investigation was made of the links between 41 different cytokines and growth factors and 10.7 million DNA variations.

"We wanted to find out the molecular-level processes that lead to an increased risk of developing inflammatory diseases. Understanding these processes will enable more effective treatment of diseases," explains Professor Olli Raitakari, Director of the Research Centre.

Researchers noticed that the medicine daclizumab, previously used for treating organ rejection reactions, could possibly also be used in the treatment of multiple sclerosis and Crohn's disease. In addition, an increase in the activity of MIP1b-cytokine could also serve as a method of treatment against coeliac disease and Behcet disease. Further clinical studies are required to confirm the observations.

Evidence from human genetics speeds up medical development

Technological development has enabled the practice of genome-wide association studies since the turn of the century.

In these kinds of studies, millions of DNA variations are examined and their impact is assessed for each property being studied. The studies carried out so far have succeeded in uncovering, for example, over one hundred genomic loci which have an impact on the risk of developing Crohn's disease or ulcerous colitis.

In studies of connections between genetic variations and disease risks, the precise molecular process causing the increased risk often remains unclear. In order to uncover this molecular process, genome-wide association studies use as response variables molecules that mediate disease-risk through the bloodstream, such as cytokines and growth factors, instead of using the diseases themselves.

"It has been shown that for those drug candidates where there is evidence from human genetics of their effectiveness, the chance of being approved in clinical studies testing effectiveness and safety is increased two-fold. Various estimates made of the costs of developing for market a single medicinal molecule have come out at around 800 million dollars. Genetics research can offer significant savings for

medical development," Professor Raitakari points out.

The data used in the study was composed of internationally unique long-term research data covering risk factors for cardiovascular diseases among Finns.

The Cardiovascular Risk in Young Finns Study is one of the largest follow-up studies into cardiovascular risk from childhood to adulthood. Using 1980 as the baseline, 3,596 subjects participated in the first cross-sectional study, and follow-up visits have been conducted in 1983, 1986, 2001, 2007, and 2011.

The national FINRISK surveys have been conducted at 5-year intervals between 1972 and 2012 to monitor cardiovascular risk factor levels in Finland. A new independent sample has been collected for each survey and a total of 53,589 subjects aged 25–74 have participated in these surveys.

The research findings were published in The *American Journal of Human Genetics*.

More information: Ari V. Ahola-Olli et al. Genome-wide Association Study Identifies 27 Loci Influencing Concentrations of Circulating Cytokines and Growth Factors, *The American Journal of Human Genetics* (2017). DOI: 10.1016/j.ajhg.2016.11.007

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