

## Several protein biomarkers protect against disease development

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Inflammatory processes are associated with a large range of human diseases, including rheumatic diseases and allergies. Protein biomarkers are measurable molecules that can have a prognostic value in patients, be



used to diagnose disease, or indicate severity of disease. Today, a large number of plasma proteins have been identified as potential biomarkers for inflammatory diseases, where they are often highly expressed in patients with the disease.

However, the <u>causal relationship</u> between a <u>protein biomarker</u> and <u>inflammatory diseases</u> is generally unknown. The protein could either be expressed in response to the disease, to protect from tissue damage, or the high expression of the protein could be the underlying factor behind the development of disease.

In the current study, the scientists used a method called Mendelian randomisation to identify protein biomarkers that have a direct causal effect on protecting or promoting disease development.

"In Mendelian randomisation we use <u>genetic information</u> to determine whether individuals born with high natural levels of a protein will have a higher or a lower risk of developing a disease. Mendelian randomisation has often been called nature's own clinical trial since individuals are randomized at birth to receive genetic variants that might increase the protein biomarker levels," says Torgny Karlsson, statistician at the Department of Immunology, Genetics and Pathology, Uppsala University, and one of the leading researchers behind the study.

Almost one hundred protein biomarkers, previously associated with inflammatory disease, were targeted in the current study. The study showed that IL-12B protects against psoriasis and psoriatic arthropathy, LAP-TGF-b-1 against osteoarthritis, TWEAK against asthma, VEGF-A against ulcerative colitis, and LT-a against both type 1 diabetes and rheumatoid arthritis. Only one biomarker was found to have a damaging effect, namely IL-18R1, which increased the risk of developing allergy, hay fever and eczema.



"Surprisingly, we found that a larger fraction of the proteins investigated actually protect against disease development, rather than increasing the risk of disease," says Weronica Ek, associate professor at the Department of Immunology, Genetics and Pathology, Uppsala University, and one of the leading researchers behind the study.

"Our results suggest that, in healthy individuals, such proteins are expressed to protect against <u>tissue damage</u>," says Ek.

The protective effects identified are important, since they can shed light on the pathogenesis of inflammatory disease. However, many of these proteins may serve, or are already being investigated, as potential drug targets.

"Since protein biomarkers are markers of disease, treatments that lower the levels of these proteins are a natural choice to treat symptoms of disease in patients. However, our results suggest that such treatments might have adverse effects in healthy tissues and possibly even increase the risk of a disease if used incorrectly," says Åsa Johansson, group leader at the Department of Immunology, Genetics and Pathology, SciLifeLab, Uppsala University, and the senior investigator behind the study.

"In addition, the proteins identified represent potential novel intervention points for disease prevention," says Johansson.

**More information:** Weronica E. Ek et al, Causal effects of inflammatory protein biomarkers on inflammatory diseases, *Science Advances* (2021). DOI: 10.1126/sciadv.abl4359. www.science.org/doi/10.1126/sciadv.abl4359



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