Medical Xpress

Large-scale proteomics in population-based studies may contribute to a better understanding of diseases

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In an article revealed in *Nature*, scientists from deCODE Genetics, a subsidiary of the pharmaceutical company Amgen, demonstrated how plasma proteomics can contribute to a better understanding of diseases.

The study's focus on the plasma proteome led the team to find associations between various diseases and the levels of specific proteins. "Measuring a great number of proteins in a population-based cohort enables the discovery of circulating biomarkers and the early detection of disease," says Patrick Sulem, scientist at deCODE genetics and one of the senior authors on the paper.

Additionally, the scientists leveraged genetic factors influencing protein levels to illuminate the biological ties between sequence variant associations and pathogenesis of disease occurrence. "The biological relationship between an association of a sequence variant with disease can often be elusive. Incorporating proteo-genomics into the analysis can uncover the molecular mechanisms of disease development," says Kári Stefánsson, scientist at deCODE genetics.

The scientists analyzed data from about 50,000 individuals of European, African and Asian ancestry from the UK Biobank, using 2,941 immunoassays on the Olink Explore platform. The data were generated by the UK Biobank Pharma Proteomics Project (UKB-PPP), a consortium of thirteen biopharmaceutical companies, including Amgen, studying circulating protein biomarkers.

The authors compared these findings to a previous study where they analyzed data from around 40,000 Icelanders using 4,907 aptamer-based assays on the SomaScan platform. In total they identified over 80,000 associations between sequence variants and protein levels and over 500,000 associations of diseases and other traits with protein levels.

The scientists observed discrepancies in the measurements of protein levels when a subset of samples was examined using both platforms. These differences between platforms affected the discovery of circulating disease biomarkers and the detection of genetic factors that influence both protein levels and disease manifestation at the same time.

By examining large cohorts in Iceland and the UK, a substantial number of associations could be detected, making the comparison meaningful. The authors emphasized the value of validation of individual assays on a case-by-case basis.

"While these two proteomics platforms serve as useful instruments for simultaneous testing of thousands of proteins in large datasets, careful validation is necessary for individual proteins," says Kári Stefánsson, CEO of deCODE genetics and one of the senior authors on the paper.

More information: Patrick Sulem, Large-scale plasma proteomics comparisons through genetics and disease associations, *Nature* (2023). DOI: 10.1038/s41586-023-06563-x. www.nature.com/articles/s41586-023-06563-x

Provided by deCODE genetics