Proteomics and genomics as risk predictors of cardiometabolic diseases

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Cardiovascular disease (CVD) and type 2 diabetes (T2D) are interconnected chronic conditions, collectively considered cardiometabolic disease, which cause significant morbidity and mortality worldwide. To identify biomarkers for earlier detection and disease prevention, we are developing predictors of cardiometabolic disease endpoints using genomics and proteomics. We develop a Protein Risk Score (ProtRS) for incident disease prediction in the Trøndelag Health Study and FinnGen using targeted measurements from blood plasma. We evaluate the discrimination and calibration of these ProtRSs as novel predictors of disease in addition to polygenic scores and other conventional risk factors. We also characterize the gene ontology biological pathways indicated by the protein associations with CVD and T2D. Finally, we identify genome-wide protein quantitative trait loci (pQTL) for over 7,000 proteins measured on the SomaScan v4.1 assay. We use these to create pQTL-based polygenic scores and evaluate their predictive performance as well. These findings highlight the potential of the plasma proteome in disease risk stratification. Future validation in additional population biobanks will help determine the clinical utility of these protein-based risk predictors.