INVITED EDITORIAL

A novel urinary proteomic classifier predicts the risk of coronary artery disease

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Proteomics is a rapidly evolving field of molecular biology that studies the structure, function, and interactions of proteins within a cell, tissue, or organism. It involves the analysis of a set of proteins expressed by an organism or a particular cell type under specific conditions. The main goal of proteomics is to understand the complex network of protein interactions and their regulation in health and disease.[1]

Cardiovascular disease is a leading cause of mortality worldwide,[2] and there is a growing interest in using proteomics to predict cardiovascular risk. Proteomics can be used to identify proteins that are differentially expressed or modified in patients with cardiovascular disease compared to healthy individuals. By analyzing the patterns of protein expression or modification, researchers can identify potential biomarkers of disease and develop new diagnostic and therapeutic strategies.[3]

For example, proteomics can be used to identify proteins that are associated with atherosclerosis. Several studies have shown that changes in the levels of specific proteins, such as lipoprotein particles, apolipoproteins, and complement proteins, are associated with an increased risk of cardiovascular disease. Proteomics can also be used to study the effects of lifestyle interventions, such as diet and exercise, on cardiovascular risk. By analyzing changes in the expression or modification of specific proteins, researchers can identify molecular mechanisms underlying the protective effects of these interventions.[4,5]

In summary, proteomics is a powerful tool for studying the complex molecular mechanisms underlying cardiovascular disease and for identifying potential biomarkers and therapeutic targets. In this issue of the *European Journal of Preventive Cardiology*, Dongmei Wei and collaborators[6] assess the association of biomarkers derived from urine proteomics with development of coronary artery disease (CAD) in a retrospective analysis of longitudinal data.

A derivation cohort of 72 individuals free of CAD matched by age, sex, hypertension, renal function, and total cholesterol were evaluated. Urine biomarkers were compared in those who developed or not CAD after 8 years (36 with and 36 without CAD, respectively). The validation cohort comprised 893 individuals (115 with CAD) from the Flemish Study on Environment, Genes and Health Outcomes study[7] as well 156 individuals (80 with CAD) from the Human Urinary Proteome Database,[8] followed up to 8 years. Intriguingly, 160 urinary peptides related to collagen turnover, lipid metabolism, and inflammation were selected. New classifiers were compared with 2 sets of urine proteomic classifiers that had been previously tested (CAD238 and ACSP75).[9,10] Biomarkers were selected using robust statistical methods and machine learning. In the validation cohort, biomarkers were tested by multivariate Cox models.

The new proteomic classifier was positively associated with CAD, independent of the Framingham risk score (adjusted HR: 1.44, 95% CI: 1.01–2.95) or the SCORE2 risk score, recommended by the European Society of Cardiology[11] (adjusted HR:1.67, 95% CI: 1.14–2.45). Overall, the new classifier provided a strong discrimination for CAD that was superior to the two previous classifiers, improving both risk discrimination and reclassification (*Figure 1*).

These findings are in agreement with a previous report demonstrating that higher plasma concentrations of 15 inflammatory proteins were associated with higher risks of myocardial infarction after adjustment for medications and established cardiovascular risk factors; among these 15 biomarkers, five (IL-6, IL-18R1, CXCL1, CD6, and CDCP1) were independently associated with myocardial infarction.[12] Equally important, a proteomic approach had identified the pathways involved in cardiovascular disease attributable to physical inactivity,[13] leading to the understanding of a number of proteins and enzymes involved in atherosclerotic processes in sedentary individuals, emphasizing that physical activity is linked to protective pathways including anti-oxidation and anti-inflammation.[14]

Unfortunately, Wei *et al.* did not investigate the association between the urinary proteomic classifier and the severity or subtypes of CAD. Further studies, ideally prospective and with a large population, are warranted to evaluate whether the new urinary proteomic classifier can identify plaque volume and composition measured by ultrasound or computerized tomography. The peptides constituting the proteomic classifier were involved in diverse pathways associated with atherosclerosis, including inflammation, lipid metabolism, and collagen turnover (*Figure 1*); however, the exact molecular mechanisms linking these markers to CAD need to be determined in dedicated studies.
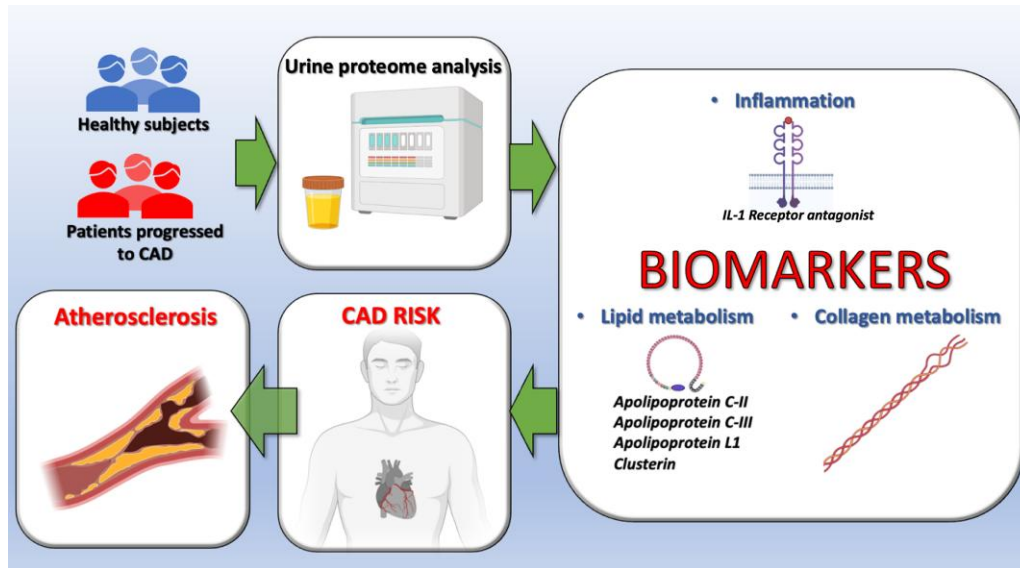

Figure 1 The peptides constituting the proteomic classifier used to predict coronary artery disease (CAD) are involved in diverse pathways associated with atherosclerosis, including inflammation, lipid metabolism, and collagen turnover.

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