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Commentary

Plasma lipid profiles differ among chronic inflammatory diseases

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Lipids participate in many biological processes and take part in a complex network of bioactive compounds and biochemical reactions. They act as inducers, suppressors, modulators, cellular structuring and signaling compounds, and mediators in many pathways, including inflammatory pathways [1,2]. Profiling lipids in human samples might advance the discovery of diagnostic, prognostic, and monitoring disease biomarkers, in addition to allowing the exploration of biological mechanisms [3]. Despite their utility, the variety of lipid species and the different ways to profile them has resulted in a lack of consensus targets that, ultimately, retarded the translation of findings into clinical practices. Mass spectrometry (MS)-based shotgun lipidomics simplifies methodological standardization because it uses no prior chromatographic separation to perform global analysis of lipids from crude biological lipid extracts and is potentially more translatable to clinical applications [4].

Lipidomics can be used to develop new clinical tools and advance the understanding of homeostatic and inflammatory processes related to chronic inflammatory systemic diseases such as atherosclerosis-related vascular diseases, including cardiovascular diseases (CVD), stable and unstable angina pectoris, myocardial infarction, and ischemic stroke (IS), as well as diseases with a high incidence of atherosclerotic and cardiovascular events such as systemic lupus erythematosus (SLE) [5,2]. The etiological mechanisms of inflammation for these chronic inflammatory diseases involve a complex and dynamic network that has not been fully elucidated. Delayed diagnosis gives rise to irreversible pathologic changes, and the scarcity of personalized therapeutic strategies causes severe loss of quality of life and life span for patients suffering from these illnesses, highlighting the need for facilitated diagnosis and identification of high-risk patients [6].

In this article of *EBiomedicine* [7], Matthiesen et al. are the first to use MS-based shotgun lipidomics to profile plasma lipids of two chronic inflammatory diseases with different etiologies. They analyzed plasma samples from healthy volunteers (n = 85) and patients diagnosed with CVD (n = 217), IS (n = 21), and SLE (n = 104). CVD patients were also stratified according to their stage of disease. The authors investigated 596 plasma lipids and, using machine learning statistical modeling, they pointed out commonalities in dysregulated lipids in vascular diseases and to a lesser extent in SLE, supporting the notion of a common etiology for vascular diseases (i.e., involving atherosclerotic lesions in blood vessels). All these diseases could be distinguished from one another and the healthy group based on molecular signatures. The authors also showed that the plasma lipid profiles of patients with the same disease (i.e., CVD) at different stages could be stratified, allowing new possibilities for patient management and risk-stratification.

The methodology of Matthiesen et al. could assist screening individuals at high risk for cardiovascular complications and could represent a valuable tool for early diagnosis. Follow-up of disease progression could also enable tailored therapeutic approaches, e.g. by identifying subpopulations [8]. Ideally, disease stratification could also be explored by this approach, especially in cases such as inflammatory bowel diseases [9], rheumatoid arthritis, and infectious diseases, the latter being exemplified by coronavirus disease 2019 [10].

Nevertheless, validation of the findings from Matthiesen et al. must be performed in larger cohorts with broad ranges of age, body mass index, gender, and race. This limitation pertains to most studies that search for new biomarkers. Collecting and analysing representative groups with substantial numbers of subjects is only possible in multicenter studies, which requires the cooperation of institutions across borders aimed at validating common biomarker models. In addition to using samples to propose new methodologies, it is time to combine efforts to achieve actual clinical gains using MS-based lipidomics and other omics.

Contributors

PHGS, AARS, and AMP co-wrote this commissioned commentary.

Declaration of Competing Interest

The authors declare no conflicts of interest.

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