

The nutritional metabolomics crossroads: how to ensure success for dietary biomarkers

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The application of metabolomics in nutrition research has increased in recent years. Although it holds great promise, there are a number of issues or limitations that urgently need attention to enable it to deliver its full potential in the nutrition field. First, many studies do not report quantitative data, which makes any cross-study comparison difficult or the development of any reference values impossible. Second, there is an overreliance on association studies, with little understanding of the underlying biological processes. Third, replication in an independent cohort is often not possible due to a lack of resources. Notwithstanding these and other issues, the application of metabolomics in nutrition research has made important advancements in recent years. Examples include, but are not limited to, 1) the development of new biomarkers of dietary intake and 2) the application to intervention studies to understand the underlying mechanism of action.

In this issue of the Journal, Playdon et al. (1) identify a series of associations between 4 diet quality indexes and serum metabolite concentrations. Although some of the associations confirm previously identified dietary biomarkers, some novel findings are also reported. The utility of these findings in terms of dietary assessment for the nutrition community is very limited because of the lack of established dose responses and the lack of quantitative metabolite data and corresponding cutoffs or calibration curves. However, the demonstration yet again that dietary patterns are reflected in metabolite profiles supports previous findings and adds weight to the concept that metabolites may be potential objective measures of dietary intake (2, 3). The strength of the study lies in the robust determination of the 4 diet quality indexes, which the authors argue eloquently are more reproducible than the data-driven approaches. An examination of metabolic pathways at the diet quality level showed some potential pathways associated with healthy eating patterns. Interrogation of the metabolite profiles associated with healthy eating patterns has the potential to enable our understanding of the underlying mechanisms that lead to the health benefits. In this regard, the study by Playdon et al. lays the foundations for such work. Interestingly, AlEsa et al. (4) show that adherence to healthful dietary patterns is associated with favorable concentrations of many cardiometabolic and endocrine biomarkers. Applications of metabolomics in such a context may shed light

into the mechanisms by which the health benefits are mediated. Furthermore, this knowledge could be used in the development of future diet quality indexes that are directly related to metabolic health.

With respect to dietary biomarkers derived from metabolomics, the time has come when it is imperative that we develop standardization and a clear demonstration of the utility of dietary biomarkers in terms of dietary assessment. Similar to previous editorials in which there was a call for standardization in measurement approaches for nutritional biomarkers such as folate, there is now an urgent need for the community to adapt a more standardized approach to the measuring and reporting of metabolomics data (5). We now have had ~10 y of reported associations between food intake and biomarkers, and although there is no question about the links, it is now imperative to move these biomarkers into practice. To permit the use of dietary biomarkers in dietary assessment, it is essential that dose-response studies are performed with accurate and quantitative measurement of the biomarkers. The field now needs to progress in this direction to realize the full potential of metabolomics for the nutrition community. Also in this issue of the Journal, Lampe et al. (6) describe the type of study that needs to be performed to show the utility of identified candidate biomarkers for dietary assessment measurements. They show through a controlled-feeding study that a series of dietary biomarkers, including carotenoids, tocopherols, folate, vitamin B-12, and phospholipid fatty acids, performed as well as established energy (doubly labeled water) and protein (urinary nitrogen) recovery biomarkers in representing nutrient intake. Although these dietary biomarkers were not derived from metabolomics studies, the positive results and comparability with the accepted approaches are promising. For those of us who work in the area, this is an important example of what can be achieved.

The field of dietary biomarkers is at a crossroads: the continuation of reporting only associations with candidate biomarkers has the potential to extinguish the vision whereby these biomarkers can aid dietary assessment by acting as objective measures of intake. The true demonstration of the potential of these biomarkers is necessary in combination with the measurement

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First published online January 18, 2017; doi: 10.3945/ajcn.116.150847.

and reporting of quantitative metabolite data. Following this path should result in a bright future for dietary biomarkers and hopefully deliver on the promise of objective measures of intake.

The sole author was responsible for all aspects of the manuscript. The author had no conflicts of interest to declare.

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