Guest: Dr. Marta Guasch-Ferre is a research fellow at the Department of Nutrition at Harvard T.H. Chan School of Public Health.

Bob Barrett: This is a podcast from *Clinical Chemistry,* sponsored by the Department of Laboratory Medicine at Boston Children's Hospital. I am Bob Barrett.

In the era of precision medicine, it is no surprise that there is an emerging interest in personalizing one's diet based on their genetic make-up. This concept called, "precision nutrition," refers to the application of -omics techniques such as genomics and metabolomics, to achieve better prevention or treatment of disease to optimize nutrition.

There is a particular interest in metabolomics, which examines the vast and varied component of the metabolome and its potential to provide a comprehensive picture of overall dietary intake. This involves measuring expanded profiles of small molecule metabolites in saliva, blood, or urine and associating the resulting patterns with dietary intake and phenotypic information. Nutritional metabolomics may help researchers elucidate metabolic pathways relevant to human nutrition and identify objective dietary biomarkers or profiles that are associated with specific food exposures.

Currently, nutritional epidemiologic studies rely on self-reported dietary assessment methods that are subject to recall bias and measurement error and measure individual food intake versus true exposure as may be possible with metabolomics.

Though many metabolite biomarkers of individual foods and dietary patterns have been identified, some lack required sensitivity and specificity or may represent short-term intakes rather than long-term dietary habits. Additionally, there are technological and experimental challenges that must considered and resolved to advance efforts in applying metabolomics for examining the role of diet in human health.

The January 2017 *Clinical Chemistry* special issue on obesity includes a review article that summarizes the current and future roles of nutritional metabolomics.

For this podcast, we're joined by Dr. Marta Guasch-Ferre, the article's primary author. Dr. Guasch-Ferre is a research fellow at the Department of Nutrition at Harvard T.H. Chan School of Public Health. Her research interests include the role of the Mediterranean diet on type two diabetes and cardiovascular disease.

So doctor, first of all, to put your research into some context, what is the background of this work and what is nutritional metabolomics?

Dr. Guasch-Ferre: In the past few years, the scientific community has focused on a more integrated systems epidemiology approach, in which several fields converge to integrate the traditional knowledge with novel -omics techniques such as genomics and metabolomics. Nutritional epidemiology, which is the study of nutrition in large populations, has not been the exception and several studies having incorporated this -omics data in the past decade.

And along these lines and to answer your second question, the concept of nutritional metabolomics has emerged and refers to the integration of metabolomics profiling which is the identification of small molecules present in the biological sample with nutrition in complex bio systems. And in our article, we have provided an extensive review of the users of nutritional metabolomics, the study design, and the statistical approach used in these studies, as well as a review of the studies identifying metabolomics profiles related to its diet.

Bob Barrett: Can you tell us some of the key biomarkers of nutrients in foods or dietary patterns that were identified using nutritional metabolomics?

Dr. Guasch-Ferre: The most extensively studied food groups in nutritional metabolomics includes fruits, vegetables, meat, fish also whole grain cereals, nuts, wine, coffee, and chocolate. And biomarkers identified with the use of these metabolomic techniques include metabolites of different species such as amino acids, acetylcarnitine, carbohydrates, bio acids and pyrimidine and purine metabolites as well as lipid metabolites.

For example, proline and betaine have been identified as biomarkers of citrus intake in several studies. And other potential biomarkers, for example, of nut intake identified to include conjugated fatty acids certain in metabolites as well as microbial variety phenolic metabolites. However, most of these biomarkers still need to be validated and replicated in other studies.

And also, some studies have also evaluated metabolite signatures, of instead of a specific nutrients or food associated with dietary patterns. Dietary patterns that come to mind include vegetarian diets, western dietary patterns or Nordic and Mediterranean diets as well.

For example, our western dietary patterns have been associated with metabolite signatures that were characterized by high concentrations of branched-chain amino acids, aromatic acids and short-chain L-carnitines or Mediterranean diet interventions have been characterized by metabolites like olay, phospholipids and lysophospholipid.

I think an important thing to note here is that although these studies identified many metabolite biomarkers, these biomarkers sometimes are not sensitive or specific to dietary intakes and consequently they may not be good biomarkers of intake.

For example, this is the case of vitamin C that several character carotenoids and flavonoids are common to many fruits and vegetables and hence they can be used as genetic biomarkers for total fruit and vegetable intake but not maybe specific to individual fruits or vegetables. And nonetheless, I would say that nutritional metabolomics holds promise for the development of robust and unbiased strategy for measuring diet.

Bob Barrett: What are some of the applications of metabolomics in the field of nutritional epidemiology?

Dr. Guasch-Ferre: Nutritional metabolomics has two major uses. The first one is to identify biomarkers of intake in a more objective manner and trying to overcome some of the limitations of traditional methods such as record errors, health consciousness bias, and errors in nutrient estimation from food composition diets.

For example, nutritional metabolomics can discover novel biomarkers of intake and can be used to discriminate between non-consumers versus consumers of a specific food or diet and they can also generate biomarker patterns to evaluate the efficacy of nutritional interventions for maintaining and improving health at the individual level. And the second major use of nutritional metabolomics is to help disentangle molecular mechanisms by which diet affects health and disease. And although there has been much progress in identifying noble biomarkers of intake, there are several issues that need to be considered.

For example, as I mentioned before, some of these biomarkers may not be sensitive or specific to a particular food or dietary pattern. Second, because many biomarkers

have a short half-life and we would need multiple measurements to get our usual intake. And finally, sometimes, these biomarkers and metabolomic techniques are more expensive to measure than the use of traditional dietary instruments. Given these limitations, it is unlikely that, for now, metabolomics biomarkers will replace traditional dietary assessment using self-reported methods. Therefore, these biomarkers identified from metabolomics and traditional self-reported methods suggest validated food frequency questionnaires should be used in a complementary fashion rather than to substitute the traditional methods.

Bob Barrett: Well, finally doctor, where do you think research in this field is headed? Will nutritional metabolomics still be a buzzword, say, 10 years down the line?

Dr. Guasch Ferre: Wow, that's a good question. In the future, reproducible metabolomics biomarkers may be used to validate self-reported measurements of dietary intake. Also, they can be used to correlate estimates of dietary intake, identify novel biomarkers of food consumption, and probably provide objective biomarkers of adherence to dietary interventions and dietary patterns. From the standpoint of public health and procedure nutrition, the incorporation of nutritional metabolomics into traditional nutritional epidemiology can help to identify subgroups that differ in the response to specific dietary components, so that interventions can be tailored to those individuals who will benefit the most, thus reducing the cost and side effects for those who will not.

Bob Barrett: Dr. Marta Guasch-Ferre is a research fellow at The Department of Nutrition at Harvard T.H. Chan School of Public Health. She has been our guest in this podcast from *Clinical Chemistry*. I'm Bob Barrett. Thanks for listening.