Understanding the Interaction of Diet Quality with the Gut Microbiome and Their Effect on Disease

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As evidence emerges that higher diet quality predicts lower mortality (1) and incidence of type 2 diabetes (2), possible biologic mechanisms for this relation have been hypothesized. Besides the positive influence of diet quality on body weight, body fat distribution, and inflammatory status, food components and dietary patterns have been linked to the composition of gut microbiota (3). In addition, evidence has accumulated for a relation between gut microbial characteristics and type 2 diabetes (4). The cross-sectional investigation among Swedish adults in the current issue of the *Journal of Nutrition* adds new evidence to the triangular relation of dietary patterns, the presence of prediabetes as an indicator of risk to develop diabetes, and gut microbiota composition (5).

After applying principal component analysis to data from 4-d food records, the authors identified 2 dietary patterns: a Health-conscious and a Sugar and High-Fat Dairy pattern. Both explained relatively low proportions of dietary variation (6.8% and 5.2%, respectively). Positive contributors to the Health-conscious pattern included fruits/berries, nuts/seeds, vegetables/legumes, yogurt/cheese, and high-fiber grains, while sugar-sweetened beverages and red/processed meat had negative factor loadings. The Sugar and High-Fat Dairy pattern was characterized by high intakes of pastry/desserts, high-fat milk/cream, low-fiber bread, potatoes, and processed/red meat. The fact that tea, coffee, and butter loaded in the same direction for the 2 patterns illustrates 1 of the limitations of the a posteriori data-driven approach to assess diet quality.

Sequencing of the 16S ribosomal RNA gene (V1–V3 region) identified 64 genera and 8 phyla (5). Significant associations with the microbiota were primarily detected in relation to the Health-conscious pattern and not the Sugar and High-Fat Dairy pattern. This is in contrast to other cross-sectional studies that have linked long-term Westernized diet patterns to features in the microbial community composition (6, 7). The findings can be summarized as follows: *1)* participants with high scores on the Health-conscious patterns were ~50% less likely to present with prediabetes, an association that lost significance after adjustment for BMI, likely indicating an indirect action of diet quality on the microbiota through modifications of body weight; *2)* higher scores of the Health-conscious pattern were related to the abundance of 6 bacteria of the phylum *Firmicutes*: positively with *Roseburia*, *Lachnospira*, and unclassified in order RF39, and negatively to *Blautia*, *Eubacterium*, and *Anaerotruncus*; *3)* of the 6 bacteria associated with the dietary pattern, only *Roseburia* was related to a lower prevalence of prediabetes. *Roseburia* attenuated the association of the Health-conscious pattern with prediabetes, suggesting that a possible mediation effect may be present.

How do these findings compare to previous reports? As to the first side of the triangle, the existing evidence about an association between diet patterns and incidence of type 2 diabetes is extensive and strong, both for a priori and a posteriori dietary patterns (2). A meta-analysis showed that data-derived patterns characterized by red/processed meat, refined grains, high-fat dairy, and fried products were associated with a 44% higher diabetes risk, whereas a diet rich in vegetables, legumes, fruits, poultry, and fish predicted a 16% lower risk (2). The results for a priori patterns were similar; the Mediterranean diet, the most commonly studied pattern, predicted a 30% lower diabetes risk (2).

In terms of the second side of the triangle, not so many investigations have examined diet quality in relation to the gut microbiome. Nevertheless, the evidence is strong that dietary components bioavailable to microbiota, such as carbohydrates, dietary fats, proteins, and polyphenols, influence the gut microbiome (3). Beneficial effects of the Mediterranean diet on diversity and composition of gut microbiota have been detected in several investigations (8, 9). The authors of this commentary recently reported associations of several a priori dietary indices, including the Healthy Eating Index (HEI-2010) and the alternate Mediterranean Diet (aMED), with measures of fecal microbial community structure in the Multiethnic Cohort (MEC) (9). Among participants who had completed a validated quantitative FFQ 20 y before stool collection, dietary indices were positively associated with α diversity, lower abundance of the phyla Actinobacteria, and with 21 of the 103 genera tested. Of these, 12 genera within *Firmicutes* were positively associated and 9 (5 *Firmicutes*, 1 *Actinobacteria*, 3 *Proteobacteria*) were inversely associated with diet quality. The significant genera from the phyla *Firmicutes* included 7 members of the *Lachnospiraceae* family, although not *Roseburia*. Lower HEI-2005 scores were also associated with a lower relative abundance of *Roseburia* in a recent report (10).

A plausible biologic mechanism linking diet to the gut microbiome is that *Roseburia* and *Lachnospira* both metabolize fermentable carbohydrates, i.e., dietary fiber, and produce butyrate and other short-chain fatty acids that influence glucose metabolism and diabetes risk as reviewed recently [11]. *Lachnospira* uses pectin found in fruits and vegetables for acetate production. Fiber intake may lead to the presence of *Roseburia*, a butyrogenic bacteria that condenses 2 moles of acetate to form 1 mole of butyrate [12]. Interestingly, the MEC report also detected an inverse association of the HEI-2010 with *Anaerotruncus*, which has been associated with a Westernized diet pattern among older men [7].

As to the third side of the triangle, a role for *Roseburia* in type 2 diabetes has been previously indicated by a study showing that *Roseburia* discriminated between normoglycemic women and those with type 2 diabetes [13]. However, only nominal increases in *Escherichia/Shigella* related to diabetes were identified despite many associations of bacteria with obesity in another report [14].

The boon in molecular tools available to study the microbiome has opened up a myriad of opportunities to understand the complex impact of diet on the microbiome and the microbiome on human health. Although tools to measure bacterial taxa have been useful, the genetic plasticity of bacteria can result in a very different functional capacity within genera. To integrate the microbiome in human health requires an understanding of the functional capacity (metagenomics) and the activity of the microbiome (metatranscriptomics and metaproteomics). Standardization of methodologies ranging from sample collection to laboratory methods to bioinformatics approaches will allow valid comparisons across large human population studies [15]. High-quality bacterial reference genomes associated with pure cultures will establish the link from gene to functionality as this area advances [16, 17]. Shuttling between functional potential and activity using multiple 'omics methods and expanding reference databases will help to uncover the functional link between the microbiome and human health [17].

The current study confirms that certain dietary patterns are associated with specific bacteria [5] and provides novel information linking the 3 corners of the triangle between dietary patterns, type 2 diabetes, and the gut microbiome. Yet, given the complexity of these associations, obesity and other factors will have to be included in causal pathways and long-term studies with repeated sampling will be required to answer many of the open questions. Dietary patterns, both data-derived and based on dietary recommendations, broadly agree on components of a healthy diet: primarily high intakes of fruits/vegetables, nuts, and whole grain products and low intakes of red/processed meats and products high in sugar and certain fats. The beneficial health outcomes are likely a result, in part, of higher levels of short-chain fatty acids derived from plant-based nutrients typical for a Mediterranean diet [8]. Whereas defining optimal dietary patterns will remain challenging in light of the difficulties in long-term dietary assessment, a focus on well-defined dietary patterns such as the HEI or the aMED will improve the comparability of future investigations. As these patterns are based on dietary recommendations, they will be easier to translate into dietary interventions than data-derived patterns.

Acknowledgments

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