Commentary

Dairy alters the microbiome, are we but skimming the surface?

Thomaz F.S. Bastiaanssen[a,b], John F. Cryan[a,b,*]

[a] Department of Anatomy & Neuroscience, School of Medicine, College of Medicine & Health, University College Cork, Cork, Ireland
[b] APC Microbiome Ireland, University College Cork, Cork, Ireland

ARTICLE INFO

In a recent issue of *EBioMedicine*, Shuai, Zuo and colleagues show that dairy consumption affects both composition and diversity of the microbiome in a large longitudinal cohort focusing on inhabitants of Guangzhou, China. They also find that the microbiome in turn is associated with several serum metabolite levels [1]. Notably, the bacterial genera that were positively associated with dairy intake are typically associated with milk fermentation. This is not the first time diary was shown to influence the microbiome and it stands to reason that enriching the gut environment with a dairy-rich diet would result in a shift in the microbiome towards milk-fermenting microbes [2]. Indeed, this study can be seen as part of a recent trend of large-scale studies showing a link between microbiome and diet [3−5]. Taking these and the current study together, it is clear that dietary intake is one of the major drivers of microbiome composition [6].

However, it is also becoming evident that diet-microbiome interactions are perhaps more subtle than previously thought and hard to disentangle, especially at the compositional level of the microbiome. Furthermore, it is not completely obvious how to move forward with the knowledge that diet affects the microbiome in many subtle ways. There exists a large degree of variance in dietary habits in the general population and dietary data by itself is complex, making it non-trivial to control and account for the effects of diet on the microbiome. To complicate matters further, there exist hidden biases in microbiome metagenomic sequencing experiments, even within the same study, which complicates attempts to compare microbiome feature abundances between studies [7].

Having acknowledged the challenges, it remains clear that both diet and microbiome play a crucial role in maintaining health. Indeed, in one of the large studies mentioned previously, the well-known beneficial effects of the Mediterranean diet were shown to be dependent on the availability of *Prevotella copri* in the microbiome [5]. Fortunately, numerous approaches remain available to take advantage of existing studies. For instance, associations between microbiome features and host phenotype can be verified in different cohorts.

Recently, there have been promising developments in using ratios between microbial features to reduce complexity of the data but retain a large proportion of the information within [8]. Furthermore, in situations where longitudinal sampling is available, shifts in the functional microbiome have been reported to be robust to cohort effects and indeed conserved between host organisms, underlining the utility of longitudinal microbiome datasets [9]. Finding and implementing ways in which microbiome cohorts can be effectively compared is essential to the field moving forward.

Another important challenge in the field is linking the microbiome to concrete changes in host metabolism. In the current study, Shuai, Zuo and colleagues report improvements in serum metabolites that are associated with cardiovascular health [1]. Though they acknowledge that this study was not equipped to statistically establish causality, it is worth noting that some of the metabolites that were altered are generally thought to be microbial in origin. It has been shown that serum metabolites are linked to the microbiome, indeed, many of the metabolites that were associated with the microbiome were labelled as xenobiotics or even unidentified compounds [4]. This implies that many serum metabolites with microbial origins are still poorly annotated, meaning that a substantial aspect of host-microbe communication is still undocumented. In future studies, using a biologically informed framework to infer the origin of metabolites will be essential.

Large studies such as the one led by Shuai, Zuo and colleagues here, tend to shed light on new parts of the host-microbe interaction puzzle. However, they also tend to confront us with the many open questions and uncertainties that remain in the microbiome field. As this research field is constantly developing, new discoveries will inevitably update past conclusions. This makes the availability of well-characterized large multi-omics datasets especially valuable and, indeed, the dataset associated with the current study represents a welcome addition to the field. Together, these studies promise to lead to a deeper understanding of the interactions between diet, microbiome and host, which will in turn help us maintain and improve our health and quality of life.

E-mail address: j.cryan@ucc.ie (J.F. Cryan).

Contributors

Both authors planned, wrote, and edited the manuscript.

Declaration of Competing Interest

The authors declare no conflict of interest.

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