MICROBIOLOGY

The Guts of Dietary Habits

Can dietary intervention change an individual's gut microbiome composition?

Uri Gophna

There is a multimillion-dollar industry based on the concept that introducing beneficial bacteria into the human intestines will improve our health. The trillions of symbionts in the large intestine profoundly affect our metabolism and immunity. Accordingly, abnormal bacterial communities have been identified in several human diseases such as inflammatory bowel diseases (*1–3*), colon cancer (*4, 5*), irritable bowel syndrome (*6*), and nonalcoholic fatty liver disease (*7*). The composition of microbial communities is generally stable within each individual. Past studies of the gut microbiota emphasized the huge impact of nutrition (*8*), which is likely to outweigh that of the host genotype (*9*). On page 105 of this issue. Wu *et al.* (*10*) further explore how dietary factors can influence the profile and stability of intestinal microbes.

The dissimilarity in gut bacterial composition between individuals is huge, even between identical twins (*11*), complicating the extraction of clinically relevant generalizations from studies of the microbiota. Recent analysis shows that it is possible to simplify matters, because all people, including those with chronic intestinal disease, can be classified into just three broad "enterotypes" dominated by three different genera: *Bacteroides* and *Prevotella* (both belonging to the phylum Bacteroidetes), and *Ruminococcus* (*12*). More surprisingly, these enterotypes were independent not just of sex and body mass index but also of nationality, despite the profound differences in long-term dietary habits between western nations and east Asian countries.

By combining detailed nutritional analysis and microbiome determination in 98 individuals, Wu *et al.* sought to identify nutrients that substantially affect abundances of microbial species. They found that higher fat intake and lower fiber intake are associated with particular bacterial groups. Intriguingly, enterotypes appeared to be determined by long-term diet: The *Bacteroides* enterotype was positively associated with animal protein and saturated fats, whereas the *Prevotella* enterotype was associated with a predominantly plant-based nutrition with high carbohy-

drates and low meat and dairy consumption. These findings are in agreement with a previous study comparing children from Italy and Burkina-Faso, which showed that the African children, who have practically no animal fat and protein in their diets, are colonized by members of *Prevotella* (or *Xylanibacter*, a closely related genus), whereas their European counterparts have high *Bacteroides* levels (*13*). The third enterotype, *Ruminococcus*, previously shown to be the most commonly encountered (*12*), was not well separated and often merged with the *Bacteroides* enterotype. This is perhaps unsurprising given that the abundance of the *Ruminococcus* genus in that cluster was relatively low to begin with, resulting in more egalitarian microbial communities with no dominant genus. Thus, it may be that this "definition by exclusion" enterotype may not represent a stable state.

Wu *et al.* then performed a dietary inter-

vention with 10 individuals, all with a *Bacteroides* enterotype, to examine the short-term (10 days) effects of nutrition on bacterial communities and enterotypes (see the figure). In agreement with a previous study in mice, changes were detectable within the first 24 hours, testifying to the rapid effects that diet can have on quickly dividing bacteria. Remarkably, however, no stable changes to the *Prevotella* enterotype were observed in the five individuals who were switched to a high-fiber/low-fat diet, although one showed a temporary 1-day switch. Thus, enterotypes appear to reflect long-term nutritional habits, and altering them may require a more prolonged dietary intervention, unless it is preceded by antibiotic treatment, which is usually undesirable. Is the goal of switching enterotypes really desirable, even if one enterotype should be shown to correlate with increased disease risk? Establishing causa-
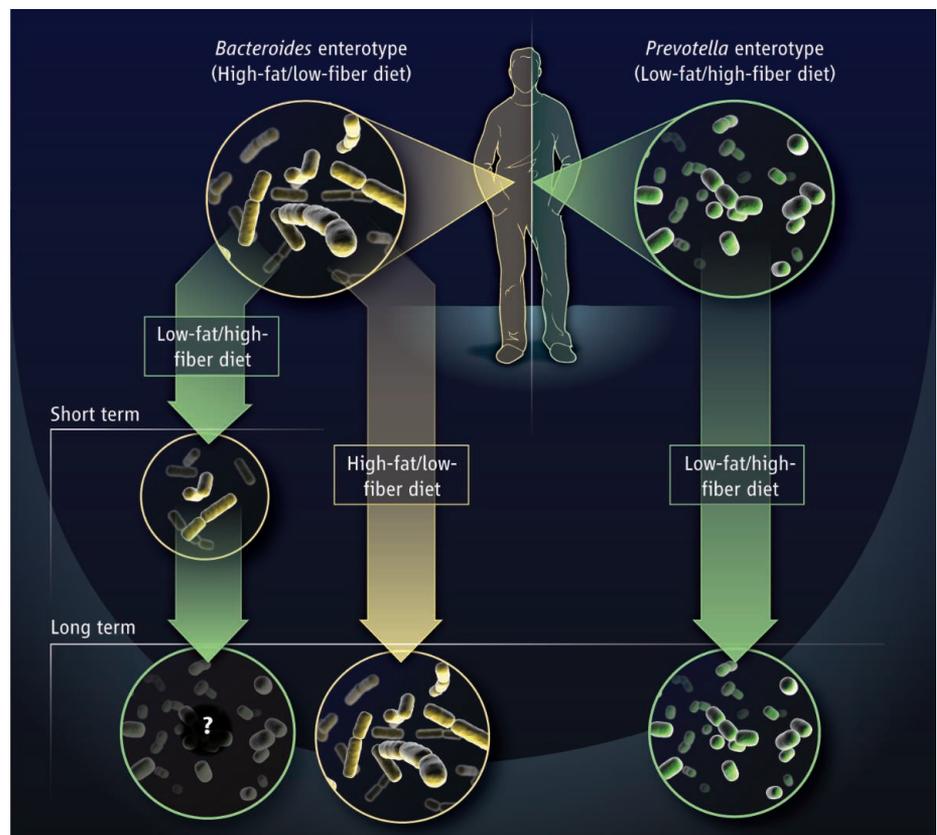
Long- and short-term effects. Nutrients affect the composition of the intestinal microbiota. Two different long-term diets are associated with a distinct gut microbe population (enterotypes). These microbial profiles are stable, and short-term dietary changes are not sufficient to alter them.

Molecular Microbiology and Biotechnology, George S. Wise Faculty of Life Sciences, Tel Aviv University, Ramat Aviv, Tel Aviv 69000, Israel. E-mail: urigo@tauex.tau.ac.il

tion from microbiota-disease associations is difficult. Moreover, bacteria to which health benefits have been attributed, such as *Faecalibacterium prausnitzii* (*14*), have not been associated with a particular enterotype. Thus, although the enterotypes represent a useful framework for the study of the gut microbiota, the clinical value of knowing one's enterotype remains to be determined.

Wu *et al*. also show that several dietary factors that have an impact on gut bacteria, such as red wine and the artificial sweetener aspartame, are not correlated with enterotypes. That an artificial sweetener can modify bacterial communities is surprising. How even minor concentrations of such a sweetener are sufficient to cause substantial changes in some gut inhabitants warrants further study. Undoubtedly, consumers of these food additives, which are otherwise perceived as safe, are unaware that these substances may influence their gut bacteria. This may be of particular importance to patients with dis-

eases correlated with modifications of the gut microbiota, such as irritable bowel syndrome and inflammatory bowel diseases. These individuals often adhere to self-imposed diets that they have empirically found to reduce symptoms such as diarrhea, but are unlikely to anticipate that an artificial sweetener may affect their indigenous microbiota and possibly their well-being.

It is anticipated that the study by Wu *et al*. will be followed up by larger diet-microbiome association studies that will help refine the picture of nutrients that affect the composition of the intestinal microbiota. Follow-up work is important because the large number of dietary parameters forced the authors to use a relatively lenient false discovery rate, and thus it is possible that a small number of links that they discovered are the product of chance. Further insights into diet-microbiome relationships could eventually have an impact on nutritional guidelines for both healthy individuals and patients with chronic

intestinal diseases and metabolic diseases such as obesity and diabetes. We are still only at the beginning stages of considering microbiomes as a diagnostic and engineering microbiome structure as treatment.

References
1. U. Gophna, K. Sommerfeld, S. Gophna, W. F. Doolittle, S. J. Veldhuyzen van Zanten, *J. Clin. Microbiol.* **44**, 4136 (2006).
2. C. Manichanh *et al*., *Gut* **55**, 205 (2006).
3. D. N. Frank *et al*., *Proc. Natl. Acad. Sci. U.S.A.* **104**, 13780 (2007).
4. P. D. Scanlan *et al*., *Environ. Microbiol.* **10**, 789 (2008).
5. T. Wang *et al*., *ISME J.* 10.1038/ismej.2011.109 (2011).
6. A. Kassinen *et al*., *Gastroenterology* **133**, 24 (2007).
7. M. D. Spencer *et al*., *Gastroenterology* **140**, 976 (2011).
8. P. J. Turnbaugh *et al*., *Sci. Transl. Med.* **1**, 6ra14 (2009).
9. A. Kovacs *et al*., *Microb. Ecol.* **61**, 423 (2011).
10. G. D. Wu *et al*., *Science* **334**, 105 (2011).
11. P. J. Turnbaugh *et al*., *Nature* **457**, 480 (2009).
12. M. Arumugam *et al*., *Nature* **473**, 174 (2011).
13. C. De Filippo *et al*., *Proc. Natl. Acad. Sci. U.S.A.* **107**, 14691 (2010).
14. H. Sokol *et al*., *Proc. Natl. Acad. Sci. U.S.A.* **105**, 16731 (2008).

10.1126/science.1213799

ECOLOGY

Resilience to Blooms

Justin D. Brookes[1] and Cayelan C. Carey[2]

Managing nitrogen and phosphorus pollution of fresh water may decrease the risk of cyanobacterial blooms, even in the face of warming temperatures.

Cyanobacterial blooms (see the figure) present health risks worldwide for humans and livestock that drink or use contaminated water, and also represent substantial economic costs to communities due to water treatment, lost tourism and recreation revenue, and declining property values (*1*). These explosive growths occur in fresh and marine water, and may be increasing globally. One recommendation is that water managers must address the effects of climate change when combating cyanobacterial blooms (*2*). However, recent studies suggest that controlling nutrients may be more important in increasing aquatic ecosystem resilience to these blooms.

A number of factors may potentially contribute to an increase in blooms, primarily climate change and changing land use. Most climate change modeling scenarios predict that aquatic systems will experience increases in temperature, thermal stratification (*2*), and water column stability, all

[1]School of Earth and Environmental Science, University of Adelaide, Adelaide 5005, Australia. [2]Department of Ecology and Evolutionary Biology, Cornell University, Ithaca, NY 14853, USA. E-mail: justin.brookes@adelaide.edu.au, ccc99@cornell.edu

factors that favor cyanobacteria over other phytoplankton (*2*, *3*). Thermal stratification leads to a greater propensity for cyanobacterial blooms, as many cyanobacteria have

Big bloom. A cyanobacterial bloom in Lake Windermere, England, in June 2007. See SOM text for suggested resources related to cyanobacerial blooms.

gas-filled vesicles that enable them to rise to the water surface and form dense blooms (*2*, *4*). In addition to climate change, deforestation, human and commercial animal waste, and agricultural fertilization have increased nutrient runoff into aquatic systems (*5*), also favoring cyanobacterial blooms.

What is the relative importance of warming temperature versus nutrient (nitrogen and phosphorus) loading in driving cyanobacterial dynamics? Many modeling studies (*6*, *7*), historical data analyses (*4*, *8*), and experimental studies (*9*, *10*) show increased nutrient concentrations as a consistently more important driver of blooms than warming temperatures. For example, in Lake Müggel (Müggelsee), Germany, cyanobacteria did not directly benefit from increased water temperatures; rather, blooms decreased as nutrient loading was reduced (*4*, *11*). Whereas some studies indicate that increasing nutrients and temperatures may exert a synergistic effect on cyanobacterial dominance (*4*, *6*, *7*), nutrient loading, notably nitrogen and phosphorus, is the primary factor in the expansion of blooms (*12*).

There are several mechanisms by which increased nutrients lead to the dominance of