microbial genome databases. The proportion of the various microbial species was inferred from the relative abundance of DNA. The analysis showed that, similar to other studies, only two major bacterial divisions and one archaeal member were represented in the samples.

After analyzing the fecal microbial community, the authors scanned the DNA libraries for the sequences of enzymes that participate in known metabolic pathways. In previous analyses, the scanned enzyme sequences were only compared to other microbial genomes. Gill and colleagues, however, compared the enzyme sequences to the human (that is, the host) genome. Compared to the human genome, the microbiome was highly enriched in metabolic pathways that facilitate degradation of plant polysaccharides, synthesize short-chain fatty acids (such as butyryl–coenzyme A, a principal energy source for colonocytes), remove toxic products of bacterial fermentation and xenobiotic compounds, and synthesize vitamin and isoprenoid precursors (**Fig. 1a**). As expected, statistically significant intersubject variability was found, as flora varies between individuals.

Taken together, these findings emphasize the important contributions the gut microbiome makes to our existence. The microbiome affects host metabolism by enhancing energy production and maximizing the energy value in food, contributes to biosynthetic pathways and promotes host homeostasis, and decontaminates the intestine, thereby minimizing exposure to toxic substances that could result in malignancies or other problems. Symbiosis with resident bacteria endows us with a colossal metabolic diversity and capacity.

This study supports the theory that we are in fact 'superorganisms' whose metabolism integrates microbial and human features. To further elucidate the details of this composite 'supermetabolism', deeper sequencing analysis of additional subjects will need to be performed.

The experimental approach taken by the authors can now be used to answer several key questions about the function of microbiota in health and disease. Microbiota has been implicated in various disease states, such as obesity[10], inflammatory bowel disease[11], cardiovascular disease[12] and late-onset autism[13]. Animal models and metagenomic comparisons such as this one will help flesh out the details. They will also aid in understanding how an imbalance in the carefully calibrated microbial community could lead to disease or be disrupted by it.

As we learn more about the interdependence on our resident bacteria, new therapeutic avenues may come into sight. Drug development efforts could be directed toward discovery of high-tech prebiotics with narrow and specific target ranges, and advances in bacterial isolation and culturing techniques could allow creation of probiotic cocktails suited for individual diseases and disorders. Additionally, individual differences in microbiota composition—such as that between the two subjects in this study—could be evaluated using the metagenomic comparison, and used to fine-tune dietary recommendations and therapeutic regimens. Individualized medicine will only become truly individualized when all aspects of an individual, human and bacterial alike, can be considered.

A potential model is emerging, in which a disruption in the microbiome results in a functional imbalance, contributing to a pathological state (**Fig. 1b**). Treatments such as drugs, changes in diet or re-seeding efforts could facilitate a return to the steady state between the human body and resident microbiota, thereby restoring the functions of supermetabolism. We are just beginning to realize the implications of being a superorganism, and the benefits of better knowing our intestinal inhabitants.

1. Eckburg, P.B. *et al. Science* **308**, 1635–1638 (2005).
2. Gill, S.R. *et al. Science* **312**, 1355–1359 (2006).
3. Lupp, C. & Finlay, B.B. *Curr. Biol.* **15**, R235–R236 (2005).
4. Ley, R.E., Peterson, D. & Gordon, J.I. *Cell* **124**, 837–848 (2006).
5. Backhed, F. *et al. Science* **307**, 1915–1920 (2005).
6. Alam, M., Midtvedt, T. & Uribe, A. *Scand. J. Gastroenterol.* **29**, 445–451 (1994).
7. Gustafsson, B.E., Midtvedt, T. & Strandberg, K. *Scand. J. Gastroenterol.* **5**, 309–314 (1970).
8. Husebye, E., Hellstrom, P.M. & Midtvedt, T. *Dig. Dis. Sci.* **39**, 946–956 (1994).
9. Sonnenburg, J.L. *et al. Science* **307**, 1955–1959 (2005).
10. Ley, R.E. *et al. Proc. Natl. Acad. Sci. USA* **102**, 11070–11075 (2005).
11. Guarner, F. & Malagelada, J. *Lancet* **361**, 512–519 (2003).
12. Ordovas, J.M. & Mooser, V. *Curr. Opin. Lipidol.* **17**, 157–161 (2006).
13. Song, Y., Liu,C. & Finegold, S.M. *Appl. Environ. Microbiol.* **70**, 6459–6465 (2004).

Microbes plump up mice

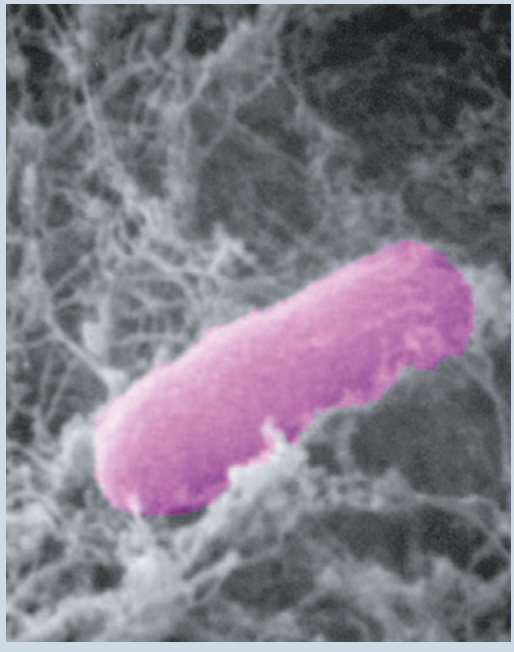
Interactions among the microbes in our gut could contribute to obesity, suggest findings by Buck Samuel and Jeffrey Gordon (*Proc. Natl. Acad. Sci. USA* **103**, 10011–10016).

Gordon and his colleagues had previously found that germ-free mice gained fat after they were inoculated with a suite of gut microbes. To ask why, the researchers inoculated germ-free mice with only a few species. These included two common inhabitants of the human large intestine, the polysaccharide-munching bacterium *Bacteroides thetaiotaomicron* (shown here) and the archaeal species *Methanobrevibacter smithii*.

Mice inoculated with both species did not gain weight—but they got 50 percent fatter. They also had 100–1,000-fold more microbes in their gut than mice inoculated with either microbe alone. Clearly, the microbes were somehow interacting. The researchers found that *M. smithii* influenced the metabolism of *B. thetaiotaomicron,* prompting it to consume mainly fructose-containing polysaccharides that break down into several substances, including formate—the preferred food of *M. smithii*.

Exactly why the mice get fatter is unclear. But the findings suggest that the collaboration between the microbes increases the efficiency of polysaccharide metabolism— increasing the yields of short-chain fatty acids such as acetate, which are used by the mouse to stimulate fat production and storage. The authors say that differences in our gut microbial communities may affect our predisposition to obesity. For some people, a diet rich in certain polysaccharides, such as fructose-containing sweeteners, could expand the waistline.

Charlotte Schubert



Justin Sonnenburg, Jaime Dant, Jeffrey Gordon; AAAS