Nature Reviews Gastroenterology & Hepatology **8**, 241 (2011); doi:10.1038/nrgastro.2011.60

MICROBIOME

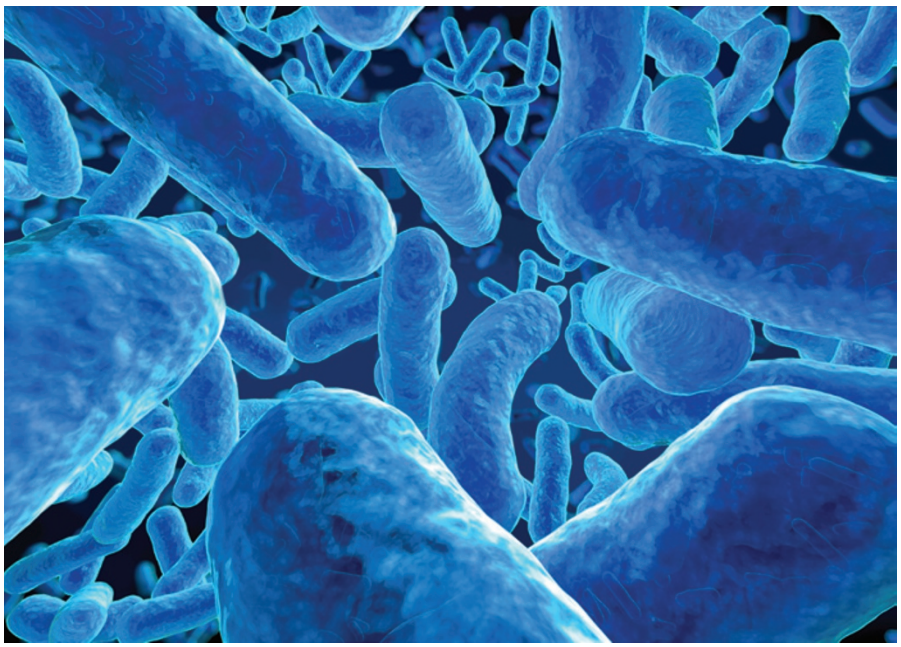
Human gut microbiota can be readily cultured, manipulated and archived

A team at Washington University School of Medicine has shown that individualized, human gut microbiota collections can be grown and manipulated in the laboratory. "This research helps set up a discovery pipeline in which we can deliberately manipulate collections of human intestinal microbes from people of different ages and cultures who are either healthy or sick," explains group leader Jeffrey Gordon. "It gives us the ability to test the contributions of specific microbes or groups of microbes and their influence on a person's health."

Dysbiosis of human gut microbiota has been implicated in the setting of Crohn's disease, obesity and malnutrition; however, using culture-independent methods, such as metagenomics, it has been difficult to identify the underlying mechanisms that link members of the microbial community to host disease phenotypes. In addition, although it has long been possible to culture bacteria in the laboratory, questions have remained about how much of the microbiota can be cultured and whether it is representative in taxonomic and functional terms.

The aims of this study were, therefore, threefold: to see how representative readily cultured phylotypes were of human gut microbiota; to transplant cultured communities into a mammalian gut ecosystem to study their dynamics; and to create a clonally arrayed, personalized strain collection as the basis for *in vitro* or *in vivo* reassembly of elements of the human gut microbiota.

A fresh stool sample was taken from two unrelated humans at four different time points. Part of each sample was grown under strict anaerobic conditions mimicking those of the human gut. The 16S rRNA genes of the cultured and uncultured samples were sequenced to evaluate how much of the uncultured gut community was represented in the readily cultured subset. "We were able to capture a remarkable proportion of the diversity of each person's intestinal bacteria in the samples we grew in the laboratory," says Andrew Goodman, lead author. "99% of the 16S rRNA reads derived from the complete fecal samples from either donor belong to the phylum-, class- and order-level taxa that are also present in the corresponding cultured sample; 89% are derived from readily cultured family-level taxa, and 70% and 56% belong to readily cultured genus- and species-level taxa, respectively."



© iStockphoto

Next, samples of the uncultured and cultured microbiota were transplanted into the intestinal tract of gnotobiotic mice. The colonization dynamics and distribution of both communities were found to be similar, as was their response to a change in nutrition—from a low-fat, plant-polysaccharide-rich chow diet to a high-fat, high-sugar Western diet. Goodman, Gordon and colleagues also found that by manipulating the diet consumed by the gnotobiotic mice they could shape the composition of the cultured communities.

Finally, the group created a clonally archived, taxonomically mapped, personalized microbiota collection for one of the human donors. To do this they adopted a multiwell format (ten 384-well trays per donor) that avoided the need for colony picking, which makes it difficult to capture sufficient bacterial diversity.

The researchers now want to understand how key taxa contribute to microbial community function. "We are developing personalized gut microbiota collections from humans with diverse physiologic traits and reuniting these communities *in vitro* and in gnotobiotic mice, potentially after genome-wide mutagenesis of selected community members," explains Goodman.

"One central question we hope to answer is how much of a person's overall nutritional status can be ascribed to their gut microbes and whether nutritional status can be improved by therapeutic interventions directed to gut microbial communities," concludes Gordon.

Natalie J. Wood

Original article Goodman, A. L. *et al*. Extensive personal human gut microbiota culture collections characterized and manipulated in gnotobiotic mice. *Proc. Natl Acad. Sci. USA* doi:10.1073/pnas.1102938108