Human gut microbiota, containing at least 100 trillion bacteria, resides in the mucosal surface of the human intestine. Each individual is host to a distinct set of at least 160 species in the gut. The collective microbial genome encodes 500 times more genes than the human genome, and so it is tempting to consider human genes as noise in the storm of microbial signals [1]. Recent data suggest that, while microbial signals modulate crucial functions of the healthy human body, there are also accumulating data suggesting that many human diseases have their origin in distorted gut microbiota composition [2].

Intestinal mucus is produced by goblet cells and forms a highly organized glycoprotein network, mainly consisting of mucin 2 (MUC2), but also containing a stable core proteome [3]. Despite the mucus layer long being considered a simple lubricator to facilitate the passage of the fecal material through the intestinal channel, recent interest in the gut microbiota has also brought intestinal mucus into the focus of research. Bacterial mucin degradation that exceeds mucus renewal by the host is an evident factor that leads to barrier dysfunction and likely contributes to inflammation or infection. For example, in inflammatory bowel disease patients, a mucus-degrading bacterium such as Ruminococcus gravis is frequently observed, suggesting that defects of the intestinal mucus layer play important roles in intestinal inflammation [4]. Also, diet can affect the gut bacteria, thereby influencing the integrity of the mucus layer. Diets with limiting dietary fiber may foster bacteria species that can degrade host glycans of the mucus layer. In contrast, some gut bacteria, such as Bifidobacterium longum, can help to mend diet-related mucus defects. Schroeder [5] recently demonstrated that the application of two murine-derived lactobacilli strains could ameliorate colitis in Muc2−/− mice [5]. Although the molecular mechanism is so far unclear, it is possible that distinct metabolic or structural components of specific Lactobacillus strains prevent intestinal disease by modulating the function of the mucus layer (Figure 1).

While we are still only at the beginning of understanding the function and importance of the mucus layer, recent studies have already shown that its interaction with the gut microbiota is more intense than previously thought. The gut microbiota not only affects the physiology of the intestine, but also signals to distant organs, thereby affecting whole-body metabolism [6]. As such, gut bacteria have been identified as a contributing factor to metabolic diseases and a defective intestinal mucosal barrier may be the crucial interface between host and microbes. Indeed, Schroeder [5] revealed that translocation of the bacterial endotoxin lipopolysaccharide (LPS) from the gut due to a defective mucus layer induces adipose tissue inflammation and that obese humans and mice have increased levels of LPS in their plasma [5]. Considering the crucial effect of the gut microbiota on the mucus layer, targeting the microbe involved in regulating the intestinal mucus layer will be a good strategy for diseases with a dysfunctional mucus layer including ulcerative colitis and metabolic diseases.

Despite recent progress in gut microbiota studies, gut microbiota analyses and microbiota transplantations often focus on bacterial community members, neglecting the potential influence of viruses and fungi that are likewise transplanted in complex communities. Especially bacteriophages have been shown to localize to the mucosal surface and are specifically enriched in the mucus when compared with the surrounding...
environment [7], further suggesting the importance of bacteriophages in the intestine may be also relevant for health and disease.

In conclusion, targeting the gut microbiota to improve mucosal barrier function is a feasible strategy that drives research in this area. It will thus be important to resolve the question of cause or consequence: does an altered gut microbiota contribute to disease, or does it merely reflect a disease status? To this end, prospective, as well as intervention, studies in humans are required. In addition, it is important to identify the molecular mechanisms by which some bacteria are beneficial in terms of barrier strengthening effect while other strains are not.

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