Bugs as Drugs

THERAPEUTIC MICROBES FOR THE PREVENTION AND TREATMENT OF DISEASE

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ASM PRESS
Washington, DC
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Dr. Patrice D. Cani is a Professor at the Université catholique de Louvain (UCL) and investigator for WELBIO (Walloon Excellence in Lifesciences Biotechnology) and the Fund for Scientific Research (FRS-FNRS). He is a member of the Royal Academy of Medicine of Belgium and the recipient of prestigious grants and prizes. He has published more than 200 papers, reviews, and chapter books in the field of gut microbiota, prebiotics/probiotics, and metabolism. In the early 2000s, he started to investigate the interactions between gut microbes and complex biological systems (endocannabinoids, immunity) by using prebiotics. In 2007, he discovered the concept of metabolic endotoxemia and more recently the role of specific bacteria (e.g., Akkermansia). Twitter: @MicrObesity.
The reinvigoration of research into the human microbiome—the collection of microbes that reside within and on our body—has resulted in novel insights into the role of these microorganisms in health and disease. Associations between the composition of the intestinal microbiome and many human diseases, including inflammatory bowel disease, cardiovascular disease, metabolic disorders, and cancer, have been elegantly described in the past decade. Because of these seminal discoveries and the increased public interest in the use of probiotics and prebiotics to impact health, many researchers and entrepreneurs are working toward translating the human microbiome into novel diagnostics and therapeutics. Thus, one of the main objectives of this volume is to provide insights into how one may capitalize on the enormous amount of knowledge being generated in microbe-human interactions for the translation into products that will benefit humankind.

We note that microbiome research, and the use of microbes as therapeutics, is not of recent origin. Elie Metchnikoff posited over 100 years ago that lactic acid bacteria found in fermented milk were beneficial to health and prevented intestinal “putrefaction.” Ben Eiseman and colleagues began using fecal enema as an adjunct therapy in the treatment of pseudomembranous enterocolitis in 1958, a full 20 years prior to *Clostridium difficile* being identified as one of the main causative agents of this disease. Indeed, fecal transplantation for the treatment of disease dates back centuries to the 4th century, when Ge Hong, a well-known traditional Chinese medicine doctor, described the use of human fecal material by mouth to treat his patients with severe diarrhea.

Why, then, the increase in developing novel therapeutics and diagnostics using microbes now? Significant improvements in genetic engineering of non-model organisms, next-generation sequencing technology, and metabolic profiling have certainly stimulated much confidence in being able to harness microbes to improve health. In addition, systems biology approaches and synthetic engineering of microbes are now high-throughput and cost-effective enough to explore a much wider range of therapeutic possibilities to be vetted.

Finally, we note there is much hype and enthusiasm over the use of microbes—not only classical probiotics but also future next-generation beneficial microbes and engineered bacteria—to make significant impacts on many human diseases and to restore healthy microbial communities. However, our understanding of how microbial communities function to influence health is still quite shallow, and translation to therapeutics will require patience and basic research. For example, the linking of many diseases to altered microbial communities is only
by association, and in many cases these correlations have only been uncovered in mouse models. We must acknowledge that despite the explosion of science in the gut microbiome in the past decade, much of the work has described associations between the microbiome and disease with few instances of causation. Until microbiome shifts that are associated with disease are shown to be truly driving disease manifestation, it will be difficult to know which diseases can be tackled via microbiome manipulation. It is important to remind the scientific community that just because one or several bacteria are increased or decreased in a specific pathological situation, this does not necessarily mean they play a role in disease. Therefore, a deeper understanding of the mechanisms and functions of microbiome-human interaction will be required to fully realize the potential of developing drugs for the treatment of acute and chronic diseases. Another objective of this book is for readers to identify key gaps that exist in their respective fields that need to be closed in order to assist in moving therapeutic microbes from the bench to the bedside.

We are indebted to the authors for their contributions to this book, which we know took a considerable amount of time to produce. We hope you find the chapters informative and useful in your endeavors.

Robert A. Britton
Patrice D. Cani
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