

The background of the cover is a microscopic image of various green, rod-shaped bacteria. The bacteria are shown in different orientations and focus, creating a sense of depth and movement. The overall color palette is a range of green tones, from light lime to deep forest green.

# INTESTINAL MICROBIOTA PROBIOTICS AND PREBIOTICS

COMPREHENSIVE TEXTBOOK  
FOR HEALTH PROFESSIONALS

Edited by  
Rok Orel

# INTESTINAL MICROBIOTA PROBIOTICS AND PREBIOTICS

COMPREHENSIVE TEXTBOOK  
FOR HEALTH PROFESSIONALS

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Textbook of Intestinal Microbiota, Probiotics and Prebiotics

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# INTESTINAL MICROBIOTA PROBIOTICS AND PREBIOTICS

*»Life's a Piece of Shit, When You Look at It.«*

*Monty Python*

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## Preface

Awareness of the importance of intestinal microbiota for human health and disease, and of the possibilities of influencing its composition and function with probiotics and prebiotics, is growing. In western communities, the idea of modifying the intestinal microbiota to promote good health, and prevent or even cure different diseases, faded away after the first few decades of the 20<sup>th</sup> century despite the research and interest of pioneers. Until its renaissance in late 80s and 90s, this field was only covered by a few enthusiasts. Thereafter, interest increased through nutritional sciences and the food industry rather than through medical sciences and pharmaceutical companies. Professionals in the latter were very skeptical about the field. Despite the results of numerous high quality clinical studies over the last two decades showing that specific probiotic strains and prebiotic substances undoubtedly have significant effects on certain clinical conditions, a number of health professionals remain skeptical for several reasons. Some companies with an interest in the pre and probiotic business effectively “bombarded” both health professionals and end consumers with often misleading information, which resulted in reservation in professional communities. Due to lenient legislation and poor quality control, many products on the market were of questionable quality and were not backed up by sufficient clinical evidence. In order to regulate this sector, the European Food Safety Authority (EFSA) produced a series of policies; however, these were unsuccessful at protecting consumers. As a result, the EFSA has virtually banned the use of health claims for probiotics, even though the efficacy of some strains is supported by a level of evidence comparable with that needed for registering drugs. As health claims cannot be made about food supplements, finding information about the efficacy of a particular product is difficult. This represents another missed opportunity to develop a meaningful instrument to help both health professionals and end consumers to make decisions about which pro or prebiotic products to use and for which condition.

Another reason is that without fully knowing or understanding about the substances, reasonable decisions cannot be made. From the initial concept of using “good” bacteria, or probiotics, to improve health and prevent disease, we came to understand that the effects of probiotics are strain specific and dose dependent. We can only partially predict the utility of a specific strain when we know its specific mechanisms of action but have no clinical evidence of its efficacy. Moreover, we realized that there is no such thing as a “universal” probiotic that is efficient for all indications. Even strains that show a very high level of efficacy in some conditions may be completely ineffective

in the others. While quality and comprehensive information is relatively easy to find through specified meetings and journals by dedicated experts on this field, they are not so readily accessible to the majority of professional users. A lack of such information in professional groups not only results in less use of pre and probiotic products in general, but also in the wrong choice of product for a specific purpose. Both of these are detrimental to patients.

The basic idea behind this textbook is to provide health professionals, such as medical doctors, pharmacists and nutritionists/dietitians, with comprehensive, understandable, user friendly, up to date information on the intestinal microbiota, probiotics and prebiotics. It focuses on a basic understanding of their mechanisms of action and the level of evidence to support their clinical efficacy in improving health and treating diseases. The main mission of this textbook, however, is to change health professionals from being “believers” or “nonbelievers” to being more knowledgeable about the field. As editor, I invited selected authors who are considered to be among the most prominent experts in the world to write about their fields in dedicated chapters. I want to thank them all for their invaluable contribution to the comprehensiveness and quality of the book. The authors of the individual chapters were requested to specify those probiotic strains, prebiotic substances and their combinations that have been proven to be efficient in specified indications. Whenever possible, specific recommendations were made based on available literature of clinical trials, meta-analyses, systematic reviews and positional papers from expert groups. I believe we have written a book that is both interesting and understandable to the readership. Moreover, I sincerely hope that information in this book will help different health professionals in their everyday practical work with patients.

Rok Orel  
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A handwritten signature in black ink, consisting of a large, stylized 'R' followed by a smaller 'O' and a final flourish.

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Juan M. Rodríguez is a professor at the Department of Nutrition, Food Science & Food Technology at the Complutense University in Madrid, Spain. He is a director of the research group “Human microbiota in the perinatal period and its application in mother-infant nutrition”. He is also a research leader of projects dealing with the selection of probiotics for their use in the mother-infant pair, and microbiological, biochemical and immunological aspects of pregnancy, lactation and infancy, including the microbiota/microbiome of human milk, that of pre-term neonates, and

the mother-to-child transmission of HIV-1 through breastfeeding. He is a co-founder and director of ProbiSearch, a spin-off company from Complutense University of Madrid, devoted to the study of complex microbiotas by using a variety of microbiological, immunological and biochemical methods, including –omics approaches; and the isolation, selection and characterization of probiotic strains.

**Prof. Irena Rogelj, PhD**

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Irena Rogelj has been involved in education and research work since she graduated from Food Science and Technology at the Biotechnical faculty, University of Ljubljana in 1978. She became a Doctor of Science in Food Science in 1990 and was appointed as a full professor in Dairy Science and Nutrition in 2003. She holds the Chair of Dairy Science at the Biotechnical faculty, and since 2010 she has been a Head of the Institute of Dairy Science and Probiotics. From 2001 to 2009, she was a member of the Commission for scientific research work at the Biotechnical faculty, and from 2005 to 2009, a member of Commission for research work at the University of Ljubljana. She has 30 years of research

experience in the field of biochemistry and microbiology of milk and milk products, with a focus on the study of lactic acid bacteria (LAB) isolated from fermented dairy products, the digestive tract, bacteriocinogenic LAB, properties of probiotic strains and their effects, and their possible use in protective starter cultures and probiotic products. The results of the research group she leads were presented at several international conferences and have been published in many scientific articles and book chapters. From 2010 to 2013 she was a principal researcher of the research project “The role of breast milk in the development of a breastfed child’s intestinal microbiota”. She has experience in testing probiotic bacterial action in animal models (pigs, mice) and in humans, as well as in the field of quality control of probiotic dietary supplements.

**Mary Ellen Sanders, PhD**

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Mary Ellen Sanders is consultant in the area of probiotic microbiology. She works with food and supplement companies to develop new probiotic products, provides technical support for enhancing existing probiotic product lines and offers perspective on paths to scientific substantiation of probiotic product label claims. Through numerous written, oral and video pieces, including a website, [www.usprobiotics.org](http://www.usprobiotics.org), she strives to provide objective, evidence-based information on probiotics for consumers and professionals. Dr. Sanders serves as Chief Science Officer for the International Scientific Association for Probiotics and Prebiotics (ISAPP) ([www.isapp.net](http://www.isapp.net)).

**Assoc. Prof. Elena Daniela Serban, M.D., PhD**

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Elena Daniela Şerban is an associate professor of pediatrics at the “Mother and Child” Department at the Second Chair of Pediatrics “Iuliu Hatieganu” University of Medicine and Pharmacy in Cluj–Napoca, Romania. She is also a senior consultant in pediatrics at the Emergency Children’s Hospital. Her scientific work is focused on pediatric bowel diseases, probiotics and prebiotics, and gastroesophageal reflux disease. Lately, her research work has focused on the genetic, environmental and microbial interactions in inflammatory bowel disease. She has published many papers in international medical journals and several book chapters. She is an active member of national and

international societies, including the European Crohn’s and Colitis Organization, and European Society of Pediatric Gastroenterology, Hepatology and Nutrition. She is the president of the Gastroenterology Committee and a member of the Leading Council of the Romanian Pediatric Society of Gastroenterology, Hepatology and Nutrition.

**Prof. Hania Szajewska, M.D., PhD**

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Hania Szajewska is a Professor and Chair of the Department of Pediatrics at the Medical University of Warsaw. She has broad interests in pediatric nutrition, but her research focuses on probiotics and prebiotics, the effects of early dietary interventions on later outcomes, acute and chronic diarrheal diseases, and celiac disease. She is actively involved in several European Union-funded projects (e.g., PREVENTCD; NUTRIMENTHE; EarlyNutrition). She is an enthusiastic advocate for the practice of evidence-based medicine. She served as a member of the Council of the European Society for Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN), and more recently as the General Secretary of ESPGHAN. She also served as a member, and then as the Secretary, of the ESPGHAN Committee on Nutrition. Currently, she serves as the co-chairperson of the ESPGHAN Working Group on Probiotics and Prebiotics, and the chairperson of the ESPGHAN Working Group on Outcomes in Nutrition Trials. She is also an Associate Editor of the Journal of Pediatric Gastroenterology and Nutrition, and a reviewer for journals in the field of pediatrics and pediatric gastroenterology and nutrition. She has published numerous scientific works and book chapters.

**Prof. Borut Štrukelj, PhD**

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Borut Štrukelj is a full professor at the Department for Pharmaceutical Biology at the Faculty of Pharmacy, Ljubljana where he leads the group for Pharmaceutical Biotechnology. At the Jozef Stefan Institute, he is a Member of the biotechnology group. Through his post-doc EMBO award, he was able to work at the CPRO-DLO, PRI Institute for plant molecular biology in Wageningen, Netherlands. Prof. Štrukelj has published a great number of scientific and professional articles many of them in the important international scientific journals. He is a member of many Slovenian and international pharmaceutical and biomedical

associations. In 1991, he was awarded the Kidirč award for his scientific contribution in the field of molecular biology. In 2007 he received a national award for his excellent scientific contribution (Zois award). From 1996 to 2012 he was appointed as an expert in the European Pharmacopoeia in a Group for biological pharmaceuticals as well as at the European Agency for Medicines in London (EMA). In 2010, he received the Fulbright Award for visiting professorship at the Duquesne University, Pittsburgh, USA.

**Prof. Yvan Vandenplas, M.D., PhD**

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Yvan Vandenplas completed his medical studies at the "Vrije Universiteit Brussel" and trained in pediatrics (1981-1986) at the same institute. He became Head of the Unit for Pediatric Gastroenterology and Nutrition in 1987, is Head of the Department of Pediatrics at the University Hospital, Brussels (UZ Brussel), and has been the Chair of Pediatrics since 1994. His PhD Thesis was on "Esophageal pH monitoring for Gastro-Esophageal Reflux in Infants and Children" in April 1991. He has numerous publications listed on Medline. His main interests are gastro-esophageal reflux (diagnostic procedures, treatment), probiotics and prebiotics, cow's milk protein allergy, constipation, infant

nutrition, and *Helicobacter pylori*. He has published many original research and review papers on topics such as infant nutrition and gastro-esophageal reflux, and other gastro-intestinal disorders. He is now the associate editor of the Journal of Pediatric Gastroenterology and Nutrition, and serving ESPGHAN as President of the committee of Gastroenterology.

**Prof. Zvi Weizman, M.D.**

Institution: Pediatric Gastroenterology and Nutrition Unit, Soroka Medical Center and Faculty of Health Sciences, Ben-Gurion University, Beer-Sheva, Israel

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Zvi Weizman is the founder and head of the Pediatric Gastroenterology and Nutrition Unit at the Soroka University Medical Center in Beer-Sheva, Israel. He is a full professor of Pediatrics at the Faculty of Health Sciences at the Ben-Gurion University. His main research interests are: infant nutrition, nutrition education, and the clinical effects of probiotics and prebiotics. He coordinates the European Society of Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) Working Group of Probiotics and Prebiotics. He initiated and coordinated the pre-graduate nutrition education courses for medical and nursing students in his Medical School at Ben-Gurion University. He has published many scientific papers.

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- The background of the slide is a microscopic image of green, rod-shaped bacteria, likely Bacillus or Clostridium species, arranged in various orientations. The bacteria are illuminated from the side, creating a strong sense of depth and texture. The overall color palette is a vibrant, monochromatic green.
- Overview of the Human Intestinal Microbiota
  - The Immune System and Intestinal Microbiota
  - Dysbiosis – the Concept of Dysfunctional Intestinal Microbiota
  - Probiotics – Historical Overview, General Concepts and Mechanism of Action
  - Breast Milk: a Source of Bacteria for the Infant Gut
  - Probiotics and Prebiotics in Infant Formula
  - Probiotics and Prebiotics in the Prevention of Respiratory Tract Infections
  - Probiotics and Prebiotics in Treatment and Prevention of Gastrointestinal Infections
  - Antibiotic-Associated Diarrhea and *Clostridium difficile*-Associated Diarrhea
  - *Helicobacter pylori* Infection – What Place Does Probiotic Use Have in Its Treatment?
  - Probiotics and Prebiotics in Inflammatory Bowel Disease
  - Probiotics and Prebiotics in Prevention and Therapy of Allergy
  - Intestinal Microbiota, Probiotics and Prebiotics in Functional Gastrointestinal Disorders
  - Probiotics in Functional Gastrointestinal Disorders of Infancy
  - Emerging Fields of Probiotic and Prebiotic Use