#### Preface

The human gastrointestinal tract microorganisms, termed the "microbiota," have been 113 investigated since the beginning of microbiological studies, when Anthonie van 114 Leeuwenhoek investigated the microorganisms in his own stools. The human microbiota 115 comprises trillions of microbes distributed in various niches throughout the intestinal tract 116 and is one of the most complex microbial ecosystems on earth. The host and its 117 microbiota have co-evolved together, and considering the staggering numbers and 118 diversity, it is therefore not surprising that the microbiota exert a major influence on the 119 host. The original term for the microbiota upon discovery was the "flora" or "microflora," 120 literally translated as "small plants," which has a botanical connotation. These terms are 121 still used widely today and internationally recognized. Nevertheless, it is considered more 122 appropriate to use the term microbiota, i.e., "small life" taking into account that the 123 microbiota is predominately comprised of bacteria, a smaller number of yeasts, and some 124 protozoa; hence, this term is used throughout this book. With this book, we have made an 125 attempt to cover all issues associated with the gastrointestinal microbiota, from health to 126 disease and from sampling to identification. Although various books have addressed the 127 intestinal microbiota, this has mainly been from the perspective of disease or nutrition, 128 while the microbiota itself has rarely been the focus. This current book aims to fill this gap 129 and provide the reader with a comprehensive overview of all aspects related to the 130 gastrointestinal microbiota. There have been major scientific advances especially in 131 human intestinal microbiology in the recent past, which are also covered by the 132 contributions. 133

Early studies were limited to description of the culturable microbes, which as we 134 now realize, made up only a minority of the gastrointestinal tract microbiota. Due to the 135 development of molecular biological techniques over the last decade, microbes can now 136 be detected and studied to a large extent, without the need for culturing. In the first chapter, 137 Kaouther Ben Amor and Elaine Vaughan review the major achievements of recent times in 138 determining the diversity of the microbiota using modern molecular techniques, based on 139 16S ribosomal RNA, as well as methods to evaluate their activity within the various 140niches. Research of the gastrointestinal tract microbiota, especially in the case of humans, 141 is often restricted to fecal material. In fact, a range of other sampling techniques are 142 available, which are presented by Angelé Kerckhoffs and colleagues, to access the small 143 intestine, as well as noninvasive sampling methods that are routinely used in medical 144 practice. This is an important issue since feces represent only the luminal material of the 145 terminal colon and will provide insufficient information about other locations of the gut. 146 Anne McCartney and Glenn Gibson describe the succession of the microbiota in infants, as 147 well as the earlier culturing studies, and the methodology to characterize the microbiota 148

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down to subspecies level. It has long been recognized that the intestinal microbiota plays an important role in maintaining health in infants. Currently, much attention is also focused on the intestinal microbiota of the elderly, as is discussed in the chapter by Fang He. In western nations, the elderly are becoming an increasingly important segment of the population, and it is becoming increasingly established that intestinal health has a major role in their quality of life.

While establishing the microbiota diversity and their activity (live versus dead) is a 157 major challenge, it is essential to know and understand their effects on the host. The 158 intestinal microbiota has a major influence on the development and maintenance of our 159 immune system as described by Marie-Christiane Moreau. Because of their direct contact 160 with the host, the activity and interaction of the microbiota with the intestinal mucosa may 161 be more important than the activity of microbes in the lumen, as described by Wai Ling 162 Chow and Yuan-Kun Lee. The human microbiota also play a major role in our nutrition. 163 Barry Goldin reviews the myriad of metabolic possibilities of the human microbiota 164 concerning the metabolism of food ingredients and drugs we consume, as well as host-165 derived substrates. Max Bingham focuses on the metabolism by the microbiota of 166 polyphenols, which are considered to be key active constituents of fruits and vegetables 167 and responsible for many of the health protective effects of diets rich in these foods. 168 Today, functional genomics technologies are developing and will facilitate our ability to 169 detect the microbes and determine the molecular mechanisms of their impact on the host. 170 Through the sequencing of an ever-increasing number of microbiota genomes, and elegant 171 molecular studies, a further understanding is being obtained into the molecular functioning 172 of the host-microbiota interactions, a dynamic area that is discussed by Peter Bron, 173 Michiel Kleerebezem, and Willem de Vos. 174

In the past, the gastrointestinal tract microbiota has received attention in particular in 175 relation to disease. Fergus Shanahan, Barbara Sheil, and coworkers review the relationship 176 between the intestinal microbiota and inflammatory bowel diseases, as well as give an 177 overview of the probiotic clinical trials and the potential mechanisms of probiotics for 178 ameliorating these intestinal diseases. Through its metabolism, the intestinal microbiota is 179 thought to play an important role in both the etiology and prevention of colorectal cancer, 180 as discussed by Patricia Heavey, Ian Rowland, and Joseph Rafter. In addition to diseases 181 of the gastrointestinal tract, Pirkka Kirjavainen and Gregor Reid also discuss that diseases 182 such as allergy are being recognized to have an "intestinal component," again mediated 183 through the interaction between the microbiota and the intestinal immune system. 184

In order to gain a better understanding of the composition and functioning of the 185 intestinal microbiota and how this can be influenced, intestinal models have been 186 developed; this allows for a simplification of the complex intestinal ecosystem as presented 187 by Harri Mäkivuokko and Päivi Nurminen. For our understanding, experimental animals 188 have been and are indispensable, as described by Anders Henriksson, especially with the 189 availability of various knockout animal models for disease. Also the use of animals with 190 a "human" microbiota provide valuable models to investigate the influence of substances on 191 the microbiota and host physiology. The best animal models to show the importance of 192 the intestinal microbiota are germ-free animals. Their physiological differences compared 193 to conventional animals are striking and show clearer than any other model the role 194 intestinal microbes play, as discussed by Elisabeth Norin and Tore Midtvedt. Because of its 195 influence on the health and well being of the host, strategies have been devised to alter the 196 composition and/or activity of the intestinal microbiota. Antibiotics have long been known 197 to alter the composition of the intestinal microbiota, as discussed by Asa Sullivan and Carl 198 Erik Nord, which may lead to various side effects, depending on the activity spectrum of the 199 antibiotic. Methods to improve the activity and composition of the intestinal microbiota 200

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include probiotics, microbes ingested orally that provide beneficial effects, and prebiotics
substrates that are selectively metabolized by the beneficial native gastrointestinal tract
microbes, as discussed in the chapters by Chandraprakash Khedkar and Arthur Ouwehand,
and Ross Crittenden and Martin Playne, respectively.

The major part of the book deals with the microbiota of humans, and when animals 205 are studied, it is often as a model for humans. Minna Rinkinen describes the microbiota of 206 companion animals, an area that has received very little attention to date, although the 207 well being of pets can contribute significantly to the well being of the owner. In the case of 208 farm animals, discussed by Alojz Bomba and colleagues, there is an important economic 209 drive where the role of the microbiota on performance is a major focus. This will only 210 become more important from 2006 onward as antimicrobial growth promoters will be 211 prohibited in the European Union. 212

We are most grateful to the authors who have been willing to share their knowledge 213 and experience in their field of intestinal microbiology. They are all busy researchers 214 and yet they committed themselves to writing these chapters. It has been a pleasure to 215 cooperate with these experts for the production of this book. Together their excellent 216 contributions provide state-of-the-art research on the human intestinal microbiology, as 217 well as informative chapters about the animal microbiota for comparative purposes. Elaine 218 Vaughan also acknowledges the staff and colleagues of Unilever Research and 219 Development, Vlaardingen, Laboratory of Microbiology, Wageningen University, and 220 Wageningen Center of Food Sciences, for inspiring discussions on intestinal micro-221 biology. Arthur Ouwehand similarly acknowledges the support and inspiration from the 222 colleagues at Danisco Innovation and the Functional Foods Forum, University of Turku. 223 We hope all readers will share our excitement for this dynamic subject that impacts on all 224 our lives. 225

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