# Preface

Members of the genus *Shigella* are responsible for a moderate to severe dysenteric syndrome called shigellosis. This form of bacillary dysentery is ubiquitous around the world with greatly elevated morbidity and mortality in developing nations. Typical symptoms include diarrhea, fever, and stomach cramps starting one or two days after ingestion of contaminated food or water. In many cases the initial diarrhea then turns bloody and contains mucus. Patients in developed nations do not usually require hospitalization, however, children can develop severe symptoms that require immediate medical care to prevent dehydration and longer term effects. This is especially true for children between the ages of two and five in underdeveloped parts of the world where there are simultaneous threats of malnourishment and high incidence of other infectious diseases.

As considered here, the genus *Shigella* is considered a stand-alone group of species that specifically cause diarrhea in humans. They were discovered over 100 years ago and classified as four distinct species containing numerous O antigen serotypes. In reality, the *Shigella* species are so closely related to *Escherichia coli* that they should possibly not be classified as a genus but rather a distinctive species within the genus *Escherichia* (for example, see: Fukushima, et al. (2002) Phylogenetic Analysis of *Salmonella*, *Shigella*, and *Escherichia coli* Strains on the Basis of the *gyrB* Gene Sequence. J. Clin. Microbiol. 40:2779-85 & van den Beld and Reubsaet (2012) Differentiation between Shigella, enteroinvasive Escherichia coli (EIEC) and noninvasive Escherichia coli. Eur. J. Clin. Microbiol. 31:899-904). Nevertheless, the vast majority of cases of bacillary dysentery are attributable to what we refer to here as *Shigella* and they thus warrant special consideration as a diarrheal pathogen of global public health importance.

This book is roughly divided into three sections that bring us up to date on the molecular biology of *Shigella*. The first section will explore essential aspects of metabolism and gene regulation in this human adapted pathogen. Topics here include the acquisition of limiting iron as an essential means for survival within the host, the evolution of the *Shigella* genome to make its pathogenic lifestyle compatible with its metabolism, and the mechanisms by which virulence genes are expressed. This section explores critical aspects of the molecular and cellular biology of *Shigella* as it has diversified from its evolutionary place among the *Escherichia coli*. While there is much more to be learned about the metabolomics and genomics of *Shigella*, this section provides the reader with a flavor of often overlooked features of bacterial pathogens and the recently developed appreciation for RNA-based regulation of gene expression.

The second section of this work focuses on the important area of host-pathogen interplay. *Shigella* is among a group of organisms for which a wealth of information exists on its ability to subvert host signaling processes for the benefit of the pathogen. Humans have evolved to fight infections by a variety of innate and adaptive processes, however, the most successful human pathogens have developed exquisite means for avoiding these processes to allow them to gain a foothold to ultimately allow colonization and cause host cell damage. *Shigella* has evolved specific mechanisms to trigger pathways for the destruction of phagocytes (macrophage killing) that are portrayed differently to intestinal epithelial cells which are prompted to internalize the bacterial pathogen to provide an intracellular niche where it can replicate and spread to neighboring cells. All three of these topics are covered in excellent detail in this section of the book, however, *Shigella*

interplay with the host is only beginning to be fully appreciated. The ability for this pathogen to alter signaling pathways within tissues is also a topic of interest and this is evident from its manipulation of host innate immunity and its ability to elicit signals across the intestinal epithelium. A full understanding of all of these events is prompting the development of novel methods for assessing the host cell targets that are subverted by the effector proteins that *Shigella* skillfully delivers, which is also addressed in this section. Lastly, an overview of the adaptive immunity elicited by *Shigella* infection is presented along with a comparison of this response with that induced by current *Shigella* vaccine candidates.

In the final section of this book, two aspects of what is probably *Shigella*'s most prominent virulence are discussed. The *Shigella* type III secretion system is considered one of the paradigms for type III secretion in Gram-negative bacteria. The T3SS is recognized as a highly evolved nanomachine for promoting cross-species communications between prokaryotes and eukaryotes in what are often pathogenic relationships, but which can be symbiotic in some cases. While we have not gone into tremendous detail on the overall structure of the type III secretion apparatus (T3SA), two chapters are dedicated to dynamic aspects of the *Shigella* T3SS. One is the nature of the needle tip complex of the T3SA which is essential for sensing contact with host cells and ultimately creating the translocon pore through which effector proteins are delivered into host cells. The second chapter describes new methods that are allowing the identification of newly recognized effector proteins that are the tools by which *Shigella* alters target cell behavior. It should be noted, however, that previous chapters also touch upon the topics of type III secretion and the manipulation of host cell signaling by effector proteins. Thus, all the sections of this book should be viewed as an integrated overview of the molecular and cellular biology of *Shigella* and its human host.

There are many important facets of *Shigella* that are not covered in this book, but these are by no means to be slighted by their omission. The overall goal of this compendium is to provide the researcher, especially those new to the field, with a flavor of some of the topics that are important as we move forward in understanding *Shigella* the pathogen and the delicate balance it has with its primary host – human beings. Just a few of the topics not covered here would include the importance of lipopolysaccharide as a virulence factor and the effect of newly developed antibiotic resistances on the changing epidemiology of shigellosis. We hope it is thus clear to the reader that much remains to be learned about this organism and the public health problem it poses.

We would like to express our gratitude to the authors who contributed to this book and we thank them for their important contributions to our current understanding of *Shigella* and shigellosis. We also thank the publisher for realizing the importance of providing this overview of the research being done on the cellular and molecular biology of this pathogen and how they contribute to bacillary dysentery.

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