Preface

Understanding bacterial infections is more important than ever. Despite the development of antibacterial agents during the last century, bacterial infections are still one of the leading causes to worldwide morbidity and mortality. What is especially alarming is that we are entering a postantibiotic era where we have no, or very limited, treatment options to several bacterial infections previously not considered as threats (CDC. Antibiotic resistance: threat report 2013). A fundamental issue in infection biology has been, and still is: What is virulence and how does it relate to pathogenesis? There is no simple answer to this and the theoretical framework is continuously developing. The molecular dissection of Koch's postulates made possible by the molecular genetics revolution has been instrumental in understanding bacterial-host interactions at the molecular level, but this somewhat bacteria-centered view has had its limitations in describing the whole process ranging all the way from commensalism to severe infections. Here, more recent frameworks taking both the bacterial properties and the host responses into account have gained recognition. However, theoretical frameworks will remain theoretical until they can be experimentally tested. Therefore, methodologies assessing many different aspects of bacterial infections are absolutely crucial in moving our understanding forward, for the sake of knowledge itself, and for developing novel means of controlling bacterial infections.

In this volume, *Bacterial Pathogenesis*: *Methods and Protocols*, we have had the privilege of recruiting researchers with very different methodological approaches, with the common goal of understanding bacterial pathogenesis from molecules to whole organisms. The methods describe experimentation of a wide range bacterial species, such as *Streptococcus pyogenes*, *Streptococcus dysgalactiae*, *Staphylococcus aureus*, *Helicobacter pylori*, *Propionibacterium acnes*, *Streptococcus pneumoniae*, *Enterococcus faecalis*, *Listeria monocytogenes*, *Pseudomonas aeruginosa*, *Escherichia coli*, *Salmonella typhimurium*, and *Mycobacterium marinum*. However, many of the protocols can be modified and generalized to study any bacterial pathogen of choice. Part I details very different approaches to identifying and characterizing bacterial effector molecules, from high-throughput gene-based methods, via advanced proteomics, to classical protein chemistry methods. Part II deals with structural biology of bacterial pathogenesis and how to overcome folding and stability problems with recombinantly expressed proteins. Part III describes methodology that with precision can identify bacteria in complex communities and develop our understanding of how genomes of bacterial pathogens have evolved. Part IV, the largest section, reflects the rapid development of advanced imaging techniques that can help us answer questions about molecular properties of individual live bacteria, ultrastructure of surfaces, subcellular localization of bacterial proteins, motility of bacteria within cells, and localization of bacteria within live hosts. Part V describes methods from in vitro and in vivo modeling of bacterial infections, including using zebra fish as a surrogate host, bacterial platelet activation, antimicrobial activity of host proteases, assessment of biofilms in vitro and in vivo, and using a fish pathogen as a surrogate infectious agent in a mouse model of infection. Finally, Part VI is based on the notion that bacterial pathogens are the true experts of our immune system. Therefore, immune evasion bacterial factors can, when taken out of their infectious context, be used as

powerful tools or therapeutics against immunological disorders. This is exemplified by the use of proteases from pathogenic bacteria for characterization of therapeutic antibodies, measurements of antibody orientation on bacterial surfaces, and finally the potential use of immunoglobulin active enzymes as therapy against antibody-mediated diseases.

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