DEDICATION

We dedicate this volume to the memory of our colleague Ira Herskowitz, whose lifetime effort exemplified what was best in the Phage Group. Ira’s work with Ethan Signer on late gene expression in λ (see reference 11 in the Preface) presaged the recent work discussed in Chapter 7 on the mechanism of Shiga toxin expression from λ-related prophages. His work with David Botstein in constructing hybrid phages between coliphage λ and the Salmonella phage P22 (see reference 3 in the Preface) showed that phages specific for different species under the right conditions can recombine, adding to the early experimental evidence leading to the ideas discussed in (Continues)
Chapter 4 regarding phage evolution. Although Ira's career blossomed with his seminal contributions to the yeast field, he never lost his love for \( \lambda \). Even in the midst of making that career change, he wrote an insightful review on the subject of the \( \lambda \) lysis-lysogeny decision in Annual Review of Genetics (see reference 10 in the Preface) and even later joined with colleagues from two other laboratories to write a definitive review on \( \lambda \)-host interactions (see reference 7 in the Preface). More than two decades later, the lysis-lysogeny review is still regarded by the field as a masterful and useful presentation of the topic. Ira's wisdom and enthusiasm are missed.
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A skeptical reader may well ask, “Why publish a volume dedicated to the subject of phage and bacterial pathogenesis at this time?” After all, the idea that phage genomes include genes encoding virulence factors is certainly not new. Over a half a century has passed since Freeman reported that nontoxicogenic *Corynebacterium diphtheriae* could be converted to a toxigenic state through phage infection and lysogeny (6). This suggested that a phage encodes and/or controls expression of the toxin gene. The former was proven to be the correct interpretation more than 30 years ago when Uchida et al. (16) provided the genetic and physiological proof that a phage indeed carries the gene encoding diphtheria toxin. Moreover, the idea of using phages as antibacterial agents goes back to a discoverer of phage. As pointed out by Summers in Chapter 1, Félix d’Herelle, the codiscoverer of phage, was an early advocate of the use of phage to combat bacterial infections; he even conducted phage therapy trials on humans. What then has occurred to warrant the publication of this book on phage and bacterial pathogenesis?

A number of factors have aligned themselves to make this, in our opinion, a propitious time to assemble such a monograph. First, the results of the sequencing of a large number of the genomes from bacterial pathogens made it clear that prophages make up a relatively large component of these genomes (see chapters 7, 8, and 16). For example, most of the differences between the genomes of enterohemorrhagic *Escherichia coli* (EHEC) and *E. coli* K-12 are accounted for by the 18 prophage-like elements found in the EHEC genome (see chapter 7). Comparative analyses of the genomes of several group A streptococcus (GAS) strains revealed that most of the variation in gene content among different GAS strains is accounted for by differences in their phage contents (see chapter 16). Moreover, sequence analysis of the genomes of a number of pathogens makes it quite clear that the presence of virulence genes on phage genomes is far more common than was previously thought. These studies show that many genes encoding known virulence factors and open reading frames
homologous to genes that encode virulence factors are carried within prophages. Second, the extensive body of knowledge collected over the years on phage biology, particularly at the molecular level, was productively applied to phages carrying virulence genes (see chapters 7, 8, and 9). Third, there has been recent heightened interest in how the ecological niche influences the interaction between phages and bacteria (see chapter 5). One needs only to look at the enthusiastic response to the recent ASM-sponsored meeting on the “New Phage Biology” (2) that attracted over 350 participants from 24 countries for confirmation of the resurgence of interest in phage biology and related technologies.

In preparing this volume, we have tried to bring together the new findings on phage in pathogenesis with sufficient background information on important aspects of phage biology that directly impinge on the role of phage in pathogenesis. The book is divided into three sections. The chapters in Section I present overviews of the phage world that are designed to provide updates of relevant information for those with more than a cursory knowledge of phage lore and sufficient background for the non-cognoscenti to assist in understanding the chapters focusing on specific pathogens and their phages. The chapters in Section II explore the role of phages in the biology and pathogenicity of specific infectious bacteria. It is these chapters that obviously provide the rationale for initiating this endeavor. The chapters in Section III present new information regarding applications of phage biology in biotechnology as well as a critical assessment of therapeutic and diagnostic use of phage. We hope this last section provides information of practical value for the research efforts of the reader.

The editors feel privileged to have attracted such a group of renowned experts to write chapters and thank them for their cooperation in getting the volume to press in a timely manner. We would also like to remind the reader of the spirit of cooperation that imbued the phage group, a spirit that was institutionalized by the annual Cold Spring Harbor phage meeting and the Cold Spring Harbor Phage Course. Through the inspired efforts of that group, work on phage contributed significantly over the last 60 years to fundamental advances in biology. It is our intention for this volume to become a worthy successor to previous noteworthy books on phage. These include the classic earlier works of Mark Adams (1) and Gunther Stent (14) that served as primers to the phage world as well as the seven volumes dedicated specifically to single-stranded DNA phages (5), RNA phages (17), λ (8, 9), T4 (12, 13), and Mu (15). The more encompassing two-volume set edited by Richard Calendar (4), soon to be updated, covers information on most of the intensely studied phages.

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