PREFACE

When writing about phages, one must remember to consider their practical applications, as even results of early phage studies opened a plethora of phage usage possibilities. Phage therapy, phage typing, phage display of antibodies, transductional mapping of bacterial chromosomes and phage-mediated bacterial mutagenesis are only a few of the examples. As we can now see, the application of phages in the past was significantly curtailed by limited possibilities of exploring the phage world, as well as by technical difficulties in getting an insight into phage structure and biology. These limitations have been decreasing with the advent of new research possibilities initiated, e.g., by the development of omics and mass spectrometry, as well as different kinds of fluorescent, atomic force and electron microscopy technologies.

Ironically, despite the above mentioned possibilities, the most complex obligatorily virulent phages revealed their genomic structure only within the recent decade, after the publication of the first draft of the human genome sequence. Numerous genes of these phages encoding proteins toxic to bacteria prevented the determination of their complete genomic sequences until the development of cloning-independent sequencing technologies and their common use. Thus, only since the beginning of the XXI century, which has been called by some "the age of phage", have we been able to discover the full richness of the phage world, its remarkable diversity and the huge impact of phages on bacterial populations. We can use modern research tools to get a deeper insight into those phage properties and structures that were detected or predicted by researchers a long time ago. Finally, having nowadays the possibility to study phages at a molecular level, we can widen our understanding of their nature, interactions with each other and with organisms of the surrounding world to the extent that enables a more and more deliberate use of phage-encoded proteins and complex macromolecular structures as well as complete phages, single or in mixtures. This volume concerns the above-mentioned issues.

An early interest in phages was partially motivated by their potential bactericidal activity and hence, the possibility of their therapeutic use. Although the therapeutic application of phages has been nearly abandoned for years, especially in Western countries, it once again became the focus of attention with the emergence and spread of antibiotic-resistant bacterial pathogens. Thus, the first part of this volume is devoted entirely to phage therapy. In the context of a possible return to these clinical

approaches, results of early studies on phage therapy that have remained unknown for most of the readers for decades, but are outlined here in a chapter by Nina Chanishvili, should become of special value. Although their original interpretation by former researchers may seem currently too speculative and not always justified, and although proper controls were often lacking, now, at the time of costly and restricted studies on humans, they are a valuable source of information. The molecular basis of some of the methods that were used at that time and may seem "suspicious" at first glance can be understood today as a reader may learn from Chapter 5. Also, the efficacy of phage therapy that was often estimated in the past just on the basis of a "patient's feeling of getting better", can be verified now in well designed scientific or medical experiments, as one can learn from chapters by Andrzej Górski and co-authors, by Ryszard Międzybrodzki and co-authors, and by Emilie Saussereau and Laurent Debarbieux. It is becoming clear that one can consider various phages as specific medicines. To be effective, they have to be applied in a certain way and at a certain time, similarly to traditional medicines that work more or less efficiently depending on the illness, patient and certain other factors. The molecular structure of many of these potential phage medicines is no longer a mystery, which opens a way for future genetic engineering to obtain phages of better therapeutic potential and wider specificities. Phage engineering is relatively fast and easy in the present era of synthetic biology.

Interactions and selected applications of phage proteins and macromolecular complexes are the subject of the second part of this volume. A chapter by Roman Häuser and co-authors reveals how phage protein interactomes can be reconstructed based on the results of high-throughput studies and presents a detailed overview of protein interactomes of several model phages. Hui Zhang and co-authors describe the structure, action and potential application of the most powerful biological nanomotors – complexes of phi29 phage portal proteins with other macromolecular components of phage DNA packaging machinery. A chapter by Kenan Murphy is focused on phage recombinases, which became a primary tool in various types of DNA manipulations *in vivo* and *in vitro*, even supplanting restriction enzymes in cloning protocols. Other phage enzymes, endolysins, are the subject of a chapter by Daniel Nelson and co-workers. As bacterial peptidoglycan-hydrolysing proteins, they are an attractive alternative to analogously acting antibiotics, and, in addition to phages that encode them, may become useful in the fight with antibiotic-resistant bacterial pathogens.

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