Preface

Cellular membranes are crucial for the survival of organisms and maintaining the lipid membrane structure is therefore paramount for the proper functioning of cells. Many efficient strategies for damaging membranes have evolved and pore formation is one of the most intensely studied and best understood. Pore formation is frequently used in toxic attack on cells, as it can lead to efficient disruption of cell metabolism or even cell death. There are several different ways in which proteins efficiently attach to lipid membranes, oligomerize, and punch holes in them. This book describes the functioning of two important pore-forming protein families, cholesterol-dependent cytolysins (CDC), and proteins of the membrane attack complex/perforin (MACPF) family, which are nowadays understood to belong together. Cholesterol-dependent cytolysins are key virulence factors of many pathogenic bacteria, while proteins of the membrane attack complex and perforin family enable removal of unwanted cells from organisms. CDC and MACPF proteins represent perhaps the best studied pore forming protein families and in the last couple of years we have witnessed a significant increase in our understanding of how they function. Perhaps the most surprising discovery was the realization that MACPFs and CDCs are evolutionarily linked through a common domain that forms the basis for transmembrane pore formation, and the two protein families are now collectively referred to as the MACPF/CDC superfamily. Many new members have been described and functionally characterized in recent years and the different contributors to this book provide a comparative analysis of the structure and function of a diverse range of MACPF/CDC superfamily members.

The introductory two chapters by Gregor Anderluh, Robert Gilbert and colleagues, and Masaru Nonaka set the stage for the rest of this book by providing an overview of the MACPF/CDC members and their evolutionary relationships. Next, the book deals with the structural properties of the cholesterol-dependent cytolysins (Robert Gilbert) and MACPF proteins (chapter by Andreas Sonnen and Philipp Henneke). The chapter by Benjamin Johnson and Alejandro Heuck provides a mechanistic explanation of membrane interaction and pore formation by perfringolysin O, one of the best-studied MACPF/CDCs. The next part of the book describes functional properties of MACPF/CDC proteins. A general chapter by Gregor Anderluh and colleagues provides an overview and general information about membrane interactions, pore formation, and effects on cells. Functional

properties and the biological role of several MACPF/CDC members are then described in more detail: pneumolysin (by Tim Mitchell and Catherine Dalziel), listeriolysin O (by Stephanie Seveau), perforin (by Judy Lieberman and Jerome Thiery, and Apolonija Bedina Zavec and colleagues), MACPF proteins of apicomplexan parasites (by Robert Menard and colleagues), and chlamydial MACPF proteins (by Lacey Taylor and David Nelson). Next, an interesting group of MACPF proteins from fungi that require a second, accessory protein for efficient pore formation is described by Peter Maček and colleagues. This book finishes with a chapter on fluorescence imaging of MACPF/CDC proteins by Michael Senior and Mark Wallace. This will be an important biophysical approach for study of MACPF/CDC interactions with the membrane, their assembly mechanism, and the properties of the final pore.

We hope that this book will set the stage for future studies on the evolution, structure, and function of MACPF/CDC members, particularly those that are as yet not so well known. There is certainly a lot more we need to learn and understand about these proteins, and it will be especially interesting to see what is discovered in the coming years about their roles in development, as part of the toxic arsenal of marine organisms and in the pathogenic mechanisms of bacteria and apicomplexan parasites. We enjoyed editing this volume and would like to thank our contributors very much for their involvement in the project, and for providing excellent chapters and enabling this book to offer fresh insights into the subject. We thank them for their engagement and hard work toward their contributions and are also grateful to Gisou van der Goot for her historical overview of pore-forming proteins. We would also like to express our sincere gratitude to the production staff at Springer, particularly to Thijs van Vlijmen for his patience and answers to our endless inquiries.

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