

# Preface

One of the most fascinating riddles in immune biology is how vertebrates can sense the presence of a broad variety of highly diverse pathological agents. In response to this challenge, the two branches of the immune system, innate and adaptive immunity, evolved during evolution. The innate immune system represents the more ancient and more rapid defense instrument against infectious microbes or other pathophysiological stimuli. This system relies on a repertoire of germline-encoded receptors that sense pathogen-associated molecules (“non-self”) and endogenous stress signals (“danger”). About 15 years ago, the term “inflammasome” was introduced as a new concept in this fascinating research field. Inflammasomes represent a conserved set of macromolecular signaling complexes in immune cells that sense “hazard” and trigger the inflammatory machinery. The inflammasome concept contributed significantly to a renaissance in the fields of innate immunity and cell death. In recent years, the overall importance of inflammasomes was and still is increasingly recognized, as the complex biology of various pathological scenarios is better understood. The concerted actions of inflammasomes and other components of the innate immune system are of great significance for responding adequately to harmful microbial infections. However, accumulating data also support the view that deregulated inflammasome signaling is connected to a variety of inflammatory human pathologies, including inflammatory bowel disease, rheumatoid arthritis as well as hereditary periodic fever syndromes. Unlike this high importance for human and animal health, it appears that a comprehensive volume on inflammasome biology is still not available.

With the breathtaking expansion of research on inflammasome signaling cascades in recent years, this is an opportune time to review present knowledge about inflammasome action. Accordingly, a comprehensive collection of reviews on the multiple facets of inflammasome signal transduction seems both timely and appropriate for a book series. The present volume on “Inflammasome Signaling and Bacterial Infections” summarizes our current scientific understanding of inflammasome biology in 13 chapters by experts in this research area. It is designed to provide an introduction to inflammasomes and bacterial pathogenesis for advanced

undergraduates, graduate students, medical students, postdocs, and (bio)medical investigators, who are interested in infectious diseases and immunology. We discuss the most recent insights in the major components of known canonical and non-canonical inflammasome complexes and highlight their mechanism of action, in particular in response to infection with important bacterial model organisms and the corresponding disease pathologies.

The first two chapters are designed to provide the necessary background and a general overview for understanding the topics covered in the following chapters. This introduction includes advances in understanding the inflammasome structure at the molecular level and general strategies of up- and downstream signaling events. In the subsequent chapters, we specifically discuss the composition and activity of distinct inflammasomes during infection with various gut pathogens (*Salmonella*, *Shigella*, *Yersinia*, *Listeria*, and *Helicobacter*), respiratory pathogens (*Mycobacterium*, *Legionella*, *Burkholderia*, and *Streptococcus*) as well as skin and soft tissue pathogens (*Francisella* and *Staphylococcus*). As will become evident from these detailed review articles, there is much more complexity in inflammasome signaling pathways than was originally anticipated, adding greatly to the interest into these signaling factor cascades. Within the individual chapters, readers will find not only consensus and paradigm, but also differing perspectives on the regulation and functions of the multitude of inflammasome factors. Importantly, all of the reviews point out specific areas, where the lack of sufficient knowledge and understanding raises intriguing new questions for further experimentation. These outstanding questions often pertain to the increasingly complex biological functions of inflammasome components and diverse mechanisms of regulation in a variety of systems, ranging from mouse models to humans. Recurring themes are (i) how the regulation and function of inflammasome proteins are highly dependent on the cell type and activating stimulus, (ii) how pyroptotic cell death is regulated in detail, and (iii) how persistent pathogens can dampen the canonical inflammasome machinery in order to establish long-term infection. In the future, better characterization of the cellular and molecular biology of the inflammasomes will pinpoint important new therapeutic targets for the treatment and prevention of multiple infectious diseases and pathological conditions. If this comprehensive collection of reviews on inflammasomes stimulates fresh new thinking and research on the involved signaling pathways, this book will have accomplished its goal.

The above-discussed advances in the field have helped to shape the core of this volume. I am very grateful to the scientific contributors from around the globe, who have participated in the preparation of these outstanding chapters covering our growing knowledge of this important innate immune mechanism. I hope that this volume brings an invaluable resource to readers new to the field and expands the resources for those professionals already working in the inflammasome area. I would like to thank all participants for their support and help in making this book a success.

Inflammasome Signaling and Bacterial Infections

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