

METHODS IN MOLECULAR BIOLOGY

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Mouse Models of Innate Immunity

Methods and Protocols

Second Edition

Edited by

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Cover Figure: (Figure 6F from Chapter 1) Post-natal day 14 chimeric F0 founder mice generated following CRISPR/Cas9 genetic modification. Contributed by Artiom Gruzdev and colleagues.

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Preface

Humans are exposed to millions of potentially dangerous pathogens on a daily basis. Our innate and adaptive immune systems work together to evade infection and minimize the impact of contact, ingestion, and inhalation of these agents. While the adaptive immune system is critical for providing a pathogen-specific immune response and long-lasting memory, the innate immune system provides the initial response during the critical first hours and days following exposure to new pathogens. The innate immune system is evolutionarily conserved, with elements found across vertebrates, invertebrates, and plant species. This is particularly true in terms of pattern recognition receptors and their respective signaling cascades that are responsible for the recognition of specific pathogen-associated or damage-associated molecular patterns. These receptors drive the molecular and cellular responses that enable effective host defense against extracellular and intracellular pathogens, damage, and cellular stress.

The ultimate goal of biomedical research is to improve the health and well-being of human patients. Because many of the elements associated with the innate immune system are evolutionarily conserved across species in terms of both structure and function, mouse models have become a preferred human surrogate or complementary model for clinical studies. The readily available assortment of genetically modified mouse strains provides potent tools to define the complex interactions associated with innate immune system function and host–microbe interactions. Indeed, advances in mouse models have occurred in unison with progress in human clinical studies, which together have had tremendous impacts on our understanding of the innate immune system across species.

In this second edition of *Mouse Models of Innate Immunity*, we have again assembled a highly diverse and well-regarded group of active researchers with extensive experience in immunology, microbiology, genetics, and animal models. Similar to the other volumes in the *Methods in Molecular Biology* series, these contributors have provided a unique group of highly detailed protocols to aid in the design and execution of experiments to fully evaluate essential elements associated with the innate immune response. The emphasis of this second edition has been placed on *in vitro*, *ex vivo*, and *in vivo* mouse models that accurately mimic physiologically and clinically relevant disease processes. The first half of the book contains protocols that focus on assessments of specific cells and/or pathogens that are critical for understanding innate immune function. These *in vitro* and *ex vivo* studies are designed to provide simplified model systems to evaluate novel hypotheses and deduce mechanistic insight, without the complexity and confounding factors commonly associated with *in vivo* studies. Building beyond these simplified models, the second half of the book provides robust protocols that are highly useful to evaluate innate immune system function and characterize phenotypes in complex *in vivo* model systems. These *in vivo* protocols describe methods to evaluate innate immune function in the skin, eye, lung, gut, and systemically. In addition to our focus on infectious disease models, in this

second edition we have also included several new protocols associated with autism, cancer, microfluidics platforms, and CRISPR systems. Thus, it is my genuine hope and expectation that the second edition of *Mouse Models of Innate Immunity* will benefit the biomedical research community by providing expert insight and protocols that will allow investigators at all levels to rigorously plan, implement, and assess mechanisms associated with the innate immune response.

Blacksburg, VA, USA

Irving C. Allen

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