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Series Editor:
John M. Walker
School of Life and Medical Sciences
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Mouse Models of Innate Immunity

Methods and Protocols

Second Edition

Edited by

Irving C. Allen

Department of Biomedical Sciences, Virginia–Maryland Regional College, Blacksburg, VA, USA

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Editor
Irving C. Allen
Department of Biomedical Sciences
Virginia-Maryland Regional College
Blacksburg, VA, USA

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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***

Contents

Contributors

Irving C. Allen • *Department of Biomedical Sciences, Virginia-Maryland Regional College, Blacksburg, VA, USA*

Janelle C. Arthur • *Department of Microbiology and Immunology, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA; Lineberger Comprehensive Cancer Center, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA; Center for Gastrointestinal Biology and Disease, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA*

Brittany P. Boribong • *Genetics, Bioinformatics, and Computational Biology, Virginia Tech, Blacksburg, VA, USA*

Michael A. Casasanta • *Department of Biochemistry, Virginia Polytechnic Institute, State University, Blacksburg, VA, USA*

Clayton C. Caswell • *Department of Biomedical Sciences and Pathobiology, Center for One Health Research, Virginia Maryland College of Veterinary Medicine, Virginia Tech, Blacksburg, VA, USA*

Sheryl Coutermarsh-Ott • *Department of Biomedical Sciences and Pathobiology, Virginia-Maryland College of Veterinary Medicine, Virginia Tech, Blacksburg, VA, USA*

Beckley K. Davis • *Department of Biology, Franklin & Marshall College, Lancaster, PA, USA*

Frank R. DeLeo • *Laboratory of Bacteriology, Rocky Mountain Laboratories, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Hamilton, MT, USA*

Kristin Eden • *Department of Basic Science Education, Virginia Tech Carilion School of Medicine, Roanoke, VA, USA*

Michael B. Fessler • *Immunity, Inflammation, and Disease Laboratory, National Institute of Environmental Health Sciences, National Institutes of Health, Research Triangle Park, NC, USA*

Kristin A. Gabor • *Immunity, Inflammation, and Disease Laboratory, National Institute of Environmental Health Sciences, National Institutes of Health, Research Triangle Park, NC, USA*

Michael Glogauer • *Faculty of Dentistry, University of Toronto, Toronto, ON, Canada*

Wei Gong • *Department of Hepatobiliary Surgery and Liver Transplantation, Shandong Provincial Hospital Affiliated to Shandong University, Jinan, China*

Kymberly M. Gowdy • *Department of Pharmacology and Toxicology, Brody School of Medicine, East Carolina University, Greenville, NC, USA*

Artiom Gruzdev • *Knockout Mouse Core, Reproductive and Developmental Biology Laboratory, National Institute of Environmental Health Sciences, National Institutes of Health, Research Triangle Park, NC, USA*

Thomas B. Hagler • *Knockout Mouse Core, Reproductive and Developmental Biology Laboratory, National Institute of Environmental Health Sciences, National Institutes of Health, Research Triangle Park, NC, USA*

Caroline N. Jones • *Department of Biological Sciences, Virginia Tech, Blacksburg, VA, USA*
Brita Kilburg-Basnyat • *Department of Pharmacology and Toxicology, Brody School of Medicine, East Carolina University, Greenville, NC, USA*
Scott D. Kobayashi • *Laboratory of Bacteriology, Rocky Mountain Laboratories, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Hamilton, MT, USA*
Lisa K. Kozicky • *Division of Gastroenterology, Department of Pediatrics, BC Children's Hospital Research Institute, University of British Columbia, Vancouver, BC, Canada*
Catherine R. Lammert • *Department of Neuroscience, Center for Brain Immunology and Glia, University of Virginia, Charlottesville, VA, USA; Graduate Program in Neuroscience, University of Virginia, Charlottesville, VA, USA*
Yu L. Lei • *Department of Periodontics and Oral Medicine, University of Michigan School of Dentistry, Ann Arbor, MI, USA; University of Michigan Rogel Cancer Center, Ann Arbor, MI, USA; Department of Otolaryngology—Head and Neck Surgery, University of Michigan Health System, Ann Arbor, MI, USA*
Jamie Lovaglio • *Rocky Mountain Veterinary Branch, Rocky Mountain Laboratories, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Hamilton, MT, USA*
John R. Lukens • *Department of Neuroscience, Center for Brain Immunology and Glia, University of Virginia, Charlottesville, VA, USA; Graduate Program in Neuroscience, University of Virginia, Charlottesville, VA, USA*
Natalia Malachowa • *Laboratory of Bacteriology, Rocky Mountain Laboratories, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Hamilton, MT, USA*
Dylan K. McDaniel • *Department of Biomedical Sciences and Pathobiology, Virginia-Maryland College of Veterinary Medicine, Virginia Tech, Blacksburg, VA, USA*
Charles E. McGee • *Duke Human Vaccine Institute, Duke University Medical Center, Durham, NC, USA*
Kenneth J. Oestreich • *Virginia Tech Carilion Research Institute, Roanoke, VA, USA; Department of Biomedical Sciences and Pathobiology, Virginia-Maryland College of Veterinary Medicine, Virginia Tech, Blacksburg, VA, USA; Virginia Tech Carilion School of Medicine, Roanoke, VA, USA*
Michael D. Powell • *Virginia Tech Carilion Research Institute, Roanoke, VA, USA; Graduate Program in Translational Biology, Medicine, and Health, Virginia Tech, Blacksburg, VA, USA*
Amina Rahimi • *Department of Biochemistry, Virginia Tech, Blacksburg, VA, USA*
Kota V. Ramana • *Department of Biochemistry and Molecular Biology, University of Texas Medical Branch, Galveston, TX, USA*
Manas K. Ray • *Knockout Mouse Core, Reproductive and Developmental Biology Laboratory, National Institute of Environmental Health Sciences, National Institutes of Health, Research Triangle Park, NC, USA*
Kaitlin A. Read • *Virginia Tech Carilion Research Institute, Roanoke, VA, USA*
Veronica M. Ringel-Scaia • *Department of Biomedical Sciences and Pathobiology, Virginia-Maryland College of Veterinary Medicine, Virginia Tech, Blacksburg, VA, USA; Graduate Program in Translational Biology, Medicine, and Health, Virginia Tech, Blacksburg, VA, USA*

Kelly Roney • *Rho, Chapel Hill, NC, USA*
Aaron Rothemich • *Department of Microbiology and Immunology, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA*
Christopher J. Sample • *Duke Human Vaccine Institute, Duke University Medical Center, Durham, NC, USA*
Greg J. Scott • *Knockout Mouse Core, Reproductive and Developmental Biology Laboratory, National Institute of Environmental Health Sciences, National Institutes of Health, Research Triangle Park, NC, USA*
Philip M. Sherman • *Cell Biology Program, Research Institute, Hospital for Sick Children, University of Toronto, Toronto, ON, Canada; Faculty of Dentistry, University of Toronto, Toronto, ON, Canada*
Daniel J. Slade • *Department of Biochemistry, Virginia Polytechnic Institute, State University, Blacksburg, VA, USA*
Laura M. Sly • *Division of Gastroenterology, Department of Pediatrics, BC Children's Hospital Research Institute, University of British Columbia, Vancouver, BC, Canada*
Bharath K. Sreekumar • *Virginia Tech Carilion Research Institute, Roanoke, VA, USA; Graduate Program in Translational Biology, Medicine, and Health, Virginia Tech, Blacksburg, VA, USA*
Yee Sun Tan • *Department of Periodontics and Oral Medicine, University of Michigan School of Dentistry, Ann Arbor, MI, USA; University of Michigan Rogel Cancer Center, Ann Arbor, MI, USA*
Linda Vong • *Cell Biology Program, Research Institute, Hospital for Sick Children, University of Toronto, Toronto, ON, Canada*
Haitao Wen • *Department of Microbial Infection and Immunity, The Ohio State University College of Medicine, Columbus, OH, USA; Infectious Disease Institute, The Ohio State University College of Medicine, Columbus, OH, USA*
Umesh C. S. Yadav • *Department of Biochemistry and Molecular Biology, University of Texas Medical Branch, Galveston, TX, USA*