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## Preface

In the face of frequent threats of either exogenous (usually infection) or endogenous (neoplastic transformation) origin, humans and other mammals are endowed with a vigorous and versatile capacity for host defense. This contributes to the maintenance of homeostasis and in the face of millions of years of evolutionary pressure, mammalian species developed two parallel yet highly interdependent systems to protect against infection and malignancy. Thus, the innate and acquired immune systems together perform remarkably well in responding to threats, thereby favoring survival. Not only are these two systems seamlessly integrated, but they also both support and cross-regulate each other at multiple levels. Hence, knowledge of the critical nodes that unite these systems is fundamental to a comprehensive understanding of mammalian host defense. Macrophages and dendritic cells are sentinels and effectors of innate immunity. Far beyond this, however, they are also perhaps more than any other cell type, poised at the interface with the acquired immune system where they critically influence the development of antigen-specific immune responses and long-term memory. The involvement of macrophages and dendritic cells in health and disease is not, however, limited to the realm of classical immunology. Research findings over the past several decades have made it abundantly clear that these cells are also centrally involved in heterogeneous inflammatory conditions and disease processes such as atherosclerosis, neurodegenerative disease, wound healing, and graft-versus-host disease to name only a few. In light of their critical contributions to diverse inflammatory diseases and to immunity and host defense, a contemporaneous understanding of state-of-the-art approaches to investigate the behaviors of macrophages and dendritic cells is useful, and is something this volume seeks to achieve.

An essential starting point to any research concerned with the properties or functions of macrophages and dendritic cells is the availability of adequate numbers of cells representing a highly purified homogeneous population. As such, four chapters are presented that address the isolation and cultures of these cells, including generating growth factor-dependent cell lines, methods for phenotypic characterization, and analysis of ontogeny.

Much of the work of macrophages and dendritic cells is initiated at the level of cell surface receptors that survey the environment for cognate ligands. Recognizing the centrality of receptor ligand interactions to the biology of these cells, two chapters are included that address the identification of novel myeloid cell surface receptors, while two complementary chapters describe approaches aimed at identifying novel ligands.

Phagocytosis is one of the most prominent functional properties of macrophages and to a lesser extent dendritic cells. Consequently, no contemporary volume of research approaches would be complete without addressing this area. Just as whole cell analysis is simplified when adequate quantities of pure starting material are available, this is also one of the challenges facing researchers studying phagosome biology. Furthermore, one of the areas of greatest interest to macrophage biologists is the fate of a phagosome once it is formed or “phagosome maturation.” Consequently, chapters are included that address topics including large-scale phagosome isolation, quantitative and real-time analysis of phagosome maturation, and the role of GTPases in regulating phagosome biogenesis.

Macrophages and dendritic cells are inherently resistant to the introduction and expression of foreign genes. This has consistently been a significant obstacle confronting researchers whose aim has been to assign function to individual genes and the proteins they encode. This volume takes advantage of recent advances in the area of genetic manipulation of macrophages and dendritic cells with three chapters addressing this area with a particular emphasis on siRNA approaches.

Macrophages are required to undergo an activation program in order to maximize their effector functions and macrophage activation is an area of intense interest. Controlling cell activation is also critically important to limiting collateral damage resulting from excessive inflammation. In recent years, it has become clear that macrophage activation is not a homogeneous process and that the phenotypic outcome is very much influenced by the local environment, most importantly cytokines, but other factors as well. Currently, two major macrophage activation programs have been described leading to the generation of either M1, proinflammatory, or M2 anti-inflammatory macrophages. Given the importance of this rapidly advancing area of research, three chapters in this volume address the M1 vs. M2 or “classical vs. alternative” paradigm of macrophage activation.

Macrophage activation and for that matter all other stimulus-dependent responses by these cells are brought about through tightly regulated and highly integrated signaling pathways. Cell regulation in these cells has been studied intensively and recently it has become clear that lipid signaling plays an important role in determining phenotype. As such, two chapters address the role of lipid signaling and lipid signaling intermediates in macrophage biology.

Finally, macrophages are endowed with a vast array of degradative enzymes that they use to carry out functional programs and which contribute profoundly to both health and disease. A chapter dealing with the secretion of matrix metalloproteinases by macrophages provides a window into advances in this area and offers a vantage point for future research concerned with how the enzymatic machinery of these cells is linked to tissue inflammation.

It is my hope that readers, both neophytes and seasoned investigators, will find *Macrophages and Dendritic Cells: Methods and Protocols* to be both timely and useful in their research. Most importantly, I thank the authors for valuable time spent in preparing their chapters and for sharing their experience and knowledge. Thanks is also due to John Walker for his editorial advice and Jessica Lin for her critical editorial assistance.

***Vancouver, BC***

***Neil E. Reiner***



<http://www.springer.com/978-1-58829-972-7>

Macrophages and Dendritic Cells

Methods and Protocols

Reiner, N.E. (Ed.)

2009, XII, 368 p., Hardcover

ISBN: 978-1-58829-972-7

A product of Humana Press