

## FUNDAMENTALS OF INFLAMMATION

The acute inflammatory response is the body's first system of alarm signals that are directed toward containment and elimination of microbial invaders. Uncontrolled inflammation has emerged as a pathophysiologic basis for many widely occurring diseases in the general population that were not initially known to be linked to the inflammatory response, including cardiovascular disease, asthma, arthritis, and cancer. To better manage treatment, diagnosis, and prevention of these wide-ranging diseases, multidisciplinary research efforts are under way in both academic and industry settings. The purpose of this book is to provide an introduction to the cell types, chemical mediators, and general mechanisms of the host's first response to invasion. World-class experts from institutions around the world have written chapters for this introductory text. The text is presented as an introductory springboard for graduate students, postdoctoral Fellows, medical scientists, and researchers from other disciplines who wish to gain an appreciation and working knowledge of current cellular and molecular mechanisms fundamental to inflammation.

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## PREFACE

The acute inflammatory response is the body's first system of alarm signals that are directed toward containment and elimination of microbial invaders. Uncontrolled inflammation has emerged as a pathophysiologic basis to many of the widely occurring diseases in the general population that were not initially known to be linked to events in the inflammatory response. These include cardiovascular diseases and neurodegenerative diseases (including Alzheimer's disease), and it has now become apparent that inflammation is an important component of cancer progression and the persistence of neuropathic pain. These are diseases that cross many disciplines. To better manage treatment, diagnosis, and prevention of diseases, multidisciplinary research efforts are under way in both academic and industry settings. Since knowledge of the acute inflammatory response in itself spans many disciplines, the editors' mission is to provide in this text an introduction to the cell types, chemical mediators, and general mechanisms that are involved in this primordial first response of the host to invasion. It is also now clear that the termination or the resolution of the acute inflammatory response is an active process, which is pivotal and is the outcome of the acute response. As an endogenous programmed response, the terrain of resolution holds many new possibilities for treatment and prevention of uncontrolled inflammation in a wide range of diseases.

World-class experts from many different universities and fields have written the chapters of this introductory textbook. The main sections of this book are focused on the cell types, processes, and molecular events that constitute the acute inflammatory response as we know it today. They cross the biomedical disciplines of hematology, infectious disease, pulmonary medicine, gastroenterology, oral medicine and dentistry, biochemistry, immunology, immunopharmacology, and general pathology. Given the need to gain a more complete understanding of the acute

inflammatory response and its resolution, the scope of this text is presented as an introductory springboard intended for graduate students, postdoctoral Fellows, medical scientists, and senior researchers from other disciplines who wish to gain an appreciation and working knowledge of the current cellular and molecular mechanisms of the effector immune system that are fundamental in inflammation.

Part I of this text is devoted to examining acute inflammation, chronic inflammation, wound healing, and resolution, with an emphasis on current concepts in molecular and cellular events and their relevance to health and disease. The first three chapters in Part I thus provide a general view of the terrain and cellular players in inflammation.

Part II of this text brings into focus the individual cell types important in acute and chronic inflammation, their cellular and molecular biology, and, importantly, an introduction of their role in disease processes. Attention is also directed toward the importance of cell–cell interactions in the acute inflammatory response and our current understanding of the key interface between vascular, blood-borne cell types and their relation to interstitial events within inflamed tissues.

Part III stresses the importance of endogenous chemical mediators and local mediators in this process. In this regard, an update is provided on the important role of lipid-derived mediators and protein-derived mediators, including chemokines and cytokines, as well as nucleotide mediators such as adenosine and oxygen-derived reactive oxygen species. The importance of surface adhesion molecules in these processes is also stressed. The role and molecular mechanisms of each of these systems as well as their contributions to host defense is presented in view of their physiology and pathobiology in inflammation.

Since there is considerable interest in understanding the endogenous control mechanisms, as well as

new therapeutic approaches to control inflammation in disease, Part IV of this text is devoted to an introduction to immunopharmacology, with a view of current mediators and mechanisms involved in inflammatory pain, currently used nonsteroidal anti-inflammatory drugs, and the importance of cytokines in our current appreciation of the interface between cancer and inflammation.

Part V brings us to one of the unique features of this introductory textbooks. Each of these chapters focuses on the tissue face or histology of inflammation as viewed in human diseases that are characterized by excessive inflammation. The chapters in this part are short and include histology and case reports. This part aims to discuss clinician scientists' and academic pathologists' views about inflammation in relation to widely occurring diseases. The goal is to give readers a picture of inflamed tissues and disease processes that we need to address as researchers to develop better approaches for prevention and treatment via new knowledge and innovative research of these diseases. Part V includes examples from airway inflammation, neural inflammation, sepsis, gastrointestinal diseases, and skin diseases characterized by inflammation, as well as kidney and cardiovascular diseases.

Part VI presents current and widely used animal models that are particularly useful in understanding experimental approaches to study inflammation. This part includes chapters with an emphasis on methodological approaches to address tissue injury and

reperfusion of tissues, as these events can be viewed as rapid local acute inflammatory responses in vivo. Chapters are also included that evaluate current asthma, arthritis, ocular, atherosclerosis, and oral inflammation. Chapters in this part include the host's response to pathogens as a classic approach to gain an in-depth appreciation of the cellular and molecular events that have evolved in concert with the microbial world and their dynamic interplay in inflammation.

Each of the chapters is presented as an introduction by experts who are involved in cutting-edge research in their area of expertise. The aim of the editors is to provide a springboard for new investigators and research centers currently devoted to cutting-edge research in these areas. It exposes the reader to the exciting and fascinating cellular and molecular events that are involved in acute inflammation, chronic inflammation, their termination, and our quest for precise pharmacologic control in these life-sparing processes.

Experts worldwide have contributed concise chapters to launch this textbook for students new to this field. The text should be of interest to both students and investigators in academic and industrial settings. The editors trust that the reader will share our enthusiasm and continued excitement for studying the cellular and molecular events in this first response of the human body to invasion, injury, and tissue damage from within the area of inflammation research.

*The Editors*