
Immunology of Aging

Ahmad Massoud • Nima Rezaei
Editors

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 Springer

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Foreword

The rapidity of scientific progress over the last few years emphasizes the utility of a new collection of state-of-the-art reviews on the immunology of aging, as edited here by Drs Massoud and Rezaei. They have succeeded in putting together a remarkable set of contributions from many well-known scientists in the immunosenescence research field.

Because the number of elderly people is increasing, both in the rich world and in developing countries, aging is a huge challenge for society globally and for the science of biogerontology. Our knowledge of aging processes has exploded during this last decade, and we are starting really to understand what aging means and what causes it, even if our knowledge is still fragmentary. Nonetheless, most of this knowledge has not yet been translated meaningfully into the clinical setting. In addition to comprehensive coverage of basic research in immunity and aging, this book emphasizes the eventual clinical implications of this work.

One essential target of the complex physiological changes occurring in all organ systems with aging is the immune system. We can conceptualize this change in the immune system either as a dynamic dysregulation or an adaptation to an ever-changing universe of pathogen exposures. There is no current consensus on what the exact changes covered by the general term “immunosenescence” actually are. There is even less consensus on the causes of these changes. Also because of these controversies, it seems timely to publish a book featuring different viewpoints as represented by the many different authors. Thus, this book comprehensively treats most aspects of the immunology of aging.

The first three chapters deal with the concept of integrating age-associated changes of the immune system in the general dynamic changes of the organism, by a holistic approach. Thus, knowledge of immune system interactions (either positive or negative) with other physiological systems such as the neuroendocrine system is essential for understanding immunosenescence. Moreover, the immune system appears to be a more sensitive “marker” or “surrogate” for biological aging, being more indicative of the state of bodily functioning than chronological age. This exceptional natural aging of the immune system has been integrated and experimentally challenged in the oxy-inflamm-aging theory and the altered functions of somatic stem cells. Thereafter, Chap. 4 deals with the many different theories of aging and concludes that the inflammation theory, stated as mostly integrative of all the

others, is supported by much experimental evidence, such as in the domain of oxidative stress, autophagy, and DNA repair pathways.

Because the immune system is divided into the two main arms of innate and adaptive immunity, the next four chapters deal with the innate immune system separately by describing the behavior of the individual cells which constitute it. Alterations to neutrophil, eosinophil, and basophil functions in aging are concluded to be mainly due to signaling alterations; this offers potential therapeutic targets in these cells. Another chapter discusses the essential role of dendritic cell alterations in immunosenescence. The next is devoted to changes in NK cell phenotypes and functions with aging. Their potentially important role in connection with cancer is discussed in detail. Finally, the role of the pattern recognition receptors in innate cells is reviewed from a functional and evolutionary perspective in the context of aging.

The next six chapters review changes in the adaptive immune system with age. Five of these chapters are about T-cell alterations as the most well-studied and important changes in immunosenescence, but B cells are not neglected as well. One chapter reviews the repertoire changes in T cells with aging leading to increased incidence of infections by newly encountered pathogens and an altered vaccination response. Reciprocal to this change is the increase of memory T cells, especially CD8+ T cells, induced by chronic antigenic challenges such as CMV infection. The next two chapters on T cells are dedicated to functional changes in T cells with aging and to the underlying mechanisms. The potential biomarker role of these changes for healthy aging is also mentioned. These chapters additionally describe how such alterations to T-cell function are related to many age-related diseases such as infections and cancer. T-cell aging may be considered as a hallmark of many pathological processes and changes observed with aging. The next chapter enlarges our understanding of the causes of these age-associated alterations in T cells by describing the metabolic alterations in different T-cell subsets. Finally, changes to Tregs are discussed in the next chapter in relation to aging and age-associated diseases. The last chapter in this part dealing with the adaptive immune response is devoted to B cells, changes to which are discussed in relation to the increased susceptibility to infections and decreased vaccine response in elderly subjects. Chapter 15 moves to the essential role of miRNAs in immunosenescence in relation to other genetic alterations, while the next chapter explains immunogenetics of aging. The next three chapters deal with the higher incidence of infections in elderly subjects, especially influenza infection and its prevention by vaccination. The incidence of several infections is increasing in the elderly, including sepsis due to *E. coli* or Staphylococcus infections as described in the first chapter of this section. This increased incidence of infections either at home or in hospitals is mainly due to age-associated dysregulated immune system. The next chapter specifically discusses the effects of influenza in the elderly and the possible causative immune alterations involved. Influenza is typically a disease of the elderly, and most mortality occurs in people over 60 years old. Finally, the last chapter reviews the requirement for new vaccines and new vaccine strategies in the elderly and specifically discusses recent progress in the field of

influenza vaccination (such as adjuvant addition, different routes of administration, or the enhanced antigenicity of the vaccines).

The next part of the book includes three chapters dealing with an important aspect of aging and especially of immunity, specifically the effects of nutrition and diet. The first chapter in this part describes the role of body reserves and nutritional uptake as essential prerequisites for well-functioning immune responses, which do take a large amount of energy delivered by nutrients that can be deficient in most of the elderly people. The second chapter in this section describes the role and importance of a diet adequate for major nutrients, vitamins, and oligoelements as being essential for healthy aging and for a well-functioning immune system. The gut microbiota also depends on an adequate diet. Malnutrition associated with aging may largely contribute to immunosenescence. Caloric restriction and the Mediterranean diet may have some beneficial roles and are to be favored by the elderly. The last chapter discusses the specific role of Zn which intervenes in enzyme and protein functions and in genomic stability. There are several causes for decreased Zn availability in the elderly, but supplementation can yield conflicting results. Nutrigenomics and how it should be applied to the elderly need to be considered in future studies.

The next two chapters discuss the role of oxidative stress in the aging process and in immunosenescence. Oxidative stress plays an important role in cell senescence by modulating proliferative and functional capacities. There is an interplay between oxidative stress and the inflammatory process characterizing the aging immune system.

One chapter is devoted to skin aging and immunosenescence. The visible changes and the underlying molecular alterations are largely influenced by the dysregulated immune system with aging in some way specific to the skin.

The last chapter discusses the effect of physical exercise on the immune system with aging. Physical activity has many beneficial effects on the modulation of age-related diseases and even on longevity and healthy aging. Most studies are cross-sectional, but some longitudinal studies have been performed. Many immune parameters have been studied, often with disparate results. Nonetheless, it seems that exercise is able to enhance immune function in elderly subjects and possibly even postpone the occurrence of immunosenescence. Physical activity is thus beneficial for the elderly and their immune functions.

Considering the broad overview of immunosenescence and its consequences, and their potential modulation, this book should fill a gap in a timely manner. It should be on the shelves of every library as a very useful tool for researchers as well as students.

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Preface

Aging is defined as the accumulation of changes in a person over time. It is well established that the overall immune function declines with advancing age, a phenomenon referred to as immunosenescence. Several studies have been performed during recent decades, indicating the pathological consequences of age-related changes in the immune system, leading to a variety of manifestations such as increased susceptibility to infections and an increased tendency toward autoimmunity and immunopathology. Immune function in elderly is not deteriorating by random; rather, it appears to be under genetic control, as well as environmental factors such as diet and lifestyle. Therefore, maintaining a healthy lifestyle is an important contributing factor in supporting a more functional immune system during aging. It should be noted that average age of the world's population is increasing at an unprecedented rate. The concept that changes in the immune system may be a fundamental predisposing factor to the overall aging complications is a field of scientific inquiry and remained ambiguous in many aspects.

We are delighted to edit the book *The Immunology of Aging*, the book which is a result of extensive collaboration of more than sixty great thinkers and scholars in collaboration with a number of juniors in this field, from more than ten different countries. While we are thankful to all of them for making it possible, we would also like to acknowledge the effort of one of our medical students, Armin Hirbod-Mobarakeh, who not only contributed in drafting a chapter but also helped in technical and language edition of the whole chapters.

Whether your interests are immunological aspects of aging, age-related diseases, and longevity, this book can serve as an appropriate venue. Contributing authors in this book present a broad multidisciplinary background on the immunological facets of aging. The aim of this book is to summarize the most up-to-date information on the scientific issues in aging of the immune system research with an insight into the effect of this process on susceptibilities to diseases which are most common among elders. The retrieval strategies to slow down the decline in the immune system in the elderly are another subject detailed extensively. We hope that the book would be welcomed by the scientists and clinicians with interest in the field of aging.

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