

Immunology is the quintessential medical science. Indeed, no branch of the medical sciences has improved the health of people more than the application of immunologic principles to prevention of disease. Smallpox has been eliminated from the planet as a natural infection, as has poliomyelitis from the Western Hemisphere. Hepatitis B vaccine has prevented more cancers than any intervention other than smoking cessation. The newly introduced human papilloma virus vaccine promises to cut strikingly the toll of cervical cancer.

The continued need for progress in immunology is clear. The HIV epidemic roars on. Disappointing results from vaccine trials require a redoubled effort to understand how to build the new generations of vaccines that can attack the really hard problems, including HIV, tuberculosis, and malaria, among infectious diseases. Highly effective therapeutic vaccines for cancers still elude us, but progress in understanding the innate immune system and regulatory T cells places new tools in our hands to continue the attack on this major problem.

Understanding the basis of inflammation and the cytokine world has given us effective drugs to treat rheumatoid arthritis and other autoinflammatory/autoimmune diseases. The value of the interventions based on this knowledge, such as the use of tumor necrosis factor (TNF), interleukin-6 (IL-6), and IL-1 blockers, is now established. The application of anti-CD20 in the treatment of autoimmune disorders shows great promise.

Fundamental Immunology has the goal of aiding in the education of a new generation of immunologists who can both probe more deeply into the organizing principles of the immune system and can translate this new information into effective treatments and preventatives that can extend and enlarge on the record of immunologic science in bettering the lot of humankind.

Were I beginning the task of preparing a comprehensive text of immunology today, I might have titled it *Immunology, Endless Fascination*. Certainly that describes my own view of this science over the more than 25 years that I have been working on the six editions of *Fundamental Immunology*. I had believed that scientific progress was marked by periods of intense creativity, during which new concepts were established, followed by longer periods of consolidation, when work that made important but anticipated advances would dominate. Perhaps that will prove to be true of modern immunology as well when it is looked at

by a disinterested observer, but for one in the midst, the pace of discovery seems to speed up with each passing year. *Endless fascination* certainly describes my experience of immunology.

During the interval since the previous edition, there have been major advances in every field of immunology. Indeed, in one of the most striking pieces of work, an entirely new adaptive immune system has been discovered. Pancer, Cooper, and their colleagues have shown that jawless vertebrates, rather than using an adaptive immune system based on the immunoglobulin superfamily T-cell and B-cell receptors, evolved an entirely distinct adaptive system based on the use of leucine-rich repeat molecules as the recognition elements. The understanding of innate immunity continues to grow with the deepening understanding of the range of microbial sensors and of how they link to the adaptive immune system. The 2007 Lasker Prize for Basic Medical Sciences went to Ralph Steinman for his discovery of dendritic cells, which interpret the messages of the innate system to the adaptive system. The importance of regulatory T cells continues to grow, as does our insight into the mechanisms of their action. The cytokine biology field expands and broadens in its importance. The number of interleukins is now into the mid-30s, and some of the more recently discovered molecules have the most important functions. The application of imaging technologies that allow the visualization of the *in vivo* behavior of the cells and tissues of the immune system has provided spectacular insights into the structure and dynamics of the system and promises still more amazing results in the future. The field of systems immunology, still in its infancy, has given notice that it will be a major approach to our science in the next decades.

I hope that this sixth edition will convey this dynamism and provide the reader with both a solid grounding in our field and with much of the very latest that has been achieved. As with each of the previous editions, most of the chapters are entirely new and not simple reworkings of the chapter in the previous edition. In order to contain the sixth edition within one volume, a decision was made to limit the number of references that will be printed in the text. For those chapters in which there are substantially in excess of 200 references cited in the text, the authors have selected 200 to be included in the print version of the book. All are included in the electronic version. The electronic version can be accessed at www.fundamentalimmunology.com.

As before, this edition begins with an introductory chapter, "The Immune System," aimed at giving an overview of modern immunology and providing those new to the field with the basis to go on to the subsequent chapters. This is followed by an "expanded introduction" provided by the sections, "Organization and Evolution of the Immune System," "Immunoglobulins and B Lymphocytes," and "T lymphocytes." I have introduced a new and extended section, "The Intersection of Innate and Adaptive Immunity," which is followed by the section, "Regulation and Effector Functions of the Immune Response." The book concludes with sections devoted to the immune system's role in protection against pathogenic microorganisms, "Immu-

nity to Infectious Agents," and on how the immune system is involved in a variety of human disorders, "Immunologic Mechanisms in Disease."

I repeat a word of caution that has been in the Preface to each edition. Immunology is moving very fast. Each of the chapters is written by an expert in the field, but in some areas there may be differences of opinion expressed by equally accomplished authors. I ask the reader to take note of the differences and to follow developments in the field.

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