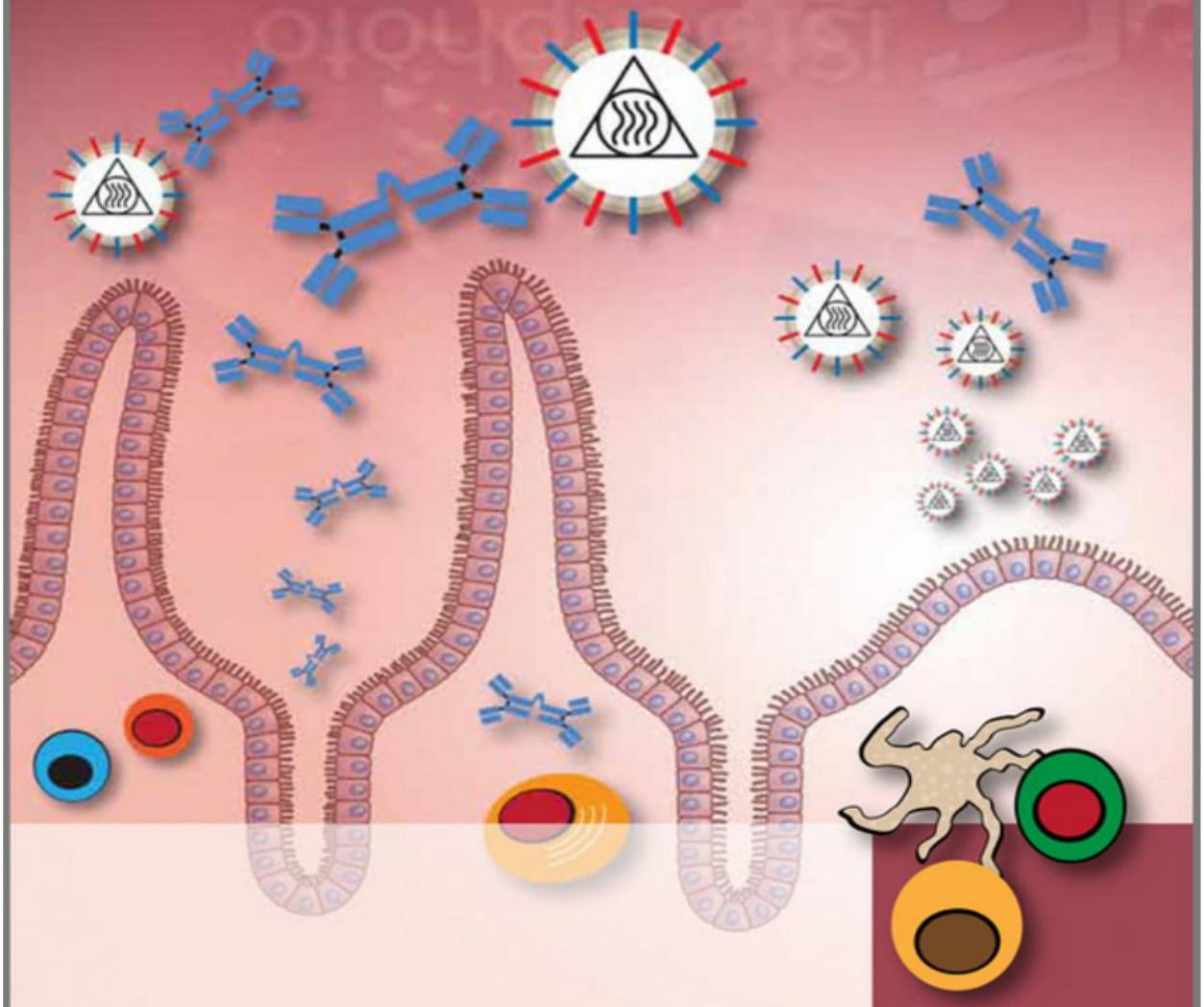
Andrew E. Williams

Immunology

Mucosal and Body Surface Defences



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Preface

For thousands of years humans have marvelled at how the body is able to protect itself from infectious pathogens. Even the ancient Chinese and Greeks acknowledged the protective effects of the immune system, noting how one is rendered resistant to catching the same disease a second time. The first empirical studies were performed by Edward Jenner, and later Louis Pasteur, who developed vaccines against smallpox and anthrax, respectively. Indeed, vaccination has become such an important aspect of human health it is sometimes easy to forget the central role the immune system plays in affording protection against so many diseases.

The vast majority of medically important pathogens infect their host across a body surface such as the skin, or across a mucosal tissue such as the respiratory tract or intestines, as these sites are the ones exposed to the external environment. Vertebrates have therefore evolved elaborate immune defence mechanisms to protect against infection across mucosal linings and body surfaces. Mucosal immune defence mechanisms are therefore integral to our survival. However, conventional immunology textbooks largely overlook this aspect of the immune system, even though it remains fundamental for the prevention of infectious disease. Many have continued to teach immunology based on knowledge of the central immune system of the blood and spleen, rather than teaching immunology from the perspective of mucosal and body surfaces. After all, these are the places where host–pathogen interactions actually take place. Therefore I have tried to redress this bias by focusing on immunity at mucosal and body surfaces. This book should therefore prove useful for science undergraduates studying immunology, medical students undertaking academic studies, postgraduate students working toward a higher degree and the broad spectrum of

professional academic and clinical scientists working in the field of immunology.

Knowledge of how the immune system operates has increased extensively in the past 50 years, including our insight into mucosal immunology. The first three chapters describe the basic architecture of the immune system and the elements of innate and adaptive immunity that contribute to protective immune responses. A more focused description of the innate immune system is given in Chapter 2, including aspects of barrier, chemical and mechanical defence, components of innate immunity which are so often overlooked. A description of the effector functions of the cells of the innate immune system, such as macrophages, granulocytes and NK cells, is also given. A similar approach is used in Chapter 3 to illustrate the ways in which adaptive immune responses are orchestrated, including how B cells produce antibodies and how T cells elicit their effector functions. This includes a discussion of B cell and T cell selection and the generation of memory cells, which are key to providing long-lasting protection and is a central concept in immunology.

The next two chapters focus on two important families of signalling molecules, the cytokines and chemokines, which have fundamental roles in orchestrating the spatial and temporal mechanics of an immune response. These chapters define just how important cytokines and chemokines are to the organization of the immune system.

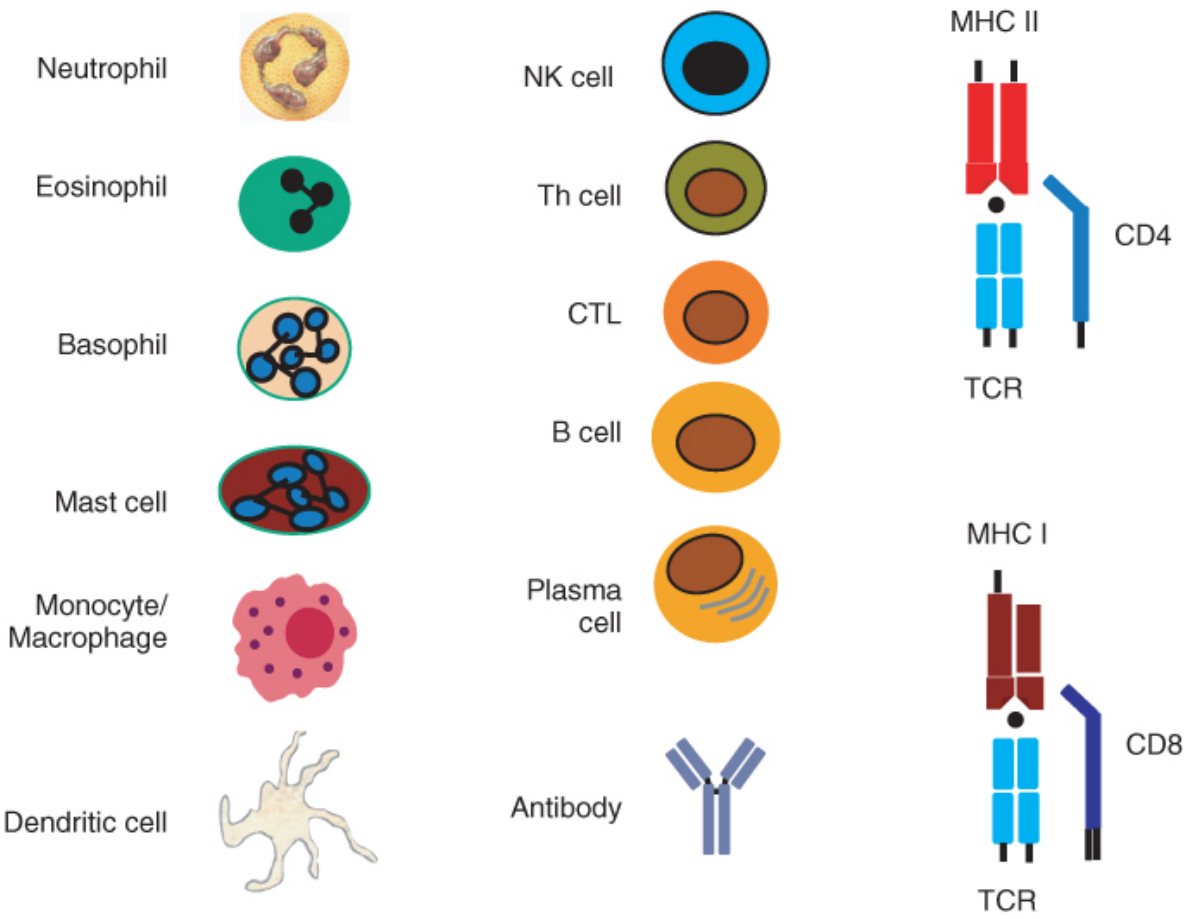
Chapters 6 to 10 describe the central thesis of this textbook, in that they describe the workings of the mucosal immune system. An introductory chapter outlines the central concepts of the mucosal immune system that differentiates it from the central or peripheral immune systems. The key structural and cellular components and the common themes that link mucosal tissues are explored. For example, epithelial barrier formation, aggregation of

organized lymphoid tissues, the importance of secretory IgA in mucosal defence and the need to balance immunity with homeostasis, are discussed. The concept of inductive sites, where immune responses are initiated, and effector sites, where immune cell functions take place, are discussed. From there, a description of the major tissues that form mucosal associated lymphoid tissue (MALT) is described, including the gastrointestinal tract, respiratory tract, urogenital tract and the conjunctiva of the eye. In addition, the importance of the skin in body surface immunity is examined.

The next four chapters are devoted to studying immunity against the four major groups of pathogen, the viruses, bacteria, fungi and parasites, with particular emphases on those infectious microorganisms that infect mucosal or body surfaces. This discussion includes the innate and adaptive immune mechanisms that are responsible for protection and the evasion strategies that these pathogens employ in order to subvert host immune responses.

Chapter 15 focuses on immune-mediated diseases that affect mucosal and body surfaces, including hypersensitivity reactions, allergies and autoimmunity. Chapter 16 details the various aspects of mucosal tumour immunology, in particular how the tumour and the immune system are constantly competing with each other. Finally, Chapter 17 describes the process of vaccination, from the conventional strategies most commonly used today, to novel regimens that specifically target the mucosal immune system and to cutting edge technologies used in modern vaccine development.

List of Standard Cells and Symbols



Chapter 1

Basic Concepts in Immunology

1.1 The Immune System

The immune system evolved so as to defend our bodies against infectious microorganisms such as viruses, bacteria, fungi and parasites. Throughout history it has been observed that people who survive an infectious disease acquire protection against that disease, which is otherwise known as immunity. As far back as the fifteenth century attempts have been made to induce immunity against infectious diseases, a process referred to as vaccination. The realisation that immunity can be transferred from one person to another demonstrated that soluble factors exist in the blood and body fluids that protect against pathogens. It is now known that cellular components of the immune system are also present throughout the entire body and that these immune cells engage with any harmful substance or microorganism in order to preserve the integrity of host tissues. The defence against microorganisms is fought on many fronts and there are immune cells and innate components of the immune system within every tissue and organ. There are a multitude of cells and soluble factors that can be considered part of the immune system. For example, the barrier function of the outer layers of the skin, the mucus produced in the airways, the antibodies secreted into the gut lumen or the circulating lymphocytes that destroy virus-infected cells. The immune system comprises a number of different cell types and a multitude of secreted factors and surface bound molecules.