FOREWORD

FOCUS CONTENTS

Mucosal matters

Abstract | The field of mucosal immunology covers a lot of territory, given that it comprises the large physical surfaces that line the body's passages and cavities and that link the external environment to the immune system. New insights into the workings of the mucosal immune system, together with clinical and genetic advances, offer exciting opportunities for translational research.

This Focus issue of *Nature Reviews Immunology* presents a series of specially commissioned Review articles that update us on the importance and breadth of current research in the field of mucosal immunology, and that reveal the emerging translational and therapeutic opportunities for infectious, inflammatory, autoimmune and allergic diseases that involve mucosal tissues. This issue is produced in collaboration with the Federation of Clinical Immunology Societies (FOCIS), which is dedicated to encouraging education and research across multiple scientific and medical disciplines to integrate immunological approaches to disease.

The mucosal surfaces of the gastrointestinal, reproductive and respiratory tracts are in direct contact with the external environment and are therefore susceptible to invasion by pathogens. To exploit mucosal routes for optimal vaccination or restore the integrity of the mucosa at sites of immunopathology, we need to understand the cells, molecules and mechanisms involved in immune responses at mucosal sites. What is particularly unique about mucosal sites is their continuous exposure to environmental antigens and commensal microorganisms. So immune cells distributed throughout the gut-associated lymphoid tissues (GALTs) must balance the need to remain hyporesponsive to commensal bacteria with retaining their capacity to respond to a pathogenic insult. Such a feat is achieved through an elaborate crosstalk between the epithelium and transient and resident components of the innate and adaptive immune systems. In addition, the response is constantly moulded by interactions with the bacterial communities.

In this issue, David Artis discusses these interactions and considers how microorganisms are sampled in the intestine; how intestinal epithelial cells (IECs), which were once considered to provide a simple physical barrier to the external environment, discriminate between commensal and pathogenic bacteria; and how epithelial-cell-derived factors, through effects on dendritic cells (DCs) and lymphocytes, regulate intestinal immune homeostasis.

One of the oldest known components of mucosal immunity, IgA, is revisited by Andrea Cerutti, who reviews recent evidence indicating that bacteria regulate IgA responses by promoting links between B cells and components of the mucosal innate immune system, including epithelial cells and DCs. A better understanding of this crosstalk may help us to develop more effective mucosal vaccines, as well as new therapeutic and preventive measures against inflammatory diseases.

At the juncture of innate and adaptive immune responses in the intestinal mucosa lie intestinal DCs, which drive both protective responses against oral pathogens and tolerogenic responses to commensal microflora and dietary antigens. As reviewed by Janine Coombes and Fiona Powrie, these DCs represent an appealing target for the modulation of intestinal immune responses, given their diverse functions in promoting IgA production, regulating T-helper-cell responses and facilitating regulatory T-cell development.

Florian Hladik and Juliana McElrath draw to our attention the fact that HIV infects millions of people worldwide each year through mucosal transmission. They review our current understanding of the immediate events that follow viral exposure at genital mucosal sites. The development of effective strategies for the prevention of HIV infection may hinge on understanding the early steps of HIV invasion of the immunological barrier that occurs at these sites.

Translational research in inflammatory bowel disease (IBD) is a prime example of the new era of personalized medicine, in which genetic variation between individuals underlies specific immune responses that lead to tissue pathology. Judy Cho reviews the recent insights into immune pathways and mechanisms gained from gene discovery in IBD; several of the polymorphic genes associated with disease could represent candidates for targeted immune intervention. Remarkably, some of the genes associated with IBD are also associated with other organ-specific autoimmune diseases, suggesting common mechanisms and similar potential treatments.

The diversity of the underlying mechanisms for the control of mucosal immune responses presents both a challenge and an opportunity to researchers. Much remains to be learned, but the studies highlighted in this issue illustrate the potential for information exchange between research and clinical disciplines in the field of immunology to lead to medical innovation — a goal shared by *Nature Reviews Immunology* and FOCIS.

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