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An Antigen Depository of the Immune System: Follicular Dendritic Cells

Edited by Marie H. Kosco-Vilbois

With 39 Figures

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Cover illustration: The cover illustration which combines a background of scanning electron micrographs with two contrasting cartoon overlays, is designed to emphasize the changing morphology of the FDC from filiform to beaded dendrities during its functional relationship with B cells of the developing germinal center. The yellow overlay depicts the mystery of the FDC (blue)-antigen (red)-iccosome (beads)-B cell (maroon) microenvironment. In this unique setting, the FDC transfers the retained antigen via iccosomes to germinal center B cells. The blue overlay shows the B cell endocytosing the iccosomes for antigen-processing. Via the Golgi apparatus and transport vesicles, the processed iccosomal antigens are then re-expressed at the B cell's surface for presentation to T cells. (Professor Andras K. Szakal, Department of Anatomy, Medical College of Virginia, Virginia Commonwealth University, Richmond, Virginia)

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Preface

Follicular dendritic cells (FDC) are unique among cells of the immune system. While their morphological characteristics resulted in their inclusion as a 'dendritic cell type', they differ quite significantly from the other members of the dendritic cell family. In contrast to T-cell-associated dendritic cells or the Langerhans cells found in the skin, FDC reside in highly organized B cell follicles within secondary lymphoid tissues. This site of residence provided a nomenclature committee in 1982 with the second descriptive factor for the derivation of their name. The cardinal feature of FDC is to trap and retain antigen on the surface of their dendritic processes for extended amounts of time and it is this feature that provides the conceptual component for the title of this book.

In response to an antigenic challenge, primary B cell follicles undergo dynamic events, giving rise to germinal centers which are associated with activation, expansion, and differentiation processes of B cells. The interactions of B cells with FDC and T cells in the germinal centers are essential for generating the complete repertoire of antibody isotypes obtained during an antibody response. In addition, stimuli either initiated or maintained during the germinal center reponse leads to production of high affinity antibodies through the processes of somatic mutation and clonal selection. In this context, FDC act as a pivotal source of antigen. They accumulate foreign proteins (e.g., viruses and bacteria) in an unprocessed form on their plasma membranes. They then alter their morphology, forming iccosomes, and deliver the immunogen to specific B cells which subsequently internalize, process, and present the material to elicit help from the surrounding T cells. As the response continues, FDC appear to provide soluble and cell-surface-associated stimuli that aid in directing the reaction. Finally, as the germinal center response subsides, FDC undergo morphological changes that cause the immune complexes to become buried within labyrinthian patterns of membrane formed by the braiding of their dendritic processes. This capacity to preserve unpro-

cessed antigen within the body has been linked to the long-term maintenance of circulating high-affinity antibody and B memory cells.

In addition to the benefits associated with this feature of long-term antigen retention, viral trapping is especially significant in the pathogenesis associated with the acquired immunodeficiency syndrome (AIDS). It has now gained widespread acceptance that the FDC-retained human immunodeficiency virus (HIV) provides an important reservoir for this infectious agent. FDC are also involved in other pathological conditions such as certain neoplasias, and ectopic germinal centers are associated with autoimmune diseases. Thus continued accumulation of information for the role of FDC during maintenance of a healthy individual as well as their contribution to disease states will provide insight into means of affecting the humoral and cellular immune response.

The contributions within this book represent reviews of recent work carried on by many of the main laboratories worldwide pursuing questions concerning FDC. The influence of FDC on B cell activation, survival and differentiation are addressed using several different model systems. While the full extent of the molecules involved in these interactions are yet to be revealed, the latest experimental data are presented. In addition to the discussion of their accessory activities, the highly controversial issue for the origin of FDC is also included. While the reader will find a wealth of important information contained in these chapters, hopefully, one will also begin to realize the multitude of questions that remain to be both addressed and answered concerning the full involvement of FDC in immune responses.

Geneva — Marie H. Kosco-Vilbois

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List of Contributors

(Their addresses can be found at the beginning of their respective chapters.)