Preface

Discovery of the BLyS (also known as BAFF) family of ligands and receptors has yielded a paradigm shift in our view of B-lymphocyte selection, survival, activation, and homeostasis. Previously, the B-cell antigen receptor (BCR) was viewed as the sole mediator of these parameters, in which BCR signals were not only dominant but were also linearly related to consequent outcomes. However, appreciating that BLyS signaling is an equal partner in establishing and maintaining B-cell pools indicated that additional regulatory complexity – apparently based on population density and homeostatic demands – had to be included in models of B-cell behavior. This mounting interest was amplified by evidence of a clear relationship to autoimmunity. The resulting flurry of research activity has yielded a wealth of information and insights, impacting basic concepts in B-cell tolerance and activation as well as revealing novel translational strategies for autoimmunity, neoplasia, and transplant tolerance. This book includes 12 chapters that together yield an overview of these advances and ideas.

The initial excitement generated by associations with humoral autoimmunity, coupled with profound B lineage phenotypes in knockout mouse models, prompted immediate questions: What do these receptors and cytokines look like, how do they interact, what cells express them, and how does this inform our understanding of their biology? Indeed, probing the structural features of BLyS family ligands and receptors has afforded substantial insight, as have studies directed toward understanding the basic biological actions of these molecules. These features are detailed in the first several chapters. The structural features of BLyS family ligands and receptors are detailed in Chapter 1, with emphasis on how these are related to biological interactions and activities. The next several chapters explore how these molecules function in B-cell development, selection, and activation and detail current thinking about signal transduction and downstream mediators of the various receptor ligand pairs.

How advancing knowledge of BLyS family molecules impacts our understanding of human disease states, as well as whether these molecules may serve as therapeutic targets, remains areas of intense scrutiny. Because the associations of BLyS with systemic lupus erythematosis and rheumatoid arthritis were recognized early, these questions have been extensively interrogated from the standpoint of humoral autoimmunity. Chapters 7 through 10 provide an overview of this burgeon-
ing area, from both mechanistic and translational perspectives. Finally, because of their preferential expression in B lineage cells and their impact on survival, similar basic and translational questions exist about the roles of BLyS family members in B-cell neoplasia. The last two chapters examine these relationships.

Although this volume reveals the wealth of concepts and possibilities catalyzed by the last 10 years’ research on the BLyS family, it is unlikely the plateau has yet been reached. Indeed, implications for the manipulation of pre-immune and antigen-experienced B-cell pools promise even more during the next decade, as current thoughts reach maturity and are extended to transplant tolerance and vaccine development.

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