B Cell Trophic Factors and B Cell Antagonism in Autoimmune Disease
Current Directions in Autoimmunity

Vol. 8

Series Editor

A.N. Theofilopoulos  La Jolla, Calif.
B Cell Trophic Factors and B Cell Antagonism in Autoimmune Disease

Volume Editor

William Stohl  Los Angeles, Calif.

36 figures, 4 in color, and 11 tables, 2005
Contents

VII  Foreword
  Stohl, W. (Los Angeles, Calif.)

1  Determinations of B Cell Fate in Immunity and Autoimmunity
  Noelle, R.J.; Erickson, L.D. (Lebanon, N.H.)

25  Regulatory Roles for Cytokine-Producing B Cells in Infection and Autoimmune Disease
  Lund, F.E. (Saranac Lake, N.Y.); Garvy, B.A. (Lexington, Ky.);
  Randall, T.D.; Harris, D.P. (Saranac Lake, N.Y.)

55  The CD19-CD21 Signal Transduction Complex of B Lymphocytes Regulates the Balance between Health and Autoimmune Disease: Systemic Sclerosis as a Model System
  Tedder, T.F.; Poe, J.C. (Durham, N.C.); Fujimoto, M. (Tokyo);
  Haas, K.M. (Durham, N.C.); Sato, S. (Kanazawa)

91  Marginal Zone B Cell Physiology and Disease
  Lopes-Carvalho, T.; Kearney, J.F. (Birmingham, Ala.)

124  Dendritic Cells Control B Cell Growth and Differentiation
  Jego, G.; Pascual, V.; Palucka, A.K.; Banchereau, J. (Dallas, Tex.)

140  The Biology of CD20 and Its Potential as a Target for mAb Therapy
  Cragg, M.S.; Walshe, C.A.; Ivanov, A.O.; Glennie, M.J. (Southampton)

175  B Lymphocyte Depletion in Rheumatoid Arthritis: Targeting of CD20
193 Treatment of SLE with Anti-CD20 Monoclonal Antibody
Looney, R.J.; Anolik, J.; Sanz, I. (Rochester, N.Y.)

206 The Biochemistry and Biology of BAFF, APRIL and Their Receptors
Kalled, S.L.; Ambrose, C.; Hsu, Y.-M. (Cambridge, Mass.)

243 The BAFF/APRIL System: An Important Player in Systemic Rheumatic Diseases
Mackay, F.; Sierro, F.; Grey, S.T. (Darlinghurst); Gordon, T.P. (Bedford Park)

266 Human B Lymphocyte Malignancies: Exploitation of BLyS and APRIL and Their Receptors
Jelinek, D.F.; Darce, J.R. (Rochester, Minn.)

289 BlySfulness Does Not Equal Blissfulness in Systemic Lupus Erythematosus: A Therapeutic Role for BLyS Antagonists
Stohl, W. (Los Angeles, Calif.)

305 Author Index

306 Subject Index
Thirty years ago, when I was still a medical student, understanding B cell biology was rather simple. The raison d’être of B cells was to produce antibodies – period. A large quiescent collection of individual B cells, each uniquely expressing a different antigen receptor (Ig), would ‘hang around’ either in the circulation or in secondary lymphoid tissues. The B cells were ‘waiting patiently’ to become activated and programmed into antibody-secreting cells. Given that the vast majority of B cells at any one time was not secreting antibodies, it was felt that most B cells at any single point in time were essentially inert. Following immunization, some B cells would advance from the ‘inert’ stage to a ‘memory’ stage, but, again, the overriding raison d’être of memory B cells was to generate antibodies in a manner quantitatively greater and more vigorous than that which could occur in the absence of immunization. Indeed, autoimmunity was considered to be largely a product of ‘forbidden’ B cell clones. For some unknown and mysterious reason, B cell clones which should have normally disappeared were persistent in some unfortunate individuals. These forbidden clones were immunized by self antigens and, consequent to some abstruse sequence of events, matured into autoantibody-secreting cells. The poor hosts harboring these forbidden clones were ravaged by the resulting pernicious autoantibodies.

Thirty years may be a very short time-span in terms of world history, but our understanding of B cells has increased and expanded by many orders of magnitude during this short period of time. We now know that B cells, in addition to differentiating into antibody-secreting cells, serve many other vital functions. The roles of B cells as antigen-presenting cells, as cytokine-producing cells, and as
effector and regulatory cells are well-appreciated today. It is increasingly accepted that the role of B cells in autoimmune diseases is not limited to their production of autoantibodies. Indeed, the pathologic role of B cells in many autoimmune disorders may be largely, if not totally, autoantibody-independent. It is still true that T cells continue to receive much attention by those investigating the pathogenesis of autoimmune diseases and by those treating patients with autoimmune diseases. Nevertheless, interest in B cells is no longer limited to the reclusive immunologist focused on esoteric topics – today the B cell has grabbed the avid attention of the mainstream clinicians and scientists alike.

The current volume covers cutting-edge topics ranging from the very basic through the clinical. The study of autoimmunity is no longer limited to the laboratory bench but includes the patient examination room and infusion center as well. Just as clinicians need to have a working knowledge of Western blots and microarray analyses, so too scientists need to have a working knowledge of biologic therapeutics and clinical trials. It is hoped that this volume will contain something for everyone interested in the broad field of B cells and autoimmunity.

I wish to conclude by thanking several individuals without whom I would have no reason to write this foreword. First, I convey my most sincere thanks and gratitude to Ari Theofilopoulos, the series editor of Current Directions in Autoimmunity, for entrusting me to organize this volume. Ari has been an invaluable guide and wellspring of insight. Second, I thank all the contributors to this volume. They kindly and patiently tolerated my frequent nagging, and the exemplary quality of the final product is testimony to their collective scholarship and clarity of thought. Finally and most importantly, there are no words which can adequately express how truly lucky I am to have the love of my life, my wife Avivya, at my side. For the past 30 years, she has continually advised me, cheered for me, encouraged me when times got tough, and chastised me when I went off track (a common and recurrent problem). I would be completely lost without her. To Avivya and to our five precious and priceless children, Shelly, Hindi, Rafi, Adina, and Chumi, I lovingly dedicate this volume.

William Stohl
Los Angeles, Calif.

Foreword VIII