

Editorial

Cytokines coming of age in South America

An active and integrated scientific community plays an essential role in the evolution of developing countries. Not only does the scientific community promote cultural growth and technological advancement, but importantly, contributes to improvements in the quality of life, economic independence, and the transfer of basic creative knowledge to solve major regional problems. Despite serious economic and political challenges in the region, a tradition of fundamental research has been fostered in South America by Nobel Prize winners and international scientific leaders such as Bernardo Houssay, Luis F. Leloir, César Milstein, Carlos Chagas Filho, Mauricio Rocha e Silva, Héctor Croxato, Pablo Valenzuela and Gustavo Hoecker (among others). This strong tradition of excellence continues to thrive within the atmosphere of many South American institutions of higher learning. However, these inspirational examples of scientific excellence may remain isolated examples if we are unable to support career development of thousands of young, motivated scientists who dedicate their lives to the advancement of scientific competitiveness in the region.

Despite significant efforts of the scientific community in South America, fundamental research is often viewed by public and private leaders as a marginal activity. This attitude has and will continue to cause an excessive brain-drain of talented South Americans to developed countries, thus ultimately widening the gap between developed and developing countries. In this regard, much remains to be done in terms of increasing scientific competitiveness in the region, such as fostering international collaborations (particularly between neighboring countries), creating stronger ties with industry, and stimulating governmental awareness of the importance of scientific knowledge for national development.



This special issue of *Cytokine and Growth Factor Reviews* entitled “**Cytokines Coming of Age in South America**” reflects the efforts and enthusiasm of immunologists from Buenos Aires, Córdoba, Rosario, Santiago de Chile, Rio de Janeiro, Sao Paulo and Montevideo (see Figure) who have already made a significant impact on the scientific community in South America, despite the context of unfavorable financial and political climates. These 16 excellent mini-review articles illustrate the fascinating interplay of cytokines, growth factors, and chemokines in several physiological and pathological processes linked to innate and adaptive immune responses.

In the first chapter, **Jorge Geffner and colleagues** provide a detailed review of the delicate interplay of

pathogens, cytokines and stress signals in the regulation of dendritic cell physiology and highlight the concept that dendritic cells are critical in sensing environmental signals and integrating this information to determine the profile of adaptive immunity. **Alexis Kalergis and his team** contribute a comprehensive article illustrating newly emerging concepts concerning the functional cross-talk between antigen binding, chemokines and cytokines in the assembly of the immunological synapse and the impact of these interactions in controlling the decision between immune cell activation and immune cell tolerance. “The essential role of chemokines in the selective regulation of lymphocyte homing” by **Mario Roseblatt, María Rosa Bono and colleagues** clearly summarize our current understanding of the role of cytokines and chemokines as regulators of lymphocyte migration through normal and inflamed tissues. **Eduardo Arzt and colleagues** provide a critical overview of the molecular cross-talk between glucocorticoids and transcription factors in the regulation of cytokine signaling and function, focusing on the physiologic relevance of this intricate network. Then, **Marta Toscano and colleagues** thoroughly examine the immunoregulatory role of endogenous lectins in innate and adaptive immune response, highlighting the functional relevance of these proteins as targets for immunointervention during inflammation and cancer. In “Cytokines and chemokines shaping the B-cell compartment” **Adriana Gruppi and her group** critically discuss interesting new observations detailing how cytokines can impact the development, survival and differentiation of different B-cell subsets, thus influencing the decision between memory B cells or antibody-secreting plasma cells. **Eduardo Chuluyan and Verónica García** highlight the importance of costimulatory molecules in the regulation of cytokine responses in human immune cells and the functional interplay between these intricate pathways during intracellular human infection.

Parasitic diseases have medical and economical impact in South America, and therefore deserve a central place in this special issue. In this context, **George Dos Reis, Marcela Lopes and colleagues** summarize their pioneering work on cross-talk between apoptosis and cytokines in the control of parasitic infections. **Susana Gea, Wilson Savino, Oscar Bottaso** and colleagues in an authentic international effort (Córdoba-Rio de Janeiro and Rosario), successfully summarize the complex network of cytokines, chemokines and extracellular adhesion molecules in the regulation of Chagas disease. By integrating different aspects of cytokine research, **Silvia Correa and colleagues** have contributed with a challenging view of the neuroendocrine-immune network during host–pathogen interactions and autoimmune settings. In their article “The role of cytokines in the regulation of ocular autoimmune inflammation” **Luiz Rizzo and colleagues** summarize two decades of ingenious work on the role of cytokines in the regulation of immune privilege and ocular autoimmunity. In

addition, **Leonardo Fainboim and his group** contribute a timely review illustrating the dual role of cytokines in the regulation of immune cell tolerance or immune-mediated liver pathology.

Norberto Zwirner and colleagues provide a comprehensive review on a newly emerging theme—“The role of MICA-NKG2D system in cytokine-driven regulation of natural killer (NK) cell functions”. Such mechanisms appear to be critical for tumor growth and the understanding of these processes may contribute to innovative approaches for potentiating NK cell-mediated tumor immunity. Tumors have devised multiple strategies to evade immune attack, an intriguing area revisited by **Flavio Salazar and colleagues** who illustrate the paradoxical role of cytokines in promoting tumor immunity or favoring tumor-immune escape. An exciting area of exploration at the interface of fundamental and applied Immunology is represented by gene therapy approaches aimed at delivering cytokines for therapeutic purposes in neoplastic and infectious processes. In this regard, **Oswaldo Podhajcer, Verónica Lopez and Guillermo Mazzolini** contribute with a wide-ranging and timely review discussing the fundamentals, applications and limitations of cytokine-based cancer gene therapy. Finally, **Alejandro Chabalgoity, Adriana Baz and colleagues** close this special issue with an article summarizing new innovative strategies to manipulate the cytokine network in order to polarize immune responses during vaccination and immunotherapy.

We would sincerely like to thank all our colleagues who contributed with this unique Special Issue of *Cytokine and Growth Factor Reviews*; it has been an honor and a pleasure to work together in the preparation of this volume. These mini-reviews by no means represent a comprehensive survey of the range of important, international caliber cytokine and immunological research in South America and we apologize to the many excellent scientists working in these areas who could not be invited to contribute to this issue due to space restrictions. Finally, I would like to express my sincere thanks to Dr. John Hiscott for trusting on me for serving as Guest Editor of this special issue.



Dr. Gabriel Rabinovich is an independent researcher of CONICET (National Research Council in Argentina), associate professor of Immunology at the Faculty of Exact and Natural Sciences (University of Buenos Aires) and visiting professor at the University of Maryland (Center of Marine Biotechnology; Baltimore, USA). He works at the Division of Immunogenetics, Hospital de Clínicas “José de San Martín”, University of Buenos Aires and is currently moving to the Institute of Biology and Experimental Medicine (CONICET). The main interest of his group is toward unveiling the role of protein–glycan interactions in immunoregulation. Their current research interests include the role of galectins in inflammation, tumor-immune escape and autoimmune settings, as well as the impact of differential glycosylation in these processes. He received his BS and PhD in biochemistry from the Faculty of Chemical Sciences of the National University of Córdoba (Argentina), and completed his studies at the Kennedy Institute of Rheumatology (Imperial

College, London). He serves as associate editor and is a member of the editorial board of international journals including *Cell Death & Differentiation*, *Emerging Infectious Diseases*, *European Journal of Inflammation* and *Inmunología* and served as invited editor for this Special Issue of *Cytokines and Growth Factor Reviews*. At present, he published 69 original papers and reviews in international peer-reviewed journals, including invited reviews in *Annual Reviews Immunology* and *Nature Reviews Cancer* and acted as author and editor of the book “*Molecular Immunopathology: Novel frontiers in Medicine; a link between biomedical research and clinical practice*” published by “*Editorial Médica Panamericana*” (Latin America and Spain). His work was distinguished by several awards and grants including “*The John Simon Guggenheim Memorial Foundation Award*” (2006; New York), “*Elaine R. Shepard Memorial Investigator Award of the Cancer Research Institute*” (2006; New York), “*The Mizutani Foundation for Glycoscience Award*” (2005; Tokyo); “*The Wellcome Trust*” (2003; London), “*Bunge Born Award*” to the Young Talent Scientist in Argentina (2005; Buenos Aires), “*The Bernardo Houssay Prize for the Young Talent Scientist of the Year*” (2004; Buenos Aires) and “*The Ten*

Young Persons of the Year in Argentina TOYP 2004” (2004; Buenos Aires). His work was also highlighted by editorials in *Nature* and *Nature Reviews Cancer* (August 1999 and May 2004).

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