

Preface

THE TERM "CYTOKINES" WAS COINED BY Stanley Cohen in 1974 to refer to secreted molecules, primarily of immunological importance, that both are produced by and execute actions on immune cells. Typically, cytokines act over limited distances, either directly on the cytokine-producing cell by an autocrine mechanism or instead on a proximal cell in a paracrine fashion. This attribute distinguishes cytokines from growth factors that act more distally, but only partially, as some cytokines indeed act over large distances. At times, the distinction between cytokines and other types of factors is more one of semantics. Cytokines typically act on multiple types of target cells, and accordingly can have broad, often pleiotropic actions. Although many cytokines promote proliferation and survival, some potently drive differentiation and others can be immunosuppressive or promote cell death.

The cytokine field has truly exploded over the years, beginning with observations of relatively poorly defined activities that were transformed by recombinant DNA technology into defined molecules that have since been rigorously studied *in vitro* and *in vivo* by biochemical and cell biological approaches, sophisticated imaging, structural biology, mouse models, and next generation sequencing approaches. Moreover, the development of cytokine mutants and specific antibodies have allowed additional new insights.

This volume includes a range of chapters covering a large number of cytokines that collectively span multiple families, including type I four- α -helical bundle cytokines, type II cytokines (which include the interferons and IL-10 family cytokines), as well as other structurally distinct molecules, such as members of the IL-1 and IL-17 families of cytokines, that exhibit other modes of signaling. Some chapters focus primarily on basic mechanisms of signaling or gene regulation, whereas others focus more on the biological actions and/or clinical utility.

The book is necessarily not all-inclusive, but hopefully this compendium of chapters highlights many critical aspects of and the tremendous ongoing excitement within the broader field. One must appreciate the incredible importance of cytokines related to the potency of their biological actions, the mechanisms by which they signal and control gene regulation, and how their actions are now being harnessed and manipulated—either augmented or inhibited—with clinical benefit. In fact, the manipulation of cytokines or their actions represent the basis of therapy for many diseases, including cancer, immunodeficiency, allergy, and autoimmune diseases, and it is noteworthy that the first successful human gene therapy was for X-linked severe combined immunodeficiency, a disease of defective cytokine signaling. The interested reader will presumably go well beyond the limits of this one volume, as the field is rapidly advancing, with surging numbers of publications.

I particularly wish to thank my co-editor, Bob Schreiber, who co-formulated the vision of this book. All of the authors who contributed are extremely busy, so I thank them for their enthusiasm, substantial time, and hard work in writing and revising state-of-the-art chapters in their respective fields. I also wish to thank Harvey Lodish for suggesting that Richard Sever contact me about such a book, Richard Sever for discussing the general vision, and Barbara Acosta and her colleagues at Cold Spring Harbor Press for their wonderful help, patience related to delays, and their ability to "nudge" the right amount to get things done without offending anyone. Hopefully many, including graduate and medical students as well as more senior scientists, will greatly appreciate the product that this book represents and be inspired to pursue new ideas and additional innovative research in the area of cytokines.

WARREN J. LEONARD