Preface

Chemokines and their receptors play a central role in the pathogenesis of numerous, perhaps all, acute and chronic inflammatory diseases. About 50 distinct chemokines produced by a variety cell types and tissues either constitutively or in response to inflammatory stimuli are involved in a plethora of biological processes. These small secreted proteins exert their exquisitely variegated functions upon binding to a family of seven-transmembrane spanning G-protein coupled receptors (GPCRs) composed of almost 20 distinct entities. The biological activities of chemokines range from the control of leukocyte trafficking in basal and inflammatory conditions to the regulation of hematopoiesis, angiogenesis, tissue architecture, and organogenesis. The basis for such diversified activities rests, on one hand, upon the ubiquitous nature of chemokine production and chemokine receptor expression. Virtually every cell type can produce chemokines and expresses a unique combination of chemokine receptors. On the other hand, chemokine receptors make use of a flexible and complex network of intracellular signaling machineries that can regulate a variety of cellular functions ranging from cell migration, growth, and differentiation to death.

As knowledge of the size of chemokine and chemokine receptor families rapidly reaches completeness, much is still to be uncovered in terms of functional architecture of the chemokine system. The disparity between the large number of chemokines and that smaller number of receptors is balanced by the promiscuity in ligand–receptor interactions, with multiple chemokines binding to the same receptor and several chemokines binding to more than one receptor. Although most investigators now agree that this apparent redundancy in the chemokine system may actually be a powerful way to diversify their biological activities, we still do not fully understand how this can be achieved.

Evidence for the role of many chemokines and receptors in the pathogenesis of different acute or chronic inflammatory diseases is rapidly increasing. Optimistically, every chemokine receptor may be an interesting pharmacological target for therapeutic intervention. The challenge for the future is to identify the unique pathogenic process and specific disease in which any given chemokine receptor may potentially be implicated. The rapidly expanding knowledge of viral strategies for manipulation of the chemokine system lends support to the notion that chemokines have a crucial biological role. From the revolutionary discovery of chemokine receptors as coreceptors for HIV, and more recently smallpox, a whole range of virally encoded chemokine receptor

analogs, chemokine receptor agonists and antagonists, and chemokine inhibitors has been identified, each hinting at the potent effects and potential benefits of manipulating the chemokine system. These findings, together with the knowledge that chemokine receptors belong to the superfamily of GPCRs that constitute a large fraction of current targets for therapeutic intervention in human diseases, explain why these receptors have become the focus of great interest in the pharmaceutical industry.

The aim of *Cell Migration in Inflammation and Immunity* is to provide a range of protocols and practical approaches to the study of chemokine receptor biology. Innovative techniques and useful protocols are illustrated by leading scientists in the field. Our hope is to provide a useful guide to researchers with various levels of experience who wish to investigate the many areas of chemokine receptor biology ranging from cloning and characterization of novel receptors, to the use of animal models to dissect chemokine receptor function in vivo. This book strives to cover a wide range of chemokine receptor biology, with an emphasis on experimental approaches useful in dissecting their involvement in the pathogenesis of both acute and chronic inflammatory diseases. Each manuscript provides a detailed description of methods and background information, and also includes a short but useful bibliography for a more in depth analysis of each specific topic.

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