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BOOK REVIEWS

Interleukins: Molecular Biology and Immunology, *edited by T. Kishimoto, Basel, Switzerland:Karger Publishers, 330 pages, $256.00 (hardcover), 1992*

Since the initial biochemical characterization of interleukin 1 (IL-1) and IL-2 a little more than a decade ago, the interleukins, which represent secreted regulatory proteins of the immune system, have emerged alongside neurotransmitters, endocrine hormones and growth factors as major regulators of cell and tissue function. *Interleukins: Molecular Biology and Immunology* is a concise series of chapters by different authors that focus on the structure and function of IL-1 to IL-8. The editor, Dr. Kishimoto, has directed attention to the areas of change in this field. In the past few years, the rapid movement from the identification of a new interleukin to the availability of recombinant interleukin has yielded a number of texts which have emphasized their role in haematopoiesis, inflammatory responses, and disease. Each interleukin is a multifunctional molecule with numerous biological activities, often overlapping those of several other interleukins. This book captures another theme, interleukin receptors and signal transduction mechanisms. While the primary structure of the interleukins does not reveal homology, their receptors show significant homology. Some receptor cDNAs encode membrane polypeptides that are responsible individually for expression of high-affinity ligand binding; others such as the IL-2, IL-3, and IL-6 receptors require cooperation of multiple subunits. A comparison of receptor structures suggests that there exist several receptor families, each of which appears to contain members derived from a common ancestral gene. The significance of the patterns of sequence conservation await the determination of the three-dimensional structure of at least one member of each family. It would appear likely that sequence homologies in the receptors may reflect a conservation in three-dimensional structure, needed to retain high-affinity ligand binding since analysis of the sequence of the interleukins themselves suggests that these molecules are all likely to have a four helix bundle structure.

The largest of the receptor families has been termed the hematopoietin receptor family. This type of receptor structure is characterised by specifically conserved cysteine residues that may be found in either single or multiple copies in the extra-cellular domain of the receptors. Members of this gene family also contain a characteristic motif, serine-tryptophan-X-serine-tryptophan (where X is any amino acid), that is usually present as a single copy just proximal to the extracellular side of the membrane spanning region of the receptor. Members of the hematopoietin receptor-gene family also contain single or multiple copies of fibronectin type 3 binding motifs throughout the extracellular domain. The sequence homologies between the extracellular regions are not carried over to the cytoplasmic domains of the receptors, which appear unrelated for the most part. Members of the hematopoietin receptor family include the β-subunit of the IL-2 receptor; both subunits of IL-3; granulocyte-macrophage colony stimulating factor (GM-CSF) and IL-6 receptors; IL-4, IL-5, and IL-7 receptors; erythropoietin and leukemia inhibitory factor (LIF) receptors; as well as the growth hormone prolactin and G-CSF receptors. IL-1 receptors have extracellular regions that are members of the immunoglobulin superfamily, being composed of several immunoglobulin-like domains. This group includes the two IL-1 receptors, the M-CSF receptor, the various fibroblast growth factor receptors, and the platelet-derived growth factor receptors.

Receptors that fall into common families based on extracellular domain homology do not show significant overall cytoplasmic domain sequence homology with each other or with other receptors or proteins of known biochemical function. The field of signal transduction is now poised to take advantage of the interleukins. One may assume either that the receptors that do not have identifiable sequence homology defining a biochemical function activate as yet unknown signalling pathways, or that these receptors contain as yet unidentified subunits that have known signalling functions. The nature of signal transduction pathway for interleukin receptors is a growing field of interest as it is envisaged that while activation of any particular receptor must be associated with some specific intracellular pathways, these pathways must interweave with signals generated from other

receptors. It appears that the number of identified intracellular signals activated by growth factors are far fewer than the different patterns of biological responses that these molecules can elicit. As a corollary, the same type of response, activation of protein kinase C, for example, can be shown to occur in response to many signals. It seems likely that the temporal sequence and relative magnitude of the early biochemical changes induced by a particular interleukin are likely to constitute much of its characteristic signature, determining in turn the pattern of gene transcription elicited. Identifying the biochemical steps and components of these pathways and how they operate in ensemble is a challenge, as it will lead to an understanding of how growth and differentiation events are regulated and lead to new ways of treating disorders that involve defects in growth factor production or cellular signalling processes. The final two chapters deal with mechanisms of IL-2 and IL-6 gene expression. While little is known about how information is transmitted from ligand-activated cell surface receptors to the nucleus, analysis of IL-2 and IL-6 gene expression is directing attention to families of nuclear binding proteins.

This book is very readable, being concisely written. For a series of multi-authored chapters it is a coherent text. It is a very good entry into problems of developmental biology and gene expression. It is a sign of how rapidly the field is changing that we now number 12 interleukins, and that another text must be produced to continue the sequence. The field of cloned receptors or receptor subunits has increased, and LIF and a new molecule, oncostatin M, have receptors that also utilize the gp130 subunit of the IL-6 receptor. This book will appeal both to the basic researcher and to the clinician seeking an understanding of both modern research trends and where new therapies will emerge.

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