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Volume 351

THE CHEMOKINES

Biology of the Inflammatory Peptide Supergene Family II

Edited by I. J. D. Lindley, J. Westwick, and S. Kunkel

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Edited by

I. J. D. Lindley
Sandoz Research Institute
Vienna, Austria

J. Westwick
University of Bath
Bath, United Kingdom

and

S. Kunkel
University of Michigan
Ann Arbor, Michigan

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PREFACE

The first symposium in this series was held at the Royal College of Surgeons of England in December 1988 and was entitled "Novel Neutrophil Stimulating Peptides". That symposium successfully brought together the majority of laboratories working in the area of interleukin-8 and related peptides; see *Immunology Today* 10: 146-147 (1989). The Second International Symposium on Chemotactic Cytokines was held at the same venue in June 1990, and a much-increased attendance reflected the accelerating pace of work in the area of these chemotactic cytokines. The proceedings of that meeting were published in *Advances in Experimental Medicine and Biology, vol.* 305 (1991).

The rapid advances made in the field of chemotactic cytokines over the last 18 months necessitated a third Symposium in this series to collate and place in perspective an explosion of new data. The Third International Symposium on Chemotactic Cytokines was held between August 31 and September 1, 1992 in Baden-bei-Wien, Austria.

However, the lack of a clear nomenclature system was creating some confusion in the area, especially as new factors continue to be discovered and classified as family members. In the past, these inflammatory mediators had been placed arbitrarily under the broad heading of "intercrines" or "chemotactic cytokines" with no clear classification guidelines to follow. This nomenclature issue was addressed at the Symposium, where investigators in the field were invited to reach a consensus regarding a collective name for these mediators. The resulting decision was to identify the major family as **chemokines**, to replace all previous terms.

The chemokines are involved in recruitment and activation of specific immune cells and regulation of adhesion molecules on the cell surface, and have been implicated in many disease states, including atherosclerosis, asthma, renal disease, rheumatoid arthritis, psoriasis and allergy. Exciting new findings in the area involve cloning of new members of the family, new activities of known members, and cloning of specific receptors, in addition to new clinical and experimental data.

We are extremely grateful to the companies listed overleaf, for without their support the symposium and this book would not have been possible.

I.J.D. Lindley
S.L. Kunkel
J. Westwick

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CHEMOTACTIC AND INFLAMMATORY CYTOKINES -- CXC AND CC PROTEINS

Marco Baggiolini

Theodor-Kocher Institute
University of Bern
P.O. Box
CH-3000- BERN-9, Switzerland

INTRODUCTION

This is the third meeting in about three years on a family of cytokines that became fancy with the discovery of interleukin-8 (IL-8). The IL-8-related cytokines are small, and relatively easy to work with. They are characterized by four conserved cysteine residues. Alignment of these residues differentiates two subfamilies: one with the first two cysteines separated by one amino acid (CXC cytokines), and the other with adjacent cysteines (CC cytokines). The genes for the two clans inhabit different chromosomes, number 4 for the CXC and number 17 for the CC, and the cytokines that they produce have different target cell preferences.

Platelet factor 4 (PF4) was the first protein of this class to be characterized. Its sequence was reported in 1977 (1-4), ten years before the discovery of IL-8 (5-7). PF4 is stored in the α—granules of blood platelets together with two other CXC proteins, platelet basic protein (PBP) and its N-terminal truncation derivative, connective tissue-activating peptide III (CTAP-III) (8,9). ß—Thromboglobulin, a truncation derivative of PBP and CTAP-III, was characterized early on (10). A gamma-interferon-inducible protein (IP10) was then identified. Unlike the CXC proteins stored in the platelet, IP10 was found to be *induced* in cells upon stimulation, and gamma-interferon is particularly potent (11,12).

This area of research was interesting, but rather quiet until several related proteins were found that are strongly chemotactic for leukocytes (13). When IL-8 came along, many research groups were apparently ready to enter the field, and within a few years our knowledge about CXC proteins increased enormously. The full sequence of IL-8 was quickly established in several laboratories, and today we know its three-dimensional structure (14), the structure and chromosomal location of its gene (15,16), the sequence and binding properties of its receptors (17-20), and we have gained detailed information on its biological activities, and the mechanism of signal transduction in neutrophils (21).

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