科技资料

REGULATION OF THE ACUTE PHASE AND IMMUNE RESPONSES: INTERLEUKIN-6

ANNALS OF THE NEW YORK ACADEMY OF SCIENCES

Volume 557

REGULATION OF THE ACUTE PHASE AND IMMUNE RESPONSES: INTERLEUKIN-6

Edited by Pravinkumar B. Sehgal, Gerd Grieninger, and Giovanna Tosato

The New York Academy of Sciences
New York, New York
1989

Library of Congress Cataloging-in-Publication Data

Regulation of the acute phase and immune responses: interleukin-6/edited by Pravinkumar B. Sehgal, Gerd Grieninger, and Giovanna Tosato.

p. cm. — (Annals of the New York Academy of Sciences, ISSN 0077-8923; v. 557)
Based on papers presented at a conference held Dec. 12-14, 1988 in New York City; cosponsored by the New York Academy of Sciences and the National Foundation for Cancer Research.
Includes bibliographies and index.
ISBN 0-89766-531-7 (alk. paper). — ISBN 0-89766-532-5 (pbk.: alk. paper).
1. Immune response—Regulation—Congresses. 2. Interleukins—Physiological effect—Congresses. 3. Alpha macroglobulins—Physiological effect—Congresses. I. Sehgal, Pravinkumar B. II. Grieninger, Gerd. III. Tosato, Giovanna. IV. New York Academy of Sciences. V. National Foundation for Cancer Research. VI. Series.
[DNLM: 1. Acute Phase Proteins—congresses. 2. Gene Expression Regulation—congresses. 3. Genes, Immune Response—congresses. 4. Inflammation—congresses. 5. Interleukins—congresses. W1 AN626YL v. 557/QW 541 R3445 1988]
Q11.N5 vol. 557
[QR186]
500 s—dc20
[616.07'9]
DNLM/DLC
for Library of Congress 89-9264
CIP

PCP
Printed in the United States of America
ISBN 0-89766-531-7 (cloth)
ISBN 0-89766-532-5 (paper)
ISSN 0077-8923

REGULATION OF THE ACUTE PHASE AND IMMUNE RESPONSES: INTERLEUKIN-6

December 14, 1988

We the undersigned participants at the conference entitled "Regulation of the Acute Phase and Immune Responses: A New Cytokine" sponsored by the New York Academy of Sciences and the National Foundation for Cancer Research, held in New York City on December 12-14, 1988, recommend that the cytokine previously called "interferon-β_2", "26-kDa protein", "B-cell stimulatory factor 2", "hybridoma/plasmacytoma growth factor", "hepatocyte stimulating factor", "interleukin-HP1", and "monocyte granulocyte inducer type 2" be referred to as "interleukin-6". Investigators may use additional synonyms when referring to particular products derived from the interleukin-6 gene.

Kushner, I.	Paul, W. E.	Tosato, G.
Gauldie, J.	Aarden, L. A.	Content, J.
Grieninger, G.	Van Snick, J.	Revel, M.
Clark, S.	Van Damme, J.	Sehgal, P. B.
Fuller, G. M.	Hirano, T.	Koj, A.
Kishimoto, T.	Nordan, R.	Schreiber, G.
Sachs, L.		

(The order of the names above was determined by random draw.)

The Cover

The cover illustration is a reproduction of figure 1 in: Fåhræus, R. 1921. *Acta Med. Scand.* **55:** 1-228. Excerpts from the accompanying text are reproduced below.

"One of the most elementary properties of the blood, from a physico-chemical point of view, is that it constitutes a suspension. The blood-corpuscles may be said to be suspended in plasma. . . .

"The principal theme [. . .] is that the subsiding speed of the blood corpuscles differs under various physiological and pathological conditions to a very great extent—in other words, that *the suspension-stability of the blood is subjected to considerable and constitutional changes.* . . .

"In most diseases the evacuated blood had quite a different appearance to that when in a state of health. When coming from a sick person it secreted a whitish substance of solid consistency which was [. . .] lacking in the blood taken from a healthy person, but which in more severe cases of illness could perhaps take up more than half of the liquid volume evacuated. This substance which could change in quantity, always secreted itself, however, when it made its appearance, in the form of a superficial layer above the rest of the bloodcake which was normally conditioned. This layer was the so-called *crusta sanguinis*, or, the *buffy coat.*[1]

"The most important cause of the origin of this phenomenon was this, that the subsiding speed of the blood corpuscles was increased. The appearance of the blood cake thus showed various degrees of that property in the blood which I have called its suspension-stability. *The buffy coat was a sign indicating that the suspension-stability of the blood was reduced.*

"There is probably no observation in the history of medicine which has played such a big part as has this phenomenon. The white layer of the blood [. . .] formed for generation after generation for more than two and a half thousand years the fundamental fact, thanks to which the solution was thought to have been found to what has in all times been the burning problem of the nature of disease and the remedy therefor. The fundamental theory of the pathological philosophy of antiquity and the middle-ages and the greater part of more modern times was the *humoral pathology*, according to which all diseases were ascribed to alterations in the body fluids. This theory was not, as we generally imagine, a rootless abstraction, but was founded on the fact that the unhealthy blood, by reason of the presence of the white layer, differed so conspicuously from the healthy blood. . . .

"[1] Amongst other terms for the buffy coat may be mentioned: *Crusta* (*corium*) *pseudomembranacea, lardacea, adiposa, pellea, alba.* The most usual name which really only characterised a certain type of buffy coat was *crusta inflammatoria* or *phlogistica.* On account of the especially thick development of the buffy coat in lung-complaints, it was also called *crusta pleuritica.* . . ."

"As far as I know, there is only one scientist [. . .] who has observed and carried out systematic experiments on clinical material respecting the sinking rapidity of the corpuscles, namely, BIERNACKI of Warschau, who in the nineties [*1890s*] published several essays on this subject.[1] . . . BIERNACKI has the merit of being the first to have sought to call attention to a practical clinical method of measuring in bloodtests in which coagulation has been prevented, the sinking rapidity of the corpuscles, or rather the sedimentation speed. . . ."

"[1] BIERNACKI. Über die Beziehung des Plasmas zu den rothen Blutkörperchen und über den Werth verschiedener Methoden der Blutkörperchenvolumbestimmung. Zeitschrift f. physiologishe Chemie. Vol. 19. 1894. . . ."

A Merging of Disciplines

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The "acute phase" alterations in the composition of blood have been known for more than 2500 years. Today, we understand that the increase in erythrocyte sedimentation rate during acute illness reflects, in large part, a change in plasma protein composition, particularly an increase in the fibrinogen level. It is now clear that interleukin-6 is a major enhancer of the synthesis of fibrinogen (and numerous other plasma proteins) by the liver. It is a humbling thought that interleukin-6, around which there is so much new excitement, participates in a phenomenon that lies at the historical roots of modern medicine.

The idea for this conference arose in September 1987 when it became apparent that investigators in a number of separate fields of research were working with the same cytokine from different perspectives. During the three days of this meeting, it became evident that yet more investigators have independently discovered interleukin-6. It is becoming increasingly clear that the literature contains an enormous amount of information about this one cytokine, which can be tapped by simply knowing the appropriate synonyms. Each of us at this conference benefited by increasing our awareness of relevant areas of research that, prior to this occasion, we may not have been following closely. Our coming together at this conference constituted a relatively rare and marvelous opportunity to promote the confluence of many different lines of scientific investigation relating to interleukin-6. We wish to express our appreciation of the overwhelmingly enthusiastic response that this conference elicited. We thank all of the investigators who participated and who, in many instances, went out of their way to accommodate our requests. It speaks greatly for the flexibility afforded us by the New York Academy of Sciences that, even after final approval of the program by the Conference Committee, we were able to add speakers in newly emergent areas of interleukin-6 research. We hope that the participants were rewarded by the scientific nourishment at this conference, as well as by the joyful atmosphere of the city at this festive time of the year. For many of us, this volume of the *Annals* marks a watershed in our scientific careers.

In one sense, this meeting follows up on themes last presented at the New York Academy of Sciences in September 1981 at the conference entitled "C-Reactive Protein

and the Plasma Protein Response to Tissue Injury" (1982. Ann. N. Y. Acad. Sci. Volume 389). We are gratified that the last speaker at that conference, Dr. Emil Gotschlich, consented to be the first speaker at this conference.

We wish to express our gratitude to Ellen Marks, Conference Director, and Reneé Wilkerson-Brown, Conference Coordinator, and the rest of the staff of the NYAS Conference Department for their superb and smooth professionalism in putting this conference together. We also appreciate the efforts of Bill Boland and Stefan Malmoli in producing this volume of the *Annals* with lightning speed.

ANNALS OF THE NEW YORK ACADEMY OF SCIENCES

Volume 557
June 15, 1989

REGULATION OF THE ACUTE PHASE AND IMMUNE RESPONSES: INTERLEUKIN-6 [a]

Editors and Conference Chairs
PRAVINKUMAR B. SEHGAL, GERD GRIENINGER, and GIOVANNA TOSATO

CONTENTS

[a] The papers in this volume were presented at a conference entitled Regulation of the Acute Phase and Immune Responses: A New Cytokine, which was held in New York City on December 12-14, 1988. The conference was cosponsored by the New York Academy of Sciences and the National Foundation for Cancer Research.

Part VII. Poster Papers

Major funding was received from:

- NATIONAL FOUNDATION FOR CANCER RESEARCH
- NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES—NATIONAL INSTITUTES OF HEALTH

Financial assistance was received from:

- AIDS PROGRAM—NATIONAL INSTITUTES OF HEALTH
- BURROUGHS WELLCOME COMPANY
- CIBA-GEIGY
- EASTMAN PHARMACEUTICALS
- HOECHST-ROUSSEL PHARMACEUTICALS, INC.
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- MERCK SHARP & DOHME RESEARCH LABORATORIES
- OFFICE OF NAVAL RESEARCH GRANT N00014-89-J-1162
- PFIZER CENTRAL RESEARCH
- RORER CENTRAL RESEARCH
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