IMMUNOPATHOLOGY

VII[th] International Symposium
Bad Schachen (Germany) 1976

Edited by
Prof. Dr. Peter A. Miescher, Geneva

Immunopathology

VIITH INTERNATIONAL SYMPOSIUM

Held at Bad Schachen (Germany)
June 14–19, 1976

Edited by
PETER A. MIESCHER, GENEVA

SCHWABE & CO · PUBLISHERS · BASEL/STUTTGART

This Symposium was sponsored
by "Deutsche Forschungsgemeinschaft" and World Health Organization

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Printed in Switzerland
ISBN 3-7965-0673-9

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When the committee organized the first symposium on immunopathology in 1958, the impact of immunology on medicine had been very small: little was known and much had to be discovered. However, the basic work being carried out already permitted one to predict a rapid development in this new field. In the meantime, the expectations have been surpassed by the actual progress in clinical immunology. Today, there is almost no field of medicine that has not felt the impact of immunopathology.

The VIIth Immunopathology Symposium reflects the main present trends: first, immunogenetics has emerged as a very important part of immunopathology. Great advances in molecular biology have relied on the application of the methodology of genetics to the elucidation of the fundamental processes of life at the cellular level.

Various papers dealt with the regulation of the immune response. First of all, the immune response is genetically determined. Furthermore, this phenomenon is being increasingly assessed at a molecular and cellular level. The old question concerning the nature of the T cell receptor for antigenic recognition has been reinvestigated by EICHMANN. This receptor does not appear to possess an immunoglobulin-like light chain. Rather, his data indicate that the variable region of the immunoglobulin heavy chain is shared between the T cell receptor and the antibody molecules.

Microbial immunopathology is another field which demonstrates an increasing impact of immunology on medicine. The pathogenesis of protozoal diseases such as malaria and Kala Azar's disease is dominated by immune phenomena, particularly of the immune complex type. Furthermore, scientists are intrigued by the possible role that slow viruses may play in a number of pathological conditions such as systemic lupus erythematosus, rheumatoid arthritis and sclerosing panencephalitis. During recent years, results have been obtained concerning the role of eosinophils in the immune response to parasitic diseases. Rather than being just an indicator, they appear to be active in the defence mechanism against parasites.

Research on biomediators in effector mechanisms is continuously producing new results of importance in the understanding of a number of pathogenic mechanisms of disease. On one hand, biomediators are generated by the complement system, on the other hand by lymphocytes. Other cells such as neutrophils and basophils are also discussed. Dr Müller-Eberhard's contribution on the properdin pathway arrived after page proofing and for this reason we have had to place it at the end of the proceedings.

Research on immune deficiency has permitted the better assessment of the level of immunological incompetence. In the studies on immunocyte differentiation, it has been recognized that infantile x-linked agammaglobulinemia is due to an

arrest in B cell differentiation. Patients with antibody-deficiency syndromes may possibly also suffer from a differentiation arrest at the B lymphocyte level for which either T or B lymphocytes, or a combination of the two, may be responsible. A new type of immune deficiency has been described by SELIGMANN as "a consequence of anti-B cell autoantibodies".

Immune stimulation has been discussed for many decades. However, it is just now that it appears to have emerged from the alchemistic level to proper scientific assessment. Yet, clinicians cannot wait to apply immune stimulation in therapy, and particularly in the treatment of cancer.

This symposium would not have been possible without the help of the "Deutsche Forschungsgemeinschaft" and the World Health Organization. Furthermore, we obtained financial support from the following organizations: Paul-Martini-Stiftung, Frankfurt/Main; Bayer AG, Behringwerke AG, Berghof GmbH, Boehringer AG, Ciba-Geigy AG, Deutsche Wellcome, Immuno GmbH, Sandoz AG, Thomae AG. We are very grateful for this generous support. Furthermore, we would like to thank Dr. RIETHMUELLER for taking care of the local organization with such competence as meeting secretary. We would also like to thank all discussion editors and our editorial assistants, Mrs. A. GENZ and Mrs. J. RINGROSE, who helped to prepare the proceedings. Finally, we are indebted to Dr. CHR. OVERSTOLZ and Dr. U. BREITENSTEIN from the Schwabe Company who have made a major effort to have these proceedings published within a short period of time.

Geneva, March 1st, 1977 P. A. MIESCHER

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Regulation of the Immune Response

Microbial Immunopathology

Immunogenetics and Immunopathology

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The identification of genes which determine biological phenomena, and the study of the control they exert on these phenomena has proven to be a most successful approach to a detailed understanding of their mechanism. The greatest advances in molecular biology have relied upon the application of the methodology of genetics to the elucidation of the fundamental processes of life at the cellular level. The same statement may be made concerning our understanding of immunological phenomena. The genetic approach has again proven extremely productive and has permitted us to identify many fundamental questions in immunobiology and to resolve some of them successfully.

Among the problems with which the young discipline of immunogenetics has been concerned are the structural genes of the immunoglobulin chains (reviewed in refs. 11 and 18). These genes have been identified by their control of allotypic antigenic determinants on the constant segment of L chains and on both the constant and variable regions of rabbit H chains. These studies have provided the first evidence of the control of a single polypeptide chain by two distinct structural genes. I shall not dwell further on this aspect of immunogenetics.

Another area of rapid progress has been the study of transplantation antigens and the genes which control their expression on cell surfaces. A considerable debt is owed to GORER and to SNELL for their pioneer work in this field which permitted the identification of the major histocompatibility complex (MHC) and of minor histocompatibility loci in the mouse, and for the development of congenic resistance strains of mice selected to differ only at the MHC, the *H-2* complex (reviewed in ref. 28). These studies proved to be invaluable when it became known that the MHC of mammals controlled many essential immunological functions in addition to histocompatibility antigens.

Originally recognized and studied as that portion of the genome coding for the major transplantation antigens [28], it is now abundantly clear that the MHC genes code for a variety of molecules which are integrally involved in control mechanism of immune responses [3, 27]. The relationships of these various molecules to one another and the degree of functional and chemical heterogeneity among them will

Table 1. Subregions of the mouse *H-2* complex

K	*I-A*	*I-B*	*I-J*	*I-C*	*S*	*D*

Table 2. Assignment of immunological phenomena to regions of the major histocompatibility complex (MHC)

Functions of the MHC	*H-2* regions
1. Antigens stimulating tissue rejection and specific cytolytic T cells	K and D > I
2. Cytolytic T cells specific for cell membrane antigens: virally coded, chemically modified, tumor associated or minor histocompatibility	K and D
3. Mixed leukocyte reaction. Graft-versus-host reactions	I > K and D
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provide fundamental clues to the genetic mechanisms involved in controlling lymphocyte function.

In Table 1, we show a map of the genetic subdivisions of the mouse major histocompatibility complex, the *H-2* complex. And in Table 2, we present the assignments of immunological phenomena to distinct regions of the major histocompatibility complex of the mouse. The various functions which have been shown to be controlled by this most important cluster of genes are (1) the expression of antigens which stimulate specific tissue rejections [28], and the stimulation of specific cytolytic T cells [27, 28]; (2) the stimulation of cytolytic T cells specific for cell membrane antigens coded by viruses [33], chemically modified [26], or associated with the malignant process, such as TSTA [13]; (3) the mixed leukocyte reaction and the graft-versus-host reaction [27, 28]; (4) the control of specific immune responses to thymus dependent antigens by genes which have been termed "histocompatibility linked *Ir* genes" [1, 3]; (5) the control of specific immune suppression by T cells by genes which have been termed "specific immune suppression genes" [2, 7]; (6) an antigen found on suppressor cells [21] and on suppressor factor [29]; (7) The regulation of T and B cell cooperative interactions in

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