CONTEMPORARY TOPICS IN
MOLECULAR IMMUNOLOGY
VOLUME 4
CONTEMPORARY TOPICS IN MOLECULAR IMMUNOLOGY

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There are many unanswered questions regarding the molecular nature of antibodies, components of complement, and other substances which participate in the immune response. The list of substances which need to be analyzed chemically is increasing. Plasma cell products, of course, have long been of great interest because the most prevalent ones are immunoglobulins. Other cell types, however, are the source of the broad spectrum of additional substances which classically fall into the sanctum of the molecular immunologist. It is these substances, and especially those more recently discovered, which are responsible for the broadening investigative interests of immunologists.

In this volume we have provided you with descriptions of research being done with immunoglobulins and with complement. Additionally, we have included two reports that deal with molecules which are among the more recent acquisitions of the molecular immunologist.

The components of complement are known to react in a cascading manner which results in the lysis of cellular antigens. The first step in the classical pathway requires the activation of C1 by the antibody–antigen aggregates. This volume of *Contemporary Topics in Molecular Immunology* begins with the report of Reid and Porter which describes their investigation of the mechanism of activation of C1. Their descriptions of C1q and of the reaction of C1 with immunoglobulins are especially intriguing. It is clearly apparent from their report that activation of the components of complement is a complex phenomenon.

While it has long been known that antibody–antigen reactions are very fast, it was only within recent years that special techniques became available for making accurate and meaningful kinetic measurements. Froese and Sehon utilized the techniques for investigating the antibody’s combining site and its epitope as they combined. Kinetic studies provided additional information about the mechanism of the reaction, and about the structure of the combining site.

Rabbit immunoglobulin allotypes are an exciting and controversial subject in immunology. This will become evident to readers of the contribution of Knight and Hanly who describe in considerable detail the genetic control of rabbit α chains. The treatise begins with a complete but concise description of
our up-to-date understanding of immunoglobulin allotypes, which includes nomenclature, genetic notations, etc. Then the authors deal with the complexities of the variable and constant region allotypes. Finally, they bring into proper perspective the inter-relationships of all the variable and constant region heavy chain genes.

Franklin and Frangione have reviewed the structurally altered proteins associated with plasma cell and lymphocyte neoplasms in humans and mice. These proteins, besides being interesting from the structural point of view, are being used to obtain genetic information that cannot be derived from studies of intact molecules. The authors have described chemically the γ, α, and μ heavy chain disease proteins and myeloma proteins which have altered heavy and light chains. They have concluded by drawing attention to the nonrandomness of mutations. Within the framework of present knowledge possible mechanisms for synthesis of the structurally altered immunoglobulins are discussed.

The sequences of heavy and light chains and their relationships to the three-dimensional structure of IgG are described by Davies, Padlan, and Segal. The hypervariable regions of the V domains are brought together to form the antigen-binding sites of two Fab fragments with binding activity. The remarkable crystallographic studies of these investigators have made it clear that insertions, deletions, and simple substitutions in the hypervariable regions will produce profound changes in the specificity of the site.

Poulik and Reisfeld have prepared a comprehensive review of the literature concerned with β2-microglobulin. They have described the physical-chemical properties of the protein and have concluded that it is probably a free circulating domain functionally analogous to CH₃. Further, all human nucleated cells appear to be able to produce β2-microglobulins and contain the protein on their membranes. The β2-microglobulins are a part of native HL-A antigens, and the mode of their association is discussed in detail. The authors also have considered the possible biological and immunological functions of the protein.

The nature and activities of lymphokines have generated considerable interest recently. The book concludes with the discussion by Granger, Daynes, Runge, Prieur, and Jeffes of the lymphokines and some factors which may be instrumental in governing their secretion. The authors describe several models for direct and indirect cytodestruction in in vitro systems by activated lymphotoxin or lymphotoxin-like molecules on the surface of the target cell, and it is this substance which ultimately is responsible for cytolysis. Recent data which support this premise are discussed.

We wish to thank the writers for providing us with such exciting manuscripts, and we cannot help but feel confident that you, the reader, will be enlightened as you read this volume.

F. P. Inman
W. J. Mandy
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