CELL SURFACE REVIEWS, Volume 2

VIRUS INFECTION AND THE CELL SURFACE

VIRUS INFECTION AND THE CELL SURFACE

Edited by

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General preface

Research on membranes and cell surfaces today occupies center stage in many areas of biology and medicine. This dominant position reflects the growing awareness that many important biological processes in animal and plant cells and in microorganisms are mediated by these structures. The extraordinary and unprecedented expansion of knowledge in molecular biology, genetics, biochemistry, cell biology, microbiology and immunology over the last fifteen years has resulted in dramatic advances in our understanding of the properties of the cell surface and heightened our appreciation of the subtle, yet complex, nature of cell surface organization.

The rapid growth of interest in all facets of research on cell membranes and surfaces owes much to the convergence of ideas and results from seemingly disparate disciplines. This, together with the recognition of common patterns of biological organization in membranes from highly different forms of life, has led to a situation in which the sharp boundaries between the classical biological disciplines are rapidly disappearing. The investigator interested in cell surfaces must be at home in many fields, ranging from the detailed biochemical and biophysical properties of the molecules and macromolecules found in membranes to morphological and phenomenological descriptions of cellular structure and cell-to-cell interactions. Given the broad front on which research on cell surfaces is being pursued, it is not surprising that the relevant literature is scattered in a diverse range of journals and books, making it increasingly difficult for the active investigator to collate material from several areas of research. Thus, while scientists are becoming increasingly specialized in their techniques, and in the nature of the problems they study, they must interpret their results against an intellectual and conceptual background of rapidly expanding dimension. It is with these conflicting demands and needs in mind that this series, to be known under the collective title of CELL SURFACE REVIEWS, was conceived.

CELL SURFACE REVIEWS will present up-to-date surveys of recent advances in our understanding of membranes and cell surfaces. Each volume will

contain authoritative and topical reviews by investigators who have contributed to progress in their respective research fields. While individual reviews will provide comprehensive coverage of specialized topics, all of the reviews published within each volume will be related to an overall common theme. This format represents a departure from that adopted by most of the existing series of "review" publications which usually provide heterogeneous collections of reviews on unrelated topics. While this latter format is considerably more convenient from an editorial standpoint, we feel that publication together of a number of related reviews will better serve the stated aims of this series – to bridge the information and specialization "gap" among investigators in related areas. Each volume will therefore present a fairly complete and critical survey of the more important and recent advances in well defined topics in biology and medicine. The level will be advanced, directed primarily to the needs of the research worker and graduate students.

Editorial policy will be to impose as few restrictions as possible on contributors. This is appropriate since the volumes published in this series will represent collections of review articles and will not be definitive monographs dealing with all aspects of the selected subject. Contributors will be encouraged, however, to provide comprehensive, critical reviews that attempt to integrate the available data into a broad conceptual framework. Emphasis will also be given to identification of major problems demanding further study and the possible avenues by which these might be investigated. Scope will also be offered for the presentation of new and challenging ideas and hypotheses for which complete evidence is still lacking.

The first four volumes of this series will be published within one year, after which volumes will appear at approximately one year intervals.

George Poste
Garth L. Nicolson
Editors

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Preface

Viruses are intracellular parasites which multiply by redirecting the synthetic machinery of host cells to the production of new infectious virus particles. Virus multiplication thus represents a highly specific pattern of altered biosyntheses in an otherwise normal cell. The more-or-less complete integration of viruses with the activities of the host cell presents a major obstacle to the therapeutic control of virus infection, yet it is this property that makes viruses of considerable value as probes for examining cellular organization. Thus many of the questions concerning specificity, replication and pathogenicity in virus infection can in fact be viewed as problems in investigative cell biology and a number of problems pertinent to both virology and cytology can be formulated in common terms.

The diverse properties shown by the major groups of animal viruses in their mode of entry into the cell, the mechanism and site of their intracellular replication and the way in which newly synthesized virus subunits are assembled and released from the cell as progeny virions create a broad pattern of virus–host cell interactions. This diversity reflects the great potential of viruses as probes for studying cellular organization, since different viruses or even individual strains of the same virus can be selected to induce any one of a wide range of changes affecting various cellular functions. The value of this approach is well illustrated by the considerable body of information on the basic properties of cellular membranes derived from observations of virus-infected cells.

The information gained from the study of the interaction of animal viruses with host cell membranes is quite diverse. Analysis of the initial attachment and binding of viruses to the cell surface and the subsequent invasion (penetration) of the cell not only offers insight into those factors which can determine whether the cell will be infected successfully but also provides useful information on the functional organization of the cellular plasma membrane. Host cell membranes also play major roles in many aspects of the virus replication process itself. Evidence is accumulating that the synthesis of many viral components, including nucleic acids, takes place in association with subcellular membranes. Characterization of these membrane-associated functions in virus replication may there-

fore offer some insight into the likely role of cell membranes in controlling the synthesis of similar types of molecules in the normal uninfected cell. In the case of the enveloped animal viruses, the membranes of the host cell are also involved in the final assembly and release of new virions. With the exception of the pox viruses in which the virus envelope is apparently synthesized de novo, all of the enveloped animal viruses derive their envelope from pre-existing cellular membranes. This flow of virus-specified proteins and glycoproteins, together with most membrane lipids and perhaps certain other host cell components, into newly forming virus particles can be used as an experimental system for studying a number of questions concerning membrane biogenesis, including: the site(s) of synthesis of different membrane macromolecules; the interaction of proteins, lipids and other macromolecules in membranes; and the mechanism(s) for translocation of membrane components between intracellular membranes and the plasma membrane. Since many animal viruses inhibit cellular biosynthetic processes during their own replication, these questions can often be studied against a low or non-existent background of cell-directed synthesis. Another attractive feature is that the morphogenesis of different classes of enveloped viruses involves different cellular membrane systems. By selection of an appropriate virus it is thus possible to study virus-induced modification of the nuclear membrane, the endoplasmic reticulum and the plasma membrane. Since the lipid composition of most enveloped animal viruses closely resembles that of their membrane of origin, the new progeny virions released from various cellular membranes can serve as probes for studying the lipid composition of the membranes in question.

Other aspects of the interaction between viruses and membranes are also of interest. Some of the cytopathic effects of viruses reflect alterations in membrane function. Virus-induced antigenic modification of the cellular plasma membrane assumes significance not only in determining the effectiveness of the host's immune response to infection but also in influencing the extent and nature of the tissue and cell damage accompanying virus infection. Finally, viral modification of the cellular plasma membrane can produce changes in the social behavior of infected cells such as cell agglutination, cell fusion and, in the case of cells transformed by oncogenic viruses, aberrant patterns of cell growth control and cell-to-cell recognition.

This volume contains nine reviews describing virus-induced changes in mammalian cell membranes. It is clearly impossible within the limits of a single volume to fully review the large repertoire of virus-membrane interactions already identified in productive and transforming infections caused by the various major groups of animal viruses. In selecting the topics for review in this volume we have placed deliberate emphasis on studies done with non-oncogenic viruses. This decision was motivated by two considerations. Firstly, studies on the membrane alterations found in cells transformed by oncogenic viruses have received considerable attention over the past few years and further review in this volume would serve little purpose. Secondly, it is our conviction, and that of the contributors to this volume, that experimental studies on the effects of non-

oncogenic animal viruses on mammalian cells and their membranes, though often less publicized than comparable work with tumor viruses, can serve as a valuable research tool for studying membrane organization and function.

We thank the contributors for their efforts in preparing their respective articles. While every attempt has been made to ensure rapid publication, it is often difficult in a multi-author volume to achieve exact synchrony in the receipt of contributions. We therefore extend our apologies to those contributors who helpfully supplied their reviews earliest but now find them the least up-to-date. We also thank Adele Brodginski, Judy Kaiser, Molly Terhaar, Shirley Guagliardi and Alice MacKearnin for their assistance in preparing the edited manuscripts.

George Poste
Buffalo, New York
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