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Comprehensive Virology

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Regulation and Genetics

Genetics of Animal Viruses

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Foreword

The time seems ripe for a critical compendium of that segment of the biological universe we call viruses. Virology, as a science, having passed only recently through its descriptive phase of naming and numbering, has probably reached that stage at which relatively few new—truly new—viruses will be discovered. Triggered by the intellectual probes and techniques of molecular biology, genetics, biochemical cytology, and high-resolution microscopy and spectroscopy, the field has experienced a genuine information explosion.

Few serious attempts have been made to chronicle these events. This comprehensive series, which will comprise some 6000 pages in a total of about 22 volumes, represents a commitment by a large group of active investigators to analyze, digest, and expostulate on the great mass of data relating to viruses, much of which is now amorphous and disjointed, and scattered throughout a wide literature. In this way, we hope to place the entire field in perspective, and to develop an invaluable reference and sourcebook for researchers and students at all levels.

This series is designed as a continuum that can be entered anywhere, but which also provides a logical progression of developing facts and integrated concepts.

Volume 1 contains an alphabetical catalogue of almost all viruses of vertebrates, insects, plants, and protists, describing them in general terms. Volumes 2–4 deal primarily, but not exclusively, with the processes of infection and reproduction of the major groups of viruses in their hosts. Volume 2 deals with the simple RNA viruses of bacteria, plants, and animals; the togaviruses (formerly called arboviruses), which share with these only the feature that the virion's RNA is able to act as messenger RNA in the host cell; and the reoviruses of animals and plants, which all share several structurally singular features, the most important being the double-strandedness of their multiple RNA molecules.

Volume 3 addresses itself to the reproduction of all DNA-containing viruses of vertebrates, encompassing the smallest and the largest viruses known. The reproduction of the larger and more complex RNA viruses is the subject matter of Volume 4. These viruses share the property of being enclosed in lipoprotein membranes, as do the togaviruses included in Volume 2. They share as a group, along with the reoviruses, the presence of polymerase enzymes in their virions to satisfy the need for their RNA to become transcribed before it can serve messenger functions.

Volumes 5 and 6 represent the first in a series that focuses primarily on the structure and assembly of virus particles. Volume 5 is devoted to general structural principles involving the relationship and specificity of interaction of viral capsid proteins and their nucleic acids, or host nucleic acids. It deals primarily with helical and the simpler isometric viruses, as well as with the relationship of nucleic acid to protein shell in the T-even phages. Volume 6 is concerned with the structure of the picornaviruses, and with the reconstitution of plant and bacterial RNA viruses.

Volumes 7 and 8 deal with the DNA bacteriophages. Volume 7 concludes the series of volumes on the reproduction of viruses (Volumes 2-4 and Volume 7) and deals particularly with the single- and double-stranded virulent bacteriophages.

Volume 8, the first of the series on regulation and genetics of viruses, covers the biological properties of the lysogenic and defective phages, the phage-satellite system P 2-P 4, and in-depth discussion of the regulatory principles governing the development of selected lytic phages.

The present volume provides a truly comprehensive analysis of the genetics of all animal viruses that have been extensively studied to date. Described in ten detailed chapters are genotypes and phenotypic expression of conditional, host range, and deletion mutants of three major classes of animal DNA viruses followed by seven genera of RNA viruses. Principles and methodology are presented and compared to provide insight into mechanisms of mutagenesis, selection of mutants, complementation analysis, and gene mapping with restriction endonucleases and other methods. Whenever appropriate, the genetic properties of viruses are related to nucleic acid structure and function as well as recombination, integration of viral with host genome, malignant transformation, and alteration of host cell functions.

The following volume (10) will deal with transcriptional and translational regulation of viral gene expression, defective virions, and

integration of tumor virus genomes into host cell chromosomes. Later volumes will be concerned with regulation of plant virus development, covirus systems, satellitism and virioids. Two or three additional volumes will be devoted largely to structural aspects and the assembly of bacteriophages and animal viruses, as well as to special groups of newer viruses.

The complete series will endeavor to encompass all aspects of the molecular biology and the behavior of viruses. We hope to keep this series up to date at all times by prompt and rapid publication of all contributions, and by encouraging the authors to update their chapters by additions or corrections whenever a volume is reprinted.

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CHAPTER 1

Genetics of Polyoma Virus and Simian Virus 40

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1. INTRODUCTION*

Polyoma virus and simian virus 40 (SV40) are the smallest known tumor viruses. Their genomes are double-stranded circular DNA molecules, approximately 3.4×10^6 daltons in molecular weight, sufficient to code for the synthesis of approximately 200,000 daltons of protein. Infection of cells by polyoma and SV40 results in alterations in cell growth properties, sometimes leading to malignancy. Cells having altered growth properties are referred to as "transformed" or "neoplastic," and the process which leads to the acquisition of new growth properties is called "cell transformation." It should be emphasized that viral genes are not the only determinants of altered cell growth properties. Cellular genes and regulatory systems are major factors in the emergence of a malignant cell from a normal population.

* Much of the earlier work included in this chapter is described in *The Molecular Biology of Tumor Viruses* (Tooze, 1973) and a recent review (Eckhart, 1974). To avoid unnecessary references in the text, publications prior to 1973 which can be found in these volumes will generally not be cited here. The biochemistry of polyoma and SV40 infection has been described in detail by N. Salzman and G. Khoury in "Reproduction of Papovaviruses" in Volume 3 of this series. Interested readers should also consult the 1974 *Cold Spring Harbor Symposium on Tumor Viruses* (Vol. 39, 1975), which contains many pertinent articles.