

The Herpesviruses Volume 2

Edited by

BERNARD ROIZMAN

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Foreword

The first volume of the series entitled *Comprehensive Virology* was published in 1974 and the last is yet to appear. We noted in 1974 that virology as a discipline has passed through its descriptive and phenomenological phases and was joining the molecular biology revolution. The volumes published to date were meant to serve as an in-depth analysis and standard reference of the evolving field of virology. We felt that viruses as biological entities had to be considered in the context of the broader fields of molecular and cellular biology. In fact, we felt then, and feel even more strongly now, that viruses, being simpler biological models, could serve as valuable probes for investigating the biology of the far more complex host cell. During the decade-long compilation of a series of books like *Comprehensive Virology*, some of the coverage will obviously not remain up-to-date. The usual remedy to this aspect of science publishing is to produce a second edition. However, in view of the enormous increase in knowledge about viruses, we felt that a new approach was needed in covering virology in the 1980s and 1990s. Thus we decided to abandon the somewhat arbitrary subgrouping of the subject matter of *Comprehensive Virology* under the titles Reproduction, Structure and Assembly, Regulation and Genetics, Additional Topics, and Virus-Host Interactions. Instead we have organized a new series entitled *The Viruses*. This series will consist of individual volumes or groups of volumes, each to deal with a single virus family or group, each to be edited with full responsibility by an acknowledged authority on that topic, and each to cover all aspects of these viruses, ranging from physicochemistry to pathogenicity and ecology. Thus, over the next several years we plan to publish single volumes or multiple-volume sets devoted to each of the following virus families: Herpesviridae, Adenoviridae, Papovaviridae, Parvoviridae, Poxviridae, Reoviridae, Retroviridae, Picornaviridae, Togaviridae, Rhabdoviridae, Myxoviridae, and Paramyxoviridae, as well as

hepatitis viruses, plant viruses, bacterial viruses, insect viruses, and perhaps other groups of viruses if and when they are deemed appropriate for comprehensive coverage and analysis.

This volume of THE VIRUSES is part of a set that will provide comprehensive coverage of herpesviruses. The editor of these books is Bernard Roizman. The Herpesviridae comprise a family of viruses widespread throughout the animal kingdom, many of which are extremely important pathogens. Diseases caused by herpesviruses are of ever-increasing significance as serious medical problems. In addition, research on the molecular biology, genetics, pathogenicity, and immunology of these complex viruses has in recent years undergone a veritable metamorphosis, which promises to continue for some years to come.

The first volume of this group dealt largely with viruses associated with malignancy in their natural or experimental hosts. The present volume covers the cytomegaloviruses, varicella-zoster virus, and bovine, equine, fish, reptilian, and amphibian herpes viruses.

Heinz Fraenkel-Conrat
Robert R. Wagner

Preface

Volume 1 of *Herpesviruses* appeared in December of 1982; it dealt with current nomenclature and classification of herpesviruses and with *Gamma herpesviridae*—the newest and most tantalizing of the various herpesvirus subfamilies. The viruses belonging to this subfamily that were discussed in Volume 1 included the Epstein-Barr virus, the virus associated with Marek's disease, and several herpesviruses isolated from New World monkeys. The organization of the topics by subfamilies is not, however, followed in the second volume. Rather, the editor (that is I) prevailed on Charles C. Randall and his disciples, Dennis J. O'Callaghan and Glenn Gentry who contributed much of what is known regarding the molecular biology of equine herpesviruses, and on Hanns Ludwig who, with his associates, has become the major contributor to our knowledge about bovine herpesviruses. Although the herpesviruses isolated from horses and bovines, respectively, belong to different subfamilies, it was not only convenient but also fortuitous to have each group discussed in one chapter. The same logic governed the inclusion of all amphibian herpesviruses in a single chapter written by Allan Granoff and of the fish and reptilian herpesviruses in another chapter by their main exponent—Ken Wolf. I am grateful to Fred Rapp and Mark F. Stinski for an extensive coverage of the structure, function and biology of human cytomegalovirus, to Richard W. Hyman for the chapter on varicella-zoster and again to Hanns Ludwig for bringing together the available knowledge on B virus.

Our knowledge concerning the more than 80 different herpesviruses is uneven. While one author could still cover authoritatively all that is known about the herpesviruses of fishes and reptiles, this is no longer possible for herpes simplex viruses and will no longer be possible for many others because of the exponentially increasing flow of information on just about every facet of the biology of these viruses. Whereas Volume 4 will be dedicated entirely to the Immunobiology of Human Herpesvi-

uses, Volume 3 will consist of chapters exploring in depth specific aspects of the biology of individual and groups of herpesviruses, and, like Volume 2, will not have a unifying theme.

Editing, like writing, is a discipline one learns by making mistakes. The most profitable advice I can pass on to aspiring editors is to repeat Murphy's immortal words that if anything can go wrong, it will. Of the errors I attribute solely to myself, the most amusing is that Volume 1 credits me with a Ph.D. instead of an Sc.D.; the less amusing is the disappearance of my preface to Volume 1 between Chicago and the publisher's office in New York. As a consequence neither the intent of this series or acknowledgements appropriate to that volume appear in their proper place. The proverbial editorial license is most likely a myth; nevertheless it may not be too late to express at least some of the sentiments whose proper place would have been Volume 1.

Science is a systematic exploration not so much of the unknown as of the curious, the challenging, and of the observation that does not fit the conceptual rubric in which it has been placed. Among the virus families, few present the modern scholar with as much diversity, as many questions, puzzles, and ambiguities as the family *Herpesviridae*. The appreciation of both their significance in human and animal health and our ignorance concerning their biology is reflected in the ever increasing number of investigators focusing their research interests on these viruses.

It is characteristic of science that the facts of today become the foundation, the backdrop, and occasionally the ruins upon which the facts of tomorrow emerge. The *Herpesviruses* are intended to be a meaningful compilation of what we know, to help us interpret what we see today, and to assist us in designing the experiments of tomorrow. To dedicate the knowledge of the present to those who will contribute to our knowledge on herpesviruses in the future is superfluous; without them, all that is done today is of little value and of no consequences.

Bernard Roizman

Chicago
December 1982

Contents

Chapter 1

The Biology of Cytomegaloviruses

Fred Rapp

I. Properties of Cytomegaloviruses	1
A. Physical Properties	1
B. Biological Properties	3
C. Molecular Properties	7
II. <i>In Vitro</i> Infection of Host Cells	23
A. Human Cytomegaloviruses	23
B. Murine Cytomegalovirus	32
C. Guinea Pig Cytomegalovirus	34
D. Other Cytomegaloviruses	36
III. Pathogenesis in Natural Hosts	36
A. Pathogenicity in Rodents	36
B. Pathogenesis in Monkeys	43
IV. Transmission	44
V. Latency, Persistence, and Reactivation	45
VI. Cell Transformation by Cytomegaloviruses	48
VII. Control of Cytomegalovirus Infections	50
A. Antiviral Therapy	50
B. Interferon	50
C. Vaccines	51
References	53

Chapter 2

Molecular Biology of Cytomegaloviruses

Mark F. Stinski

I. Introduction.....	67
II. Rate of Infectious Virus Production: Comparisons between Herpes Simplex Virus and Cytomegalovirus.....	69
III. Viral Genome.....	71
A. Physical Properties of the Cytomegalovirus Genome....	71
B. Viral Genome Arrangement.....	72
C. Comparisons among Different Strains of Human Cytomegaloviruses.....	74
D. Defective Cytomegalovirus DNA.....	75
IV. Transcription of the Viral Genome.....	76
A. Sequential Viral Genome Expression.....	76
B. Mapping the Immediate Early Viral Genes.....	82
C. Mapping the Early and Late Viral Genes.....	83
D. Comparisons between Cytomegalovirus and Herpes Simplex Virus Transcription.....	85
V. Virus-Induced Protein and Glycoprotein Synthesis in Infected Cells.....	86
A. Protein Synthesis.....	86
B. Criteria for the Identification of Virus-Induced Proteins and Glycoproteins.....	87
C. Immediate Early Proteins.....	88
D. Early Proteins.....	91
E. Late Proteins.....	91
F. Early and Late Virus-Induced Glycoproteins.....	94
VI. Virus-Induced Enzymes.....	95
A. Host-Cell Enzymes.....	95
B. Virus-Specified Enzymes.....	96
VII. Viral DNA Replication.....	97
VIII. Virions and Dense Bodies of Cytomegalovirus.....	98
IX. Nonproductive Infection.....	101
A. Nonproductive Cells of Animal Origin.....	103
B. Nonproductive Cells of Human Origin.....	104
X. Conclusion.....	107
References.....	108

Chapter 3

Molecular Biology of Varicella-Zoster Virus

Richard W. Hyman

I. Introduction.....	115
II. <i>In Vitro</i> Growth Problem.....	116

III. Varicella-Zoster-Virus-Related Proteins.....	120
IV. Varicella-Zoster Virus DNA.....	121
V. Conclusions.....	131
References	132

Chapter 4

Bovine Herpesviruses

Hanns Ludwig

I. Introduction.....	135
II. History.....	135
III. Classification	138
IV. Morphology and Morphogenesis.....	138
V. Genetic Material	145
A. Genome of Bovid Herpesvirus 1	145
B. Genome of Bovid Herpesvirus 2	150
C. DNAs of Bovid Herpesviruses 3 and 4	154
D. DNA of Bovid Herpesvirus 5	156
E. DNA of Bovid Herpesvirus 6	156
VI. Proteins and Antigens.....	158
A. Virus-Specific Proteins	158
B. Serological Identification of Strains and Individual Strain Differences.....	158
C. Virus-Specific Antigens	163
D. Antigenic Diversity of Bovine Herpesviruses and Immunological Cross-Reactivities with Other Herpesviruses	164
VII. Properties of the Viruses	174
A. <i>In Vitro</i>	174
B. <i>In Vivo</i>	180
VIII. Immune Response and Other Defense Mechanisms	183
A. Humoral Immune Response.....	183
B. Cell-Mediated Immunity.....	185
C. Interferon	185
D. Role of Host Defense Mechanisms	186
IX. Diseases, Experimental Infections, and Pathology.....	187
A. Bovid Herpesvirus 1 Infections.....	187
B. Bovid Herpesvirus 2 Infections.....	189
C. Bovid Herpesvirus 3 Infections.....	189
D. Bovid Herpesvirus 4 Infections.....	190
E. Bovid Herpesvirus 5 Infections.....	191
F. Bovid Herpesvirus 6 Infections.....	191
X. Pathogenesis	194
XI. Diagnosis.....	195

XII. Epidemiology	197
XIII. Concluding Remarks.....	198
References	200

Chapter 5

The Equine Herpesviruses

Dennis J. O'Callaghan, Glenn A. Gentry, and Charles C. Randall

I. Introduction.....	215
II. Classification and Clinical Features	216
A. Equine Herpesvirus Type 1	216
B. Equine Herpesvirus Type 2	225
C. Equine Herpesvirus Type 3	226
III. Structure and Molecular Anatomy of Equine Herpesvirus Virions and Their Components.....	228
A. Morphology.....	228
B. Properties of Equine Herpesvirus DNAs	231
IV. Replication.....	245
A. Introduction	245
B. Early Events: Morphological.....	246
C. Transcription	246
D. DNA Synthesis.....	247
E. New Enzymatic Activities following Infection with Equine Herpesviruses.....	248
F. Protein Synthesis	253
G. Capsid Assembly and Envelopment	255
H. Effect of Equine Herpesvirus Infection on Host Macromolecular Synthesis.....	257
V. Defective Interfering Particles and Systems of Persistent Infection.....	258
A. Generation of Equine Herpesvirus Type 1 Defective Interfering Particles <i>in Vivo</i>	259
B. Biochemical and Biological Properties of Equine Herpesvirus Type 1 Defective Interfering Particles Generated in Cell Culture	260
C. Coestablishment of Persistent Infection and Oncogenic Transformation by Equine Herpesvirus Type 1 Defective Interfering Particle Preparations	268
D. Mechanism for Maintenance of Equine Herpesvirus Type 1 Persistent Infection	273
E. Coestablishment of Persistent Infection and Oncogenic Transformation by High-Multiplicity Infection with Equine Cytomegalovirus	277

VI. Oncogenic Potential of Equine Herpesviruses	280
A. Properties of Equine Herpesvirus Type 1 Oncogenically Transformed Cells	280
B. Identification of Equine Herpesvirus Type 1 DNA Sequences Integrated in LSEH Transformed and Tumor Hamster Embryo Cell Lines	285
C. Blot Hybridization Analyses of Defective Interfering Tumor Cells	290
D. Construction and Mapping of Recombinant Phages Containing LSEH-4 Conjoint Sequences	294
E. Oncogenic Transformation of Hamster Embryo Cells by Equine Cytomegalovirus	296
F. Oncogenic Transformation of Hamster Embryo Cells by Equine Herpesvirus Type 3	299
G. Concluding Remarks Concerning Equine Herpesvirus Oncogenesis	300
VII. Evolutionary Relationships	301
A. Among the Equine Herpesviruses	301
B. Between the Equine and Other Herpesviruses	302
C. Origins of the Herpesviruses	302
VIII. Antiviral Prospects	303
A. Predictive Value of the Equine Herpesvirus Type 1-Hamster Model	303
B. Control of Equine Herpesviral Disease by Chemotherapy	305
References	305

Chapter 6

Biology and Properties of Fish and Reptilian Herpesviruses

Ken Wolf

I. Introduction	319
II. Reptilian Herpesviruses	322
A. Painted Turtle Herpesvirus	322
B. Pacific Pond Turtle Herpesvirus	324
C. Green Sea Turtle Herpesvirus (Gray Patch Disease)	325
D. Iguana Herpesvirus	328
E. Green Lizard Herpesvirus	331
F. Elapid Snake Herpesvirus	331
III. Teleost Fish Herpesviruses	334
A. <i>Oncorhynchus masou</i> Virus	334
B. <i>Herpesvirus salmonis</i> (Salmonid Herpesvirus Disease)	336
C. Carp Pox Herpesvirus (<i>Herpesvirus epithelioma</i>)	347
D. Channel Catfish Herpesvirus (Channel Catfish Virus)	349

E. Turbot Herpesvirus (<i>Herpesvirus scophthalmi</i>)	358
F. Walleye Herpesvirus	362
References	363

Chapter 7

Amphibian Herpesviruses

Allan Granoff

I. Introduction	367
II. Lucké Tumor	368
III. Lucké Tumor Herpesvirus	369
A. Morphology and Structure	369
B. Virus DNA	369
C. Relationship of Temperature to Virus Replication and Expression of Virus Genes	372
D. Oncogenicity	375
E. Effect of Physical and Chemical Agents on Lucké Herpesvirus Oncogenicity	377
F. Natural Transmission	377
G. Cultivation <i>in Vitro</i>	377
IV. Frog Virus 4	378
A. Isolation	378
B. Morphology and Structure	378
C. Virus DNA	379
D. Virus-Cell Interaction	380
E. Effect of Physical and Chemical Agents	381
V. Conclusions	382
References	382

Chapter 8

B Virus (*Herpesvirus simiae*)

Hanns Ludwig, G. Pauli, H. Gelderblom, G. Darai, H.-G. Koch,
R.M. Flugel, B. Norrild, and M. D. Daniel

I. Introduction and History	385
II. Morphogenesis and Morphology	386
A. Virus-Cell Interaction	386
B. Morphogenesis	387
C. Morphology	389
III. Genetic Material	390
A. Guanosine Plus Cytosine Content of the DNA	390
B. Measurement of the DNA Contour Length by Electron Microscopy	390

C. Infectivity of B Virus DNA	392
D. Restriction-Endonuclease Cleavage Patterns	392
IV. Antigens and Proteins	399
A. Proteins	400
B. Antigens	401
V. Serology	411
A. B Virus and Other Herpesvirus Infections: Serological Diagnosis	411
B. Antibody-Dependent Cellular Cytotoxicity Tests	412
C. Considerations on the Function of Common Antigenic Determinants in B Virus, Herpes Simplex Virus, and Bovid Herpesvirus 2	414
VI. Pathogenesis and Pathology	415
A. Disease in Monkeys	416
B. Disease in Man	417
C. Latency	418
VII. Epidemiology	419
VIII. Conclusions	421
References	423
 Index	 429

CHAPTER 1

The Biology of Cytomegaloviruses

FRED RAPP

I. PROPERTIES OF CYTOMEGALOVIRUSES

The initial isolations of human cytomegaloviruses (HCMVs) occurred in 1956 and 1957 (Rowe *et al.*, 1956; M. G. Smith, 1956; Weller *et al.*, 1957). Many investigators have since isolated CMVs or CMV-like agents from a variety of hosts including monkeys (Black *et al.*, 1963; Ablashi *et al.*, 1972; Asher *et al.*, 1974; Nigida *et al.*, 1979; Rangan and Chaiban, 1980), horses (Plummer and Waterson, 1963; Hsiung *et al.*, 1969), rats (Rabson *et al.*, 1969), squirrels (Diosi and Babusceac, 1970), pigs (Plowright *et al.*, 1976), mice (M. G. Smith, 1954; Kim *et al.*, 1975), guinea pigs (Jackson, 1920; Cole and Kuttner, 1926), and sheep (Hartley and Done, 1963).

As early as 1920, Leila Jackson reported the detection of "an intracellular protozoan parasite" in the salivary gland ducts of the guinea pig. This report was followed by a similar one (Cole and Kuttner, 1926) in which a filterable virus was detected in the submaxillary glands of guinea pigs. Cole and Kuttner recognized that the cells had characteristics of herpes simplex virus (HSV)-infected cells, although they were enlarged, which is not typical of HSV infection.

A. Physical Properties

The cytomegaloviruses (CMVs) are morphologically similar to other members of the herpesvirus group; they have an icosahedral capsid con-