



*Assembly of
Enveloped RNA Viruses*

*Monique Dubois-Dalcq
Kathryn V. Holmes
Bernard Rentier*

Editorial Assistance: David W. Kingsbury

Springer-Verlag Wien New York

Dr. *Monique Dubois-Dalq*

Head of Section on Neural and Molecular Ultrastructure, Laboratory of Molecular Genetics,
National Institute of Neurological and Communicative Disorders and Stroke,
National Institutes of Health, Bethesda, Maryland, U.S.A.

Professor Dr. *Kathryn V. Holmes*

Department of Pathology, Uniformed Services, University of the Health Sciences,
Bethesda, Maryland, U.S.A.

Dr. *Bernard Rentier*

“Premier Assistant” and “Maître de Conférences”, Laboratory of General and Medical Microbiology,
University of Liege, Belgium

Professor Dr. *David W. Kingsbury*

St. Jude Children’s Research Hospital, Memphis, Tenn., U.S.A.

This work is subject to copyright.

All rights are reserved, whether the whole or part of the materials is concerned, specifically those of translation, reprinting, re-use of illustrations, broadcasting, reproduction by photocopying machine or similar means, and storage in data banks.

©1984 by Springer-Verlag/Wien

Softcover reprint of the hardcover 1st edition 1984

With 94 partly coloured Figures

Library of Congress Cataloging in Publication Data. Dubois-Dalq, Monique. Assembly of enveloped RNA viruses. Includes bibliographical references and index. 1. Viruses, RNA-Reproduction. I. Holmes, Kathryn V. II. Rentier, Bernard. III. Kingsbury, David W. IV. Title. V. Title: Assembly of enveloped R.N.A. viruses. QR395.D83. 1984. 576'.64. 84-14111.

ISBN-13:978-3-7091-8758-6 e-ISBN-13:978-3-7091-8756-2

DOI: 10.1007/978-3-7091-8756-2

Foreword

This book is a collection of critical reviews about a diverse group of virus families with two features in common: the stable repository of genetic information in each virus is RNA, and each virus modifies and appropriates a particular patch of the eukaryotic cell membrane system to complete its structure. The reviews take the reader from the level of virus genome structure and expression through the quaternary interactions between virus-specified elements and cellular components that cooperate to produce virus particles. There are spectacular illustrations in this volume, but it is much more than a picture gallery. Reading widely in this book can be an effective antidote to overspecialization: in these pages, you are likely to learn much about viruses and about cells that you didn't know before; you'll discover illuminating parallels between diverse virus families; you'll come away with a sharpened awareness of important things that are still to be learned.

Memphis, Tenn., Summer 1984

David W. Kingsbury

Preface

This book was written at the suggestion of Dr. David W. Kingsbury made at a workshop on viruses organized by the Multiple Sclerosis Society in Aspen, Colorado, U.S.A., three years ago. Originally, we had thought to focus on the morphological aspects of viral assembly. Later, during our discussions on the process of budding of enveloped RNA viruses, it became evident that we should include biochemical data in our review and correlate them with the structural aspects of virus maturation. To highlight the way in which various viruses use the cellular machinery for maturation, we have composed a series of schemes. We also decided to add to the well known budding RNA viruses a description of the rotaviruses, since budding appears essential to their maturation. Dr. Kingsbury accepted the difficult task of critically reading and editing each one of our ten chapters. His broad views and in-depth knowledge of the virological literature were most valuable. We are extremely grateful to Dr. Kingsbury for his dedication and promptness in editing.

Summer, 1984

The Authors

Acknowledgements

Many scientists have contributed in various manners to this book. We are very thankful to all of them. Their specific contributions are listed below. We thank:

- F. V. Alonzo, University of Alabama, Birmingham, for Fig. 4-5 a.
- J. C. Armstrong, European Molecular Biology Organization, Heidelberg, Federal Republic of Germany, for data on coronavirus RNA in advance of publication.
- H. Arnheiter, Laboratory of Molecular Genetics, National Institute of Neurological and Communicative Disorders and Stroke, National Institutes of Health, Bethesda, Maryland, for critical review of Chapter I, for advice on rhabdoviruses and orthomyxoviruses and for Fig. 2-2 and 4-2 b.
- T. Bächli, Institute for Immunology and Virology, Zürich, Switzerland, for Fig. 3-5 and 4-2 a, c and d.
- J. N. Behnke, Uniformed Services University of the Health Sciences, Bethesda, Maryland, for helpful discussions on coronaviruses and Fig. 7-6 a.
- W. J. Bellini, Laboratory of Molecular Genetics, National Institute of Neurological and Communicative Disorders and Stroke, National Institutes of Health, Bethesda, Maryland, for advice and for sharing data on paramyxoviruses.
- J. Boyle, Uniformed Services University of the Health Sciences, Bethesda, Maryland, for advice on coronaviruses and rotaviruses.
- W. Brandt, Walter Reed Army Institute of Research, Washington, D. C., for advice on Flaviviruses and Figs. 8-11 and 8-12.
- D. T. Brown, University of Texas, Austin, for sharing data on Alphaviruses in advance of publication.
- J. C. Brown, University of Virginia, Charlottesville, for advice on rhabdoviruses and Fig. 2-8 c.
- M. J. Buchmeier, Scripps Clinic and Research Foundation, La Jolla, California, for advice on arenaviruses and for Figs. 6-2 b and 6-3 a and b.
- C. M. Calberg-Bacq, University of Liege, Belgium, for advice on retroviruses and for Figs. 3-10, 9-1 e, 9-7, and 9-11 b.
- E. O. Caul, Public Health Laboratory, Bristol, England, for Figs. 7-1 b and 7-4.
- D. Cavanagh, Houghton Poultry Research Station, England, for sharing data on coronavirus RNA in advance of publication.
- R. W. Compans, University of Alabama, Birmingham, for Fig. 4-5 a.
- S. Dales, University of Western Ontario, London, Canada, for Fig. 7-5.
- E. de Harven, University of Toronto, Canada, for Fig. 9-1 a.
- E. W. Doller, Uniformed Services University of the Health Sciences, Bethesda, Maryland, for helpful discussions on coronaviruses and Fig. 7-3.
- M. K. Estes, Baylor University, Houston, Texas, for advice on rotaviruses and information in advance of publication.

- M. F. Frana, Uniformed Services University of the Health Sciences, Bethesda, Maryland, for advice on coronaviruses.
- H. Frank, Max-Planck Institute for Virus Research, Tübingen, W. Germany, for sharing data on orthomyxoviruses and for Figs. 4-5 b and c, 4-6, 9-8, 9-10 b, and 9-11 a, c, d and f.
- P. M. Grimley, Uniformed Services University of the Health Sciences, Bethesda, Maryland, for advice on togaviruses and Figs. 8-3, 8-4, 8-5, 8-13, 8-14, 8-15, and 8-16.
- A. K. Harrison, Centers for Disease Control, Atlanta, Georgia, for Figs. 2-5, 2-6, and 2-9 b.
- R. N. Hogan, Laboratory of Molecular Genetics, National Institute of Neurological and Communicative Disorders and Stroke, National Institutes of Health, Bethesda, Maryland, for Figs. 3-2 a and b and 3-6 a.
- C. R. Howard, London School of Hygiene and Tropical Medicine, for advice on arenaviruses and for Figs. 6-3 c and 6-4.
- A. Kapikian, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland, for advice on rotaviruses and for Fig. 10-1.
- D. Kolakofsky, University of Geneva, Switzerland, for sharing data on paramyxoviruses and for Fig. 2-4.
- S. Kozma, University of Liege, Belgium, for Fig. 9-5.
- C.-J. Lai, Laboratory of Infectious Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland, for advice and sharing data on orthomyxoviruses.
- R. A. Lamb, Northwestern University, Evanston, Illinois, for sharing preprints on orthomyxoviruses.
- R. A. Lazzarini, Laboratory of Molecular Genetics, National Institute of Neurological and Communicative Disorders and Stroke, National Institutes of Health, Bethesda, Maryland, for advice on rhabdoviruses.
- R. B. Luftig, University of South Carolina, Columbia, for Fig. 9-4.
- L. Markoff, Laboratory of Infectious Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland, for sharing data on orthomyxoviruses.
- B. Murphy, Laboratory of Infectious Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland, for advice on orthomyxoviruses.
- F. A. Murphy, Colorado State University, Fort Collins, for Figs. 2-5, 2-9 b, 6-2 a and c, and 6-3 d.
- W. Odenwald, Laboratory of Molecular Genetics, National Institute of Neurological and Communicative Disorders and Stroke, National Institutes of Health, Bethesda, Maryland, for advice on rhabdoviruses and Figs. 2-8 a and b.
- L. Oshiro, California State Department of Health, Berkeley, for Figs. 7-1 a, 7-7 a, and 7-8 a.
- B. Petrie, Baylor University, Houston, Texas, for advice on rotaviruses and Figs. 10-2, 10-3, and 10-4.
- A. Pinter, Memorial Sloan-Kettering Cancer Center, New York, for Fig. 9-3.
- C. S. Raine, Albert Einstein College of Medicine, Yeshiva University, New York, for Figs. 3-3 a, 3-4, and 3-9.
- C. D. Richardson, Laboratory of Molecular Genetics, National Institute of Neurological and Communicative Disorders and Stroke, National Institutes of Health, Bethesda, Maryland, for advice on paramyxoviruses and retroviruses.
- F. Rickaert, Laboratory of Molecular Genetics, National Institute of Neurological and Communicative Disorders and Stroke, National Institutes of Health, Bethesda, Maryland, for Figs. 3-2 c and d.
- M. Reginster, University of Liege, Belgium, for advice on orthomyxoviruses.
- S. G. Robbins, Uniformed Services University of the Health Sciences, Bethesda, Maryland for advice on coronaviruses.
- E. Rodriguez-Boulan, State University of New York, Brooklyn, for Figs. 1-3 b and 1-4.
- M. Schubert, Laboratory of Molecular Genetics, National Institute of Neurological and Communicative Disorders and Stroke, National Institutes of Health, Bethesda, Maryland, for advice on rhabdoviruses.
- J. L. Sever, Infectious Diseases Branch, National Institute of Neurological and Communicative Disorders and Stroke, National Institutes of Health, Bethesda, Maryland, for his sustained support to the electron microscopic studies of viral assembly by M.D.D. and B.R.

- J. K. Smith, U.S. Army Medical Research Institute of Infectious Diseases, Fort Dietrick, Maryland for advice on bunyaviruses and Fig. 5-2.
- E. Strauss, California Institute of Technology, Pasadena, for helpful advice on togaviruses and for sharing data in advance of publication.
- J. Strauss, California Institute of Technology, Pasadena, for helpful advice on togaviruses and for sharing data in advance of publication.
- V. Stollar, Rutgers Medical School, Piscataway, New Jersey, for sharing data on Alphaviruses in advance of publication.
- L. S. Sturman, New York State Department of Health, Albany, for advice on coronaviruses.
- M. M. Sveda, Laboratory of Molecular Genetics, National Institute of Neurological and Communicative Disorders and Stroke, National Institutes of Health, Bethesda, Maryland, for advice and sharing data on orthomyxoviruses.
- J. Turner, New York State Department of Health, Albany, for assistance with high voltage electron microscopy and with Fig. 7-7 e.
- W. W. Newcomb, University of Virginia, Charlottesville, for advice on rhabdoviruses and Fig. 2-8 c.
- G. Warren, European Molecular Biology Organization, Heidelberg, Federal Republic of Germany, for Figs. 8-2, 8-6 and 8-7.
- J. S. Wolinsky, University of Texas, Houston, for Fig. 3-8.
- R. G. Wyatt, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland, for advice on rotaviruses.
- P. R. Young, London School of Hygiene and Tropical Medicine, for advice on arenaviruses and Figs. 6-3 c and 6-4.

We gratefully acknowledge the excellent collaboration of Judy Hertler. She organized the bibliography and correspondence, spent many hours working on the word processor and actively participated in the final editing of the book. Her contribution to the index was invaluable. The diagrams designed by B. Rentier were skillfully executed by Trudy Nickelson. Ray Rusten printed the micrographs from our laboratory.

This work was supported in part by grant # 17899 from the National Institutes of Health and by grant # 2 H-13 from the United States Agency for International Development and by grants from the "Fonds National de la Recherche Scientifique" of Belgium.

The opinions expressed in this report are the private views of the authors and should not be construed as official or as necessarily reflecting the views of the Uniformed Services University or the Department of Defense.

Contents

1. An Overview of the Assembly of Enveloped RNA Viruses	1
I. Introduction	1
II. Virus Entry	3
III. Virus Genomes	3
IV. Synthesis of Virus Components	5
Sites of Virus Protein Synthesis	5
Synthesis of Virus Glycoproteins	5
Glycosylation	9
Transport of Virus Glycoproteins	10
Cleavage of Precursor Proteins	10
Other Post-Translational Modifications	12
V. Assembly of Virus Components	12
Nucleocapsid (NC) Assembly (Encapsidation)	12
Structure of NCs	13
Sites of Budding	13
Early Interactions Between NC and Envelope Proteins	14
Virus Budding	18
Virus Release	18
Defective Assembly	19
VI. New Avenues	20
2. Assembly of <i>Rhabdoviridae</i>	21
I. Introduction	21
II. Molecular Organization	21
Replication and Transcription	22
Virus Proteins	23
III. Intracellular Synthesis of Virus Components	26
IV. Assembly of Virus Components	30
NC Assembly	30
Sites of Budding	32

	Interactions Between NC and Envelope Proteins	35
	Virus Budding	36
	Defective Assembly	40
V.	Virus Release and Organization of the Virion	41
3.	Assembly of <i>Paramyxoviridae</i>	44
I.	Introduction	44
II.	Molecular Organization	45
	Virus Proteins	46
III.	Intracellular Synthesis of Virus Components	48
IV.	Assembly of Virus Components	51
	NC Assembly	51
	Association of Envelope Proteins	51
	Interactions Between NC and Envelope Proteins	54
	Virus Budding	57
	Defective Assembly	60
V.	Post-Release Maturation and Organization of the Virion.	64
4.	Assembly of <i>Orthomyxoviridae</i>	66
I.	Introduction	66
II.	Molecular Organization	66
	Virus Proteins	68
III.	Intracellular Synthesis of Virus Components	71
IV.	Assembly of Virus Components	77
	NC Assembly	77
	Interaction Between NC and Envelope Proteins	77
	Virus Budding	77
	Defective Assembly	79
V.	Virus Release and Organization of the Virion	80
5.	Assembly of <i>Bunyaviridae</i>	83
I.	Introduction	83
II.	Molecular Organization	83
	Virus Proteins	85
III.	Intracellular Synthesis of Virus Components	85
IV.	Assembly of Virus Components	86
V.	Virus Release and Organization of the Virion	87
6.	Assembly of <i>Arenaviridae</i>	90
I.	Introduction	90
II.	Molecular Organization	90
	Virus Proteins	92
III.	Intracellular Synthesis of Virus Components	92
IV.	Assembly of Virus Components	92
	NC Assembly	92
	Virus Budding	95

Defective Budding	95
V. Organization of the Virion	95
7. Assembly of <i>Coronaviridae</i>	100
I. Introduction	100
II. Molecular Organization	101
Transcription	101
Replication	102
Virus Proteins	103
III. Synthesis, Transport and Processing of Virus Proteins.	105
IV. Assembly of Virus Components	108
NC Assembly	108
Interaction of NC and Envelope Proteins and Virus Budding	109
Release of Virions from the Cell and Post-Release Maturation.	111
Defective Assembly	115
V. Organization of the Virion	117
8. Assembly of <i>Togaviridae</i>	120
Introduction	120
Alphaviruses	120
I. Introduction	120
II. Molecular Organization	121
Virus Proteins	122
III. Protein Synthesis, Transport and Post-Translational Modifica- tions	124
IV. Assembly of Virus Components	126
NC Assembly	126
Interactions Between NC and Envelope Proteins	127
V. Defective Assembly	131
VI. Organization of the Virion	135
Flaviviruses	136
I. Introduction	136
II. Molecular Organization	137
III. Protein Synthesis, Transport and Post-Translational Modifica- tions	139
IV. Assembly of Virus Components	140
V. Defective Budding	144
VI. Organization of the Virion	146
Rubiviruses	147
Pestiviruses	148
Non-Arthropod-Borne Togaviruses	148
Conclusion	148
9. Assembly of <i>Retroviridae</i>	149
I. Introduction	149

II.	Molecular Organization	149
	Virus Proteins	153
III.	Intracellular Synthesis of Virus Components	155
IV.	Assembly of Virus Components	160
	NC Assembly Occurs Independently from Budding	160
	NC Assembly Is Coordinated with Budding.	161
	Interactions Between NC and Enveloped Proteins.	163
	Virus Budding	163
	Virus Release and Post-Release Maturation.	166
V.	Organization of the Virion	170
10.	Assembly of Rotaviruses	171
I.	Introduction	171
II.	Molecular Organization	173
III.	Translation, Transport and Processing of Virus Proteins.	175
IV.	Assembly of Virus Components.	177
	NC Assembly	177
	Virus Budding	177
	Modification After Budding.	177
	Release of Virions from Infected Cells	179
	Defective Assembly	179
V.	Organization of the Virion	181
	References	183
	Subject Index	217