

CONTENTS

Contributors

xi

Preface

xv

1. Unity in Diversity: Shared Mechanism of Entry Among Paramyxoviruses **1**

Jean-Louis Palgen, Eric M. Jurgens, Anne Moscona, Matteo Porotto,
and Laura M. Palermo

- | | | |
|----|---|----|
| 1. | Introduction to Paramyxoviruses | 2 |
| 2. | Structure and Function of the Paramyxovirus Glycoproteins | 8 |
| 3. | Proposed Mechanisms of Receptor-Binding Protein and Fusion Protein Interactions | 13 |
| 4. | Conclusions | 22 |
| | Acknowledgments | 23 |
| | References | 23 |

2. Alphavirus Entry into Host Cells **33**

Ricardo Vancini, Raquel Hernandez, and Dennis Brown

- | | | |
|----|--|----|
| 1. | Introduction | 34 |
| 2. | Alphavirus Interaction with Host Cells | 36 |
| 3. | Measuring Viral Entry | 41 |
| 4. | Alphavirus Genome Delivery | 45 |
| 5. | Alphavirus Entry in the Absence of Membrane Fusion | 47 |
| 6. | Challenges and Perspectives | 57 |
| | Acknowledgments | 57 |
| | References | 57 |

3. The Mechanism of HCV Entry into Host Cells **63**

Florian Douam, Dimitri Lavillette, and François-Loïc Cosset

- | | | |
|----|---|----|
| 1. | Introduction | 64 |
| 2. | The Viral Particle Organization and Composition: A Fundamental Key to Decrypt Virus Entry | 65 |
| 3. | Early Steps of Virus Entry | 68 |
| 4. | Receptor Binding and Clustering | 72 |
| 5. | Postbinding Steps and Virus Fusion | 83 |
| 6. | Concluding Remarks | 94 |

Acknowledgments	97
References	97

4. The Evolution of HIV-1 Interactions with Coreceptors and Mannose C-Type Lectin Receptors **109**

Marie Borggren and Marianne Jansson

1. Introduction	110
2. Chemokine Receptors as Critical HIV-1 Coreceptors	110
3. Evolution of Coreceptor Use During Virus Transmission and Establishment in the New Host	112
4. Intrapatient Evolution of HIV-1 Coreceptor Use	114
5. The Switch Pathway	114
6. The CCR5-Restricted Pathway	117
7. CLRs in HIV-1 Infection	119
8. CLRs and HIV-1 Interactions During Virus Transmission	122
9. CLRs and HIV-1 Interactions During the Chronic Infection Phase	124
10. Clinical Aspects of Virus Evolution at the Interface of Coreceptors and Mannose CLR	126
Acknowledgments	128
References	128

5. A Game of Numbers: The Stoichiometry of Antibody-Mediated Neutralization of Flavivirus Infection **141**

Theodore C. Pierson and Michael S. Diamond

1. Introduction	142
2. Flavivirus Structure	144
3. A Multiple-Hit Model for the Neutralization of Flaviviruses	146
4. The Stoichiometry of Neutralization and Enhancement of Flaviviruses	150
5. Factors That Modulate the Stoichiometry of Neutralization	154
6. The Stoichiometry of ADE	159
7. Insights into Vaccines and Therapeutics	160
Acknowledgments	160
References	161

6. TRIM21-Dependent Intracellular Antibody Neutralization of Virus Infection **167**

William A. McEwan and Leo C. James

1. Introduction	168
2. The Tripartite Motif Family	169

3. TRIM21 Is a High-Affinity Cytosolic Fc Receptor	170
4. TRIM21 Mediates Antibody-Dependent Intracellular Neutralization	171
5. TRIM21 Is a Sensor for Cytoplasmic Antibody	173
6. TRIM21 Functions are Ubiquitin Dependent	173
7. <i>In Vivo</i> Relevance	174
8. Viral Determinants of TRIM21-Mediated Neutralization	175
9. TRIM21 Exerts Highly Efficient Incremental Neutralization	177
10. The Persistent Fraction	180
11. Comparison of TRIM21 with TRIM5 α	180
12. Conclusions	183
Acknowledgments	183
References	183
 7. Picornavirus-Host Interactions to Construct Viral Secretory Membranes	 189
Alexander L. Greninger	
1. Back on the Radar	190
2. Getting to 3A	190
3. GBF1	192
4. PI4KB	193
5. ACBD3	195
6. Cholesterol	198
7. 2B-2C Pore Forming With ER-Golgi Membranes	199
8. Next Steps	200
9. Conclusion	204
Acknowledgments	205
References	205
 8. Retroviral Factors Promoting Infectivity	 213
Emilia Cristiana Cuccurullo, Chiara Valentini, and Massimo Pizzato	
1. Introduction	214
2. Retroviral Auxiliary Factors that Promote Infectivity	219
3. Retrovirus Factors that Promote Virion Infectivity with a Yet Unknown Mechanism: The Nef and glycoGag Enigma	228
4. Final Remarks	237
References	238

9. The Cytoplasmic Tail of Retroviral Envelope Glycoproteins	253
Philip R. Tedbury and Eric O. Freed	
1. Introduction	254
2. Retroviral Assembly	258
3. Synthesis and Function of Env	259
4. Function of the Retroviral Env CT	261
5. Conclusions	271
Acknowledgments	272
References	272
10. Molecular Determinants of the Ratio of Inert to Infectious Virus Particles	285
P.J. Klasse	
1. Introduction: A Wide Range of Particle-to-Infectious-Unit Ratio	286
2. Infectious or Infecting?	287
3. Defective from the Start	295
4. Decay in Suspension	307
5. Abortive Infection	309
6. Conclusions	315
Acknowledgment	317
References	317
11. The Role of Chance in Primate Lentiviral Infectivity: From Protomer to Host Organism	327
Roland R. Regoes and Carsten Magnus	
1. Introduction	327
2. Host Entry	329
3. Cell Entry	335
4. Synthesis and Outlook	343
Acknowledgments	345
References	346
12. Virus-Encoded 7 Transmembrane Receptors	353
Ann-Sofie Møllekov-Jensen, Martha Trindade Oliveira, Helen Elizabeth Farrell, and Nick Davis-Poynter	
1. Evolutionary Context of v7TMRs	354
2. Functional Divergence from Cellular Chemokine Receptors	362

3. Biological Roles of Viral CKRs	371
4. Concluding Remarks	382
References	382
13. EBV, the Human Host, and the 7TM Receptors: Defense or Offense?	395
Kristine Niss Arfelt, Suzan Fares, and Mette M. Rosenkilde	
1. EBV Infection	396
2. Immune Response and Immune Evasion	402
3. EBV-BILF1—A Virus-Encoded 7TM Receptor with Immune Evasive Functions	404
4. EB12: An Endogenous 7TM Receptor Manipulated by EBV	407
5. Manipulation of the Host Immune System 7TM Receptors and Ligands by EBV—The Chemokine System	411
6. EBV-Associated Diseases	414
7. Drug-Target Potential	418
8. Conclusions	419
Acknowledgment	419
References	419
Index	429