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Title: Host factors in nidovirus replication

Issue Date: 2013-11-13

References

REFERENCES

1. **Morens, D. M., and A. S. Fauci.** 2013. Emerging Infectious Diseases: Threats to Human Health and Global Stability. *PLoS Pathog.* **9**:e1003467.
2. http://www.who.int/topics/emerging_diseases/en/
3. <http://www.who.int/topics/influenza/en/>
4. <http://www.who.int/hiv/>
5. <http://www.who.int/mediacentre/factsheets/fs164/en/>
6. **Drosten, C., S. Gunther, W. Preiser, S. van der Werf, H. R. Brodt, S. Becker, H. Rabenau, M. Panning, et al.** 2003. Identification of a novel coronavirus in patients with severe acute respiratory syndrome. *N. Engl. J. Med.* **348**:1967-1976.
7. **Ksiazek, T. G., D. Erdman, C. S. Goldsmith, S. R. Zaki, T. Peret, S. Emery, S. Tong, C. Urbani, et al.** 2003. A novel coronavirus associated with severe acute respiratory syndrome. *N. Engl. J. Med.* **348**:1953-1966.
8. **Kuiken, T., R. A. Fouchier, M. Schutten, G. F. Rimmelzwaan, G. van Amerongen, D. van Riel, J. D. Laman, T. de Jong, et al.** 2003. Newly discovered coronavirus as the primary cause of severe acute respiratory syndrome. *Lancet* **362**:263-270.
9. http://www.who.int/csr/sars/country/table2004_04_21/
10. **Keogh-Brown, M. R., and R. D. Smith.** 2008. The economic impact of SARS: how does the reality match the predictions? *Health policy* **88**:110-120.
11. **Lau, S. K., P. C. Woo, K. S. Li, Y. Huang, H. W. Tsoi, B. H. Wong, S. S. Wong, S. Y. Leung, et al.** 2005. Severe acute respiratory syndrome coronavirus-like virus in Chinese horseshoe bats. *Proc. Natl. Acad. Sci. USA* **102**:14040-14045.
12. **Li, W., Z. Shi, M. Yu, W. Ren, C. Smith, J. H. Epstein, H. Wang, G. Crameri, et al.** 2005. Bats are natural reservoirs of SARS-like coronaviruses. *Science* **310**:676-679.
13. **Li, W., C. Zhang, J. Sui, J. H. Kuhn, M. J. Moore, S. Luo, S. K. Wong, I. C. Huang, et al.** 2005. Receptor and viral determinants of SARS-coronavirus adaptation to human ACE2. *EMBO J.* **24**:1634-1643.
14. **de Groot, R. J., S. C. Baker, R. S. Baric, C. S. Brown, C. Drosten, L. Enjuanes, R. A. Fouchier, M. Galiano, et al.** 2013. Middle East Respiratory Syndrome Coronavirus (MERS-CoV); Announcement of the Coronavirus Study Group. *J. Virol.*
15. **Zaki, A. M., S. van Boheemen, T. M. Bestebroer, A. D. Osterhaus, and R. A. Fouchier.** 2012. Isolation of a novel coronavirus from a man with pneumonia in Saudi Arabia. *N. Engl. J. Med.* **367**:1814-1820.
16. **van Boheemen, S., M. de Graaf, C. Lauber, T. M. Bestebroer, V. S. Raj, A. M. Zaki, A. D. Osterhaus, B. L. Haagmans, et al.** 2012. Genomic characterization of a newly discovered coronavirus associated with acute respiratory distress syndrome in humans. *MBio* **3**:e00473-00412.
17. http://www.who.int/csr/don/archive/disease/coronavirus_infections/en/
18. **Muller, M. A., V. S. Raj, D. Muth, B. Meyer, S. Kallies, S. L. Smits, R. Wollny, T. M. Bestebroer, et al.** 2012. Human Coronavirus EMC Does Not Require the SARS-Coronavirus Receptor and Maintains Broad Replicative Capability in Mammalian Cell Lines. *MBio* **3**:e00515-00512.
19. **van der Hoek, L.** 2007. Human coronaviruses: what do they cause? *Antivir. Ther.* **12**:651-658.
20. **McIntosh, K., J. H. Dees, W. B. Becker, A. Z. Kapikian, and R. M. Chanock.** 1967. Recovery in tracheal organ cultures of novel viruses from patients with respiratory disease. *Proc. Natl. Acad. Sci. USA* **57**:933-940.

21. **Hamre, D., and J. J. Procknow.** 1966. A new virus isolated from the human respiratory tract. *Proc. Soc. Exp. Biol. Med.* **121**:190-193.
22. **van der Hoek, L., K. Pyrc, M. F. Jebbink, W. Vermeulen-Oost, R. J. Berkhout, K. C. Wolthers, P. M. Wertheim-van Dillen, J. Kaandorp, et al.** 2004. Identification of a new human coronavirus. *Nat. Med.* **10**:368-373.
23. **Woo, P. C., S. K. Lau, C. M. Chu, K. H. Chan, H. W. Tsoi, Y. Huang, B. H. Wong, R. W. Poon, et al.** 2005. Characterization and complete genome sequence of a novel coronavirus, coronavirus HKU1, from patients with pneumonia. *J. Virol.* **79**:884-895.
24. **Huynh, J., S. Li, B. Yount, A. Smith, L. Sturges, J. C. Olsen, J. Nagel, J. B. Johnson, et al.** 2012. Evidence supporting a zoonotic origin of human coronavirus strain NL63. *J. Virol.* **86**:12816-12825.
25. **www.promedmail.org**
26. **Snijder, E. J., and M. Kikkert.** 2013. Arteriviruses, p. 859-879. In D. M. Knipe and P. M. Howley (ed.), *Fields Virology*, 6 ed. Lippincott Williams & Wilkins, Philadelphia, PA.
27. **Holtkamp, D. J., J. B. Kliebenstein, E. J. Neumann, J. J. Zimmerman, H. Rotto, T. K. Yoder, C. Wang, P. Yeske, et al.** 2011. Presented at the 2011 International PRRS Symposium, Chicago, Illinois, USA.
28. **Belov, G. A., and F. J. van Kuppeveld.** 2012. (+)RNA viruses rewire cellular pathways to build replication organelles. *Current opinion in virology*.
29. **Knoops, K., M. Barcena, R. W. Limpens, A. J. Koster, A. M. Mommaas, and E. J. Snijder.** 2012. Ultrastructural characterization of arterivirus replication structures: reshaping the endoplasmic reticulum to accommodate viral RNA synthesis. *J. Virol.* **86**:2474-2487.
30. **Knoops, K., M. Kikkert, S. H. Worm, J. C. Zevenhoven-Dobbe, Y. van der Meer, A. J. Koster, A. M. Mommaas, and E. J. Snijder.** 2008. SARS-coronavirus replication is supported by a reticulo-vesicular network of modified endoplasmic reticulum. *PLoS Biol.* **6**:e226.
31. **Gosert, R., A. Kanjanahaluethai, D. Egger, K. Bienz, and S. C. Baker.** 2002. RNA replication of mouse hepatitis virus takes place at double-membrane vesicles. *J. Virol.* **76**:3697-3708.
32. **van der Meer, Y., E. J. Snijder, J. C. Dobbe, S. Schleich, M. R. Denison, W. J. Spaan, and J. Krijnse Locker.** 1999. Localization of mouse hepatitis virus nonstructural proteins and RNA synthesis indicates a role for late endosomes in viral replication. *J. Virol.* **73**:7641-7657.
33. **van der Meer, Y., H. van Tol, J. Krijnse Locker, and E. J. Snijder.** 1998. ORF1a-encoded replicase subunits are involved in the membrane association of the arterivirus replication complex. *J. Virol.* **72**:6689-6698.
34. **Brockway, S. M., C. T. Clay, X. T. Lu, and M. R. Denison.** 2003. Characterization of the expression, intracellular localization, and replication complex association of the putative mouse hepatitis virus RNA-dependent RNA polymerase. *J. Virol.* **77**:10515-10527.
35. **Stertz, S., M. Reichelt, M. Spiegel, T. Kuri, L. Martinez-Sobrido, A. Garcia-Sastre, F. Weber, and G. Kochs.** 2007. The intracellular sites of early replication and budding of SARS-coronavirus. *Virology* **361**:304-315.
36. **Ulasli, M., M. H. Verheije, C. A. de Haan, and F. Reggiori.** 2010. Qualitative and quantitative ultrastructural analysis of the membrane rearrangements induced by coronavirus. *Cell. Microbiol.* **12**:844-861.
37. **Gorbalenya, A. E., L. Enjuanes, J. Ziebuhr, and E. J. Snijder.** 2006. Nidovirales: evolving the largest RNA virus genome. *Virus Res.* **117**:17-37.

38. **Nga, P. T., C. Parquet Mdel, C. Lauber, M. Parida, T. Nabeshima, F. Yu, N. T. Thuy, S. Inoue, et al.** 2011. Discovery of the first insect nidovirus, a missing evolutionary link in the emergence of the largest RNA virus genomes. *PLoS Pathog.* **7**:e1002215.
39. **Sawicki, S. G., and D. L. Sawicki.** 1995. Coronaviruses use discontinuous extension for synthesis of subgenome-length negative strands. *Adv. Exp. Med. Biol.* **380**:499-506.
40. **Pasternak, A. O., W. J. Spaan, and E. J. Snijder.** 2006. Nidovirus transcription: how to make sense...? *J. Gen. Virol.* **87**:1403-1421.
41. **Snijder, E. J., S. Siddell, and A. E. Gorbalenya.** 2005. The order Nidovirales, p. 390–404. In B. W. Mahy and V. ter Meulen (ed.), *Topley and Wilson's Microbiology and Microbial Infections: Virology Volume*. Hodder Arnold, London.
42. **den Boon, J. A., E. J. Snijder, E. D. Chirside, A. A. de Vries, M. C. Horzinek, and W. J. Spaan.** 1991. Equine arteritis virus is not a togavirus but belongs to the coronaviruslike superfamily. *J. Virol.* **65**:2910-2920.
43. **Brierley, I., and F. J. Dos Ramos.** 2006. Programmed ribosomal frameshifting in HIV-1 and the SARS-CoV. *Virus Res.* **119**:29-42.
44. **Brierley, I., P. Digard, and S. C. Inglis.** 1989. Characterization of an efficient coronavirus ribosomal frameshifting signal: requirement for an RNA pseudoknot. *Cell* **57**:537-547.
45. **Van Hemert, M. J., and E. J. Snijder.** 2008. The Arterivirus Replicase. In S. Perlman, T. Gallagher, and E. J. Snijder (ed.), *Nidoviruses*. ASM Press.
46. **Ziebuhr, J.** 2006. The coronavirus replicase: insights into a sophisticated enzyme machinery. *Adv. Exp. Med. Biol.* **581**:3-11.
47. **Fang, Y., and E. J. Snijder.** 2010. The PRRSV replicase: exploring the multifunctionality of an intriguing set of nonstructural proteins. *Virus Res.* **154**:61-76.
48. **Lauber, C., J. Ziebuhr, S. Junglen, C. Drosten, F. Zirkel, P. T. Nga, K. Morita, E. J. Snijder, and A. E. Gorbalenya.** 2012. Mesoniviridae: a proposed new family in the order Nidovirales formed by a single species of mosquito-borne viruses. *Arch. Virol.* **157**:1623-1628.
49. **Ulferts, R., and J. Ziebuhr.** 2011. Nidovirus ribonucleases: Structures and functions in viral replication. *RNA Biol.* **8**:295-304.
50. **Denison, M. R., R. L. Graham, E. F. Donaldson, L. D. Eckerle, and R. S. Baric.** 2011. Coronaviruses: an RNA proofreading machine regulates replication fidelity and diversity. *RNA Biol.* **8**:270-279.
51. **Bouvet, M., I. Imbert, L. Subissi, L. Gluais, B. Canard, and E. Decroly.** 2012. RNA 3'-end mismatch excision by the severe acute respiratory syndrome coronavirus nonstructural protein nsp10/nsp14 exoribonuclease complex. *Proc. Natl. Acad. Sci. USA* **109**:9372-9377.
52. **van Hemert, M. J., A. H. de Wilde, A. E. Gorbalenya, and E. J. Snijder.** 2008. The *in vitro* RNA synthesizing activity of the isolated arterivirus replication/transcription complex is dependent on a host factor. *J. Biol. Chem.* **283**:16525-16536.
53. **van Hemert, M. J., S. H. van den Worm, K. Knoops, A. M. Mommaas, A. E. Gorbalenya, and E. J. Snijder.** 2008. SARS-coronavirus replication/transcription complexes are membrane-protected and need a host factor for activity *in vitro*. *PLoS Pathog.* **4**:e1000054.
54. **Prentice, E., W. G. Jerome, T. Yoshimori, N. Mizushima, and M. R. Denison.** 2004. Coronavirus replication complex formation utilizes components of cellular autophagy. *J. Biol. Chem.* **279**:10136-10141.
55. **Reggiori, F., I. Monastyrska, M. H. Verheije, T. Cali, M. Ulasli, S. Bianchi, R. Bernasconi, C. A. de Haan, and M. Molinari.** 2010. Coronaviruses Hijack the LC3-I-positive EDEMosomes, ER-derived vesicles exporting short-lived ERAD regulators, for replication. *Cell Host Microbe* **7**:500-508.

56. **Miller, S., and J. Krijnse-Locker.** 2008. Modification of intracellular membrane structures for virus replication. *Nat. Rev. Microbiol.* **6**:363-374.
57. **Krijnse-Locker, J., M. Ericsson, P. J. Rottier, and G. Griffiths.** 1994. Characterization of the budding compartment of mouse hepatitis virus: evidence that transport from the RER to the Golgi complex requires only one vesicular transport step. *J. Cell. Biol.* **124**:55-70.
58. **Wieringa, R., A. A. de Vries, J. van der Meulen, G. J. Godeke, J. J. Onderwater, H. van Tol, H. K. Koerten, A. M. Mommaas, et al.** 2004. Structural protein requirements in equine arteritis virus assembly. *J. Virol.* **78**:13019-13027.
59. **Griffiths, G., and P. Rottier.** 1992. Cell biology of viruses that assemble along the biosynthetic pathway. *Semin. Cell. Biol.* **3**:367-381.
60. **Nagy, P. D., and J. Pogany.** 2012. The dependence of viral RNA replication on co-opted host factors. *Nat. Rev. Microbiol.* **10**:137-149.
61. **Li, Z., and P. D. Nagy.** 2011. Diverse roles of host RNA binding proteins in RNA virus replication. *RNA Biol.* **8**:305-315.
62. **Ahlquist, P., A. O. Noueiry, W. M. Lee, D. B. Kushner, and B. T. Dye.** 2003. Host factors in positive-strand RNA virus genome replication. *J. Virol.* **77**:8181-8186.
63. **Moriishi, K., and Y. Matsuura.** 2007. Host factors involved in the replication of hepatitis C virus. *Rev. Med. Virol.* **17**:343-354.
64. **Watanabe, T., S. Watanabe, and Y. Kawaoka.** 2010. Cellular networks involved in the influenza virus life cycle. *Cell Host Microbe* **7**:427-439.
65. **Zhong, Y., Y. W. Tan, and D. X. Liu.** 2012. Recent progress in studies of arterivirus- and coronavirus-host interactions. *Viruses* **4**:980-1010.
66. **Walsh, D., and I. Mohr.** 2011. Viral subversion of the host protein synthesis machinery. *Nat. Rev. Microbiol.* **9**:860-875.
67. **Jackson, R. J., C. U. Hellen, and T. V. Pestova.** 2010. The mechanism of eukaryotic translation initiation and principles of its regulation. *Nat. Rev. Mol. Cell Biol.* **11**:113-127.
68. **Dauber, B., and T. Wolff.** 2009. Activation of the Antiviral Kinase PKR and Viral Countermeasures. *Viruses* **1**:523-544.
69. **Wang, X., Y. Liao, P. L. Yap, K. J. Png, J. P. Tam, and D. X. Liu.** 2009. Inhibition of protein kinase R activation and upregulation of GADD34 expression play a synergistic role in facilitating coronavirus replication by maintaining de novo protein synthesis in virus-infected cells. *J. Virol.* **83**:12462-12472.
70. **Cruz, J. L., I. Sola, M. Becares, B. Alberca, J. Plana, L. Enjuanes, and S. Zuniga.** 2011. Coronavirus gene 7 counteracts host defenses and modulates virus virulence. *PLoS Pathog.* **7**:e1002090.
71. **Xiao, H., L. H. Xu, Y. Yamada, and D. X. Liu.** 2008. Coronavirus spike protein inhibits host cell translation by interaction with eIF3f. *PLoS One* **3**:e1494.
72. **Lokugamage, K. G., K. Narayanan, C. Huang, and S. Makino.** 2012. SARS coronavirus nsp1 protein is a novel eukaryotic translation inhibitor that represses multiple steps of translation initiation. *J. Virol.*
73. **Kamitani, W., C. Huang, K. Narayanan, K. G. Lokugamage, and S. Makino.** 2009. A two-pronged strategy to suppress host protein synthesis by SARS coronavirus Nsp1 protein. *Nat. Struct. Mol. Biol.* **16**:1134-1140.
74. **Kamitani, W., K. Narayanan, C. Huang, K. Lokugamage, T. Ikegami, N. Ito, H. Kubo, and S. Makino.** 2006. Severe acute respiratory syndrome coronavirus nsp1 protein suppresses host gene expression by promoting host mRNA degradation. *Proc. Natl. Acad. Sci. USA* **103**:12885-12890.

75. **Mackenzie, J.** 2005. Wrapping things up about virus RNA replication. *Traffic* **6**:967-977.
76. **Welsch, S., S. Miller, I. Romero-Brey, A. Merz, C. K. Bleck, P. Walther, S. D. Fuller, C. Antony, et al.** 2009. Composition and three-dimensional architecture of the dengue virus replication and assembly sites. *Cell Host Microbe* **5**:365-375.
77. **Gillespie, L. K., A. Hoenen, G. Morgan, and J. M. Mackenzie.** 2010. The endoplasmic reticulum provides the membrane platform for biogenesis of the flavivirus replication complex. *J. Virol.* **84**:10438-10447.
78. **Kopeck, B. G., G. Perkins, D. J. Miller, M. H. Ellisman, and P. Ahlquist.** 2007. Three-dimensional analysis of a viral RNA replication complex reveals a virus-induced mini-organelle. *PLoS Biol.* **5**:e220.
79. **Spuul, P., G. Balistreri, L. Kaariainen, and T. Ahola.** 2010. Phosphatidylinositol 3-kinase-, actin-, and microtubule-dependent transport of Semliki Forest Virus replication complexes from the plasma membrane to modified lysosomes. *J. Virol.* **84**:7543-7557.
80. **Belov, G. A., V. Nair, B. T. Hansen, F. H. Hoyt, E. R. Fischer, and E. Ehrenfeld.** 2012. Complex dynamic development of poliovirus membranous replication complexes. *J. Virol.* **86**:302-312.
81. **Romero-Brey, I., A. Merz, A. Chiramel, J. Y. Lee, P. Chlanda, U. Haselman, R. Santarella-Mellwig, A. Habermann, et al.** 2012. Three-dimensional architecture and biogenesis of membrane structures associated with hepatitis C virus replication. *PLoS Pathog.* **8**:e1003056.
82. **Norbury, C., and P. Nurse.** 1992. Animal cell cycles and their control. *Annu. Rev. Biochem.* **61**:441-470.
83. **Nigg, E. A.** 1995. Cyclin-dependent protein kinases: key regulators of the eukaryotic cell cycle. *BioEssays : news and reviews in molecular, cellular and developmental biology* **17**:471-480.
84. **Davy, C., and J. Doorbar.** 2007. G2/M cell cycle arrest in the life cycle of viruses. *Virology* **368**:219-226.
85. **Xu, L. H., M. Huang, S. G. Fang, and D. X. Liu.** 2011. Coronavirus infection induces DNA replication stress partly through interaction of its nonstructural protein 13 with the p125 subunit of DNA polymerase delta. *J. Biol. Chem.* **286**:39546-39559.
86. **Xu, L., S. Khadijah, S. Fang, L. Wang, F. P. Tay, and D. X. Liu.** 2010. The cellular RNA helicase DDX1 interacts with coronavirus nonstructural protein 14 and enhances viral replication. *J. Virol.* **84**:8571-8583.
87. **Bhardwaj, K., P. Liu, J. L. Leibowitz, and C. C. Kao.** 2012. The coronavirus endoribonuclease Nsp15 interacts with retinoblastoma tumor suppressor protein. *J. Virol.* **86**:4294-4304.
88. **Chen, C. J., and S. Makino.** 2004. Murine coronavirus replication induces cell cycle arrest in G0/G1 phase. *J. Virol.* **78**:5658-5669.
89. **Chen, C. J., K. Sugiyama, H. Kubo, C. Huang, and S. Makino.** 2004. Murine coronavirus non-structural protein p28 arrests cell cycle in G0/G1 phase. *J. Virol.* **78**:10410-10419.
90. **Jensen, S., and A. R. Thomsen.** 2012. Sensing of RNA viruses: a review of innate immune receptors involved in recognizing RNA virus invasion. *J. Virol.* **86**:2900-2910.
91. **Schoggins, J. W., and C. M. Rice.** 2011. Interferon-stimulated genes and their antiviral effector functions. *Current opinion in virology* **1**:519-525.
92. **Jiang, X., and Z. J. Chen.** 2012. The role of ubiquitylation in immune defence and pathogen evasion. *Nat. Rev. Immunol.* **12**:35-48.
93. **Versteeg, G. A., and A. Garcia-Sastre.** 2010. Viral tricks to grid-lock the type I interferon system. *Curr. Opin. Microbiol.* **13**:508-516.

94. **Barretto, N., D. Jukneliene, K. Ratia, Z. Chen, A. D. Mesecar, and S. C. Baker.** 2005. The papain-like protease of severe acute respiratory syndrome coronavirus has deubiquitinating activity. *J. Virol.* **79**:15189-15198.
95. **Zheng, D., G. Chen, B. Guo, G. Cheng, and H. Tang.** 2008. PLP2, a potent deubiquitinase from murine hepatitis virus, strongly inhibits cellular type I interferon production. *Cell Res.* **18**:1105-1113.
96. **Chen, Z., Y. Wang, K. Ratia, A. D. Mesecar, K. D. Wilkinson, and S. C. Baker.** 2007. Proteolytic processing and deubiquitinating activity of papain-like proteases of human coronavirus NL63. *J. Virol.* **81**:6007-6018.
97. **Lindner, H. A., N. Fotouhi-Ardakani, V. Lytvyn, P. Lachance, T. Sulea, and R. Menard.** 2005. The papain-like protease from the severe acute respiratory syndrome coronavirus is a deubiquitinating enzyme. *J. Virol.* **79**:15199-15208.
98. **Wojdyła, J. A., I. Manolaridis, P. B. van Kasteren, M. Kikkert, E. J. Snijder, A. E. Gorbalenya, and P. A. Tucker.** 2010. Papain-like protease 1 from transmissible gastroenteritis virus: crystal structure and enzymatic activity toward viral and cellular substrates. *J. Virol.* **84**:10063-10073.
99. **Clementz, M. A., Z. Chen, B. S. Banach, Y. Wang, L. Sun, K. Ratia, Y. M. Baez-Santos, J. Wang, et al.** 2010. Deubiquitinating and interferon antagonism activities of coronavirus papain-like proteases. *J. Virol.* **84**:4619-4629.
100. **Sun, Z., Z. Chen, S. R. Lawson, and Y. Fang.** 2010. The cysteine protease domain of porcine reproductive and respiratory syndrome virus nonstructural protein 2 possesses deubiquitinating and interferon antagonism functions. *J. Virol.* **84**:7832-7846.
101. **van Kasteren, P. B., C. Beugeling, D. K. Ninaber, N. Frias-Staheli, S. van Boheemen, A. Garcia-Sastre, E. J. Snijder, and M. Kikkert.** 2012. Arterivirus and nairovirus ovarian tumor domain-containing Deubiquitinases target activated RIG-I to control innate immune signaling. *J. Virol.* **86**:773-785.
102. **van Kasteren, P. B., B. A. Bailey-Elkin, T. W. James, D. K. Ninaber, C. Beugeling, M. Khajehpour, E. J. Snijder, B. L. Mark, and M. Kikkert.** 2013. Deubiquitinase function of arterivirus papain-like protease 2 suppresses the innate immune response in infected host cells. *Proc. Natl. Acad. Sci. USA* **110**:E838-847.
103. **Totura, A. L., and R. S. Baric.** 2012. SARS coronavirus pathogenesis: host innate immune responses and viral antagonism of interferon. *Current opinion in virology* **2**:264-275.
104. **Wathelet, M. G., M. Orr, M. B. Frieman, and R. S. Baric.** 2007. Severe acute respiratory syndrome coronavirus evades antiviral signaling: role of nsp1 and rational design of an attenuated strain. *J. Virol.* **81**:11620-11633.
105. **Frieman, M., B. Yount, M. Heise, S. A. Kopecky-Bromberg, P. Palese, and R. S. Baric.** 2007. Severe acute respiratory syndrome coronavirus ORF6 antagonizes STAT1 function by sequestering nuclear import factors on the rough endoplasmic reticulum/Golgi membrane. *J. Virol.* **81**:9812-9824.
106. **Kopecky-Bromberg, S. A., L. Martinez-Sobrido, M. Frieman, R. A. Baric, and P. Palese.** 2007. Severe acute respiratory syndrome coronavirus open reading frame (ORF) 3b, ORF 6, and nucleocapsid proteins function as interferon antagonists. *J. Virol.* **81**:548-557.
107. **Patel, D., Y. Nan, M. Shen, K. Ritthipichai, X. Zhu, and Y. J. Zhang.** 2010. Porcine reproductive and respiratory syndrome virus inhibits type I interferon signaling by blocking STAT1/STAT2 nuclear translocation. *J. Virol.* **84**:11045-11055.

108. **Wang, R., Y. Nan, Y. Yu, and Y. J. Zhang.** 2013. Porcine reproductive and respiratory syndrome virus Nsp1beta inhibits interferon-activated JAK/STAT signal transduction by inducing karyopherin-alpha1 degradation. *J. Virol.* **87**:5219-5228.
109. **Zhou, P., H. Li, H. Wang, L. F. Wang, and Z. Shi.** 2012. Bat severe acute respiratory syndrome-like coronavirus ORF3b homologues display different interferon antagonist activities. *J. Gen. Virol.* **93**:275-281.
110. **Frieman, M., K. Ratia, R. E. Johnston, A. D. Mesecar, and R. S. Baric.** 2009. Severe acute respiratory syndrome coronavirus papain-like protease ubiquitin-like domain and catalytic domain regulate antagonism of IRF3 and NF-kappaB signaling. *J. Virol.* **83**:6689-6705.
111. **Wang, G., G. Chen, D. Zheng, G. Cheng, and H. Tang.** 2011. PLP2 of mouse hepatitis virus A59 (MHV-A59) targets TBK1 to negatively regulate cellular type I interferon signaling pathway. *PLoS One* **6**:e17192.
112. **Siu, K. L., K. H. Kok, M. H. Ng, V. K. Poon, K. Y. Yuen, B. J. Zheng, and D. Y. Jin.** 2009. Severe acute respiratory syndrome coronavirus M protein inhibits type I interferon production by impeding the formation of TRAF3.TANK.TBK1/IKKepsilon complex. *J. Biol. Chem.* **284**:16202-16209.
113. **Devaraj, S. G., N. Wang, Z. Chen, M. Tseng, N. Barretto, R. Lin, C. J. Peters, C. T. Tseng, et al.** 2007. Regulation of IRF-3-dependent innate immunity by the papain-like protease domain of the severe acute respiratory syndrome coronavirus. *J. Biol. Chem.* **282**:32208-32221.
114. **Enjuanes, L., F. Almazan, I. Sola, S. Zuniga, E. Alvarez, J. Reguera, and C. Capiscol.** 2006. Biochemical aspects of coronavirus replication. *Adv. Exp. Med. Biol.* **581**:13-24.
115. **Spagnolo, J. F., and B. G. Hogue.** 2000. Host protein interactions with the 3' end of bovine coronavirus RNA and the requirement of the poly(A) tail for coronavirus defective genome replication. *J. Virol.* **74**:5053-5065.
116. **Galan, C., I. Sola, A. Nogales, B. Thomas, A. Akoulitchev, L. Enjuanes, and F. Almazan.** 2009. Host cell proteins interacting with the 3' end of TGEV coronavirus genome influence virus replication. *Virology* **391**:304-314.
117. **Wang, X., J. Bai, L. Zhang, X. Wang, Y. Li, and P. Jiang.** 2012. Poly(A)-binding protein interacts with the nucleocapsid protein of porcine reproductive and respiratory syndrome virus and participates in viral replication. *Antiviral Res.* **96**:315-323.
118. **Beura, L. K., P. X. Dinh, F. A. Osorio, and A. K. Pattnaik.** 2011. Cellular poly(c) binding proteins 1 and 2 interact with porcine reproductive and respiratory syndrome virus nonstructural protein 1beta and support viral replication. *J. Virol.* **85**:12939-12949.
119. **Wang, Y., and X. Zhang.** 1999. The nucleocapsid protein of coronavirus mouse hepatitis virus interacts with the cellular heterogeneous nuclear ribonucleoprotein A1 *in vitro* and *in vivo*. *Virology* **265**:96-109.
120. **Luo, H., Q. Chen, J. Chen, K. Chen, X. Shen, and H. Jiang.** 2005. The nucleocapsid protein of SARS coronavirus has a high binding affinity to the human cellular heterogeneous nuclear ribonucleoprotein A1. *FEBS Lett.* **579**:2623-2628.
121. **Li, H. P., X. Zhang, R. Duncan, L. Comai, and M. M. Lai.** 1997. Heterogeneous nuclear ribonucleoprotein A1 binds to the transcription-regulatory region of mouse hepatitis virus RNA. *Proc. Natl. Acad. Sci. USA* **94**:9544-9549.
122. **Huang, P., and M. M. Lai.** 2001. Heterogeneous nuclear ribonucleoprotein a1 binds to the 3'-untranslated region and mediates potential 5'-3'-end cross talks of mouse hepatitis virus RNA. *J. Virol.* **75**:5009-5017.

123. **Jourdan, S. S., F. Osorio, and J. A. Hiscox.** 2012. An interactome map of the nucleocapsid protein from a highly pathogenic North American porcine reproductive and respiratory syndrome virus strain generated using SILAC-based quantitative proteomics. *Proteomics* **12**:1015-1023.
124. **Tijms, M. A., and E. J. Snijder.** 2003. Equine arteritis virus non-structural protein 1, an essential factor for viral subgenomic mRNA synthesis, interacts with the cellular transcription co-factor p100. *J. Gen. Virol.* **84**:2317-2322.
125. **Kwak, H., M. W. Park, and S. Jeong.** 2011. Annexin A2 binds RNA and reduces the frameshifting efficiency of infectious bronchitis virus. *PLoS One* **6**:e24067.
126. **Nanda, S. K., and J. L. Leibowitz.** 2001. Mitochondrial aconitase binds to the 3' untranslated region of the mouse hepatitis virus genome. *J. Virol.* **75**:3352-3362.
127. **Tan, Y. W., W. Hong, and D. X. Liu.** 2012. Binding of the 5'-untranslated region of coronavirus RNA to zinc finger CCHC-type and RNA-binding motif 1 enhances viral replication and transcription. *Nucleic Acids Res.* **40**:5065-5077.
128. **Maines, T. R., M. Young, N. N. Dinh, and M. A. Brinton.** 2005. Two cellular proteins that interact with a stem loop in the simian hemorrhagic fever virus 3'(+)NCR RNA. *Virus Res.* **109**:109-124.
129. **Li, H. P., P. Huang, S. Park, and M. M. Lai.** 1999. Polypyrimidine tract-binding protein binds to the leader RNA of mouse hepatitis virus and serves as a regulator of viral transcription. *J. Virol.* **73**:772-777.
130. **Kellam, P.** 2006. Attacking pathogens through their hosts. *Genome Biol.* **7**:201.
131. **Schwegmann, A., and F. Brombacher.** 2008. Host-directed drug targeting of factors hijacked by pathogens. *Sci. Signal* **1**:re8.
132. **Yeh, K. M., T. S. Chiueh, L. K. Siu, J. C. Lin, P. K. Chan, M. Y. Peng, H. L. Wan, J. H. Chen, et al.** 2005. Experience of using convalescent plasma for severe acute respiratory syndrome among healthcare workers in a Taiwan hospital. *J. Antimicrob. Chemother.* **56**:919-922.
133. **Cheng, Y., R. Wong, Y. O. Soo, W. S. Wong, C. K. Lee, M. H. Ng, P. Chan, K. C. Wong, et al.** 2005. Use of convalescent plasma therapy in SARS patients in Hong Kong. *Eur. J. Clin. Microbiol. Infect. Dis.* **24**:44-46.
134. **Tong, T. R.** 2009. Therapies for coronaviruses. Part I of II – viral entry inhibitors. *Expert Opin. Ther. Pat.* **19**:357-367.
135. **van den Brink, E. N., J. Ter Meulen, F. Cox, M. A. Jongeneelen, A. Thijsse, M. Throsby, W. E. Marissen, P. M. Rood, et al.** 2005. Molecular and biological characterization of human monoclonal antibodies binding to the spike and nucleocapsid proteins of severe acute respiratory syndrome coronavirus. *J. Virol.* **79**:1635-1644.
136. **ter Meulen, J., A. B. Bakker, E. N. van den Brink, G. J. Weverling, B. E. Martina, B. L. Haagmans, T. Kuiken, J. de Kruif, et al.** 2004. Human monoclonal antibody as prophylaxis for SARS coronavirus infection in ferrets. *Lancet* **363**:2139-2141.
137. **ter Meulen, J., E. N. van den Brink, L. L. Poon, W. E. Marissen, C. S. Leung, F. Cox, C. Y. Cheung, A. Q. Bakker, et al.** 2006. Human monoclonal antibody combination against SARS coronavirus: synergy and coverage of escape mutants. *PLoS Med.* **3**:e237.
138. **Takano, T., Y. Katoh, T. Doki, and T. Hohdatsu.** 2013. Effect of chloroquine on feline infectious peritonitis virus infection *in vitro* and *in vivo*. *Antiviral Res.* **99**:100-107.
139. **Keyaerts, E., S. Li, L. Vijgen, E. Rysman, J. Verbeeck, M. Van Ranst, and P. Maes.** 2009. Antiviral activity of chloroquine against human coronavirus OC43 infection in newborn mice. *Antimicrob. Agents Chemother.* **53**:3416-3421.
140. **Krzystyniak, K., and J. M. Dupuy.** 1984. Entry of mouse hepatitis virus 3 into cells. *J. Gen. Virol.* **65 (Pt 1)**:227-231.

141. **Payne, H. R., J. Storz, and W. G. Henk.** 1990. Initial events in bovine coronavirus infection: analysis through immunogold probes and lysosomotropic inhibitors. *Arch. Virol.* **114**:175-189.
142. **Kreutz, L. C., and M. R. Ackermann.** 1996. Porcine reproductive and respiratory syndrome virus enters cells through a low pH-dependent endocytic pathway. *Virus Res.* **42**:137-147.
143. **Kono, M., K. Tatsumi, A. M. Imai, K. Saito, T. Kuriyama, and H. Shirasawa.** 2008. Inhibition of human coronavirus 229E infection in human epithelial lung cells (L132) by chloroquine: involvement of p38 MAPK and ERK. *Antiviral Res.* **77**:150-152.
144. **Keyaerts, E., L. Vijgen, P. Maes, J. Neyts, and M. Van Ranst.** 2004. In vitro inhibition of severe acute respiratory syndrome coronavirus by chloroquine. *Biochem. Biophys. Res. Commun.* **323**:264-268.
145. **Du, L., Y. He, Y. Zhou, S. Liu, B. J. Zheng, and S. Jiang.** 2009. The spike protein of SARS-CoV--a target for vaccine and therapeutic development. *Nat. Rev. Microbiol.* **7**:226-236.
146. **Fernandez-Montero, J. V., P. Barreiro, and V. Soriano.** 2009. HIV protease inhibitors: recent clinical trials and recommendations on use. *Expert Opin. Pharmacother.* **10**:1615-1629.
147. **Clark, V. C., J. A. Peter, and D. R. Nelson.** 2013. New therapeutic strategies in HCV: second-generation protease inhibitors. *Liver Int.* **33 Suppl 1**:80-84.
148. **Yang, H., W. Xie, X. Xue, K. Yang, J. Ma, W. Liang, Q. Zhao, Z. Zhou, et al.** 2005. Design of wide-spectrum inhibitors targeting coronavirus main proteases. *PLoS Biol.* **3**:e324.
149. **Ghosh, A. K., J. Takayama, K. V. Rao, K. Ratia, R. Chaudhuri, D. C. Mulhearn, H. Lee, D. B. Nichols, et al.** 2010. Severe acute respiratory syndrome coronavirus papain-like novel protease inhibitors: design, synthesis, protein-ligand X-ray structure and biological evaluation. *J. Med. Chem.* **53**:4968-4979.
150. **Hsu, J. T., C. J. Kuo, H. P. Hsieh, Y. C. Wang, K. K. Huang, C. P. Lin, P. F. Huang, X. Chen, and P. H. Liang.** 2004. Evaluation of metal-conjugated compounds as inhibitors of 3CL protease of SARS-CoV. *FEBS Lett.* **574**:116-120.
151. **Kuo, C. J., H. G. Liu, Y. K. Lo, C. M. Seong, K. I. Lee, Y. S. Jung, and P. H. Liang.** 2009. Individual and common inhibitors of coronavirus and picornavirus main proteases. *FEBS Lett.* **583**:549-555.
152. **Wu, C. Y., J. T. Jan, S. H. Ma, C. J. Kuo, H. F. Juan, Y. S. Cheng, H. H. Hsu, H. C. Huang, et al.** 2004. Small molecules targeting severe acute respiratory syndrome human coronavirus. *Proc. Natl. Acad. Sci. USA* **101**:10012-10017.
153. **Ratia, K., S. Pegan, J. Takayama, K. Sleeman, M. Coughlin, S. Baliji, R. Chaudhuri, W. Fu, et al.** 2008. A noncovalent class of papain-like protease/deubiquitinase inhibitors blocks SARS virus replication. *Proc. Natl. Acad. Sci. USA* **105**:16119-16124.
154. **Crotty, S., D. Maag, J. J. Arnold, W. Zhong, J. Y. Lau, Z. Hong, R. Andino, and C. E. Cameron.** 2000. The broad-spectrum antiviral ribonucleoside ribavirin is an RNA virus mutagen. *Nat. Med.* **6**:1375-1379.
155. **Morgenstern, B., M. Michaelis, P. C. Baer, H. W. Doerr, and J. Cinatl, Jr.** 2005. Ribavirin and interferon-beta synergistically inhibit SARS-associated coronavirus replication in animal and human cell lines. *Biochem. Biophys. Res. Commun.* **326**:905-908.
156. **Stroher, U., A. DiCaro, Y. Li, J. E. Strong, F. Aoki, F. Plummer, S. M. Jones, and H. Feldmann.** 2004. Severe acute respiratory syndrome-related coronavirus is inhibited by interferon- alpha. *J. Infect. Dis.* **189**:1164-1167.
157. **Saijo, M., S. Morikawa, S. Fukushi, T. Mizutani, H. Hasegawa, N. Nagata, N. Iwata, and I. Kurane.** 2005. Inhibitory effect of mizoribine and ribavirin on the replication of severe acute respiratory syndrome (SARS)-associated coronavirus. *Antiviral Res.* **66**:159-163.

158. **Knowles, S. R., E. J. Phillips, L. Dresser, and L. Matukas.** 2003. Common adverse events associated with the use of ribavirin for severe acute respiratory syndrome in Canada. *Clin. Infect. Dis.* **37**:1139-1142.
159. **te Velthuis, A. J., S. H. van den Worm, A. C. Sims, R. S. Baric, E. J. Snijder, and M. J. van Hemert.** 2010. Zn(2+) inhibits coronavirus and arterivirus RNA polymerase activity *in vitro* and zinc ionophores block the replication of these viruses in cell culture. *PLoS Pathog.* **6**:e1001176.
160. **Liu, K., X. Feng, Z. Ma, C. Luo, B. Zhou, R. Cao, L. Huang, D. Miao, et al.** 2012. Antiviral activity of phage display selected peptides against Porcine reproductive and respiratory syndrome virus *in vitro*. *Virology* **432**:73-80.
161. **Tanner, J. A., B. J. Zheng, J. Zhou, R. M. Watt, J. Q. Jiang, K. L. Wong, Y. P. Lin, L. Y. Lu, et al.** 2005. The adamantane-derived bananins are potent inhibitors of the helicase activities and replication of SARS coronavirus. *Chem. Biol.* **12**:303-311.
162. **Yang, N., J. A. Tanner, Z. Wang, J. D. Huang, B. J. Zheng, N. Zhu, and H. Sun.** 2007. Inhibition of SARS coronavirus helicase by bismuth complexes. *Chem. Commun. (Camb)*:4413-4415.
163. **Yang, N., J. A. Tanner, B. J. Zheng, R. M. Watt, M. L. He, L. Y. Lu, J. Q. Jiang, K. T. Shum, et al.** 2007. Bismuth complexes inhibit the SARS coronavirus. *Angew. Chem. Int. Ed. Engl.* **46**:6464-6468.
164. **Yu, M. S., J. Lee, J. M. Lee, Y. Kim, Y. W. Chin, J. G. Jee, Y. S. Keum, and Y. J. Jeong.** 2012. Identification of myricetin and scutellarein as novel chemical inhibitors of the SARS coronavirus helicase, nsP13. *Bioorg. Med. Chem. Lett.* **22**:4049-4054.
165. **Kim, M. K., M. S. Yu, H. R. Park, K. B. Kim, C. Lee, S. Y. Cho, J. Kang, H. Yoon, et al.** 2011. 2,6-Bis-arylmethoxy-5-hydroxychromones with antiviral activity against both hepatitis C virus (HCV) and SARS-associated coronavirus (SCV). *Eur. J. Med. Chem.* **46**:5698-5704.
166. **Bouvet, M., C. Debarnot, I. Imbert, B. Selisko, E. J. Snijder, B. Canard, and E. Decroly.** 2010. *In vitro* reconstitution of SARS-coronavirus mRNA cap methylation. *PLoS Pathog.* **6**:e1000863.
167. **He, R., A. Adonov, M. Traykova-Adonova, J. Cao, T. Cutts, E. Grudesky, Y. Deschambaul, J. Berry, et al.** 2004. Potent and selective inhibition of SARS coronavirus replication by aurintricarboxylic acid. *Biochem. Biophys. Res. Commun.* **320**:1199-1203.
168. **Ke, M., Y. Chen, A. Wu, Y. Sun, C. Su, H. Wu, X. Jin, J. Tao, et al.** 2012. Short peptides derived from the interaction domain of SARS coronavirus nonstructural protein nsp10 can suppress the 2'-O-methyltransferase activity of nsp10/nsp16 complex. *Virus Res.* **167**:322-328.
169. **Wilson, L., P. Gage, and G. Ewart.** 2006. Hexamethylene amiloride blocks E protein ion channels and inhibits coronavirus replication. *Virology* **353**:294-306.
170. **Neuman, B. W., D. A. Stein, A. D. Kroeker, M. J. Churchill, A. M. Kim, P. Kuhn, P. Dawson, H. M. Moulton, et al.** 2005. Inhibition, escape, and attenuated growth of severe acute respiratory syndrome coronavirus treated with antisense morpholino oligomers. *J. Virol.* **79**:9665-9676.
171. **Burrer, R., B. W. Neuman, J. P. Ting, D. A. Stein, H. M. Moulton, P. L. Iversen, P. Kuhn, and M. J. Buchmeier.** 2007. Antiviral effects of antisense morpholino oligomers in murine coronavirus infection models. *J. Virol.* **81**:5637-5648.
172. **Ahn, D. G., W. Lee, J. K. Choi, S. J. Kim, E. P. Plant, F. Almazan, D. R. Taylor, L. Enjuanes, and J. W. Oh.** 2011. Interference of ribosomal frameshifting by antisense peptide nucleic acids suppresses SARS coronavirus replication. *Antiviral Res.* **91**:1-10.
173. **van den Born, E., D. A. Stein, P. L. Iversen, and E. J. Snijder.** 2005. Antiviral activity of morpholino oligomers designed to block various aspects of Equine arteritis virus amplification in cell culture. *J. Gen. Virol.* **86**:3081-3090.

174. **Zhang, Y. J., D. A. Stein, S. M. Fan, K. Y. Wang, A. D. Kroeker, X. J. Meng, P. L. Iversen, and D. O. Matson.** 2006. Suppression of porcine reproductive and respiratory syndrome virus replication by morpholino antisense oligomers. *Vet. Microbiol.* **117**:117-129.
175. **Patel, D., T. Opriessnig, D. A. Stein, P. G. Halbur, X. J. Meng, P. L. Iversen, and Y. J. Zhang.** 2008. Peptide-conjugated morpholino oligomers inhibit porcine reproductive and respiratory syndrome virus replication. *Antiviral Res.* **77**:95-107.
176. **Han, X., S. Fan, D. Patel, and Y. J. Zhang.** 2009. Enhanced inhibition of porcine reproductive and respiratory syndrome virus replication by combination of morpholino oligomers. *Antiviral Res.* **82**:59-66.
177. **Opriessnig, T., D. Patel, R. Wang, P. G. Halbur, X. J. Meng, D. A. Stein, and Y. J. Zhang.** 2011. Inhibition of porcine reproductive and respiratory syndrome virus infection in piglets by a peptide-conjugated morpholino oligomer. *Antiviral Res.* **91**:36-42.
178. **He, Y. X., R. H. Hua, Y. J. Zhou, H. J. Qiu, and G. Z. Tong.** 2007. Interference of porcine reproductive and respiratory syndrome virus replication on MARC-145 cells using DNA-based short interfering RNAs. *Antiviral Res.* **74**:83-91.
179. **Li, G., P. Jiang, Y. Li, X. Wang, J. Huang, J. Bai, J. Cao, B. Wu, et al.** 2009. Inhibition of porcine reproductive and respiratory syndrome virus replication by adenovirus-mediated RNA interference both in porcine alveolar macrophages and swine. *Antiviral Res.* **82**:157-165.
180. **Heinrich, A., D. Riethmuller, M. Gloger, G. F. Schusser, M. Giese, and S. Ulbert.** 2009. RNA interference protects horse cells *in vitro* from infection with Equine Arteritis Virus. *Antiviral Res.* **81**:209-216.
181. **Zhang, Y., T. Li, L. Fu, C. Yu, Y. Li, X. Xu, Y. Wang, H. Ning, et al.** 2004. Silencing SARS-CoV Spike protein expression in cultured cells by RNA interference. *FEBS Lett.* **560**:141-146.
182. **Wu, C. J., H. W. Huang, C. Y. Liu, C. F. Hong, and Y. L. Chan.** 2005. Inhibition of SARS-CoV replication by siRNA. *Antiviral Res.* **65**:45-48.
183. **DeVincenzo, J. P.** 2012. The promise, pitfalls and progress of RNA-interference-based antiviral therapy for respiratory viruses. *Antivir. Ther.* **17**:213-225.
184. **Burnett, J. C., J. J. Rossi, and K. Tiemann.** 2011. Current progress of siRNA/shRNA therapeutics in clinical trials. *Biotechnol. J.* **6**:1130-1146.
185. **Shi, Y., D. H. Yang, J. Xiong, J. Jia, B. Huang, and Y. X. Jin.** 2005. Inhibition of genes expression of SARS coronavirus by synthetic small interfering RNAs. *Cell Res.* **15**:193-200.
186. **Li, B. J., Q. Tang, D. Cheng, C. Qin, F. Y. Xie, Q. Wei, J. Xu, Y. Liu, et al.** 2005. Using siRNA in prophylactic and therapeutic regimens against SARS coronavirus in Rhesus macaque. *Nat. Med.* **11**:944-951.
187. **Stockman, L. J., R. Bellamy, and P. Garner.** 2006. SARS: systematic review of treatment effects. *PLoS Med.* **3**:e343.
188. **Garlinghouse, L. E., Jr., A. L. Smith, and T. Holford.** 1984. The biological relationship of mouse hepatitis virus (MHV) strains and interferon: *in vitro* induction and sensitivities. *Arch. Virol.* **82**:19-29.
189. **Taguchi, F., and S. G. Siddell.** 1985. Difference in sensitivity to interferon among mouse hepatitis viruses with high and low virulence for mice. *Virology* **147**:41-48.
190. **Haagmans, B. L., T. Kuiken, B. E. Martina, R. A. Fouchier, G. F. Rimmelzwaan, G. van Amerongen, D. van Riel, T. de Jong, et al.** 2004. Pegylated interferon-alpha protects type 1 pneumocytes against SARS coronavirus infection in macaques. *Nat. Med.* **10**:290-293.
191. **Paragas, J., L. M. Blatt, C. Hartmann, J. W. Huggins, and T. P. Endy.** 2005. Interferon alfacon1 is an inhibitor of SARS-corona virus in cell-based models. *Antiviral Res.* **66**:99-102.

192. **Zheng, B., M. L. He, K. L. Wong, C. T. Lum, L. L. Poon, Y. Peng, Y. Guan, M. C. Lin, and H. F. Kung.** 2004. Potent inhibition of SARS-associated coronavirus (SCOV) infection and replication by type I interferons (IFN-alpha/beta) but not by type II interferon (IFN-gamma). *J. Interferon Cytokine Res.* **24**:388-390.
193. **Dusheiko, G.** 1997. Side effects of alpha interferon in chronic hepatitis C. *Hepatology* **26**:1125-1215.
194. **Mitsuki, Y. Y., K. Ohnishi, H. Takagi, M. Oshima, T. Yamamoto, F. Mizukoshi, K. Terahara, K. Kobayashi, et al.** 2008. A single amino acid substitution in the S1 and S2 Spike protein domains determines the neutralization escape phenotype of SARS-CoV. *Microbes Infect.* **10**:908-915.
195. **Salonen, A., T. Ahola, and L. Kaariainen.** 2005. Viral RNA replication in association with cellular membranes. *Curr. Top. Microbiol. Immunol.* **285**:139-173.
196. **Sawicki, S. G., D. L. Sawicki, and S. G. Siddell.** 2007. A contemporary view of coronavirus transcription. *J. Virol.* **81**:20-29.
197. **Ng, L. F., and D. X. Liu.** 2002. Membrane association and dimerization of a cysteine-rich, 16-kilodalton polypeptide released from the C-terminal region of the coronavirus infectious bronchitis virus 1a polyprotein. *J. Virol.* **76**:6257-6267.
198. **Harcourt, B. H., D. Jukneliene, A. Kanjanahaluethai, J. Bechill, K. M. Severson, C. M. Smith, P. A. Rota, and S. C. Baker.** 2004. Identification of severe acute respiratory syndrome coronavirus replicase products and characterization of papain-like protease activity. *J. Virol.* **78**:13600-13612.
199. **Shi, S. T., J. J. Schiller, A. Kanjanahaluethai, S. C. Baker, J. W. Oh, and M. M. Lai.** 1999. Colocalization and membrane association of murine hepatitis virus gene 1 products and De novo-synthesized viral RNA in infected cells. *J. Virol.* **73**:5957-5969.
200. **Denison, M. R., W. J. Spaan, Y. van der Meer, C. A. Gibson, A. C. Sims, E. Prentice, and X. T. Lu.** 1999. The putative helicase of the coronavirus mouse hepatitis virus is processed from the replicase gene polyprotein and localizes in complexes that are active in viral RNA synthesis. *J. Virol.* **73**:6862-6871.
201. **Pedersen, K. W., M. Y. van der, N. Roos, and E. J. Snijder.** 1999. Open reading frame 1a-encoded subunits of the arterivirus replicase induce endoplasmic reticulum-derived double-membrane vesicles which carry the viral replication complex. *J. Virol.* **73**:2016-2026.
202. **van Dinten, L. C., A. L. Wassenaar, A. E. Gorbalenya, W. J. Spaan, and E. J. Snijder.** 1996. Processing of the equine arteritis virus replicase ORF1b protein: identification of cleavage products containing the putative viral polymerase and helicase domains. *J. Virol.* **70**:6625-6633.
203. **Bi, W., J. D. Pinon, S. Hughes, P. J. Bonilla, K. V. Holmes, S. R. Weiss, and J. L. Leibowitz.** 1998. Localization of mouse hepatitis virus open reading frame 1A derived proteins. *J. Neurovirol.* **4**:594-605.
204. **Bost, A. G., R. H. Carnahan, X. T. Lu, and M. R. Denison.** 2000. Four proteins processed from the replicase gene polyprotein of mouse hepatitis virus colocalize in the cell periphery and adjacent to sites of virion assembly. *J. Virol.* **74**:3379-3387.
205. **Bost, A. G., E. Prentice, and M. R. Denison.** 2001. Mouse hepatitis virus replicase protein complexes are translocated to sites of M protein accumulation in the ERGIC at late times of infection. *Virology* **285**:21-29.
206. **Ivanov, K. A., V. Thiel, J. C. Dobbe, Y. van der Meer, E. J. Snijder, and J. Ziebuhr.** 2004. Multiple enzymatic activities associated with severe acute respiratory syndrome coronavirus helicase. *J. Virol.* **78**:5619-5632.

207. **Prentice, E., J. McAuliffe, X. Lu, K. Subbarao, and M. R. Denison.** 2004. Identification and characterization of severe acute respiratory syndrome coronavirus replicase proteins. *J. Virol.* **78**:9977-9986.
208. **Snijder, E. J., M. Y. van der, J. Zevenhoven-Dobbe, J. J. Onderwater, M. J. van der, H. K. Koerten, and A. M. Mommaas.** 2006. Ultrastructure and origin of membrane vesicles associated with the severe acute respiratory syndrome coronavirus replication complex. *J. Virol.* **80**:5927-5940.
209. **Pol, J. M., F. Wagenaar, and J. E. Reus.** 1997. Comparative morphogenesis of three PRRS virus strains. *Vet. Microbiol.* **55**:203-208.
210. **Wood, O., N. Tauraso, and H. Liebhaber.** 1970. Electron microscopic study of tissue cultures infected with simian haemorrhagic fever virus. *J. Gen. Virol.* **7**:129-136.
211. **Goldsmith, C. S., K. M. Tatti, T. G. Ksiazek, P. E. Rollin, J. A. Comer, W. W. Lee, P. A. Rota, B. Bankamp, et al.** 2004. Ultrastructural characterization of SARS coronavirus. *Emerg. Infect. Dis.* **10**:320-326.
212. **Ng, M. L., S. H. Tan, E. E. See, E. E. Ooi, and A. E. Ling.** 2003. Proliferative growth of SARS coronavirus in Vero E6 cells. *J. Gen. Virol.* **84**:3291-3303.
213. **Snijder, E. J., and J. J. Meulenberg.** 1998. The molecular biology of arteriviruses. *J. Gen. Virol.* **79** (Pt 5):961-979.
214. **Van Aken, D., J. Zevenhoven-Dobbe, A. E. Gorbalenya, and E. J. Snijder.** 2006. Proteolytic maturation of replicase polyprotein pp1a by the nsp4 main proteinase is essential for equine arteritis virus replication and includes internal cleavage of nsp7. *J. Gen. Virol.* **87**:3473-3482.
215. **Beerens, N., B. Selisko, S. Ricagno, I. Imbert, L. van der Zanden, E. J. Snijder, and B. Canard.** 2007. De novo initiation of RNA synthesis by the arterivirus RNA-dependent RNA polymerase. *J. Virol.*
216. **Seybert, A., L. C. van Dinten, E. J. Snijder, and J. Ziebuhr.** 2000. Biochemical characterization of the equine arteritis virus helicase suggests a close functional relationship between arterivirus and coronavirus helicases. *J. Virol.* **74**:9586-9593.
217. **Snijder, E. J., H. van Tol, N. Roos, and K. W. Pedersen.** 2001. Non-structural proteins 2 and 3 interact to modify host cell membranes during the formation of the arterivirus replication complex. *J. Gen. Virol.* **82**:985-994.
218. **Franklin, R. M.** 1967. Replication of bacteriophage ribonucleic acid: some physical properties of single-stranded, double-stranded, and branched viral ribonucleic acid. *J. Virol.* **1**:64-75.
219. **Sawicki, S. G., and D. L. Sawicki.** 1990. Coronavirus transcription: subgenomic mouse hepatitis virus replicative intermediates function in RNA synthesis. *J. Virol.* **64**:1050-1056.
220. **de Vries, A. A., E. D. Chirnside, M. C. Horzinek, and P. J. Rottier.** 1992. Structural proteins of equine arteritis virus. *J. Virol.* **66**:6294-6303.
221. **Igarashi, A.** 1978. Isolation of a Singh's *Aedes albopictus* cell clone sensitive to Dengue and Chikungunya viruses. *J. Gen. Virol.* **40**:531-544.
222. **Snijder, E. J., A. L. Wassenaar, and W. J. Spaan.** 1994. Proteolytic processing of the replicase ORF1a protein of equine arteritis virus. *J. Virol.* **68**:5755-5764.
223. **van Dinten, L. C., S. Rensen, A. E. Gorbalenya, and E. J. Snijder.** 1999. Proteolytic processing of the open reading frame 1b-encoded part of arterivirus replicase is mediated by nsp4 serine protease and is essential for virus replication. *J. Virol.* **73**:2027-2037.
224. **van Marle, G., L. C. van Dinten, W. J. Spaan, W. Luytjes, and E. J. Snijder.** 1999. Characterization of an equine arteritis virus replicase mutant defective in subgenomic mRNA synthesis. *J. Virol.* **73**:5274-5281.

225. **van Marle, G., J. C. Dobbe, A. P. Gultyaev, W. Luytjes, W. J. Spaan, and E. J. Snijder.** 1999. Arterivirus discontinuous mRNA transcription is guided by base pairing between sense and antisense transcription-regulating sequences. *Proc. Natl. Acad. Sci. USA* **96**:12056-12061.
226. **Chu, P. W., and E. G. Westaway.** 1985. Replication strategy of Kunjin virus: evidence for recycling role of replicative form RNA as template in semiconservative and asymmetric replication. *Virology* **140**:68-79.
227. **Grun, J. B., and M. A. Brinton.** 1986. Characterization of West Nile virus RNA-dependent RNA polymerase and cellular terminal adenylyl and uridylyl transferases in cell-free extracts. *J. Virol.* **60**:1113-1124.
228. **Barton, D. J., S. G. Sawicki, and D. L. Sawicki.** 1991. Solubilization and immunoprecipitation of alphavirus replication complexes. *J. Virol.* **65**:1496-1506.
229. **Uchil, P. D., and V. Satchidanandam.** 2003. Characterization of RNA synthesis, replication mechanism, and *in vitro* RNA-dependent RNA polymerase activity of Japanese encephalitis virus. *Virology* **307**:358-371.
230. **Hardy, S. F., T. L. German, L. S. Loesch-Fries, and T. C. Hall.** 1979. Highly active template-specific RNA-dependent RNA polymerase from barley leaves infected with brome mosaic virus. *Proc. Natl. Acad. Sci. USA* **76**:4956-4960.
231. **Snijder, E. J., A. L. Wassenaar, L. C. van Dinten, W. J. Spaan, and A. E. Gorbalenya.** 1996. The arterivirus nsp4 protease is the prototype of a novel group of chymotrypsin-like enzymes, the 3C-like serine proteases. *J. Biol. Chem.* **271**:4864-4871.
232. **Wassenaar, A. L., W. J. Spaan, A. E. Gorbalenya, and E. J. Snijder.** 1997. Alternative proteolytic processing of the arterivirus replicase ORF1a polyprotein: evidence that NSP2 acts as a cofactor for the NSP4 serine protease. *J. Virol.* **71**:9313-9322.
233. **Snijder, E. J., A. L. Wassenaar, and W. J. Spaan.** 1992. The 5' end of the equine arteritis virus replicase gene encodes a papainlike cysteine protease. *J. Virol.* **66**:7040-7048.
234. **Tijms, M. A., D. D. Nedialkova, J. C. Zevenhoven-Dobbe, A. E. Gorbalenya, and E. J. Snijder.** 2007. Arterivirus subgenomic mRNA synthesis and virion biogenesis depend on the multifunctional nsp1 autoprotease. *J. Virol.*
235. **Tijms, M. A., L. C. van Dinten, A. E. Gorbalenya, and E. J. Snijder.** 2001. A zinc finger-containing papain-like protease couples subgenomic mRNA synthesis to genome translation in a positive-stranded RNA virus. *Proc. Natl. Acad. Sci. USA* **98**:1889-1894.
236. **Brayton, P. R., M. M. Lai, C. D. Patton, and S. A. Stohlman.** 1982. Characterization of two RNA polymerase activities induced by mouse hepatitis virus. *J. Virol.* **42**:847-853.
237. **Brayton, P. R., S. A. Stohlman, and M. M. Lai.** 1984. Further characterization of mouse hepatitis virus RNA-dependent RNA polymerases. *Virology* **133**:197-201.
238. **Mahy, B. W., S. Siddell, H. Wege, and V. ter Meulen.** 1983. RNA-dependent RNA polymerase activity in murine coronavirus-infected cells. *J. Gen. Virol.* **64** (Pt 1):103-111.
239. **Compton, S. R., D. B. Rogers, K. V. Holmes, D. Fertsch, J. Remenick, and J. J. McGowan.** 1987. *In vitro* replication of mouse hepatitis virus strain A59. *J. Virol.* **61**:1814-1820.
240. **Dennis, D. E., and D. A. Brian.** 1982. RNA-dependent RNA polymerase activity in coronavirus-infected cells. *J. Virol.* **42**:153-164.
241. **Sawicki, S. G., and D. L. Sawicki.** 1986. Coronavirus minus-strand RNA synthesis and effect of cycloheximide on coronavirus RNA synthesis. *J. Virol.* **57**:328-334.
242. **Barton, D. J., and J. B. Flanagan.** 1993. Coupled translation and replication of poliovirus RNA *in vitro*: synthesis of functional 3D polymerase and infectious virus. *J. Virol.* **67**:822-831.

243. **Ehrenfeld, E., and D. Brown.** 1981. Stability of poliovirus RNA in cell-free translation systems utilizing two initiation sites. *J. Biol. Chem.* **256**:2656-2661.
244. **Chu, P. W., and E. G. Westaway.** 1987. Characterization of Kunjin virus RNA-dependent RNA polymerase: reinitiation of synthesis *in vitro*. *Virology* **157**:330-337.
245. **Tomassini, J. E., E. Boots, L. Gan, P. Graham, V. Munshi, B. Wolanski, J. F. Fay, K. Getty, and R. LaFemina.** 2003. An *in vitro* Flaviviridae replicase system capable of authentic RNA replication. *Virology* **313**:274-285.
246. **Sreevalsan, T., and F. H. Yin.** 1969. Sindbis virus-induced viral ribonucleic acid polymerase. *J. Virol.* **3**:599-604.
247. **Polatnick, J., and R. B. Arlinghaus.** 1967. Foot-and-mouth disease virus-induced ribonucleic acid polymerase in baby hamster kidney cells. *Virology* **31**:601-608.
248. **Rosenberg, H., B. Diskin, L. Oron, and A. Traub.** 1972. Isolation and subunit structure of polycytidylate-dependent RNA polymerase of encephalomyocarditis virus. *Proc. Natl. Acad. Sci. USA* **69**:3815-3819.
249. **Quadt, R., and E. M. Jaspars.** 1990. Purification and characterization of brome mosaic virus RNA-dependent RNA polymerase. *Virology* **178**:189-194.
250. **Baltimore, D., and R. M. Franklin.** 1963. A New Ribonucleic Acid Polymerase Appearing after Mengovirus Infection of L-Cells. *J. Biol. Chem.* **238**:3395-3400.
251. **Svitkin, Y. V., and N. Sonenberg.** 2003. Cell-free synthesis of encephalomyocarditis virus. *J. Virol.* **77**:6551-6555.
252. **Yin, F. H., and E. Knight, Jr.** 1972. *In vivo* and *in vitro* synthesis of human rhinovirus type 2 ribonucleic acid. *J. Virol.* **10**:93-98.
253. **Warrilow, D., W. B. Lott, S. Greive, and E. J. Gowans.** 2000. Properties of the bovine viral diarrhoea virus replicase in extracts of infected MDBK cells. *Arch. Virol.* **145**:2163-2171.
254. **Lai, V. C., S. Dempsey, J. Y. Lau, Z. Hong, and W. Zhong.** 2003. *In vitro* RNA replication directed by replicase complexes isolated from the subgenomic replicon cells of hepatitis C virus. *J. Virol.* **77**:2295-2300.
255. **Hardy, R. W., J. Marcotrigiano, K. J. Blight, J. E. Majors, and C. M. Rice.** 2003. Hepatitis C virus RNA synthesis in a cell-free system isolated from replicon-containing hepatoma cells. *J. Virol.* **77**:2029-2037.
256. **Takegami, T., and S. Hotta.** 1989. *In vitro* synthesis of Japanese encephalitis virus (JEV) RNA: membrane and nuclear fractions of JEV-infected cells possess high levels of virus-specific RNA polymerase activity. *Virus Res.* **13**:337-350.
257. **Qureshi, A. A., and D. W. Trent.** 1972. Saint Louis encephalitis viral ribonucleic acid replication complex. *J. Virol.* **9**:565-573.
258. **Li, M. L., Y. H. Lin, and V. Stollar.** 2005. A cell-free system for the synthesis of Sindbis virus subgenomic RNA: importance of the concentration of the initiating NTP. *Virology* **341**:24-33.
259. **Baltimore, D., H. J. Eggers, R. M. Franklin, and I. Tamm.** 1963. Poliovirus-induced RNA polymerase and the effects of virus-specific inhibitors on its production. *Proc. Natl. Acad. Sci. USA* **49**:843-849.
260. **Ali, N., K. D. Tardif, and A. Siddiqui.** 2002. Cell-free replication of the hepatitis C virus subgenomic replicon. *J. Virol.* **76**:12001-12007.
261. **Sun, J. H., S. Adkins, G. Faurote, and C. C. Kao.** 1996. Initiation of (-)-strand RNA synthesis catalyzed by the BMV RNA-dependent RNA polymerase: synthesis of oligonucleotides. *Virology* **226**:1-12.

262. **Molenkamp, R., B. C. Rozier, S. Greve, W. J. Spaan, and E. J. Snijder.** 2000. Isolation and characterization of an arterivirus defective interfering RNA genome. *J. Virol.* **74**:3156-3165.
263. **Egger, D., N. Teterina, E. Ehrenfeld, and K. Bienz.** 2000. Formation of the poliovirus replication complex requires coupled viral translation, vesicle production, and viral RNA synthesis. *J. Virol.* **74**:6570-6580.
264. **Barton, D. J., E. P. Black, and J. B. Flanagan.** 1995. Complete replication of poliovirus *in vitro*: preinitiation RNA replication complexes require soluble cellular factors for the synthesis of VPg-linked RNA. *J. Virol.* **69**:5516-5527.
265. **Shi, S. T., K. J. Lee, H. Aizaki, S. B. Hwang, and M. M. Lai.** 2003. Hepatitis C virus RNA replication occurs on a detergent-resistant membrane that cofractionates with caveolin-2. *J. Virol.* **77**:4160-4168.
266. **Westaway, E. G., A. A. Khromykh, and J. M. Mackenzie.** 1999. Nascent flavivirus RNA colocalized *in situ* with double-stranded RNA in stable replication complexes. *Virology* **258**:108-117.
267. **Arlinghaus, R. B., and J. Polatnick.** 1969. *In vitro* products of a membrane-free foot-and-mouth disease virus ribonucleic acid polymerase. *Virology* **37**:252-261.
268. **Etchison, D., and E. Ehrenfeld.** 1981. Comparison of replication complexes synthesizing poliovirus RNA. *Virology* **111**:33-46.
269. **Ehrenfeld, E., J. V. Maizel, and D. F. Summers.** 1970. Soluble RNA polymerase complex from poliovirus-infected HeLa cells. *Virology* **40**:840-846.
270. **Molenkamp, R., H. van Tol, B. C. Rozier, M. Y. van der, W. J. Spaan, and E. J. Snijder.** 2000. The arterivirus replicase is the only viral protein required for genome replication and subgenomic mRNA transcription. *J. Gen. Virol.* **81**:2491-2496.
271. **Bose, S., M. Mathur, P. Bates, N. Joshi, and A. K. Banerjee.** 2003. Requirement for cyclophilin A for the replication of vesicular stomatitis virus New Jersey serotype. *J. Gen. Virol.* **84**:1687-1699.
272. **Briggs, C. J., D. E. Ott, L. V. Coren, S. Oroszlan, and J. Tozser.** 1999. Comparison of the effect of FK506 and cyclosporin A on virus production in H9 cells chronically and newly infected by HIV-1. *Arch. Virol.* **144**:2151-2160.
273. **Kambara, H., H. Tani, Y. Mori, T. Abe, H. Katoh, T. Fukuhara, S. Taguwa, K. Moriishi, and Y. Matsuura.** 2011. Involvement of cyclophilin B in the replication of Japanese encephalitis virus. *Virology* **412**:211-219.
274. **Nakagawa, M., N. Sakamoto, N. Enomoto, Y. Tanabe, N. Kanazawa, T. Koyama, M. Kurosaki, S. Maekawa, et al.** 2004. Specific inhibition of hepatitis C virus replication by cyclosporin A. *Biochem. Biophys. Res. Commun.* **313**:42-47.
275. **Qing, M., F. Yang, B. Zhang, G. Zou, J. M. Robida, Z. Yuan, H. Tang, and P. Y. Shi.** 2009. Cyclosporine inhibits flavivirus replication through blocking the interaction between host cyclophilins and viral NS5 protein. *Antimicrob. Agents Chemother.* **53**:3226-3235.
276. **de Wilde, A. H., J. C. Zevenhoven-Dobbe, Y. van der Meer, V. Thiel, K. Narayanan, S. Makino, E. J. Snijder, and M. J. van Hemert.** 2011. Cyclosporin A inhibits the replication of diverse coronaviruses. *J. Gen. Virol.* **92**:2542-2548.
277. **Pfefferle, S., J. Schopf, M. Kogl, C. C. Friedel, M. A. Muller, J. Carbajo-Lozoya, T. Stellberger, E. von Dall'armi, et al.** 2011. The SARS-Coronavirus-Host Interactome: Identification of Cyclophilins as Target for Pan-Coronavirus Inhibitors. *PLoS Pathog.* **7**:e1002331.
278. **Tanaka, Y., Y. Sato, S. Osawa, M. Inoue, S. Tanaka, and T. Sasaki.** 2012. Suppression of feline coronavirus replication *in vitro* by cyclosporin A. *Vet. Res.* **43**:41.

279. **Davis, T. L., J. R. Walker, V. Campagna-Slater, P. J. Finerty, R. Paramanathan, G. Bernstein, F. MacKenzie, W. Tempel, et al.** 2010. Structural and biochemical characterization of the human cyclophilin family of peptidyl-prolyl isomerases. *PLoS Biol.* **8**:e1000439.
280. **Barik, S.** 2006. Immunophilins: for the love of proteins. *Cell. Mol. Life Sci.* **63**:2889-2900.
281. **Nagy, P. D., R. Y. Wang, J. Pogany, A. Hafren, and K. Makinen.** 2011. Emerging picture of host chaperone and cyclophilin roles in RNA virus replication. *Virology* **411**:374-382.
282. **Tedesco, D., and L. Haragsim.** 2012. Cyclosporine: a review. *J. Transplant.* **2012**:230386.
283. **Flisiak, R., S. V. Feinman, M. Jablkowski, A. Horban, W. Kryczka, M. Pawlowska, J. E. Heathcote, G. Mazzella, et al.** 2009. The cyclophilin inhibitor Debio 025 combined with PEG IFNalpha2a significantly reduces viral load in treatment-naive hepatitis C patients. *Hepatology* **49**:1460-1468.
284. **Flisiak, R., A. Horban, P. Gallay, M. Bobardt, S. Selvarajah, A. Wiercinska-Drapalo, E. Siwak, I. Cielniak, et al.** 2008. The cyclophilin inhibitor Debio-025 shows potent anti-hepatitis C effect in patients coinfecting with hepatitis C and human immunodeficiency virus. *Hepatology* **47**:817-826.
285. **Lawitz, E., E. Godofsky, R. Rouzier, T. Marbury, T. Nguyen, J. Ke, M. Huang, J. Praetgaard, et al.** 2011. Safety, pharmacokinetics, and antiviral activity of the cyclophilin inhibitor NIM811 alone or in combination with pegylated interferon in HCV-infected patients receiving 14 days of therapy. *Antiviral Res.* **89**:238-245.
286. **de Groot, R. J., J. A. Cowley, L. Enjuanes, K. S. Faaberg, S. Perlman, P. J. Rottier, E. J. Snijder, J. Ziebuhr, and A. E. Gorbalenya.** 2012. Order of Nidovirales, p. 785-795. In A. King, M. Adams, E. Carstens, and E. J. Lefkowitz (ed.), *Virus Taxonomy, the 9th Report of the International Committee on Taxonomy of Viruses*. Academic Press.
287. **Snijder, E. J., and W. J. M. Spaan.** 2007. Arteriviruses, p. 1337-1355. In D. M. Knipe and P. M. Howley (ed.), *Fields Virology*, 5 ed. Lippincott, Williams & Wilkins, Philadelphia, Pa.
288. **Nedialkova, D. D., A. E. Gorbalenya, and E. J. Snijder.** 2010. Arterivirus Nsp1 modulates the accumulation of minus-strand templates to control the relative abundance of viral mRNAs. *PLoS Pathog.* **6**:e1000772.
289. **Kim, H. S., J. Kwang, I. J. Yoon, H. S. Joo, and M. L. Frey.** 1993. Enhanced replication of porcine reproductive and respiratory syndrome (PRRS) virus in a homogeneous subpopulation of MA-104 cell line. *Arch. Virol.* **133**:477-483.
290. **Bryans, J. T., M. E. Crowe, E. R. Doll, and W. H. McCollum.** 1957. Isolation of a filterable agent causing arteritis of horses and abortion by mares; its differentiation from the equine abortion (influenza) virus. *Cornell Vet.* **47**:3-41.
291. **van den Born, E., C. C. Posthuma, K. Knoops, and E. J. Snijder.** 2007. An infectious recombinant equine arteritis virus expressing green fluorescent protein from its replicase gene. *J. Gen. Virol.* **88**:1196-1205.
292. **Fang, Y., R. R. Rowland, M. Roof, J. K. Lunney, J. Christopher-Hennings, and E. A. Nelson.** 2006. A full-length cDNA infectious clone of North American type 1 porcine reproductive and respiratory syndrome virus: expression of green fluorescent protein in the Nsp2 region. *J. Virol.* **80**:11447-11455.
293. **Sun, Z., Y. Li, R. Ransburgh, E. J. Snijder, and Y. Fang.** 2012. Nonstructural protein 2 of porcine reproductive and respiratory syndrome virus inhibits the antiviral function of interferon-stimulated gene 15. *J. Virol.* **86**:3839-3850.
294. **MacLachlan, N. J., U. B. Balasuriya, J. F. Hedges, T. M. Schweidler, W. H. McCollum, P. J. Timoney, P. J. Hullinger, and J. F. Patton.** 1998. Serologic response of horses to the structural proteins of equine arteritis virus. *J. Vet. Diagn. Invest.* **10**:229-236.

295. **Knoops, K., C. Swett-Tapia, S. H. van den Worm, A. J. Te Velthuis, A. J. Koster, A. M. Mommaas, E. J. Snijder, and M. Kikkert.** 2010. Integrity of the early secretory pathway promotes, but is not required for, severe acute respiratory syndrome coronavirus RNA synthesis and virus-induced remodeling of endoplasmic reticulum membranes. *J. Virol.* **84**:833-846.
296. **Schreiber, S. L., and G. R. Crabtree.** 1992. The mechanism of action of cyclosporin A and FK506. *Immunol. Today* **13**:136-142.
297. **Hopkins, S., B. Dimassimo, P. Rusnak, D. Heuman, J. Lalezari, A. Sluder, B. Scorenaux, S. Mosier, et al.** 2012. The cyclophilin inhibitor SCY-635 suppresses viral replication and induces endogenous interferons in patients with chronic HCV genotype 1 infection. *J. Hepatol.* **57**:47-54.
298. **Wenger, R., M. Mutter, P. Garrouste, R. Lysek, O. Turpin, G. Vuagniaux, V. Nicolas, L. Novaroli Zanolari, and R. Crabbé.** November 2009. Cycloundecadepsipeptide compounds and use of said compounds as a medicament. patent WO 2010/052559.
299. **Watashi, K., M. Hijikata, M. Hosaka, M. Yamaji, and K. Shimotohno.** 2003. Cyclosporin A suppresses replication of hepatitis C virus genome in cultured hepatocytes. *Hepatology* **38**:1282-1288.
300. **Damaso, C. R., and S. J. Keller.** 1994. Cyclosporin A inhibits vaccinia virus replication *in vitro*. *Arch. Virol.* **134**:303-319.
301. **Chatterji, U., P. Lim, M. D. Bobardt, S. Wieland, D. G. Cordek, G. Vuagniaux, F. Chisari, C. E. Cameron, et al.** 2010. HCV resistance to cyclosporin A does not correlate with a resistance of the NS5A-cyclophilin A interaction to cyclophilin inhibitors. *J. Hepatol.* **53**:50-56.
302. **Fernandes, F., I. U. Ansari, and R. Striker.** 2010. Cyclosporine inhibits a direct interaction between cyclophilins and hepatitis C NS5A. *PLoS One* **5**:e9815.
303. **Gaither, L. A., J. Borawski, L. J. Anderson, K. A. Balabanis, P. Devay, G. Joberty, C. Rau, M. Schirle, et al.** 2010. Multiple cyclophilins involved in different cellular pathways mediate HCV replication. *Virology* **397**:43-55.
304. **Coelmont, L., X. Hanouille, U. Chatterji, C. Berger, J. Snoeck, M. Bobardt, P. Lim, I. Vliegen, et al.** 2010. DEB025 (Alisporivir) inhibits hepatitis C virus replication by preventing a cyclophilin A induced cis-trans isomerisation in domain II of NS5A. *PLoS One* **5**:e13687.
305. **Foster, T. L., P. Gallay, N. J. Stonehouse, and M. Harris.** 2011. Cyclophilin A interacts with domain II of hepatitis C virus NS5A and stimulates RNA binding in an isomerase-dependent manner. *J. Virol.* **85**:7460-7464.
306. **Chatterji, U., M. Bobardt, S. Selvarajah, F. Yang, H. Tang, N. Sakamoto, G. Vuagniaux, T. Parkinson, and P. Gallay.** 2009. The isomerase active site of cyclophilin A is critical for hepatitis C virus replication. *J. Biol. Chem.* **284**:16998-17005.
307. **Liu, Z., F. Yang, J. M. Robotham, and H. Tang.** 2009. Critical role of cyclophilin A and its prolyl-peptidyl isomerase activity in the structure and function of the hepatitis C virus replication complex. *J. Virol.* **83**:6554-6565.
308. **Kaul, A., S. Stauffer, C. Berger, T. Pertel, J. Schmitt, S. Kallis, M. Zayas, V. Lohmann, et al.** 2009. Essential role of cyclophilin A for hepatitis C virus replication and virus production and possible link to polyprotein cleavage kinetics. *PLoS Pathog.* **5**:e1000546.
309. **Watashi, K., N. Ishii, M. Hijikata, D. Inoue, T. Murata, Y. Miyanari, and K. Shimotohno.** 2005. Cyclophilin B is a functional regulator of hepatitis C virus RNA polymerase. *Mol. Cell* **19**:111-122.
310. **Castro, A. P., T. M. Carvalho, N. Moussatche, and C. R. Damaso.** 2003. Redistribution of cyclophilin A to viral factories during vaccinia virus infection and its incorporation into mature particles. *J. Virol.* **77**:9052-9068.

311. **Liu, X., L. Sun, M. Yu, Z. Wang, C. Xu, Q. Xue, K. Zhang, X. Ye, et al.** 2009. Cyclophilin A interacts with influenza A virus M1 protein and impairs the early stage of the viral replication. *Cell. Microbiol.*
312. **Luo, C., H. Luo, S. Zheng, C. Gui, L. Yue, C. Yu, T. Sun, P. He, et al.** 2004. Nucleocapsid protein of SARS coronavirus tightly binds to human cyclophilin A. *Biochem. Biophys. Res. Commun.* **321**:557-565.
313. **Almazan, F., C. Galan, and L. Enjuanes.** 2004. The nucleoprotein is required for efficient coronavirus genome replication. *J. Virol.* **78**:12683-12688.
314. **Schelle, B., N. Karl, B. Ludewig, S. G. Siddell, and V. Thiel.** 2006. Nucleocapsid protein expression facilitates coronavirus replication. *Adv. Exp. Med. Biol.* **581**:43-48.
315. **Pang, X., M. Zhang, L. Zhou, F. Xie, H. Lu, W. He, S. Jiang, L. Yu, and X. Zhang.** 2011. Discovery of a potent peptidic cyclophilin A inhibitor Trp-Gly-Pro. *Eur. J. Med. Chem.* **46**:1701-1705.
316. **Puyang, X., D. L. Poulin, J. E. Mathy, L. J. Anderson, S. Ma, Z. Fang, S. Zhu, K. Lin, et al.** 2010. Mechanism of resistance of hepatitis C virus replicons to structurally distinct cyclophilin inhibitors. *Antimicrob. Agents Chemother.* **54**:1981-1987.
317. **Perlman, S., and J. Netland.** 2009. Coronaviruses post-SARS: update on replication and pathogenesis. *Nat. Rev. Microbiol.* **7**:439-450.
318. **Tong, T. R.** 2009. Drug targets in severe acute respiratory syndrome (SARS) virus and other coronavirus infections. *Infect. Disord. Drug Targets* **9**:223-245.
319. **Vincent, M. J., E. Bergeron, S. Benjannet, B. R. Erickson, P. E. Rollin, T. G. Ksiazek, N. G. Seidah, and S. T. Nichol.** 2005. Chloroquine is a potent inhibitor of SARS coronavirus infection and spread. *Virol. J.* **2**:69.
320. **de Haan, C. A., and P. J. Rottier.** 2006. Hosting the severe acute respiratory syndrome coronavirus: specific cell factors required for infection. *Cell. Microbiol.* **8**:1211-1218.
321. **Vogels, M. W., B. W. van Balkom, D. V. Kaloyanova, J. J. Batenburg, A. J. Heck, J. B. Helms, P. J. Rottier, and C. A. de Haan.** 2011. Identification of host factors involved in coronavirus replication by quantitative proteomics analysis. *Proteomics* **11**:64-80.
322. **Zhang, L., Z. P. Zhang, X. E. Zhang, F. S. Lin, and F. Ge.** 2010. Quantitative proteomics analysis reveals BAG3 as a potential target to suppress severe acute respiratory syndrome coronavirus replication. *J. Virol.* **84**:6050-6059.
323. **Nakagawa, M., N. Sakamoto, Y. Tanabe, T. Koyama, Y. Itsui, Y. Takeda, C. H. Chen, S. Kakimoto, et al.** 2005. Suppression of hepatitis C virus replication by cyclosporin A is mediated by blockade of cyclophilins. *Gastroenterology* **129**:1031-1041.
324. **Sims, A. C., S. E. Burkett, B. Yount, and R. J. Pickles.** 2008. SARS-CoV replication and pathogenesis in an *in vitro* model of the human conducting airway epithelium. *Virus Res.* **133**:33-44.
325. **Cervantes-Barragan, L., R. Züst, R. Maier, S. Sierro, J. Janda, F. Levy, D. Speiser, P. Romero, et al.** 2010. Dendritic cell-specific antigen delivery by coronavirus vaccine vectors induces long-lasting protective antiviral and antitumor immunity. *MBio* **1**:e00171-00110.
326. **Das Sarma, J., E. Scheen, S. H. Seo, M. Koval, and S. R. Weiss.** 2002. Enhanced green fluorescent protein expression may be used to monitor murine coronavirus spread *in vitro* and in the mouse central nervous system. *J. Neurovirol.* **8**:381-391.
327. **Ishii, N., K. Watashi, T. Hishiki, K. Goto, D. Inoue, M. Hijikata, T. Wakita, N. Kato, and K. Shimotohno.** 2006. Diverse effects of cyclosporine on hepatitis C virus strain replication. *J. Virol.* **80**:4510-4520.
328. **Manel, N., B. Hogstad, Y. Wang, D. E. Levy, D. Unutmaz, and D. R. Littman.** 2010. A cryptic sensor for HIV-1 activates antiviral innate immunity in dendritic cells. *Nature* **467**:214-217.

329. **te Velthuis, A. J., J. J. Arnold, C. E. Cameron, S. H. van den Worm, and E. J. Snijder.** 2010. The RNA polymerase activity of SARS-coronavirus nsp12 is primer dependent. *Nucleic Acids Res.* **38**:203-214.
330. **Paeshuysse, J., A. Kaul, E. De Clercq, B. Rosenwirth, J. M. Dumont, P. Scalfaro, R. Bartenschlager, and J. Neyts.** 2006. The non-immunosuppressive cyclosporin DEBIO-025 is a potent inhibitor of hepatitis C virus replication *in vitro*. *Hepatology* **43**:761-770.
331. **Ciesek, S., E. Steinmann, H. Wedemeyer, M. P. Manns, J. Neyts, N. Tautz, V. Madan, R. Bartenschlager, et al.** 2009. Cyclosporine A inhibits hepatitis C virus nonstructural protein 2 through cyclophilin A. *Hepatology* **50**:1638-1645.
332. **Chatterji, U., M. D. Bobardt, P. Lim, and P. A. Gallay.** 2010. Cyclophilin A-independent recruitment of NS5A and NS5B into hepatitis C virus replication complexes. *J. Gen. Virol.* **91**:1189-1193.
333. **Goto, K., K. Watashi, D. Inoue, M. Hijikata, and K. Shimotohno.** 2009. Identification of cellular and viral factors related to anti-hepatitis C virus activity of cyclophilin inhibitor. *Cancer Sci.* **100**:1943-1950.
334. **Krishnan, M. N., A. Ng, B. Sukumaran, F. D. Gilfoy, P. D. Uchil, H. Sultana, A. L. Brass, R. Adametz, et al.** 2008. RNA interference screen for human genes associated with West Nile virus infection. *Nature* **455**:242-245.
335. **Sessions, O. M., N. J. Barrows, J. A. Souza-Neto, T. J. Robinson, C. L. Hershey, M. A. Rodgers, J. L. Ramirez, G. Dimopoulos, et al.** 2009. Discovery of insect and human dengue virus host factors. *Nature* **458**:1047-1050.
336. **Zhou, H., M. Xu, Q. Huang, A. T. Gates, X. D. Zhang, J. C. Castle, E. Stec, M. Ferrer, et al.** 2008. Genome-scale RNAi screen for host factors required for HIV replication. *Cell Host Microbe* **4**:495-504.
337. **Ng, T. I., H. Mo, T. Pilot-Matias, Y. He, G. Koev, P. Krishnan, R. Mondal, R. Pithawalla, et al.** 2007. Identification of host genes involved in hepatitis C virus replication by small interfering RNA technology. *Hepatology* **45**:1413-1421.
338. **Tai, A. W., Y. Benita, L. F. Peng, S. S. Kim, N. Sakamoto, R. J. Xavier, and R. T. Chung.** 2009. A functional genomic screen identifies cellular cofactors of hepatitis C virus replication. *Cell Host Microbe* **5**:298-307.
339. **Li, Q., A. L. Brass, A. Ng, Z. Hu, R. J. Xavier, T. J. Liang, and S. J. Elledge.** 2009. A genome-wide genetic screen for host factors required for hepatitis C virus propagation. *Proc. Natl. Acad. Sci. USA* **106**:16410-16415.
340. **Reiss, S., I. Rebhan, P. Backes, I. Romero-Brey, H. Erfle, P. Matula, L. Kaderali, M. Poenisch, et al.** 2011. Recruitment and activation of a lipid kinase by hepatitis C virus NS5A is essential for integrity of the membranous replication compartment. *Cell Host Microbe* **9**:32-45.
341. **Supekova, L., F. Supek, J. Lee, S. Chen, N. Gray, J. P. Pezacki, A. Schlapbach, and P. G. Schultz.** 2008. Identification of human kinases involved in hepatitis C virus replication by small interference RNA library screening. *J. Biol. Chem.* **283**:29-36.
342. **Randall, G., M. Panis, J. D. Cooper, T. L. Tellinghuisen, K. E. Sukhodolets, S. Pfeffer, M. Landthaler, P. Landgraf, et al.** 2007. Cellular cofactors affecting hepatitis C virus infection and replication. *Proc. Natl. Acad. Sci. USA* **104**:12884-12889.
343. **Hao, L., A. Sakurai, T. Watanabe, E. Sorensen, C. A. Nidom, M. A. Newton, P. Ahlquist, and Y. Kawaoka.** 2008. *Drosophila* RNAi screen identifies host genes important for influenza virus replication. *Nature* **454**:890-893.

344. **Karlas, A., N. Machuy, Y. Shin, K. P. Pleissner, A. Artarini, D. Heuer, D. Becker, H. Khalil, et al.** 2010. Genome-wide RNAi screen identifies human host factors crucial for influenza virus replication. *Nature* **463**:818-822.
345. **Pyrk, K., B. Berkhout, and L. van der Hoek.** 2007. The novel human coronaviruses NL63 and HKU1. *J. Virol.* **81**:3051-3057.
346. **Narayanan, K., C. Huang, and S. Makino.** 2008. SARS coronavirus accessory proteins. *Virus Res.* **133**:113-121.
347. **Ratia, K., K. S. Saikatendu, B. D. Santarsiero, N. Barretto, S. C. Baker, R. C. Stevens, and A. D. Mesecar.** 2006. Severe acute respiratory syndrome coronavirus papain-like protease: structure of a viral deubiquitinating enzyme. *Proc. Natl. Acad. Sci. USA* **103**:5717-5722.
348. **Zust, R., L. Cervantes-Barragan, M. Habjan, R. Maier, B. W. Neuman, J. Ziebuhr, K. J. Szretter, S. C. Baker, et al.** 2011. Ribose 2'-O-methylation provides a molecular signature for the distinction of self and non-self mRNA dependent on the RNA sensor Mda5. *Nat. Immunol.* **12**:137-143.
349. **Ye, Y., K. Hauns, J. O. Langland, B. L. Jacobs, and B. G. Hogue.** 2007. Mouse hepatitis coronavirus A59 nucleocapsid protein is a type I interferon antagonist. *J. Virol.* **81**:2554-2563.
350. **Kopecky-Bromberg, S. A., L. Martinez-Sobrido, and P. Palese.** 2006. 7a protein of severe acute respiratory syndrome coronavirus inhibits cellular protein synthesis and activates p38 mitogen-activated protein kinase. *J. Virol.* **80**:785-793.
351. **Hussain, S., S. Perlman, and T. M. Gallagher.** 2008. Severe acute respiratory syndrome coronavirus protein 6 accelerates murine hepatitis virus infections by more than one mechanism. *J. Virol.* **82**:7212-7222.
352. **Coyne, C. B., R. Bozym, S. A. Morosky, S. L. Hanna, A. Mukherjee, M. Tudor, K. S. Kim, and S. Cherry.** 2011. Comparative RNAi screening reveals host factors involved in enterovirus infection of polarized endothelial monolayers. *Cell Host Microbe* **9**:70-82.
353. **Hsu, N. Y., O. Ilnytska, G. Belov, M. Santiana, Y. H. Chen, P. M. Takvorian, C. Pau, H. van der Schaar, et al.** 2010. Viral reorganization of the secretory pathway generates distinct organelles for RNA replication. *Cell* **141**:799-811.
354. **de Wilde, A. H., Y. Li, Y. van der Meer, G. Vuagniaux, R. Lysek, Y. Fang, E. J. Snijder, and M. J. van Hemert.** 2013. Cyclophilin inhibitors block arterivirus replication by interfering with viral RNA synthesis. *J. Virol.* **87**:1454-1464.
355. **van den Worm, S. H., K. K. Eriksson, J. C. Zevenhoven, F. Weber, R. Zust, T. Kuri, R. Dijkman, G. Chang, et al.** 2012. Reverse genetics of SARS-related coronavirus using vaccinia virus-based recombination. *PLoS One* **7**:e32857.
356. **Boutros, M., L. P. Bras, and W. Huber.** 2006. Analysis of cell-based RNAi screens. *Genome Biol.* **7**:R66.
357. **Beck, R., M. Rawet, F. T. Wieland, and D. Cassel.** 2009. The COPI system: molecular mechanisms and function. *FEBS Lett.* **583**:2701-2709.
358. **Niu, T. K., A. C. Pfeifer, J. Lippincott-Schwartz, and C. L. Jackson.** 2005. Dynamics of GBF1, a Brefeldin A-sensitive Arf1 exchange factor at the Golgi. *Mol. Biol. Cell.* **16**:1213-1222.
359. **Cherry, S., T. Doukas, S. Armknecht, S. Whelan, H. Wang, P. Sarnow, and N. Perrimon.** 2005. Genome-wide RNAi screen reveals a specific sensitivity of IRES-containing RNA viruses to host translation inhibition. *Genes Dev.* **19**:445-452.
360. **Chang, Y. J., C. Y. Liu, B. L. Chiang, Y. C. Chao, and C. C. Chen.** 2004. Induction of IL-8 release in lung cells via activator protein-1 by recombinant baculovirus displaying severe acute respiratory syndrome-coronavirus spike proteins: identification of two functional regions. *J. Immunol.* **173**:7602-7614.

361. **Zhang, X., K. Wu, D. Wang, X. Yue, D. Song, Y. Zhu, and J. Wu.** 2007. Nucleocapsid protein of SARS-CoV activates interleukin-6 expression through cellular transcription factor NF-kappaB. *Virology* **365**:324-335.
362. **Liao, Y., X. Wang, M. Huang, J. P. Tam, and D. X. Liu.** 2011. Regulation of the p38 mitogen-activated protein kinase and dual-specificity phosphatase 1 feedback loop modulates the induction of interleukin 6 and 8 in cells infected with coronavirus infectious bronchitis virus. *Virology* **420**:106-116.
363. **Banerjee, S., K. Narayanan, T. Mizutani, and S. Makino.** 2002. Murine coronavirus replication-induced p38 mitogen-activated protein kinase activation promotes interleukin-6 production and virus replication in cultured cells. *J. Virol.* **76**:5937-5948.
364. **Oostro, M., E. G. te Lintelo, M. Deijs, M. H. Verheije, P. J. Rottier, and C. A. de Haan.** 2007. Localization and membrane topology of coronavirus nonstructural protein 4: involvement of the early secretory pathway in replication. *J. Virol.* **81**:12323-12336.
365. **Verheije, M. H., M. Raaben, M. Mari, E. G. Te Lintelo, F. Reggiori, F. J. van Kuppeveld, P. J. Rottier, and C. A. de Haan.** 2008. Mouse hepatitis coronavirus RNA replication depends on GBF1-mediated ARF1 activation. *PLoS Pathog.* **4**:e1000088.
366. **Neuman, B. W., J. S. Joseph, K. S. Saikatendu, P. Serrano, A. Chatterjee, M. A. Johnson, L. Liao, J. P. Klaus, et al.** 2008. Proteomics analysis unravels the functional repertoire of coronavirus nonstructural protein 3. *J. Virol.* **82**:5279-5294.
367. **Belov, G. A., N. Altan-Bonnet, G. Kovtunovych, C. L. Jackson, J. Lippincott-Schwartz, and E. Ehrenfeld.** 2007. Hijacking components of the cellular secretory pathway for replication of poliovirus RNA. *J. Virol.* **81**:558-567.
368. **Belov, G. A., M. H. Fogg, and E. Ehrenfeld.** 2005. Poliovirus proteins induce membrane association of GTPase ADP-ribosylation factor. *J. Virol.* **79**:7207-7216.
369. **Gazina, E. V., J. M. Mackenzie, R. J. Gorrell, and D. A. Anderson.** 2002. Differential requirements for COPI coats in formation of replication complexes among three genera of Picornaviridae. *J. Virol.* **76**:11113-11122.
370. **Wang, J., Z. Wu, and Q. Jin.** 2012. COPI Is Required for Enterovirus 71 Replication. *PLoS One* **7**:e38035.
371. **van der Linden, L., H. M. van der Schaar, K. H. Lanke, J. Neyts, and F. J. van Kuppeveld.** 2010. Differential effects of the putative GBF1 inhibitors Golgicide A and AG1478 on enterovirus replication. *J. Virol.* **84**:7535-7542.
372. **Cureton, D. K., R. Burdeinick-Kerr, and S. P. Whelan.** 2012. Genetic inactivation of COPI coat-omer separately inhibits vesicular stomatitis virus entry and gene expression. *J. Virol.* **86**:655-666.
373. **Cherry, S., A. Kunte, H. Wang, C. Coyne, R. B. Rawson, and N. Perrimon.** 2006. COPI activity coupled with fatty acid biosynthesis is required for viral replication. *PLoS Pathog.* **2**:e102.
374. **Konig, R., S. Stertz, Y. Zhou, A. Inoue, H. H. Hoffmann, S. Bhattacharyya, J. G. Alamares, D. M. Tscherne, et al.** 2010. Human host factors required for influenza virus replication. *Nature* **463**:813-817.
375. **He, D., C. Overend, J. Ambrogio, R. J. Maganti, M. J. Grubman, and A. E. Garmendia.** 2011. Marked differences between MARC-145 cells and swine alveolar macrophages in IFNbeta-induced activation of antiviral state against PRRSV. *Vet. Immunol. Immunopathol.* **139**:57-60.
376. **Rowland, R. R., B. Robinson, J. Stefanick, T. S. Kim, L. Guanghua, S. R. Lawson, and D. A. Benfield.** 2001. Inhibition of porcine reproductive and respiratory syndrome virus by interferon-gamma and recovery of virus replication with 2-aminopurine. *Arch. Virol.* **146**:539-555.

377. **Krahling, V., D. A. Stein, M. Spiegel, F. Weber, and E. Muhlberger.** 2009. Severe acute respiratory syndrome coronavirus triggers apoptosis via protein kinase R but is resistant to its antiviral activity. *J. Virol.* **83**:2298-2309.
378. **Woo, P. C., M. Wang, S. K. Lau, H. Xu, R. W. Poon, R. Guo, B. H. Wong, K. Gao, et al.** 2007. Comparative analysis of twelve genomes of three novel group 2c and group 2d coronaviruses reveals unique group and subgroup features. *J. Virol.* **81**:1574-1585.
379. **Vijaykrishna, D., G. J. Smith, J. X. Zhang, J. S. Peiris, H. Chen, and Y. Guan.** 2007. Evolutionary insights into the ecology of coronaviruses. *J. Virol.* **81**:4012-4020.
380. **Fouchier, R. A., N. G. Hartwig, T. M. Bestebroer, B. Niemeyer, J. C. de Jong, J. H. Simon, and A. D. Osterhaus.** 2004. A previously undescribed coronavirus associated with respiratory disease in humans. *Proc. Natl. Acad. Sci. USA* **101**:6212-6216.
381. **Raj, V. S., H. Mou, S. L. Smits, D. H. Dekkers, M. A. Muller, R. Dijkman, D. Muth, J. A. Demmers, et al.** 2013. Dipeptidyl peptidase 4 is a functional receptor for the emerging human coronavirus-EMC. *Nature* **495**:251-254.
382. **Randall, R. E., and S. Goodbourn.** 2008. Interferons and viruses: an interplay between induction, signalling, antiviral responses and virus countermeasures. *J. Gen. Virol.* **89**:1-47.
383. **Versteeg, G. A., P. J. Bredenbeek, S. H. van den Worm, and W. J. Spaan.** 2007. Group 2 coronaviruses prevent immediate early interferon induction by protection of viral RNA from host cell recognition. *Virology* **361**:18-26.
384. **Sims, A. C., S. C. Tilton, V. D. Menachery, L. E. Gralinski, A. Schafer, M. M. Matzke, B. J. Webb-Robertson, J. Chang, et al.** 2013. Release of severe acute respiratory syndrome coronavirus nuclear import block enhances host transcription in human lung cells. *J Virol* **87**:3885-3902.
385. **Yoshikawa, T., T. E. Hill, N. Yoshikawa, V. L. Popov, C. L. Galindo, H. R. Garner, C. J. Peters, and C. T. Tseng.** 2010. Dynamic innate immune responses of human bronchial epithelial cells to severe acute respiratory syndrome-associated coronavirus infection. *PLoS One* **5**:e8729.
386. **Zeng, F. Y., C. W. Chan, M. N. Chan, J. D. Chen, K. Y. Chow, C. C. Hon, K. H. Hui, J. Li, et al.** 2003. The complete genome sequence of severe acute respiratory syndrome coronavirus strain HKU-39849 (HK-39). *Exp. Biol. Med.* **228**:866-873.
387. **Weber, F., V. Wagner, S. B. Rasmussen, R. Hartmann, and S. R. Paludan.** 2006. Double-stranded RNA is produced by positive-strand RNA viruses and DNA viruses but not in detectable amounts by negative-strand RNA viruses. *J. Virol.* **80**:5059-5064.
388. **Belouzard, S., J. K. Millet, B. N. Licitra, and G. R. Whittaker.** 2012. Mechanisms of coronavirus cell entry mediated by the viral spike protein. *Viruses* **4**:1011-1033.
389. **Snijder, E. J., P. J. Bredenbeek, J. C. Dobbe, V. Thiel, J. Ziebuhr, L. L. Poon, Y. Guan, M. Roza-nov, et al.** 2003. Unique and conserved features of genome and proteome of SARS-coronavirus, an early split-off from the coronavirus group 2 lineage. *J. Mol. Biol.* **331**:991-1004.
390. **Vijgen, L., E. Keyaerts, E. Moes, I. Thoelen, E. Wollants, P. Lemey, A. M. Vandamme, and M. Van Ranst.** 2005. Complete genomic sequence of human coronavirus OC43: molecular clock analysis suggests a relatively recent zoonotic coronavirus transmission event. *J. Virol.* **79**:1595-1604.
391. **Pfefferle, S., S. Oppong, J. F. Drexler, F. Gloza-Rausch, A. Ipsen, A. Seebens, M. A. Muller, A. Annan, et al.** 2009. Distant relatives of severe acute respiratory syndrome coronavirus and close relatives of human coronavirus 229E in bats, Ghana. *Emerg. Infect. Dis.* **15**:1377-1384.
392. **Cameron, M. J., A. A. Kelvin, A. J. Leon, C. M. Cameron, L. Ran, L. Xu, Y. K. Chu, A. Danesh, et al.** 2012. Lack of innate interferon responses during SARS coronavirus infection in a vaccination and reinfection ferret model. *PLoS One* **7**:e45842.

393. **Roth-Cross, J. K., L. Martinez-Sobrido, E. P. Scott, A. Garcia-Sastre, and S. R. Weiss.** 2007. Inhibition of the alpha/beta interferon response by mouse hepatitis virus at multiple levels. *J. Virol.* **81**:7189-7199.
394. **Cervantes-Barragan, L., R. Zust, F. Weber, M. Spiegel, K. S. Lang, S. Akira, V. Thiel, and B. Ludewig.** 2007. Control of coronavirus infection through plasmacytoid dendritic-cell-derived type I interferon. *Blood* **109**:1131-1137.
395. **Kindler, E., H. R. Jonsdottir, D. Muth, O. J. Hamming, R. Hartmann, R. Rodriguez, R. Geffers, R. A. Fouchier, et al.** 2013. Efficient Replication of the Novel Human Betacoronavirus EMC on Primary Human Epithelium Highlights Its Zoonotic Potential. *MBio* **4**:e00611-00612.
396. **Rose, K. M., R. Elliott, L. Martinez-Sobrido, A. Garcia-Sastre, and S. R. Weiss.** 2010. Murine coronavirus delays expression of a subset of interferon-stimulated genes. *J. Virol.* **84**:5656-5669.
397. **Bergman, S. J., M. C. Ferguson, and C. Santanello.** 2011. Interferons as therapeutic agents for infectious diseases. *Infect. Dis. Clin. North. Am.* **25**:819-834.
398. **Breban, R., J. Riou, and A. Fontanet.** 2013. Interhuman transmissibility of Middle East respiratory syndrome coronavirus: estimation of pandemic risk. *Lancet.*
399. **Roberts, A., E. W. Lamirande, L. Vogel, J. P. Jackson, C. D. Paddock, J. Guarner, S. R. Zaki, T. Sheahan, et al.** 2008. Animal models and vaccines for SARS-CoV infection. *Virus Res.* **133**:20-32.
400. **Martin, J. E., M. K. Louder, L. A. Holman, I. J. Gordon, M. E. Enama, B. D. Larkin, C. A. Andrews, L. Vogel, et al.** 2008. A SARS DNA vaccine induces neutralizing antibody and cellular immune responses in healthy adults in a Phase I clinical trial. *Vaccine* **26**:6338-6343.
401. **Hopkins, A. L., and C. R. Groom.** 2002. The druggable genome. *Nat. Rev. Drug Discov.* **1**:727-730.
402. **Bienz, K., D. Egger, T. Pfister, and M. Troxler.** 1992. Structural and functional characterization of the poliovirus replication complex. *J. Virol.* **66**:2740-2747.
403. **Zebovitz, E., J. K. Leong, and S. C. Doughty.** 1974. Involvement of the host cell nuclear envelope membranes in the replication of Japanese encephalitis virus. *Infect. Immun.* **10**:204-211.
404. **Quinkert, D., R. Bartenschlager, and V. Lohmann.** 2005. Quantitative analysis of the hepatitis C virus replication complex. *J. Virol.* **79**:13594-13605.
405. **Ahlquist, P., S. X. Wu, P. Kaesberg, C. C. Kao, R. Quadt, W. DeJong, and R. Hershberger.** 1994. Protein-protein interactions and glycerophospholipids in bromovirus and nodavirus RNA replication. *Arch. Virol. Suppl.* **9**:135-145.
406. **Kovalev, N., J. Pogany, and P. D. Nagy.** 2012. A Co-Opted DEAD-Box RNA helicase enhances tobusvirus plus-strand synthesis. *PLoS Pathog.* **8**:e1002537.
407. **Rodriguez, P. L., and L. Carrasco.** 1992. Gliotoxin: inhibitor of poliovirus RNA synthesis that blocks the viral RNA polymerase 3Dpol. *J. Virol.* **66**:1971-1976.
408. **Gerber, L., T. M. Welzel, and S. Zeuzem.** 2013. New therapeutic strategies in HCV: polymerase inhibitors. *Liver Int.* **33 Suppl 1**:85-92.
409. **Tsai, C. H., P. Y. Lee, V. Stollar, and M. L. Li.** 2006. Antiviral therapy targeting viral polymerase. *Curr. Pharm. Des.* **12**:1339-1355.
410. **Law, G. L., M. J. Korth, A. G. Benecke, and M. G. Katze.** 2013. Systems virology: host-directed approaches to viral pathogenesis and drug targeting. *Nat. Rev. Microbiol.* **11**:455-466.
411. **Johnson, S. A., and T. Hunter.** 2005. Kinomics: methods for deciphering the kinome. *Nat. Methods* **2**:17-25.
412. **Dar, A. C., and K. M. Shokat.** 2011. The evolution of protein kinase inhibitors from antagonists to agonists of cellular signaling. *Annu. Rev. Biochem.* **80**:769-795.
413. **Schang, L. M.** 2011. Cellular Protein Kinases as Antiviral Targets, p. 305-347. In B. Klebl, G. Müller, and M. Hamacher (ed.), *Protein Kinases as Drug Targets*. Wiley-VCH Verlag GmbH & Co. KGaA.

414. **Lupberger, J., M. B. Zeisel, F. Xiao, C. Thumann, I. Fofana, L. Zona, C. Davis, C. J. Mee, et al.** 2011. EGFR and EphA2 are host factors for hepatitis C virus entry and possible targets for antiviral therapy. *Nat. Med.* **17**:589-595.
415. **Moser, T. S., R. G. Jones, C. B. Thompson, C. B. Coyne, and S. Cherry.** 2010. A kinome RNAi screen identified AMPK as promoting poxvirus entry through the control of actin dynamics. *PLoS Pathog.* **6**:e1000954.
416. **Song, S., J. Bi, D. Wang, L. Fang, L. Zhang, F. Li, H. Chen, and S. Xiao.** 2013. Porcine reproductive and respiratory syndrome virus infection activates IL-10 production through NF-kappaB and p38 MAPK pathways in porcine alveolar macrophages. *Dev. Comp. Immunol.* **39**:265-272.
417. **Josset, L., V. D. Menachery, L. E. Gralinski, S. Agnihothram, P. Sova, V. S. Carter, B. L. Yount, R. L. Graham, et al.** 2013. Cell Host Response to Infection with Novel Human Coronavirus EMC Predicts Potential Antivirals and Important Differences with SARS Coronavirus. *MBio* **4**.
418. **Wannee, K. F., A. H. De Wilde, M. Rabelink, R. Hoebe, J. J. Goeman, P. ten Dijke, E. J. Snijder, M. Kikkert, and M. J. van Hemert.** 2013. Kinome-targeted siRNA library screening identifies common cellular factors and signaling pathways influencing the replication of distantly related nidoviruses. Manuscript in Preparation.
419. **Novina, C. D., and P. A. Sharp.** 2004. The RNAi revolution. *Nature* **430**:161-164.
420. **Bushman, F. D., N. Malani, J. Fernandes, I. D'Orso, G. Cagney, T. L. Diamond, H. Zhou, D. J. Hazuda, et al.** 2009. Host cell factors in HIV replication: meta-analysis of genome-wide studies. *PLoS Pathog.* **5**:e1000437.
421. **Jackson, A. L., and P. S. Linsley.** 2010. Recognizing and avoiding siRNA off-target effects for target identification and therapeutic application. *Nat. Rev. Drug Discov.* **9**:57-67.
422. **Echeverri, C. J., P. A. Beachy, B. Baum, M. Boutros, F. Buchholz, S. K. Chanda, J. Downward, J. Ellenberg, et al.** 2006. Minimizing the risk of reporting false positives in large-scale RNAi screens. *Nat. Methods* **3**:777-779.
423. **Dancourt, J., and C. Barlowe.** 2010. Protein sorting receptors in the early secretory pathway. *Annu. Rev. Biochem.* **79**:777-802.
424. **Bethune, J., F. Wieland, and J. Moelleken.** 2006. COPI-mediated transport. *J. Membr. Biol.* **211**:65-79.
425. **Brass, A. L., D. M. Dykxhoorn, Y. Benita, N. Yan, A. Engelman, R. J. Xavier, J. Lieberman, and S. J. Elledge.** 2008. Identification of host proteins required for HIV infection through a functional genomic screen. *Science* **319**:921-926.
426. **Tanaka, Y., Y. Sato, and T. Sasaki.** 2013. Suppression of coronavirus replication by cyclophilin inhibitors. *Viruses* **5**:1250-1260.
427. **Gething, M. J., and J. Sambrook.** 1992. Protein folding in the cell. *Nature* **355**:33-45.
428. **Schinzel, A. C., O. Takeuchi, Z. Huang, J. K. Fisher, Z. Zhou, J. Rubens, C. Hetz, N. N. Danial, et al.** 2005. Cyclophilin D is a component of mitochondrial permeability transition and mediates neuronal cell death after focal cerebral ischemia. *Proc. Natl. Acad. Sci. USA* **102**:12005-12010.
429. **Teigelkamp, S., T. Achsel, C. Mundt, S. F. Gothel, U. Cronshagen, W. S. Lane, M. Marahiel, and R. Luhrmann.** 1998. The 20kD protein of human [U4/U6.U5] tri-snRNPs is a novel cyclophilin that forms a complex with the U4/U6-specific 60kD and 90kD proteins. *RNA* **4**:127-141.
430. **Horowitz, D. S., E. J. Lee, S. A. Mabon, and T. Misteli.** 2002. A cyclophilin functions in pre-mRNA splicing. *EMBO J.* **21**:470-480.
431. **Steinbach, W. J., J. L. Reedy, R. A. Cramer, Jr., J. R. Perfect, and J. Heitman.** 2007. Harnessing calcineurin as a novel anti-infective agent against invasive fungal infections. *Nature reviews. Microbiology* **5**:418-430.

432. **Wainberg, M. A., A. Dascal, N. Blain, L. Fitz-Gibbon, F. Boulterice, K. Numazaki, and M. Tremblay.** 1988. The effect of cyclosporine A on infection of susceptible cells by human immunodeficiency virus type 1. *Blood* **72**:1904-1910.
433. **Montano-Loza, A. J., S. Wasilenko, J. Bintner, and A. L. Mason.** 2010. Cyclosporine A inhibits *in vitro* replication of betaretrovirus associated with primary biliary cirrhosis. *Liver Int.* **30**:871-877.
434. **Luban, J., K. L. Bossolt, E. K. Franke, G. V. Kalpana, and S. P. Goff.** 1993. Human immunodeficiency virus type 1 Gag protein binds to cyclophilins A and B. *Cell* **73**:1067-1078.
435. **Yang, F., J. M. Robotham, H. B. Nelson, A. Irsigler, R. Kenworthy, and H. Tang.** 2008. Cyclophilin A is an essential cofactor for hepatitis C virus infection and the principal mediator of cyclosporine resistance *in vitro*. *J. Virol.* **82**:5269-5278.
436. <http://www.clinicaltrials.gov/>
437. **Fischer, G., P. Gallay, and S. Hopkins.** 2010. Cyclophilin inhibitors for the treatment of HCV infection. *Curr. Opin. Investig. Drugs* **11**:911-918.
438. **Liu, Z., J. M. Robida, S. Chinnaswamy, G. Yi, J. M. Robotham, H. B. Nelson, A. Irsigler, C. C. Kao, and H. Tang.** 2009. Mutations in the hepatitis C virus polymerase that increase RNA binding can confer resistance to cyclosporine A. *Hepatology* **50**:25-33.
439. **Carbajo-Lozoya, J., M. A. Muller, S. Kallies, V. Thiel, C. Drosten, and A. von Brunn.** 2012. Replication of human coronaviruses SARS-CoV, HCoV-NL63 and HCoV-229E is inhibited by the drug FK506. *Virus Res.* **165**:112-117.
440. **McHutchison, J. G., E. J. Lawitz, M. L. Shiffman, A. J. Muir, G. W. Galler, J. McCone, L. M. Nyberg, W. M. Lee, et al.** 2009. Peginterferon alfa-2b or alfa-2a with ribavirin for treatment of hepatitis C infection. *N. Engl. J. Med.* **361**:580-593.
441. **Manns, M. P., J. G. McHutchison, S. C. Gordon, V. K. Rustgi, M. Shiffman, R. Reindollar, Z. D. Goodman, K. Koury, et al.** 2001. Peginterferon alfa-2b plus ribavirin compared with interferon alfa-2b plus ribavirin for initial treatment of chronic hepatitis C: a randomised trial. *Lancet* **358**:958-965.
442. **Fried, M. W., M. L. Shiffman, K. R. Reddy, C. Smith, G. Marinos, F. L. Goncales, Jr., D. Haussinger, M. Diago, et al.** 2002. Peginterferon alfa-2a plus ribavirin for chronic hepatitis C virus infection. *N. Engl. J. Med.* **347**:975-982.
443. **McHutchison, J. G., M. P. Manns, A. J. Muir, N. A. Terrault, I. M. Jacobson, N. H. Afdhal, E. J. Heathcote, S. Zeuzem, et al.** 2010. Telaprevir for previously treated chronic HCV infection. *N. Engl. J. Med.* **362**:1292-1303.
444. **Flisiak, R., J. Jaroszewicz, I. Flisiak, and T. Lapinski.** 2012. Update on alisporivir in treatment of viral hepatitis C. *Expert Opin Investig Drugs* **21**:375-382.
445. **Chan-Yeung, M., and R. H. Xu.** 2003. SARS: epidemiology. *Respirology* **8 Suppl**:S9-14.
446. **Roberts, A., D. Deming, C. D. Paddock, A. Cheng, B. Yount, L. Vogel, B. D. Herman, T. Sheahan, et al.** 2007. A mouse-adapted SARS-coronavirus causes disease and mortality in BALB/c mice. *PLoS Pathog.* **3**:e5.
447. **McCray, P. B., Jr., L. Pewe, C. Wohlford-Lenane, M. Hickey, L. Manzel, L. Shi, J. Netland, H. P. Jia, et al.** 2007. Lethal infection of K18-hACE2 mice infected with severe acute respiratory syndrome coronavirus. *J. Virol.* **81**:813-821.
448. **Munster, V. J., E. de Wit, and H. Feldmann.** 2013. Pneumonia from human coronavirus in a macaque model. *N. Engl. J. Med.* **368**:1560-1562.
449. **Madrid, P. B., S. Chopra, I. D. Manger, L. Gilfillan, T. R. Keepers, A. C. Shurtleff, C. E. Green, L. V. Iyer, et al.** 2013. A systematic screen of FDA-approved drugs for inhibitors of biological threat agents. *PLoS One* **8**:e60579.

450. **Falzarano, D., E. de Wit, C. Martellaro, J. Callison, V. J. Munster, and H. Feldmann.** 2013. Inhibition of novel beta coronavirus replication by a combination of interferon-alpha2b and ribavirin. *Sci. Rep.* **3**:1686.
451. **Chan, R. W., M. C. Chan, S. Agnihothram, L. L. Chan, D. I. Kuok, J. H. Fong, Y. Guan, L. L. Poon, et al.** 2013. Tropism and innate immune responses of the novel human betacoronavirus lineage C virus in human ex vivo respiratory organ cultures. *J. Virol.*
452. **Zielecki, F., M. Weber, M. Eickmann, L. Spiegelberg, A. M. Zaki, M. Matrosovich, S. Becker, and F. Weber.** 2013. Human cell tropism and innate immune system interactions of human respiratory coronavirus EMC compared to those of severe acute respiratory syndrome coronavirus. *J. Virol.* **87**:5300-5304.