

Viral Interactions with Adaptor-Protein Complexes

Subjects: **Virology**

Contributor: Ivana Strazic Geljic

Numerous viruses hijack cellular protein trafficking pathways to mediate cell entry or to rearrange membrane structures thereby promoting viral replication and antagonizing the immune response. Adaptor protein complexes (AP), which mediate protein sorting in endocytic and secretory transport pathways, are one of the conserved viral targets. We present here different mechanisms of viral interference with AP complexes and the functional consequences that allow for efficient viral propagation and evasion of host immune defense. The best described examples are interactions of human immunodeficiency virus and human herpesviruses with AP complexes. Several other viruses, like Ebola, Nipah, and SARS-CoV-2, are pointed out as high priority disease-causative agents supporting the need for deeper understanding of virus-AP interplay which can be exploited in the design of novel antiviral therapies

adaptor protein complexes

protein sorting

viruses

HIV

herpesviruses

AP-1

AP-2

AP-3

AP-4

AP-5

1. Introduction

Viruses are obligate intracellular pathogens that rely on host cell machinery in various stages of their life cycles. A great number of host factors that are indispensable or contribute to successful viral infections has been identified. Multiple studies have shed light onto the unique strategies employed by individual viruses, but the accumulating data also indicate the overlapping patterns of viral-host interplay ^{[1][2]}. Viruses have evolved a plethora of strategies to counteract the mechanisms of host's immune response at various stages of their life cycles. From internalization of viral particles and replication of the viral genome to viral assembly and release of mature virions, the interference with cellular trafficking and sorting machinery appears to be an asset for viral propagation and antagonizing of host antiviral response ^[3]. Clathrin-mediated endocytosis (CME), a major cellular ubiquitous route of receptor internalization, is a common route utilized by viruses, particularly of small and intermediate size. Regardless of the viral receptor used, CME is dependent on the oligomeric clathrin and adaptor-protein (AP) complexes that coordinate the recruitment of endocytic cargo proteins and assembly of clathrin into a polyhedral lattice at the plasma membrane and the trans-Golgi network (TGN) ^{[4][5][6][7][8]}. A large body of evidence showed that many viral genera take advantage of cellular AP complexes, making them conserved viral targets ^[9]. It was established long ago that CME can be a part of the productive infectious cascade with the example of Semliki Forest virus ^[10]. Since then, numerous interactions of clathrin components and viral proteins or virions have been documented. During coevolution with host organisms, viruses have acquired genome sequences identical or closely resembling to

motifs used by host proteins for the interaction with AP complexes. This enables them not only to maximize their own replication and assembly but importantly to interfere with the proper sorting and expression of host molecules hazardous to their survival.

2. Viral Interactions with Adaptor-Protein Complexes

We will present different mechanisms of viral interference with cellular AP complexes and their functional consequences that allow for efficient viral propagation and evasion of host's immune defense. Viruses discussed in the review are listed in [Table 1](#) and presented following the Baltimore classification of viruses which is based on the structure of the viral genome and the manner of messenger RNA (mRNA) synthesis.

Table 1. Viral families and their respective AP interaction complexes.

Group	Viral Family Members included in the Review		Viral Protein Involved	AP Complex Involved	References
dsDNA Viruses	Adenoviridae	Human Adenoviruses (HAdV, HAdV2, HAdV5)	RIDα, RIDβ	AP-1, AP-2	[11] [12] [13]
		Herpesviridae			
	α-herpesvirinae	Herpes simplex virus 1 and 2 (HSV-1, HSV-2)	gE/gI, VP22	AP-1	[14] [15] [16]
		Pseudorabiesvirus (PRV)	gB, gE	AP-1, AP-2	[17]
		Varicella zoster virus (VZV)	ORF9p	AP-1	[18]
	β-herpesvirinae	Murine Cytomegalovirus (MCMV)	m154, gp48, m04	AP-1, AP-2, AP-3	[19] [20] [21]
		Human Cytomegalovirus (HCMV)	UL20	AP-1	[22]
		Human herpes virus 6, -7 (HHV-6, -7)	U21	AP-1, AP-3	[23]
		Epstein-Barr virus (EBV)	BILF1, BMRF,	AP-1, AP-4	[24] [25]
	γ-herpesvirinae	Kaposi's sarcoma-associated	unknown	AP-2	[26]

Group	Viral Family Members included in the Review		Viral Protein Involved	AP Complex Involved	References
		herpesvirus (KSHV)			
		Polyomaviridae	Human polyomavirus (JCV)	agnoprotein	AP-2, AP-3 [27]
		Poxviridae	Vaccinia virus (VACV)	VACV F13, VACV A33	AP-2 [28] [29]
ssDNA viruses (+ strand or "sense")	not identified	/	/	/	/
dsRNA viruses	not identified	/	/	/	/
(+) ssRNA viruses (+ strand or sense)	Coronaviridae	Severe acute respiratory syndrome coronavirus (SARS-CoV, SARS-CoV-2)	unknown	AP-2	[9] [30] [31]
		Murine hepatitis virus (MHV)	unknown	AP-2	[32] [33]
	Flaviviridae	Dengue virus (DENV)	unknown	AP-1, AP-2	[34] [35]
		Hepatitis C virus (HCV)	NS2, NS5A, core	AP-1, AP-2, AP-4	[36] [37] [38] [39] [40] [1]
	Rhinoviridae	Human rhinovirus (hRV)	LDLR (minor group)	AP-2	[41]
(–) ssRNA viruses (– strand or antisense) RNA	Filoviridae	Zaire ebolavirus (EBOV)	unknown	AP-1, AP-2	[42] [43]
	Nairoviriade	Crimean-congo hemorrhagic fever (CCHFV)	unknown	AP-2	[44]
	Orthomyxoviridae	Influenza A (IAV)	Hemagglutinin	AP-2	[9] [45] [46]
	Paramyxoviridae	Hendra virus	M-protein	AP-3	[47]

Group	Viral Family Members included in the Review		Viral Protein Involved	AP Complex Involved	References
	(HeV)				
		Nipah virus (NiV)	NiV-F, M-protein	AP-1, AP-3	[47][48]
	Pneumoviridae	Human respiratory syncytial virus (RSV)	M-protein	AP-2, AP-3	[49][50][51]
	Rhabdoviridae	Vesicular stomatitis Indiana virus (VSV)	VSV-G	AP-2, AP-3	[52][53]
ssRNA-RT viruses (+ strand or sense) RNA with DNA intermediate in life-cycle		Ecotropic murine leukemia virus (eMuLV)	Env	AP-3?	[54]
	Retroviridae	Human immunodeficiency virus 1 (HIV-1)	Nef, Gag, Vpu	AP-1, AP-2, AP-3	[55][56][57][58]
		Human immunodeficiency virus 2 (HIV-2)	Nef, Env, Gag	AP-1, AP-2, AP-3, AP-5	[59][60][61]
dsDNA-RT viruses DNA with RNA intermediate in life-cycle	Hepadnaviridae	Hepatitis B virus (HVB)	preS1	AP-2	[62][63][64]

EBV, and NiV are listed in the WHO Research and Development Blueprint, an effort aimed at reducing the time of development and distribution of vaccines and treatments in public health emergencies. Identification and targeting of host trafficking pathways universal for unrelated viral pathogens is a promising approach to advance the discovery of new antiviral therapeutics. As an example, *N*-(*p*-amylcinnamoyl) anthranilic acid (ACA) was found to interrupt μ 2-adaptin-virus interaction and exhibits in vivo activity against several viruses, including IAV, Zika virus, MERS, and SARS-CoV-2 [9]. Deeper understanding of virus-AP interplay is a premise for better characterization of currently known and yet uncovered host targets hijacked by multiple viral families.

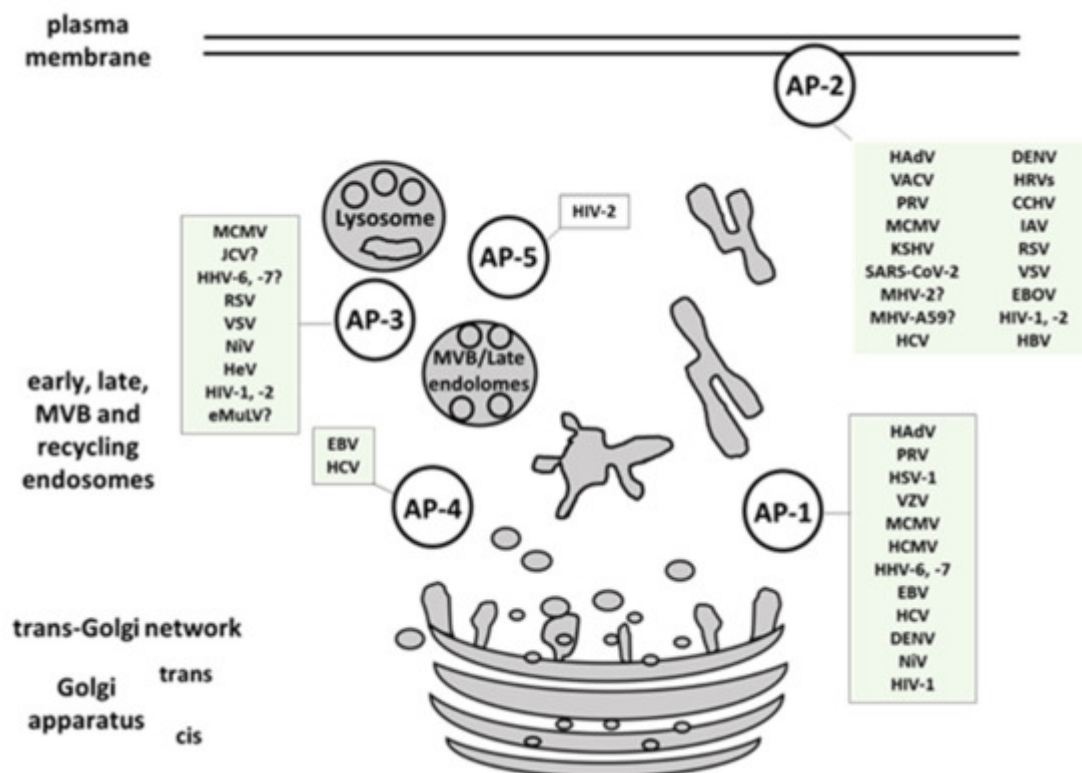


Figure 1. Multiple viruses exploit host AP complexes in different stages of their life cycles. AP-1 complex is involved in viral proteins intracellular trafficking, reduction of the surface MHC I molecules, release of viral particles and in viral replication. AP-2 complex is widely exploited for viral entry, and endocytosis of immune signaling molecules targeted by viruses. AP-3 is implicated in endolysosomal sorting and trafficking of viral proteins, and in viral particles production. AP-4 is shown to be important for viral replication, intracellular transport, and virion release. AP-5 mediates intracellular transport of HIV-2 Gag. MVB- multivesicular body. (For full virus species names refer to [Table 1](#).)

References

1. Robinson, M.; Schor, S.; Barouch-Bentov, R.; Einav, S. Viral journeys on the intracellular highways. *Cell Mol Life Sci.* 2018, 75, 3693–3714.
2. Ren, S.; Ding, C.; Sun, Y. Morphology Remodeling and Selective Autophagy of Intracellular Organelles during Viral Infections. *Int. J. Mol. Sci.* 2020, 21, 3689.
3. Agrawal, T.; Schu, P.; Medigeshi, G.R. Adaptor protein complexes-1 and 3 are involved at distinct stages of flavivirus life-cycle. *Sci. Rep.* 2013, 3, 1813.
4. Boehm, M.; Bonifacino, J.S. Adaptins. *Mol. Biol. Cell* 2001, 12, 2907–2920.
5. Hirst, J.; D. Barlow, L.; Francisco, G.C.; Sahlender, D.A.; Seaman, M.N.J.; Dacks, J.B.; Robinson, M.S. The Fifth Adaptor Protein Complex. *PLoS Biol.* 2011, 9, e1001170.

6. Robinson, M.S.; Bonifacino, J.S. Adaptor-related proteins. *Curr. Opin. Cell Biol.* 2001, 13, 444–453.
7. Hirst, J.; Itzhak, D.N.; Antrobus, R.; Borner, G.H.H.; Robinson, M.S. Role of the AP-5 adaptor protein complex in late endosome-to-Golgi retrieval. *PLoS Biol.* 2018, 16, e2004411.
8. Brodsky, F.M. Diversity of clathrin function: New tricks for an old protein. *Annu. Rev. Cell Dev. Biol.* 2012, 28, 309–336.
9. Yuan, S.; Chu, H.; Huang, J.; Zhao, X.; Ye, Z.W.; Lai, P.M.; Wen, L.; Cai, J.P.; Mo, Y.; Cao, J.; et al. Viruses harness YxxO motif to interact with host AP2M1 for replication: A vulnerable broad-spectrum antiviral target. *Sci. Adv.* 2020, 6, eaba7910.
10. Helenius, A.; Kartenbeck, J.; Simons, K.; Fries, E. On the entry of Semliki forest virus into BHK-21 cells. *J. Cell Biol.* 1980, 84, 404–420.
11. Carvajal-Gonzalez, J.M.; Gravotta, D.; Mattera, R.; Diaz, F.; Perez Bay, A.; Roman, A.C.; Schreiner, R.P.; Thuenauer, R.; Bonifacino, J.S.; Rodriguez-Boulan, E. Basolateral sorting of the coxsackie and adenovirus receptor through interaction of a canonical YXXPhi motif with the clathrin adaptors AP-1A and AP-1B. *Proc. Natl. Acad. Sci. USA* 2012, 109, 3820–3825.
12. Cianciola, N.L.; Crooks, D.; Shah, A.H.; Carlin, C. A tyrosine-based signal plays a critical role in the targeting and function of adenovirus RIDalpha protein. *J. Virol.* 2007, 81, 10437–10450.
13. Flatt, J.W.; Butcher, S.J. Adenovirus flow in host cell networks. *Open Biol.* 2019, 9, 190012.
14. DNAM-1 and PVR regulate monocyte migration through endothelial junctions. *J. Exp. Med.* 2004, 199, 1331–1341.
15. Johnson, D.C.; Webb, M.; Wisner, T.W.; Brunetti, C. Herpes Simplex Virus gE/gI Sorts Nascent Virions to Epithelial Cell Junctions, Promoting Virus Spread. *J. Virol.* 2001, 75, 821–833.
16. Liu, J.; Gallo, R.M.; Duffy, C.; Brutkiewicz, R.R. A VP22-Null HSV-1 Is Impaired in Inhibiting CD1d-Mediated Antigen Presentation. *Viral Immunol.* 2016, 29, 409–416.
17. Van Minnebruggen, G.; Favoreel, H.W.; Nauwynck, H.J. Internalization of Pseudorabies Virus Glycoprotein B Is Mediated by an Interaction between the YQRL Motif in Its Cytoplasmic Domain and the Clathrin-Associated AP-2 Adaptor Complex. *J. Virol.* 2004, 78, 8852–8859.
18. Lebrun, M.; Lambert, J.; Riva, L.; Thelen, N.; Rambout, X.; Blondeau, C.; Thiry, M.; Snoeck, R.; Twizere, J.-C.; Dequiedt, F.; et al. Varicella-Zoster Virus ORF9p Binding to Cellular Adaptor Protein Complex 1 Is Important for Viral Infectivity. *J. Virol.* 2018, 92, e00295-18.
19. Reusch, U.; Bernhard, O.; Koszinowski, U.; Schu, P. AP-1A and AP-3A Lysosomal Sorting Functions. *Traffic* 2002, 3, 752–761.

20. Strazic Geljic, I.; Kucan Brlic, P.; Angulo, G.; Brizic, I.; Lisnic, B.; Jenus, T.; Juranic Lisnic, V.; Pietri, G.P.; Engel, P.; Kaynan, N.; et al. Cytomegalovirus protein m154 perturbs the adaptor protein-1 compartment mediating broad-spectrum immune evasion. *eLife* 2020, 9, e50803.
21. Fink, A.; Blaum, F.; Babic Cac, M.; Ebert, S.; Lemmermann, N.A.; Reddehase, M.J. An endocytic YXXPhi (YRRF) cargo sorting motif in the cytoplasmic tail of murine cytomegalovirus AP2 'adapter adapter' protein m04/gp34 antagonizes virus evasion of natural killer cells. *Med. Microbiol. Immunol.* 2015, 204, 383–394.
22. Jelcic, I.; Reichel, J.; Schlude, C.; Treutler, E.; Sinzger, C.; Steinle, A. The Polymorphic HCMV Glycoprotein UL20 Is Targeted for Lysosomal Degradation by Multiple Cytoplasmic Dileucine Motifs. *Traffic* 2011, 12, 1444–1456.
23. Kimpler, L.A.; Glosson, N.L.; Downs, D.; Gonyo, P.; May, N.A.; Hudson, A.W. Adaptor Protein Complexes AP-1 and AP-3 Are Required by the HHV-7 Immune-evasin U21 for Rerouting of Class I MHC Molecules to the Lysosomal Compartment. *PLoS ONE* 2014, 9, e99139.
24. Xiao, J.; Palefsky, J.M.; Herrera, R.; Berline, J.; Tugizov, S.M. EBV BMRF-2 facilitates cell-to-cell spread of virus within polarized oral epithelial cells. *Virology* 2009, 388, 335–343.
25. Zuo, J.; Quinn, L.L.; Tamblyn, J.; Thomas, W.A.; Feederle, R.; Delecluse, H.-J.; Hislop, A.D.; Rowe, M. The Epstein-Barr Virus-Encoded BILF1 Protein Modulates Immune Recognition of Endogenously Processed Antigen by Targeting Major Histocompatibility Complex Class I Molecules Trafficking on both the Exocytic and Endocytic Pathways. *J. Virol.* 2011, 85, 1604–1614.
26. Veettil, M.; Bandyopadhyay, C.; Dutta, D.; Chandran, B. Interaction of KSHV with Host Cell Surface Receptors and Cell Entry. *Viruses* 2014, 6, 4024–4046.
27. Suzuki, T.; Orba, Y.; Makino, Y.; Okada, Y.; Sunden, Y.; Hasegawa, H.; Hall, W.W.; Sawa, H. Viroporin activity of the JC polyomavirus is regulated by interactions with the adaptor protein complex 3. *Proc. Natl. Acad. Sci. USA* 2013, 110, 18668–18673.
28. Husain, M.; Moss, B. Evidence against an essential role of COPII-mediated cargo transport to the endoplasmic reticulum-Golgi intermediate compartment in the formation of the primary membrane of vaccinia virus. *J. Virol.* 2003, 77, 11754–11766.
29. Ward, B.M.; Moss, B. Golgi network targeting and plasma membrane internalization signals in vaccinia virus B5R envelope protein. *J. Virol.* 2000, 74, 3771–3780.
30. Wang, P.G.; Tang, D.J.; Hua, Z.; Wang, Z.; An, J. Sunitinib reduces the infection of SARS-CoV, MERS-CoV and SARS-CoV-2 partially by inhibiting AP2M1 phosphorylation. *Cell Discov.* 2020, 6, 71.
31. Cantuti-Castelvetri, L.; Ojha, R.; Pedro, L.D.; Djannatian, M.; Franz, J.; Kuivanen, S.; van der Meer, F.; Kallio, K.; Kaya, T.; Anastasina, M.; et al. Neuropilin-1 facilitates SARS-CoV-2 cell entry

- and infectivity. *Science* 2020, 370, 856–860.
32. Eifart, P.; Ludwig, K.; Bottcher, C.; de Haan, C.A.; Rottier, P.J.; Korte, T.; Herrmann, A. Role of endocytosis and low pH in murine hepatitis virus strain A59 cell entry. *J. Virol.* 2007, 81, 10758–10768.
 33. Pu, Y.; Zhang, X. Mouse hepatitis virus type 2 enters cells through a clathrin-mediated endocytic pathway independent of Eps15. *J. Virol.* 2008, 82, 8112–8123.
 34. Ang, F.; Wong, A.P.; Ng, M.M.; Chu, J.J. Small interference RNA profiling reveals the essential role of human membrane trafficking genes in mediating the infectious entry of dengue virus. *Virol. J.* 2010, 7, 24.
 35. Yasamut, U.; Tongmuang, N.; Yenchitsomanus, P.T.; Junking, M.; Noisakran, S.; Puttikhunt, C.; Chu, J.J.; Limjindaporn, T. Adaptor Protein 1A Facilitates Dengue Virus Replication. *PLoS ONE* 2015, 10, e0130065.
 36. Ricotta, D.; Conner, S.D.; Schmid, S.L.; von Figura, K.; Honing, S. Phosphorylation of the AP2 mu subunit by AAK1 mediates high affinity binding to membrane protein sorting signals. *J. Cell Biol.* 2002, 156, 791–795.
 37. Jackson, L.P.; Kelly, B.T.; McCoy, A.J.; Gaffry, T.; James, L.C.; Collins, B.M.; Honing, S.; Evans, P.R.; Owen, D.J. A large-scale conformational change couples membrane recruitment to cargo binding in the AP2 clathrin adaptor complex. *Cell* 2010, 141, 1220–1229.
 38. Xiao, F.; Wang, S.; Barouch-Bentov, R.; Neveu, G.; Pu, S.; Beer, M.; Schor, S.; Kumar, S.; Nicolaescu, V.; Lindenbach, B.D.; et al. Interactions between the Hepatitis C Virus Nonstructural 2 Protein and Host Adaptor Proteins 1 and 4 Orchestrate Virus Release. *mBio* 2018, 9, e02233-17.
 39. Li, X.; Niu, Y.; Cheng, M.; Chi, X.; Liu, X.; Yang, W. AP1S3 is required for hepatitis C virus infection by stabilizing E2 protein. *Antiviral Res.* 2016, 131, 26–34.
 40. Neveu, G.; Barouch-Bentov, R.; Ziv-Av, A.; Gerber, D.; Jacob, Y.; Einav, S. Identification and targeting of an interaction between a tyrosine motif within hepatitis C virus core protein and AP2M1 essential for viral assembly. *PLoS Pathog.* 2012, 8, e1002845.
 41. Snyers, L.; Zwickl, H.; Blaas, D. Human rhinovirus type 2 is internalized by clathrin-mediated endocytosis. *J. Virol.* 2003, 77, 5360–5369.
 42. Bhattacharyya, S.; Hope, T.J.; Young, J.A. Differential requirements for clathrin endocytic pathway components in cellular entry by Ebola and Marburg glycoprotein pseudovirions. *Virology* 2011, 419, 1–9.
 43. Bekerman, E.; Neveu, G.; Shulla, A.; Brannan, J.; Pu, S.Y.; Wang, S.; Xiao, F.; Barouch-Bentov, R.; Bakken, R.R.; Mateo, R.; et al. Anticancer kinase inhibitors impair intracellular viral trafficking and exert broad-spectrum antiviral effects. *J. Clin. Investig.* 2017, 127, 1338–1352.

44. Garrison, A.R.; Radoshitzky, S.R.; Kota, K.P.; Pegoraro, G.; Ruthel, G.; Kuhn, J.H.; Altamura, L.A.; Kwilas, S.A.; Bavari, S.; Haucke, V.; et al. Crimean-Congo hemorrhagic fever virus utilizes a clathrin- and early endosome-dependent entry pathway. *Virology* 2013, 444, 45–54.
45. Keren, T.; Roth, M.G.; Henis, Y.I. Internalization-competent influenza hemagglutinin mutants form complexes with clathrin-deficient multivalent AP-2 oligomers in live cells. *J. Biol. Chem.* 2001, 276, 28356–28363.
46. Wang, G.; Jiang, L.; Wang, J.; Zhang, J.; Kong, F.; Li, Q.; Yan, Y.; Huang, S.; Zhao, Y.; Liang, L.; et al. The G Protein-Coupled Receptor FFAR2 Promotes Internalization during Influenza A Virus Entry. *J. Virol.* 2020, 94, e01707-19.
47. Sun, W.; McCrory, T.S.; Khaw, W.Y.; Petzing, S.; Myers, T.; Schmitt, A.P. Matrix proteins of Nipah and Hendra viruses interact with beta subunits of AP-3 complexes. *J. Virol.* 2014, 88, 13099–13110.
48. Mattera, R.; Farias, G.G.; Mardones, G.A.; Bonifacino, J.S. Co-assembly of viral envelope glycoproteins regulates their polarized sorting in neurons. *PLoS Pathog.* 2014, 10, e1004107.
49. Kolokoltsov, A.A.; Deniger, D.; Fleming, E.H.; Roberts, N.J., Jr.; Karpilow, J.M.; Davey, R.A. Small interfering RNA profiling reveals key role of clathrin-mediated endocytosis and early endosome formation for infection by respiratory syncytial virus. *J. Virol.* 2007, 81, 7786–7800.
50. Krzyzaniak, M.A.; Zumstein, M.T.; Gerez, J.A.; Picotti, P.; Helenius, A. Host cell entry of respiratory syncytial virus involves macropinocytosis followed by proteolytic activation of the F protein. *PLoS Pathog.* 2013, 9, e1003309.
51. Ward, C.; Maselko, M.; Lupfer, C.; Prescott, M.; Pastey, M.K. Interaction of the Human Respiratory Syncytial Virus matrix protein with cellular adaptor protein complex 3 plays a critical role in trafficking. *PLoS ONE* 2017, 12, e0184629.
52. Nishimura, N.; Plutner, H.; Hahn, K.; Balch, W.E. The delta subunit of AP-3 is required for efficient transport of VSV-G from the trans-Golgi network to the cell surface. *Proc. Natl. Acad. Sci. USA* 2002, 99, 6755–6760.
53. Cureton, D.K.; Massol, R.H.; Saffarian, S.; Kirchhausen, T.L.; Whelan, S.P. Vesicular stomatitis virus enters cells through vesicles incompletely coated with clathrin that depend upon actin for internalization. *PLoS Pathog.* 2009, 5, e1000394.
54. Fujisawa, R.; Masuda, M. Ecotropic murine leukemia virus envelope protein affects interaction of cationic amino acid transporter 1 with clathrin adaptor protein complexes, leading to receptor downregulation. *Virology* 2007, 368, 342–350.
55. Buffalo, C.Z.; Iwamoto, Y.; Hurley, J.H.; Ren, X. How HIV Nef Proteins Hijack Membrane Traffic To Promote Infection. *J. Virol.* 2019, 93, e01322-19.

56. Pereira, E.A.; daSilva, L.L. HIV-1 Nef: Taking Control of Protein Trafficking. *Traffic* 2016, 17, 976–996.
57. Jia, X.; Weber, E.; Tokarev, A.; Lewinski, M.; Rizk, M.; Suarez, M.; Guatelli, J.; Xiong, Y. Structural basis of HIV-1 Vpu-mediated BST2 antagonism via hijacking of the clathrin adaptor protein complex 1. *Elife* 2014, 3, e02362.
58. Chu, H.; Wang, J.J.; Spearman, P. Human immunodeficiency virus type-1 gag and host vesicular trafficking pathways. *Curr. Top. Microbiol. Immunol.* 2009, 339, 67–84.
59. Alford, J.E.; Marongiu, M.; Watkins, G.L.; Anderson, E.C. Human Immunodeficiency Virus Type 2 (HIV-2) Gag Is Trafficked in an AP-3 and AP-5 Dependent Manner. *PLoS ONE* 2016, 11, e0158941.
60. Hirao, K.; Andrews, S.; Kuroki, K.; Kusaka, H.; Tadokoro, T.; Kita, S.; Ose, T.; Rowland-Jones, S.L.; Maenaka, K. Structure of HIV-2 Nef Reveals Features Distinct from HIV-1 Involved in Immune Regulation. *iScience* 2020, 23, 100758.
61. Noble, B.; Abada, P.; Nunez-Iglesias, J.; Cannon, P.M. Recruitment of the adaptor protein 2 complex by the human immunodeficiency virus type 2 envelope protein is necessary for high levels of virus release. *J. Virol.* 2006, 80, 2924–2932.
62. Cooper, A.; Shaul, Y. Clathrin-mediated endocytosis and lysosomal cleavage of hepatitis B virus capsid-like core particles. *J. Biol. Chem.* 2006, 281, 16563–16569.
63. Huang, H.C.; Chen, C.C.; Chang, W.C.; Tao, M.H.; Huang, C. Entry of hepatitis B virus into immortalized human primary hepatocytes by clathrin-dependent endocytosis. *J. Virol.* 2012, 86, 9443–9453.
64. Iwamoto, M.; Saso, W.; Nishioka, K.; Ohashi, H.; Sugiyama, R.; Ryo, A.; Ohki, M.; Yun, J.H.; Park, S.Y.; Ohshima, T.; et al. The machinery for endocytosis of epidermal growth factor receptor coordinates the transport of incoming hepatitis B virus to the endosomal network. *J. Biol. Chem.* 2020, 295, 800–807.

Retrieved from <https://encyclopedia.pub/entry/history/show/25595>