Virologica Sinica 37 (2022) 321–330

Contents lists available at ScienceDirect

Virologica Sinica

journal homepage: www.keaipublishing.com/en/journals/virologica-sinica
www.virosin.org

Review

The emerging roles of retromer and sorting nexins in the life cycle of viruses

Yue Lu [a,b,c], Ping He [b,c], Yuxuan Zhang [b,c], Yongwen Ren [a,b,c], Leiliang Zhang [a,b,c,*]

[a] Department of Clinical Laboratory Medicine, The First Affiliated Hospital of Shandong First Medical University & Shandong Provincial Qianfoshan Hospital, Jinan, 250013, China
[b] Department of Pathogen Biology, School of Basic Medical Sciences, Shandong First Medical University & Shandong Academy of Medical Sciences, Jinan, 250117, China
[c] Medical Science and Technology Innovation Center, Shandong First Medical University & Shandong Academy of Medical Sciences, Jinan, 250117, China

ARTICLE INFO

Keywords:
Retromer
Coronaviridae
Flaviviridae
Retroviridae
Sorting nexin (SNX)

ABSTRACT

Retromer and sorting nexins (SNXs) transport cargoes from endosomes to the trans-Golgi network or plasma membrane. Recent studies have unveiled the emerging roles for retromer and SNXs in the life cycle of viruses, including members of *Coronaviridae*, *Flaviviridae* and *Retroviridae*. Key components of retromer/SNXs, such as Vps35, Vps26, SNX5 and SNX27, can affect multiple steps of the viral life cycle, including facilitating the entry of viruses into cells, participating in viral replication, and promoting the assembly of virions. Here we present a comprehensive updated review on the interplay between retromer/SNXs and virus, which will shed mechanistic insights into controlling virus infection.

1. Introduction

Retrograde transport is a highly regulated and selective process, which is widely described as the flow of proteins and lipids from the plasma membrane to the Golgi, from endosomes to the Golgi, or from Golgi to the endoplasmic reticulum (ER) (Bonifacino and Rojas, 2006; Johannes and Popoff, 2008). The endocytic recycling pathway is responsible for sending the endocytic cargoes back to the plasma membrane, maintaining the stability of the plasma membrane composition and ensuring the normal progress of a variety of cellular biological processes.

An important protein complex for vesicle transport is the retromer complex (Bujny et al., 2007). Retromer is an endosomal membrane-binding protein complex and its main function is to select the cargoes for retrograde transport from the early endosome to the Golgi (Seaman, 2012; Burd and Cullen, 2014). In eukaryotic cells, retromer transports cargoes from mature endosomes to newly synthesized endosomal tubules through recognizing and sorting, and then transports back to the Golgi (Arighi et al., 2004; Seaman, 2004, 2012; Bonifacino and Hurley, 2008). There are growing evidences that retromer is also involved in transport processes from endosome to plasma membrane (Temkin et al., 2011; Choy et al., 2014). Transport pathways mediated by retromer were outlined in Fig. 1.

In mammalian cells, retromer is comprised of Vps35, Vps26 and Vps29 (Seaman et al., 1998; Seaman, 2005; Wassmer et al., 2007; Attar and Cullen, 2010). The cargo-selective trimer Vps26-Vps29-Vps35 forms a stable tertiary structure, which participates in the binding of cargoes (Haft et al., 2000; Arighi et al., 2004; Kerr et al., 2005; Bugarcic et al., 2011). Retromer-mediated trafficking in cargoes works by directly binding to Vps35 or Vps26 (Arighi et al., 2004; Shi et al., 2006; Seaman, 2007; Belenkaya et al., 2008; Tabuchi et al., 2010; Fjorback et al., 2012).

Sorting nexins (SNXs) are consisted of a series of proteins that are involved in the identification and sorting of cargoes during retrograde transport from endosome to the Golgi or plasma membrane (Cullen and Korswagen, 2011). At present, 33 kinds of SNXs are known in mammals (Cullen, 2008), some of which can bind to retromer (Arighi et al., 2004). SNX1, SNX2, SNX5, SNX6 and SNX32 can associate with retromer to deform membrane (Carlton et al., 2004; Griffin et al., 2005; Wassmer et al., 2007). Many studies have shown that mammalian SNXs are able to function in recognizing and trafficking cargoes, independently of retromer (Kvainickas et al., 2017; Simonetti et al., 2017; Yong et al., 2020).

Many protein cargoes reach the cell surface through endocytic recycling by retromer, which requires the participation of COMMD/CCDC22/CCDC93 (CCC), Wiskott-Aldrich syndrome protein and SCAR homologue (WASH) complex and SNX27 (Li et al., 2015; Phillips-Krawczak et al., 2015; Bartuzi et al., 2016; Lee et al., 2016). WASH complex is fundamental for endosomal cargo sorting, which is composed of five proteins, in which FAM21 is located on the endosome near retromer by binding to Vps35 (Harbour et al., 2012). The WASH complex is able to promote the formation of actin fiber network

* Corresponding author.
E-mail address: armzhang@hotmail.com (L. Zhang).

https://doi.org/10.1016/j.virs.2022.04.014
Received 28 December 2021; Accepted 12 April 2022
Available online 2 May 2022

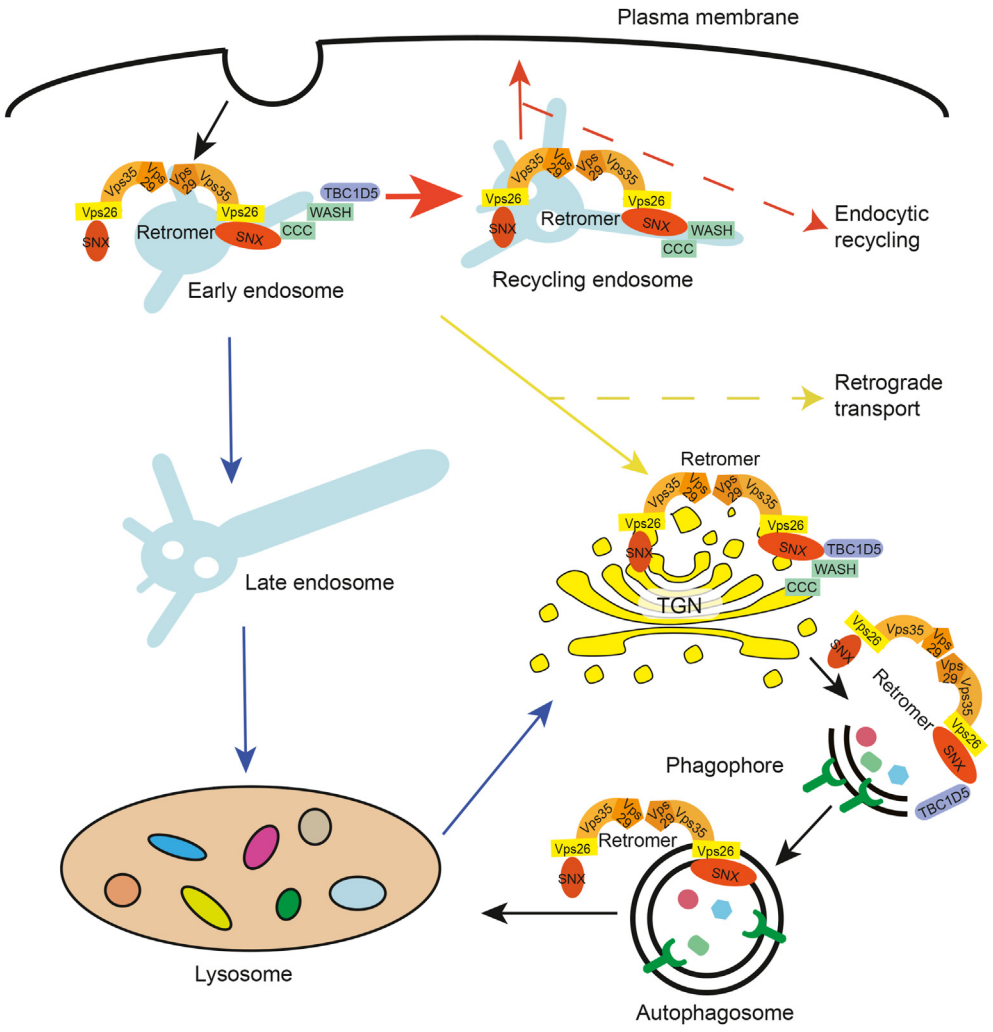

Fig. 1. Transport pathways mediated by retromer and SNXs in the absence of virus. Retromer and SNXs mediate two transport pathways including endocytic recycling from the recycling endosome to the plasma membrane and retrograde transport from the endosome to TGN. Retromer also bridges the endosome and autophagosome. SNX, sorting nexin; TGN, trans-Golgi network; Vps, vacuolar protein sorting; WASH, Wiskott-Aldrich syndrome protein and SCAR homologue; CCC, COMMD/CCDC22/CCDC93; TBC1D5, Tre2-Bub2-Cdc16 (TBC) Domain Family Member 5.

in the part of the endosome, thus boosting the sorting of cargoes into retromer, while FAM21 can direct SNX27/retromer cargoes to the plasma membrane (Phillips-Krawczak et al., 2015; Bartuzi et al., 2016; Lee et al., 2016).

Rab protein is a small guanosine triphosphatase (GTPase) that regulates membrane transport events by cycling between the membrane-related GTP-binding and GDP-binding types (Guerra and Bucci, 2016; Stroupe, 2018). Tre2-Bub2-Cdc16 (TBC) Domain Family Member 5 (TBC1D5) is a Rab7-specific GTPase activating protein, which binds closely to retromer *in vitro* and is a pivotal component of the retromer complex (Seaman et al., 2009). TBC1D5 not only bridges the endosome and autophagosome via its C-terminal LIR motif (Popovic et al., 2012), but also associates with ATG9 and the active ULK1 complex during autophagy (Popovic and Dikic, 2014). ATG9A is recycled to the trans-Golgi network (TGN) in a SNX4/retromer-dependent manner (Ravussin et al., 2021). The involvement of retromer complex in autophagy is shown in Fig. 1.

Retrograde transport and endocytic recycling pathways have been used by various viral proteins to mediate cytotoxicity and pathogenic mechanisms. Accumulating studies have revealed the emerging roles for retromer/SNXs in the life cycle of viruses, including severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and human Papillomavirus (HPV). Retromer/SNXs components may participate in multiple steps of the viral life cycle directly or indirectly. In this review, we will summarize the interplay between retromer/SNXs and virus sorted by virus families.

2. The roles for retromer in the life cycle of virus

2.1. *Coronaviridae*

The coronavirus disease 2019 (COVID-19) pandemic, caused by SARS-CoV-2, is a huge threat to public health and global economy. Several protein-protein interaction studies and functional genome-wide screening studies have shown that the involvement of retromer in the life cycle SARS-CoV-2. Daniloski et al. found a consistent theme among the enriched complexes for SARS-CoV-2 life cycle was endosome function, of which Vps26A, Vps29, Vps35 and SNX27 were identified (Daniloski et al., 2021).

The SARS-CoV-2 entry is mediated by membrane fusion at the plasma membrane, while the deletion of RRAR furin cleavage site in spike (S) protein drives virus entry to endosomal pathway. Genome-wide CRISPR screening with RRAR deletion mutant identified a series of SARS-CoV-2 host factors related to intracellular transport, such as Vps35, Vps29, SNX27, CCC, WASH, Arp2/3 (Zhu et al., 2021). Knockout of key

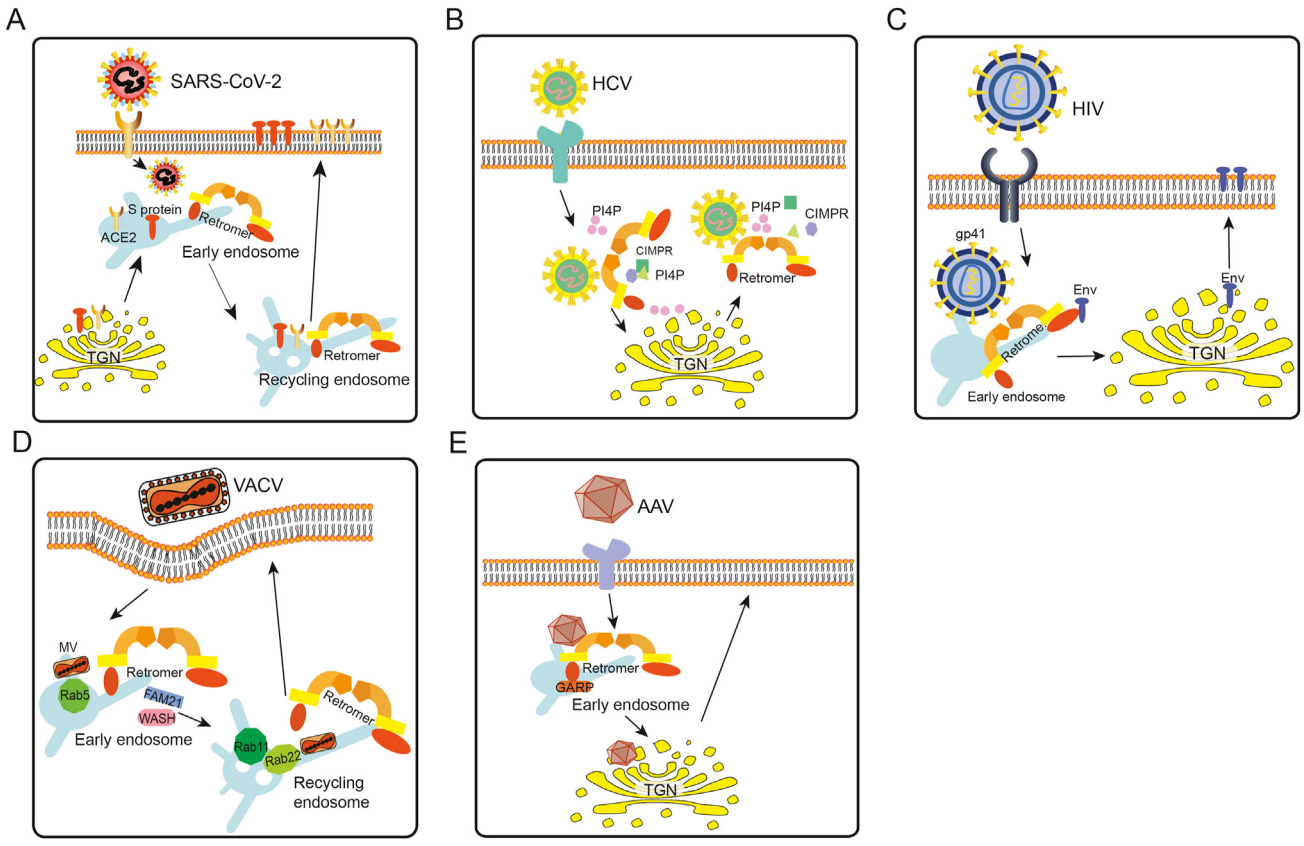

Fig. 2. The schematic models that demonstrate the mechanistic view of the function of retromer and SNXs for typical viruses. **A** SARS-CoV-2 receptor ACE2 and S protein are transported to cell surface by SNX27-retromer. **B** Retromer and its cargo CIMPR are required for HCV replication. **C** Retromer affects HIV through trafficking Env. **D** VACV uncoating requires WASH component FAM21. **E** Retromer facilitates AAV to enter the cell. SNX, sorting nexin; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; ACE2, angiotensin-converting enzyme 2; S, spike; NSP, non-structural protein; TGN, trans-Golgi network; HCV, hepatitis C virus; CIMPR, cation-independent mannose-6-phosphate receptor; PI4P, phosphatidylinositol-4-phosphate; Env, envelope glycoprotein envelope; HIV, human immunodeficiency virus; VACV, vaccinia virus; MV, mature virion; WASH, Wiskott-Aldrich syndrome protein and SCAR homologue; AAV, adeno-associated virus; GARP, Golgi associated retrograde protein complex.

components of retromer, such as SNX27 and CCC, reduced surface level of angiotensin-converting enzyme 2 (ACE2), indicating the key role for SNX27/retromer in SARS-CoV-2 entry (Zhu et al., 2021). SNX27 PDZ domain recognizes SNX27/retromer complex cargoes and mediates the recycling of transmembrane cargoes from the endosome to the plasma membrane (Ghai et al., 2013; Gallon et al., 2014; Kliche et al., 2021). Interestingly, C-terminal cytoplasmic tail of ACE2 possesses a type I PDZ binding motif (PBM) and associates with SNX27 PDZ domain (Kliche et al., 2021), raising the possibility that ACE2 is a SNX27/retromer cargo. Thus SNX27 may promote SARS-CoV-2 entry by regulating the endocytic recycling of ACE2 (Fig. 2A). Indeed, silencing SNX27 or knockout of SNX27 reduced the surface level of ACE2 (Yang et al., 2022).

In addition to ACE2, S protein of SARS-CoV-2 could interact with SNX27 (Cattin-Ortolá et al., 2021; Zhao et al., 2021). PDZ domain of SNX27 associated with the "MTSC" motif of S protein (Cattin-Ortolá et al., 2021; Zhao et al., 2021). One study showed that S mutant deficient for SNX27 binding did not alter its accumulation on the plasma membrane (Cattin-Ortolá et al., 2021). However, in another study, S mutant losing SNX27 binding ability reduced surface level of S protein (Zhao et al., 2021). Moreover, knockout of SNX27 decreased S protein cell surface expression and reduced S-based pseudovirus production. Therefore, SNX27 could mediate the endocytic recycling pathway of S (Fig. 2A).

2.2. *Flaviviridae*

Hepatitis C virus (HCV) infection is an important cause of liver disease. More than 170 million people worldwide are chronically infected with HCV (Shepard et al., 2005). Chronic HCV usually develops into liver fibrosis, cirrhosis and hepatocellular carcinoma (HCC) (Yamane et al., 2013), which seriously affects human health. The completion of the life cycle of HCV requires the participation of many host factors. Among host factors of HCV, phosphatidylinositol-4-phosphate (PI4P) is a specific inositol phosphate rich in the HCV replication region, which plays a vital role in the replication of HCV (Hsu et al., 2010; Reiss et al., 2011; Tai and Salloum, 2011; Bianco et al., 2012; Hong et al., 2014; Li et al., 2014). The effectors of PI4P are involved in many steps of the life cycle of HCV. PI4P could promote the dissociation of retromer and its cargoes on the TGN (Niu et al., 2013), while retromer and other PI4P effectors OSBP, FAPP2, GOLPH3 and CERT jointly promote the process of virus life cycle (Amako et al., 2009; Lim and Hwang, 2011; Khan et al., 2014; Wang et al., 2014; Yin et al., 2016). The domain I of NS5A protein interacts with Vps35, the core component of retromer. Moreover, PI4P induced by HCV can elevate the unloading of a typical retromer cargo cation-independent mannose-6-phosphate receptor (CIMPR) in the virus replication region (Yin et al., 2016) (Fig. 2B). Knockdown of retromer and its cargo CIMPR inhibited HCV replication. Given that the CIMPR is necessary for

trafficking lysosomal hydrolases to lysosomes (via endosomes) and that retromer regulates the endosome-to-Golgi retrieval of the CIMPR, it seems likely that loss of retromer is impacting on CIMPR localization, altering lysosome function which is then affecting virus replication. In the process of HCV replication, retromers located in autophagosomes, indicating that retromers may also regulate the replication of virus through autophagy (Yin et al., 2017).

2.3. Retroviridae

Human T cell leukemia virus type 1 (HTLV-1) was the first discovered human retrovirus (Poiesz et al., 1980). The HTLV-1 endemic areas are spread all over the world, such as Japan, the Caribbean Islands, Central America, South America, and Africa. HTLV-1 is the pathogen of adult T cell leukemia (ATL), and associated myelopathy/tropic spastic paraparesis (Yoshida et al., 1982; Goncalves et al., 2010).

The regulatory gene *Tax-1* is required for efficient virus replication, as it drives transcription of viral gene products. PBM at the carboxyl terminus of Tax-1 is significant for HTLV-1 induced cellular transformation. SNX27 is an interacting partner of Tax-1, and their interaction is mediated by the Tax-1 PBM and SNX27 PDZ domain. SNX27 can promote the plasma membrane localization of glucose transport 1 (GLUT1). Tax-1 alters GLUT1 localization via its interaction with SNX27. Through their observations, Al-Saleem et al. demonstrated that overexpression of Tax-1 in cells reduced the level of GLUT1 on the plasma membrane, while knockdown of SNX27 increased virion release and decreased HTLV-1 infectivity (Al-Saleem et al., 2019).

The envelope glycoprotein envelope (Env) of human immunodeficiency virus (HIV) is not only the key determinant of virus infection, but also the main target of humoral immunity. Env is composed of 856 amino acids and synthesizes a 160 kDa leader chain (gp160) in the ER, which is then split into two subunits (Checkley et al., 2011): the receptor-bound surface subunit gp120 and transmembrane subunit gp41. Subunit gp41 has cytoplasmic binding domain and can regulate the intracellular transport of Env. In addition, the long cytoplasmic tail of Env has a potential effect on the assembly of infectious virions and prevents Env from being exposed to the immune system. Under normal circumstances, most of the envelope glycoproteins are located on the Golgi and traverse the whole pathway from the Golgi to the plasma membrane. The envelope glycoproteins that are not packaged into the virus will be endocytosed back to the Golgi (Berlioz-Torrent et al., 1999; Wyss et al., 2001; Byland et al., 2007). Nevertheless, little is known about the detailed mechanism of this process.

Experiments have shown that retromer regulates the intracellular transport of Env and promotes the retrograde transport from endosome to Golgi (Fig. 2C). In virus-infected cells, HIV-1 envelope glycoprotein Env can co-localize with retromer (Groppelli et al., 2014). Knockdown of the retromer component Vps26 or Vps35 increases Env expression on the plasma membrane. These functions depend on the direct interaction between C-terminal 100 amino acids of Env gp41 and retromer complex (Groppelli et al., 2014). Interfering with the function of retromer could inhibit the transport of envelope glycoproteins, resulting in the inability of endogenous envelope glycoproteins to return to the Golgi, changing the location of Env, and ultimately affecting the process of Env incorporation into newly synthesized virions (Groppelli et al., 2014).

Using high-throughput small interference RNA (siRNA) screening, Bayliss et al. identified the trafficking proteins, including Rab7L1 also known as Rab29, are required for HIV virological synapses (VS) formation (Bayliss et al., 2020). Rab7L1/Rab29 functions in intracellular transport and endosomal sorting of lysosome-bound membrane proteins and participates in retromer activity (Kuwahara et al., 2016). By using the retromer pathway, internalized HIV virions can be delivered onto the plasma membrane, promoting the formation of VS, and enabling trans-infection between monocyte derived Dendritic cell (MDDC) and T cell (Bayliss et al., 2020). Retromer affects the late step of HIV-1 replication and regulates virus assembly, which is a new discovery of its function. It also provides a new direction for the future research on the relationship between virus and retromer.

2.4. Papillomaviridae

HPV is a non-enveloped DNA virus that mainly infects epithelial cells of the skin and mucous membranes (Griffin et al., 2014). More than 200 types of human papillomavirus have been identified, among which HPV16 and HPV18 subtypes are the most common high risk strains. Genome-wide siRNA screening confirmed that retromer was a crucial protein for HPV to enter cells (Lipovsky et al., 2013). The capsid protein of HPV penetrates the plasma membrane and employs retromer to transport to TGN. Its genome is transmitted to TGN during infection. Studies have demonstrated that inhibition of TGN function significantly reduces virus infectivity. After endocytosis, the incoming HPV virions remain in the membrane vesicles until they reach the nucleus, where viral DNA replication occurs (Schelhaas et al., 2012; Day et al., 2013, 2019; Lipovsky et al., 2013; DiGiuseppe et al., 2016; Aydin et al., 2017; Siddiqa et al., 2018).

The entry of HPV16 into cells was mediated by retromer (Pim et al., 2021). Upon knocking down the core components of retromer, Vps26, Vps29 or Vps35, respectively, HPV16 infection is restricted. Moreover, other types of *Papillomaviridae* such as HPV18 also require retromer to enter the host cells (Ganti et al., 2016a). The internalized HPV exists in the endosome cavity. Although the L2 capsid protein is not a transmembrane protein, it is still a cargo transported by retromer. Part of the viral L2 capsid protein extends into the cytoplasm through the membrane, where it can bind to retromer and several other L2 binding partners (such as SNX17) (Bergant Marusic et al., 2012; Bronnimann et al., 2013; Lipovsky et al., 2013; Popa et al., 2015). Retromer directly binds to a highly conserved sequence motif at the C-terminal of L2 protein (Zhang et al., 2018), which is considered as a retromer binding motif mimic. The knockdown or mutation of this motif will interfere with the ability of L2 to bind to retromer, resulting in the accumulation of L2 protein *in vivo* and inhibiting the transport of virus from early endosome to TGN (Popa et al., 2015; Lipovsky et al., 2017). This defect was remedied by replacing the main binding site of retromer on L2 with retromer sorting signal from intracellular proteins. *In vitro* experiments illustrated that this site on L2 could directly bind to retromer (Popa et al., 2015). L2 protein also contains a cationic cell-penetrating peptide (CPP) sequence, which triggers retromer-mediated HPV transport during virus entry (Zhang et al., 2018, 2020). CPP from L2 mediates transient insertion of L2 into the endosome membrane, which is stabilized by retromer-L2 binding. Those results demonstrated that retromer plays a key role in CPP-mediated membrane insertion (Xie et al., 2021).

SNX17 and SNX27 play an important role in the process of HPV infection. SNX17 can interact with L2, which is related to the transport of L2 from late endosomes. A PDZ domain in SNX27 is critical for the interaction between HPV16 L2 and SNX27, which modulates virion trafficking (Pim et al., 2015). Knockdown of SNX17 decreased the level of L2 in late endosomes and weakened pseudoviral infection (Bergant and Banks, 2013). SNX27 exists in the early endosomes and binds to cargo through its carboxyl terminal amino acid residues (Cai et al., 2011). Knocking down SNX27 limits pseudoviral particles infection. When both SNX17 and SNX27 were knocked down, the viral infection efficiency were further decreased. However, overexpression of these two proteins led to different localization of L2 protein. SNX27 overexpression did not change the nuclear localization of L2, while overexpression of SNX17 caused L2 to localize only in the cytoplasm, suggesting that SNX17 may participate in the late stage of virus entry (Zhang et al., 2016).

GTPase cycle of Rab7b is critical for HPV trafficking (Day et al., 2013; Lipovsky et al., 2013; Young et al., 2019). During HPV infection, binding of the retromer to L2 recruits Rab7-specific GTPase activating protein TBC1D5 to retromer, inducing the disassembly of retromer-HPV complex from the membrane (Seaman et al., 2009; Jia et al., 2016; Borg Distefano

et al., 2018; Jimenez-Orgaz et al., 2018). Cargo binding plays a central role in membrane recruitment and assembly of active retromer complexes (Harrison et al., 2014; Lucas et al., 2016). TBC1D5 stimulates the hydrolysis of Rab7-GTP, driving the disintegration of the retromer-HPV complex, which in turn causes dissociation of the retromer from the endosomal membrane, and vesicles containing cargoes are transported to TGN, where the cargoes are delivered through membrane fusion to coordinate retrograde transport (Rojas et al., 2008; Seaman et al., 2009; Liu et al., 2012; Harrison et al., 2016; Lucas et al., 2016; Jimenez-Orgaz et al., 2018).

Oncoprotein E6 from multiple high-risk HPV types associates with SNX27 by a classical PBM-PDZ interaction. E6, SNX27 and the retromer form a complex, which facilitates the SNX27 cargoes, such as GLUT1, recycling back to the cell surface. Thus, E6 plays an important role to maintaining high levels of glucose uptake by regulating GLUT1 transport (Ganti et al., 2016b).

Stannin is an important regulator of HPV entry. It is located in the lysosomal compartment and does not affect the binding of HPV16 to cells, virus absorption or virus uncoating, whereas can selectively inhibit the entry of several types of HPV. It is expressed in human keratinocytes and interacts with L1 major capsid proteins. Stannin could weaken the interaction between L2 capsid protein and retromer, inhibit HPV16 transport into TGN in the cell, and stimulate HPV degradation, thus leading to the low infectivity of HPV. Although endogenous level of Stannin inhibits HPV16 infection, its role in natural infection remains unclear (Lipovsky et al., 2017).

2.5. Herpesviridae

Herpesvirus saimiri (HVS) tyrosine kinase-interacting protein (Tip) is needed for the immortalization of T lymphocytes *in vitro*. Tip interacts with Vps35 through a conserved glutamate-rich N-terminal motif. CIMPR is a receptor for lysosomal hydrolases and other endosomal proteins. The expression of Tip diminishes the level of CIMPR, leading to lysosomal degradation and reducing the redistribution of Vps35 into lysosomes. Conversely, the existence of Tip does not affect the stability of the retromer subunit. Tip inhibition of retromer activity is related to down-regulation of CD4 expression on cell surface and the transformation of human initial T cells *in vitro* (Kingston et al., 2011).

Human cytomegalovirus (HCMV) belongs to the beta herpesvirus subfamily of herpesviruses (Davison et al., 2009). It causes asymptomatic infection in healthy people and poses a serious threat to patients with low immune function. HCMV induces the formation of cytoplasmic viral assembly center (cVAC), where mature virus particles are formed by a variety of viral proteins. HCMV *UL35* gene encodes the envelope protein ppUL35, which participates in the assembly of cytomegalovirus. Maschkowitz et al. found that SNX5 interacted with UL35 protein. The expression of wild-type protein rather than SNX5 binding deficient mutant leads to the redistribution of intracellular CIMPR, indicating that UL35 protein binds to SNX5 and negatively regulates the cellular transport pathway. In addition, the binding of UL35 proteins to SNX5 is necessary for efficient viral replication and transport of the most abundant HCMV glycoprotein B (gB, gpUL55) to cVAC (Maschkowitz et al., 2018). cVAC consists of circular vesicles from the Golgi and endosomal network (Das et al., 2007; Das and Pellett, 2011). In the late stages of HCMV infection, the viral capsid is transported to cVAC, where it is surrounded by a membrane protein layer and a viral membrane.

Viruses could induce the degradation of key components of immune system by selective autophagy of aggregates (aggrephagy). Murine cytomegalovirus (MCMV) M45 and herpes simplex virus type 1 (HSV-1) ICP6 recruit Vps26B and TBC1D5 to facilitate the degradation of receptor-interacting protein kinase 1 (RIPK1) by aggrephagy, which represents a novel viral immune-evasion mechanism (Muscolino et al., 2020).

2.6. Poxviridae

Vaccinia virus (VACV) belongs to Orthopoxvirus genus of *Poxviridae* family. It is a large double-stranded DNA virus, which is capable of infecting a wide range of cell lines and animals (Van Vliet et al., 2009). VACV mature virion (MV) enters the host cells through macropincytosis (Mercer and Helenius, 2008). In the stage of intracellular cargo transport, Rab5 exists in the early endosome, while Rab7 is located at the late endosome and lysosome (Hsiao et al., 2015). Studies have shown that before membrane fusion and virus decapitation, MV is transported to early endosomes, where Rab5 is active and further binds to recycling endsomes marked by Rab11 and Rab22. Rab11 and Rab22 work together to regulate VACV entry into cells.

In early endosome, FAM21-retromer protein complex is required for MV sorting (Hsiao et al., 2015) (Fig. 2D). The invasion of vaccinia virus MV into HeLa cells depends on FAM21 (Huang et al., 2008). FAM21 is a key component of WASH protein, which is necessary for endosomal sorting of vesicles containing MV. The sorting of endosome containing MV also requires the interaction of FAM21 with retromer complex components Vps26, Vps29 and Vps35 (Harbour et al., 2012; Jia et al., 2012). WASH and retromer cause membrane fusion and VACV core uncoating in the cytoplasm. The discovery of FAM21-retromer complex regulating the intracellular transport of VACV has enlightened us on the relationship between VACV and early endosomal MV sorting.

Western Reserve (WR) strain of VACV open reading frame (ORF) WR039 (K7R) encodes a non-essential VACV protein K7 (Schroder et al., 2008; Benfield et al., 2013). Li et al. found that K7 preferentially bound to host proteins related to vesicle transport, including COPI, retromer and class C Homologues in Endosome-Vesicle Interaction complex (CHEVI) (Li et al., 2017). Experiments uncovered that K7 interaced with Vps35, Vps26A and Vps26B, and the C-terminal leucine in K7 was required for retromer binding (Li et al., 2017). Therefore, K7 may be involved in the intracellular transport of the virus and combine with FAM21-retromer complex, thereby promoting the uncoating of vaccinia virus. Another possibility is that K7 blocks the cargo binding site of retromer by interacting with retromer (Li et al., 2017).

2.7. Parvoviridae

Recombinant adeno-associated virus (AAV) has low immunogenicity which infects a variety of tissues *in vivo* and provides long-term transgene expression in tissues after mitotic (Grimm and Kay, 2003). Thus it is considered to be one of the most powerful tools for gene therapy, which is a promising way to treat life-threatening diseases that cannot be cured by any other form of medicine. AAV vectors are currently being evaluated for the treatment of Duchenne muscular dystrophy, hemophilia, heart failure, Parkinson's disease and other diseases.

AAV capsids accumulate in TGN and Golgi (Bantel-Schaal et al., 2002; Pajusola et al., 2002; Johnson et al., 2011; Nonnenmacher and Weber, 2011), which indicates that AAV exploits the retrograde transport mechanism from endosome to TGN, involving retromer complex (Vps29 and Vps35) and Golgi associated retrograde protein complex (GARP) (Vps51, Vps52, Vps53, and Vps54) (Fig. 2E). Using recently developed Golgi targeting drugs and siRNA-mediated knockdown of a specific transporter protein, Nonnenmacher et al. have proved that transport to the Golgi is necessary for AAV transduction. SNX5-mediated retrograde transport to the Golgi is a widely conserved feature of AAV transport, which seems to have nothing to do with the identity of the receptor used for virus attachment. They also observed that virions escaped the endosomal system directly from the TGN/Golgi compartment (Nonnenmacher et al., 2015). Different AAV serotypes may vary in endocytosis rate and transport mechanism (Keiser et al., 2011; Weinberg et al., 2014). Unexpectedly, all the capsids of AAV will converge into a common retrograde transport

route to TGN. These results suggest that retromer/SNXs and retrograde transport mechanism play a vital role in the transportation of AAV.

2.8. Orthomyxoviridae

For centuries, influenza viruses have been the cause of recurrent epidemics (Taubenberger and Morens, 2010). Although a variety of new drugs and vaccines have been developed, drug resistance has emerged because influenza A virus (IAV) has the strong ability to mutate and evolve. IAV has a segmented single-stranded negative sense RNA genome (Cheung and Poon, 2007), and matrix protein 2 (M2) is the spliced product of the seventh segment of IAV genome. It is a type III transmembrane protein that forms a homotetramer and belongs to ion channel proteins. Although a small amount of M2 was incorporated in virions, a large number of M2 existed in the endosomal chamber of infected cells (Henkel et al., 1998). Bhowmick et al. detected that M2 was retrogradely transported to the cytoplasm through endosome and Golgi network (Bhowmick et al., 2017). It prevents the fusion of endosome and lysosome when moving from endosome to TGN. M2 colocalized with SNX1 and SNX4 proteins and was considered as a retromer cargo. In addition, the exit of M2 to the cytoplasm from ER required the interaction with wild-type p97ATPase. Accordingly, the M2 is transported from the endoplasmic reticulum to the cytoplasm bypassing the cytoplasmic proteasome, and then transported to TGN to escape degradation (Bhowmick et al., 2017).

2.9. Pneumoviridae

Human respiratory syncytial virus (HRSV) is one of the most common viruses causing respiratory tract infections every year (Nair et al., 2011). HRSV belongs to the genus *Orthopneumoviruses* of the family *Pneumoviridae*, and its negative-stranded RNA genome encodes 11 kinds of proteins. Among those viral proteins, nucleoprotein (N) protein associates with viral RNA and plays the key role in inclusion bodies formation induced by virus, whereas the matrix protein (M) protein is involved in virus assembly and budding on the cell surface.

HRSV N and M proteins interact with retromer component SNX2 evidenced by proximity ligation assay and co-immunoprecipitation experiment (Cardoso et al., 2020). Another retromer component Vps26 also exists in inclusion bodies and filamentous structures. Silencing SNX1 and SNX2 causes the decrease of viral protein, the size of HRSV inclusion body, the formation of syncytia, and the generation of progeny viruses (Cardoso et al., 2020). In summary, SNX2 plays a significant role in the transport of HRSV structural proteins to assembly sites, indicating the role for retromer/SNXs in the biogenesis of HRSV particles (Cardoso et al., 2020).

2.10. Togaviridae

Alphaviruses belong to a group of viruses vectored in nature by blood-feeding insects. Sindbis virus (SINV), chikungunya virus (CHIKV) and Mayaro virus (MAYV) are pathogenic alphaviruses which pose great challenges to public health in the world. However, there are few specific drugs or vaccines available against these viruses (Chattopadhyay et al., 2013).

One host protein SNX5 was shown to be critical for the replication of these pathogenic alphaviruses. Schuchman et al. constructed a stable HEK293 SNX5 gene knockout cell line (Schuchman et al., 2018). Compared with wild-type HEK293 cells, they found that the production of SINV was significantly inhibited, and similar results were revealed in MAYV and CHIKV (Schuchman et al., 2018). Thus, it is speculated that SNX5 is essential for the growth of these three arboviruses viruses.

3. Conclusions

During infection, viruses hijack many host transport pathways for their own benefit. Here, we review the roles of the host protein trafficking complex retromer/SNXs in viral infection. What is striking is the large diversity of viruses that require retromer/SNXs or retromer-associated proteins. With the extensive study of the interplay between virus and retromer/SNXs, scientists found that numerous viruses utilized retromer/SNXs, most often for cell entry (Fig. 3). Retromer/SNXs

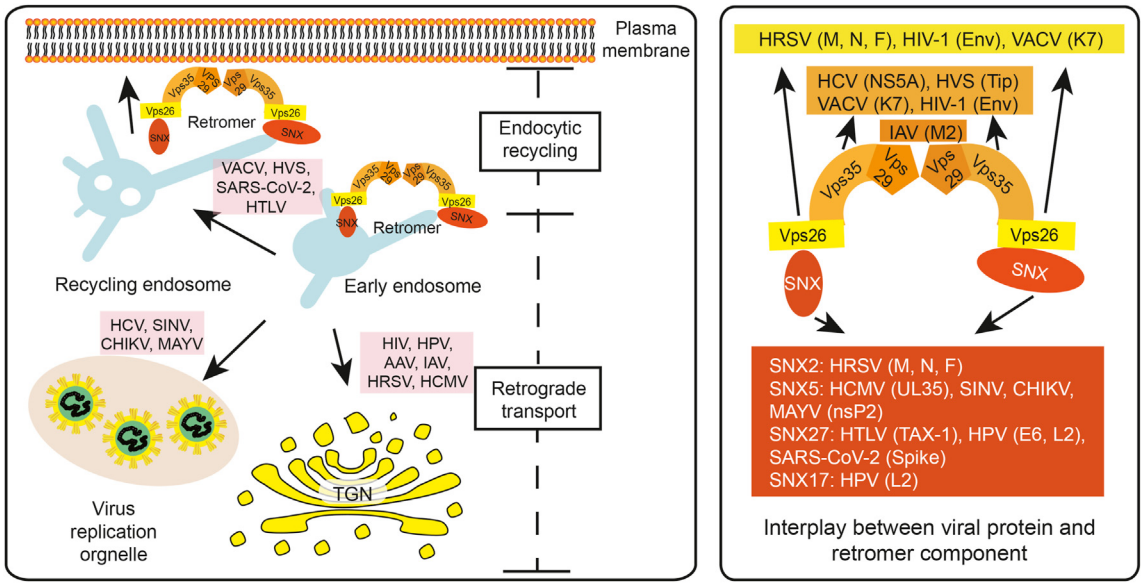

Fig. 3. Transport pathways mediated by retromer and SNXs in the presence of virus. HCV, SINV, CHIKV, MAYV, HIV, HPV, AAV, IAV, HRSV and HCMV use the retrograde transport pathway of retromer to promote infection. SARS-CoV-2, VACV, HVS and HTLV hijack the recycling pathway of retromer and SNXs. The detailed interaction between virus proteins and retromer components was illustrated in the right. HCV, hepatitis C virus; SINV, Sindbis virus; CHIKV, chikungunya virus; MAYV, Mayaro virus; HIV, human immunodeficiency virus; HPV, human papillomavirus; AAV, adeno-associated virus; IAV, influenza A virus; HRSV, human respiratory syncytial virus; HCMV, human cytomegalovirus; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; VACV, vaccinia virus; HVS, Herpes saimiri virus; HTLV, human T-cell leukemia virus; SNX, sorting nexin; Vps, vacuolar protein sorting.

Table 1
Selected examples of the interplay between virus and retromer/SNXs.

Virus	Viral protein	Retromer/SNXs component	Interplay between virus and retromer/SNXs	Reference
SARS-CoV-2	S, NSP2, NSP7, NSP12, NSP16	WASH, CCDC22, SNX1/2, Vps26A, Vps29, Vps35, SNX27	Retromer promotes the endocytic recycling of ACE2.	(Daniloski et al., 2021; Kliche et al., 2021; Papa et al.,. 2021; Zhu et al., 2021)
HCV	NS5A	Vps35	Retromer participates in the replication of HCV.	Yin et al., (2016)
HIV-1	Env	Vps35, Vps26	Retromer participates in the assembly of HIV-1 virions.	Groppelli et al., (2014)
HPV	L2, E6	SNX17, SNX27, Vps complex, TBC1D5	Retromer facilitates HPV to enter the cell.	(Bergant and Banks, 2013; Lipovsky et al., 2013; Pim et al., 2015; Popa et al., 2015; Xie et al., 2020)
VACV	–	WASH, FAM21	Retromer facilitates VACV to enter the cell.	Hsiao et al., (2015)
HVS	Tip	Vps35	Tip inhibits the activity of retromer, which in turn downregulates the level of CD4 on the cell surface.	Kingston et al., (2011)
AAV	–	Vps29, Vps35, SNX5	Retromer facilitates AAV to enter the cell.	Nonnenmacher et al., (2015)
IAV	M2	SNX complex	M2 is transported to TGN via retromer and escapes degradation.	Bhowmick et al., (2017)
HRSV	M, N, F	SNX2, Vps26	Retromer facilitates HRSV to enter the cell.	Cardoso et al., (2020)
HCMV	UL35	SNX5	Retromer participates in the assembly of HCMV virions.	Maschkowitz et al., (2018)
SINV, CHIKV, MAYV	nsP2	SNX5	SNX5 affects the replication pathway of SINV, CHIKV and MAYV.	Schuchman et al., (2018)
HTLV	TAX-1	SNX27	The interaction between SNX27 and TAX-1 alters GLUT1 localization.	Al-Saleem et al., (2019)

SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; *S*, spike; *NSP*, non-structural protein; *WASH*, Wiskott-Aldrich syndrome protein and SCAR homologue; *SNX*, sorting nexin; *Vps*, vacuolar protein sorting; *ACE2*, angiotensin-converting enzyme 2; *HCV*, hepatitis C virus; *HIV*, human immunodeficiency virus; *HPV*, human papillomavirus; *VACV*, vaccinia virus; *HVS*, Herpesvirus saimiri; *Tip*, tyrosine kinase-interacting protein; *AAV*, adeno-associated virus; *IAV*, influenza A virus; *TGN*, trans-Golgi network; *HRSV*, human respiratory syncytial virus; *HCMV*, human cytomegalovirus; *SINV*, Sindbis virus; *CHIKV*, chikungunya virus; *MAYV*, Mayaro virus; *HTLV*, human T-cell leukemia virus; *GLUT1*, human glucose transporter 1.

associates with a variety of virus proteins to affect virus entry and replication (Table 1). For some viruses, the role of retromer/SNXs is fairly well understood, and in others the data just hint at a role. In several cases, SNX proteins interact with virus proteins. It is possible that retromer/SNXs is also involved in the life cycle of those viruses.

There are two transport routes regulated by retromer/SNXs: (1) retrograde transport, in which retromer/SNXs transports protein cargo from the endosome to TGN (Fig. 1); (2) endocytic recycling pathway, in which retromer/SNXs transports proteins from the recycling endosome to the cell surface (Fig. 1). Endocytic pathway is widely hijacked by viruses beneficial for their infection. Key components of host cellular machineries that function at endosomes including retromer components will likely be involved in viral infection. HCV, SINV, CHIKV, MAYV, HIV, HPV, AAV, IAV, HRSV and HCMV use the retrograde transport pathway of retromer/SNXs to promote infection (Fig. 3). In addition, retromer and SNXs regulate the recycling of many cell surface proteins, some of which are virus receptors. For instance, SARS-CoV-2 receptor ACE2 is a SNX27-retromer cargo. Therefore, retromer and SNXs may regulate virus infection by controlling the cell surface levels of virus receptors. SARS-CoV-2, VACV, HVS and HTLV proteins manipulate the recycling pathway of retromer (Fig. 3). Thus retromer and SNXs could regulate viral infection directly or indirectly. Additional, retromer and SNXs play important roles in other pathogens such as bacteria and parasites. Thus, retromer and SNXs could be potential drug targets to combat infectious diseases.

Conflict of interest

The authors declare that there are no conflicts of interest.

Acknowledgments

This work was supported by grants from National Natural Science Foundation of China (81871663 and 82072270), Undergraduate Science and Technology Innovation Plan of International Class of Clinical Medicine in Shandong First Medical University (ZYKC2019-016), and Academic promotion programme of Shandong First Medical University (2019LJ001). Thanks for the insightful comments from the reviewers.

References

Al-Saleem, J., Dirksen, W.P., Martinez, M.P., Shkriabai, N., Kvaratskhelia, M., Ratner, L., Green, P.L., 2019. HTLV-1 Tax-1 interacts with SNX27 to regulate cellular localization of the HTLV-1 receptor molecule, GLUT1. PLoS One 14, e0214059.
Amako, Y., Sarkeshik, A., Hotta, H., Yates 3rd, J., Siddiqui, A., 2009. Role of oxysterol binding protein in hepatitis C virus infection. J. Virol. 83, 9237–9246.
Arighi, C.N., Hartnell, L.M., Aguilar, R.C., Haft, C.R., Bonifacino, J.S., 2004. Role of the mammalian retromer in sorting of the cation-independent mannose 6-phosphate receptor. J. Cell Biol. 165, 123–133.
Attar, N., Cullen, P.J., 2010. The retromer complex. Adv. Enzym. Regul. 50, 216–236.
Aydin, I., Villalonga-Planells, R., Greune, L., Bronnimann, M.P., Calton, C.M., Becker, M., Lai, K.Y., Campos, S.K., Schmidt, M.A., Schelhaas, M., 2017. A central region in the minor capsid protein of papillomaviruses facilitates viral genome tethering and membrane penetration for mitotic nuclear entry. PLoS Pathog. 13, e1006308.
Bantel-Schaal, U., Hub, B., Kartenbeck, J., 2002. Endocytosis of adeno-associated virus type 5 leads to accumulation of virus particles in the Golgi compartment. J. Virol. 76, 2340–2349.
Bartuzi, P., Billadeau, D.D., Favier, R., Rong, S., Dekker, D., Fedoseienko, A., Fieten, H., Wijers, M., Levels, J.H., Huijkman, N., Kloosterhuis, N., van der Molen, H., Brufau, G., Groen, A.K., Elliott, A.M., Kuivenhoven, J.A., Plecko, B., Grangl, G., McGaughran, J., Horton, J.D., Burstein, E., Hofker, M.H., van de Sluis, B., 2016. CCC- and WASH-mediated endosomal sorting of LDLR is required for normal clearance of circulating LDL. Nat. Commun. 7, 10961.

Bayliss, R., Wheeldon, J., Caucheteux, S.M., Niessen, C.M., Piguet, V., 2020. Identification of host trafficking genes required for HIV-1 virological synapse formation in dendritic cells. J. Virol. 94, e01597-19.
Belenkaya, T.Y., Wu, Y., Tang, X., Zhou, B., Cheng, L., Sharma, Y.V., Yan, D., Selva, E.M., Lin, X., 2008. The retromer complex influences Wnt secretion by recycling wntless from endosomes to the trans-Golgi network. Dev. Cell 14, 120–131.
Benfield, C.T.O., Ren, H., Lucas, S.J., Bahsoun, B., Smith, G.L., 2013. Vaccinia virus protein K7 is a virulence factor that alters the acute immune response to infection. J. Gen. Virol. 94, 1647–1657.
Bergant, M., Banks, L., 2013. SNX17 facilitates infection with diverse papillomavirus types. J. Virol. 87, 1270–1273.
Bergant Marusic, M., Ozbun, M.A., Campos, S.K., Myers, M.P., Banks, L., 2012. Human papillomavirus L2 facilitates viral escape from late endosomes via sorting nexin 17. Traffic 13, 455–467.
Berlioz-Torrent, C., Shacklett, B.L., Erdtmann, L., Delamarre, L., Bouchaert, I., Sonigo, P., Dokhelar, M.C., Benarous, R., 1999. Interactions of the cytoplasmic domains of human and simian retroviral transmembrane proteins with components of the clathrin adaptor complexes modulate intracellular and cell surface expression of envelope glycoproteins. J. Virol. 73, 1350–1361.
Bhowmick, S., Chakravarty, C., Sellathamby, S., Lal, S.K., 2017. The influenza A virus matrix protein 2 undergoes retrograde transport from the endoplasmic reticulum into the cytoplasm and bypasses cytoplasmic proteasomal degradation. Arch. Virol. 162, 919–929.
Bianco, A., Reghellin, V., Donnici, L., Fenu, S., Alvarez, R., Baruffa, C., Peri, F., Pagani, M., Abrignani, S., Neddermann, P., De Francesco, R., 2012. Metabolism of phosphatidylinositol 4-kinase IIIalpha-dependent PI4P Is subverted by HCV and is targeted by a 4-anilino quinazoline with antiviral activity. PLoS Pathog. 8, e1002576.
Bonifacino, J.S., Hurley, J.H., 2008. Retromer. Curr. Opin. Cell Biol. 20, 427–436.
Bonifacino, J.S., Rojas, R., 2006. Retrograde transport from endosomes to the trans-Golgi network. Nat. Rev. Mol. Cell Biol. 7, 568–579.
Borg Distefano, M., Hofstad Haugen, L., Wang, Y., Perdreau-Dahl, H., Kjos, I., Jia, D., Morth, J.P., Neefjes, J., Bakke, O., Progida, C., 2018. TBC1D5 controls the GTPase cycle of Rab7b. J. Cell Sci. 131, jcs216630.
Bronnimann, M.P., Chapman, J.A., Park, C.K., Campos, S.K., 2013. A transmembrane domain and GxxxG motifs within L2 are essential for papillomavirus infection. J. Virol. 87, 464–473.
Bugarcic, A., Zhe, Y., Kerr, M.C., Griffin, J., Collins, B.M., Teasdale, R.D., 2011. Vps26A and Vps26B subunits define distinct retromer complexes. Traffic 12, 1759–1773.
Bujny, M.V., Popoff, V., Johannes, L., Cullen, P.J., 2007. The retromer component sorting nexin-1 is required for efficient retrograde transport of Shiga toxin from early endosome to the trans Golgi network. J. Cell Sci. 120, 2010–2021.
Burd, C., Cullen, P.J., 2014. Retromer: a master conductor of endosome sorting. Cold Spring Harbor Perspect. Biol. 6, a016774.
Byland, R., Vance, P.J., Hoxie, J.A., Marsh, M., 2007. A conserved dileucine motif mediates clathrin and AP-2-dependent endocytosis of the HIV-1 envelope protein. Mol. Biol. Cell 18, 414–425.
Cai, L., Loo, L.S., Atlashkin, V., Hanson, B.J., Hong, W., 2011. Deficiency of sorting nexin 27 (SNX27) leads to growth retardation and elevated levels of N-methyl-D-aspartate receptor 2C (NR2C). Mol. Cell Biol. 31, 1734–1747.
Cardoso, R.S., Tavares, L.A., Jesus, B.L.S., Criado, M.F., de Carvalho, A.N., Souza, J.P., Bedi, S., de Souza, M.M., Silva, M.L., Lanfredi, G.P., Vitti, B.C., Scudero, O.B., Faca, V.M., Ono, A., Ventura, A.M., daSilva, L.L.P., Arruda, E., 2020. Host retromer protein sorting nexin 2 interacts with human respiratory syncytial virus structural proteins and is required for efficient viral production. mBio 11, e01869-20.
Carlton, J., Bujny, M., Peter, B.J., Oorschot, V.M., Rutherford, A., Mellor, H., Klumperman, J., McMahon, H.T., Cullen, P.J., 2004. Sorting nexin-1 mediates tubular endosome-to-TGN transport through coincidence sensing of high- curvature membranes and 3-phosphoinositides. Curr. Biol. 14, 1791–1800.
Cattin-Ortolá, J., Welch, L.G., Maslen, S.L., Papa, G., James, L.C., Munro, S., 2021. Sequences in the cytoplasmic tail of SARS-CoV-2 Spike facilitate expression at the cell surface and syncytia formation. Nat. Commun. 12, 5333.
Chattopadhyay, A., Wang, E., Seymour, R., Weaver, S.C., Rose, J.K., 2013. A chimeric vesiculo/alphavirus is an effective alphavirus vaccine. J. Virol. 87, 395–402.
Checkley, M.A., Luttge, B.G., Freed, E.O., 2011. HIV-1 envelope glycoprotein biosynthesis, trafficking, and incorporation. J. Mol. Biol. 410, 582–608.
Cheung, T.K., Poon, L.L., 2007. Biology of influenza a virus. Ann. N. Y. Acad. Sci. 1102, 1–25.
Choy, R.W., Park, M., Temkin, P., Herring, B.E., Marley, A., Nicoll, R.A., von Zastrow, M., 2014. Retromer mediates a discrete route of local membrane delivery to dendrites. Neuron 82, 55–62.
Cullen, P.J., 2008. Endosomal sorting and signalling: an emerging role for sorting nexins. Nat. Rev. Mol. Cell Biol. 9, 574–582.
Cullen, P.J., Korswagen, H.C., 2011. Sorting nexins provide diversity for retromer-dependent trafficking events. Nat. Cell Biol. 14, 29–37.
Daniloski, Z., Jordan, T.X., Wessels, H.H., Hoagland, D.A., Kasela, S., Legut, M., Maniatis, S., Mimitou, E.P., Lu, L., Geller, E., Danziger, O., Rosenberg, B.R., Phatnani, H., Smibert, P., Lappalainen, T., tenOever, B.R., Sanjana, N.E., 2021. Identification of required host factors for SARS-CoV-2 infection in human cells. Cell 184, 92–105.
Das, S., Pellett, P.E., 2011. Spatial relationships between markers for secretory and endosomal machinery in human cytomegalovirus-infected cells versus those in uninfected cells. J. Virol. 85, 5864–5879.
Das, S., Vasanji, A., Pellett, P.E., 2007. Three-dimensional structure of the human cytomegalovirus cytoplasmic virion assembly complex includes a reoriented secretory apparatus. J. Virol. 81, 11861–11869.
Davison, A.J., Eberle, R., Ehlers, B., Hayward, G.S., McGeoch, D.J., Minson, A.C., Pellett, P.E., Roizman, B., Studdert, M.J., Thiry, E., 2009. The order Herpesvirales. Arch. Virol. 154, 171–177.
Day, P.M., Thompson, C.D., Schowalter, R.M., Lowy, D.R., Schiller, J.T., 2013. Identification of a role for the trans-Golgi network in human papillomavirus 16 pseudovirus infection. J. Virol. 87, 3862–3870.
Day, P.M., Weisberg, A.S., Thompson, C.D., Hughes, M.M., Pang, Y.Y., Lowy, D.R., Schiller, J.T., 2019. Human papillomavirus 16 capsids mediate nuclear entry during infection. J. Virol. 93, e00454-19.
DiGiuseppe, S., Luszczek, W., Keiffer, T.R., Bienkowska-Haba, M., Guion, L.G., Sapp, M.J., 2016. Incoming human papillomavirus type 16 genome resides in a vesicular compartment throughout mitosis. Proc. Natl. Acad. Sci. U. S. A. 113, 6289–6294.
Fjorback, A.W., Seaman, M., Gustafsen, C., Mehmedbasic, A., Gokool, S., Wu, C., Militz, D., Schmidt, V., Madsen, P., Nyengaard, J.R., Willnow, T.E., Christensen, E.I., Mobley, W.B., Nykjaer, A., Andersen, O.M., 2012. Retromer binds the FANSHY sorting motif in SorLA to regulate amyloid precursor protein sorting and processing. J. Neurosci. 32, 1467–1480.
Gallon, M., Clairfeuille, T., Steinberg, F., Mas, C., Ghai, R., Sessions, R.B., Teasdale, R.D., Collins, B.M., Cullen, P.J., 2014. A unique PDZ domain and arrestin-like fold interaction reveals mechanistic details of endocytic recycling by SNX27-retromer. Proc. Natl. Acad. Sci. U. S. A. 111, E3604–E3613.
Ganti, K., Massimi, P., Manzo-Merino, J., Tomaic, V., Pim, D., Playford, M.P., Lizano, M., Roberts, S., Kranjec, C., Doorbar, J., Banks, L., 2016a. Interaction of the human papillomavirus E6 oncoprotein with sorting nexin 27 modulates endocytic cargo transport pathways. PLoS Pathog. 12, e1005854.
Ganti, K., Massimi, P., Manzo-Merino, J., Tomaić, V., Pim, D., Playford, M.P., Lizano, M., Roberts, S., Kranjec, C., Doorbar, J., Banks, L., 2016b. Interaction of the human papillomavirus E6 oncoprotein with sorting nexin 27 modulates endocytic cargo transport pathways. PLoS Pathog. 12, e1005854.
Ghai, R., Bugarcic, A., Liu, H., Norwood, S.J., Skeldal, S., Coulson, E.J., Li, S.S., Teasdale, R.D., Collins, B.M., 2013. Structural basis for endosomal trafficking of diverse transmembrane cargos by PX-FERM proteins. Proc. Natl. Acad. Sci. U. S. A. 110, E643–E652.
Goncalves, D.U., Proietti, F.A., Ribas, J.G., Araujo, M.G., Pinheiro, S.R., Guedes, A.C., Carneiro-Proietti, A.B., 2010. Epidemiology, treatment, and prevention of human T-cell leukemia virus type 1-associated diseases. Clin. Microbiol. Rev. 23, 577–589.
Griffin, C.T., Trejo, J., Magnuson, T., 2005. Genetic evidence for a mammalian retromer complex containing sorting nexins 1 and 2. Proc. Natl. Acad. Sci. U. S. A. 102, 15173–15177.
Griffin, L.M., Cicchini, L., Xu, T., Pyeon, D., 2014. Human keratinocyte cultures in the investigation of early steps of human papillomavirus infection. Methods Mol. Biol. 1195, 219–238.
Grimm, D., Kay, M.A., 2003. From virus evolution to vector revolution: use of naturally occurring serotypes of adeno-associated virus (AAV) as novel vectors for human gene therapy. Curr. Gene Ther. 3, 281–304.
Groppelli, E., Len, A.C., Granger, L.A., Jolly, C., 2014. Retromer regulates HIV-1 envelope glycoprotein trafficking and incorporation into virions. PLoS Pathog. 10, e1004518.
Guerra, F., Bucci, C., 2016. Multiple roles of the small GTPase Rab7. Cells 5, 34.
Haft, C.R., de la Luz Sierra, M., Bafford, R., Lesniak, M.A., Barr, V.A., Taylor, S.I., 2000. Human orthologs of yeast vacuolar protein sorting proteins Vps26, 29, and 35: assembly into multimeric complexes. Mol. Biol. Cell 11, 4105–4116.
Harbour, M.E., Breusegem, S.Y., Seaman, M.N., 2012. Recruitment of the endosomal WASH complex is mediated by the extended 'tail' of Fam21 binding to the retromer protein Vps35. Biochem. J. 442, 209–220.
Harrison, K., Haga, I.R., Pechenick Jowers, T., Jasim, S., Cintrat, J.C., Gillet, D., Schmitt-John, T., Digard, P., Beard, P.M., 2016. Vaccinia virus uses retromer-independent cellular retrograde transport pathways to facilitate the wrapping of intracellular mature virions during virus morphogenesis. J. Virol. 90, 10120–10132.
Harrison, M.S., Hung, C.S., Liu, T.T., Christiano, R., Walther, T.C., Burd, C.G., 2014. A mechanism for retromer endosomal coat complex assembly with cargo. Proc. Natl. Acad. Sci. U. S. A. 111, 267–272.
Henkel, J.R., Apodaca, G., Altschuler, Y., Hardy, S., Weisz, O.A., 1998. Selective perturbation of apical membrane traffic by expression of influenza M2, an acid-activated ion channel, in polarized madin-darby canine kidney cells. Mol. Biol. Cell 9, 2477–2490.
Hong, Z., Yang, X., Yang, G., Zhang, L., 2014. Hepatitis C virus NS5A competes with PI4KB for binding to ACBD3 in a genotype-dependent manner. Antivir. Res. 107, 50–55.
Hsiao, J.C., Chu, L.W., Lo, Y.T., Lee, S.P., Chen, T.J., Huang, C.Y., Ping, Y.H., Chang, W., 2015. Intracellular transport of vaccinia virus in HeLa cells requires WASH-VPEF/FAM21-Retromer complexes and recycling molecules Rab11 and Rab22. J. Virol. 89, 8365–8382.
Hsu, N.Y., Ilnytska, O., Belov, G., Santiana, M., Chen, Y.H., Takvorian, P.M., Pau, C., van der Schaar, H., Kaushik-Basu, N., Balla, T., Cameron, C.E., Ehrenfeld, E., van Kuppeveld, F.J., Altan-Bonnet, N., 2010. Viral reorganization of the secretory pathway generates distinct organelles for RNA replication. Cell 141, 799–811.
Huang, C.Y., Lu, T.Y., Bair, C.H., Chang, Y.S., Jwo, J.K., Chang, W., 2008. A novel cellular protein, VPEF, facilitates vaccinia virus penetration into HeLa cells through fluid phase endocytosis. J. Virol. 82, 7988–7999.
Jia, D., Gomez, T.S., Billadeau, D.D., Rosen, M.K., 2012. Multiple repeat elements within the FAM21 tail link the WASH actin regulatory complex to the retromer. Mol. Biol. Cell 23, 2352–2361.
Jia, D., Zhang, J.S., Li, F., Wang, J., Deng, Z., White, M.A., Osborne, D.G., Phillips-Krawczak, C., Gomez, T.S., Li, H., Singla, A., Burstein, E., Billadeau, D.D., Rosen, M.K., 2016. Structural and mechanistic insights into regulation of the retromer coat by TBC1d5. Nat. Commun. 7, 13305.

Jimenez-Orgaz, A., Kvainickas, A., Nagele, H., Denner, J., Eimer, S., Dengjel, J., Steinberg, F., 2018. Control of RAB7 activity and localization through the retromer-TBC1D5 complex enables RAB7-dependent mitophagy. EMBO J. 37, 235–254.
Johannes, L., Popoff, V., 2008. Tracing the retrograde route in protein trafficking. Cell 135, 1175–1187.
Johnson, J.S., Gentzsch, M., Zhang, L., Ribeiro, C.M., Kantor, B., Kafri, T., Pickles, R.J., Samulski, R.J., 2011. AAV exploits subcellular stress associated with inflammation, endoplasmic reticulum expansion, and misfolded proteins in models of cystic fibrosis. PLoS Pathog. 7, e1002053.
Keiser, N.W., Yan, Z., Zhang, Y., Lei-Butters, D.C., Engelhardt, J.F., 2011. Unique characteristics of AAV1, 2, and 5 viral entry, intracellular trafficking, and nuclear import define transduction efficiency in HeLa cells. Hum. Gene Ther. 22, 1433–1444.
Kerr, M.C., Bennetts, J.S., Simpson, F., Thomas, E.C., Flegg, C., Gleeson, P.A., Wicking, C., Teasdale, R.D., 2005. A novel mammalian retromer component, Vps26B. Traffic 6, 991–1001.
Khan, I., Katikaneni, D.S., Han, Q., Sanchez-Felipe, L., Hanada, K., Ambrose, R.L., Mackenzie, J.M., Konan, K.V., 2014. Modulation of hepatitis C virus genome replication by glycosphingolipids and four-phosphate adaptor protein 2. J. Virol. 88, 12276–12295.
Kingston, D., Chang, H., Ensser, A., Lee, H.R., Lee, J., Lee, S.H., Jung, J.U., Cho, N.H., 2011. Inhibition of retromer activity by herpesvirus saimiri tip leads to CD4 downregulation and efficient T cell transformation. J. Virol. 85, 10627–10638.
Kliche, J., Kuss, H., Ali, M., Ivarsson, Y., 2021. Cytoplasmic short linear motifs in ACE2 and integrin beta3 link SARS-CoV-2 host cell receptors to mediators of endocytosis and autophagy. Sci. Signal. 14, eabf1117.
Kuwahara, T., Inoue, K., D'Agati, V.D., Fujimoto, T., Eguchi, T., Saha, S., Wolozin, B., Iwatsubo, T., Abeliovich, A., 2016. LRRK2 and RAB7L1 coordinately regulate axonal morphology and lysosome integrity in diverse cellular contexts. Sci. Rep. 6, 29945.
Kvainickas, A., Jimenez-Orgaz, A., Nägele, H., Hu, Z., Dengjel, J., Steinberg, F., 2017. Cargo-selective SNX-BAR proteins mediate retromer trimer independent retrograde transport. J. Cell Biol. 216, 3677–3693.
Lee, S., Chang, J., Blackstone, C., 2016. FAM21 directs SNX27-retromer cargoes to the plasma membrane by preventing transport to the Golgi apparatus. Nat. Commun. 7, 10939.
Li, H., Koo, Y., Mao, X., Sifuentes-Dominguez, L., Morris, L.L., Jia, D., Miyata, N., Faulkner, R.A., van Deursen, J.M., Vooijs, M., Billadeau, D.D., van de Sluis, B., Cleaver, O., Burstein, E., 2015. Endosomal sorting of Notch receptors through COMMD9-dependent pathways modulates Notch signaling. J. Cell Biol. 211, 605–617.
Li, H., Yang, X., Yang, G., Hong, Z., Zhou, L., Yin, P., Xiao, Y., Chen, L., Chung, R.T., Zhang, L., 2014. Hepatitis C virus NS5A hijacks ARFGAP1 to maintain a phosphatidylinositol 4-phosphate-enriched microenvironment. J. Virol. 88, 5956–5966.
Li, Y., Zhang, L., Ke, Y., 2017. Cellular interactome analysis of vaccinia virus K7 protein identifies three transport machineries as binding partners for K7. Virus Gene. 53, 814–822.
Lim, Y.S., Hwang, S.B., 2011. Hepatitis C virus NS5A protein interacts with phosphatidylinositol 4-kinase type IIIalpha and regulates viral propagation. J. Biol. Chem. 286, 11290–11298.
Lipovsky, A., Erden, A., Kanaya, E., Zhang, W., Crite, M., Bradfield, C., MacMicking, J., DiMaio, D., Schoggins, J.W., Iwasaki, A., 2017. The cellular endosomal protein stannin inhibits intracellular trafficking of human papillomavirus during virus entry. J. Gen. Virol. 98, 2821–2836.
Lipovsky, A., Popa, A., Pimienta, G., Wyler, M., Bhan, A., Kuruvilla, L., Guie, M.A., Poffenberger, A.C., Nelson, C.D., Atwood, W.J., DiMaio, D., 2013. Genome-wide siRNA screen identifies the retromer as a cellular entry factor for human papillomavirus. Proc. Natl. Acad. Sci. U. S. A. 110, 7452–7457.
Liu, T.T., Gomez, T.S., Sackey, B.K., Billadeau, D.D., Burd, C.G., 2012. Rab GTPase regulation of retromer-mediated cargo export during endosome maturation. Mol. Biol. Cell 23, 2505–2515.
Lucas, M., Gershlick, D.C., Vidaurrazaga, A., Rojas, A.L., Bonifacino, J.S., Hierro, A., 2016. Structural mechanism for cargo recognition by the retromer complex. Cell 167, 1623–1635 e1614.
Maschkowitz, G., Gartner, S., Hofmann-Winkler, H., Fickenscher, H., Winkler, M., 2018. Interaction of human cytomegalovirus tegument proteins ppUL35 and ppUL35A with sorting nexin 5 regulates glycoprotein B (gpUL55) localization. J. Virol. 92, e00013–18.
Mercer, J., Helenius, A., 2008. Vaccinia virus uses macropinocytosis and apoptotic mimicry to enter host cells. Science 320, 531–535.
Muscolino, E., Schmitz, R., Loroch, S., Caragliano, E., Schneider, C., Rizzato, M., Kim, Y.H., Krause, E., Juranić Lisnić, V., Sickmann, A., Reimer, R., Ostermann, E., Brune, W., 2020. Herpesviruses induce aggregation and selective autophagy of host signalling proteins NEMO and RIPK1 as an immune-evasion mechanism. Nat. Microbiol. 5, 331–342.
Nair, H., Brooks, W.A., Katz, M., Roca, A., Berkley, J.A., Madhi, S.A., Simmerman, J.M., Gordon, A., Sato, M., Howie, S., Krishnan, A., Ope, M., Lindblade, K.A., Carosone-Link, P., Lucero, M., Ochieng, W., Kamimoto, L., Dueger, E., Bhat, N., Vong, S., Theodoratou, E., Chittaganpitch, M., Chimah, O., Balmaseda, A., Buchy, P., Harris, E., Evans, V., Katayose, M., Gaur, B., O'Callaghan-Gordo, C., Goswami, D., Arvelo, W., Venter, M., Briese, T., Tokarz, R., Widdowson, M.A., Mounts, A.W., Breiman, R.F., Feikin, D.R., Klugman, K.P., Olsen, S.J., Gessner, B.D., Wright, P.F., Rudan, I., Broor, S., Simoes, E.A., Campbell, H., 2011. Global burden of respiratory infections due to seasonal influenza in young children: a systematic review and meta-analysis. Lancet 378, 1917–1930.
Niu, Y., Zhang, C., Sun, Z., Hong, Z., Li, K., Sun, D., Yang, Y., Tian, C., Gong, W., Liu, J.J., 2013. PtdIns(4)P regulates retromer-motor interaction to facilitate dynein-cargo dissociation at the trans-Golgi network. Nat. Cell Biol. 15, 417–429.
Nonnenmacher, M., Weber, T., 2011. Adeno-associated virus 2 infection requires endocytosis through the CLIC/GEEC pathway. Cell Host Microbe 10, 563–576.
Nonnenmacher, M.E., Cintrat, J.C., Gillet, D., Weber, T., 2015. Syntaxin 5-dependent retrograde transport to the trans-Golgi network is required for adeno-associated virus transduction. J. Virol. 89, 1673–1687.
Pajusola, K., Gruchala, M., Joch, H., Luscher, T.F., Yla-Herttuala, S., Bueler, H., 2002. Cell-type-specific characteristics modulate the transduction efficiency of adeno-associated virus type 2 and restrain infection of endothelial cells. J. Virol. 76, 11530–11540.
Papa, G., Mallery, D.L., Albecka, A., Welch, L.G., Cattin-Ortola, J., Luptak, J., Paul, D., McMahon, H.T., Goodfellow, I.G., Carter, A., Munro, S., James, L.C., 2021. Furin cleavage of SARS-CoV-2 Spike promotes but is not essential for infection and cell-cell fusion. PLoS Pathog. 17, e1009246.
Phillips-Krawczak, C.A., Singla, A., Starokadomskyy, P., Deng, Z., Osborne, D.G., Li, H., Dick, C.J., Gomez, T.S., Koenecke, M., Zhang, J.S., Dai, H., Sifuentes-Dominguez, L.F., Geng, L.N., Kaufmann, S.H., Hein, M.Y., Wallis, M., McGaughran, J., Gecz, J., Sluis, B., Billadeau, D.D., Burstein, E., 2015. COMMD1 is linked to the WASH complex and regulates endosomal trafficking of the copper transporter ATP7A. Mol. Biol. Cell 26, 91–103.
Pim, D., Broniarczyk, J., Bergant, M., Playford, M.P., Banks, L., 2015. A novel PDZ domain interaction mediates the binding between human papillomavirus 16 L2 and sorting nexin 27 and modulates virion trafficking. J. Virol. 89, 10145–10155.
Pim, D., Broniarczyk, J., Siddiqa, A., Massimi, P., Banks, L., 2021. Human papillomavirus 16 L2 recruits both retromer and retriever complexes during retrograde trafficking of the viral genome to the cell nucleus. J. Virol. 95, e02068, 20.
Poiesz, B.J., Ruscetti, F.W., Gazdar, A.F., Bunn, P.A., Minna, J.D., Gallo, R.C., 1980. Detection and isolation of type C retrovirus particles from fresh and cultured lymphocytes of a patient with cutaneous T-cell lymphoma. Proc. Natl. Acad. Sci. U. S. A. 77, 7415–7419.
Popa, A., Zhang, W., Harrison, M.S., Goodner, K., Kazakov, T., Goodwin, E.C., Lipovsky, A., Burd, C.G., DiMaio, D., 2015. Direct binding of retromer to human papillomavirus type 16 minor capsid protein L2 mediates endosome exit during viral infection. PLoS Pathog. 11, e1004699.
Popovic, D., Akutsu, M., Novak, I., Harper, J.W., Behrends, C., Dikic, I., 2012. Rab GTPase-activating proteins in autophagy: regulation of endocytic and autophagy pathways by direct binding to human ATG8 modifiers. Mol. Cell Biol. 32, 1733–1744.
Popovic, D., Dikic, I., 2014. TBC1D5 and the AP2 complex regulate ATG9 trafficking and initiation of autophagy. EMBO Rep. 15, 392–401.
Ravussin, A., Brech, A., Tooze, S.A., Stenmark, H., 2021. The phosphatidylinositol 3-phosphate-binding protein SNX4 controls ATG9A recycling and autophagy. J. Cell Sci. 134, jcs250670.
Reiss, S., Rebhan, I., Backes, P., Romero-Brey, I., Erfle, H., Matula, P., Kaderali, L., Poenisch, M., Blankenburg, H., Hiet, M.S., Longerich, T., Diehl, S., Ramirez, F., Balla, T., Rohr, K., Kaul, A., Buhler, S., Pepperkok, R., Lengauer, T., Albrecht, M., Eils, R., Schirmacher, P., Lohmann, V., Bartenschlager, R., 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.
Rojas, R., van Vlijmen, T., Mardones, G.A., Prabhu, Y., Rojas, A.L., Mohammed, S., Heck, A.J., Raposo, G., van der Sluijs, P., Bonifacino, J.S., 2008. Regulation of retromer recruitment to endosomes by sequential action of Rab5 and Rab7. J. Cell Biol. 183, 513–526.
Schelhaas, M., Shah, B., Holzer, M., Blattmann, P., Kuhling, L., Day, P.M., Schiller, J.T., Helenius, A., 2012. Entry of human papillomavirus type 16 by actin-dependent, clathrin- and lipid raft-independent endocytosis. PLoS Pathog. 8, e1002657.
Schroder, M., Baran, M., Bowie, A.G., 2008. Viral targeting of DEAD box protein 3 reveals its role in TBK1/IKKepsilon-mediated IRF activation. EMBO J. 27, 2147–2157.
Schuchman, R., Kilianski, A., Piper, A., Vancini, R., Ribeiro, J.M.C., Sprague, T.R., Nasar, F., Boyd, G., Hernandez, R., Glaros, T., 2018. Comparative characterization of the Sindbis virus proteome from mammalian and invertebrate hosts identifies nsP2 as a component of the virion and sorting nexin 5 as a significant host factor for alphavirus replication. J. Virol. 92, e00694, 18.
Seaman, M.N., 2004. Cargo-selective endosomal sorting for retrieval to the Golgi requires retromer. J. Cell Biol. 165, 111–122.
Seaman, M.N., 2005. Recycle your receptors with retromer. Trends Cell Biol. 15, 68–75.
Seaman, M.N., 2007. Identification of a novel conserved sorting motif required for retromer-mediated endosome-to-TGN retrieval. J. Cell Sci. 120, 2378–2389.
Seaman, M.N., 2012. The retromer complex - endosomal protein recycling and beyond. J. Cell Sci. 125, 4693–4702.
Seaman, M.N., Harbour, M.E., Tattersall, D., Read, E., Bright, N., 2009. Membrane recruitment of the cargo-selective retromer subcomplex is catalysed by the small GTPase Rab7 and inhibited by the Rab-GAP TBC1D5. J. Cell Sci. 122, 2371–2382.
Seaman, M.N., McCaffery, J.M., Emr, S.D., 1998. A membrane coat complex essential for endosome-to-Golgi retrograde transport in yeast. J. Cell Biol. 142, 665–681.

Shepard, C.W., Finelli, L., Alter, M.J., 2005. Global epidemiology of hepatitis C virus infection. Lancet Infect. Dis. 5, 558–567.
Shi, H., Rojas, R., Bonifacino, J.S., Hurley, J.H., 2006. The retromer subunit Vps26 has an arrestin fold and binds Vps35 through its C-terminal domain. Nat. Struct. Mol. Biol. 13, 540–548.
Siddiqa, A., Massimi, P., Pim, D., Broniarczyk, J., Banks, L., 2018. Human papillomavirus 16 infection induces VAP-dependent endosomal tubulation. J. Virol. 92, e01514–e01517.
Simonetti, B., Danson, C.M., Heesom, K.J., Cullen, P.J., 2017. Sequence-dependent cargo recognition by SNX-BARs mediates retromer-independent transport of CI-MPR. J. Cell Biol. 216, 3695–3712.
Stroupe, C., 2018. This is the end: regulation of Rab7 nucleotide binding in endolysosomal trafficking and autophagy. Front. Cell Dev. Biol. 6, 129.
Tabuchi, M., Yanatori, I., Kawai, Y., Kishi, F., 2010. Retromer-mediated direct sorting is required for proper endosomal recycling of the mammalian iron transporter DMT1. J. Cell Sci. 123, 756–766.
Tai, A.W., Salloum, S., 2011. The role of the phosphatidylinositol 4-kinase PI4KA in hepatitis C virus-induced host membrane rearrangement. PLoS One 6, e26300.
Taubenberger, J.K., Morens, D.M., 2010. Influenza: the once and future pandemic. Publ. Health Rep. 125 (Suppl. 3), 16–26.
Temkin, P., Lauffer, B., Jäger, S., Cimermancic, P., Krogan, N.J., von Zastrow, M., 2011. SNX27 mediates retromer tubule entry and endosome-to-plasma membrane trafficking of signalling receptors. Nat. Cell Biol. 13, 715–721.
Van Vliet, K., Mohamed, M.R., Zhang, L., Villa, N.Y., Werden, S.J., Liu, J., McFadden, G., 2009. Poxvirus proteomics and virus-host protein interactions. Microbiol. Mol. Biol. Rev. 73, 730–749.
Wang, H., Perry, J.W., Lauring, A.S., Neddermann, P., De Francesco, R., Tai, A.W., 2014. Oxysterol-binding protein is a phosphatidylinositol 4-kinase effector required for HCV replication membrane integrity and cholesterol trafficking. Gastroenterology 146, 1373–1385 e1371-1311.
Wassmer, T., Attar, N., Bujny, M.V., Oakley, J., Traer, C.J., Cullen, P.J., 2007. A loss-of-function screen reveals SNX5 and SNX6 as potential components of the mammalian retromer. J. Cell Sci. 120, 45–54.
Weinberg, M.S., Nicolson, S., Bhatt, A.P., McLendon, M., Li, C., Samulski, R.J., 2014. Recombinant adeno-associated virus utilizes cell-specific infectious entry mechanisms. J. Virol. 88, 12472–12484.
Wyss, S., Berlioz-Torrent, C., Boge, M., Blot, G., Honing, S., Benarous, R., Thali, M., 2001. The highly conserved C-terminal dileucine motif in the cytosolic domain of the human immunodeficiency virus type 1 envelope glycoprotein is critical for its association with the AP-1 clathrin adaptor [correction of adapter]. J. Virol. 75, 2982–2992.
Xie, J., Heim, E.N., Crite, M., DiMaio, D., 2020. TBC1D5-Catalyzed cycling of Rab7 is required for retromer-mediated human papillomavirus trafficking during virus entry. Cell Rep. 31, 107750.
Xie, J., Zhang, P., Crite, M., Lindsay, C.V., DiMaio, D., 2021. Retromer stabilizes transient membrane insertion of L2 capsid protein during retrograde entry of human papillomavirus. Sci. Adv. 7, eabh4276.
Yamane, D., McGivern, D.R., Masaki, T., Lemon, S.M., 2013. Liver injury and disease pathogenesis in chronic hepatitis C. Curr. Top. Microbiol. Immunol. 369, 263–288.
Yang, B., Jia, Y., Meng, Y., Xue, Y., Liu, K., Li, Y., Liu, S., Li, X., Cui, K., Shang, L., Cheng, T., Zhang, Z., Hou, Y., Yang, X., Yan, H., Duan, L., Tong, Z., Wu, C., Liu, Z., Gao, S., Zhuo, S., Huang, W., Gao, G.F., Qi, J., Shang, G., 2022. SNX27 suppresses SARS-CoV-2 infection by inhibiting viral lysosome/late endosome entry. Proc. Natl. Acad. Sci. U. S. A. 119, e2117576119.
Yin, P., Hong, Z., Yang, X., Chung, R.T., Zhang, L., 2016. A role for retromer in hepatitis C virus replication. Cell. Mol. Life Sci. 73, 869–881.
Yin, P., Hong, Z., Zhang, L., Ke, Y., 2017. Retromer localizes to autophagosomes during HCV replication. Virol. Sin. 32, 245–248.
Yong, X., Zhao, L., Deng, W., Sun, H., Zhou, X., Mao, L., Hu, W., Shen, X., Sun, Q., Billadeau, D.D., Xue, Y., Jia, D., 2020. Mechanism of cargo recognition by retromer-linked SNX-BAR proteins. PLoS Biol. 18, e3000631.
Yoshida, M., Miyoshi, I., Hinuma, Y., 1982. Isolation and characterization of retrovirus from cell lines of human adult T-cell leukemia and its implication in the disease. Proc. Natl. Acad. Sci. U. S. A. 79, 2031–2035.
Young, J.M., Zine El Abidine, A., Gomez-Martinez, R.A., Ozbun, M.A., 2019. The known and potential intersections of rab-GTPases in human papillomavirus infections. Front. Cell Dev. Biol. 7, 139.
Zhang, P., Monteiro da Silva, G., Deatherage, C., Burd, C., DiMaio, D., 2018. Cell-penetrating peptide mediates intracellular membrane passage of human papillomavirus L2 protein to trigger retrograde trafficking. Cell 174, 1465–1476.
Zhang, P., Moreno, R., Lambert, P.F., DiMaio, D., 2020. Cell-penetrating peptide inhibits retromer-mediated human papillomavirus trafficking during virus entry. Proc. Natl. Acad. Sci. U. S. A. 117, 6121–6128.
Zhang, Q.Y., Tan, M.S., Yu, J.T., Tan, L., 2016. The role of retromer in Alzheimer's disease. Mol. Neurobiol. 53, 4201–4209.
Zhao, L., Zhong, K., Zhao, J., Yong, X., Tong, A., Jia, D., 2021. SARS-CoV-2 spike protein harnesses SNX27-mediated endocytic recycling pathway. Med. Comm. 2, 798–809.
Zhu, Y., Feng, F., Hu, G., Wang, Y., Yu, Y., Zhu, Y., Xu, W., Cai, X., Sun, Z., Han, W., Ye, R., Qu, D., Ding, Q., Huang, X., Chen, H., Xu, W., Xie, Y., Cai, Q., Yuan, Z., Zhang, R., 2021. A genome-wide CRISPR screen identifies host factors that regulate SARS-CoV-2 entry. Nat. Commun. 12, 961.