Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
Host endomembrane recruitment for plant RNA virus replication
Romain Grangeon, Jun Jiang and Jean-François Laliberté

Although there is a significant amount of literature that deals with the identification of plant viral proteins involved in membrane remodeling and vesicle production in infected cells, there are very few investigations that report on the impact that infection has on the overall architecture and dynamics of the early secretory endomembranes. Recent investigations have shown that for some viruses the endoplasmic reticulum, Golgi bodies and other organelles are heavily recruited into virus-induced perinuclear structures. These structures are not isolated organelles and are dynamically connected to the bulk of non-modified endomembranes. They also have a functional link with peripheral motile vesicles involved in virus intracellular movement. The full molecular events that constitute a perinuclear remodeling and virion assembly are probably taking place within these structures.

Introduction
Recent advances in cell fluorescent imaging and tomography coupled to electron microscopy are bringing growing interest in understanding the architecture and role of the cellular remodeling that is taking place upon infection by viruses (for extensive reviews on the subject, refer to [1,2]). Because most investigations on cellular remodeling in plant cells have been conducted using positive-sense (+)RNA viruses, this review will mainly focus on this class of viruses. Replication by plant (+)RNA viruses, like their vertebrate homologs, leads to the formation in the infected cell of elaborate membranous, organelle-like, platforms that sustain viral RNA synthesis and cell-to-cell movement. These membrane modifications are believed to increase the local concentrations of viral and host proteins needed to produce new genomes, which probably enhance replication efficiency, and possibly to provide protection from host defense response [3]. They also act as vehicles for the egress of viral RNA for systemic infection throughout the plant (for a review on the subject, refer to [4]).

Different plant virus groups induce the formation of diverse structures from host endomembranes, both in terms of architecture and membrane/organelle origin. Endomembranes are defined here as a system of interconnected membranes that fills the cell interior and connects the cell boundary with the double membrane organelles – nucleus, plastids and mitochondria. Essentially, every single organelle found in a plant cell is targeted by one virus or another. For example, Tomato bushy stunt virus (TBSV) replicates in peroxisomes [5], Carnation Italian ringspot virus in mitochondria [6] and Turnip yellow mosaic virus in chloroplasts [7]. The significance of this organelar diversity is unknown, but specific membrane targeting appears not to be a strict requirement for efficient viral infection as replication complexes can be redirected to an alternate subcellular localization [8,9]. There are also many examples indicating that membrane remodeling is the consequence of plant viruses replicating or moving on endoplasmic reticulum (ER)-derived membranes. This results in the formation of mini-organelles referred to as spherules, vesicles or multivesicular bodies [10,11,12,13*,14,15*,16,17]. These vesicles may be single or double membrane structures that are often connected to the cytosol by a narrow neck, allowing exchange of components needed for replication [18]. The ER is a major component of the cell’s secretory pathway, which is a series of steps a cell uses to move host components to their final functional location. The secretory pathway was thus shown to be used for intracellular and intercellular viral movement [19*,20*,21*,22,23**,24,25]. Virus use of the secretory pathway not only has a morphological impact on ER, it also leads to an inhibition of protein secretion [26] and may promote specific lipid synthesis [27]. Although there is a significant amount of literature that deals with the identification of the viral proteins involved in membrane remodeling and vesicle production, there are very few investigations that report on the impact that plant virus infection has on the overall architecture and dynamics of the early secretory endomembranes. This review will look at recent works that show that Potato virus X (PVX) and Turnip mosaic virus (TuMV) infections lead to endomembrane recruitment into large perinuclear globular structures that are functionally linked to smaller peripherally located motile vesicles that ultimately become associated with plasmodesmata. This connection would provide an...
assembly line for viral genome replication and virus egress into neighboring cells.

Plant cell biology

Before looking at endomembrane recruitment during plant virus infections, it may be important to provide an overview of the general morphology of plant cells. For those interested in a more detailed account of plant cell morphology, they are invited to consult The Illuminated Plant Cell website (http://www.illuminatedcell.com/Home.html). First, it must be realized that for many plant cells there is limited free cytosolic space, which is restricted by the presence of large central vacuoles and by the sheer number of chloroplasts. Within this constricted space, the ER pervades the cell and has an extremely dynamic, multifunctional and pleomorphic nature [28,29]. Morphologically, it is characterized by a nuclear envelope-connected ER and a peripheral (cortical) tubular and cisternal ER juxtaposing the plasma membrane. Transvacuolar ER strands provide a direct link between the perinuclear and the cortical ER and act as distribution routes for metabolites, organelles [30] and are also thought to be involved in anchoring the nucleus within the cell [31*]. The plant Golgi apparatus is present in the form of several motile bodies that are distributed throughout the cytoplasm and are associated with microfilaments [32]. Golgi bodies also move in close association with ER tubules and traffic rapidly within transvacuolar strands [33], whereas in animal cells the Golgi apparatus occupies a rather stationary perinuclear position [34]. Another important difference is the absence in plant cells of an intermediate compartment between ER and the Golgi apparatus, which is present in mammalian cells and known as the ER-Golgi intermediate compartment (ERGIC) [35]. Finally, plant cells have plasmodesmata that provide cytoplasmic continuity between neighboring cells that supports the cell-to-cell and long-distance trafficking of small molecules as well as of a wide spectrum of endogenous proteins and ribonucleoprotein complexes. These plasma membrane lined channels contain ER-derived desmotubules and actin filaments and are used for virus cell-to-cell spread (for a review on the topic see [4,36]). These distinctive features may explain the relationship between ER-associated virus replication centers and virus egress through plasmodesmata [37].

Recruitment of endomembranes into virus-induced structures

Membrane-associated replication complexes contain viral RNA as well as viral and host replication factors but not much is known about their host endomembrane composition. This question has recently been addressed in the case of potato virus X (PVX, genus potexivirus). At late infection stages, PVX induces the formation of large inclusion bodies often localized next to the nucleus, which have historically been termed ‘X-bodies’, that contain viral RNA [38], PVX replication proteins, virions and ribosomes [12,39]. Very recently, Tilsner et al. [40**] have analyzed the contribution of endomembranes to these X-bodies. First, they found that the triple gene block protein 1 (TGBp1) forms the core of the X-bodies, which have a layered structure with TGBp1 aggregates at the center, vRNA in the middle and virions at the cytoplasmic periphery (Figure 1). They found that the ER and Golgi (as well as actin filaments) are heavily recruited into these structures, apparently reorganized into densely stacked membranes (Figure 1). Since TGB proteins are not needed for PVX replication, the authors propose that this elaborate structure provides a restricted environment that would link replication with movement and possibly encapsidation.

Grangeon et al. [41**] have reported that turnip mosaic virus (TuMV, genus potyvirus) infection also leads to the formation of perinuclear globular structures similar to X-bodies. The 6K2-Vpg-Pro precursor protein of potyviruses has been shown to be a scaffold protein around which the viral replication complex assembles [15*,42–46]. VPg binds several viral and host proteins, in particular translation factors (for a review, refer to [47]) while the 6K2 is responsible for membrane recruitment [47]. They examined the distribution of well characterized ER and Golgi organelle markers in TuMV-infected cells by confocal microscopy. In TuMV-infected cells, the cortical ER does not show any apparent modification but is speckled with 6K2-tagged vesicles (from now on designated as peripheral vesicles). On the contrary, the perinuclear ER is enlarged into a large irregular shaped globular-like structure that contained 6K2 and is linked to the cortical ER by transvacuolar strands. The ER is compacted within this structure and does not show a polygonal tubular pattern. Golgi bodies, COPII coatomers and chloroplasts are also recruited into this perinuclear globular structure (Figure 1). Disruption of the early secretory pathway by Brefeldin A (BFA) or by co-expression of a dominant-negative mutant of Arf1, which regulates membrane traffic between the Golgi and ER, does not affect the formation of the globular structure. Similarly, BFA does not affect replication of Melon necrotic spot virus whereas it has a negative impact on cell-to-cell movement [19*]. This situation is also observed during coronavirus infection where virus-induced remodeling of endoplasmic reticulum membranes and viral replication, albeit reduced, still take place in the presence of BFA [48].

However, despite their close association, ER and Golgi recruitment may not take place in tandem for all plant viruses. For instance, cowpea mosaic virus infection induces massive proliferation of ER and its recruitment into virus-induced vesicles, but not of Golgi membranes [14]. A similar situation is found for Grapevine fanleaf virus [11]. This noticeable dissimilarity suggests the
existence of different mechanisms for host endomembrane recruitment during plant virus infection.

Dynamics of virus-induced structures
The plant ER and Golgi bodies are dynamic secretory organelles, constantly undergoing remodeling [49,50]. Since the perinuclear globular structure observed in TuMV-infected cells contains an amalgam of condensed ER and Golgi membranes, investigations have been performed to observe if this compartment is nevertheless functionally linked to the bulk of non-modified endomembranes [41]. Fluorescence recovery after photobleaching (FRAP) experiments and the use of photoactivatable GFP (PAGFP) [51] indicated that the TuMV-induced perinuclear structure is not an isolated subcellular compartment, Golgi and ER being connected to the bulk of the host cell endomembranes. It also appears that this compartment is a reservoir that can hold a large quantity of ER membranes. It has been reported that plant viral infections stimulate de novo membrane synthesis [14,52,53] and perhaps the bulk of newly synthesized lipids accumulate in these perinuclear structures. On the contrary, the perinuclear globular structure is not rapidly restocked in viral components following photobleaching, with no input of viral proteins from near-by perinuclear structures. Similarly, the
internal architecture of Hepatitis C virus membranous webs appears relatively static, with limited exchange of viral proteins within and between neighboring replication complexes [54].

However, this apparent inactivity in restocking for viral components does not mean that the globular structure is a closed entity for viral proteins. PAGFP is used for fluorescent pulse labeling of fusion proteins at a specific position within a cell, which allows their subsequent cellular redistribution to be monitored [51]. When 6K2 was fused to PAGFP and expressed in infected cells and photoactivation performed within the globular structure, activated 6K2-PAGFP fluorescence was found to rapidly fill up the globular structure and motile 6K2-tagged vesicles were seen to originate and to move away from this same structure. These experiments then provide evidence for a functional link between the perinuclear globular structure and peripheral vesicles. Tilsner et al. [40**] also demonstrated that there is continuity between the X-bodies and peripheral vesicles associated with movement proteins and thus viral egress.

TuMV peripheral vesicles show rapid trafficking along transvacuolar strands as if they were traveling on a highway out and into the perinuclear globular structure [41**] (Figure 2). This trafficking is probably brought by rearrangements in the actin cytoskeleton [30]. Several groups have looked at the contribution of the cytoskeleton in the intracellular trafficking of virus-induced structures (for a review on the subject, refer to [22,55]). For example, the group of Nelson analyzed the association of tobacco mosaic virus-induced bodies with microfilaments [16]. Time-lapse imaging shows that the peripheral bodies traffic along microfilaments with average velocities of 1 μm/s with top speed approaching 8 μm/s. The movement of these bodies has subsequently been shown to depend on myosin motors [15*,20*,21*]. Plasmodesmata are the ultimate destination of this trafficking.

Endomembranes are not only recruited to virus replication complexes, they are actively remodeled. For example, TBSV recruits ESCRT (endosomal sorting complexes required for transport) factors [3] and Brome mosaic virus (BMV) host reticulon proteins [56,57] to facilitate membrane curving during virus-induced structure formation.

**Recruitment of endomembranes in Arabidopsis thaliana mutant lines**

Interestingly, defects in the early secretory pathway can produce similar recruitment of endomembranes into perinuclear structures as those observed in PVX-infected and TuMV-infected cells. Faso et al. [58**] characterized an Arabidopsis thaliana mutant that partially accumulates Golgi membrane markers and a soluble secretory marker in perinuclear globular structures entwined with actin cables and composed of a mass of convoluted ER tubules that maintain a connection with the bulk ER. The mutation also leads to impaired traffic of proteins at the ER/Golgi interface. In the same vein, Nakano et al. [59**] isolated two A. thaliana mutants with defects in ER morphology and designated them endoplasmic reticulum morphology1 (ermo1) and ermo2. The cells of both

---

**Figure 2**

(a) TuMV-infected cells expressing 6K2-mCherry showing that transvacuolar strands provide a direct link between the perinuclear structure and the cell periphery highlighted by brightfield. (b) TuMV-infected cells expressing 6K2-mCherry showing association of peripheral vesicles with cortical ER (HDEL-GFP). n indicates nucleus position. Arrows indicate a peripheral vesicle moving within a transvacuolar strand. Bar = 10 μm.
Host endomembrane recruitment for plant RNA virus replication
Grangeon, Jiang and Laliberté

mutants develop a number of ER-derived spherical bodies, approximately 1 µm in diameter, that also contain Golgi bodies. The above lines have a defect in one of the Sec24 isomers that causes a partial loss of function for the binding of cargo protein intended for secretion. Faso et al. [58**] hypothesized that if constitutive traffic is disrupted, inappropriate fusion of vesicles between the ER and the Golgi may occur, creating an aberrant compartment. It is then plausible that the formation of the perinuclear globular structure is the consequence of an interfering event between a viral protein and Sec24 or another host protein of that nature.

Such interfering events have been documented for vertebrate viruses. The viral proteins involved are membrane-associated and interact or interfere with cellular membrane trafficking proteins of the early secretory pathway [60*,61–63]. However, there is as yet no report showing a specific interaction with a plant viral protein and a host secretory pathway component but there is one investigation indicating that this may be the case. The triple gene block protein 3 (TGBp3) of bamboo mosaic virus (genus potyvirus) induces by itself the production of peripheral vesicles that are associated with the cortical ER. Wu et al. [23**] showed that mutations in the C-terminal region of the protein no longer formed vesicles in the cortical ER but exhibited perinuclear ER localization and concluded that C-terminal region of TGBp3 probably contains a sorting signal specifying cortical ER localization, implying interaction with a secretory pathway component. The tobacco etch virus (genus potyvirus) 6K2 protein may also have an ER export signal [64]. It will be interesting to see if these viral proteins target a component of the early secretory pathway at the ER/Golgi interface that leads to inhibition of protein secretion and formation of the perinuclear globular structure.

We suggest the following model to describe the cellular remodeling taking place during TuMV infection that shares many features with PVX replication (Figure 3). Early in the infection process, the incoming viral RNA is translated and the viral gene products contribute to the formation of the perinuclear globular structure. Replication events (i.e., negative and positive-sense RNA transcription) take place within this globular structure and these events would still happen even if the ER-Golgi interface is disrupted during viral infection. After this step, viral egress is initiated by the budding of 6K2 vesicles at ERES in the globular structure, which then traffic along the ER/microfilaments towards the plasma membrane and plasmodesmata for ultimate delivery of the virus into neighboring cells.

**Conclusion**

The full molecular events that consubstantiate with this endomembrane recruitment in virus-induced structures remain however to be elucidated. Evidently viral genome replication and probably virion assembly are taking place within these structures. The fact that there is heavy
recruitment of organelles into these structures would also reflect a need for sustained high synthetic activity that is required for virus production. Future investigations will thus aim at identifying host proteins that are involved in the formation of the perinuclear structure. Additionally, considering the large size of these structures, other events may take place concomitantly. For instance, the unfolded protein response has been proposed to be an element of PVX infection [65]. The active role of the host endomembranes in other plant (+)RNA virus replication should also be explored to broaden our understanding of general and unique aspects of these membranes in supporting viral processes.

Acknowledgements
We thank the anonymous reviewer for his/her constructive comments. Studies in J-F. Laliberté are supported by grants from the Natural Sciences and Engineering Research Council of Canada and from Le Fonds québécois de recherche sur la nature et les technologies.

References and recommended reading
Papers of particular interest, published within the period of review, have been highlighted as:

• of special interest

•• of outstanding interest

1. den Boon JA, Ahlquist P: Organelle-like membrane compartmentalization of positive-strand RNA virus replication factories. Annual Review of Microbiology 2010, 64:241-256.

2. Laliberté J-F, Sanfaçon H: Cellular remodeling during plant virus infection. Annual Review of Phytopathology 2010, 48:69-91.

3. Barajas D, Jiang Y, Nagy PD: A unique role for the host ESCRT proteins in replication of Tomato bushy stunt virus. PLoS Pathogens 2009, 5:e1000705.

4. Niehl A, Heinlein M: Cellular pathways for viral transport through plasmodesmata. Proteoplasma 2011, 248:75-99.

5. McCartney AW, Greenwood JS, Fabian MR, White KA, Mullen RT: Localization of the tomato bushy stunt virus replication protein p32 reveals a peroxisome-to-endoplasmic reticulum sorting pathway. The Plant Cell 2005, 17:3510-3531.

6. Hwang YT, McCartney AW, Gidda SK, Mullen RT: Localization of the Carnation Italian ringspot virus replication protein p36 to the mitochondrial outer membrane is mediated by an internal targeting signal and the TOM complex. BMC Cell Biology 2008, 9:54.

7. Prod’homme D, Jakubiec A, Tourner V, Druegeon G, Jupin I: Targeting of the turnip yellow mosaic virus 69K replication protein to the chloroplast envelope is mediated by the 140K protein. JIournal of Virology 2003, 77:9124-9135.

8. Jonczyk M, Pathak KB, Sharma M, Nagy PD: Exploiting alternative subcellular location for replication: tombusvirus replication switches to the endoplasmic reticulum in the absence of peroxisomes. Virology 2007, 362:320-330.

9. Miller DJ, Schwartz MD, Dye BT, Ahlquist P: Engineered retargeting of viral RNA replication complexes to an alternative intracellular membrane. Journal of Virology 2003, 77:12193-12202.

10. Schwartz M, Chen J, Lee WM, Janda M, Ahlquist P: Alternative, virus-induced membrane rearrangements support positive-strand RNA virus genome replication. Proceedings of the National Academy of Sciences of the United States of America 2004, 101:11263-11268.

11. Ritzenhaler C, Laporte C, Gaire F, Dunoyer P, Schmitt C, Duval S, Piequet A, Loudes AM, Rohfristsch O, Stussi-Garaud C et al.: Grapevine fanleaf virus replication occurs on endoplasmic reticulum-derived membranes. Journal of Virology 2002, 76:8808-8819.

12. Ju HJ, Samuels TD, Wang YS, Blancaflor E, Payton M, Mitra R, Krishnamurthy K, Nelson RS, Verchot-Lubicz J: The potato virus X TGBp2 movement protein associates with endoplasmic reticulum-derived vesicles during virus infection. Plant Physiology 2005, 138:1877-1895.

13. Banumunisenghe D, See J-K, Rao ALN: Subcellular localization and rearrangement of endoplasmic reticulum by brome mosaic virus capsid protein. Journal of Virology 2011, 85:2953-2963.

Authors provide EM data of BMV vesicle production in infected cells.

14. Carette JE, Stuiver M, Van Lent J, Wellink J, Van Kammbr AB: Cowpea mosaic virus infection induces a massive proliferation of endoplasmic reticulum but not Golgi membranes and is dependent on de novo membrane synthesis. Journal of Virology 2000, 74:6556-6563.

15. Wei TY, Huang TS, McNiel J, Laliberté JF, Hong J, Nelson RS, Wang AM: Sequential recruitment of the endoplasmic reticulum and chloroplasts for plant potyvirus replication. Journal of Virology 2010, 84:799-809.

Authors provide evidence for the association of chloroplasts with replication vesicles.

16. Liu JZ, Blancaflor EB, Nelson RS: The tobacco mosaic virus 126-kilodalton protein, a constituent of the virus replication complex, alone or within the complex aligns with and traffics along microfilaments. Plant Physiology 2005, 138:1853-1856.

17. Kusumanegara K, Mine A, Hyodo K, Kaido M, Mise K, Okuno T: Identification of domains in p27 auxillary replicase protein essential for its association with the endoplasmic reticulum membranes in Red clover necrotic mosaic virus. Virology 2012, 433:131-141.

18. Pogany J, Nagy PD: Authentic replication and recombinion of Tomato bushy stunt virus RNA in a cell-free extract from yeast. Journal of Virology 2008, 82:5967-5980.

19. Genoves A, Navarro JA, Pallas V: The intra- and intercellular movement of Melon necrotic spot virus (MNSV) depends on an active secretory pathway. Molecular Plant-Microbe Interactions 2010, 23:263-272.

The authors show that the Golgi apparatus is involved in virus movement.

20. Amari K, Lerich A, Schmitt-Keichinger C, Dolja VV, Ritzenhaler C: Tubule-guided cell-to-cell movement of a plant virus requires class XI myosin motors. PLoS Pathogens 2011, 7:e1002327.

The authors show that intercellular movement through plasmodesmata depends on myosin motor.

21. Harries PA, Park JW, Sasaki N, Ballard KD, Maule AJ, Nelson RS: Differing requirements for actin and myosin by plant viruses for sustained intercellular movement. Proceedings of the National Academy of Sciences of the United States of America 2009, 106:17594-17599.

First evidence for myosin motor involved in virus movement.

22. Harries PA, Schoels JE, Nelson RS: Intracellular transport of viruses and their components: utilizing the cytoskeleton and membrane highways. Molecular Plant-Microbe Interactions 2010, 23:1381-1393.

23. Wu CH, Lee SC, Wang CW: Viral protein targeting to the cortical endoplasmic reticulum is required for cell-cell spreading in plants. Journal of Cell Biology 2011, 193:521-535.

The authors introduce the notion that vesicle-inducing viral proteins have a targeting signal for exit from perinuclear to cortical ER.

24. Schepetilnikov MV, Solovyev AG, Gorshkova EN, Schiemann J, Prokhnnevsky AJ, Dolja VV, Morozov SY: Intracellular targeting of a hordeiviral membrane-spanning movement protein: sequence requirements and involvement of an unconventional mechanism. Journal of Virology 2008, 82:1284-1293.

25. Haviv S, Moskovitz Y, Mawassi M: The ORF3-encoded proteins of vitiviruses GVA and GVB induce tubule-like and punctuate structures during virus infection and localize to the plasmodesmata. Virus Research 2012, 163:291-301.

26. Wei TY, Wang AM: Biogenesis of cytoplasmic membranous vesicles for plant potyvirus replication occurs at endoplasmic reticulum.
Host endomembrane recruitment for plant RNA virus replication

Beauchemin B, Bamunusinghe U, Yang J, Hoffmann Z, Zhang J, Lacomme L, Ye B, Robinson KJ, Harries LA, Linnik B, Bortolotti I, Verchot-Lubicz X, Cruz MJ, Nebenfuhr A, Robinson ER, Oparka KJ, Host AJWT, Oparka KM, Harries LA, Laliberte JF, Koster LM, Lauritsen EJ, Kikker M, Wolk T, Wang A, Lacomme L, Burelle S, Wang S, Yang P, Mathieu I, Dechagant C, Beesley DL, Dufresne PJ, Snijder EJ, Bubeck N, Bortolotti I, Neill D, Harries L, Ahlquist P, Cheung S, Lang MA, Boulter D, Oparka KM, Hoffmann Z, Grondin S, Bortolotti I, Webb S, Oparka KJ, Host AJWT, Natera V, Martinez-Huitle CA, Lacomme L, Linnik B, Bortolotti I, Verchot-Lubicz X, Laliberte JF, Koster LM, Opperman L, Seemann T, Ahlquist P, Edake N, Cande WZ, Kikker M, Bortolotti I, Harries L, Burelle S, Wang S, Yang P, Mathieu I, Dechagant C, Beesley DL, Dufresne PJ, Snijder EJ, Bubeck N, Bortolotti I, Neill D, Harries L, Ahlquist P, Cheung S, Lang MA, Boulter D, Oparka KM, Hoffmann Z, Grondin S, Bortolotti I, Webb S, Oparka KM, Hoffmann Z, Grondin S, Bortolotti I, Webb S, Oparka KM, Hoffmann Z, Grondin S, Bortolotti I, Webb S, Oparka KM, Hoffmann Z, Grondin S, Bortolotti I, Webb S, Oparka KM, Hoffmann Z, Grondin S, Bortolotti I, Webb S.
59. Nakano RT, Matsushima R, Ueda H, Tamura K, Shimada T, Li L, Hayashi Y, Kondo M, Nishimura M, Hara-Nishimura I: GNOM-LIKE1/ERMO1 and SEC24a/ERMO2 are required for maintenance of endoplasmic reticulum morphology in Arabidopsis thaliana. *The Plant Cell* 2009, 21:3672-3685. Another example of the disruption of the secretory pathway may have on cellular remodeling.

60. Sharp TM, Guix S, Katayama K, Crawford SE, Estes MK: Inhibition of cellular protein secretion by Norwalk virus nonstructural protein p22 requires a mimic of an endoplasmic reticulum export signal. *PLoS ONE* 2010, 5:e13130. This article shows many parallel with plant viruses of a vertebrate virus hijacking the secretory pathway.

61. Moffat K, Knox C, Howell G, Clark SJ, Yang H, Belshaw GJ, Ryan M, Wileman T: Inhibition of the secretory pathway by foot-and-mouth disease virus 2BC protein is reproduced by coexpression of 2B with 2C, and the site of inhibition is determined by the subcellular location of 2C. *Journal of Virology* 2007, 81:1129-1139.

62. Belov GA, Altan-Bonnet N, Kovtunovych G, Jackson CL, Lippincott-Schwartz J, Ehrenfeld E: Hijacking components of the cellular secretory pathway for replication of poliovirus RNA. *Journal of Virology* 2007, 81:558-567.

63. Belov GA, Feng Q, Nikovics K, Jackson CL, Ehrenfeld E: A critical role of a cellular membrane traffic protein in poliovirus RNA replication. *PLoS Pathogens* 2008, 4:e1000216.

64. Lerich A, Langhans M, Sturm S, Robinson DG: Is the 6 kDa tobacco etch viral protein a bona fide ERES marker? *Journal of Experimental Botany* 2011, 62:5013-5023.

65. Ye C, Dickman MB, Whitham SA, Payton M, Verchot J: The Unfolded Protein response is triggered by a plant viral movement protein. *Plant Physiology* 2011, 156:741-755.