

Review Article

Viral Infection and Mitochondria in Eukaryotic Mammalian, Insect and Plant Cells

Mohammadreza Rezapanah^{1,2}, Vahideh Hamidi Sofiani³, Malihe Naderi^{4,5}, Arefeh Ebrahimian Shiadeh³, Behnam Baghdadi⁶, Iliad Moradi⁷, Mohammadreza Kalani^{8,9}, Abdolvahab Moradi^{3*}

1. Iranian Research Institute of Plant Protection (IRIPP), Agricultural Research Education and Extension Organization (AREEO), Tehran 1985713133, Iran.
2. Iranian Network for Research in Viral Diseases, Tehran, Iran.
3. Department of Microbiology, Faculty of Medicine, Golestan University of Medical Science, Gorgan, Iran.
4. Hiroshima Institute of Life Sciences, 7-21, Nishi Asahi-Machi, Minami-ku, Hiroshima-shi, Hiroshima, 734-0002 Japan.
5. Department of Microbiology and Microbial Biotechnology, Faculty of Life Sciences and Biotechnology, Shahid Beheshti University, Tehran, Iran.
6. Department of Biology, Arts and Science Faculty, Eastern Mediterranean University, Turkey.
7. Department of Laboratory Sciences, School of Allied Medical Sciences, Iran University of Medical Sciences, Tehran, Iran.
8. School of Cell and Molecular Biology, University of Illinois at Urbana-Champaign, Urbana, United States.
9. Department of Molecular Medicine, Golestan University of Medical Sciences, Golestan, Iran.

Abstract

Background and Aims: Viruses manipulate intracellular organelles such as mitochondria, endoplasmic reticulum, cytoskeleton, and lipid droplets to facilitate their own replication. In response, host cells initiate antiviral defenses and reorganize these organelles to combat infection. Mitochondria are a primary target in this process, as viral proteins exploit them to inhibit the host's antiviral mechanisms. In plants, viral manipulation of mitochondria can disrupt energy production, impacting overall plant health. Similarly, in insects, which serve as crucial vectors for many plant viruses, viral interactions can alter mitochondrial function, affecting both vector competence and the dynamics of disease transmission. The intricate relationship between viruses and mitochondrial dynamics highlights the complexity of host-virus interactions across various biological systems. This paper explores mitochondrial communication with viral infections in mammals, insects, and plants.

Keywords: Eukaryotic cells, Mitochondria, Viral infection

Introduction

Mitochondria are complex organelles involved in numerous cellular signaling and metabolic pathways, playing a critical role in calcium homeostasis and triggering antiviral responses, including innate immunity and apoptosis. Viruses as intracellular parasites hinge strongly on host metabolic functions and,

to varying extents, manipulate these functions to facilitate their replication (1). Although only a few viruses with large coding capacities encode their own metabolic enzymes, all viruses utilize host resources such as lipids, amino acids, and energy to support processes like viral assembly and release. Recent research has increasingly focused on the metabolomics of viral infections and the impacts of viral manipulation on mitochondrial metabolism (2). Viral-induced mitochondrial redistribution within host cells can often be inhibited through disruption of the microtubule network (3).

* Corresponding author;

Abdolvahab Moradi, Ph.D,
Department of Microbiology, faculty of medicine, Golestan
University of Medical Science, Gorgan, Iran.
Email: abmoradi@gmail.com, Tel: +989111772107.

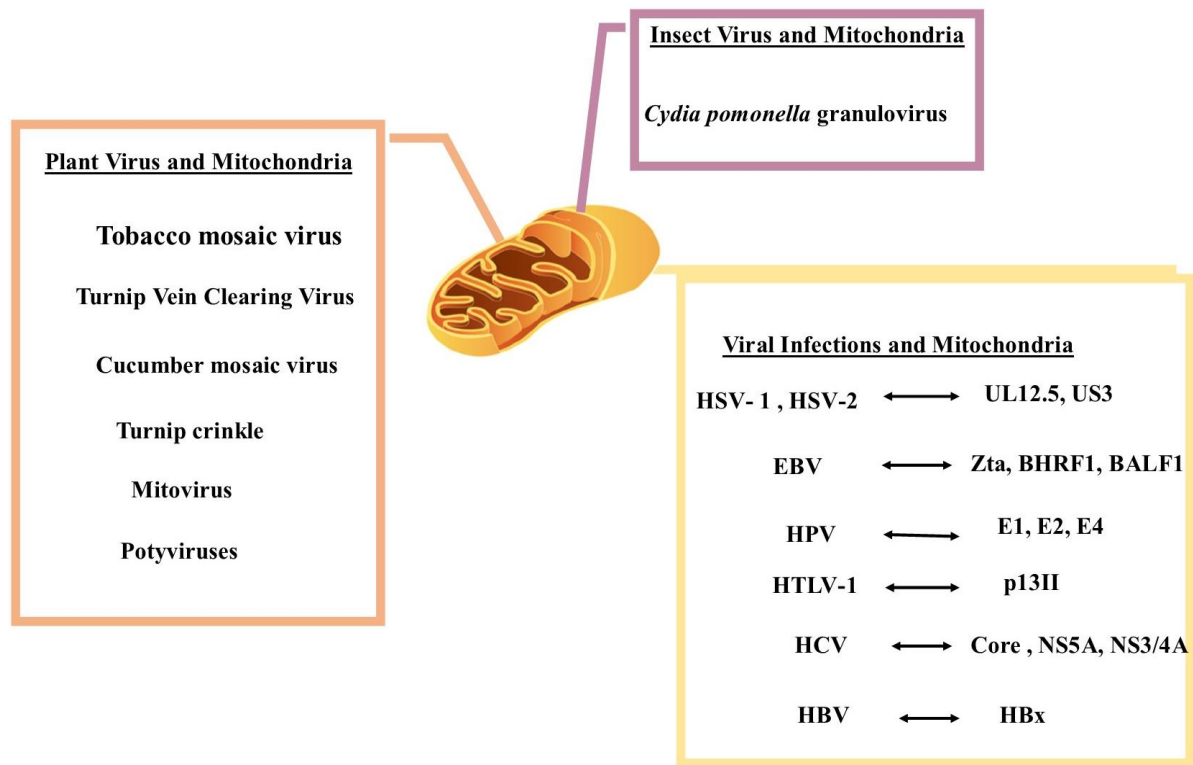


Fig. 1. Graphical Abstract

Mitochondria are specifically targeted by viruses and their proteins to suppress the host's antiviral response (4). During viral infection, pattern recognition receptors such as PRRs roust the production of interferons (IFNs). Mitochondrial antiviral-signaling protein (MAVS) serves as a critical signaling hub for pathways activated by RIG-I-like receptors that detect viral RNA(5). Viruses also impact host cell metabolism, causing notable disruptions in cellular and physiological functions (6). Although the duty of mitochondrial activity patterns during viral infections is being explored, mitochondria are central to both innate and cellular immunity, positioning them as a valuable focus for further molecular studies in viral pathogenesis (7). This paper reviews current insights into factors affecting mitochondria during viral infections (Figure 1).

Viral Infections and Mitochondria

In addition to the essential role in cellular metabolism, mitochondria are key players in the function of innate immunity, especially during viral

infections. Immune signaling can be triggered through interactions on the mitochondrial surface, as well as through the release of damage-associated molecular patterns (DAMPs) like mtDNA as mitochondrial DNA, that occurs alongside dynamic changes in mitochondrial morphology (8).

mtDNA is typically tightly bound by Transcription Factor A Mitochondrial (TFAM) within the mitochondrial matrix (9). Studies show that TFAM-coated mtDNA is more stable and less susceptible to oxidative damage from reactive oxygen species (ROS), while newly synthesized, uncoated mtDNA is more prone to leakage and oxidation into the cytosol (10). This release of mtDNA is linked to reduced TFAM binding, driven by an increase in PKA-mediated phosphorylation of TFAM (11).

During viral infections, RNA degradation pathways-especially those targeting defective or misprocessed RNAs can be hijacked or disrupted by viruses to evade immune detection and manipulate host cell functions. The PNPase-SUV3 complex, for instance, can modulate antiviral signaling pathways, including those mediated by mitochondrial antiviral signaling (MAVS) proteins (12). Many viruses encode

proteins that target mitochondria to regulate the apoptosis process of infected cells. Proapoptotic proteins of viruses translocate to the mitochondrial membranes, inducing mitochondrial membrane permeabilization (MMP), almost accompanied by mitochondrial fragmentation and swelling (13).

Mammalian Cells Mitochondria and Viral Infections

The genomes of HSV-1 and HSV-2 encode a conserved viral serine/threonine protein kinase, US3, found in all α -herpesviruses. While US3 is not important for viral growth *in vitro*, it demonstrates a significant role in various aspects of HSV replication and pathogenesis (14). US3 expression significantly influences several signal transduction pathways, including the JNK and PKB/Akt pathways, and inhibits mitochondrial electron transport in HSV-1-infected cells. Additionally, US3 phosphorylates numerous cellular and viral proteins in infected cells and exhibits potent anti-apoptotic activity in both transfected and infected cells (15).

The replication cycle of HSV-1 progresses rapidly, with viral genome replication beginning early in the infection. This dependence on cellular metabolites is reflected in NADH₂ levels, a critical cofactor for various cellular metabolic processes. HSV-1 can tolerate a decrease in intracellular NADH₂, often due to the activation of poly(ADP-ribose) polymerase (PARP) family members in response to replication-associated DNA damage (16). Emphasizing the importance of mtDNA in infection, certain viral factors specifically target this genome. One such factor is UL12.5, an N-terminally truncated isoform of the HSV-1 UL12 protein, which localizes to mitochondria and promotes mitochondrial DNA depletion (17).

HIV-1 (Human immunodeficiency virus type 1), is among the most prevalent viruses worldwide and carries a significant pathogenic impact. It is also one of the best-characterized viruses, with considerable research devoted to understanding the mitochondrial metabolic aspects of its life cycle. Notably, both HIV infection itself and antiretroviral therapy,

especially HAART (highly active antiretroviral therapy), are associated with mitochondrial toxicity (18). Nucleoside analogue reverse transcriptase inhibitors, a component of HAART, are responsible for mtDNA depletion, leading to disruptions in cellular energy production. Since mtDNA encodes subunits essential for the respiratory chain complexes, mtDNA depletion inevitably affects mitochondrial respiration. However, studies suggest a different impact in asymptomatic HIV-infected pediatric patients (19).

In another context, the Epstein-Barr virus (EBV) Zeta protein, a DNA-binding protein, hijacks the mitochondrial single-stranded binding (mtSSB) protein by directly attaching to it and redirecting it to the nucleus, where the viral genome is located. This interaction is crucial for facilitating EBV lytic replication while simultaneously suppressing mtDNA replication (20). The Epstein-Barr virus (EBV) encodes two Bcl-2 homologs: BHRF1 and BALF1 (21). BHRF1 shares similar three-dimensional structures, localization profiles, and positive effects on cell survival with Bcl-2. It effectively suppresses apoptosis, and mitochondrial membrane permeabilization (MMP) enforced by various stimulants, including c-myc activation, heterologous viral infections, antitumor chemotherapeutic drugs, and gamma radiation. BHRF1 significantly inhibits TRAIL-mediated apoptosis, which involves caspase-8 function and loss of mitochondrial membrane potential.

However, unlike Bcl-2 and Bcl-xL, BHRF1 lacks an exposed, preformed BH-3 binding groove, preventing it from sequestering and inhibiting proapoptotic BH-3-only proteins (22). Although BHRF1 can bind the proapoptotic BH-3-only protein Bim, it does not interact with Bak, offering some protection.

Interestingly, the content of Bim bound with BHRF1 is relatively small compared to the levels of Bim expression induced during apoptosis, suggesting that BHRF1 may function through Bim to inhibit apoptosis (23). BALF1, another Bcl-2 homolog, also interacts with the proapoptotic proteins Bax and Bak and may counteract the effects of BHRF1, although its role in the viral life cycle remains controversial. Additionally, the nuclear antigens EBNA-3C

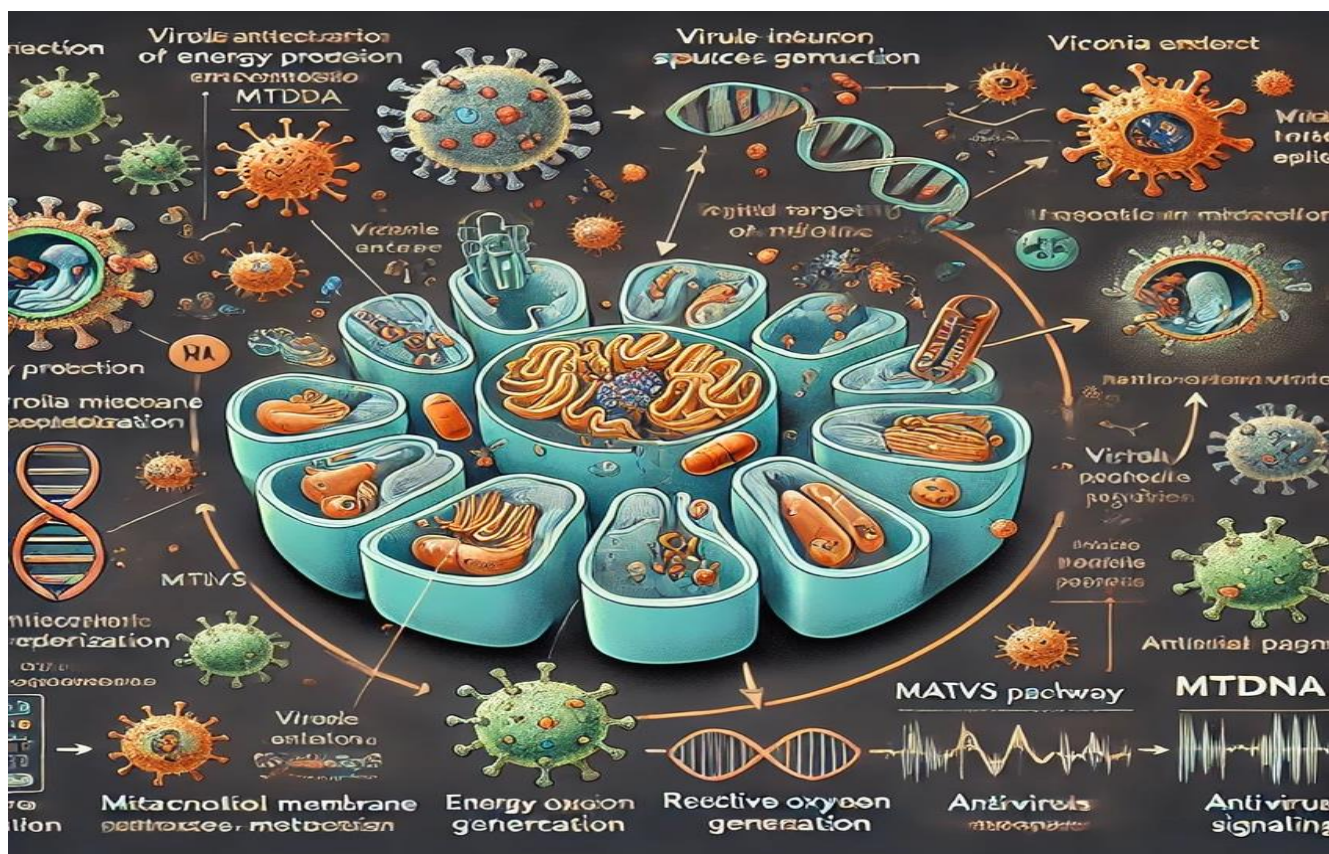


Fig. 2. This figure illustrates the complex interplay between mitochondria and human viral infection within mammalian cells, emphasizing how viral infections manipulate mitochondrial functions and host immune responses (This figure drawn by Chatgpt).

EBNA3A, are responsible for lymphoblastoid cell lines, exhibiting anti-apoptotic properties. They cooperate to down-regulate the expression of the BH-3-only protein Bim (24). Since Bim is an important regulator of B-cell survival and acts as a tumor suppressor in B cells, its depletion by the nuclear EBNA3 proteins may facilitate EBV-mediated lymphomagenesis. The EBNA-leader protein (LP) disrupts host transcription and the cytoplasmic apoptotic machinery, interacting with Bcl-2 via the cellular HS1-associated protein X-1 (HAX-1), a mitochondrial inhibitor of apoptosis regulated by Omi/HtrA2 (25). The E2 protein of human papillomavirus (HPV) indirectly affects mitochondrial function by inducing p32 (26), an RNA-binding protein that associates with TFAM, which is crucial for mitochondrial transcription and translation (27). Additionally, the mitochondrial localization of the E1[^]E4 protein is ascribed to a leucine-rich

area in its N-terminus (28). Through a mechanism that remains unclear, E1[^]E4 promotes the detachment of mitochondria from microtubules, leading to the formation of a single large cluster of mitochondria adjacent to the nucleus (13). Human T-lymphotropic virus type 1 (HTLV-1), a causative agent of adult T-cell leukemia, encodes several unique regulatory and accessory proteins within the pX area of its provirus, including p13II, derived from open reading frame II. The p13II protein specifically localizes to the region of the inner mitochondrial membrane, where it influences mitochondrial function and morphology (29); Within the mitochondria, p13II induces internal potassium (K⁺) current, resulting in mitochondrial swelling, membrane depolarization, enhanced respiratory chain function, and increased generation of ROS (reactive oxygen species) (30, 31). Additionally, p13II sensitizes cells to apoptosis induced by Fas ligand and ceramide, while suppressing cell proliferation and tumorigenesis in cells co-expressing Myc and Ras (32). HCV (Hepatitis C virus) has been demonstrated to impact mitochondrial biogenesis and transcription. The virus disrupts mitochondrial trans-

cription through its two NS5A and core proteins, resulting in endoplasmic reticulum (ER) stress and increased calcium (Ca^{2+}) transmission from the ER to mitochondria. This dysregulation can cause to increased generation of ROS, increased susceptibility to mitochondrial permeability transition, impaired oxidative phosphorylation, and cell death, all of which contribute to viral pathogenesis (33). Additionally, the NS3/4A protein of HCV, functioning as a serine protease, specifically inhibits RIG-I-mediated signaling by cleaving MAVS (mitochondrial antiviral signaling) at Cys508 (34).

Beta-oxidation generates acetyl-CoA, which is a crucial substrate for mitochondrial function and is necessary for the replication cycle of some viruses. HCV serves as a well-characterized example of viral manipulation for this metabolic pathway. HCV replication depends on the act of the enzyme dodecanoyl coenzyme A delta isomerase (DCI), that is associated in the degradation of long-chain unsaturated fatty acids that have double bonds at odd-numbered carbon positions (35). The significance of beta-oxidation, particularly DCI in HCV replication, is supported by several lines of evidence: (I) Knockdown of DCI, (II) pharmacological inhibition of long-chain fatty acid transport into mitochondria using etomoxir, both result in reduced HCV replication in Huh7 hepatoma cells, and (III) mitochondrial fatty acid oxidation and the availability of its associated enzymes are generally enhanced during HCV infection (3). The X protein from Hepatitis B virus (HBx) plays a significant role in the development of hepatocellular carcinomas by acting as a transcriptional activator for both viral and cellular genes. HBx is communicated with mitochondria, likely through an assumed transmembrane area (amino acids 54–70), and it transfects cells and sensitizes infected to apoptosis induced by $\text{TNF-}\alpha$ (36).

Recent studies have demonstrated that HBx induces cyclophilin D-mediated mitochondrial penetrance transmission, leading to calcium influx into the cytoplasm. Additionally, HBx communicates with the mitochondrial matrix chaperone Hsp60 and Hsp70. Further research is needed to clarify the mechanisms underlying

HBx-related mitochondrial regulation (37). Interaction between mammalian cells and viral infection demonstrated in Figure 2.

Plant Cells Mitochondria and Viral Infections

Different studies have been managed to elucidate the functions of plant viruses due to replication and movement by using cell biological, biochemical, genetical, and molecular methods. Specially, studies related to cell biology contributed extremely to the description of the plasmodesmata structure, the intra/intercellular movement of viral proteins, and the interplay between viral factors and cells. Presumably, there are yet undetermined, complex relations between virus movement and virus replication (38). As plant cell systems are intricately, it is important to note that several plant viruses demonstrated various reactions to distinct host factors or hosts. For instance, actin filament affects the motions of Tobacco Mosaic Virus (TMV), but the motions of Turnip Vein Clearing Virus (TVCV) are not linked to the actin filaments (39). Despite significant efforts to understand virus infections, further research is still needed to find answers to many unresolved questions. Numerous host factors must be identified to fully understand the precise mechanisms employed by viruses for the replication of intracellular/intercellular movement. Although *Nicotiana benthamiana* is a commonly used plant model for studying plant viruses, its use has only recently expanded due to previously limited genomic resources (40). Since the *N. benthamiana* genome became available, more precise genetic studies can now be carried out to identify (41).

Plant viruses exhibit a high level of diversification and can induce significant alterations and deformations within a plant host cell. Their genomes can be composed of single-stranded DNA (ssDNA), double-stranded DNA (dsDNA), double-stranded RNA (dsRNA), or single-stranded RNA (ssRNA), all encapsulated by a capsid made of coat protein molecules (42). Generally, the viral genome encodes proteins essential for the initiation and maintenance

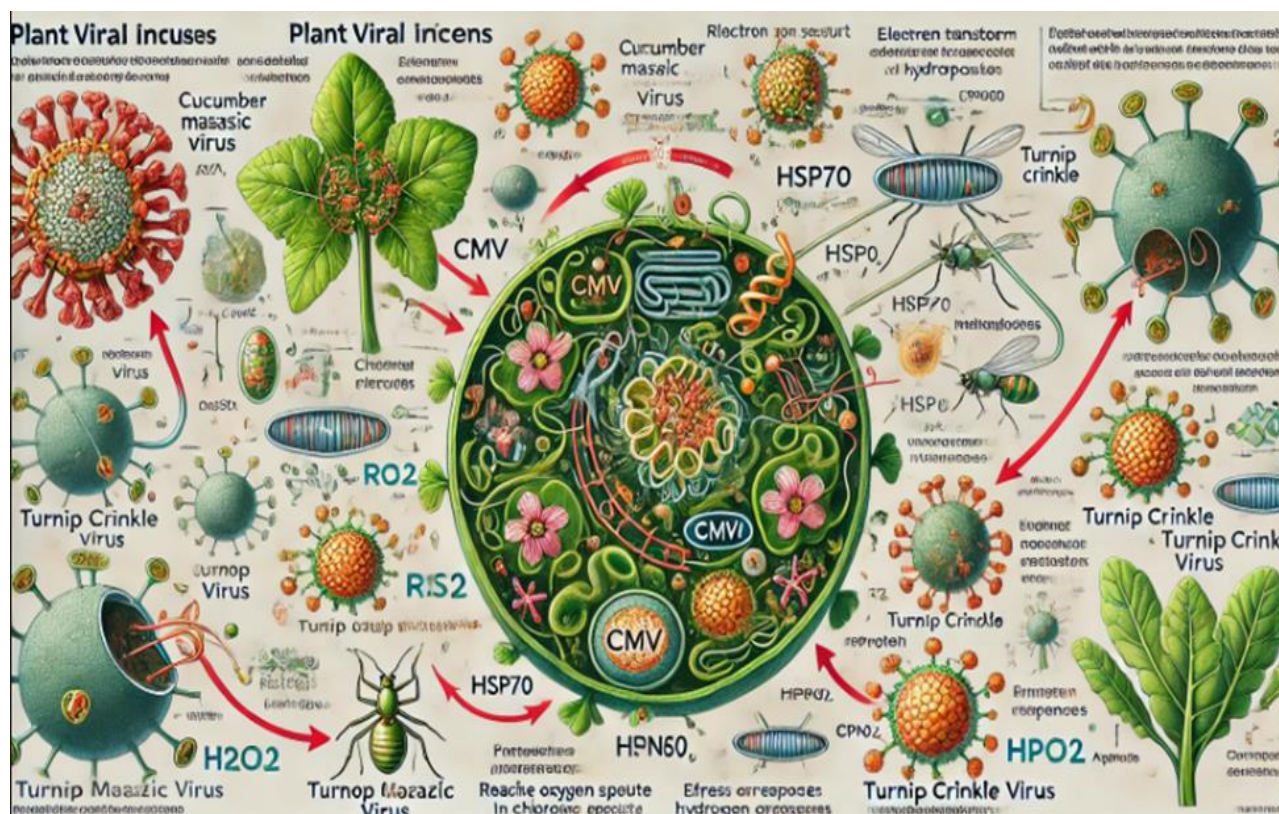


Fig. 3. Here's a scientific diagram depicting plant viral infections and their interactions with mitochondria in plant cells. It highlights key elements like CMV and Turnip crinkle virus effects on mitochondrial and chloroplast function, stress response proteins, and transmission via insect vectors (This figure drawn by Chatgpt).

of viral infection through local and systemic transport mechanisms. As a result, plant viruses operate exclusively within the host cell, triggering multilayered alterations in its internal systems during the infection process (43). Mitochondria play an important role in the electron transport chain. Infection by Cucumber mosaic virus (CMV) disrupts the electron transport chains in both chloroplasts and mitochondria, resulting in increased electron flow to oxygen (O_2) and a heightened accumulation of hydrogen peroxide (H_2O_2) (44). Due to infection with TVCV, the expression of mitochondrial matrix proteins HSP70 and CPN60 elevates in infected plants as a stress response to mitochondrial injury caused by the virus (45).

In quinoa plants that were infected with a Mitovirus, mitochondria-rich fractions were separated through cell fractionation to examine the impact of viral infection on the mitochond-

rial proteome. The analysis indicated that infection leads to the upregulation of proteins communicated with stress responses to drought (46, 47). Mitovirus possess small positive-sense RNA genomes, replicate with mitochondria, and have been shown to infect just fungi to date (48). Potyviruses can replicate and express their own genomes in the cytoplasm, primarily within closely affiliated membranous structures including the endoplasmic reticulum (ER) or in its vicinity. Our findings provide the first evidence of Potato virus Y (PVY) capsid proteins and particles being present inside the mitochondria during compatible interactions, while in hypersensitive reflexes, these interplays were detected within chloroplasts (49). Many plant viruses that pose significant agricultural challenges are transferred by insect vectors, such as thrips, aphids, leafhoppers, and planthoppers, persistently. Increasing evidence suggests that the persistent transmission of viruses results in only limited adverse effects, rather than full-blown pathogenesis, in their insect vectors (50). Interaction between plant cells and viral infection demonstrated in Figure 3.



Downloaded from journal.isv.org.ir on 2026-10-10]

Downloaded from journal.isv.org.ir on 2026-10-10]

Downloaded from journal.isv.org.ir on 2026-10-10]

Downloaded from journal.isv.org.ir on 2026-10-10]

Downloaded from journal.isv.org.ir on 2026-10-10]

Downloaded from journal.isv.org.ir on 2026-10-10]

Downloaded from journal.isv.org.ir on 2026-10-10]

tunities for developing innovative antiviral strategies.

Acknowledgment

None

Conflict of Interest

No conflict of interest is declared.

Funding

This study was not financially supported by any agency, or institution.

Ethics Approval and Consent to Participate

Not applicable.

References

1. Williamson CD, DeBiasi RL, Colberg-Poley AM. Viral product trafficking to mitochondria, mechanisms and roles in pathogenesis. *Infect Disord Drug Targets*. 2012;12(1):18-37.
2. El-Bacha T, Da Poian AT. Virus-induced changes in mitochondrial bioenergetics as potential targets for therapy. *Int J Biochem cell Biol*. 2013;45(1):41-6.
3. Claus C, Liebert UG. A renewed focus on the interplay between viruses and mitochondrial metabolism. *Arch Virol*. 2014;159(6):1267-77.
4. Purandare N, Ghosalkar E, Grossman LI, Aras S. Mitochondrial Oxidative Phosphorylation in Viral Infections. *Viruses*. 2023;15(12):2380.
5. Singh S, Dirani K, Kumar A. Intricacy of Mitochondrial Dynamics and Antiviral Response During RNA Virus Infection. *Front Virol* 2022;2:918806.
6. Thaker SK, Ch'ng J, Christofk HR. Viral hijacking of cellular metabolism. *BMC Biol*. 2019;17(1):59.
7. Elesela S, Lukacs NW. Role of Mitochondria in Viral Infections. *Life (Basel)*. 2021;11(3):232.
8. Sorouri M, Chang T, Hancks DC. Mitochondria and Viral Infection: Advances and Emerging Battlefronts. *mBio*. 2022;13(1):e0209621.
9. Hu MM, Shu HB. Mitochondrial DNA-triggered innate immune response: mechanisms and diseases. *Cell Mol Immunol*. 2023;20(12):1403-12.
10. Zhong Z, Liang S, Sanchez-Lopez E, He F, Shalpour S, Lin XJ, et al. New mitochondrial DNA synthesis enables NLRP3 inflammasome activation. *Nature*. 2018;560(7717):198-203.
11. Lai JH, Wang MY, Huang CY, Wu CH, Hung LF, Yang CY, et al. Infection with the dengue RNA virus activates TLR9 signaling in human dendritic cells. *EMBO Rep*. 2018;19(8):e46182.
12. Chen PL. SUV3 Helicase and Mitochondrial Homeostasis. *Int J Mol Sci*. 2023;24(11):9233.
13. Boya P, Pauleau AL, Poncet D, Gonzalez-Polo RA, Zamzami N, Kroemer G. Viral proteins targeting mitochondria: controlling cell death. *Biochim Biophys Acta*. 2004;1659(2-3):178-89.
14. Kato A, Tanaka M, Yamamoto M, Asai R, Sata T, Nishiyama Y, et al. Identification of a physiological phosphorylation site of the herpes simplex virus 1-encoded protein kinase Us3 which regulates its optimal catalytic activity in vitro and influences its function in infected cells. *J Virol*. 2008;82(13):6172-89.
15. Mou F, Forest T, Baines JD. US3 of herpes simplex virus type 1 encodes a promiscuous protein kinase that phosphorylates and alters localization of lamin A/C in infected cells. *J Virol*. 2007;81(12):6459-70.
16. Grady SL, Hwang J, Vastag L, Rabinowitz JD, Shenk T. Herpes simplex virus 1 infection activates poly (ADP-ribose) polymerase and triggers the degradation of poly(ADP-ribose) glycohydrolase. *J Virol*. 2012;86(15):8259-68.
17. Duguay BA, Smiley JR. Mitochondrial nucleases ENDOG and EXOG participate in mitochondrial DNA depletion initiated by herpes simplex virus 1 UL12.5. *J Virol*. 2013;87(21):11787-97.
18. Miró O, López S, Pedrol E, Rodríguez-Santiago B, Martínez E, Soler A, et al. Mitochondrial DNA depletion and respiratory chain enzyme deficiencies are present in peripheral blood mononuclear cells of HIV-infected patients with HAART-related lipodystrophy. *Antivir Ther*. 2003;8(4):333-8.
19. Romero-Cordero S, Kirwan R, Noguera-Julian A, Cardellach F, Fortuny C, Morén C. A Mitocentric View of the Main Bacterial and Parasitic Infectious Diseases in the Pediatric Population. *Int J Mol Sci*. 2021;22(6):3272.
20. Wiedmer A, Wang P, Zhou J, Rennekamp AJ, Tiranti V, Zeviani M, et al. Epstein-Barr virus immediate-early protein Zta co-opts mitochondrial single-stranded DNA binding protein to promote viral and inhibit mitochondrial DNA replication. *J Virol*. 2008;82(9):4647-55.
21. Altmann M, Hammerschmidt W. Epstein-Barr virus provides a new paradigm: a requirement for the immediate inhibition of apoptosis. *PLoS Biol*. 2005;3(12):e404.
22. Huang Q, Petros AM, Virgin HW, Fesik SW, Olejniczak ET. Solution structure of the BHRF1 protein from Epstein-Barr virus, a homolog of human Bcl-2. *J Mol Biol*. 2003;332(5):1123-30.
23. Desbien AL, Kappler JW, Marrack P. The Epstein-Barr virus Bcl-2 homolog, BHRF1, blocks apoptosis by binding to a limited amount of Bim. *Proc Natl Acad Sci U S A*. 2009;106(14):5663-8.

24. Anderton E, Yee J, Smith P, Crook T, White RE, Allday MJ. Two Epstein-Barr virus (EBV) oncoproteins cooperate to repress expression of the proapoptotic tumour-suppressor Bim: clues to the pathogenesis of Burkitt's lymphoma. *Oncogene*. 2008;27(4):421-33.
25. Cilenti L, Soundarapandian MM, Kyriazis GA, Stratico V, Singh S, Gupta S, et al. Regulation of HAX-1 anti-apoptotic protein by Omi/HtrA2 protease during cell death. *J Biol Chem*. 2004;279(48):50295-301.
26. Gao LJ, Gu PQ, Zhao W, Ding WY, Zhao XQ, Guo SY, et al. The role of globular heads of the C1q receptor in HPV 16 E2-induced human cervical squamous carcinoma cell apoptosis is associated with p38 MAPK/JNK activation. *J Transl Med*. 2013;11:118.
27. Boczonadi V, Ricci G, Horvath R. Mitochondrial DNA transcription and translation: clinical syndromes. *Essays Biochem*. 2018;62(3):321-40.
28. Raj K, Berguerand S, Southern S, Doorbar J, Beard P. E1 empty set E4 protein of human papillomavirus type 16 associates with mitochondria. *J Virol*. 2004;78(13):7199-207.
29. Hilaragi H, Kim SJ, Phipps AJ, Silic-Benussi M, Ciminale V, Ratner L, et al. Human T-lymphotropic virus type 1 mitochondrion-localizing protein p13(II) is required for viral infectivity in vivo. *J Virol*. 2006;80(7):3469-76.
30. Silic-Benussi M, Biasiotto R, Andresen V, Franchini G, D'Agostino DM, Ciminale V. HTLV-1 p13, a small protein with a busy agenda. *Mol Aspects Med*. 2010;31(5):350-8.
31. Silic-Benussi M, Marin O, Biasiotto R, D'Agostino DM, Ciminale V. Effects of human T-cell leukemia virus type 1 (HTLV-1) p13 on mitochondrial K⁺ permeability: A new member of the viroporin family? *FEBS letters*. 2010;584(10):2070-5.
32. Silic-Benussi M, Cavallari I, Zorzan T, Rossi E, Hilaragi H, Rosato A, et al. Suppression of tumor growth and cell proliferation by p13II, a mitochondrial protein of human T cell leukemia virus type 1. *Proc Natl Acad Sci U S A*. 2004;101(17):6629-34.
33. Wang T, Weinman SA. Interactions Between Hepatitis C Virus and Mitochondria: Impact on Pathogenesis and Innate Immunity. *Curr Pathobiol Rep*. 2013;1(3):179-87.
34. Meylan E, Curran J, Hofmann K, Moradpour D, Binder M, Bartenschlager R, et al. Cardif is an adaptor protein in the RIG-I antiviral pathway and is targeted by Hepatitis C virus. *Nature*. 2005;437(7062):1167-72.
35. Rasmussen AL, Diamond DL, McDermott JE, Gao X, Metz TO, Matzke MM, et al. Systems virology identifies a mitochondrial fatty acid oxidation enzyme, dodecanoyl coenzyme A delta isomerase, required for hepatitis C virus replication and likely pathogenesis. *J Virol*. 2011;85(22):11646-54.
36. Tan C, Guo H, Zheng M, Chen Y, Huang W. Involvement of mitochondrial permeability transition in hepatitis B virus replication. *Virus Res*. 2009;145(2): 307-11.
37. Ohta A, Nishiyama Y. Mitochondria and viruses. *Mitochondrion*. 2011;11(1):1-12.
38. Tilsner J, Oparka KJ. Missing links? The connection between replication and movement of plant RNA viruses. *Curr Opin Virol*. 2012;2(6):705-11.
39. 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. *Proc Natl Acad Sci U S A*. 2009;106(41):17594-9.
40. Bombarely A, Rosli HG, Vrebalov J, Moffett P, Mueller LA, Martin GB. A draft genome sequence of *Nicotiana benthamiana* to enhance molecular plant-microbe biology research. *Mol plant Microbe Interact*. 2012;25(12):1523-30.
41. Hong JS, Ju HJ. The Plant Cellular Systems for Plant Virus Movement. *Plant Pathol J*. 2017;33(3):213-28.
42. Hull R. *Plant virology*: Academic press; 2013.
43. Koziel E, Otulak-Koziel K, Bujarski JJ. Plant Cell Wall as a Key Player During Resistant and Susceptible Plant-Virus Interactions. *Front Microbiol*. 2021;12: 656809.
44. Song XS, Wang YJ, Mao WH, Shi K, Zhou YH, Nogués S, et al. Effects of cucumber mosaic virus infection on electron transport and antioxidant system in chloroplasts and mitochondria of cucumber and tomato leaves. *Physiol Plant*. 2009;135(3):246-57.
45. Blake J, Lee KW, Morris TJ, Elthon TE. Effects of turnip crinkle virus infection on the structure and function of mitochondria and expression of stress proteins in turnips. *Physiol Plant*. 2007;129(4):698-706.
46. Gomaa AE, El Mounadi K, Parperides E, Garcia-Ruiz H. Cell Fractionation and the Identification of Host Proteins Involved in Plant-Virus Interactions. *Pathogens*. 2024;13(1):53.
47. Di Silvestre D, Passignani G, Rossi R, Ciuffo M, Turina M, Vigani G, et al. Presence of a Mitovirus Is Associated with Alteration of the Mitochondrial Proteome, as Revealed by Protein-Protein Interaction (PPI) and Co-Expression Network Models in *Chenopodium quinoa* Plants. *Biology (Basel)*. 2022;11(1):95.
48. Nibert ML, Vong M, Fugate KK, Debat HJ. Evidence for contemporary plant mitoviruses. *Virology*. 2018; 518:14-24.
49. Otulak K, Garbaczewska G. The participation of plant cell organelles in compatible and incompatible potato virus Y-tobacco and -potato plant interaction. *Acta Physiol Plant*. 2014;36(1):85-99.
50. Chen Q, Zheng L, Mao Q, Liu J, Wang H, Jia D, et al. Fibrillar structures induced by a plant reovirus target mitochondria to activate typical apoptotic response and promote viral infection in insect vectors. *PLoS Pathog*. 2019;15(1):e1007510.
51. Rezapanah M. Screening *Cydia pomonella* granulovirus (CpGV) isolates via comparative bioassays. *Iran J Virol*. 2015;9(3):1-5.
52. Zhang ZD, Zhong B. Regulation and function of the cGAS-MITA/STING axis in health and disease. *Cell Insight*. 2022;1(1):100001.
53. Meki IK, Huditz HI, Strunov A, van der Vlugt RAA, Kariithi HM, Rezapanah M, et al. Characterization and Tissue Tropism of Newly Identified Iflavirus and Nege-

viruses in *Glossina morsitans morsitans* Tsetse Flies. *Viruses*. 2021;13(12):2472.

54. Lakhova TN, Tsygichko AA, Klimenko AI, Ismailov VY, Vasiliev GV, Asaturova AM, et al. Assembly and Genome Annotation of Different Strains of Apple Fruit

Moth Virus (*Cydia pomonella* granulovirus). *Int J Mol Sci*. 2024;25(13):7146.

55. Miller DP, Luque T, Crook NE, Winstanley D, O'Reily DR. Expression of the *Cydia pomonella* granulovirus iap3 gene. *Arch Virol*. 2002;147(6):1221-36.