Review

Tropical Fruit Virus Resistance in the Era of Next-Generation Plant Breeding

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Abstract: Plant viral diseases constitute a major contributor to agricultural production losses, significantly impacting the economies of exporting countries by more than USD 30 billion annually. Understanding and researching the biology and genomics of viruses is crucial for developing virus-resistant genetically edited or genetically modified plants. Genetic modifications can be targeted to specific regions within genes of target plants which are important or essential for the virus to establish a systemic infection, thus fostering resistance or enabling plants to effectively respond to invading agents while preserving their yield. This review provides an overview of viral incidence and diversity in tropical fruit crops and aims to examine the current state of the knowledge on recent research efforts aimed at reducing or eliminating the damage caused by viral diseases, with emphasis on genetically edited products that have reached the market in recent years.

Keywords: virus genetic diversity; gene editing; plant disease; biotechnology

1. Introduction

A notable uptick in world exports of major tropical fruit crops was observed in 2023, with an estimated 12% increase compared to previous years, resulting in a total value exceeding USD 11 billion [1]. This surge marks the highest level recorded thus far, highlighting the growing demand for tropical fruit in the global market. Fruit crops constitute a significant portion of the global agricultural output, accounting for 17% of the total production value of crops in 2021 [2]. This sector not only fulfills domestic food requirements but also sustains employment, engaging approximately 5 million workers in Brazil, and generating around 190 million jobs in China and India [3,4].

Countries in Asia and the Americas are collectively responsible for 76.2% of global production of tropical fruit crops [5]. The major crops cultivated worldwide are avocado, banana, citrus (orange, tangerine, lemon, and lime), mango, melon, papaya, pineapple, and watermelon [1,6,7]. Plant viruses in tropical fruits can cause annual losses exceeding USD 30 billion [8]. Bananas, citrus, pineapple, papaya, and melon appear to be particularly susceptible to viral infections, representing economic challenges for the main producing and exporting countries.

Specific export projections anticipate a 4% expansion in global pineapple exports, reaching 3.2 million tonnes in 2023; conversely, papaya exports are forecasted to decrease by 3%, amounting to 365,000 tonnes [1]. Despite an overall positive supply outlook, concerns persist regarding adverse weather events and the spread of plant diseases, particularly impacting papaya cultivation. These challenges highlight the importance of improving mitigation strategies and adopting sustainable practices to protect tropical fruit production and trade.

Most plant viruses feature RNA as their genetic material, with geminiviruses (ssDNA viruses) representing a notable exception; in fruit crops, Umer et al. reviewed that over 70% of the economically important viruses have (+)ssRNA genomes [9]. Genetic diversity relies on the constant changes occurring in DNA or RNA viral genomes, which generate new variants through genetic mechanisms such as mutation, recombination, and reassortment, as well as non-genetic mechanisms such as gene flow and genetic drift [10]. Fruit crops are exposed to several viral infections, and coinfections (a necessary occurrence to generate recombinants) are common in the field.

Biotechnology emerges as an essential ally to face the challenge of controlling viral diseases in the fruit sector, employing precise scientific methodologies to confer resistance, combat infections in orchards, and improve new cultivars [11]. This review emphasizes the use of contemporary gene-editing techniques, notably CRISPR/Cas9, while providing historical insights into classical methods such as genetically modified organisms ("transgenics"). Considering the genetic diversity exhibited by viruses, we initially explore the impact of viral infections on tropical fruit crops, examine the correlation between viral modes of action and the extensive possibilities for manipulating host genomes, and conclude by presenting products which have been approved by national and international regulatory bodies and are available for consumers.

2. Viral Infections in Tropical Fruit Crops

Plants face constant threats from pathogens like fungi, bacteria, and viruses, resulting in an annual economic toll of around USD 220 billion; notably, viral infections alone make up half of the emerging and reemerging diseases caused by microorganisms [12]. Until 2019, the International Committee on Taxonomy of Viruses (ICTV) had identified 1484 plant viruses, among which those with RNA genomes stand out as the most detrimental to crops [13]. Table 1 details the tropical fruit crops highlighted in this review and their main viral diseases.

Table 1. Tropical fruit crop inventory and their most common viral infections.

Fruit Crop	Symptoms	Disease	Virus(es)	Family (Genome Type)	Geographic Distribution
Banana	Mosaic and streak on the inflorescence bracts and petioles	Bract mosaic	banana bract mosaic virus (BBrMV)	*Potyviridae* (+ssRNA)	Asia, Africa, South America and South Pacific Islands
	Dwarfism, dark green streaks/marks	Bunchy top	banana bunchy top virus (BBTV)	*Nanoviridae* (ssDNA)	Asia, Africa, Oceania, South Pacific Islands
	Discontinuous chlorotic streak, necrosis	Streak disease	banana streak virus (BSV)	*Caulimoviridae* (dsDNA)	Asia, Africa, Oceania and South Pacific Islands
	Mosaic in leaves (dark/light green and yellowish areas)	Mosaic disease	cucumber mosaic virus (CMV)	*Bromoviridae* (+ssRNA)	Tropical and subtropical countries
Citrus	Green or yellow, smooth and circular lesions	Leprosis	citrus leprosis virus (CiLV)	*Kitaviridae* (+ssRNA)	South and Central America
	Dwarfism, intense yellowing	Tristeza	citrus tristeza virus (CTV)	*Closteroviridae* (+ssRNA)	Mediterranean region, North and South America
	Leaves show yellowing and mottling; coloring ringspot in fruit	Mosaic	citrus mosaic virus (CiMV)	*Secoviridae* (+ssRNA)	Mediterranean region and Asia
	Bark scaling in both the trunk and branches	Citrus Psorosis	citrus psorosis virus (CPsV)	*Aspiviridae* (-ssRNA)	North and South America
Pineapple	Red–bronze or yellow coloring on central leaves; margins tend to curve down	Mealybug wilt	pineapple mealybug wilt-associated virus complex (PMWaV-1, 2, 3)	*Closteoviridae* (+ssRNA)	South and Central America, Australia and West Africa

Table 1. *Cont.*

Fruit Crop	Symptoms	Disease	Virus(es)	Family (Genome Type)	Geographic Distribution
Papaya	Aqueous latex exudation	Sticky disease	papaya meleira virus complex (PMeV-1, 2)	PMeV *Fusagraviridae* (dsRNA) PMeV2 *Tombusviridae* (+ssRNA)	Central and South America
	Mosaic, ringspot on the fruit	Ringspot (mosaic)	papaya ringspot virus (PRSV)	*Potyviridae* (+ssRNA)	Tropical and subtropical countries
	Curling and distortion of the leaves	Leaf curl disease	papaya leaf curl virus (PaLCuV)	*Geminiviridae* (ssDNA)	Indian Subcontinent
Melon	Leaves with yellow spots; the same can occur to fruits	Watermelon mosaic	watermelon mosaic virus (WMV)	*Potyviridae* (+ssRNA)	Mediterranean region, Eastern Asia, North and South America
	Yellow mosaic, leaf distortion and blistering	Zucchini yellow mosaic	zucchini yellow mosaic virus (ZYMV)	*Potyviridae* (+ssRNA)	Tropical and subtropical countries
	Mosaic with puckering and blistering on leaves	Mosaic	papaya ringspot virus—watermelon strain (PRSV-W)	*Potyviridae* (+ssRNA)	Tropical and subtropical countries
	Interveinal chlorosis, leaves become thickened	Yellow stunting	cucurbit yellow stunting disorder virus (CYSDV)	*Closteroviridae* (+ssRNA)	Mediterranean region, North America, Africa and Asia
	Chlorotic mottle in leaves	Cucurbit yellows disease	cucurbit chlorotic yellows virus (CCYV)	*Closteroviridae* (+ssRNA)	Middle East, Mediterranean region and North America

The infection process begins with the transmission of viral particles to the plant via vectors such as mites, aphids, leafhoppers, whiteflies, and scale insects. Cellular susceptibility occurs when the virus bypasses the defense-response system of plant cells [14], which can be physical, such as cell wall and cuticle, or induced after pathogen exposure, such as the expression of *R* genes [15,16]. Viral infections cause several cell wall modifications that may lead to resistance, such as the production of endoxylanases (e.g., β-1,4 xylane) during potyvirus attack, which loosens cell wall structure and leads to deposits of xilan [17]; such modifications will appear after the interaction between pathogen and host, which differ for each one of the crops described here (Table 2). Those interactions compose multifactorial, dynamic, and complex mechanisms that play important roles in the success or failure of the viral life cycle, and at the same time, in biotechnological research.

Table 2. Description of reported interactions between plant viruses and host factors involved in the establishment of viral infection.

Host	Virus(es)	Viral Protein	Host Factors	Function	Reference
Banana	BBrMV	eIF4E	VPg	Genome viral translation	[18]
	CMV	CMV 2b	AGO1	Viral suppression of RNA silencing	[19]
	CMV	CMV 1a	AGO1	Regulation of CMV 2b-AGO1 interaction, and inhibition of another layer of AGO2-mediated antiviral silencing	

Table 2. *Cont.*

Host	Virus(es)	Viral Protein	Host Factors	Function	Reference
Citrus	CiLV	p29	Fib2	Possible promotion of viral movement and/or suppression of the plant's antiviral defense RNA silencing mechanism	[20]
	CTV	p23 and CP	CaFKBP17-2	Intracellular trafficking movement of the p23-CP-CaFKBP17-2 complex	[21]
	CPsV	24K	miR156/miR171	Affects the normal processing of miRNA biogenesis and reduces mature miRNAs in citrus	[22]
Pineapple	PMWaV-1	p61	RNAi system	Systemic RNA silencing suppressive activity	[23]
	PMWaV-2	p20/CP		Local and systemic RNA silencing suppressive activity	
Papaya	PRSV-P	NIa-Po	PaMsrB1	Interferes with the elimination of reactive oxygen species (ROS) by PaMsrB1 in chloroplasts due to viral infection	[24]
		MG132	proteasome 20s	Increased viral accumulation due to inhibition of protease and RNAse functions of the 20s proteasome protein	[25]
		HcPro	proteasome 20s PAA domain		
	PMeV-1	CP2 and CP4	50S ribosomal protein L17 (RPL17)	Downregulation of RPL17 delays papaya sticky disease symptoms	[26]
Melon	WMV	P3N-PIPO	Wmr	Disruption of viral virulence of the *wmr* gene resulting in cell death phenotype	[27]
	CCYV	P22 (L127 residue)	RNAi system	Maintains the stability of the RNA silencing suppression system and is essential for increasing virulence	[28]
		P22(F-Box motif)	CsSKP1LB1	Inhibition of the suppressive activity of RNA silencing mediated by the viral protein P22	[29]
		P22	CsRPS21		[30]

2.1. Banana

Banana bract mosaic virus (BBrMV) is transmitted through suckers and aphid vectors, and constitute a major problem in southern India, the Philippines, Sri Lanka, and Hawaii [31]. BBrMV encodes the three proteases typical of potyviruses, named P1, HC-Pro, and NIa-Pro. HC-Pro is a major RNA silencing suppressor protein, acting as a pathogenicity factor in most potyvirus infections. It has also been suggested by in silico analysis that BBrMV may encode miRNAs, which could affect the expression of host genes, but this requires experimental validation [32].

Banana bunchy top virus (BBTV), also transmitted by aphids, causes extensive losses in banana crops which, if not controlled, can reach 70% of production [33]. This virus encodes three proteins, CP, MP, and Clink, that act as RNA silencing suppressors, and another designated NSP, a virulence factor that blocks the host's transmembrane receptor kinase activity [34,35]. After being challenged by BBTV infection, transcriptomic analysis revealed differentially expressed genes (DEGs) of wild susceptible *Musa balbisiana* and a resistant phenotype [36]. They shared a similar pattern of expression of 62 DEGs; 151 were exclusively of susceptible cultivars and 99 belonged to resistant *M. balbisiana*. The products derived from DEGs were also different. The host's protein machinery was upregulated in the wild cultivar, such as small ribosomal subunit 40S, translation elongation factor (eEF1A), and eukaryotic translation initiation factor (eIF5A); also, RNA polymerase sigma factor 70 and phosphorolytic exoribonuclease PNP were upregulated, highlighting the essential effect of these proteins to the pathogen replication. On the other hand, the study

showed that the resistant cultivar expressed a set of different genes, such as the up- and downregulation of specific protein kinases, the downregulation of phytohormones—auxin efflux carrier component 1a and abscisic acid signaling—and changes in reactive oxygen species (ROS) and secondary metabolite production levels. These findings are crucial for understanding the viral mechanisms, which can lead to the development of novel control strategies.

In banana crops, bunchy top and streak disease (caused by banana streak virus—BSV) play an important economic role, reducing its yield and productivity [37]. BSV transmission occurs by mealybugs, but its spread through crops also occurs via endosomal BSV (eBSV) activation. eBSV is incorporated into the *M. balbisiana* (B) genome, and therefore is present in hybrids containing the B genome (e.g., allotriploid AAB plantain type). Although *M. balbisiana* is resistant to infection, AAB hybrids are susceptible to epissomal BSV released after the stress triggered by abiotic factors such as micropropagation [37,38]. Under some other stress conditions, the viral replication pathway is activated and the new infective BSV particles are able to avoid DNA cytosine methylation and transcriptional gene silencing, even after facing accumulation of siRNAs produced by the defense-response mechanism; this is supposed to explain why eBSV persists in its integrated form in plants [37,39], a challenge to biotechnological approaches.

Some viruses are not restricted to one specific group of hosts, such as cucumber mosaic virus (CMV), which infects more than 1200 plant species in more than 100 families, including *Musa* sp. [40]. The CMV genome is composed of three RNA segments: RNA1 and RNA2 encode viral replication proteins, while RNA3 encodes the coat protein and a movement protein. RNA2 also contains the *2b* gene, which suppresses the RNA silencing machinery [41]. Recent studies have focused on the use of CMV for virus-induced gene silencing (VIGS) [42]. The CMV-20 isolate obtained from *Musa acuminata* was used to silence *glutamate 1-semialdehyde aminotransferase* (GSA) and *phytoene desaturase* (PDS), reducing their transcript levels to 10% and 18% of the control, respectively.

2.2. Citrus

Citrus leprosis virus C (CiLV-C) infects orange, grapefruit, and tangerines, and the infection is restricted to the area where the vector (mites of the genus *Brevipalpus*) attacks, an intriguing process that relies on the production of reactive oxygen species (ROS) by the host, activating a hypersensible response [43]. Arena et al. described that 24 h after viral inoculum in *Arabidopsis thaliana*, the replication rate is limited to a few cells, but after 6 days, reprogramming of CiLV-C transcription occurs, increasing genomic and subgenomic RNA molecules, with downregulation of the jasmonate/ethylene (JA/ET) pathways, which are involved in the anti-herbivory defense response [44]. The authors suggest that this could be a viral strategy to increase the vector's fitness, and it may be a future target for gene editing-based modifications.

Citrus tristeza virus (CTV), transmitted by aphids (e.g., *Toxoptera citricida*), has the largest RNA genomes in plant RNA viruses, comprising 12 open reading frames (ORFs) within 19.3 kb [45]. ORF1a at the 5′ proximal end encodes a 349 kDa polyprotein, and eventually, the translation continues to ORF1b. At the 3′ proximal region, subgenomic RNAs (sgRNAs) direct the translation of viral proteins responsible for the assembly of virus particles, virus movement, and RNA silencing suppression [46]. CTV encodes three RNA silencing suppressors, p20, p23, and CP, each one with a distinct mode of action. p23 is a local (intracellular) suppressor, while p20 suppresses both local and systemic silencing. CP is also a systemic (intercellular) suppressor but does not act locally, which is a distinct mode of action from all other known viral suppressor proteins [47]. Collectively, the three CTV suppressors interfere with multiple points of the RNA silencing pathway, which may be necessary for a virus with such a long RNA genome and which causes long-term, persistent infections in perennial hosts. In addition to its repertoire of RNA silencing suppressors, CTV also produces a non-coding sgRNA named low-molecular-weight tristeza 1 (LMT1),

which downregulates the salicylic acid-based defense response, the only known case of a long, non-coding viral RNA that interferes with plant defense [48].

Citrus mosaic virus (CiMV) is a member of the *Sadwavirus* genus and is related to *Satsuma dwarf virus* (SDV), which infects satsuma mandarin (*Citrus unshiu*) [49]. CiMV has a bipartite genome, and information on virus–host interactions is limited [50]. Hyun et al. detected an interesting relationship between CiMV and CTV after a coinfection assay [51]. CiMV reduced fruit quality and symptoms were clear, but there were no CTV symptoms, probably because it was a mild strain. The authors did not discard the possibility that coinfection may have affected symptom severity.

The citrus psorosis disease is widely spread in North and South America, specially Argentina and Uruguay [52]. Citrus psorosis virus (CPsV) is transmitted by vegetative propagation, and the bark symptoms are frequently observed in sweet orange, mandarin, and grapefruit [53]. Belabess et al. reported that CPsV downregulates the RNAi machinery in *Citrus sinensis* and upregulates the gene *Scarecrow-like 6* (SCL6), activating programmed cell death and reducing chlorophyll synthesis [54]. The 24K viral protein, encoded by ORF1 of RNA1, interacts with the miRNA synthesis machinery and negatively affects their accumulation, altering the expression of their targets [22].

2.3. Pineapple

Mealybug wilt of pineapple (MWP) is described as the most significant viral disease of pineapple. It is caused by a complex composed of three viruses: pineapple mealybug-associated virus 1 (PMWaV-1), pineapple mealybug-associated virus 2 (PMWaV-2), and pineapple mealybug-associated virus 3 (PMWaV-3). Dey et al. report that the etiology of the disease, regarding symptomatic expression, depends on the interaction of ants with scale insects and also on the pineapple genotype [55]. Furthermore, Green et al. state that only pineapples infested by *Dysmicoccus brevipes* and *D. neobrevipes* and infected by PMWaV-2 develop typical symptoms, such as root drying, wilting, and gradual leaf discoloration; PMWaV-2 is responsible for encoding RNA silencing suppressor proteins, which, similarly to those encoded by CTV, act locally and systemically to prevent the degradation of viral mRNAs by the host's RNA silencing machinery [56].

2.4. Papaya

Viral infections are a continuously phytosanitary and economic problem for papaya growers, who often resort to roguing, an effective control measure that involves removing the infected plants. Delayed implementation of roguing can result in losses of up to 100% in the state of Espírito Santo, the main papaya-growing region of Brazil [57]. Papaya ringspot virus—papaya strain (PRSV-p, a potyvirus) is the etiological agent of the most devastating disease of papaya crop, named ringspot/mosaic disease, since the symptoms constitute the appearance of a mosaic in leaf tissues, and a yellow circular spot on the fruits [58,59]. During PRSV-p infection, the innate immune system is activated, specifically expressing 25 DEGs of dominant resistance (related to hypersensitive responses) and 15 related to hormone-mediated resistance (e.g., ethylene and salicylic acid), and also a biological response after exposure to light, which reduces photosynthetic activity and leads to oxidative stress [60].

Papaya sticky disease (PSD) is caused by a viral complex including papaya meleira virus 1 (PMeV-1) and papaya meleira virus 2 (PMeV-2). Symptoms include reduced latex viscosity with subsequent aqueous latex exudation, causing the fruit to become "sticky", and is often followed by necrosis of the leaf tips [61]. Interestingly, symptom expression is dependent on the plant's developmental stage, occurring only after flowering. PSD is present in Brazil [62], Mexico [63], Ecuador [64], and Australia [65], and its management imposes additional challenges to growers.

The interactions between the PMeV complex and papaya plants have not been characterized in detail, but it is known that the viruses are located primarily, if not solely, in cells of the laticiferous vessels, responsible for storing latex and having a predominance

of proteases. In an attempt to escape the viral attack, papaya cells activate defense mechanisms before the flowering period, altering the expression of genes related to the synthesis of growth regulators and encoding proteins related to the chloroplast [26]. The study also demonstrated that two regions of the putative CP ORF of PMeV-1, CP2 and CP4, interact with ribosomal proteins, specifically the 50S ribosomal protein L17 (RPL17). RPL17 is down-regulated during the pre-flowering period, which is consistent with the above-mentioned symptom expression occurring only after flowering.

Papaya leaf curl virus (PaLCuV), a member of the genus *Begomovirus*, is spread to hosts by whiteflies of the *Bemisia tabaci* cryptic species complex. The PaLCuV genome is monopartite, approx. 2.8 kb in length, and contains six ORFs. Control of leaf curl disease is extremely important in production regions because it impacts papaya exportation and the extraction of pharmaceutical properties [66]. Control strategies are particularly difficult to implement because they encompass several approaches including vector control, early detection, removal of infected plants, and development of resistant cultivars [67].

2.5. Melon

The Cucurbitaceae family includes a wide range of crop plants, such as cucumber, squash, melon, and watermelon, and an important virus disease of this group is caused by the potyvirus watermelon mosaic virus (WMV). WMV infects more than 170 plant species, and in *Cucumis melo* (melon), a mixed infection, with the phloem-limited cucurbit yellow stunting disorder virus (CYSDV), is common. An extensive study by Domingo-Calap et al. studied mixed infection with WMV and CYSDV [68,69]. CYSDV had higher titers during the first 60 days of infection, while WMV had a lower concentration; however, a positive interaction was observed as aphid vectors displayed a preference for plants with the two viruses over those with a single infection by WMV. At the molecular level, the authors identified relevant interactions among four proteins: WMV P1-HC-Pro (with P1 modulating HC-Pro silencing suppressing activity) and CYSDV P22-P25 (P22 modulating P25 suppressor activity). When a mixed infection occurs, P22 does not influence HCPro functions, but P1 has a negative effect on P25, reducing its suppressor activity in a dose-dependent fashion.

Looking to obtain genetically modified organisms (GMOs) in the form of WMV-resistant cultivars, the *rwm1* gene was reported as a recessive resistance gene for WMV in *Arabidopsis* [70]. Expression of the dominant allele causes the plant to be susceptible to viral infection by interaction of the *rwm1* product (the chloroplast-encoded phosphoglycerate kinase cPGK2) with the WMV VPg protein, but if a single amino acid substitution occurs in the cPGK2 protein, the interaction no longer occurs and WMV infection is prevented. This was the first case of recessive resistance to a potyvirus where the product of the resistance gene was not an isoform of the translation initiation factors eIF4E or eIF4F, and raised new possibilities of successfully engineering resistance to potyviruses using a host-encoded gene.

Melons can also be infected by two other potyviruses, zucchini yellow mosaic virus (ZYMV) and papaya ringspot virus—watermelon strain (PRSV-w). ZYMV is an emerging virus that was reported as a concerning pathogen around 10 years ago, and its transmission occurs mechanically and most vertically by aphids, e.g., *Aphis gossypii* [71]. The ZYMV reference genome is 9.6 kb in length, and its one ORF encodes a polyprotein that eventually will be processed and generate 10 functional proteins, such as VPg, P1, HC-Pro, and CP [72]. The viral replication process depends on the interaction between VPg and eIF4E, a translation initiation factor of *C. melo*, and this is an important mechanishm to generate transgenic lines [73]. PRSV-w is closely related to PRSV-p, but is able to infect only cucurbits. PRSV-w can be transmitted by at least 32 aphid species, and the disease development constitutes a significant factor for crop productivity [74,75]. The PRSV-w cylindrical inclusion protein interacts with the NBS2 domain of the Prv protein, a typical TIR-NLR resistance (R) protein. This interaction is hypothesized to be essential for virus infection in melon [76].

Criniviruses (genus *Crinivirus*) constitute an important group of whitefly-transmitted viruses that infect cucurbit crops [77]. Cucurbit yellow stunting disorder virus (CYSDV) has been a great concern in the Middle East and in southwestern USA (Arizona and California), causing yield losses of up to 60% [78]. Although it is known that CYSDV attacks the phloem tissue and a coinfection process with cucurbit chlorotic yellows virus (CCYV) do not affect both virus titers [79], the interaction between host factors and viral components is not fully understood. Another important crinivirus is CCYV. A transient expression assay in *Nicotiana benthamiana* revealed that a minor coat protein, P4.9, was localized at plasmodesmata, a site related to cell-to-cell movement [80]. Most interestingly, a recent study revealed that the interaction between CCYV and its vector, *B. tabaci*, affects the insect's resistance to the insecticide imidacloprid [81]. Viruliferous whiteflies have the insecticide resistance gene, CYP6CM1, upregulated compared to non-viruliferous insects. Silencing of the gene by RNA interference decreased virus acquisition by the whitefly. Those findings indicate that CYVV and *B. tabaci* establish a mutualistic relationship that promotes virus transmission and therefore increases disease incidence.

3. Management Strategies

Plants are constantly exposed to infection by plant viruses, and due to the obligatory intracellular lifestyle of these pathogens, control methods must be based on risk-reducing and preventive measures [82]. Viral infectious processes are established through the complete development of a replication cycle within the host cell and the production of new infectious progeny. Control strategies can be of chemical, physical, biological, or genetic nature.

Because insects act as vectors of several plant viruses, chemical control of the vector is often an effective way of managing virus diseases. However, insecticides cause environmental harm and generate residues in crops, and their long-term use can select resistant vector populations [83]. Moreover, chemical control of the insect vector is ineffective to control non-persistently transmitted plant viruses. Physical strategies include roguing (removal of the entire symptomatic plant) or pruning (selective removal of symptomatic portions of the plant). These methods are common in some crops, such as passion fruit, in which roguing is used to control cowpea aphid-borne mosaic virus [84]; papaya, in which it is used to control PRSV and PMeV [85,86]; and banana, in which it is a preferred technique to control BBTV [87].

Genetic modifications came to solve problems that the methods above could not: identify, at the molecular level, how the host cell interacts with the invader agent, and how to interfere with this interaction to block the viral infection or improve the defense response. Genetically modified organisms were developed that brought important benefits for agriculture, such as new virus-resistant varieties of tomato [88], banana [89], apple [90], and pineapple [91]. The recently developed gene editing technology (GEd) has already generated virus-resistant varieties of tomato [92], banana [93], apple [94], orange [95], and melon [96].

4. Disease-Resistant Crops: Research Trends in Tropical Fruit Virology

The production of virus-resistant genetically modified (GM) plants was one of the greatest achievements of plant biotechnology in the late 20th century, and constitutes a virtually assured way of controlling viral diseases in both annual and perennial crops. The main strategy for generating such plants is the expression of a non-coding, virus-derived RNA, which will form a hairpin and activate the RNA silencing machinery in advance of the arrival of the virus. One of the first crops to be engineered was a tropical fruit crop, papaya, for resistance to PRSV-p.

The two GM cultivars of papaya were obtained, named "SunUp" and "Rainbow", the first engineered using an untranslatable version of the PRSV-p HA 5-1 coat protein gene, and the latter a hybrid form of "SunUp" and "Kahopo" [97]. Planting of GM papaya started in 1998 in the Puna district of the island of Hawaii, and saved the papaya industry in that

region. According to Gonsalves et al., initially, 76% of farmers in the Puna district grew transgenic seeds, and the next year, 56% of papaya fields were transgenic [98]. Despite the great results after a field trial, the authors noticed that "SunUp" was susceptible to PRSV-p strains from outside Hawaii, and that resistance in "Rainbow" was age-dependent for Hawaiian PRSV-p, mainly found in plants that were younger than 8 weeks. Even facing this problem, "Rainbow" had its commercial market ranging from 70% of the Hawaiian papaya industry, and evolved from 32% in 2001 to 77% of the market in 2009 [99]. Presently, more than 90% of the papaya production in Hawaii is GM, with no breakdown in resistance and no harmful environmental effects.

Successful control of papaya ringspot using GM papaya also occurred in China. The transgenic construct was designed to provide resistance against the four PRSV-p variants identified in China, named Ys, Vb, Sm, and Lc, and was based on an untranslatable version of the Ys NIb (replicase) gene, which is more conserved than the *CP* gene [100]. In 1998, the Huanong No. 1 GM papaya was obtained and its commercial release was approved in 2006. Large-scale planting of Huanong No. 1 confirmed resistance to the four variants, and by 2010, 85% of the cultivated area comprised the GM cultivar.

Recent advances in plant biotechnology allow for direct, precise modifications to an organism's genome, such as the introduction, removal, or editing of specific genes, significantly accelerating and efficiently obtaining desirable traits in crops [101]. Techniques such as heterologous expression, RNA interference (RNAi), and gene editing through the clustered regularly interspaced short palindromic repeats (CRISPR)/CRISPR-associated protein (CRISPR/Cas) system enable genome alteration within the same species and facilitate genetic material exchange among different species, expanding the range of genes available for use.

Plant resistance mediated by genetic engineering follows two main pathways. In pathogen-derived resistance (PDR), part of the viral genome is inserted into the host plant to induce a resistance response [102]. This is the strategy used in the GM papaya plants expressing the PRSV-p coat protein commercialized in Hawaii and China [103].

It is also possible to utilize characteristics of the host genome itself to induce a resistance phenotype, denominated as heterologous organism-derived resistance (HoDR). The eukaryotic translation initiation factors constitute an important susceptibility/resistance pathway in several crops facing potyvirus infection, specially the eIF4E family. *eIF4E* expression is upregulated during soybean mosaic virus (SMV) and WMV in soybean crops, but after the knockout of the gene by RNAi, plants showed a resistance phenotype [104]. The CRISPR/Cas9 approach was used to silence the same gene to confer resistance to potyviruses in tomato [105] and potato [106]. Studies encompassing the use of the host genome as a source of resistance are predominant in identifying susceptible genes, thus facilitating gene modification/editing and promoting the resistance phenotype. However, with the discovery of CRISPR/Cas9, this landscape is changing in current research.

Currently, basic studies such as functional genomics are capable of indicating regions in the genome or target genes that assist in the production of genetically modified plants [107]. Techniques such as knockout of susceptible genes [108], knock-in of genes conferring resistance to stresses [109], and alteration of gene expression regulation [110] are highly effective (Figure 1). Regardless of the strategy used, whether it is pathogen-derived or host-derived resistance, targeted genetic modifications and editing mediated by biotechnological tools hold promising prospects for combating viral disease (as well as other biotic stresses) in plants.
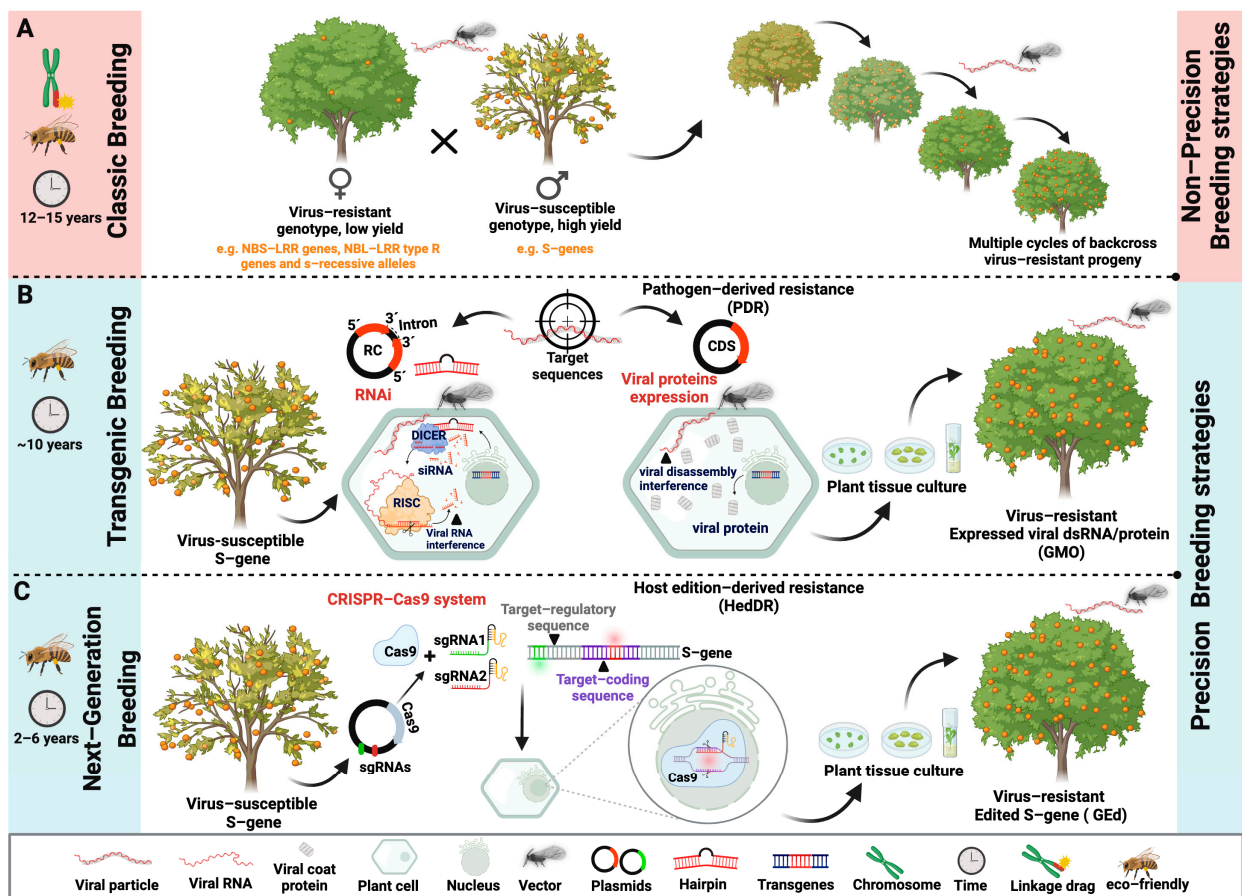
Figure 1. Evolution of the strategies for conferring resistance to viruses in plants. The scheme illustrates the two main landscapes in plant breeding to confer resistance to viral infections in plants (non–precision and precision breeding), considering the advances with the new breeding technologies (NBTs) and some particularities between strategies. (**A**) Classic breeding methods have, as their source of antiviral resistance, plant genotypes that contain canonical or similar resistance (R) genes, which through targeted crossings/backcrosses are introduced into productive, but susceptible, elite genotypes. (**B**) With the advent of genetic engineering, the prospects for obtaining virus–resistant plants have expanded, as even genomic sequences from the virus itself can be used to achieve the pathogen–derived resistance phenotype (PDR) or genes derived from heterologous organisms (HoDR), which may not be sexually compatible with the recipient plant. Both RNA interference (RNAi) using constructs with viral reverse complementary (RC) sequences to generate hairpin RNA and heterologous expression using coding sequences (CDS) from distinct sources are efficient and precise strategies that have been employed to obtain virus–resistant GM crops. (**C**) NBTs allow for an unprecedented level of precision in breeding, with the specific editing of regulatory and/or gene–coding sequences to obtain genome-edited (GEd) crops. Among the most widespread NBTs, CRISPR/Cas technology enables precise modification of the plant genome to introduce resistance against specific viral infections. Created with BioRender.com.

4.1. Pathogen-Derived Resistance by RNA Silencing

RNA interference (RNAi)-mediated post-transcriptional gene silencing (PTGS), or RNA silencing, refers to an antiviral defense response based on small (20–24 nt) RNA molecules, and involving Dicer-like (DCL), Argonaute (AGO), and RNA-dependent RNA polymerase (RDR) proteins [111]. DCL proteins (type III RNases) process double-stranded RNA (dsRNA) into small interfering RNA (siRNA) molecules. These siRNAs are then integrated into AGO endonucleases, forming the RNA-induced silencing complex (RISC). The RISC is guided by siRNAs to selectively bind to target mRNA molecules, cleaving the target mRNA and thus suppressing protein production. Additionally, the cleaved

target RNA can be recognized by RNA-dependent RNA (RDR) proteins, responsible for amplifying dsRNA, enhancing the gene silencing effect. RDRs significantly increase the efficiency of the RNAi mechanism and contribute to more robust gene silencing [112,113].

Plant-infecting viral pathogens exhibit a wide diversity of genomes, including different types of genetic material such as single-stranded RNA (ssRNA), double-stranded RNA (dsRNA), single-stranded DNA (ssDNA), or double-stranded DNA (dsDNA) [114,115]. In RNA viruses, viral-derived siRNAs (vsiRNAs) are produced from DCL-mediated cleavage of dsRNA replication intermediates. In DNA viruses, siRNAs are produced by RNA-dependent RNA (Pol II), responsible for copying regions of the viral DNA on both strands (sense and antisense), forming a perfect double-stranded RNA molecule to be cleaved by DCLs [116].

Plants engineered with viral-derived DNA sequences containing inverted repeats will express dsRNAs, which will be targeted by the RNA silencing machinery to produce vsiRNAs [117]. This has been the primary strategy to obtain virus-resistant GM plants. However, plant viruses encode RNA silencing suppressor proteins (VSRs) to bypass the siRNA-based antiviral defense response. These proteins can inhibit siRNA production, capture siRNAs, or block the spread of RNA silencing signals [118]. These evolutionary strategies allow viruses to circumvent plant immune responses and successfully establish infection. Therefore, the constant refinement of technologies for engineering virus resistance in plants is essential for successful combat against biotic stresses of viral origin in agricultural crops.

By exploring proteins responsible for viral replication (Rep), transgenic banana plants fully resistant to banana bunchy top virus (BBTV) were developed by Shekhawat et al. using RNA silencing [119]. In addition to the previously mentioned GM papayas expressing the PRVV-p coat protein, Kung et al. generated transgenic papaya lines resistant to two viruses, PRSV-p and papaya leaf distortion mosaic virus (PLDMV) [120]. Although other proteins can be used to induce resistance, the predominant strategy is based on expressing the viral CP proteins [121].

Although PDR based on RNA silencing is falling out of favor due to the rise of CRISPR-Cas, this technology remains a viable option to generate virus-resistant plants due to its efficiency, durability, increasingly simplified production, and cost reduction [122]. Significant efforts are being devoted to expanding and optimizing the arsenal of RNA silencing-based tools for topical applications, including dsRNAs, synthetic microRNAs (amiRNAs), non-coding RNAs (tasiRNAs), and miRNA mimics [123].

4.2. CRISPR/Cas

CRISPR/Cas technology is a modern biotechnological tool that employs nucleases (Cas proteins) guided by RNA to alter specific sequences in the genome with high precision [124], and which has emerged as one of the most prominent approaches due to its simplicity, effectiveness, flexibility, accuracy, and multiplexing capability [125]. Based on the adaptive immune system of *Streptococcus pyogenes*, the Cas protein forms a complex by binding to CRISPR RNA (crRNA) and trans-activating crRNA (tracrRNA) molecules, which, when fused for biotechnological purposes, is termed single guide RNA (sgRNA) [126].

This complex identifies specific genome locations which are complementary to the 5′ leader sequence of the crRNA by recognizing the PAM (protospacer adjacent motif) sequence and initiates editing upstream of the sequence [127] after forming an RNA/DNA heteroduplex structure between the crRNA and the host DNA strand [128]. The PAM sequence may vary depending on the origin of the Cas protein used in the system. In the case of the *Streptococcus pyogenes* Cas9 protein, the sequence is NGG or NAG [37]. Gene editing involves insertions and deletions (indels) or substitutions of nucleotides, promoted by repair processes after double-strand breaks (DSBs). DSB repair can be mediated by homology-directed repair (HDR) or by non-homologous end joining repair (NHEJ) [129].

Compared to RNAi, CRISPR/Cas technology offers distinct advantages in engineering virus resistance in plants. Instead of post-transcriptional gene silencing, it enables targeting

susceptible genes necessary for viral spread or the manipulation of active sites of gene expression [130]. Among all biotechnological methods involved in plant transformation, the gene editing method via CRISPR/Cas has significantly increased in use in recent years.

Several studies have demonstrated the effectiveness of the CRISPR/Cas9 system in conferring resistance to DNA and RNA viruses in plants [131–133]. Furthermore, the CRISPR/Cas method allows for the exclusion of exogenous DNA persistence in the plant transformation process.

New research covering the various applications of the CRISPR/Cas9 methodology will be essential for managing viral diseases in tropical fruit crops. The CRISPR/Cas9 system has already been applied in fruit crops grown in tropical and subtropical regions, such as banana [134–136], orange [137,138], melon [139,140], apple [141,142], and papaya [143]. However, studies on some major tropical fruit crops are either scarce (papaya) or non-existent (pineapple). To mitigate the effects of viral diseases, these versatile methodologies are adopted in both basic [144,145] and applied [146,147] research. But even with these gaps, CRISPR/Cas is quickly becoming a powerful tool in the development of transgenic and non-transgenic plant varieties resistant to viral diseases, preventing agricultural production loss and aiding food security.

5. Conclusions and Future Perspectives

The investigation into plant viral diseases is crucial given their substantial impact on agricultural production, including tropical fruit crops. Genetic modification is an indispensable tool in the development of virus-resistant plants by targeting specific regions critical for viral infection. Nevertheless, recent research emphasizes how viral evolution can surpass these modifications, presenting persistent challenges to biotechnological endeavors [148,149].

Future research should focus on exploring alternative genetic targets for modification, integrating multiple resistance mechanisms, and leveraging emerging biotechnological tools such as CRISPR-based technologies. Additionally, there is a need for increased surveillance and monitoring of viral diversity in tropical fruit crops to anticipate and mitigate the emergence of new viral variants.

Ultimately, by advancing our understanding of viral biology and genomics and leveraging innovative biotechnological solutions, we can mitigate the impact of plant viral diseases on global food security and ensure the sustainable production of tropical fruit crops.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: No new data were created in this study.

Conflicts of Interest: The authors declare no conflicts of interest.

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