Chapter

Viral Diseases of Tomato – Origins, Impact, and Future Prospects with a Focus on Tomato Spotted Wilt Virus and Tomato Yellow Leaf Curl Virus

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Abstract

Tomatoes are affected by a number of viruses, with tomato spotted wilt virus (TSWV) and tomato yellow leaf curl virus (TYLCV) being two of the most damaging. TSWV and TYLCV have severely impacted tomato production worldwide for the past several decades at levels that led to both of these viruses being included in the list of top ten most important plant viruses. While they were first described in the early 1900s, both of these viruses emerged in the 1980s to become the severe and persistent problems they are today. The emergence of both viruses was facilitated in part by the emergence and expansion of more efficient insect vectors. Natural sources of resistance, especially from wild relatives of tomato, have provided some measure of control for both viruses to date. This chapter summarizes the origins, emergence, and impacts of these viruses, along with current approaches and future prospects for control, including both natural and engineered resistance.

Keywords: tomato spotted wilt virus, TSWV, tomato yellow leaf curl virus, TYLCV, RNAi, SIGS, spray-induced gene silencing, RNA interference

1. Introduction

Tomato (*Solanum lycopersicum*) is a member of the Solanacea family of plants that also includes potato, chili and bell peppers, and eggplant. Tomato is a ubiquitous crop produced worldwide for a variety of uses ranging from high value fresh fruit to use in a variety of processed products including ketchup, pastes, soups and stews, and canned pasta sauces. Tomatoes are grown under a variety of conditions including open fields, plastic or green houses, screenhouses, and indoor growth rooms.

Tomatoes are one of the most important vegetable crops in the world, valued for both their flavor and nutritional qualities including being rich in vitamins A and C as well as minerals like calcium, potassium, and phosphorus. According to FAO statistics, tomatoes are the most widely produced vegetable, with production levels

of ~170 million tons annually and accounting for ~16% of all vegetable production worldwide [1] coming from ~5 million cultivated hectares. Tomato production has been steadily increasing over recent decades, with China, the US, and India being the largest producers.

Tomato was likely domesticated by indigenous peoples in Mexico and became an important vegetable crop in Central America prior to the arrival of Europeans. Tomatoes were first introduced to Europe by conquistadors returning from the Americas then spread across Europe and the Spanish empire. Tomatoes spread quickly around the globe and even reached China during the 16th century [2].

Tomatoes are affected by many diseases, like all domesticated crops that have been extensively bred and grown in high-density monoculture. Diseases affecting tomato include those caused by bacteria, fungi, viruses, and nematodes. Viruses cause some of the most consistent and severe losses of tomato crops (reviewed in [3–5]). This chapter will focus on two viruses that have caused serious problems in tomato production for several decades, tomato spotted wilt virus (TSWV) and tomato yellow leaf curl (TYLCV). Both of these viruses were included in the top ten most damaging plant viruses, with TSWV and TYLCV occupying the second and third spots on the list, respectively [6].

TSWV and TYLCV provide interesting contrasts on a number of levels including genome structure (RNA for TSWV and DNA for TYLCV), the origin of TSWV appearing to have been disseminated around the globe along with tomatoes and/or peppers, while TYLCV has emerged more recently and its spread has been partly facilitated by humans; TSWV has an extremely broad host range that includes plants and animals, while the host range of TYLCV is much more limited. These two viruses also share some common themes including the role of insect transmission in their emergence as leading pathogens, the strong potential for natural resistance to play a role in controlling damage, and the potential for biotech/genetic engineering solutions to reduce damage caused by these viruses. This chapter will examine some of the commonalities and differences between TSWV and TYLCV as well as current and potential future prospects for control of these highly damaging pathogens.

2. Tomato spotted wilt virus background

TSWV causes severe losses in tomato and many other crops worldwide. Symptoms of TSWV in tomato include spotting, often ring spots, and uneven ripening that renders the fruit unmarketable, along with bronzing and wilting of vegetative tissue (**Figure 1**). The first known report of spotted wilt disease on tomatoes was in 1915 in Australia [7]. This spotted wilt disease was shown to be thrips transmitted in 1927 [8] and attributed to a virus in 1930 [9]. TSWV was subsequently reported in various regions around the glove, including Hawaii and Europe, where it appeared sporadically for several decades until emerging as a more regular and profound problem in the 1980s. Since that time, TSWV has become one of the most damaging plant viruses in the world, being cited for regularly causing over $1 billion in annual crop losses worldwide since the mid-1990s [10] and being recognized as the second most damaging plant virus in the world [6].

TSWV is a member of the Tospovirus genus within the family Bunyaviridae. TSWV virions are pleomorphic pseudo-spherical, with a diameter ranging from ~70 to 120 nm, and are enveloped in a host-derived membrane [11]. The RNA genome segments inside the envelope are encapsidated in N protein [12]. The virions also

Figure 1.
Tomato spotted wilt on tomato and chili pepper fruit. Typical symptoms of TSWV, including uneven ripening and spotting of fruit on tomato (left) and chili pepper (right).

contain the L protein, which is the viral RNA-dependent polymerase [13]. TSWV is mechanically transmissible to most plant species it infects, and plants can be infected with either virions or membrane-free ribonucleoprotein complexes that contain the N protein-encapsidated genome segments [14].

Tospoviruses have a tripartite negative sense (or ambi-sense) genome (**Figure 2**). The three genomic RNAs are designated by size as large (L), medium (M), and small (S) RNAs. The L RNA have an entirely negative sense, while the M and S RNAs have ambi-sense and encode genes in both the viral genome sense and viral complement senses [15]. The TSWV genome codes for five proteins overall [16]. The L protein is coded on the viral or negative sense on the L RNA and is the viral RNA-dependent polymerase [13, 17]. The M RNA has ambi-sense and codes for the NSm protein in the genome sense and the polyprotein that is processed into the two structural glycoproteins in the genome complement sense. The non-structural protein NSm has been shown to promote cell to cell and long-distance movement during infection [16, 18]. The glycoproteins were formerly referred to as G1 and G2 but are now denoted as Gn and Gc, indicating their N- or C-terminal location in the precursor polyprotein. The glycoproteins decorate the surface of the virions and are required for thrips transmission [19, 20]. The ambi-sense S RNA codes for the nonstructural protein NSs in the genome sense and the N protein in the genome complement sense. The NSs protein promotes thrips transmission and also functions as a suppressor of RNA silencing

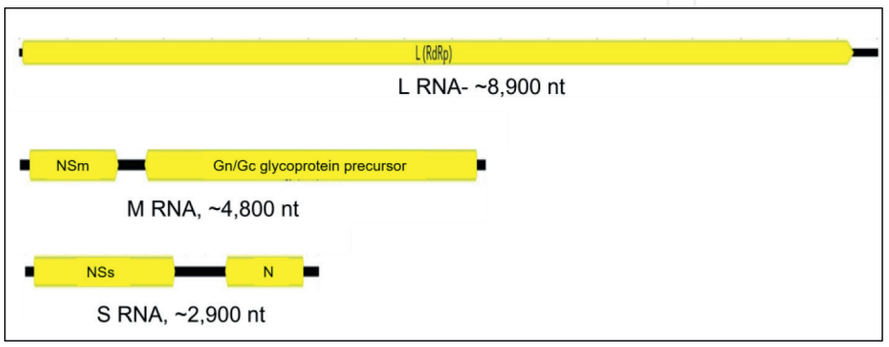

Figure 2.
Genome structure of TSWV. Cartoon representation of the tripartite TSWV genome showing the L, M, and S RNAs approximately to scale. Yellow boxes show positions of open reading frames in the genomic (L, NSm, NSs) and genome complement (glycoprotein precursor and N) senses.

[21, 22], while the N protein is the nucleocapsid that encapsidates viral RNA to form RNPs [23]. The N protein is also required for local spread, suggesting that RNPs may be the functional viral unit involved in local spread [24].

Reverse genetic systems have been a valuable tool that enabled in vitro infection from cloned cDNA and DNA copies of plant virus genomes, mutational analysis of virus genes, evaluation of chimeric viruses, and more. Unfortunately, reverse genetics systems have been unavailable or difficult to develop for viruses with negative or ambi-sense genomes, including TSWV. The recently reported rescue of TSWV from cloned cDNAs is an exciting step forward that will enable reverse genetic analysis of TSWV to TSWV researchers [25].

TSWV has an extremely broad host range and is a rare case of a virus that infects hosts in two different kingdoms as it replicates in both plants and its thrips vector [26]. This observation led to the speculation that TSWV may be a thrips-infecting virus that evolved to also infect plants, which may partially explain its severity as a plant virus. For plants, the host range of TSWV includes over 1000 different plant species in 82 botanical families encompassing both monocotyledonous and dicotyledonous plants [27]. This extremely broad host range likely contributes to TSWV disease persistence since there is a high likelihood that alternate hosts will be present even when susceptible crops are not being grown.

TSWV is transmitted by at least 10 different species of thrips with *Frankliniella occidentalis*, commonly known as the wester flower thrips, being the most efficient vector species [28, 29]. Transmission is circulative and propagative [30, 31]. While adult thrips can acquire TSWV, they are unable to transmit it, and transmission only occurs when thrips acquire TSWV as first- or second-stage larva [29, 32, 33]. While adult thrips can acquire TSWV, they are unable to transmit; thus, the acquisition of TSWV by adult thrips is a dead end for TSWV. Thrips larvae can acquire TSWV with acquisition access periods as short as 15 min although transmission efficiency increases with longer acquisition access periods, and an acquisition period of 4 days was reported to result in 74% of emerging adult thrips being competent for TSWV transmission [34]. Thrips that acquire TSWV remain infected and able to transmit TSWV for life due to the circulative propagative nature of transmission.

TSWV is thought to be acquired by thrips via an animal virus-like receptor-mediated interaction that is rare among plant viruses. The demonstration that a truncated soluble form of the TSWV glycoprotein Gn interferes with thrips transmission of TSWV, presumably by blocking TSWV receptors in the thrips midgut, suggests that the glycoproteins are the viral proteins that mediate virion acquisition [35]. Identification of thrips receptors for TSWV has been an area of interest since it may lead to strategies for blocking thrips transmission of TSWV. While early reports of thrips proteins that interact with TSWV [36] generated some excitement, these initial leads appear to have been dead ends (S. Hanson, unpublished). More recent work has identified different thrips proteins that interact with TSWV virions or glycoproteins and are therefore promising candidates for receptors that mediate TSWV acquisition in thrips [37].

TSWV was described as occurring in many different parts of the world going back to the mid-1900s. This worldwide distribution as a minor pathogen before emergence as one of the most damaging agricultural viruses suggests that TSWV may have spread around the world with host plants like tomato and pepper as they were brought back from meso-America and subsequently spread around the globe. Molecular phylogeny studies that have shown that TSWV often exists as a stable populations in geographically isolated regions and may have spread around the world

with tomatoes and/or peppers when these plants were introduced to Europe and beyond by Spanish explorers returning from the Americas [38]. The emergence of TSWV as a more widespread and damaging disease started in the 1980s, likely due to the spread of the more efficient western flower thrips vector into areas that were already infested with TSWV.

3. TYLCV background

Serious outbreaks of tomato yellow leaf curl disease were reported in the late 1920s in the Jordan Valley [39]. Typical symptoms of TYLCD include mosaic chlorosis and stunting of affected plants (**Figure 3**). Since then, numerous outbreaks of TYLCD happened around the Mediterranean in the 1960s. From there, it spread throughout the Middle East to Central Asia, Africa, and the Americas. TYLCV is now considered to be ubiquitous across tropical, subtropical, and temperate regions [40]. During the 1980s, outbreaks of TYLCV became more common and widespread, with some being noted as causing up to 100% loss in affected areas of Italy and the Dominican Republic [41, 42]. All of this led to TYLCV being recognized as one of the most severe viral pathogens of tomato worldwide [43, 44] and to TYLCV being ranked the third most important plant virus in the world [6].

TYLCV is a member of the geminiviridae family, characterized as having single stranded genomes that replicate via a rolling circle type of mechanism and unique twinned icosahedral capsids (reviewed in [45]). There are nine recognized genera within the geminiviridae, and TYLCV is part of the begomovirus genus, which is characterized as being transmitted by whiteflies and infecting dicot plants [46]. The large number of individual viruses within the begomovirus genus has led to several revisions for how groupings are determined and individual viruses are named within this group [47, 48]. The begomovirus genus contains numerous distinct tomato-infecting members, with the TYLCV subgroup being recognized as one of the most damaging to agriculture [47]. With so many closely related members, the TYLCV subgroup is often treated as a complex of closely related strains that are individually identified by including the location where the strain was recognized in the name, such as for tomato yellow leaf curl sardinia virus denoted as TYLCSV (recent listing in table 1 of [47]). In addition to the large number of strains identified to date, mixed infections that produce recombinant/chimeric variants are believed to happen frequently [49].

Figure 3.
TYLCV symptoms. Typical symptoms of TYLCV on tomato, including stunted plants (left) and mosaic chlorosis (right).

TYLCV was the first member of the begomovirus genus with a monopartite genome, with most begomoviruses having bipartite genomes (**Figure 4**). The genome of TYLCV is ~2.7 Kb and codes for genes in both the viral and complementary senses [50]. The relatively small and simple nature of geminivirus genomes has facilitated extensive reverse genetic analysis via infectious DNA clones that have been obtained for many geminiviruses including TYLCV.

The viral sense codes for two open reading frames (ORFs), with V1 encoding the capsid protein and V2 coding for a multifunctional protein that functions to both facilitate movement and suppress RNA silencing [51, 52]. The genome complementary sense strand encodes four overlapping ORFs that have broad functions in viral replication, transcription, and host interactions. The C1 ORF encodes the replication-associated protein that contains ATPase and DNA nicking domains [53]. The C1 protein promotes rolling circle replication directly by initiating and terminating rolling circle replication via DNA nicking and ligase activities and indirectly by recruiting host factors involved in viral DNA replication. The C2 ORF codes for a transcriptional activator protein (TrAP) that regulates early and late gene expression. The C3 ORF codes for a replication enhancer protein (Ren). The C4 ORF is involved in symptom development and movement [54]. Like all geminviruses, TYLCV contains a large intergenic region that facilitates bidirectional transcription and contains the origin of replication, including a requisite stem-loop sequence, where rolling circle replication begins and ends.

TYLCV, like all begomoviruses, is transmitted by whiteflies (*Bemisia tabaci*) in a circulative manner (reviewed in [55]). Acquisition and inoculation can both

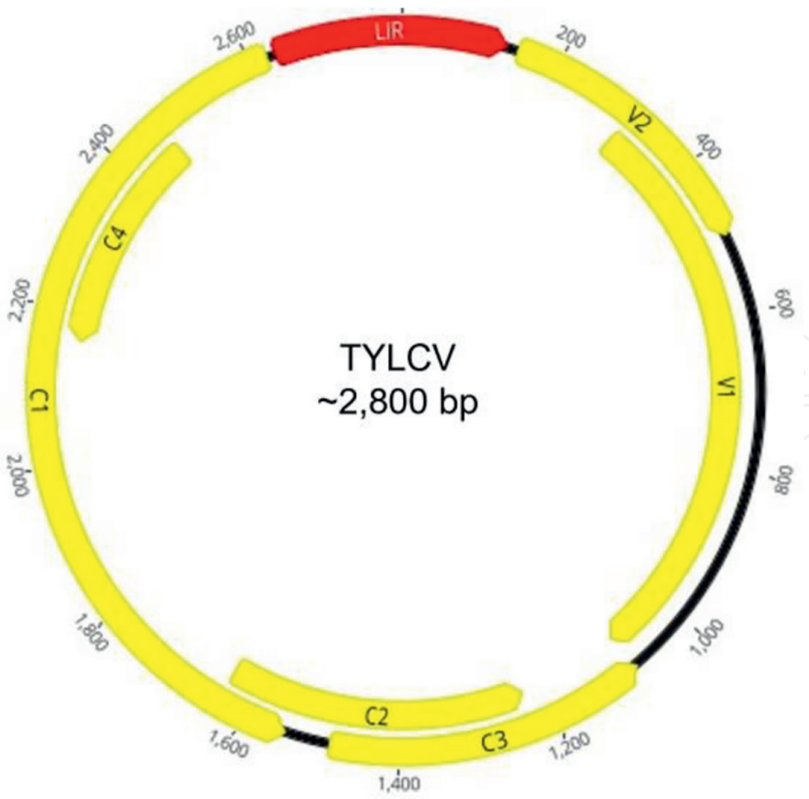

Figure 4.
TYLCV genome. Cartoon representation of the circular ssDNA genome of TYLCV. Open reading frames are shown in yellow. The large intergenic region containing the origin of replication and bidirectional promoters is shown in red.

be as quick as 15 minutes. While several *B. tabaci* biotypes are able to transmit geminiviruses, the emergence and spread of the B biotype that is highly efficient at transmitting geminiviruses played a key role in increasing the spread and severity of geminivirus diseases, including TYLCV, that started in the 1980s.

4. Management of TSWV and TYLCV

In spite of many differences in virus biology, the factors that lead to the emergence of these viruses and measures for control share a lot of commonalities. A great deal of work has gone into reducing losses caused by TSWV and TYLCV over the past few decades, with some promising advances, although much remains to be done as both viruses still cause extensive losses in tomatoes at present. Standard IPM-based practices, especially those that limit insect vectors, are widely used for controlling both TSWV and TYLCV [56–58]. Although these IPM-based approaches can produce modest reductions in disease, they are not able to prevent all diseases. Breeding for disease resistance has shown some success for both TSWV and TYLCV, and thus, resistance breeding programs are likely to continue as a focus into the future. While not broadly adopted at present, genetic engineering (GE) has shown great potential for controlling both TSWV and TYLCV. The high cost of developing GE lines, extensive regulatory requirements, and concerns about consumer acceptance of GE crops have severely limited the adoption of these approaches for control of diseases in agricultural crops (reviewed in [59]). Thus, GE-based approaches hold great promise for controlling diseases if GE crops become more widely accepted for use in agriculture.

Since the emergence and expansion of more efficient vector species was a major driver in increasing damage caused by these viruses, a number of approaches, especially integrated disease management approaches, have focused on reducing populations of insect vectors or managing production aspects like time of planting to reduce exposure of plants to viruliferous insect populations [58, 60]. Strategies based on insect vector control remain challenging for several reasons, including the lack of effective insecticides, the rapid evolution of insecticide resistance, the fact that both thrips and whiteflies are successful on a number of alternate hosts, and very quick transmission when viruliferous insects enter agricultural fields.

5. Genetic resistance

Natural resistance has been a highly successful and long-relied-upon strategy for controlling many plant pathogens. Often, wild relatives are found to contain sources of resistance that can be introgressed back into domesticated lines where resistance has been lost.

Several resistance genes have been described for TSWV. These include the single dominant R genes like the Tsw gene from *Capsicum chinense* and the Sw-5 from *Lycopersicon peruvianum* that have provided commercially useful resistance to TSWV resistance in tomato [61–63]. Both of these genes confer a typical hypersensitive response (HR)-based resistance that usually prevents systemic infection by stopping pathogens at the site of inoculation [64]. Molecular studies on TSWV strains with re-assorted genomes were used to determine that the NSm gene is the avirulence determinant recognized by the Sw-5 gene [65].

Natural resistance genes have also been described for several geminiviruses, with many of the resistance genes coming from non-domesticated relatives (reviewed in [66]). This is especially true for TYLCV [66]. The tomato relative *Solanum chilense* is noted as the most common source of TYLCV resistance genes identified to date [66]. At least twelve different sources of resistance to TYLCV were described as of 2020 (summarized in [67]). The Ty-2 gene appears to be a canonical R gene with typical nucleotide binding (NB) and leucine-rich repeat (LRR) regions [68], while others are clearly not classical R genes, but are rather genes involved in RNA metabolism, basic metabolism, cell status sensing, or signaling. The Ty-1 and Ty-3 resistance genes appear to be alleles of a gene [69] that encodes for RNA-dependent polymerase and cause increased cytosine methylation in replicated genomes [70]. Members of the WRKY group III transcription factors have been shown to play a role in TYLCV defense signaling [71]. Still other genes involve in hexose transport or other metabolic processes [72].

Unfortunately, single dominant R genes tend to have limited durability and are often overcome as pathogens evolve to escape the resistance. This is the case for many of the resistance genes described above. Resistance breaking strains of TSWV that overcome the Sw-5 genes have emerged several times independently in different areas including Europe, the US, and Australia [73–75]. Multiple independent cases of resistance breaking TSWV variants have also been reported for the Tsw genes [61, 76]. Resistance breaking has also been observed for several of the described TYLCV genes. Ty-2 mediated resistance was reported to be overcome by TYLCV-Sardinia [77] and an isolate of the mild strain of TYLCV [78]. The Ty-1 gene has been shown to be overcome occasionally under high disease pressure [79].

The generation of resistance breaking strains does not mean that R genes are not useful for control of TSWV and TYLCV. On the contrary, genetic resistance has proven to be one of the most effective tools for limiting TSWV and TYLCV losses to date. And the generation of resistance breaking strains is both typical and expected for any single dominant R gene against any evolving pathogen. For R genes to provide long-term utility, they need to be cycled through, with tomorrow's R genes being discovered while today's are in use. Fortunately, wild relatives of tomato appear to be a robust source for the discovery of new R genes that may be able to supply novel sources of genetic resistance to these viruses well into the future. This is evidenced by one recent study that has evaluated ~700 accessions derived from 13 wild tomato species, where ~140 of the lines were symptom free after inoculation with TYLCV [66]. Based on this, it is likely that wild species will continue to be a robust source of natural resistance genes that will help in reducing TSWV- and TYLCV-caused losses for the foreseeable future.

It should also be noted that while R genes are the most common form of resistance gene found historically, single dominant R genes are not the only type of genetic resistance to pathogens. There are several examples of multigenic resistance and tolerance that provide long-term stable reductions in pathogen losses. One current example is a multigenic field resistance that appears to be providing long-term durable control of TSWV in peanuts [80]. Sequence-level population analysis of multiple TSWV genes did not detect any resistance-related selection in TSWV populations, indicating that this multigenic resistance is likely to be durable. While this resistance appears to be based on high-level tolerance, it provides commercially useful control of TSWV in peanuts, a crop that suffered serious losses from TSWV prior to deployment of this

resistance. Future work using marker-assisted breeding and similar approaches may be useful for developing tomato lines with similar multigenic resistance to TSWV and TYLCV in the future.

6. Engineered resistance

Genetic engineering is an approach that has proven useful for developing resistance to many plant pathogens including many plant viruses. This is true for TSWV and TYLCV, where numerous approaches for creating engineered resistance have been reported over the past several decades. While several approaches have been described, gene silencing/RNAi approaches (reviewed in [81]) are the most common. Despite promising research results, genetically engineered virus resistance has not been widely adopted due to several barriers, including the high costs for the development of commercial lines approved for human consumption and public resistance to GMO crops (reviewed in [59]).

The first description of engineered resistance to TSWV was described in 1991 [82]. Since that time, several additional examples of engineered resistance to TSWV have been reported, including the use of chimeric RNAi-inducing genes that confer broad spectrum tospovirus resistance [83, 84]. Despite these promising results, engineered resistance to TSWV has yet to be deployed in commercial crops.

Numerous examples of engineered resistance have also been described for geminiviruses in general and TYLCV in particular (reviewed in [85]). Similar to TSWV, the first reports of engineered geminivirus resistance also date back to the 1990s, with many of these attempts using virus-derived resistance targeting the viral genes involved in replication, movement, or encapsidation [86–88]. Examples also include numerous descriptions of anti-sense RNA- and RNAi-based resistance. There are also some interesting examples of non-pathogen-derived resistance, including the use of peptide aptamers that interfere with the function of geminivirus replication-associated proteins that were found to confer high-level tolerance to several diverse begomoviruses, including TYLCV and tomato mottle virus [89]. Still other approaches have targeted host functions like those involved in modulating host defenses [90, 91]. Approaches that modulate host resistance responses have also shown promising results.

Geminiviruses are one rare example where engineered resistance has been approved and deployed in crops produced for human consumption [92]. In this case, common beans engineered to express an RNAi construct targeting the Rep gene of bean golden mosaic virus (BGMV) proved to be highly resistant to begomoviruses affecting bean production in Brazil [93]. The lack of natural resistance sources for BGMV, in spite of decades of screening, made engineered resistance an attractive alternative for BGMV. Extensive multi-year field testing showed that this gene effectively protected common beans from BGMV-caused losses, which had previously reduced yields by 40–100% [94]. So far, this resistance is only approved for use in Brazil. The effectiveness of this approach for controlling BGMV-caused losses, and similar levels of conservation among the Rep genes of TYLCV isolates, suggests that this approach has strong potential for controlling TYLCV-caused losses. While genetic engineering holds great promise for controlling TYLCV, the substantial barriers associated with development costs, regulatory approval, and consumer acceptance must still be overcome before engineered resistance approaches can be broadly utilized.

The time, cost, and consumer acceptance barriers to deploying genetically engineered resistance in crop plants intended for human consumption have spurred innovation aimed at producing similar resistance mechanisms without using transgenic plants. Promising approaches in this area include the use of exogenous double-stranded RNAs that are sprayed on plants to induce an RNAi response in a process referred to as spray-induced gene silencing (SIGS; [95]). SIGS has shown promise against several viral pathogens including TSWV [96]. Another similar approach uses endophytic bacteria engineered to express dsRNAs that can induce and RNAi response in plants. This bacterial-mediated RNAi, sometimes referred to as transkingdom RNAi, has shown promise in reducing infection by fungal and viral plant pathogens [97]. It will be interesting to see if SIGS or transkingdom RNAi evolve into useful technologies that provide control of plant pathogens while successfully skirting the barriers that have prevented more widespread adoption of genetically engineered approaches for control of plant pathogens like TSWV and TYLCV.

7. Summary

Tomatoes are the most widely produced vegetable on earth, and viruses have been a persistent problem in tomato production for as long as tomato has been cultivated as a crop. TSWV and TYLCV have been serious yield-limiting constraints on tomato production for the past several decades. Tried and true practices like traditional resistance breeding and integrated disease management have allowed continued production of tomatoes in spite of the severe losses these viruses can cause. It is likely that both of these viruses will be better controlled in the future based on the rich body of knowledge developed to date for these viruses. In particular, the abundance of natural resistance sources that are known to be present in wild relatives will continue to be a valuable source of natural resistance genes. Biotech is also likely to play a bigger role in the future on several levels. Marker-assisted breeding and other related approaches will speed introgression of natural resistance resources into commercial cultivars. And if (or when) the cost and societal acceptance barriers are reduced, approaches like engineered resistance and technologies like SIGS are certain to reduce virus caused losses.

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