Hortic. Environ. Biotechnol. 57(2):113-122. 2016.
DOI 10.1007/s13580-016-0105-x

ISSN (print) : 2211-3452
ISSN (online) : 2211-3460

Research Report

Current advances and prospectus of viral resistance in horticultural crops

Inhwa Yeam

Department of Horticulture and Breeding, Andong National University, Andong 36729, Korea

*Corresponding author: iyeam@andong.ac.kr

Received April 4, 2016 / Revised April 11, 2016 / Accepted April 19, 2016

Abstract. Viruses are a major threat causing massive yield loss and economical damage to crop production worldwide. Through complex evolutionary processes, plants encounter and overcome viral infection by developing effective resistance mechanisms. Over the past decade, remarkable progress has been made in understanding the nature of plant resistance to viruses at the molecular level. This review summarizes the major resistance strategies that plants use to prevent viral infection. Recent investigations suggest that antiviral RNA silencing is the most prevalent defense strategy in plants. Other forms of resistance include R gene-mediated resistance and host factor-related recessive resistance. Naturally occurring resistances arise and are maintained in numerous virus-plant pathosystems based mainly on arms-race relationships and the cost-efficiency of resistance acquisition. In addition to the current status of the known resistance mechanisms, this review discusses the future prospectus for the practical application of plant resistances that influence resistance durability in agricultural ecosystems. Such applications include molecular breeding strategies using advanced molecular marker systems and the utilization of trans- or cis- genetics via the acquisition of engineered disease resistances.

***Additional key words*:** durable resistance, engineered resistance, marker-assisted selection (MAS), recessive resistance, R gene-mediated resistance, RNA silencing, virus resistance

Introduction

Viral diseases are one of the major factors threatening crop production worldwide. It is estimated that about 15% of global crop production is lost due to various plant diseases, and phytopathogenic viruses are thought to cause more than one third of plant diseases (Boualem et al., 2016). Although pesticides are commonly used to reduce viral vector populations, chemical treatments cannot directly limit virus infections. In order to control agricultural losses to viral diseases, the development of disease-resistant varieties with durable and broad-spectrum resistance against various viruses has been a major goal in most plant breeding programs (Kang et al., 2005b).

Plant viruses are obligate intracellular parasites that absolutely require host cell machinery for multiplication and transmission. Viruses are nucleic acid-based pathogens that are generally packed in protein called capsids. Their genomes typically consist of single-stranded (ss) or double-stranded RNA or DNA, and the size of their genome is very small compared with that of other organisms including non-viral phytopathogens. The phytopathogenic viral life cycle of ssRNA viruses, which are considered as a major type of plant viruses, includes entry into plant cells, the uncoating of nucleic acid, the translation of viral proteins, the replication of viral nucleic acids, the assembly of progeny virions, cell-to-cell movement, systemic movement, and plant-to-plant movement (Carrington et al., 1996). Viruses lack components necessary for their own independent survival, so they rely upon numerous factors in the living host cells (Boualem et al., 2016). Although viruses are relatively simple genetic entities, the molecular mechanisms of resistance and susceptibility to viral diseases are not fully comprehended.

It is impossible to summarize all the existing disease-resistance mechanisms in a single model; however, there are several representative models based on well-characterized pathosystems (Brown, 2015; Nishimura and Dangl, 2010). Our general understanding of the molecular mechanisms of phytopathogen-host interactions has been achieved based mostly on several model bacteria-plant systems. The gene-for-gene hypothesis was proposed and has served for many years as the model of how disease resistances turn on against diverse pathogens (Flor, 1971; Keen, 1990). Based on the gene-for-gene model, a single resistance gene (R gene) encoded by the host recognizes the presence of the avirulence (Avr) proteins, effectors generally secreted by bacterial type III se-

cretion system, fungal haustoria or nematodes stylets, and triggers a resistance response, which is generally associated with the rapid appearance of cell death, a hypersensitive response (HR) (Dangl and Jones, 2001). The first characterized plant R gene was *Pto*, a protein kinase that physically interacts with either AvrPto or AvrPtoB, its avirulence determinants (Martin et al., 1993; Tang et al., 1996). Numerous R genes have since been characterized in multiple plant species. The most general types of R genes can be grouped into two classes: genes encoding nucleotide-binding leucine-rich repeat (NB-LRR) proteins and genes encoding receptor-like kinase/receptor-like proteins (Rathjen and Moffett, 2003). About a decade later, the zig-zag model was proposed (Jones and Dangl, 2006; Cook et al., 2015). In the zig-zag model, the plant defense system consists of two distinct defense responses. The primary level of defense is called PAMP/MAMP-triggered immunity (PTI), and the secondary level of defense is called effector-triggered immunity (ETI). PTI presents a basic defense mechanism by preventing pathogen invasion or thickening the cell wall in response to specific structures or proteins associated with the pathogen, so called pathogen-associated molecular patterns (PAMPs) or microbe-associated molecular patterns (MAMPs). Plants will show susceptibility only when a pathogen successfully establishes both suppression of the PTI response and facilitation of its pathogenic effectors. ETI, the second level of the defense response, is triggered when the R gene products directly or indirectly sense the presence of specific effectors, also called Avr factors. Consequently, an effective ETI will keep the plant resistant; however, an insufficient ETI will lead to disease establishment (i.e., susceptibility of the plant). Additionally, the guard hypothesis and the decoy model, a modified guard hypothesis, have been proposed and elucidated in multiple pathosystems (Dangl and Jones, 2001; Jones and Dangl, 2006; Van der Hoorn and Kamoun, 2008).

General resistance models do not fit well with viral resistance, primarily because of the intracellular parasitic nature of the virus, which, unlike other pathogens, absolutely requires the live host cell machinery. For example, pattern recognition receptors, which serve as a major defense component by triggering the first layer of resistance when a plasma-membrane receptor perceives a bacterial or fungal MAMP or PAMP (Tena et al., 2011), cannot play a role in fighting plant viruses, because viruses do not express extracellular PAMPs. Instead, RNA silencing serves as a major antiviral mechanism, although the R gene-mediated strategy is also effective against viruses as well as other phytopathogens (Nakahara and Masuta, 2014; Rodriguez et al., 2015). In the case of resistance with recessive inheritance, several recessive resistance genes have been characterized in studies of both fungal and bacterial pathogens, including *xa5*, a *Xanthomonas* resistance gene in rice (Iyer-Pascuzzi and McCouch, 2007), and *mlo*, a powdery mildew resistance gene in barley (Buschges et al., 1997). The majority of recessive resistance genes have been identified in virus-plant pathosystems, however.

This review will first focus on what is known about the naturally existing viral resistances: i) antiviral RNA silencing, ii) R gene-mediated resistanceand, and iii) recessive resistance. Second, this review will discuss the application of those known resistances from two different perspectives: molecular breeding strategies using advanced molecular marker systems and the utilization of trans or cis genetics via the acquisition of engineered disease resistances.

Overview of Virus Resistance in Plants

In the area of plant-virus interaction, *Tobacco mosaic virus* (TMV), the first virus to be discovered and isolated (Holmes, 1929), and *N*, its counterpart R gene from *Nicotiana glutinosa*, historically served as a model system for studying HR-based resistance, systemic acquired resistance (SAR), and elaboration of the gene-for-gene model. The *N* gene was the first viral R gene to be cloned and characterized, which occurred soon after the *Pto* cloning (Whitham et al., 1994). Moreover, in the case of TMV-triggered SAR, it was discovered that the mobile SAR signal can be transferred to non-infected distant tissues and maintained up to 3 weeks (Vlot et al., 2008). Despite the fact that studies of virus resistance in plants have made prominent contributions to our overall knowledge of disease resistance in plants, the critical advances in understanding the molecular mechanisms of disease resistance have primarily come from investigations of bacterial and fungal phytopathosystems. Recent studies using techniques such as RNA silencing, virus-induced gene silencing, large-scale genomic analysis, and epigenetic analysis have accelerated the exploration of plant antiviral mechanisms at the molecular level.

Genetic resistance (natural resistance) with antiviral activities comprises antiviral RNA silencing, R gene-mediated resistance, and recessive resistance in general (Fig. 1) (Kang et al., 2005b; Maule et al., 2007). R gene-mediated resistance, which is the most intensively explored form of resistance to the diverse bacteria, fungi, and viruses generally responsible for the HR, is an effective way for plants to gain viral resistance. However, because viruses are intracellular parasites consisting of a small RNA or DNA genome packed in a capsid, the RNA silencing strategy is considered as a major antiviral mechanism (Smyth, 1999; Nakahara and Masuta, 2014; Rodriguez et al., 2015). Successful antiviral RNA silencing primarily results in the degradation of the viral genome at the site of the initial infection (Voinnet, 2001). Resistance with recessive inheritance, mostly acquired via the alteration of key host factors required for the viral infection cycle, is also recognized as an effective antiviral resistance mechanism (Robaglia and Caranta, 2006). In addition to those main antiviral mechanisms, it was demonstrated in several systems that the ubiquitin proteasome

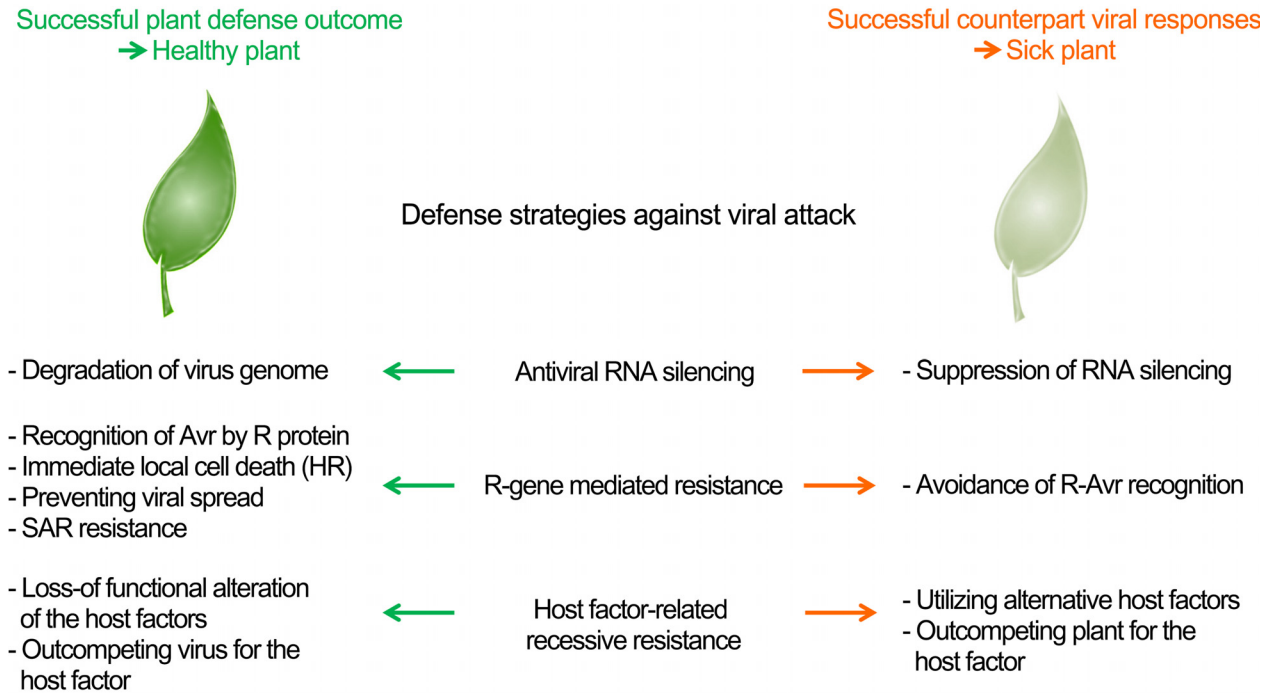

Fig. 1. Major plant defense strategies against viral attack.

system and DNA methylation processes, which are shown to have crucial resistance roles in other pathosystems, are also involved in antiviral defense (Butterbach et al., 2014).

Antiviral RNA Silencing

RNA silencing, also referred to as RNA interference (RNAi) or post-transcriptional gene silencing (PTGS), is a surveillance response triggered by double-stranded (ds) RNA (Grishok et al., 2001; Hammond et al., 2001). RNA silencing plays a major role in the regulation of gene expression during development and in defense against biotic/abiotic stresses in plants (Depicker and Mantagu, 1997; Vaucheret and Fagard, 2001; Carrington and Ambros, 2003). Plants can avoid viral infection by specifically degrading viral RNA via antiviral RNA silencing, which has been demonstrated as a common plant defense for a majority of the plant viruses (Baulcombe, 1999; Incarbone and Dunoyer, 2013). Antiviral RNA silencing is triggered by viral dsRNA segments generated either by replication intermediates or by secondary intramolecular RNA folding (hairpin) structures in the host cell (Covey et al., 1997; Ratcliff et al., 1997; Marathe et al., 2000). Inside the plant cells, viral dsRNAs are detected and processed by Dicer-like (DCL) enzymes into virus-derived small RNAs (vsRNAs) (Ding and Voinnet, 2007). The vsRNAs are incorporated into the RNA-induced silencing complex (RISC) and guide Argonaute (AGO) proteins, which induce the degradation or translational arrest of the viral RNA (Pumplin and Vionnet, 2013). The antiviral RNA silencing signal can be proliferated and transferred via the plasmodesmata and the phloem, allowing systemic viral defense (Voinnet, 2001; Molnar et al., 2010). There is increasing evidence that DNA viruses are also subject to be controlled by antiviral RNA silencing (Incarbone and Dunoyer, 2013). In the case of geminivirus, a plant virus family possessing a single-stranded circular DNA genome, vsRNA and PTGS of viral coding sequences has been observed during resistance responses (Ribeiro et al., 2007). Moreover, it was demonstrated that hypermethylation of the viral DNA genome mediated by *Ty-1*, a tomato resistance gene, results in the enhancement of transcriptional gene silencing (Butterbach et al., 2014).

In order to overcome the host defense system, plant viruses have acquired a counter-defense strategy by disrupting host antiviral silencing, which is explicable in the co-evolutionary context of arms races (Al-Kaff et al., 1998; Kasschau and Carrington, 1998; Ding and Vionnet, 2007). A number of viral suppressors of RNA silencing (VRSs) have been identified from diverse viruses without obvious sequence or structural similarities (Burgyan and Havelda, 2011). Most VRSs are multifunctional with various modes of action including the inhibition of viral RNA sensing, dicing, the RISC assembly, RNA targeting, and amplification (Burgyan and Havelda, 2011). There is increasing evidence that plants have evolved ways to fight against VRSs, which are also called "counter-counter defense responses", as the molecular arms-race theory predicts (Incarbone and Dunoyer, 2013; Pumplin and Vionnet, 2013; Zhao et al., 2016; Boualem et al., 2016).

R Gene-mediated Resistance

Dominant R genes typically confer race-specific resistance against diverse phytopathogenes encoding corresponding dominant Avr genes (Dangl et al., 1996; Hammond-Kosack and Jones, 1996). This type of resistance is associated with the HR in many cases. HR-mediated cell death immediately eliminates infected cells and prevents systemic spread of the viral infection. The HR is generally associated with mitogen-activated protein kinase (MAPK) signaling, an increase in salicylic (SA) acid and jasmonic acid (JA), calcium ion influx, callose deposition at the plasmodesmata, modification of membrane permeability, activation of defense genes, and an immediate accumulation of reactive oxygen species (ROS) and nitric oxide (NO) (Richberg et al., 1998; Yang et al., 2001).

The majority of plant R genes encode nucleotide-binding (NB) and leucine rich-repeat (LRR) domains, whereas the Avr proteins have little in common structurally (Jones and Dangl, 2006). The NB-LRR proteins consist of three domains: the nucleotide-binding site (NBS) in the center, an LRR at the C-terminal end, and a Coiled-coil (CC) or Toll and human interleukin receptor (TIR) domain at the N-terminus (Meyers et al., 2003). In addition to the conserved NBS, the NBS domain includes an Apaf-1/R protein/CED 4 (ARC) domain, which is involved in ATP hydrolysis and intramolecular interactions (Rairdan et al., 2008). Intramolecular interactions within NB-LRR proteins are conserved at certain levels and are critical for the proper functioning of the R protein (Rairdan et al., 2008). The LRR domain of NB-LRR proteins is the primary determinant conferring specificity to plant-pathogen recognition (Jones and Dangl, 2006). Additionally, the N-terminus is acknowledged as serving an important role for specific Avr interaction (Collier and Moffett, 2009). The recognition of avirulent effectors by NB-LRR proteins, which sequentially initiates down-stream defense responses, can occur directly or indirectly through cellular cofactors.

Dominant viral R genes in plants are listed in Table 1. Over 20 viral R genes with dominant inheritance are characterized so far. *N*, the first viral R gene to be cloned and characterized, is a tobacco resistance gene encoding a TIR-NB-LRR protein confering resistance to TMV (Whitham et al., 1994). The 50 kDa helicase domain p50 is the counterpart of N and is part of the viral 126 kDa protein in the TMV replicase complex (Padgett et al., 1997). In the case of TMV resistance, N recognizes the p50 helicase domain through a direct interaction (Ueda et al., 2006). Rx, a potato protein conferring resistance to *Potato virus X* (PVX), is a typical CC-NB-LRR protein. Its counterpart Avr determinant is the PVX coat protein (CP) (Bendahmane et al., 1995, 1999). The role of each functional domain and the intramolecular interactions among those domains have been intensively studied in Rx (Rairdan et al., 2008).

Recessive Virus Resistance

As intracellular parasites, viruses are exclusively dependent on host cellular mechanisms for their life cycle. When virus particles enter a plant cell, the genome is released from the capsid and early viral proteins are translated. Thereafter, the virus confronts various levels of host defense. Because of the limited number of viral gene products, the virus requires a series of host factors to pursue a successful infection cycle including replication, transcription, translation, cell-to-cell movement, and long-distance movement (Kang et al., 2005b; Truniger and Aranda, 2009). The absence or alteration of a necessary host factor can be an efficient defense strategy for the plant and is considered a form of passive resistance (Fraser, 1990, 1992). Such passive resistance generally shows recessive inheritance. The R gene-mediated resistance described in the previous section can be considered active resistance and/or dominant resistance in this context (Kang et al., 2005b).

It is predicted that more than half of the plant virus resistances are recessively inherited, although many are yet to be characterized (Kang et al., 2005b; Truniger and Aranda, 2009). A large proportion of the recessive R genes identified to date confer resistance to various potyviruses, a family of viruses that encompasses more than 30% of known plant viruses. Recessive R genes conferring potyvirus resistance have been identified and deployed for decades in numerous crops. The eukaryotic translation factor 4E (eIF4E*)* plays a major role in the initiation of host translation by recruiting messenger RNAs to the ribosomal complex and has been repeatedly identified as an essential host factor required for viral infection (Truniger and Aranda 2009). Natural variation in eIF4E preventing viral sequestration confers effective resistance to potyvirus infection in multiple crop species, suggesting that the alteration of host factors such as translation-initiation factors is a common strategy for developing viral resistance in plants (Schaad et al. 2000; Yeam et al., 2007; Cavatorta et al., 2008). Those factors include *pvr1* (*pvr2*) in pepper, *mo1* in lettuce, *sbm1* in pea, *rym4/5* in barley, *pot1* in tomato, and *zym-FL* in watermelon (Gao et al., 2004; Ling et al., 2009; Nicaise et al., 2003; Ruffel et al., 2002; Kang et al., 2005a; Wicker et al., 2005). It was demonstrated statistically that the amino acid variations in eIF4E responsible for potyviral resistance in multiple species have arisen independently and been positively selected in their evolutionary context (Cavatorta et al., 2008). The recently characterized *ty5*, which confers resistance to *Tomato yellow leaf curl virus* (TYLCV), encodes the messenger RNA surveillance factor Pelo and is another example of recessive resistance in tomato (Lapidot et al., 2015). Impaired function of Pelo, which is implicated in the ribosome recycling-phase of protein synthesis, appears to trigger the suppression of viral infection in resistant *ty5* genotypes. The known recessive resistance genes are

Table 1. Characterized virus resistance genes with dominant inheritance

Plant species	Gene/Locus	Major virus	Features of R gene	Resistance mechanism	Avirulence factor	Reference
Arabidopsis thaliana	***HRT***	*Turnip crinkle virus*	CC-NBS-LRR	HR	CP	Ren et al., 2000
Arabidopsis thaliana	***JAX1***	*Platago asiatica mosaic virus*	Jacalin like lectin	Blocking RNA accumulation	Unknown	Yamaji et al., 2012
Arabidopsis thaliana	***RCY1***	*Cucumber mosaic virus*	CC-NBS-LRR	HR	CP	Takahashi et al., 2002
Arabidopsis thaliana	***RTM1***	*Tobacco etch virus*	Jacalin family	Blocking systemic movement	CP	Chisholm et al., 2000
Arabidopsis thaliana	***RTM2***	*Tobacco etch virus*	Small heat shock protein	Blocking systemic movement	CP	Whitham et al., 2000
Arabidopsis thaliana	***RTM3***	*Tobacco etch virus*	MATH-containing protein	Blocking systemic movement	Unknown	Cosson et al., 2010
Brassica campestris	***BcTuR3***	*Turnip mosaic virus*	TIR-NB-LRR	Systemic resistance	Unknown	Ma et al., 2010
Brassica campestris	***TuRB07***	*Turnip mosaic virus*	CC-NBS-LRR	ER	Unknown	Jin et al., 2014
Capsicum spp.	***L (multi-alleles)***	*Tobacco mosaic virus*	CC-NBS-LRR	HR	CP	Tomita et al., 2011
Cucumis melo	***Prv (multi-alleles)***	*Papaya ringspot virus*	TIR-NB-LRR		Unknown	Brotman et al., 2013
Glycine max	***Rsv1***	*Soybean mosaic virus*	CC-NB-LRR	HR	P3, HC-Pro	Hayes et al., 2004
Nicotiana glutinosa	***N***	*Tobacco mosaic virus*	TIR-NBS-LRR	HR	P50 helicase domain	Whitham et al., 1994
Phaseolus vulgaris	***I***	*Bean common mosaic virus*	TIR-NBS-LRR	HR	Unknown	Vallejos, 2006
Phaseolus vulgaris	***RT4-4***	*Cucumber mosaic virus*	TIR-NBS-LRR	Systemic necrosis	2a	Seo et al., 2006
Solanum chilense	***Ty1/Ty3 (multi-alleles)***	*Tomato yellow leaf curl virus*	RDR	RNA silencing	Unknown	Butterbach et al., 2014
Solanum habrochites	***Tm1***	*Tomato mosaic virus*	TIM-barrel-like domain	Blocking replication	Replication protein	Ishibashi et al. 2007
Solanum peruvianum	***Tm2 (multi-alleles)***	*Tomato mosaic virus*	CC-NBS-LRR	Microscopic HR	MP	Lanfermeijer et al. 2003
Solanum peruvianum	***Sw5b***	*Tomato spotted wilt virus*	CC-NBS-LRR	HR	Cell-to-cell MP (NSm)	Brommonschenkel et al., 2000
Solanum tuberosum	***Rx (multi-alleles)***	*Potato virus X*	CC-NBS-LRR	Blocking replication	CP	Bendahmane et al., 2002
Solanum tuberosum	***Y1***	*Potato virus Y*	TIR-NBS-LRR	HR		Vidal et al., 2002
Vigna mungo	***CYR1***	*Mungbean yellow mosaic virus Bean common mosaic virus*	CC_NB_LRR		CP	Maiti et al., 2012

Abbreviations: MATH (meprin and TRAF domain), CP (coat protein), HC-Pro (helper component proteinase), MP (movement protein), RDR (RNA-dependent RNA polymerase), ER (extreme resistance without any necrotic local lesion)

summarized in Table 2.

Applications of Natural Virus Resistance: Molecular Breeding Aspects of Virus Resistance

The development of disease-resistant varieties, which will ultimately contribute to yield increases in crops, has been a major goal in most breeding programs. Marker-assisted selection (MAS) has been widely and successfully deployed for decades to generate disease resistance by applying genetic markers to select and combine multiple resistance genes (Foolad and Sharma 2005; Miedaner and Korzun, 2012). In the case of tomato, which is economically the most important vegetable crop worldwide, MAS has been performed actively for major virus-resistance genes including *Ty1* and *Ty2* for TYLCV, *Sw5* for *Tomato spotted wilt virus*, and *Tm2* for *Tomato mosaic virus* (reviewed in Lee et al., 2015). A molecular marker generally refers to a DNA marker and can serve as a technical tool for detecting genetic polymorphisms responsible for phenotypic variation. Various technological innovations including next-generation sequencing (NGS) techniques and single-nucleotide polymorphism (SNP) genotyping have accelerated genome-wide association studies (GWAS) and greatly improved the accuracy, cost-effectiveness, and time-efficiency of MAS (Jones et al. 2009; Salgotra et al. 2014; Thomson 2014). Increased access to genomic information has led to a considerable number of gene-based markers for disease resistances, which are greatly advantageous compared with neutral markers linked to the genes of interest (Kage et al., 2015; Kamphuis et al., 2015). PCR-gel based systems using cleaved and amplified polymorphic sequence (CAPS) markers and high-throughput SNP detection systems using high resolution-melt (HRM) markers have been utilized widely to detect multiple SNPs associated with disease-resistance traits (Lochlainn et al., 2011; Jung et al., 2015). Currently, several advanced, high-

Table 2. Characterized virus resistance genes with recessive inheritance

Plant species	Gene/Locus	Major virus	Resistance factor	Avirulence factor	Reference
Arabidopsis thaliana	***lsp1***	*Turnip mosaic virus*	eIF(iso)4E (mutagenesis)	VPg	Lellis et al., 2002
	cum1	*Cucumber mosaic virus*	eIF4E (mutagenesis)	unknown	Yoshii et al., 2004
	cum2	*Cucumber masaic virus*	eIF4G (mutagenesis)	unknown	Yoshii et al., 2004
Capsicum spp.	***pvr1/pvr2 (multi-alleles)***	*Potato virus Y, Tobacco etch virus*	eIF4E	VPg	Ruffel et al., 2002; Kang et al., 2005
Capsicum annuum	***pvr6***	*Pepper veinal mottle virus*	eIF(iso)4E	VPg	Ruffel et al., 2006
Cucumis melo	***nsv***	*Melon necrotic spot virus*	eIF4E	unknown	Nieto et al., 2006
Lactuca sativa	***mo1 (multi-alleles)***	*Lettuce mosaic virus*	eIF4E	CI- Cter, VPg	Nicaise et al., 2003
Oryza sativa	***rymv1***	*Rice yellow mottle virus*	eIF(iso)4G	VPg	Albar et al., 2006
Oryza glaberrima	***rymv2***	*Rice yellow mottle virus*	CPR5 homolog	unknown	Orjuela et al., 2013
Phaseolus vulgaris	***bc3***	*Bean common mosaic virus*	eIF4E	unknown	Naderpour et al., 2010
Solanum lycopersicum	***pot1***	*Potato virus Y, Tobacco etch virus*	eIF4E	VPg	Ruffel et al., 2005
	ty5		Pelo	unknown	Lapidot, 2015
Pisum sativum	***sbm1***	*Pea seed-born mosaic virus*	eIF4E	VPg	Gao et al., 2004
Hordeum vulgare	***rym4/5 (multi-alleles)***	*Barley yellow mosaic virus*	eIF4E	VPg	Stein et al., 2005

Abbreviations: eIF4E (eukaryotic translation initiation factor 4E), eIF(iso)4E (eukaryotic translation initiation factor iso 4E), Pelo (a messenger RNA surveillance factor), VPg (genome linked viral protein), CPR (constitutive expresser of pathogenesis related genes), CI-Cter (C terminal of cylindrical inclusion helicase)

throughput, low-cost SNP genotyping efforts are facilitated by platforms such as Fluidigm's Dynamic Arrays™, Douglas Scientific's Array Tape™, and LGC's automated systems for running KASP™ markers. Such efforts can also be pursued through genotyping-by-sequencing approaches (GBS) based on the low-cost, high-density, genome-wide scans made possible by multiplexed sequencing (Thomson et al., 2014). Those cutting-edge technologies are still in an introductory stage in the crop sciences and are rapidly attracting plant-breeding communities.

The ultimate goal in breeding programs for viral resistance is to achieve effective and durable resistance against the target viruses. The accumulation of multiple resistances by gene pyramiding was expected to be the most effective strategy for generating broad-spectrum resistance; however, there are a number of aspects that need to be considered comprehensively in order to achieve durability (Mundt, 2014). Those include the coevolutionary history of the hosts and viruses, the influences of agricultural practices on plant-virus interactions, reciprocal interactions among plants, virus and insect vectors, the reconstitution of gene frequencies and fitness levels caused by vigorous crop-improvement efforts, and global climate changes. The emergence of viral isolates that have overcome predominant R genes has been identified repeatedly (Montarry et al., 2012; Nicaise, 2014). Never-ending arms races have been demonstrated by observing host antiviral RNA silencing, viral counter responses, and host counter-counter defenses (Incarbone and Dunoyer 2013; Pumplin and Vionnet, 2013). Although more than 80% of the known viral resistances are monogenically controlled, it is assumed that polygenically controlled viral resistance exists more prevalently in natural ecosystems (Maule et al., 2007). It has been suggested that partial resistance (tolerance) or resistance controlled by quantitative trait loci would benefit durable resistance by avoiding the emergence of resistance-overcoming viruses (Richardson et al., 2006; Mundt, 2014). Furthermore, it has been demonstrated that recessive resistance is better for gaining durability than dominant resistance (Kang et al., 2005b; Sanfacon, 2015). Although it is obvious that there is still much to be revealed, recent advances in understanding naturally occurring resistance to viruses at the molecular level will bring us one step closer to accomplishing effective and durable viral resistance (Mundt, 2014; Nicaise, 2014).

Engineered Resistance to Plant Viruses

Numerous attempts have been made to develop engineered resistance against plant diseases since the development of the Agrobacterium-mediated plant-transformation technique in the early 1980s (Thomashow et al., 1980). Engineered resistance that blocks viral attack has produced a considerably large number of successes compared with other pathosystems. Pathogen-derived resistance (PDR) is conferred when a sequence from a viral genome is transgenically introduced into a host plant. The first successful PDR was shown in transgenic tobacco

expressing the CP of TMV (Abel et al., 1986). CP-mediated resistance has been widely used and reported in over 35 viruses, including *Tomato mosaic virus*, *Yellow mosaic virus*, *Cucumber mosaic virus* (CMV), and TYLCV resistances in tomato; PVX, *Potato virus Y,* and *Potato leaf roll virus* resistances in potato; CMV resistance in pepper; *Plum pox virus* resistance in plum; CMV resistance in cucumber; CMV, *Zucchini yellow mosaic virus*, and *Water melon mosaic virus* resistances in Zucchini; *Zucchini yellow mosaic virus* in melon; and *Papaya ring spot virus* in papaya (Dasgupta et al., 2003). Although the majority of PDRs to viral diseases are engineered using the viral CP, other viral genes like replicases and movement proteins are also used to generate engineered resistances (Morroni et al., 2008; Galvez et al., 2014). The molecular mechanism underlying PDR is not entirely understood. It is speculated, however, that RNA silencing plays a major role in the antiviral effects in addition to the protein interactions between viral proteins and the transgenically expressed proteins (Voinnet, 2001; Prins, 2003; Gottula and Fuchs, 2009). Modified PDRs triggered by the transgenic expression of artificial microRNAs (amiRNA) have also demonstrated effectiveness in several systems (Niu et al., 2006; Ai et al., 2011).

Besides the transgenic expression of viral gene segments, the heterologous expression of dominant or recessive resistance genes has been demonstrated to confer resistance to plant diseases in closely related host taxa (Whitham et al., 1996; Bendahmane et al., 2002; Kang et al., 2007). Several transgenic, virus-resistant varieties in squash, papaya, plum, potato, tomato, and bean have already been commercialized; however, public concerns over the potential ecological impact of the transgenic plants are still under debate (Nicaise, 2014). Intragenic or cisgenenic approaches whereby the crop is transformed with genes from within its own genome have also been introduced to generate engineered resistance to viruses (Cavatorta et al., 2011; Ilardi and Tavazza, 2015). Together with molecular insights into the mechanisms of R genes, progress in gene editing utilizing transcription activator-like effector nucleases (TALEN) and clustered regularly interspaced short palindromic repeats (CRISPRs) (Gaj et al., 2013; Gao and Zhao, 2014) might accelerate the genetic engineering of plant R genes or susceptible factors in the near future.

Conclusion

Plants developed effective antiviral resistance mechanisms through complex co-evolutionary processes. Over the past decade, the molecular mechanisms of plant resistance to viruses have been exclusively investigated, and remarkable progress has been made. Naturally occurring genetic viral resistance primarily comprises antiviral RNA silencing, R gene-mediated resistance, and recessive resistance. Since viruses are intracellular parasites consisting of a small RNA or DNA genome packed in a capsid, the RNA silencing strategy is considered a major antiviral mechanism. Successful antiviral RNA silencing primarily results in the degradation of the viral genome at the site of the initial infection. R gene-mediated resistance, which is the most intensively explored form of resistance generally responsible for the HR, is also effective in conferring viral resistance. Resistance with recessive inheritance, mostly acquired via the alteration of key host factors required for the viral infection cycle, is also recognized as an essential antiviral mechanism. The most effective resistance strategies would be selected and used in each virus-plant pathosystem, based mainly on the arms-race relationships and the fitness cost of the resistance acquisition. Profound understanding of the plant viral resistances at the molecular level will allow us one step closer to accomplishing effective and durable viral resistance. These naturally occurring viral resistances are actively utilized in major plant breeding programs mostly enabled by MAS. Current advances in high-throughput and low-cost SNP genotyping are rapidly attracting plant breeding communities and expected to accelerate MAS with improved accuracy and economic feasibility. The area of developing engineered resistance has received a great deal of attention and made several success stories in plant-virus system. Technologies involved in transgenics, cisgenics, and gene-editing will contribute to the gain of highly applicable viral resistance in addition to the breeding efforts utilizing natural resistances.

Acknowledgement: I thank Je Min Lee for useful discussions and critical review of this manuscript. This work was supported by the Golden Seed Project (Center for Horticultural Seed Development, 213003-04-4-SBG10) funded by the Ministry of Agriculture, Food and Rural Affairs (MAFRA), Ministry of Oceans and Fisheries (MOF), Rural Development Administration (RDA) and Korea Forest Service (KFS).

Literature Cited

Abel PP, Nelson RS, De B, Hoffmann N, Rogers SG, Fraley RT, Beachy RN (1986) Delay of disease development in transgenic plants that express the *Tobacco mosaic virus* coat protein gene. Science 232:738-743

Al-Kaff NS, Covey SN, Kreike MM, Page AM, Dale PJ (1998) Transcriptional and post-transcriptional gene silencing in response to a pathogen. Science 279:2113-2115

Baulcombe D (1999) Viruses and gene silencing in plants. Arch Virol Suppl 15:189-201

Bendahmane A, Farnham G, Moffett P, Baulcombe DC (2002) Constitutive gain-of-function mutants in a nucleotide binding site-leucine rich repeat protein encoded at the Rx locus of potato. Plant J 32:195-204

Bendahmane A, Kohn BA, Dedi C, Baulcombe DC (1995) The coat protein of *Potato virus X* is a strain-specific elicitor of *Rx1*-mediated virus resistance in potato. Plant J 8:933-941

Boualem A, Dogimont C, Bendahmane A (2016) The battle for survival between viruses and their host plants. Curr Opin Virol 17:32-38

Brommonschenkel SH, Frary A, Frary A, Tanksley SD (2000) The broad-spectrum *tospovirus* resistance gene *Sw-5* of tomato is a homolog of the root-knot nematode resistance gene *Mi*. Mol Plant-Microbe Interact 13:1130-1138

Brotman Y, Normantovich M, Goldenberg Z, Zvirin Z, Kovalski I, Stovbun N (2013) Dual resistance of melon to *Fusarium oxysporum* races 0 and 2 and to *Papaya ring spot virus* is controlled by a pair of head-to-head-oriented NB-LRR genes of unusual architecture. Mol Plant 6:235-238

Brown JK (2015) Durable resistance of crops to disease: a Darwinian perspective. Annu Rev Phytopathol 53:513-539

Burgyán J, Havelda Z (2011) Viral suppressors of RNA silencing. Trends Plant Sci 16:265-272

Büschges R, Hollricher K, Panstruga R, Simons G, Wolter M, Frijters A, van Daelen R, van der Lee T, Diergaarde P, Groenendijk J, et al (1997) The barley *Mlo* gene: a novel control element of plant pathogen resistance. Cell 88:695-705

Butterbach P, Verlaan MG, Dullemans A, Lohuis D, Visser RG, Bai Y, Kormelink R (2014) *Tomato yellow leaf curl virus* resistance by *Ty-1* involves increased cytosine methylation of viral genomes and is compromised by *Cucumber mosaic virus* infection. Proc Natl Acad Sci USA 111:12942-12947

Carrington JC, Ambros V (2003) Role of microRNAs in plant and animal development. Science 301:336-338

Carrington JC, Kasschau KD, Mahajan SK, Schaad MC (1996) Cell-to-cell and long-distance transport of viruses in plants. Plant Cell 8:1669-1681

Cavatorta J, Perez KW, Gray SM, Van Eck J, Yeam I, Jahn M (2011) Engineering virus resistance using a modified potato gene. Plant Biotechnol J 9:1014-1021

Cavatorta JR, Savage AE, Yeam I, Gray S, Jahn MM (2008) Positive Darwinian selection at single amino acid sites conferring plant virus resistance. J Mol Evol 67:551-559

Chisholm ST, Mahajan SK, Whitham SA, Yamamoto ML, Carrington JC (2000) Cloning of the Arabidopsis *RTM1* gene, which controls restriction of long-distance movement of tobacco etch virus. Proc Natl Acad Sci USA 97:489-494

Collier SM, Moffett P (2009) NB-LRRs work a "bait and switch" on pathogens. Trends in Plant Science 14:521-529

Cook DE, Mesarich CH, Thomma BP (2015) Understanding plant immunity as a surveillance system to detect invasion. Annu Rev Phytopathol 53:541-563

Cosson P, Sofer L, Le QH, Léger V, Schurdi-Levraud V, Whitham SA, Yamamoto ML, Gopalan S, Le Gall O, Candresse T, et al (2010) *RTM3*, which controls long-distance movement of potyviruses, is a member of a new plant gene family encoding a meprin and TRAF homology domain-containing protein. Plant Physiol 154:222-232

Covey SN, Al-Kaff NS, Langara A, Turner OS (1997) Plants combat infection by gene silencing. Nature 85:780-781

Dangl JL, Dietrich RA, Richberg MH (1996) Death don't have no mercy: Cell death programs in plant-microbe interactions. Plant Cell 8:1793-1807

Dangl JL, Jones JD (2001) Plant pathogens and integrated defense responses to infection. Nature 411:826-833

Dasgupta I, Malathi VG, Mukherjee SK (2003) Genetic engineering for virus resistance. Curr Sci 84:341-354

Depicker A, Montagu MV (1997) Post-transcriptional gene silencing in plants. Curr Opin Cell Bioi 9:373-382

Ding SW, Voinnet O (2007) Antiviral immunity directed by small RNAs. Cell 130:413-426

Flor HH (1971) Current status of the gene-for-gene concept. Annu Rev Phytopathol 9:275-296

Foolad MR, Sharma A (2005) Molecular markers as selection tools in tomato breeding. Acta Hortic 695:225-240

Fraser RSS (1990) The genetics of resistance to plant viruses. Annu Rev Phytopathol 28:179-200

Fraser RSS (1992) The genetics of plantvirus interactions: implications for plant breeding. Euphytica 63:175-185

Gaj T, Gersbach CA, Barbas CF 3rd (2013) ZFN, TALEN, and CRISPR/Cas-based methods for genome engineering. Trends Biotechnol 31:397-405

Galvez LC, Banerjee J, Pinar H, Mitra A (2014) Engineered plant virus resistance. Plant Sci 228:11-25

Gao Z, Johansen E, Eyers S, Thomas CL, Noel Ellis TH, Maule AJ (2004) The potyvirus recessive resistance gene, *sbm1*, identifies a novel role for translation initiation factor eIF4E in cell-to-cell trafficking. Plant J 40:376-385

Gao Y, Zhao Y (2014) Specific and heritable gene editing in Arabidopsis. Proc Natl Acad Sci USA 111:4357-4358

Gottula J, Fuchs M (2009) Toward a quarter century of pathogen-derived resistance and practical approaches to plant virusdisease control. Adv Virus Res 75:161-183

Grishok A, Pasquinelli AE, Conte D, Li N, Parrish S, Ha I, Baillie DL, Fire A, Ruvkun G, Mello CC (2001) Genes and mechanisms related to RNA interference regulate expression of the small temporal RNAs that control *C. elegans* developmental timing. Cell 106:23-34

Hammond SM, Caudy AA, Hannon GJ (2001) Post-transcriptional gene silencing by double-stranded RNA. Nature Rev Gen 2:110-119

Hammond-Kosack KE, Jones JD (1996) Resistance gene-dependent plant defense responses. Plant Cell 8:1773-1791

Hayes AJ, Jeong SC, Gore MA, Yu YG, Buss GR, Tolin SA (2004) Recombination within a nucleotide-binding-site/leucine-rich-repeat gene cluster produces new variants conditioning resistance to *Soybean mosaic virus* in soybeans. Genetics 166:493-503

Holmes FO (1929) Local lesions in tobacco mosaic. Bot Gaz 87:39-55

Ilardi V, Tavazza M (2015) Biotechnological strategies and tools for *Plum pox virus* resistance: trans-, intra-, cis-genesis, and beyond. Front Plant Sci 6:379

Incarbone M, Dunoyer P (2013) RNA silencing and its suppression: novel insights from in planta analyses. Trends Plant Sci 18:382-392

Ishibashi K, Masuda K, Naito S, Meshi T, Ishikawa M (2007) An inhibitor of viral RNA replication is encoded by a plant resistance gene. Proc Natl Acad Sci USA 104:13833-13838

Iyer-Pascuzzi AS, McCouch SR (2007) Recessive resistance genes and the Oryza sativa-Xanthomonas oryzae pv. oryzae pathosystem. Mol Plant Microbe Interact 20:731-739

Jin M, Lee SS, Ke L, Kim JS, Seo MS, Sohn SH, Park BS, Bonnema G (2014) Identification and mapping of a novel dominant resistance gene, TuRB07 to Turnip mosaic virus in Brassica rapa. Theor Appl Genet 127:509-519

Jones E, Chu W, Ayele M, Ho J, Bruggeman E, Yourstone K, Rafalski A, Smith OS, McMullen MD, Bezawada C, et al (2009). Development of single nucleotide polymorphism (SNP) markers for use in commercial maize (*Zea mays* L.) germplasm. Mol Breed 24:165-176

Jones JD, Dangl JL (2006) The plant immune system. Nature 444:323-329

Jung J, Kim HJ, Lee JM, Oh CS, Lee HJ, Yeam I (2015) Gene-based molecular marker system for multiple disease resistances in tomato against *Tomato yellow leaf curl virus*, late blight, and verticillium wilt. Euphytica 205:599-613

Kage U, Kumar A, Dhokane D, Karre S, Kushalappa AC (2015) Functional molecular markers for crop improvement. Crit Rev Biotechnol 16:1-14

Kamphuis LG, Hane JK, Nelson MN, Gao L, Atkins CA, Singh KB (2015) Transcriptome sequencing of different narrow-leafed lupin tissue types provides a comprehensive uni-gene assembly and extensive gene-based molecular markers. Plant Biotechnol J 13:14-25

Kang BC, Yeam I, Frantz JD, Murphy JF, Jahn MM (2005a) The

pvr1 locus in *Capsicum* encodes a translation initiation factor eIF4E that interacts with *Tobacco etch virus* VPg. Plant J 42:392-405

Kang BC, Yeam I, Jahn MM (2005b) Genetics of plant virus resistance. Annu Rev Phytopathol 43:581-621

Kang BC, Yeam I, Li H, Perez KW, Jahn MM (2007) Ectopic expression of a recessive resistance gene generates dominant potyvirus resistance in plants. Plant Biotechnol J 5:526-536

Kasschau KD, Carrington JC (1998) A counter defensive strategy of plant viruses: suppression of posttranscriptional gene silencing. Cell 95:461-470

Keen NT (1990) Gene-for-gene complementarity in plant-pathogen interactions. Annu Rev Genet 24:447-463

Lanfermeijer FC, Dijkhuis J, Sturre MJ, de Haan P, Hille J (2003) Cloning and characterization of the durable *Tomato mosaic virus* resistance gene *Tm-2(2)* from *Lycopersicon esculentum*. Plant Mol Biol 52:1037-1049

Lapidot M, Karniel U, Gelbart D, Fogel D, Evenor D, Kutsher Y, Makhbash Z, Nahon S, Shlomo H, Chen L, et al (2015) A novel route controlling begomovirus resistance by the messenger RNA surveillance factor Pelota. PLoS Genet 11:e1005538

Lee JM, Oh CS, Yeam I (2015) Molecular markers for selecting diverse disease resistances in tomato breeding programs. Plant Breed Biotechnol 3:308-322

Lellis AD, Kasschau KD, Whitham SA, Carrington JC (2002) Loss-of-susceptibility mutants of *Arabidopsis thaliana* reveal an essential role for eIF(iso)4E during potyvirus infection. Curr Biol 12:1046-1051

Ling KS, Harris KR, Meyer JD, Levi A, Guner N, Wehner TC, Bendahmane A, Havey MJ (2009) Non-synonymous single nucleotide polymorphisms in the watermelon *eIF4E* gene are closely associated with resistance to *Zucchini yellow mosaic virus*. Theor Appl Genet 120:191-200

Lochlainn SO, Amoah S, Graham NS, Alamer K, Rios JJ, Kurup S, Stoute A, Hammond JP, Ostergaard L, King GJ, et al (2011) High Resolution Melt (HRM) analysis is an efficient tool to genotype EMS mutants in complex crop genomes. Plant Methods 7:43

Ma JF, Hou XL, Xiao D, Qi L, Wang F, Sun FF, Wang Q (2010) Cloning and characterization of the *BcTuR3* gene related to resistance to *Turnip mosaic virus* (TuMV) from non-heading chinese cabbage. Plant Mol Biol Rep 28:588-596

Maiti S, Paul S, Pal A (2012) Isolation, characterization, and structure analysis of a non-TIR-NBS-LRR encoding candidate gene from MYMIV-resistant *Vigna mungo*. Mol Biotechnol 52:217-233

Marathe R, Anandalakshmi R, Smith TH, Pruss GJ, Vance VB (2000) RNA viruses as inducers, suppressors and targets of post-transcriptional gene silencing. Plant Mol Biol 43:295-306

Martin GB, Brommonschenkel S, Chunwongse J, Frary A, Ganal MW, Spivey R, Wu T, Earle ED, Tanksley SD (1993) Map-based cloning of a protein kinase gene conferring disease resistance in tomato. Science 262:1432-1436

Maule AJ, Caranta C, Boulton MI (2007) Sources of natural resistance to plant viruses: status and prospects. Mol Plant Pathol 8:223-231

Meyers BC, Kozik A, Griego A, Kuang H, Michelmore RW (2003) Genome-wide analysis of NBS-LRR-encoding genes in *Arabidopsis*. Plant Cell 13:809-834

Miedaner T, Korzun V (2012) Marker-assisted selection for disease resistance in wheat and barley breeding. Phytopathology 102:560-566

Molnar A, Melnyk CW, Bassett A, Hardcastle TJ, Dunn R, Baulcombe DC (2010) Small silencing RNAs in plants are mobile and direct epigenetic modification in recipient cells. Science 328:872-875

Montarry J, Cartier E, Jacquemond M, Palloix A, Moury B (2012) Virus adaptation to quantitative plant resistance: erosion or breakdown? J Evol Biol 25:2242-2252

Morroni M, Thompson JR, Tepfer M (2008) Twenty years of transgenic plants resistant to *Cucumber mosaic virus*. Mol Plant Microbe Interact 21:675-684

Mundt CC (2014) Durable resistance: a key to sustainable management of pathogens and pests. Infect Genet Evol 27:446-455

Naderpour M, Lund OS, Larsen R, Johansen E (2010) Potyviral resistance derived from cultivars of *Phaseolus vulgaris* carrying *bc-3* is associated with the homozygotic presence of a mutated *eIF4E* allele. Mol Plant Pathol 11:255-263

Nakahara KS, Masuta C (2014) Interaction between viral RNA silencing suppressors and host factors in plant immunity. Curr Opin Plant Biol 20:88-95

Nicaise V (2014) Crop immunity against viruses: outcomes and future challenges. Front Plant Sci 5:660

Nicaise V, German-Retana S, Sanjuan R, Dubrana MP, Mazier M, Maisonneuve B, Candresse T, Caranta C, LeGall O (2003) The eukaryotic translation initiation factor 4E controls lettuce susceptibility to the Potyvirus *Lettuce mosaic virus*. Plant Physiol 132:1272-1282

Nieto C, Morales M, Orjeda G, Clepet C, Monfort A, Sturbois B, Puigdomènech P, Pitrat M, Caboche M, Dogimont C, et al (2006) An *eIF4E* allele confers resistance to an uncapped and non-polyadenylated RNA virus in melon. Plant J 48:452-462

Nishimura MT, Dangl JL (2010) Arabidopsis and the plant immune system. Plant J 61:1053-1066

Niu QW, Lin SS, Reyes JL, Chen KC, Wu HW, Yeh SD, Chua NH (2006) Expression of artificial microRNAs in transgenic *Arabidopsis thaliana* confers virus resistance. Nat Biotechnol 24: 1420-1428

Orjuela J, Deless EF, Kolade O, Chéron S, Ghesquière A, Albar L (2013) A recessive resistance to *Rice yellow mottle virus* is associated with a rice homolog of the *CPR5* gene, a regulator of active defense mechanisms. Mol Plant Microbe Interact 26:1455-6143

Padgett HS, Watanabe Y, Beachy R (1997) Identification of the TMV replicase sequence that activates the *N* gene-mediated hypersensitive response. Mol Plant Microbe Interact 10:709-715

Prins M (2003) Broad virus resistance in transgenic plants. Trends Biotechnol 21:373-375

Pumplin N, Voinnet O (2013) RNA silencing suppression by plant pathogens: defence, counter-defence and counter-counter-defence. Nat Rev Microbiol 11:745-760

Rairdan GJ, Collier SM, Sacco MA, Baldwin TT, Boettrich T, Moffett P (2008) The coiled-coil and nucleotide binding domains of the Potato Rx disease resistance protein function in pathogen recognition and signaling. Plant Cell 20:739-751

Ratcliff F, Harrison BD, Baulcombe DC (1997) A similarity between viral defense and gene silencing in plants. Science 276:1558-1560

Rathjen JP, Moffett P (2003) Early signal transduction events in specific plant disease resistance. Curr Opin Plant Biol 6:300-306

Ren T, Qu F, Morris TJ (2000) HRT gene function requires interaction between a NAC protein and viral capsid protein to confer resistance to turnip crinkle virus. Plant Cell 12:1917-1926

Ribeiro SG, Lohuis H, Goldbach R, Prins M (2007) Tomato chlorotic mottle virus is a target of RNA silencing but the presence of specific short interfering RNAs does not guarantee resistance in transgenic plants. J Virol 81:1563-1573

Richardson KL, Vales MI, Kling JG, Mundt CC, Hayes PM (2006) Pyramiding and dissecting disease resistance QTL to barley stripe rust. Theor Appl Genet 113:485-495

Richberg MH, Aviv DH, Dangl JL (1998) Dead cells do tell tales. Curr Opin Plant Biol 1:480-485

Robaglia C, Caranta C (2006) Translation initiation factors: a weak link in plant RNA virus infection. Trends Plant Sci 11:40-45

Rodriguez E, El Ghoul H, Mundy J, Petersen M (2015) Making sense of plant autoimmunity and 'negative regulators'. FEBS J doi:10.1111/febs.13613

Ruffel S, Dussault MH, Palloix A, Moury B, Bendahmane A, Robaglia C, Caranta C (2002) A natural recessive resistance gene against *Potato virus Y* in pepper corresponds to the eukaryotic initiation factor 4E (eIF4E). Plant J 32:1067-1075

Ruffel S, Gallois JL, Lesage ML, Caranta C (2005) The recessive potyvirus resistance gene *pot-1* is the tomato orthologue of the pepper *pvr2-eIF4E* gene. Mol Genet Genomics 274:346-353

Ruffel S, Gallois JL, Moury B, Robaglia C, Palloix A, Caranta C (2006) Simultaneous mutations in translation initiation factors eIF4E and eIF(iso)4E are required to prevent *Pepper veinal mottle virus* infection of pepper. J Gen Virol 87:2089-2098

Salgotra RK, Gupta BB, Stewart Jr. CN (2014) From genomics to functional markers in the era of next-generation sequencing. Biotechnol Lett 36:417-426

Sanfaçon H (2015) Plant translation factors and virus resistance. Viruses 7:3392-3419

Schaad MC, Anderberg RJ, Carrington JC (2000) Strain-specific interaction of the *Tobacco etch virus* NIa protein with the translation initiation factor eIF4E in the yeast two-hybrid system. Virology 273:300-306

Seo YS, Rojas MR, Lee JY, Lee SW, Jeon JS, Ronald P, Lucas WJ, Gilbertson RL (2006) A viral resistance gene from common bean functions across plant families and is up-regulated in a non-virus-specific manner. Proc Natl Acad Sci USA 103:11856-11861

Smyth DR (1999) Gene silencing: plants and viruses fight it out. Curr Biol 9:R100-102

Stein N, Perovic D, Kumlehn J, Pellio B, Stracke S, Streng S, Ordon F, Graner A (2005) The eukaryotic translation initiation factor 4E confers multiallelic recessive bymovirus resistance in *Hordeum vulgare* (L.). Plant J 42:912-922

Takahashi H, Miller J, Nozaki Y, Takeda M, Shah J, Hase S, Ikegami M, Ehara Y, Dinesh-Kumar SP, Sukamto (2002) *RCY1*, an *Arabidopsis thaliana* RPP8/HRT family resistance gene, conferring resistance to *Cucumber mosaic virus* requires salicylic acid, ethylene and a novel signal transduction mechanism. Plant J 32:655-667

Tang X, Frederick RD, Zhou J, Halterman DA, Jia Y, Martin GB (1996) Initiation of plant disease resistance by physical interaction of AvrPto and Pto kinase. Science 274:2060-2063

Tena G, Boudsocq M, Sheen J (2011) Protein kinase signaling networks in plant innate immunity. Curr Opin Plant Biol 14:519-529

Thomashow MF, Nutter R, Montoya AL, Gordon MP, Nester EW (1980) Integration and organization of Ti plasmid sequences in crown gall tumors Cell 19:729-739

Thomson MJ (2014) High-throughput SNP genotyping to accelerate crop improvement. Plant Breed Biotechnol 2:195-212

Tomita R, Sekine KT, Mizumoto H, Sakamoto M, Murai J, Kiba A, Hikichi Y, Suzuki K, Kobayashi K (2011) Genetic basis for the hierarchical interaction between *Tobamovirus spp.* and L resistance gene alleles from different pepper species. Mol Plant Microbe Interact 24:108-117

Truniger V, Aranda MA (2009) Recessive resistance to plant viruses. Adv Virus Res 75:119-159

Ueda H, Yamaguchi Y, Sano H (2006) Direct interaction between the *Tobacco mosaic virus* helicase domain and the ATP-bound resistance protein, N factor during the hypersensitive response in tobacco plants. Plant Mol Biol 61:31-45

Vallejos CE, Astua-Monge G, Jones V, Plyler TR, Sakiyama NS, Mackenzie SA (2006) Genetic and molecular characterization of the *I* locus of Phaseolus vulgaris. Genetics 172:1229-1242

Van der Hoorn RA, Kamoun S (2008) From guard to decoy: a new model for perception of plant pathogen effectors. Plant Cell 20: 2009-2017

Vaucheret H, Fagard M (2001) Transcriptional gene silencing in plants: targets, inducers and regulators. Trends Genet 17:29-35

Vidal S, Cabrera H, Andersson RA, Fredriksson A, Valkonen JP (2002) Potato gene *Y-1* is an *N* gene homolog that confers cell death upon infection with *Potato virus Y*. Mol Plant Microbe Interact 15:717-727

Vlot AC, Klessig DF, Park SW (2008) Systemic acquired resistance: the elusive signal(s). Curr Opin Plant Biol 11:436-442

Voinnet O (2001) RNA silencing as a plant immune system against viruses. Trends Genet 17:449-459

Whitham SA, Anderberg RJ, Chisholm ST, Carrington JC (2000) *Arabidopsis RTM2* gene is necessary for specific restriction of *Tobacco etch virus* and encodes an unusual small heat shock-like protein. Plant Cell 12:569-582

Whitham S, Dinesh-Kumar SP, Choi D, Hehl R, Corr C, Baker B (1994) The product of the *Tobacco mosaic virus* resistance gene *N*: similarity to toll and the interleukin-1 receptor. Cell 78:1101-1115

Wicker T, Zimmermann W, Perovic D, Paterson AH, Ganal M, Graner A, Stein N (2005) A detailed look at 7 million years of genome evolution in a 439 kb contiguous sequence at the barley *Hv-eIF4E* locus: recombination, rearrangements and repeats. Plant J 41:184-194

Yamaji Y, Maejima K, Ozeki J, Komatsu K, Shiraishi T, Okano Y, Himeno M, Sugawara K, Neriya Y, Minato N, Miura C, Hashimoto M, Namba S (2012) Lectin-mediated resistance impairs plant virus infection at the cellular level. Plant Cell 24:778-793

Yang KY, Liu Y, Zhang S (2001) Activation of a mitogen-activated protein kinase pathway is involved in disease resistan in tobacco. Proc Natl Acad Sci USA 98:741-746

Yeam I, Cavatorta JR, Ripoll D, Kang B-C, Jahn MM (2007) Functional dissection of naturally occurring amino acid substitutions in eIF4E that confers recessive potyvirus resistance in plants. Plant Cell 19:2913-2928

Yoshii M, Nishikiori M, Tomita K, Yoshioka N, Kozuka R, Naito S, Ishikawa M (2004) The Arabidopsis cucumovirus multiplication 1 and 2 loci encode translation initiation factors 4E and 4G. J Virol 78:6102-6111

Zhao JH, Hua CL, Fang YY, Guo HS (2016) The dual edge of RNA silencing suppressors in the virus-host interactions. Curr Opin Virol 17:39-44