

## Review



## Plant-Virus Interactions: Disease Resistance in Focus

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**Abstract** | Crops are threatened by plant viruses worldwide as they hack the host machinery for their reproduction. Plants have undergone continuous evolution and have equipped themselves with counter defense and tolerant strategies against viral infections. In the 21<sup>st</sup> century, considerable progress has been made in understanding the available natural resistance in plants against viral threats. The review aims to explain the molecular mechanisms involved in triggering the antiviral resistance in plants. Antiviral RNA silencing, R-gene mediated resistance and host factor related recessive resistance are categorized as most beneficial plant defense approaches used by plants. The review also briefly explains about introgression of durable resistance to generate virus resistant cultivars for economically important crops through molecular breeding techniques via utilizing advanced molecular markers involving cis and trans genetics. The review adhere recent research findings regarding disease resistance against viral diseases and concludes via shedding light upon the future prospects in this exciting field of research.

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### Introduction

Worldwide crops are under continuous threat of various plant diseases. It is estimated that about 15% of global production of various crops is lost due to plant diseases. Among these diseases, phytopathogenic viruses are thought to cause more than one-third of plant diseases (Boualem et al., 2016). Although the viruses population and distribution is somehow suppressed through the management of insect vectors via application of various chemicals (Rehman et al., 2013; Islam et al., 2016a; Islam et al., 2017a) but these chemical treatments cannot directly limit plant virus infections. As the usage of chemicals have severe negative effects on human beings

and surround environment (Islam et al., 2016b; Islam and Ahmad., 2016) so the development of disease-resistant cultivars to control agricultural losses to viral diseases is considered as a major challenge in plant breeding research (Kang et al., 2005b). Plant viruses acquire host machinery for their reproduction, cell to cell movement and further transmission (Islam et al., 2017b). Viruses are nucleic acid-based pathogens that are packed with a protein called capsids. They contain single-stranded (ss) or double-stranded (ds) RNA or DNA genome and their genome size are very small as compared to other organisms like non-viral phytopathogens. Among the plant viruses, ssRNA viruses are considered as a major group. Their client characteristics include plant cells entry, nucleic acid

uncoating, viral proteins translation viral nucleic acids replication, progeny virions assembly, cell-to-cell movement, systemic movement and plant-to-plant movement (Carrington et al., 1996). Viruses lack necessary components for their independent survival, so they rely on numerous factors in the living cells of host plants (Boualem et al., 2016). Although viruses are relatively simple genetic entities, but resistance molecular mechanisms and viral diseases susceptibility are still not fully comprehended and understood. There are several mechanisms for disease resistance in plants against virus infections, but it is very difficult to explain them for various pathosystems separately (Brown, 2015). Our general understanding of plant-virus interactions and molecular mechanisms of these interactions has been achieved through the unveiling of several model bacteria-plant systems. The gene for gene theory was proposed in the early 70s (Flor, 1971) and has served as a model through explaining that how disease resistances are turned on against diverse pathogens for many years (Keen, 1990). On the base of gene for gene theory, a single resistance gene (R-gene) encoded by the host recognizes the presence of avirulence (Avr) proteins in bacterial type III secretion system secreted by effectors of fungal haustoria or nematodes stylets, and triggers a hypersensitive response of resistance leading towards the rapid cell death (HR) (Dangl and Jones, 2001). Firstly, kinase protein was characterized from host plants which exhibited its association with resistance as it clarified that R gene physically interacts with either AvrPto (Martin et al., 1993) or AvrPtoBits for a virulence determination (Tang et al., 1996). Since in multiple plant species, numerous R-genes have been characterized. The most general R genes types can be grouped into two classes, (A) genes encoding proteins nucleotide-binding leucine-rich repeat (NB-LRR), (B) genes encoding receptor-like kinase/ receptor-like proteins (Rathjen and Moffett, 2003). About a decade later, another model was proposed known as zig-zag (Jones and Dangl, 2006; Cook et al., 2015). In the zig-zag model, there are two distinct defense responses in the plant defense system. The primary defense level is called PAMP/MAMP-triggered immunity (PTI), and the secondary defense level is called effector-triggered immunity (ETI). A basic defense mechanism presented by PTI is preventing invasion of the pathogen through cell wall thickening in response to specific structures or pathogen associated proteins so-called pathogen-associated molecular patterns (PAMPs) or microbe-associated molec-

ular patterns (MAMPs). Plants show susceptibility only when a pathogen successfully establishes both PTI response suppression and its pathogenic effector's facilitation. ETI, the second defense response level is triggered when the products of R gene directly or indirectly sense specific effectors presence also called Avr factors. Consequently, an effective ETI will keep the plants resistant; however, an insufficient ETI will lead to the establishment of disease, *i.e.*, the susceptibility of the plant. A modified hypothesis called guard hypothesis proposed a decoy model and elucidated in multiple pathosystems (Van der Hoorn and Kamoun, 2008). Models of general resistance do not fit well with viral resistance primarily because of virus intracellular parasitic nature which is unlike to other pathogens as it clearly requires the machinery of the live host cell (Islam et al., 2017b). For example, receptors of pattern recognition which serve as a component of major defense by triggering the first layer of resistance when a receptor of plasma-membrane perceives a fungal or bacterial MAMP or PAMP (Tena et al., 2011), cannot play a role in plant viruses fighting because viruses do not express extracellular PAMPs. Although RNA silencing serves as a major component in the antiviral defense mechanism, however, the strategy of R-gene-mediated resistance is effective against viruses as well as other phytopathogens (Nakahara and Masuta, 2014; Rodriguez et al., 2015). In the case of recessive inheritance resistance, several recessive resistance genes have been characterized in bacterial and fungal pathogens research including xa5, a *Xanthomonas* resistance gene in rice (Iyer-Pascuzzi and McCouch, 2007), and mlo, a resistance gene for powdery mildew in barley (Buschges et al., 1997). The majority of genes related to recessive resistance have been identified in virus-plant pathosystems. The review sheds light upon naturally existing resistance against plant viruses. *i.e.* antiviral RNA silencing, R-gene-mediated resistance and recessive resistance. Secondly, this review discusses the strategies of molecular breeding using advanced molecular marker and utilization of trans or cis genetics for engineering disease resistances against plant viruses.

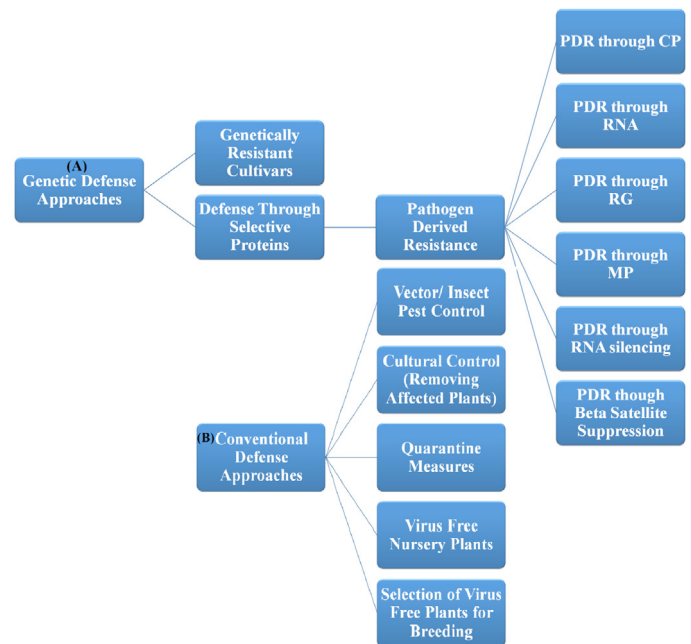
### A glimpse of viral disease resistance in plants

Tobacco mosaic virus (TMV) is the first virus discovered and isolated (Holmes, 1929) from *Nicotiana glutinosa* and its counterpart R gene served as a model for studying HR-based resistance, systemic acquired resistance (SAR), and gene-for-gene theory. *Nicotiana* gene was first viral R-gene to be cloned and char-

acterized which occurred soon after the Pto cloning (Whitham et al., 1994). Moreover, TMV-triggered SAR is thought to be consistent for at least three weeks (Vlot et al., 2008). Despite the fact that plant virus resistance studies have made prominent contributions to our overall disease resistance knowledge in plants but the critical advances in molecular mechanisms of disease resistance and their understanding models have primarily come from bacterial and fungal Phytopathosystems. Recent studies using RNA silencing, virus-induced gene silencing, large-scale genomic analysis and epigenetic analysis techniques have accelerated the plant antiviral mechanisms exploration at the molecular level. Combination of genetic resistance approaches (Figure 1A) and conventional management strategies (Figure 1B) can be helpful in exploiting natural resistance of plants against virus infections (Maule et al., 2007). R gene-mediated resistance which is the most intensively explored form of resistance towards the diverse bacteria, fungi and viruses is frequently HR responsible and is an effective way to gain resistance against plant viruses. But as the viruses are intracellular parasites consisting of a small RNA or DNA capsid packed genome, RNA silencing strategy of RNA is one of the major strategies to ensure antiviral resistance (Nakahara and Masuta, 2014; Rodriguez et al., 2015). Successful antiviral RNA silencing primarily results in the viral genome degradation at the site of initial or primary infection (Voinnet, 2001). Recessive inheritance resistance mostly acquired via alteration of key host factors which are required for establishment of viral infections and is also recognized as an effective mechanism of antiviral resistance (Robaglia and Caranta, 2006). In addition to those main antiviral mechanisms, it was demonstrated in several systems that the ubiquitin-proteasome system and processes of DNA methylation which have shown to have roles in crucial resistance in other pathosystems are also involved in antiviral defense (Butterbach et al., 2014).

### Disease resistance through antiviral RNA silencing

Antiviral RNA Silencing, also referred to as post-transcriptional gene silencing (PTGS), or RNA interference (RNAi) is a surveillance response triggered by double-stranded (ds) RNA (Hammond et al., 2001). RNA silencing plays an important role in the gene expression regulation during development and in defense against plants biotic/abiotic stresses (Carrington and Ambros, 2003). Plants can avoid infection of virus specifically by viral RNA degrading through antiviral



**Figure 1:** (A) Genetic defense strategies against viruses (B) Conventional defense approaches against plant virus diseases.

RNA silencing, which has been demonstrated as a common plant defense for a majority of the plant viruses (Incarbone and Dunoyer, 2013). Viral dsRNA segments are triggered through antiviral RNA silencing generated either by replication intermediates or by secondary intra-molecular RNA folding (hairpin) structures in the host cells (Marathe et al., 2000). Inside plant cells, plant viral dsRNAs are detected by Dicer-like (DCL) enzymes induced via virus-derived small RNAs (vsRNAs) (Ding and Voinnet, 2007). These dsRNAs incorporated the vsRNAs into the RNA-induced silencing complex (RISC) and guide Argonaute (AGO) proteins which induce the viral RNA degradation or translational arrest (Pumplin and Vionnet, 2013). Further proliferation of antiviral RNA silencing signals transferred via the phloem and plasmodesmata lead towards the systemic viral defense (Molnar et al., 2010). There is increasing evidence that antiviral RNA silencing control DNA viruses (Incarbone and Dunoyer, 2013). In gemini-viruses which have circular DNA genome (SS) vsRNA and PTGS of viral coding sequences have been observed during resistance responses (Ribeiro et al., 2007). Moreover, it was demonstrated that Ty-1 (tomato resistant gene) mediated viral DNA genome hypermethylation results in enhancement of transcriptional gene silencing (Butterbach et al., 2014). To overcome the defense system of the host plants, the viruses have acquired a counter-defense strategy by disruption of host antiviral silencing (Ding and

Vionnet, 2007). Many RNA silencing viral suppressors (VRSs) have been identified without obvious sequence or structural similarities from diverse viruses (Burgyan and Havelda, 2011). Most VRSs are multifunctional including the viral RNA sensing inhibition, dicing RISC amplification assembly and RNA targeting (Burgyan and Havelda, 2011). Several pieces of evidence increase the acceptability of molecular arms race theory as plant exhibited various counter defense responses to fight against VRSs (Zhao et al., 2016).

### Resistance through R-Gene

R-gene mediated resistance, race-specific resistance against diverse phytopathogens encoding corresponding dominant Avr genes is conferred by dominant R genes (Hammond-Kosack and Jones, 1996). This type of resistance is associated with HR in many cases. HR-mediated cell death immediately eliminates infected cells and prevents systemic spread of viral infections. The HR is generally associated with signaling of mitogen-activated protein kinase (MAPK); increase in jasmonic acid (JA), salicylic acid (SA), calcium ion influx, callose deposition at the plasmodesmata, membrane permeability modification defense genes activation and an immediate reactive oxygen species (ROS) and nitric oxide (NO) accumulation (Yang et al., 2001). The majority of plant R genes encode nucleotide-binding (NB) and leucine-rich-repeat (LRR) domains, whereas the proteins of Avr have very little common characteristics (Jones and Dangl, 2006). There are three domains of NB-LRR proteins in the center the nucleotide-binding site (NBS) at the C-terminal end, a Coiled-coil (CC) at the N-terminus toll and human interleukin receptor (TIR) domain (Meyers et al., 2003). Besides conserved NBS domain includes an Apaf-1/R protein/CED 4 (ARC) domain, which is involved in the hydrolysis of ATP and intra-molecular interactions (Rairdan et al., 2008). NB-LRR proteins with intra-molecular interactions are conserved at certain levels and are critical for proper functioning of R protein (Rairdan et al., 2008). NB-LRR proteins exhibit LRR domain which is the primary determinant for conferring the specificity to recognize plant pathogens (Jones and Dangl, 2006). The N-terminus is acknowledged serving an important role for the interaction of specific Avr (Collier and Moffett, 2009). NB-LRR proteins recognize the avirulent effectors which sequentially initiates downstream defense responses. So far more than 20 viral R genes with dominant inheritance

have been characterized. The first viral R-gene to be cloned and characterized as N is a resistance gene of tobacco encoding a protein of TIRNB-LRR conferring resistance to TMV (Whitham et al., 1994). The counterpart of N is the 50 kDa helicase domain p50 and viral 126 kDa protein part in the TMV replicase complex (Padgett et al., 1997). In the case of TMV resistance, p50 helicase domain is recognized by N through a direct interaction (Ueda et al., 2006). A potato protein Rx conferring resistance to Potato virus X (PVX) is a typical protein CC-NB-LRR. Its counterpart determinant Avr is the PVX coat protein (CP) (Bendahmane et al., 1995; 1999). The each functional domain role and intramolecular interactions among those domains have been studied intensively in Rx (Rairdan et al., 2008).

### Resistance through dominant and recessive inheritance

As intracellular parasites, viruses are exclusively dependent on cellular host mechanisms for their life cycle. When viral particles enter a plant cell, the genome is released from the capsid, and early viral proteins are translated. After that, the virus confronts various host defense levels. Because of the limited numbers of viral gene products, the virus requires a series of host factors to pursue a cycle of successful infections including replication, transcription, translation, cell to cell movement and long distance spread (Truniger and Aranda, 2009). The absence or a necessary host factor alteration can be an efficient plant defense strategy and is considered a passive form of resistance (Fraser, 1990; 1992). Such passive resistance frequently shows recessive inheritance. The resistance mediated by R gene described in the previous section can be considered in this context. It is predicted that more than half plant virus resistances are recessively inherited (Kang et al., 2005b) many are yet to be characterized (Truniger and Aranda, 2009). A large proportion of identified R genes to date confer resistance to various potyviruses. Recessive R genes conferring resistance of potyvirus have been identified and deployed for decades in numerous crops. Translation factor of eukaryotes4E (eIF4E) plays a major role in the host translation initiation by messenger RNAs recruiting the ribosomal complex and has repeatedly been identified as an essential host factor required for virus infection (Truniger and Aranda 2009). Natural variation in eIF4E preventing sequestration of virus confers effective resistance infection of potyvirus in multiple crop species suggesting that the host fac-

tors alteration such as translation initiation factors is a common strategy for developing plants viral resistance (Yeaman et al., 2007; Cavatorta et al., 2008). Those factors include pvr1 and pvr2 in pepper (Gao et al., 2004) mol in lettuce (Ling et al., 2009) sbml in pea (Nicaise et al., 2003) rym4/5 in barley (Ruffel et al., 2002) pot1 in tomato (Kang et al., 2005a) and zym-FL in watermelon (Wicker et al., 2005). It was demonstrated that the variations in the amino acid in eIF4E is responsible for potyviral resistance in multiple species have independently arisen and been selected positively in their evolutionary context (Cavatorta et al., 2008). The recently characterized ty5, which confers Tomato yellow leaf curl virus (TYLCV) resistance encodes the messenger RNA surveillance factor Pel0 and is another example of recessive resistance in tomato (Lapidot et al., 2015). Pel0 impaired functionalities which are implicated in the protein synthesis and ribosome recycling-phases appear to trigger the viral infection suppression in resistant ty5 genotypes. Various examples of genes characterized for dominant and recessive inheritance have been explained (Table 1).

### Breeding resistance against viral diseases

Development of disease resistant varieties which will ultimately contribute to increase crop yield has been a major goal in most of the breeding programs. Marker-assisted selection (MAS) has been successfully and widely deployed for decades to generate disease resistance by applying genetic markers for selection and recombination of multiple resistant genes (Miedaner and Korzun, 2012). In tomato, which is an economically important vegetable crop, MAS has been actively utilized for major genes of virus-resistance including Ty1 and Ty2 for TYLCV, Sw5 for Tomato spotted wilt virus and Tm2 for Tomato mosaic virus (Lee et al., 2015). A molecular marker refers to a DNA marker and can serve for genetic polymorphisms and detection of a technical phenotypic variation. Many technological innovations including techniques of next-generation sequencing (NGS) (Jones et al., 2009) single-nucleotide polymorphism (SNP) (Salgotra et al., 2014) genotyping have accelerated studies of genome-wide association (GWAS) and greatly improved the accuracy, cost-effectiveness, and MAS time-efficiency (Thomson, 2014). To enhance the access of genomic information, the gene-based markers have led towards the considerable number of disease resistances which is greatly advantageous compared with neutral markers linked

to the specific genes (Kage et al., 2015; Kamphuis et al., 2015). PCR-gel based systems which use cleaved and amplified polymorphic sequence (CAPS) markers and high-throughput SNP detection systems via utilization of high-resolution melt (HRM) markers have been widely utilized to detect multiple SNPs associated with traits of disease resistance (Jung et al., 2015).

There are a few success stories in introgression of resistance against the target viruses. For example, tomato-infecting viruses have been neutralized to some extent via breeding host resistance by incorporation of genes from *Solanum* species (*S. peruvianum*, *S. habrochaites*, *S. pimpinellifolium* and *S. chilense*) (Ji et al., 2007a). Molecular mapping and characterization of resistance genes via the use of molecular markers have been done (Ji et al., 2007a). TY-1 which is a major and partial dominating resistant gene was identified from *S. chilense* line # LA1969 and was introgressed, mapped towards the shorter arm of chromosome 6 (Zamir et al., 1994). Similarly, from *S. pimpinellifolium*, another major resistance QTL was exhibited and was mapped at same chromosome 6 (TG153-CT83) but conferring a different position (Chague, 1997). Another dominant gene (Ty-2) introgressed from *S. habrochaites* accession H24 was mapped to shorter arm of chromosome 11 (Hanson et al., 2000). Correspondingly, mapping of TY-3 which is categorized as partially dominant major gene extracted out from *S. chilense* accessions LA1932 and LA2779 was done at chromosome 6 (Ji et al., 2007b). The particular gene derived from LA2779 was considered to be greater in length and its linkage with TY-1 exhibited that both of these (Ty-3 and TY-1) are code specific and are allelic towards RNA-dependent polymerase (Verlaan et al., 2013). Further mapping revealed the exhibition of TY-4 mapping to chromosome 3 at its longer arm. About the development of symptoms in the host, TY-4 gene encounters 16% variation as compared to TY-3 which accounts 60% major effects (Ji et al., 2009). Alternatively, upon chromosome 4, a resistant but recessive gene TY-5 was introgressed from a genotype called Tyking (Hutton et al., 2012). The particular gene has similarities with TY-5 loci exhibiting 40% symptomatic variation (Anbinder et al., 2009). All these resistant genes encourage towards acquiring resistance against the viruses by contributing lower levels of viral particle accumulation in these genotypes. The tomato genotypes having TY-1 or Ty-3 genes exhibited 10% fewer virus symptoms than

**Table 1:** Genes characterized for dominant and recessive inheritance in various plants against plant viruses.

Plant species	Gene/Locus	Major virus	Resistance factors and features	Resistance type	Avirulence factor	Reference
Arabidopsis thaliana	HRT	Turnip crinkle virus	CC-NBS-LRR (HR)	Dominant	CP	Ren et al., 2000
	JAX1	Platago asiatica mosaic virus	Jacalin like lectin (Blocks RNA Accumulation)	Dominant	Unknown	Yamaji et al., 2012
	RCY1	Cucumber mosaic virus	CC-NBS-LRR (HR)	Dominant	CP	Takahashi et al., 2002
	RTM1	Tobacco etch virus	Jacalin family (Blocking systemic Movement)	Dominant	CP	Chisholm et al., 2000
	RTM2	Tobacco etch virus	Small heat shock Protein (Blocking systemic Movement)	Dominant	CP	Whitham et al., 2000
	RTM3	Tobacco etch virus	MATH-containing protein (Blocking systemic Movement)	Dominant	Unknown	Cosson et al., 2010
	sp1	Turnip mosaic virus	eIF(iso)4E (mutagenesis)	Recessive	VPg	Lellis et al., 2002
	cum1	Cucumber mosaic virus	eIF4E (mutagenesis)	Recessive	Unknown	Yoshii et al., 2004
	cum2	Cucumber mosaic virus	eIF4E (mutagenesis)	Recessive	Unknown	Yoshii et al., 2004
Brassica campestris	BcTuR3	Turnip mosaic virus	TIR-NB-LRR (Systemic resistance)	Dominant	Unknown	Cosson et al., 2010
	TuRB07	Turnip mosaic virus	CC-NBS-LRR (ER)	Dominant	Unknown	Ma et al., 2010
Capsicum spp.	L (multi-alleles)	Tobacco mosaic virus	CC-NBS-LRR (HR)	Dominant	CP	Tomita et al., 2011
	pvr1/pvr2 (multi-alleles)	Potato virus Y	eIF4E	Recessive	VPg	Ruffel et al., 2002;
Capsicum annuum	pvr6	Pepper veinal mottle virus	eIF(iso)4E	Recessive	VPg	Ruffel et al., 2006
Cucumis melo	nsv	Melon necrotic spot virus	eIF4E	Recessive	Unknown	Nieto et al., 2006
Glycine max,	Rsv1	Soybean mosaic virus	CC-NB-LRR (HR)	Dominant	P3, HC-Pro	Hayes et al., 2004
Hordeum vulgare	rym4/5(multi-alleles)	Barley yellow mosaic virus	eIF4E	Recessive	VPg	Stein et al., 2005
Lactuca sativa	mo1 (multi-alleles)	Lettuce mosaic virus	eIF4E	Recessive	CI- Cter, VPg	Nicaise et al., 2003
Oryza sativa	rymv1	Rice yellow mottle virus	eIF(iso)	Recessive	4G, VPg	Albar et al., 2006
Oryza glaberrima	rymv2	Rice yellow mottle virus	CPR5(H)	Recessive	unknown	Orjuela et al., 2013
Phaseolus vulgaris	I	Bean common mosaic virus	TIR-NBS-LRR (HR)	Dominant	Unknown	Vallejos, 2006
	RT4-4	Cucumber mosaic virus	TIR-NBS-LRR (Systemic necrosis)	Dominant	2a	Seo et al., 2006
	bc3	Bean common mosaic virus	eIF4E	Recessive	unknown	Naderpour et al., 2010

<i>Pisum sativum</i>	sbm1	Pea seed-born mosaic virus	eIF4E	Recessive	VPg	Gao et al., 2004
<i>Solanum chilense</i>	Ty1/Ty3 (multi-alleles)	Tomato yellow leaf curl virus	RDR (RNA silencing)	Dominant	Unknown	Butterbach et al., 2014
<i>Solanum habrochites</i>	Tm1	Tomato mosaic virus	TIM-barrel-like domain (Blocking replication)	Dominant	Replication protein	Ishibashi et al. 2007
<i>Solanum lycopersicum</i>	pot1	Potato virus Y	eIF4E	Recessive	VPg	Ruffel et al., 2005
<i>Solanum peruvianum</i>	Tm2 (multi-alleles)	Tomato mosaic virus	CC-NBS-LRR (HR)	Dominant	MP	Lanfermeijer et al. 2003
	Sw5b	Tomato spotted wilt virus	CC-NBS-LRR (HR)	Dominant	MP (NSm)	Brommonschenkel et al., 2000
<i>Solanum tuberosum</i>	Rx (multi-alleles)	Potato virus X	CC-NBS-LRR (Blocking replication)	Dominant	CP	Bendahmane et al., 2002
	Y1	Potato virus Y	TIR-NBS-LRR (HR)	Dominant	Unknown	Vidal et al., 2002
<i>Vigna mungo</i>	CYR1	Mungbean yellow mosaic virus	CC_NB_LRR	Dominant	CP	Maiti et al., 2012

Here; *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), *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)

the susceptible ones (Verlaan et al., 2013). Similarly, tomato accessions carrying TY-2 genes showed least virus particle accumulation (Barbieri et al., 2010). The other successful examples in which resistance has been tried to achieve through pyramiding of virus genes via crossing or backcrossing (Yang et al., 2013) include glycine max-soybean mosaic virus (SMV) (Shi et al., 2008), *Capsicum annuum*-pepper veinal mottle virus (PVMV) (Caranta et al., 1996), barley yellow mosaic virus (BaYMV), *Hordeum vulgare*-barley mild mosaic virus (BaMMV) (Werner et al., 2005), *Phaseolus vulgaris*-bean common mosaic virus (BCMV) (Kelly et al., 1995) and tomato leaf curl disease (ToLCD) (Kadirvel et al., 2013). Resistant accessions via pyramiding have been developed by introgression of TY-2 and TY-3 genes extracted from *S. habrochaites* and *S. chinense* respectively (Prasanna et al., 2014).

Viruses re-organize themselves and go under recombination leading towards their spread towards the cultivars which are thought to be immune to them (Islam et al., 2017). For example, tomato cultivars *i.e.* Roma and Moneymaker which were famous for their resistant characters against viruses and better yields became susceptible to ToLCD (Fufa, 2011; Camara, 2013). To manage this problem, new tomato cultivars have been adopted widely worldwide which are toler-

ant to begomoviruses infections and gives better yield even after being infected by viruses (Ozores-Hampton et al., 2013; Butterbach et al., 2014). Recently, 41 tomato genotypes were screened in Senegal for their resistance against TYLCD (Camara, 2013) out of which 12 were found to have durable resistance against the disease. But when other RNA viruses infected these 12 genotypes, they lost their considerable resistance to TYLCD (Butterbach, 2014). Similar experiments in Nigeria revealed resistant pepper and tomato cultivars against viruses (Alegbejo, 2000; Vu, 2013; Medina, 2013; Reyes, 2013). In Asian regions, cotton is the most important crop which is under constant threat of cotton leaf curl virus disease (CLCuD). Researchers evaluated that *Gossypium gossypoides* still have durable resistance against CLCuD (Azhar et al., 2013). Furthermore, considerable resistance has been achieved through transgenics showing repression genes via utilization of *Agrobacterium tumefaciens* mediated transformations (Balasubramani et al., 2003; Katageri et al., 2007; Amudha et al., 2011; Hashmi et al., 2011).

But in spite of being the best way, there are several limitations such as, (a) the resistance exploited by the breeders is mostly conferred by a single dominant gene (Frasar et al., 1990) which do not prove long-lasting

in the field and gets hammered after a couple of years in the field by the pathogen (Pelham et al., 1970), (b) unavailability of desired genetic resistance in wild-type relatives (c) linkage of non-desired traits with the resistance-conferring gene, (d) desired resistance may be multigenic which may possess difficulties in gene knockdown and transfer of genetic traits, (e) larger genomic size with higher representative DNA (f) difficulties in cloning the resistance encoded genes because of insufficient mapping of various plant species, (g) difficulty in tagging for identification and isolation of resistant genes against viruses due to lack of knowledge about available resistance in most plant species against viruses (Valkonen et al, 1998).

### Conclusion and future prospects

Effective antiviral resistance mechanisms developed by the plants through complex co-evolutionary processes. Over the past decade, plant resistance molecular mechanisms to viruses have been investigated exclusively, and remarkable progress has been made. The viral genetic resistance which is naturally occurring primarily comprises of antiviral RNA silencing, R-gene-mediated resistance and recessive resistance. As viruses are intracellular parasites consisting of a small genome of RNA or DNA packed in a capsid thus RNA silencing is considered as a major antiviral mechanism. Successful RNA antiviral silencing primarily results in the viral genome degradation at the site of the initial infection. The R-gene-mediated resistance which is the most intensively explored resistance is also effective in conferring resistance to plant viruses. Recessive inheritance resistance is mostly acquired via alteration of key host factors for viral infection is also recognized as a necessary antiviral mechanism. The most effective strategies of resistance would be selected and used in each plant pathosystem is mainly based on the arms-race relationships and the resistance acquisition fitness cost. Understanding the plant viral resistances at the molecular level will allow us one step closer for effective accomplishment of durable viral resistance. But as we know, all the viruses continuously undergo evolutionary phases and lead to the development of new strains, so more and more efforts are required to find resistant wild type plant species against viruses. These wild-type resistant traits should be characterized to incorporate into the economically important crop plants. Similarly, the interaction of begomoviruses and its insect vector should be widely studied and integrated management approaches must be utilized to minimize the vector

populations. These vectors are harbored by thousands of different weed species all around the world. So control of these weeds is also a necessary step for the management of viruses. Furthermore, biotechnological approaches like vector-enabled metagenomics (VEM), next generation sequencing (NGS), Zinc finger mechanism (ZFM) and Crisper-Cas9 are needed to be tested to stay ahead and for the development of virus free crops.

### Author's Contribution

Waqar Islam prepared the manuscript, Madiha Zaynab and Muhammad Qasim helped in compilation of figure and tables. Zujian Wu approved the manuscript for publication.

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