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Review

Sources of natural resistance to plant viruses: status and prospects

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SUMMARY

Globally, virus diseases are common in agricultural crops and have a major agronomic impact. They are countered through the deployment of genetic resistance against the virus, or through the use of a range of farming practices based upon the propagation of virus-free plant material and the exclusion of the virus vectors from the growing crop. We review here the current status of our knowledge of natural virus resistance genes, and consider the future prospects for the deployment of these genes against virus infection.

INTRODUCTION

Virus infections of crops are persistent and cannot yet be combated in ways that can be achieved for animal viruses through the stimulation of the active immune process. Hence, the best strategy is one of avoidance either through the physical separation of the pathogen and host, or through the deployment of genetic resistance to prevent or limit the extent of the infection. In practice, the former is achieved through the use of virus-free seeds or stock plants and by employing physical barriers or pesticides to deter the vectors of virus diseases. Within this armoury, however, the most effective and sustainable approach to the prevention of virus disease is through the deployment of genetic resistance targeted against viruses directly or, in theory, against their vectors. Recently there have been dramatic advances in our understanding of the molecular nature and mechanisms associated with natural virus resistance genes. Dominant and recessive resistance genes have been characterized at the molecular level and we are beginning to understand new principles of innate immunity to viruses associated with gene silencing. These advances have come about as plant biology has moved into a new phase driven by advances in technology. In the next 10 years, we will see the genomes of many of the major crop species sequenced, and technologies for faster and larger scale analyses are being developed in parallel. These advances will provide new opportunities that should change the way we tackle the problem of virus resistance. It will be possible to mine much larger collections of crop germplasm genetically for known and novel resistances, and to deliver these to industry in a more timely fashion. However, as we understand more about the principles that underlie virus replication and genome expression in plants, it should also be possible to move from a reactive to a proactive or predictive approach to tackle the problems of virus diseases.

This article will give an overview of what we know about the molecular and genetic character of the major classes of natural virus resistance genes and consider some factors that influence their practical and timely application in agriculture. Breeding for resistance, however, need not be dependent upon a full molecular characterization of the resistance gene alleles and the corresponding pathogen avirulence (avr) determinants. In a practical sense, the successful deployment of a novel resistance gene into a crop depends more upon the identification of a positive phenotype, dissection of the phenotype leading to the identification of genetic markers for marker-assisted selective breeding (MAS) and an understanding of how the novel resistance will behave in different genetic backgrounds and under pathogen pressure in the field. Hence, it is also valuable to review progress in some of the less-explored areas of resistance and to consider the future technical advances that will ease the exploitation of novel resistances.

DOMINANT RESISTANCE GENES

To date, the majority of characterized pathogen resistance (R) genes from plants have provided monogenic dominant resistance. Those characterized at the molecular level mostly confer resistance to fungal or bacterial pathogens (Hammond-Kosack and Parker, 2003), but there are currently 12 examples of such genes conferring resistance to viruses (Table 1), which have been identified from both crops (e.g. potato, tomato, tobacco, soybean and bean)

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Table 1 Dominant virus resistance genes.

Gene	Virus	avr*	Plant sp.	Reference(s)
N	*Tobacco mosaic virus* (TMV) (*Tobamovirus*)	Replicase/helicase	Tobacco	Whitham *et al.* (1994); Padgett *et al.* (1997); Erickson *et al.* (1999)
Tm2^{2}	*Tomato mosaic virus*, TMV (*Tobamoviruses*)	Movement protein	Tomato	Lanfermeijer *et al.* (2003); Weber and Pfitzner (1998)
Rx1	*Potato virus X* (PVX) (*Potexvirus*)	Coat protein	Potato	Bendahmane *et al.* (1995, 1999)
Rx2	PVX (*Potexvirus*)	Coat protein	Potato	Bendahmane *et al.* (2000)
Y-1	*Potato virus Y* (*Potyvirus*)	—†	Potato	Vidal *et al.* (2002)
Sw5	*Tomato spotted wilt virus* (*Tospovirus*)	Movement protein	Tomato	Brommonschenkel *et al.* (2000)
Rsv1	*Soybean mosaic virus* (*Potyvirus*)	—	Soybean	Hayes *et al.* (2004)
RT4-4	*Cucumber mosaic virus* (CMV) (*Cucumovirus*)	2a gene	*Phaseolus vulgaris*	Seo *et al.* (2006)
HRT	*Turnip crinkle virus* (*Carmovirus*)	Coat protein	*A. thaliana*	Cooley *et al.* (2000); Ren *et al.* (2000)
RTM1	*Tobacco etch virus* (TEV) (*Potyvirus*)	—	*A. thaliana*	Chisholm *et al.* (2000)
RTM2	TEV	—	*A. thaliana*	Whitham *et al.* (2000)
RCY1	CMV	Coat protein	*A. thaliana*	Takahashi *et al.* (2001)

*Viral avirulence determinant.
†Unknown.

and model species (*Arabidopsis thaliana*). Except for *RTM1* and *RTM2*, all fall into the nucleotide binding site-leucine rich repeat (NBS-LRR) class of resistance genes. Members within this class can be further subdivided based upon the presence of either an N-terminal Toll-interleukin-1 receptor (TIR) homology domain or an N-terminal coiled-coil (CC) domain. These genes operate through a 'gene-for-gene' recognition of pathogen avr factors, which for viruses relate to a diverse spectrum of virus gene products (Table 1). Interestingly, all the virus resistance NBS-LRR gene products lack a transmembrane domain, consistent with the intracellular lifestyle of viruses and the location of the avr products. Although it was originally believed that there was a direct physical molecular interaction between the avr and the R gene product, this now seems to be unlikely in the majority of cases. Rather, the avr appears to disrupt a complex between the resistance gene product and its negative regulator, the so-called 'guard hypothesis' (Dangl and Jones, 2001). Specific information for viral resistance genes is scarce. A direct interaction between the tobacco *N* gene product and the tobacco mosaic virus (TMV) avirulence factor has been demonstrated. Specifically, N interacts with the helicase domain (p50) of the viral replicase protein (Ueda *et al.*, 2006). This interaction has also been envisaged to play a role in the oligomerization of N prior to resistance activation (Mestre and Baulcombe, 2006). By contrast, however, the interaction between N and p50 has also been shown to be mediated by a novel N-interacting protein (NIP1) (S. P. Dinesh-Kumar, personal communication).

In common with the responses to fungi and bacteria, the NBS-LRR virus resistance genes mostly lead to complete resistance (qualitative) but are not always associated with cell death and/or tissue necrosis. The best-characterized example is *Rx* resistance against *Potato virus X* (PVX; *Potexvirus*), which confers an extreme resistance that inhibits virus replication without hypersensitive cell death being apparent. However, over-expression of the PVX avr (coat protein) in Rx-transformed *Nicotiana* spp. and potato activates cell death, indicating that the same underlying principles are operating (Bendahmane *et al.*, 1999). The same trends hold true for *Sw5* in tomato and *Rsv1* in soybean (Brommonschenkel *et al.*, 2000; Hayes *et al.*, 2004).

The use of dominant R genes controlling complete resistance appears to be an attractive option for breeders and they have been utilized when they have been available. Although R gene function is based upon precise molecular interactions that lead to the activation of resistance by pathogen avirulence determinants, virus R genes appear to have a wider specificity than might be expected. Hence, *Sw5* confers resistance to several tospoviruses (Brommonschenkel *et al.*, 2000) and *N* and *Rx* are effective against many natural variants of TMV and PVX, respectively (Dunigan *et al.*, 1987; Querci *et al.*, 1995). The determinants for this specificity reside in the LRR domains and may provide a focus of activity for the search for new resistances in wild populations of plants (Farnham and Baulcombe, 2006).

It is likely that the number of characterized R genes will rapidly increase because the common sequence features of the NBS-LRR class of dominant resistance genes provides a shortcut to their identification in new species through homology searches (Hayes *et al.*, 2004). Hence, we know that the Arabidopsis (Colombia ecotype) genome encodes approximately 149 NBS-LRR genes,

many of which have been shown to confer resistance to pathogens (Meyers *et al.*, 2003).

The non-NBS-LRR genes *RTM1* and *RTM2* effective in Arabidopsis against *Tobacco etch virus* (TEV; *Potyvirus*), were phenotypically identified as genes inhibiting TEV long-distance movement. *RTM1* encodes a protein belonging to the jacalin family, with members also involved in defence against insects and fungi (Chisholm *et al.*, 2000). *RTM2* encodes a protein with similarities to small heat shock proteins (Whitham *et al.*, 2000). A third and distinct gene (*RTM3*) conferring the same phenotype has not been characterized molecularly. Both *RTM1* and *RTM2* are expressed in phloem-associated tissues and the proteins localize to sieve elements, but the mechanism by which they restrict TEV long-distance movement has not yet been determined.

RECESSIVE RESISTANCE (IMPAIRED SUSCEPTIBILITY)

Viruses depend upon host factors to complete their infection cycle. The study of these factors provides a unique opportunity to identify mutant alleles that could confer recessive resistance to plant viruses. This approach has led to the identification of a range of plant species (tomato, lettuce, pepper, pea, melon, barley, rice) in which natural mutations of components of the eukaryotic translation initiation complex result in resistance to specific RNA viruses (for reviews see Diaz-Pendon *et al.*, 2004; Robaglia and Caranta, 2006). Interestingly, in addition to natural polymorphism in crop plants, mutagenic analysis of the same genes in Arabidopsis generated the same phenotype. The majority of these resistances function against potyvirus infection (Table 2), although, recently, eukaryotic initiation factor 4E (eIF4E) has also been implicated in recessive resistance to *Barley yellow mosaic virus* (*Bymovirus*, related to potyviruses; Kanyuka *et al.*, 2005; Stein *et al.*, 2005) and *Melon necrotic spot virus* (MNSV; *Carmovirus*; Nieto *et al.*, 2006). The eIF4E paralogue, eIF(iso)4E, has also been shown to be necessary for infection of Arabidopsis by several potyviruses (TEV; *Turnip mosaic virus*, TuMV; *Lettuce mosaic virus*, LMV; *Plum pox virus*, PPV) and recent studies suggest that potyviruses may selectively use either eIF4E or eIF(iso)4E (Sato *et al.*, 2005) or both (Ruffel *et al.*, 2006) to achieve a successful infection. Recently, the involvement of another component of the translation initiation complex, the scaffold protein eIF(iso)4G, was identified as being a susceptibility factor for *Rice yellow mottle virus* (RYMV; *Sobemovirus*) infection of rice (Albar *et al.*, 2006). For the Potyviridae, the resistance determinants have been mapped to non-conservative amino acid changes in two surface loops of eIF4E close to the cap-binding pocket. Substitutions characteristic of high resistance to RYMV were also mapped to a surface location of eIF(iso)4G. In the case of *nsv*-mediated resistance against MNSV, a single non-conservative amino acid substitution mapped to the C-terminal arm of eIF4E on an accessible region of the protein (Nieto *et al.*, 2006). Collectively, these data point towards a resistance mechanism(s) mediated by a subtle change(s) in the surface interaction of translation initiation factors. From the virus side and for most of the potyviruses listed above, and RYMV, the avr factor has been identified as the virus genome-linked protein (VPg; reviewed by Robaglia and Caranta, 2006), a protein that substitutes for the 7-methyl guanosine (m^7G) cap found in

Table 2 Recessive virus resistance genes.

	Virus	Plant sp.	Reference(s)
Natural gene			
pvr1, *pvr2*^{1}, *pvr2*^{2} + *pvr6*	PVY, TEV, *Potato vein mottling virus* (PVMV)	Pepper (*Capsicum* spp.)	Ruffel *et al.* (2002, 2006) Kang *et al.* (2005)
pot-1	PVY, TEV	Tomato (*Lycopsersicon* spp.)	Ruffel *et al.* (2005)
sbm1	*Pea seed borne mosaic virus*	Pea (*Pisum sativum*)	Gao *et al.* (2004)
mo1^1, *mo1*^{2}	*Lettuce mosaic virus* (LMV)	Lettuce (*Lactuca sativa*)	Nicaise *et al.* (2003)
rym4/5	*Barley mild mosaic virus*, *Barley yellow mosaic virus*, *Barley yellow mosaic virus 2*	Barley (*Hordeum vulgare*)	Stein *et al.* (2005); Kanyuka *et al.* (2005)
rymv1	*Rice yellow mottle virus* (RYMV)	*Oryza sativa*	Albar *et al.* (2006)
nsv	*Melon necrotic spot virus*	*Cucumis melo*	Nieto *et al.* (2006)
Mutants			
At-eIF4E1	*Clover yellow vein virus*	*A. thaliana*	Sato *et al.* (2005)
At-eIF(iso)4E	*Turnip mosaic virus*, LMV, TEV	*A. thaliana*	Duprat *et al.* (2002); Lellis *et al.* (2002)
At-eIF4E1 (cum1)	CMV	*A. thaliana*	Yoshii *et al.* (2004)
At-eIF4G (cum2)	CMV, TCV	*A. thaliana*	Yoshii *et al.* (2004)

eukaryotic host mRNAs. Intriguingly for MNSV, the determinant was found to be the RNA itself (Diaz *et al*., 2004).

The identification of members of the translation initiation complex as susceptibility factors for diverse viruses may not be unexpected as all viruses must be translated to establish an infection. Furthermore, the fact that these genes exist as paralogous and redundant gene families in all plant species studied may separate them out from other susceptibility factors as genes amenable to mutation. However, for potyviruses, where the role of eIF4E in resistance/susceptibility has been studied most extensively, the picture relating to the role of eIF4E in resistance remains somewhat confused. Examples of the direct interaction of eIF4E/eIF(iso)4E with potyvirus VPg (or its precursor NIa) have been reported (Kang *et al*., 2005; Léonard *et al*., 2000; Schaad *et al*., 2000; Wittmann *et al*., 1997) and there is evidence that indicates that this interaction may be strengthened by the incorporation of eIF4G (Grzela *et al*., 2006; Michon *et al*., 2006; Miyoshi *et al*., 2005). *In vitro* interaction studies point to precise but distinct locations for VPg- and m^7G-binding to eIF4E, although there may be some mutual antagonism (Grzela *et al*., 2006; Michon *et al*., 2006), and the products of eIF4E resistance alleles may or may not be defective for m^7G cap binding (Gao *et al*., 2004; Kang *et al*., 2005; Nieto *et al*., 2006). Furthermore, translation of potyvirus RNA *in vitro* can be eIF4E-independent. In this case, rather than eIF4E being necessary to initiate translation through an interaction with the 5′ VPg, eIF4G interacts with an RNA component in the 5′ untranslated region (5′UTR) to initiate translation (Gallie, 2001). Recently, eIF4G or its paralogues [eIF(iso)4G1 and eIF(iso)4G2] have also been demonstrated to be necessary for infection of Arabidopsis by TuMV, LMV, PPV and *Clover yellow vein virus* (ClYVV) (V. Nicaise *et al*., personal communication). However, it remains to be determined whether the role of eIF4G factors in plant–potyvirus interactions are related and dependent upon eIF4E. For *sbm1*-mediated resistance to *Pea seed borne mosaic virus* (PSbMV; *Potyvirus*) in pea, eIF4E is also implicated in cell-to-cell movement of the virus (Gao *et al*., 2004). Therefore, although eIF4E-based resistance might point to a failure of the viral RNA to be translated, the precise role of eIF4E in potyvirus infection remains uncertain. Of relevance is the identification of EMS-induced mutations *cum1* (eIF4E) and *cum2* (eIF4G) in Arabidopsis that control partial resistance to *Cucumber mosaic virus* (CMV; *Cucumovirus*) and *Turnip crinkle virus* (TCV; *Carmovirus*). In these cases, resistances are probably linked to an inefficient translation of viral RNAs for the production of viral movement proteins (Yoshii *et al*., 2004).

Although these recessive resistances can be qualitative, in many cases they are quantitative and/or are components of polygenic resistance. For example, in pepper an *eIF4E* resistance allele at the *pvr2* locus controls a partial resistance to PVY pathotypes (0,1,2) and was initially mapped as a quantitative trait locus (QTL; Caranta *et al*., 1997a). Also, from the work with mutant eIF(iso)4E in Arabidopsis (Duprat *et al*., 2002; Lellis *et al*., 2002) it appears that single mutant alleles can confer resistance to diverse related viruses. For the breeder, it is clear that the recessive resistances offer some important complementary features when compared with the dominant resistance genes. For example, in contrast to the dependence of the dominant NBS-LRR genes on induced and often common functional pathways, the recessive genes are more likely to be constitutive components of cellular activity. This mechanistic diversity has advantages in providing alternative angles of attack on target pathogens although the recessive nature of the latter class also creates some technical challenges in terms of the ease and speed of breeding.

RESISTANCE AGAINST VIRUS VECTORS

As viruses depend upon vectors for disease spread, genes that deter infestations with these vectors and/or block virus transmission have the potential to provide additional scope for genetic resistance. To date, only two genes conferring resistance to potential virus vectors have been characterized. These fall within the NBS-LRR group of plant R genes, underlining the key role of this type of gene not only against pathogens but also to pests. The tomato *Mi-1* confers resistance to the potato aphid (*Macrosiphum euphorbiae*), whitefly (*Bemisia tabaci*) and the root-knot nematodes (*Meloidogyne* spp.), the former two of which are virus vectors (Vos *et al*., 1998). Interestingly, recent work (Goggin *et al*., 2006) has shown that the *Mi-1.2* allele confers resistance against nematodes but not against aphids when placed in the distinct genetic environment of *Solanum melongena* (eggplant). This indicates that aphid resistance in tomato conferred by *Mi-1* may require additional factors. The melon *Vat* gene controls plant colonization by the aphid *Aphis gossypii* and the transmission of non-persistent viruses. A single CC-NBS-LRR gene controls this double resistance phenotype (Pauquet *et al*., 2004). In addition, there is increasing evidence that resistance to many sap-sucking and chewing insects may be mediated by single resistance genes of similar structure. For example, *Nr*, conferring resistance in lettuce against the aphid *Nasonovia ribisnigri*, shows functional similarity to *Mi-1*, and phloem-specific resistance to the blue green aphid (*Acyrthosiphon kondoi*) in *Medicago trucatula* has been mapped to a region predicted to contain CC-NBS-LRR R gene analogues (Klingler *et al*., 2005). It has been suggested that resistance mediated by NBS/LRR genes in insects may be a widespread resource for introducing important insect resistance into plants (Kaloshian, 2004).

INNATE IMMUNITY

Over the last decade our understanding of a core constitutive process termed RNA silencing (Baulcombe, 2004; Voinnet, 2005), which is common to plants, animals and fungi, has had a major

impact upon our understanding of the interaction between plants and viruses. In this process, double stranded RNA (dsRNA) is recognized as a substrate for the subsequent targeting and degradation of sequence-homologous RNAs. Through parallel pathways gene silencing serves a protective role against invading pathogens and a regulatory role for diverse aspects of growth and development. Plant viruses, which commonly have dsRNA as a secondary structural component of the genomic RNA or as a component of their replication cycle, are vulnerable to RNA silencing and as a consequence plants may recover from infection. In many ways this phenomenon is equivalent to the innate immunity found in animals. To avoid this highly effective mechanism, viruses have evolved to encode suppressors of RNA silencing and so for all virus infections a battle between constitutive defence and counter defence is in play to determine, in part, the disease outcome of the infection. Several key functional components of the RNA silencing pathway have been identified. These include the DICER-like (DCL1-4) enzymes, which cleave dsRNA into discrete small RNA products, and the RISC complex, which uses the small RNAs as guide for the degradation of homologous targets. These key components are encoded by gene families, some members of which are specific for the virus defence pathway (Voinnet, 2005; Xie *et al*., 2004). One exciting prospect is the potential for identification of alleles which specifically enhance virus resistance. These may emerge from surveying natural genetic variation in crop germplasm for enhanced innate immunity, or from screening mutant populations.

RNA silencing is the core process that has been harnessed in the generation of most transgenic virus resistant plants. The development of these plants lies outside the scope of this review but the reader is referred to Prins (2003) and Tenllado *et al*. (2004) for recent reviews of progress in this area.

NON-HOST RESISTANCE

Most plants are resistant to most viruses. Generally, when all members of a species are completely resistant to a particular pathogen they are defined as a 'non-host'. Non-host resistance is durable and therefore is valuable for exploitation towards virus-resistant plants. However, it is not tractable by classical genetics and therefore remains very poorly understood. Although this phenomenon for viruses probably relates more to an intrinsic lack of susceptibility than to active defence mechanisms, the dissection of related phenomena for other pathogens (Holub and Cooper, 2004) suggests that non-host resistance can be a multigenic trait involving layers of distinct processes. Unfortunately, the analysis of non-host mutant populations with an avirulent pathogen such as that which identified the *Pen* genes involved in non-host resistance of *Arabidopsis thaliana* to *Blumeria graminis* (Collins *et al*., 2003; Stein *et al*., 2006) appears not to have been attempted for virus pathogens.

GENETIC ANALYSIS OF QUANTITATIVE TRAITS

It is probable that to date only a small proportion of the biodiversity available for disease resistance has been used in commercial varieties. Most agronomic traits in crop plants do not segregate as single defined qualitative monogenic characters but as quantitative and polygenically controlled traits. With regard to virus resistance, this could result from the expression of an incomplete phenotype from a single gene (see eIF4E example above) or, more commonly, from the effect of modifiers of resistance gene functions. Although these traits may confer only moderate resistance, it may nevertheless be extremely valuable within an agronomic context and therefore provide a relatively untapped source of novel variation. For many disease resistances, improvement in crop yield of only a few per cent can provide the difference between profit and loss.

Relatively few QTLs for plant viral resistance have been genetically mapped (Table 3) and only *eIF4E*, which also corresponds to a major gene, has been molecularly characterized. These QTLs present particular technical challenges for their characterization and incorporation into crops. These challenges relate to the nature of the phenotypic assay used in their definition, the identification of linked markers for MAS and, ultimately, the identification of the gene in question. Although QTLs have most frequently been scored on the basis of gross symptomatic effects, there appears to be additional value in analysing the component steps of the virus infection process. Hence, in assessing resistance to CMV in pepper, reduction in virus multiplication, delays in vascular movement and restricted establishment of infection in cells individually conferred only slight delays in plant infection but collectively led to plants with near immunity (Djian-Caporalino *et al*., 2006).

NOVEL ROUTES TO RESISTANCE

The importance of translation initation factors 4E and 4G have emerged largely from fundamental studies including model systems. We anticipate that there will be many more potential resistance targets that function as host susceptibility factors. One question is how these will best be identified? They may emerge from the mining of diverse germplasm collections but this empirical approach is unlikely to be the most efficient strategy. The alternative is to build on existing fundamental work with model host–pathogen interactions. New technologies, e.g. protein–protein interaction technologies and proteomics, particularly for sequenced plant genomes make the characterization of virus-related complexes from infected cells increasingly tractable.

With respect to resistance based upon host susceptibility factors, the identification of novel recessive alleles will require either surveying natural genetic variants using high-throughput specific marker technology or the selection of plants carrying artificially induced mutations. The latter is becoming possible for increasing

Table 3 Quantitative trait loci (QTL) for plant viral resistance.

Virus	Plant sp.	Number of QTL	Resistance assays	Reference
PVY, PVMV (*Potyvirus*)	Pepper	11 QTLs +1 digenic interaction	AUSPC*	Caranta *et al.* (1997a)
CMV (*Cucumovirus*)	Pepper	2 QTLs +1 digenic interaction	Virus installation in host cells	Caranta *et al.* (1997b)
CMV (*Cucumovirus*)	Pepper	4 QTLs +2 digenic interactions	Symptom severity	Ben Chaim *et al.* (2001)
CMV (*Cucumovirus*)	Pepper	4 QTLs +2 digenic interactions	Restriction of long-distance movement	Caranta *et al.* (2002)
Potato leaf roll virus (*Polerovirus*)	Potato	3 QTLs	Virus content	Marczewski *et al.* (2001)
Tomato yellow leaf curl virus (*Begomovirus*)	Tomato	3 QTLs	Symptom severity	Zamir *et al.* (1994)
RYMV (*Sobemobvirus*)	Rice	15 QTLs	Date of symptom appearance andvirus content	Albar *et al.* (1998)
Barley yellow dwarf virus (*Luteovirus*)	Barley	4 QTLs	Tolerance (yield components)	Scheurer *et al.* (2001)
Maize chlorotic dwarf virus (*Waikavirus*)	Maize	4 QTLs	AUSPC	Jones *et al.* (2004)
Maize stripe virus (*Tenuivirus*)	Maize	4 QTLs	AUSPC	Dintinger *et al.* (2005)
Citrus tristeza virus (*Closterovirus*)	Citrus	8 QTLs +1 digenic interaction	Virus content	Asins *et al.* (2004)
Plum pox virus (*Potyvirus*)	*Prunus davidiana*	6 QTLs	Symptom severity and virus content	Decroocq *et al.* (2005)
Beet necrotic yellow vein virus (*Benyvirus*)	Sugar beet	1 major effect QTL	Virus content	Gidner *et al.* (2005)

*Area under the symptom progress curve.

numbers of species through the technology termed 'targeting induced local lesions in genomes' or 'TILLING' (Colbert *et al.*, 2001). TILLING is a reverse genetic approach for mutation generation and discovery that does not rely on transgenic technology. This technology has already demonstrated its capacity to create and identify novel alleles in wheat, one of the most challenging candidates for reverse genetics because of its complex allohexaploid genome (Slade *et al.*, 2005). TILLING technologies are available for barley, wheat, rice, maize, rape, pea and tomato and are in development for other crops.

DURABILITY OF RESISTANCE

An important factor in deciding which resistance genes may be suitable for breeding into commercial crops would be their potential durability in the face of the extreme genetic plasticity of virus pathogens or their vectors. These factors are difficult to assess although the principles governing the emergence of resistance-breaking strains of viruses may differ from those of other pathogens and be dependent upon the type of resistance employed (Garcia-Arenal and McDonald, 2003; Lecoq *et al.*, 2004; van den Bosch *et al.*, 2006). For viruses, the compact nature of the virus genome and the likelihood that most virus genetic variants will be less fit than their parents probably reduce the capacity for resistance-breaking. Nevertheless, from a molecular understanding of the basis of resistance gene function it might be predicted that genes that can only be overcome following multiple mutations in the virus avirulence determinant (avr) will be more durable. Similarly, it might be expected that resistance dependent upon avrs showing high conservation (i.e. genetically invariant) would be less easily overcome due to the fitness penalty. Although this is true for viruses that exhibit limited recombination, some viruses, for example begomoviruses (Geminiviridae), have high propensity for recombination (Morilla *et al.*, 2004; Padidam *et al.*, 1999) contributing to genetic diversification and expanded host ranges and to a potential breakdown of host resistance. The breakdown of resistance to Cotton leaf curl disease in cotton in Pakistan is likely to be a result of changes in the disease complex either as a result of recombination or the recruitment of further viruses by the promiscuous satellite (DNA β) associated with this disease (Briddon, 2003). It is likely that increased durability will be conferred by the 'pyramiding' of resistance genes, preferably operating against different components of the infection cycle, which will require simultaneous mutation in several virus gene products before resistance is broken (Caranta *et al.*, 2002; Djian-Caporalino *et al.*, 2006). The knowledge of closely linked DNA-based markers and/or the sequence of resistance genes makes it possible through MAS to trace and combine resistance factors from different sources. This has already proven useful for developing virus resistance in some important crops, e.g. beans and potatoes (Gebhardt *et al.*, 2006; Singh *et al.*, 2000).

CONCLUDING REMARKS

In the area of resistance to plant viruses, the research community has divided its efforts between building a fundamental knowledge base and responding reactively to real agronomic problems, the latter being delivered where possible to the agricultural

industry, usually in the form of markers for MAS. Ideally, in an increasingly unstable climate, which will have profound effects upon virus vectors, we should be able to predict the nature of effective resistance to potential pathogens as they appear and to provide a more rapid response time in delivery of resistance-related tools to industry. Many crop species have the drawbacks of long generation times, large (often polyploid) genomes, and limited genetic and bioinformatic resources. There is a strong strategic and financial argument for building on the advances in model species biology while also identifying pipelines whereby new findings can be effectively tested and transferred into crop species. The sequenced genomes of Arabidopsis and rice make them the pre-eminent models for dicot and monocot crop plants, although the sequencing of tomato and the legume *Medicago truncatula* will expand the repertoire of useful species. In the current socio-political climate in Europe and elsewhere these resistances are unlikely to be based upon genetically modified (GM) plants but rather will exploit diverse existing and novel stocks of crop germplasm. However, for viruses, GM approaches based upon gene silencing provide extremely powerful opportunities for deliberate and predictive resistance strategies and it would be unwise to ignore their potential for the longer term. An effective strategy to combine breadth of specificity and durability may be to combine natural and GM resistances emerging from our increasing molecular understanding of virus–host interactions in model plant species.

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