Molecular Markers for Selecting Diverse Disease Resistances in Tomato Breeding Programs

Je Min Lee¹, Chang-Sik Oh², Inhwa Yeam^{3,4}

¹Department of Horticultural Science, Kyungpook National University, Daegu 41566, Korea

²Department of Horticultural Biotechnology, College of Life Science, Kyung Hee University, Yongin 17104, Korea

³Department of Horticulture and Breeding, Andong National University, Andong 36729, Korea

⁴Institute of Agricultural Science and Technology, Andong National University, Andong 36729, Korea

ABSTRACT Tomato (*Solanum lycopersicum* L.) is an economically important crop worldwide. In addition, tomato serves as an excellent model system for plant genetics and biology, including fruit biology, abiotic stress tolerance, and plant-microbe interactions. Development and practical use of molecular markers have been actively pursued in molecular breeding programs for tomato, especially for disease resistance to allow selection of a single resistance gene and combination of multiple resistance genes. Due to insufficient genetic variation in cultivated tomatoes, various wild relatives of tomato have been investigated and utilized as disease resistance sources. In order to pursue the resistance provided by these wild relatives in developing new tomato varieties, molecular markers have been developed and intensively utilized in tomato breeding programs. In this review, we summarize the currently available molecular markers that confer resistance against major tomato diseases, including *Tomato yellow leaf curl virus* (TYLCV), *Tomato spotted wilt virus* (TSWV), *Tomato mosaic virus* (ToMV), verticillium wilt, fusarium wilt, late blight caused by *Phytophthora infestans*, leaf mold caused by *Cladosporium fulvum*, root-knot caused by *Meloidogyne* spp., bacterial spot caused by *Xanthomonas* spp., and bacterial speck caused by *Pseudomonas syringae*. The provided marker information is expected to contribute to development of marker-assisted selection for disease resistance and to exploration of novel genetic sources for a tomato breeding program.

Keywords Disease resistance, Marker-assisted breeding, SNP, Gene-based marker, Tomato breeding

INTRODUCTION

Tomato (*Solanum lycopersicum* L.) is an economically important crop worldwide, and it has been estimated that 5 million hectares of tomatoes are grown annually worldwide, producing more than 160 million tons of tomatoes (Food and Agriculture Organization 2013). Tomato also serves as an excellent academic model system for plant genetics and biology, especially for studying fruit biology, abiotic stress tolerance, and plant-microbe interactions. Development and practical use of molecular markers have been actively pursued in molecular breeding programs for tomato (Martin *et al.* 1993; Tanksley *et al.* 1995). Marker-assisted selection (MAS) and marker-assisted breeding (MAB) has been widely and successfully deployed in tomato breeding programs, especially for disease resistance, which allows

selection of a single resistance gene and combination of multiple resistance genes (Foolad and Sharma 2005; Arens *et al.* 2010).

Various technological advancements have accelerated the investigation of the whole genome and genetic loci of interest. Single nucleotide polymorphisms (SNPs) are among the most common types of genetic variation and have been widely utilized in genomics for genome mapping, phylogenetic analysis, association studies, and tagging genes of interest (Jehan and Lakhanpaul 2006; Caicedo *et al.* 2007). Numerous verified SNPs have been successfully used to develop tomato cultivars for public and commercial use (Yang *et al.* 2004; Labate and Baldo 2005). Practical DNA markers can be applied in multiple types of breeding programs such as cultivar identification, parental line selection, and selection of progenies in

Received October 20, 2015; Revised November 10, 2015; Accepted November 11, 2015; Published November 30, 2015

*Corresponding author Inhwa Yeam, iyeam@andong.ac.kr, Tel: +82-54-820-5513, Fax: +82-54-820-5785

segregating populations (Yeam *et al.* 2005; Lagudah *et al.* 2009). The release of the tomato genome sequence has expedited characterization of SNPs, allowing SNPs to be the most effective and useful genetic markers in modern tomato breeding programs (Tomato genome consortium 2012). Use of gene-based markers, which have increased due to the emergence of high-quality genome sequence information, is clearly advantageous for increasing the accuracy of MAS compared with utilization of markers generated based on DNA polymorphisms located adjacent to the gene of interest (Salgotra *et al.* 2014).

Despite decades of intensive efforts in disease resistance tomato breeding programs, a large number of diseases still threaten tomato production industries. Major diseases that challenge tomato production include *Tomato yellow leaf curl virus* (TYLCV), *Tomato spotted wilt virus* (TSWV), *Tomato mosaic virus* (ToMV), verticillium wilt caused by *Verticillium* spp., fusarium wilt caused by *Fusarium oxysporum*, late blight caused by *Phytophthora infestans*, leaf mold caused by *Cladosporium fulvum*, root-knot caused by *Meloidogyne* spp., bacterial spot caused by *Xanthomonas* spp., and bacterial speck caused by *Pseudomonas syringae*. Due to the intensive breeding efforts aimed at improving economically valuable traits, cultivated tomatoes have little variation in their gene pool. Hence, various wild relatives, including *S. pimpinellifolium*, *S. pennellii*, *S. habrochaites*, *S. peruvianum*, and *S. chilense*, have been investigated for use as disease resistance sources (Peirce 1971; Stevens *et al.* 1991; Zamir *et al.* 1994; Diwan *et al.* 1999). To pursue the resistance provided by these wild relatives in developing new tomato varieties, molecular markers have been developed and utilized in tomato breeding programs. In this review, we summarize the currently available molecular markers that confer resistance against each of the indicated diseases.

***Tomato yellow leaf curl virus* (TYLCV) resistance**

Tomato yellow leaf curl virus (TYLCV), which is transmitted by the whitefly (*Bemisia tabaci*), is one of the most serious threats to tomato production worldwide. In Korea, TYLCV incidence was first reported in Tong-Young, Gyoengsangnamdo in 2008 and has spread rapidly throughout the country (Lee *et al.* 2010). TYLCV, which is

a member of the genus Begomovirus within the family Geminiviridae, is a DNA virus with a genome of approximately 2.7–2.8 kb (Cohen and Harpaz 1964; Delatte *et al.* 2005). Several sources of TYLCV disease resistance have been identified among wild tomato species. Two major resistance loci on chromosome 6 were originated from *S. chilense*: *Ty1* from “LA1969” and *Ty3* from “LA1932” and “LA2779” (Zamir *et al.* 1994; Agrama and Scott 2006; Ji *et al.* 2007). Recently, a gene responsible for *Ty1* resistance was identified as a DFDGD-class RNA-dependent RNA polymerase and was demonstrated to be allelic with *Ty3* resistance (Verlaan *et al.* 2013). *Ty2* resistance originated from *S. habrochaites* “B6013” and was recently mapped to a 300-kb interval on chromosome 11 (Hanson *et al.* 2000; Ji *et al.* 2009a; Yang *et al.* 2014). *Ty4* was identified on chromosome 3 as an additional resistance locus in *Ty3*-carrying *S. chilense* “LA1932” and “LA2779” (Ji *et al.* 2009b). A recessive resistance locus located on chromosome 4, termed *ty5*, was identified in *S. peruvianum* (Friedmann *et al.* 1998; Anbinder *et al.* 2009). Recently, a gene responsible for *ty5* resistance has been identified as a *Pelo* gene, which is the messenger RNA surveillance factor Pelota implicated in the ribosome recycling phase of protein synthesis (Lapidot *et al.* 2015). Furthermore, *Ty6* on chromosome 10 appears to be a recessive resistance gene and has been additionally identified in *Ty3*-carrying *S. chilense* “LA2779” (Scott *et al.* 2015).

DNA markers for these TYLCV resistance genes are listed in Table 1. Since *Ty1* and *Ty3* were independently identified from different tomato accessions, different DNA markers that were closely linked to *Ty1* or *Ty3* were used in tomato breeding programs. However, it was recently confirmed that these two are in allelic relationship at a single locus (Verlaan *et al.* 2013; Caro *et al.* 2015). Resistance spectra and levels conferred by *Ty1* and *Ty3* are currently under investigation. In the case of *Ty2* resistance, a sequence characterized amplified regions (SCAR) marker, T0302, was used reliably for the selection. However, it was recently mapped to a 300-kb interval on chromosome 11, gene identification that would allow development of gene-based marker is in progress (Wolters *et al.* 2015). A gene-based derived-cleaved amplified polymorphic

Table 1. DNA markers for selecting resistant tomatoes against TYLCV.

Resistant locus (chromosome)	Marker information		References
<i>Ty1/3</i> (ch 6)	F: ATGAAGACAAAACTGCTTC R: TCAGGGTTTCACCTTCTATGAAT (<i>Ssp</i> I, <i>Bgl</i> III, or <i>Taq</i> I)	CAPS (gene-based)	Jung <i>et al.</i> 2015
<i>Ty1</i> (ch 6)	TAA TCC GTC GTT ACC TCT CCT CGGATGACTTCAATAGCAATGA3' (<i>Taq</i> I)	CAPS (closely linked)	Hoogstraten <i>et al.</i> 2005
<i>Ty3</i> (ch 6)	P6-25 F: GGTAAGTGGAAATGATGCTGCTC R: GCTCTGCCTATTGTCCCATATATAACC	SCAR (closely linked)	Ji <i>et al.</i> 2007
<i>Ty2</i> (ch 11)	T0302 F: TGG CTC ATC CTG AAG CTG ATA GCG C R: AGT GTA CAT CCT TGC CAT TGA CT	SCAR	Yang <i>et al.</i> 2014
<i>Ty4</i> (ch 3)	C2_At4g17300 (<i>Afl</i> I) F: ATTTAACCGTGTCTGGGCAACTCAATGG R: GCTCACTTTGCAAATCACATCCCCATTTCACC C2_At5g60160 (<i>Nla</i> III) F: TTCTCGCGGCCTTTTCTCCTC R: TCGTGATCGCAAACATATACTCGC	CAPS	Ji <i>et al.</i> 2009
<i>ty5</i> (ch 4)	F: TTCAAGTCCTTCTTCAAC R: ATAGATTTAAACAACAATTATAGAGATAAAAAAGTTACCTGT (<i>Rsa</i> I)	dCAPS (gene-based)	Lapidot <i>et al.</i> 2015; In this study

sequences (dCAPS) marker for *ty5* (Table 1) was developed based on the information given by Lapidot *et al.* (2015).

Tomato spotted wilt virus (TSWV) resistance

TSWV is a negative RNA virus belonging to the genus *Tospovirus* within the family *Bunyaviridae*. TSWV is effectively transmitted by thrips, and disease symptoms include bronzing, curling, necrotic spots and streaks, and stunting of stems and leaves (German *et al.* 1992). The wide host range of TSWV covers several hundred species in both monocotyledons and dicotyledons worldwide (Pappu *et al.* 2009). *Tomato chlorotic spot virus* (TCSV) and *groundnut ringspot virus* (GRSV), which are closely related to TSWV, also cause damage in the tomato production (Brommonschenkel *et al.* 2000).

Sources that are resistant to *Tospoviruses* have been found in diverse cultivars of *S. lycopersicum* (Saidi 2008). Some resistance genes for TSWV have also been identified in *S. habrochaites* (previously *L. hirsutum* “PI127826” and

“LA1353”) and in *S. habrochaites* var. *glabratum* (“PI134417” and “LA1223”). To date, eight TSWV resistance genes (*Sw1a*, *Sw1b*, *sw2*, *sw3*, *sw4*, *Sw-5*, *Sw-6*, and *Sw-7*) have been reported (Finlay 1953; Price *et al.* 2007; Saidi and Warade 2008). Among these TSWV resistance genes, *Sw-5* is the one that has been intensively studied and has been actively utilized in developing TSWV-resistant tomato varieties. *Sw-5* resistance was characterized in *S. peruvianum* on chromosome 9 (Van Zijl *et al.* 1985; Stevens *et al.* 1991) and is known to confer a broad resistance against *Tospoviruses*, including TSWV, TCSV, and GRSV (Boiteux and Giordano 1993). The *Sw-5* protein consists of a coiled-coil (CC) domain, a nucleotide-binding adapter (NB), and a leucine-rich repeat (LRR) domain (Spassova *et al.* 2001). Gene-based markers for *Sw-5* are listed in Table 2. Markers for *Sw-5* can be chosen and applied to the breeding programs, depending on the detection method of the user’s choice.

Table 2. DNA markers for a TSWV resistance gene *Sw5* on chromosome 9.

Resistant locus	Marker information		References
<i>Sw5</i>	Sw5-2 F: AATTAGGTTCTTGAAGCCCATCT R: TTCCGCATCAGCCAATAGTGT	SCAR (gene-based)	Dianese <i>et al.</i> 2010
	Sw5b F: CGGAACCTGTAACCTTGACTG R: GAGCTCTCATCCATTTTCCG	SCAR (gene-based)	Shi <i>et al.</i> 2011
	Sw5b-SNP1 F: GAGAGAGTTATTACAAGAT R: TTTCTCCTCAACATGTCGGC	SNP	Shi <i>et al.</i> 2011
	Sw5b-SNP2 F: GGTATGGGATGACTTAAGGC R: ACCCACTTCTTCAAGTCGAG	SNP	Shi <i>et al.</i> 2011
	Sw5b-SNP F: TTATTGTTTCTCGCTTTGATGTTTCG R: GAACCTGTAACCTGACTGAAAATATC	HRM* (gene-based)	Lee <i>et al.</i> In press

HRM: high-resolution melting analysis used for SNP detection.

Table 3. DNA markers for selecting ToMV resistance genes, *Tm1* and *Tm2*².

Resistant locus	Marker information		References
<i>Tm1</i>	CCACTGTATGATTTCTGCTAGTGAA AGCTTTAACAATATAAGAATAAAGAC GCAAGCTAAGGTTTACATATATGCC	SCAR (gene-based)	Ishibashi <i>et al.</i> 2007
<i>Tm2</i> ²	F: GAGTTCCTCCGTTCAAATCCTAAGCTTGAGAAG R: CTACTACACTCACGTTGCTGTGATGCAC	CAPS (gene-based)	Lanfermeijer <i>et al.</i> 2003 Lanfermeijer <i>et al.</i> 2005
	SCN13 ₁₀₀₀ (<i>AccI</i>) F: AGCGTCACTCCATACTTGAATAA R: AGCGTCACTCAAAATGTACCCAAA	CAPS (linked marker)	Sobir <i>et al.</i> 2000

Tomato mosaic virus (ToMV) resistance

ToMV, which belongs to the genus *Tobamovirus* within the family *Virgaviridae*, has a positive sense RNA genome. Two resistance genes, *Tm-1* and *Tm-2*, that confer resistance against ToMV have been introgressed to cultivated tomatoes. The *Tm-1* gene, which displays semi-dominant inheritance, was originally identified from *S. habrochites* “PI126445” (Pelham 1966; Watanabe *et al.* 1987). *Tm-1* protein does not share any functional domain with previously known resistance (R) proteins but physically binds to and functionally inhibits the replication proteins of ToMV (Ishibashi *et al.* 2007). The *Tm-2* resistance gene was characterized in *S. peruvianum* and found to confer a

higher level of resistance compared to that conferred by *Tm-1*. The *Tm-2* and the *Tm-22* resistance genes are considered to be allelic (Pelham 1966; Young and Tanksley 1989), and the *Tm-22* resistance gene is more durable than the *Tm-2* resistance gene (Fraser 1990). Consequently, *Tm-22* is both practically and economically important and thus is employed as a ToMV resistance source in tomato breeding programs. Both *Tm-2* and *Tm-22* encode a member of the coiled-coil/nucleotide binding-ARC/LRR protein class of plant resistance (R) genes (Lanfermeijer *et al.* 2003). The *Tm-22* and *Tm-2* open reading frames only differ by seven nucleotides, resulting in four amino acid differences at the protein level. Two of these differences are located in the nucleotide-binding site, and two are

located in the LRR domain (Lanfermeijer *et al.* 2005). ToMV allele-specific DNA markers derived from these above mentioned gene sequences are listed in Table 3.

Verticillium wilt resistance

Tomato verticillium wilt, which is also called vascular wilt disease, is a soil-born fungal disease caused by *Verticillium dahliae* and *V. alboatrum*, which are also responsible for the vascular wilt disease in over 200 dicotyledonous species (Fradin and Thomma 2006). A single dominant gene on chromosome 9, *Ve*, was reported to confer effective resistance against *V. alboatrum* race 1 (Schaible *et al.* 1951; Diwan *et al.* 1999). The *Ve* locus contains two closely linked, inversely oriented genes, *Ve1* and *Ve2*, and the resistance spectrums of these resistance genes have been determined (Kawchuk *et al.* 2001; Fradin *et al.* 2009). *Ve1* resistance is conferred by the extracellular LRR receptor-like protein class of disease resistance proteins (Kawchuk *et al.* 2001), which appear critical for

switching on effector-triggered immunity in the host plant. Various allele-specific molecular markers for *Ve1* and *Ve2* have been reported (Table 4; Acciarri *et al.* 2007; Kuklev *et al.* 2009; Jung *et al.* 2015). Among the DNA variations between the *Ve1* resistance allele and the *ve1* susceptibility allele, a single-bp deletion, TCA/T-A at nucleotide position 1,220, results in a premature stop codon in the *ve1* susceptibility allele, which is subsequently linked with loss of function and disease resistance (Kawchuk *et al.* 2001; Jung *et al.* 2015). Therefore, the gene-based CAPS marker derived from the single-bp deletion listed in Table 4 can be considered as a functional marker for the *Ve1* resistance locus.

Fusarium wilt resistance

The fungus *Fusarium oxysporum* causes devastating wilt diseases in many important crops, and specifically, *F. oxysporum* f. sp. *Lycopersici* (*Fol*) causes fusarium wilt of tomato. Three races of *Fol*, race 1, 2, and 3, have been

Table 4. DNA markers for selecting verticillium wilt resistance gene *Ve* on chromosome 9.

Resistant locus	Marker information		References
<i>Ve</i>	F: CCATGAACAGATGTGACTTGTGTG VeR1:AAGTTTCTTATTTTTCCTTCTCC veR2:CTCTTAGGATTTTGTGACGTGATA	SCAR (linked marker, 0.6 cM)	Kawchuk <i>et al.</i> 1998
	F: CGAAGTTGAC TACATTGACC CTG R: CAGTCTTGAAAGGTTGCTCAGCC (<i>Xba</i> I)	CAPS (gene-based)	Jung <i>et al.</i> 2015

Table 5. DNA markers for selecting resistant tomatoes against Fusarium wilt.

Resistant locus (chromosome)	Marker information		References
<i>I1</i> (ch 11)	At2 F: CGAATCTGTATATTACATCCGTCGT R: GGTGAATACCGATCATAGTCGAG	SCAR	Arens <i>et al.</i> 2010
<i>I2</i> (ch 11)	Z1063 F: ATTTGAAAGCGTGGTATTGC R: CTAAACTCACCATTAAATC	SCAR	Arens <i>et al.</i> 2010
<i>I3</i> (ch 7)	P7-43DF1/R1 F: GGTAAGAGATGCGATGATTATGTGGAG R: GTCTTTACCACAGGAACCTTATCACC	SCAR	Barillas <i>et al.</i> 2008
<i>I7</i> (ch 8)	Solyc08g077740 (<i>Age</i> I) F: AAGAAGTTCCCTTCTTCCCTTA R: GGAATAACCAAGGGGGTGT	CAPS (gene-based)	Gonzalez-Cendales <i>et al.</i> 2015

identified (Bohn and Tucker 1939; Grattidge and O'Brien 1982). Resistance against *Fol* has been characterized in multiple wild species of tomato. The *I* gene was identified in the wild tomato *S. pimpinellifolium* accession "PI79532" and confers resistance against *Fol* race 1 (Bohn and Tucker 1939). The *I-2* gene, which confers resistance to *Fol* race 2, was identified in an *S. lycopersicum* × *S. pimpinellifolium* hybrid "PI126915", and this gene encodes a coiled coil, nucleotide-binding (CC-NB)-LRR resistance protein (Stall and Walter 1965; Simons *et al.* 1998). *I-3* resistance to *Fol* race 3 was identified in *S. pennellii* "LA716" (Scott and Jones 1989) and encodes an S-receptor-like kinase (SRLK) protein (Lim *et al.* 2008; Catanzariti *et al.* 2015). Furthermore, the *I-7* resistance gene, which confers resistance to *Fol* race 1, 2, and 3, was identified in *S. pennellii* "PI414773" and encodes typical extracellular LRR receptor-like protein (LRR-RLP) (Lim *et al.* 2006; Gonzalez-Cendales *et al.* 2015). DNA markers for these resistance genes are listed in Table 5, and most of these markers are gene-based markers.

Late blight resistance

Late blight (LB) in tomato is caused by *Phytophthora infestans*, which also causes devastating LB in the potato. Although LB resistance in the potato has been extensively studied and more than 60 resistance genes have been characterized and/or located on the genetic map (Rodewald and Trognitz 2013), a few race-specific LB resistance loci have been characterized in the tomato. Two race-specific resistance genes, *Ph1* and *Ph2*, from *S. pimpinellifolium* were mapped to chromosome 7 and 10, respectively

(Peirce 1971; Moreau *et al.* 1998; Foolad *et al.* 2008). Another resistance gene from *S. pimpinellifolium* "L3708", *Ph3*, which is the most effective LB resistance gene among the known genetic sources, confers incomplete resistance against a wide range of *P. infestans* isolates (Black *et al.* 1996; Kim and Mutschler 2006; Zhang *et al.* 2013). The *Ph3* gene on chromosome 9 encodes a coiled-coil nucleotide-binding (NBS)-LRR (Zhang *et al.* 2014). *Ph4* on chromosome 2 was discovered in *S. habrochaites* LA1033 (Kole *et al.* 2006), and *Ph5-1* and *Ph5-2*, which were discovered from a novel resistance source *S. pimpinellifolium* "PSLP153", are located on chromosome 1 and 10, respectively (Merk *et al.* 2012; Merk and Foolad 2012). DNA markers for the major LB resistance genes, *Ph2* and *Ph3*, are listed in Table 6. In case of *Ph3*, a gene-based SCAR marker was developed based on two 11 bp deletions separated by 56 bp that generate a premature stop codon in the *ph3* susceptible genotype. Therefore, the gene-based SCAR marker can be considered as a functional marker for the *Ph3* resistance locus. In addition to these single dominant resistance genes, quantitative trait loci (QTL) that confer resistance to LB have also been identified in *S. habrochaites* and *S. pennellii* (Brouwer and St Clair 2004; Smart *et al.* 2007; Li *et al.* 2011; Cai *et al.* 2012).

Leaf mold resistance

Leaf mold of tomato, which is caused by the fungus *Cladosporium fulvum*, is a worldwide problem in greenhouse conditions, particularly in areas with high humidity and moderate temperatures (Rivas and Thomas 2005). The

Table 6. DNA markers for selecting late blight resistance genes *Ph2* and *Ph3*.

Resistant locus (chromosome)	Marker information		References
<i>Ph2</i> (ch 10)	dTG63 (<i>Hinf</i> I) F: CTACTCTTTCTATGCAATTTGAATTG R: AATAATTTTCAACCATAGAATGATT	CAPS	Panthee <i>et al.</i> 2012
<i>Ph3</i> (ch 9)	F: TCG ATC GTA TGT AGA CGA TG R: AGG CAA ATC TTG AAG AAG CA (<i>Msp</i> I)	CAPS (gene-based)	Jung <i>et al.</i> 2015
	F: CTACTCGTGCAAGAAGGTAC R: TCCACATCACCTGCCAGTTG	SCAR (gene-based)	Jung <i>et al.</i> 2015

genes conferring resistance against *C. fulvum*, the *Cf* genes, have been introduced into commercially grown tomato cultivars (Rivas and Thomas 2005). Among the multiple *Cf* resistance genes that originate from wild species, *Cf-2*, *Cf-4*, *Cf-4E*, *Cf-5*, and *Cf-9* genes have been most intensively studied (Jones *et al.* 1994; Dixon *et al.* 1996; Thomas *et al.* 1997; Dixon *et al.* 1998; Takken *et al.* 1999). The *Cf* genes encode membrane-anchored proteins that are largely composed of extracellular LRRs (Rivas and Thomas 2005). Although the *Cf* genes share a high degree of homology, each *Cf* gene differs in its specificity for recognizing distinct fungal effectors. The *Cf* genes, *Cf-2*, *Cf-4*, *Cf-4E*, *Cf-5*, and *Cf-9*, trigger a race-specific hypersensitive response (HR) upon plant invasion by *C. fulvum* that secretes the avirulence factors *Avr2*, *Avr4*, *Avr4E*, *Avr5*, and *Avr9*, respectively (Jones *et al.* 1994; Dixon *et al.* 1996; Thomas *et al.* 1997; Dixon *et al.* 1998; Takken *et al.* 1999). Both *Cf-4* from *S. habrochaites* and *Cf-9* from *S. pimpinellifolium* are located at the same locus on chromosome 1 in an array of five paralogs (Parniske *et al.* 1997). *Cf-2* from *S. pimpinellifolium* and *Cf-5* from the landrace of *S. lycopersicum* (formerly *L. esculentum* var. *cerasiforme*) are located in a complex locus on chromosome 6 and consist of seven *Cf-2/Cf-5* gene family homologs, which vary in LRR copy number from 25 to 38 (Dixon *et al.* 1998). A DNA marker for *Cf-9* resistance gene is listed in Table 7. Although the genes that encode *Cf-2*, *Cf-4*, *Cf-4E*,

Cf-5, and *Cf-9* have been cloned and characterized decades ago, precise MAS in differentiating each *Cf* gene has been plagued by technical difficulties, due to the existence of the gene families and complex chimeric sequences.

Root-knot nematode (RKN) resistance

RKNs of the genus *Meloidogyne* cause major economic damage to crops around the world (Williamson and Hussey 1996). These nematodes penetrate the roots and migrate to the vascular cylinder, resulting in the formation of root-knots, which affect nutrient partitioning and water uptake in the plant (Roberts and May 1986). A single, dominant gene, *Mi-1*, which originated in *S. peruvianum* “PI128657”, was introgressed into modern tomato varieties (Castagnone-Sereno *et al.* 1994). *Mi-1* encodes a CC-NBS-LRR with a nucleotide-binding site and a LRR region and confers resistance to three of the most damaging species of RKN: *M. incognita*, *M. arenaria*, and *M. javanica*. Moreover, this gene also confers resistance to potato aphid and whitefly (Milligan *et al.* 1998; Rossi *et al.* 1998; Vos *et al.* 1998). The *Mi-1* locus consists of two clusters with three and four copies of *Mi* gene homologs (Seah *et al.* 2007). *Mi-1.2*, but not the other homologs, has been suggested to be a functional resistance gene (Milligan *et al.* 1998). Other genetic determinants of RKN resistance that have been identified in *S. peruvianum* accessions include major/minor QTLs: *Mi-4* linked with *Mi-1* on

Table 7. DNA markers for selecting leaf mold resistance gene *Cf-9* on chromosome 1.

Resistant locus	Marker information	References
<i>Cf-9</i>	F: TGGGAATTTACCCGAAAGAA R: CCCAATCATTCA GTGCGTTA SCAR (gene-based)	Truong <i>et al.</i> 2011

Table 8. Allele specific markers at the root-knot nematodes resistance locus *Mi-1*.

Resistant alleles	Marker information	References
<i>Mi 1 (Rex)</i>	F: AACCGTGGACTTTGCTTTGACT R: TAAGAACAGGGACTCAGAGGATGA (<i>TaqI</i>) CAPS (closely linked)	Hoogstraten <i>et al.</i> 2005
<i>Mi-J</i>	F: CTACGGAGGATGCAAATAGAA R: AATCATTATTGT CACACTTCCCC (<i>NsiI</i>) CAPS (gene-based)	Hoogstraten <i>et al.</i> 2005
<i>Mi-1.2</i>	F: TGG AAA AAT GTT GAA TTT CTT TTG R: GCA TAC TAT ATG GCT TGT TTA CCC SCAR (gene-based)	Seah <i>et al.</i> 2007

chromosome 6, *Mi-3* and *Mi-5* on chromosome 12, *Mi-9* on chromosome 6, *Mi-2* linked to *Mi-8*, and *Mi-6* linked to *Mi-7* (Veremis *et al.* 2000; Ammiraju *et al.* 2003). The practical use of these resistance loci, however, has not yet been investigated thoroughly. Allele specific markers for *Mi-1* resistance are listed in Table 8.

Bacterial spot resistance

Bacterial spot of tomato, which is caused by a gram-negative bacterium *Xanthomonas campestris* pv. *vesicatoria* (*Xcv*), is one of the most destructive diseases both in the greenhouse and in the field, particularly in warm and humid environments (Jones *et al.* 1998). Recently, *Xcv* has been re-classified and divided into four distinct species (*X. euvesicatoria*, *X. vesicatoria*, *X. gardneri*, and *X. perforans*), which differ in their distribution, metabolic properties, and effector repertoires (Potnis *et al.* 2011).

Five races (T1 to T5) of *Xcv* are recognized by different host genotypes. *Xcv*, which causes bacterial spot disease in both pepper and tomato, has been extensively studied. Effector-triggered immunity conferred by single dominant loci, including *Xv3* and *Xv4* (also known as *RXopJ4*), are mechanisms of HR resistance. *Xv3* found in *S. lycopersicum* “H7981” and *S. pimpinellifolium* (accessions “PI126932” and “PI128216”) triggers HR resistance to T3 strains via recognition of the effector *avrXv3* (Wang *et al.* 2011). A single locus *Rx-4* on chromosome 11 (accession “PI128216”) also confers HR resistance to T3 strains; however, the degree of resistance is significantly affected by the genetic background (Robbins *et al.* 2009). Studies on *Xv3* and *Rx-4* indicated that these two genes are closely linked genes that react to the same bacterial effector or alleles of the same locus (Wang *et al.* 2011). *Xv4* (*RXopJ4*) on chromosome 3 is a dominant resistance locus that

Table 9. DNA markers for selecting bacterial spot disease resistant tomatoes.

Resistant locus (chromosome)	Marker information	References
<i>Rx-3</i> (ch 5)	Rx3-L1 (<i>Bsr</i> BI) F: CTCCGAGCGAAGAGTCTAGAGTC R: GAAGGCAAAAGGAAAAGGAGAAGGATGG CAPS	Yang <i>et al.</i> 2005
<i>Rx-4</i> (ch 11)	pcc12 (6 bp InDel) F: TCCACATCAAATGCGTTTCT R: TTCCAATCCTTTCCATTTCG InDel (0.07 cM)	Pei <i>et al.</i> 2012
<i>Xv3</i> (ch 11)	cLEC-24-C3 (restriction enzyme not indicated) F: CAGACTGGAGAGTCAAAGGT R: CCTTGCTGATAATCTGCAAGTTGTAA CAPS	Wang <i>et al.</i> 2011
	SL10027 F: GATCCAGTTTCCCTCTTACCG R: CCATTAGAGCCAAGACGCTC ASPE*	Wang <i>et al.</i> 2011
<i>Bs4</i> (ch 5)	Bs4-A02/B02 (<i>Msp</i> I) F: CTACCATCATCTCTTCAGTACCAACTC R: GAAATTGGAGGAACCGAGCTCCAG CAPS (gene-based)	Schornack <i>et al.</i> 2004
	Bs4-A03/B03 (<i>Rsa</i> I) F: GGGTTGGAGTCCGAAGAGCAGG R: GACTAACCAACGCAAGTTATTGGACAGG CAPS (gene-based)	Schornack <i>et al.</i> 2004
<i>Xv4=RXopJ4</i> (ch 3)	J350 (<i>Hinf</i> I) F: CTGCTGGAATTGTAATTATTCACG R: TTGAGCATAAACAGTCCAAAACAT CAPS	Sharlach <i>et al.</i> 2013
QTL (ch 11)	F: CCTCCAAATCCCAAACTCT R: TGTTTCATCCACTATCACGA SSR	Hutton <i>et al.</i> 2010

*ASPE: allele specific primer extension.

Table 10. DNA markers for selecting resistant tomatoes against bacterial speck disease.

Resistant locus	Marker information		References
<i>Pto</i>	F: ATCTACCCACAATGAGCATGAGCTC R: GTGCATACTCCAGTTTCCAC (<i>RsaI</i>)	CAPS (gene-based)	Yang and Francis 2005; Martin <i>et al.</i> 1993

originated from *S. pennellii* “LA716”, and *Xv4* recognizes the *Xcv* effector XopJ4 of T4 strains (Astua-Monge *et al.* 2000). *Rx-1* (chromosome 1), *Rx-2* (chromosome 1), and *Rx-3* (chromosome 5) that are responsible for HR-inducing resistance against *Xcv* T1 strains were identified in *S. lycopersicum* (accession “H7998”; Scott and Jones 1989); however, only *Rx-3* appears to be effective in conferring field resistance. *Bs4* on chromosome 5, which encodes a NB-LRR protein, recognizes the *Xcv* effector AvrBs4 (Schornack *et al.* 2004). A number of DNA markers for each *Xcv* resistance gene are summarized in Table 9. QTL that contribute *Xcv* resistance have been identified in *S. lycopersicum* “PI114490” (Hutton *et al.* 2010). In addition, the *Bs2* resistance gene identified in a pepper species is very effective against bacterial spot in transgenic tomato plants (Tai *et al.* 1999).

Bacterial speck resistance

Bacterial speck disease in tomato is caused by *Pseudomonas syringae* pv. *tomato*. The resistance gene, *Pto*, which is a member of a small gene family encoding cytoplasmic serine/threonine protein kinases, is the first disease resistance gene characterized in plants (Martin *et al.* 1993). The molecular mechanisms of *Pto* resistance have been intensively studied. Indeed, the *Pto* kinase recognizes and physically interacts with the bacterial effectors AvrPto and AvrPtoB (Tang *et al.* 1996; Shan *et al.* 2000; Kim *et al.* 2002). *Prf*, an NBS-LRR gene located within a cluster of five *Pto* homologs, is also required for resistance to *P. syringae* pv. *tomato* (Salmeron *et al.* 1996). Among the five *Pto* homologs that are tightly clustered and exhibit different functions, *PtoE* is the gene responsible for conferring resistance to bacterial speck in tomato (Kim *et al.* 2002; Abramovitch *et al.* 2006). A gene-based CAPS marker for *Pto* resistance is summarized in Table 10. A

recent study revealed that several QTLs in *S. habrochites* “LA1777” are involved in bacterial speck resistance; *bsRr1-1* on chromosome 1, *bsRr1-2* on chromosome 2, *bsRr1-12a* and *bsRr1-12b* on chromosome 12 (Thapa *et al.* 2015).

CONCLUSIONS

Due to the economic and academic importance of tomato, the genetics and molecular mechanisms of disease resistance to a variety of diseases have been intensively investigated, and the results have contributed to MAS in tomato breeding programs. In addition, extensive use of wild relatives of tomato rather than cultivated tomatoes as resistance sources required the use of molecular markers in order to track the resistance provided by these wild relatives and transfer such resistance to developing new tomato varieties. In this review, we summarized the currently available molecular markers that confer resistance to the major tomato diseases, including TYLCV, TSWV, ToMV, verticillium wilt, fusarium wilt, late blight, leaf mold, root-knot disease, bacterial spot, and bacterial speck. The provided marker information is expected to contribute to advancing MAS for disease resistance and to exploration of novel genetic sources for tomato breeding programs.

ACKNOWLEDGEMENTS

This work was supported by the Golden Seed Project (Center for Horticultural Seed Development, 213003-04-3-SBG10) funded by the Ministry of Agriculture, Food and Rural Affairs.

REFERENCES

- Abramovitch RB, Anderson JC, Martin GB. 2006. Bacterial elicitation and evasion of plant innate immunity. *Nat. Rev. Mol. Cell Biol.* 7: 601-611.
- Agrama HA, Scott JW. 2006. Quantitative trait loci for *Tomato yellow leaf curl virus* and *Tomato mottle virus* resistance in tomato. *J. Am. Hortic. Sci.* 131: 267-272.
- Ammiraju JS, Veremis JC, Huang X, Roberts PA, Kaloshian I. 2003. The heat-stable root-knot nematode resistance gene *Mi-9* from *Lycopersicon peruvianum* is localized on the short arm of chromosome 6. *Theor. Appl. Genet.* 106: 478-84.
- Anbinder I, Reuveni M, Azari R, Paran I, Nahon S, Shlomo H, Chen L, Lapidot M, Levin I. 2009. Molecular dissection of *Tomato leaf curl virus* resistance in tomato line TY172 derived from *Solanum peruvianum*. *Theor. Appl. Genet.* 119: 519-530.
- Arens P, Mansilla C, Deinum D, Cavellini L, Moretti A, Rolland S, van der Schoot H, Calvache D, Ponz F, Collonnier C, Mathis R, Smilde D, Caranta C, Vosman B. 2010. Development and evaluation of robust molecular markers linked to disease resistance in tomato for distinctness, uniformity and stability testing. *Theor. Appl. Genet.* 120: 655-664.
- Astua-Monge G, Minsavage GV, Stall RE, Vallejos CE, Davis MJ, Jones JB. 2000. Xv4-vrxv4: a new gene-for-gene interaction identified between *Xanthomonas campestris* pv. *vesicatoria* race T3 and wild tomato relative *Lycopersicon pennellii*. *Mol. Plant. Microbe Interact.* 13: 1346-1355.
- Barbary A, Djian-Caporalino C, Palloix A, Castagnone-Sereno P. 2015. Host genetic resistance to root-knot nematodes, *Meloidogyne* spp., in Solanaceae: from genes to the field. *Pest Manag. Sci.* doi: 10.1002/ps.4091.
- Barillas AC, L Mejia, A Sanchez-Perez, DP Maxwell. 2008. CAPS and SCAR markers for detection of I-3 gene introgression for resistance to *Fusarium oxysporum* f. sp. *lycopersici* race 3. *Rep. Tomato Genet. Coop.* 11-17.
- Black LL, Wang TC, Hanson PM, Chen JT. 1996. Late blight resistance in four wild tomato accessions: effectiveness in diverse locations and inheritance of resistance. *Phytopathology* 86: S24.
- Bohn G, Tucker C. 1939. Immunity to Fusarium wilt in the tomato. *Science* 89: 603-604.
- Boiteux L, Giordano LdB. 1993. Genetic basis of resistance against two Tospovirus species in tomato (*Lycopersicon esculentum*). *Euphytica* 71: 151-154.
- 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.
- Brouwer DJ, St Clair DA. 2004. Fine mapping of three quantitative trait loci for late blight resistance in tomato using near isogenic lines (NILs) and sub NILs. *Theor. Appl. Genet.* 108: 628-638.
- Cai G, Restrepo S, Myers K, Zuluaga P, Danies G, Smart C, Fry W. 2013. Gene profiling in partially resistant and susceptible near-isogenic tomatoes in response to late blight in the field. *Mol. Plant Pathol.* 14: 171-184.
- Caicedo AL, Williamson SH, Hernandez RD. 2007. Genome-wide patterns of nucleotide polymorphism in domesticated rice. *Plos Genet.* 3: 1745-1756.
- Caro M, Verlaan MG, Julián O, Finkers R, Wolters AM, Hutton SF, Scott JW, Kormelink R, Visser RG, Díez MJ, Pérez-de-Castro A, Bai Y. 2015. Assessing the genetic variation of *Ty-1* and *Ty-3* alleles conferring resistance to tomato yellow leaf curl virus in a broad tomato germplasm. *Mol. Breed.* 35: 132.
- Castagnone-Sereno P, Wajnberg E, Bongiovanni M, Leroy F, Dalmasso A. 1994. Genetic variation in *Meloidogyne incognita* virulence against the tomato *Mi* resistance gene: evidence from isofemale line selection studies. *Theor. Appl. Genet.* 88: 749-753.
- Catanzariti AM, Lim GT, Jones DA. 2015. The tomato *I-3* gene: a novel gene for resistance to Fusarium wilt disease. *New Phytol.* 207: 106-118.
- Cohen S and Harpaz I. 1964. Periodic, rather than continual acquisition of a new tomato virus by its vector, the tobacco whitefly (*Bemisia tabaci* Gennadius). *Entomol. Exp. Appl.* 7: 155-166.
- Delatte H, Martin DP, Naze F, Golbach RW, Reynaud B, eterschmitt M, Lett JM. 2005. South West Indian Ocean islands tomato begomovirus populations represent a new major monopartite begomovirus group. *J. Gen. Virol.* 86: 1533-1542.
- Diwan N, Fluhr R, Eshed Y, Zamir D, Tanksley SD. 1999. Mapping of *Ve* in tomato: a gene conferring resistance to the broadspectrum pathogen, *Verticillium dahliae* race 1. *Theor. Appl. Genet.* 98: 315-319.

- Dixon MS, Jones DA, Keddie JS, Thomas CM, Harrison K, Jones JDG. 1996. The tomato *Cf-2* disease resistance locus comprises two functional genes encoding leucine-rich repeat proteins. *Cell* 84: 451-459.
- Dixon MS, Hatzixanthis K, Jones DA, Harrison K, Jones JDG. 1998. The tomato *Cf-5* disease resistance gene and six homologs show pronounced allelic variation in leucine-rich repeat copy number. *Plant Cell* 10: 1915-1925.
- Finlay, K. 1953. Inheritance of spotted wilt resistance in the tomato II. Five genes controlling spotted wilt resistance in four tomato types. *Aust. J. Biol. Sci.* 6: 153-163.
- Foolad MR, Merk HL, Ashrafi H. 2008. Genetics, genomics and breeding of late blight and early blight resistance in tomato. *Crit. Rev. Plant. Sci.* 27: 75-107.
- Foolad MR, Panthee DR. 2012. Marker-assisted selection in tomato breeding. *Crit. Rev. Plant Sci.* 31: 93-123.
- Foolad MR, Sharma A. 2005. Molecular markers as selection tools in tomato breeding. *Acta Hort.* 695: 225-240.
- Fradin EF and Thomma BPHJ. 2006. Physiology and molecular aspects of Verticillium wilt diseases caused by *V. dahliae* and *V. albo-atrum*. *Mol. Plant Pathol.* 7: 71-86.
- Fradin EF, Zhang Z, Juarez Ayala JC, Castroverde CD, Nazar RN, Robb J, Liu CM and Thomma BP. 2009. Genetic dissection of Verticillium wilt resistance mediated by tomato *Ve1*. *Plant Physiol.* 150: 320-332.
- Fraser RSS. 1990. The genetics of resistance to plant viruses. *Annu. Rev. Phytopathol.* 28: 179-200.
- Friedmann M, Lapidot M, Cohen S, Pilowsky M 1998. A novel source of resistance to *Tomato yellow leaf curl virus* exhibiting a symptomless reaction to viral infection. *J. Am. Soc. Hortic. Sci.* 123: 1004-1007.
- Gonzalez-Cendales Y, Catanzariti AM, Baker B, Mcgrath DJ, Jones DA. 2015. Identification of *I-7* expands the repertoire of genes for resistance to Fusarium wilt in tomato to three resistance gene classes. *Mol. Plant Pathol.* doi: 10.1111/mpp.12294.
- German TL, Ullman DE, Moyer JW. 1992. *Tospoviruses*: diagnosis, molecular biology, phylogeny, and vector relationships. *Annu. Rev. Phytopathol.* 30: 315-348.
- Grattidge R, O'Brien RG. 1982. Occurrence of a third race of Fusarium wilt of tomatoes in Queensland. *Plant Dis.* 66: 165-166.
- Hanson PM, Bernacchi D, Green S, Tanksley SD, Muniyappa V, Padmaja VM, Padmaja AS, Chen H, Kuo G, Fang D, Chen J. 2000. Mapping a Wild Tomato Introgression Associated with Tomato Yellow Leaf Curl Virus Resistance in a Cultivated Tomato Line. *J. Amer. Soc. Hort. Sci.* 125: 15-20.
- Hoogstraten Jacobus Gerardus Joannes Braun, III Carl J. (2005) Methods for coupling resistance alleles in tomato. US patent 20050278804.
- Hutton SF, Scott JW, Yang W, Sim SC, Francis DM, Jones JB. 2010. Identification of QTL associated with resistance to bacterial spot race T4 in tomato. *Theor. Appl. Genet.* 121: 1275-1287.
- 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.
- Jehan T, Lakhanpaul S. 2006. Single nucleotide polymorphism (SNP)-Methods and applications in plant genetics: A review. *Indian J. Biotech.* 5: 435-459.
- Ji Y, Schuster DJ, Scott JW. 2007. Ty-3, a begomovirus resistance locus near the *Tomato yellow leaf curl virus* resistance locus Ty-1 on chromosome 6 of tomato. *Mol. Breed.* 20: 271-284.
- Ji Y, Scott JW, Schuster DJ. 2009a. Toward fine mapping of the *Tomato yellow leaf curl virus* resistance gene Ty-2 on chromosome 11 of tomato. *HortScience* 44: 614-618.
- Ji Y, Scott JW, Schuster DJ, Maxwell DP. 2009b. Molecular mapping of Ty-4, a new *Tomato yellow leaf curl virus* resistance locus on chromosome 3 of tomato. *J. Amer. Soc. Hort. Sci.* 134: 281-288.
- Jones JB, Stall RE, Bouzar H. 1998. Diversity among xanthomonads pathogenic on pepper and tomato. *Annu Rev Phytopathol.* 36: 41-58.
- Jones DA, Thomas CM, Hammond-Kosack KE, Balint-Kurti PJ, Jones JDG. 1994. Isolation of the tomato *Cf-9* gene for resistance to *Cladosporium fulvum* by transposon tagging. *Science* 266: 789-793.
- 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.
- Kawchuk LM, Hachey J, Lynch DR, Kulcsar F, van Rooijen G, Waterer DR, Robertson A, Kokko E, Byers R, Howard RJ, Fischer R, Prufer D 2001. Tomato *Ve* disease resistance genes encode cell surface-like receptors. *Proc.*

- Natl. Acad. Sci. USA 98: 6511-6515.
- Kim MJ, Mutschler MA 2006. Characterization of late blight resistance derived from *Solanum pimpinellifolium* L3708 against multiple isolates of the pathogen *Phytophthora infestans*. J. Amer. Soc. Hort. Sci. 131: 637-645.
- Kim YJ, Lin NC, Martin GB. 2002. Two distinct *Pseudomonas* effector proteins interact with the Pto kinase and activate plant immunity. Cell 109: 589-598.
- Kole C, Ashrafi H, Lin G, Foolad M. 2006. Identification and molecular mapping of a new R gene, Ph-4, conferring resistance to late blight in tomato. Solanaceae Conference, University of Wisconsin, Madison, Abstract 449
- Labate JA, Baldo AM. 2005. Tomato SNP discovery by EST mining and resequencing. Mol. Breed. 16: 343-349.
- Lagudah ES, Krattinger SG, Herrera-Foessle S, Singh RP, Huerta-Espino J, Spielmeier W, Brown-Guedira G, Selter LL, Keller B. 2009. Gene-specific markers for the wheat gene Lr34/Yr18/Pm38 which confers resistance to multiple fungal pathogens. Theor. Appl. Genet. 119: 889-898.
- 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.
- Lanfermeijer FC, Warmink J, Hille J. 2005. The products of the broken *Tm-2* and the durable *Tm-2(2)* resistance genes from tomato differ in four amino acids. J. Exp. Bot. 56: 2925-2933.
- Lapidot M, Karniel U, Gelbart D, Fogel D, Evenor D, Kutsher Y, Makhbash Z, Nahon S, Shlomo H, Chen L, Reuveni M, Levin I. 2015. A novel route controlling Begomovirus resistance by the messenger RNA surveillance factor Pelota. PLoS Genet. 11: e1005538.
- Lee H, Song W, Kwak HR, Kim J, Park J, Auh CK, Kim DH, Lee K, Lee S, Choi HS. 2010. Phylogenetic analysis and inflow route of *Tomato yellow leaf curl virus* (TYLCV) and Bemisia tabaci in Korea. Mol. Cells 30: 467-476.
- Lee HJ, Kim BY, Bae C, Kang WH, Kang BC, Yeam I, Oh CS. Development of a single-nucleotide polymorphism marker in the *Sw-5b* gene conferring disease resistance to *Tomato spotted wilt virus* in tomato. Kor. J. Hort. Sci. Technol. In press.
- Li J, Liu L, Bai Y, Finkers R, Wang F, Du Y, Yang Y, Xie B, Visser RGF, van Heusden AW. 2011. Identification and mapping of quantitative resistance to late blight (*Phytophthora infestans*) in *Solanum habrochaites* LA1777. Euphytica 179: 427-437.
- Lim GTT, Wang GP, Hemming MN, Basuki S, McGrath DJ, Carroll BJ, Jones DA. 2006. Mapping the *I-3* gene for resistance to Fusarium wilt in tomato: application of an *I-3* marker in tomato improvement and progress towards the cloning of *I-3*. Australas. Plant Pathol. 35: 671-680.
- Lim GTT, Wang GP, Hemming MN, McGrath DJ, Jones DA. 2008. High resolution genetic and physical mapping of the *I-3* region of tomato chromosome 7 reveals almost continuous microsynteny with grape chromosome 12 but interspersed microsynteny with duplications on *Arabidopsis* chromosomes 1, 2 and 3. Theor. Appl. Genet. 118: 57-75.
- Martin GB, Brommonschenkel SH, Chunwongse J, Frary A, Ganai 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.
- Merk HL, Ashrafi H, Foolad MR. 2012. Selective genotyping to identify late blight resistance genes in an accession of the tomato wild species *Solanum pimpinellifolium*. Euphytica 187: 63-75.
- Merk HL, Foolad MR. 2012. Parent-offspring correlation estimate of heritability for late blight resistance conferred by an accession of the tomato wild species *Solanum pimpinellifolium*. Plant Breeding 131: 203-210.
- Milligan SB, Bodeau J, Yaghoobi J, Kaloshian I, Zabel P, Williamson VM. 1998. The root knot nematode resistance gene *Mi* from tomato is a member of the leucine zipper, nucleotide binding, leucine-rich repeat family of plant genes. Plant Cell. 10: 1307-1319.
- Minsavage GV, Dahlbeck D, Whalen MC, Kearney B, Bonas U, Staskawicz BJ, Stall RE. 1990. Gene-for-gene relationships specifying disease resistance in *Xanthomonas campestris* pv. *vesicatoria*-pepper interactions. Mol. Plant-Microbe Interact. 3: 41-47.
- Minsavage GV, Jones JB, Stall RE. 1996. Cloning and sequencing of an avirulence gene (*avrXv3*) isolated from *Xanthomonas campestris* pv. *vesicatoria* tomato race 3. (Abstr.) Phytopathology 86: S15.
- Moreau P, Thoquet P, Olivier J, Laterrot H, Grimsley N. 1998. Genetic mapping of Ph-2, a single locus controlling partial resistance to *Phytophthora infestans* in tomato. Mol. Plant-Microbe Interact. 11: 259-269.
- Panthee DR, Foolad MR. 2012. A reexamination of molecular markers for use in marker-assisted breeding in tomato.

- Euphytica 184: 165-179.
- Pappu HR, Jones RAC, Jain RK. 2009. Global status of tospovirus epidemics in diverse cropping systems: successes achieved and challenges ahead. *Virus Res.* 141: 219-236.
- Parniske M, Hammond-Kosack KE, Golstein C, Thomas CM, Jones DA, Harrison K, Wulff BB, Jones JD. 1997. Novel disease resistance specificities result from sequence exchange between tandemly repeated genes at the Cf-4/9 locus of tomato. *Cell* 91: 821-832.
- Pei C, Wang H, Zhang J, Wang Y, Francis DM, Yang W. 2012. Fine mapping and analysis of a candidate gene in tomato accession PI128216 conferring hypersensitive resistance to bacterial spot race T3. *Theor. Appl. Genet.* 124: 533-542.
- Peirce LC. 1971. Linkage tests with *Ph* conditioning resistance to race 0, *Phytophthora infestans*. *Tomato Genet. Coop. Rep.* 21: 30.
- Pelham J. 1966. Resistance in tomato to *Tobacco mosaic virus*. *Euphytica* 15: 258-267.
- Potnis N, Krasileva K, Chow V, Almeida NF, Patil PB, Ryan RP, Sharlach M, Behlau F, Dow JM, Momol M, White FF, Preston JF, Vinatzer BA, Koebnik R, Setubal JC, Norman DJ, Staskawicz BJ, Jones JB. 2011. Comparative genomics reveals diversity among xanthomonads infecting tomato and pepper. *BMC Genomics* 12: 146.
- Price DL, Memmott FD, Scott JW, Olson SM, Stevens MR. 2007. Identification of molecular markers linked to a new Tomato spotted wilt virus resistance source in tomato. *Tomato Genet. Coop.* 57: 35-36.
- Rivas S, Thomas CM. 2005. Molecular interactions between tomato and the leaf mold pathogen *Cladosporium fulvum*. *Ann Rev Phytopathol.* 43: 395-436.
- Robbins MD, Darrigues A, Sim SC, Masud MA, Francis D M. 2009. Characterization of hypersensitive resistance to bacterial spot race T3 (*Xanthomonas perforans*) from tomato accession PI 128216. *Phytopathology* 99: 1037-1044.
- Roberts PA, May D. 1986. *Meloidogyne incognita* resistance characteristics in tomato genotypes developed for processing. *J. Nematol.* 18: 353-358.
- Rossi M, Goggin FL, Milligan SB, Kaloshian I, Ullman DE, Williamson VM. 1998. The nematode resistance gene *Mi* of tomato confers resistance against the potato aphid. *Proc. Natl. Acad. Sci. USA.* 95: 9750-9754.
- Saidi M, Warade SD. 2008. Tomato breeding for resistance to *Tomato spotted wilt virus* (TSWV): an overview of conventional and molecular approaches. *Czech J. Genet. Plant Breed.* 44: 83-92.
- 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.
- Salmeron JM, Oldroyd JED, Rommens CMT, Scofield SR, Kim HS, Lavelle DT, Dahlbeck D, Staskawicz BJ. 1996. Tomato *Prf* is a member of the leucine-rich repeat class of plant disease resistance genes and lies embedded within the *Pto* kinase gene cluster. *Cell* 86: 123-133.
- Schaible L, Cannon OS, Waddoups B. 1951. Inheritance of resistance to *Verticillium* wilt in a tomato cross. *Phytopathol.* 41: 986-990.
- Schornack S, Ballvora A, Grlebeck D, Peart J, Baulcombe D, Ganai M, Baker B, Bonas U, Lahaye T. 2004. The tomato resistance protein Bs4 is a predicted non-nuclear TIR-NB-LRR protein that mediates defense responses to severely truncated derivatives of AvrBs4 and overexpressed AvrBs3. *Plant J.* 37: 46-60.
- Scott JW, Jones J B. 1989. Inheritance of resistance to foliar bacterial spot of tomato incited by *Xanthomonas campestris* pv. *vesicatoria*. *J. Am. Soc. Hortic. Sci.* 114: 111-114.
- Scott JW, Jones JB, Somodi GC. 1995. Screening tomato accessions for resistance to *Xanthomonas campestris* pv. *vesicatoria*, race T3. *HortScience* 30: 579-581.
- Scott JW, Jones JP. 1989. Monogenic resistance in tomato to *Fusarium oxysporum* f. sp. *lycopersici* race 3. *Euphytica* 40: 49-53.
- Scott JW, Hutton SF, Freeman JH. 2015. Fla. 8638B and Fla. 8624 Tomato Breeding Lines with *Begomovirus* Resistance Genes *ty-5* Plus *Ty-6* and *Ty-6*, respectively. *HortScience* 50: 1405-1407
- Seah S, Williamson VM, Garcia BE, Meja L, Salus MS, Martin CT, Maxwell DP. 2007. Evaluation of a co-dominant SCAR marker for detection of the Mi-1 locus for resistance to root-knot nematode in tomato germplasm. *Tomato Genet. Coop.* 57: 37-40.
- Shan L, Thara VK, Martin GB, Zhou JM and Tang X. 2000. The *Pseudomonas* AvrPto protein is differentially recognized by tomato and tobacco and is localized to the plant plasma membrane. *Plant Cell* 12: 2323-2338.
- Shi A, Vierling R, Grazzini R, Chen P, Caton H, Panthee D. 2011. Identification of molecular markers for *Sw-5* gene of

- Tomato spotted wilt virus* resistance. *Amer. J. Biotechnol. Mol. Sci.* 1: 8-16.
- Simons G, Groenendijk J, Wijbrandi J, Reijans M, Groenen J, Diergaarde P, Van der Lee T, Bleeker M, Onstenk J, de Both M, Haring M, Mes J, Cornelissen B, Zabeau M, Vos P. 1998. Dissection of the *Fusarium* I2 gene cluster in tomato reveals six homologs and one active gene copy. *Plant Cell*. 10: 1055-1068.
- Smart CD, Tanksley SD, Mayton H, Fry WE. 2007. Resistance to *Phytophthora infestans* in *Lycopersicon pennellii*. *Plant Dis.* 91: 1045-1049.
- Sobir, Ohmori T, Murata M, Motoyoshi F. 2000. Molecular characterization of the SCAR markers tightly linked to the Tm-2 locus of the genus *Lycopersicon*. *Theor. Appl. Genetics* 101: 64-69.
- Spassova MI, Prins TW, Folkertsma RT, Klein-Lankhorst RM, Hille J, Goldbach RW, Prins M. 2001. The tomato gene *Sw5* is a member of the coiled coil, nucleotide binding, leucine-rich repeat class of plant resistance genes and confers resistance to TSWV in tobacco. *Mol. Breeding* 7: 151-161.
- Stall R, Walter J. 1965. Selection and inheritance of resistance in tomato to isolates of races 1 and 2 of the *Fusarium* wilt organism. *Phytopathology* 55: 1213-1215.
- Stevens M, Scott S, Gergerich R. 1991. Inheritance of a gene for resistance to Tomato spotted wilt virus (TSWV) from *Lycopersicon peruvianum* Mill. *Euphytica* 59: 9-17.
- Tai TH, Dahlbeck D, Clark ET, Gajiwala P, Pasion R, Whalen MC, Stall RE, Staskawicz BJ. 1999. Expression of the *Bs2* pepper gene confers resistance to bacterial spot disease in tomato. *Proc. Natl. Acad. Sci. USA.* 96: 14153-14158.
- Takken FLW, Thomas CM, Joosten MHAI, Golstein C, Westerink N, Hille J, et al. 1999. A second gene at the tomato *Cf-4* locus confers resistance to *Cladosporium fulvum* through recognition of a novel avirulence determinant. *Plant J.* 20: 279-288.
- Tang X, Frederick RD, Zhou J, Halterman DA, Jia Y, Martin, G.B. 1996. Initiation of plant disease resistance by physical interaction of AvrPto and Pto kinase. *Science* 274: 2060-2063.
- Tanksley SD, Ganai MW, Martin GB. 1995. Chromosome landing: a paradigm for map-based gene cloning in plants with large genomes. *Trends Genet.* 11: 63-68.
- Thapa SP, Miyao EM, Michael Davis R, Coaker G. 2015. Identification of QTLs controlling resistance to *Pseudomonas syringae* pv. *tomato* race 1 strains from the wild tomato, *Solanum habrochaites* LA1777. *Theor. Appl. Genet.* 128: 681-692.
- Thomas CM, Jones DA, Parniske M, Harrison K, Balint-Kurti PJ, Hatzixanthis K, et al. 1997. Characterization of the tomato *Cf-4* gene for resistance to *Cladosporium fulvum* identifies sequences that determine recognition specificity in *Cf-4* and *Cf-9*. *Plant Cell* 9: 2209-2224.
- Tomato Genome Consortium. 2012. The tomato genome sequence provides insights into fleshy fruit evolution. *Nature* 485: 635-641.
- Van Zijl J, Bosch S, Coetzee C. 1985. Breeding tomatoes for processing in South Africa. *International Symposium on Fruit & Vegetables for Processing* 194 (Strydom, D.K., ed). pp. 69-76. Cape Town: Acta Horticulturae.
- Veremis JC, Roberts PA. 2000. Diversity of heat-stable genotype specific resistance to *Meloidogyne* in Maranon races of *Lycopersicon peruvianum* complex. *Euphytica* 111: 9-16.
- Verlaan MG, Hutton SF, Ibrahim RM, Kormelink R, Visser RGF, Scott JW, Edwards JD, Bai Y 2013. The *Tomato yellow leaf curl virus* resistance genes *Ty-1* and *Ty-3* are allelic and code for DFDGD-class RNA-dependent RNA polymerases. *PLoS Genet* 9: e1003399.
- Vos P, Simons G, Jesse T, Wijbrandi J, Heinen L, Hogers R, Frijters A, Groenendijk J, Diergaarde P, Reijans M, Fierens-Onstenk J, de Both M, Peleman J, Liharska T, Hontelez J, Zabeau M. 1998. The tomato *Mi-1* gene confers resistance to both root-knot nematodes and potato aphids. *Nat. Biotechnol.* 16: 1365-1369.
- Wang JF, Stall RE, Vallejos CE. 1994. Genetic analysis of a complex hypersensitive reaction to bacterial spot in tomato. *Phytopathology* 84: 126-132.
- Wang H, Hutton SF, Robbins MD, Sim SC, Scott JW, Yang W, Jones JB, Francis DM. 2011. Molecular mapping of hypersensitive resistance from tomato 'Hawaii 7981' to *Xanthomonas perforans* race T3. *Phytopathology* 101: 1217-1223.
- Watanabe Y, Kishibayashi N, Motoyoshi F, Okada Y. 1987. Characterization of *Tm-1* gene action on replication of common isolates and a resistance-breaking isolate of TMV. *Virology* 161: 527-532.
- Wijkamp I, Almaraz N, Goldbach R, Peters D. 1995. Distinct levels of specificity in thrips transmission of tospoviruses.

- Phytopathology 85: 1069-1074.
- Wolters AM, Caro M, Dong S, Finkers R, Gao J, Visser RG, Wang X, Du Y, Bai Y. 2015. Detection of an inversion in the Ty-2 region between *S. lycopersicum* and *S. habrochaites* by a combination of de novo genome assembly and BAC cloning. Theor Appl Genet. 128: 1987-1997.
- Yang X, Caro M, Hutton SF, Scott JW, Guo Y, Wang X, Rashid MH, Szinay D, de Jong H, Visser RG, Bai Y, Du Y. 2014. Fine mapping of the *Tomato yellow leaf curl virus* resistance gene *Ty-2* on chromosome 11 of tomato. Mol. Breed. 34: 749-760.
- Yang W, Francis DM. 2005. Marker-assisted selection for combining resistance to bacterial spot and bacterial speck in tomato. J. Amer. Soc. Hort. Sci. 130: 716-721.
- Yang W, Sacks EJ, Lewis Ivey ML, Miller SA, Francis DM. 2005. Resistance in *Lycopersicon esculentum* intraspecific crosses to race T1 strains of *Xanthomonas campestris* pv. *vesicatoria* causing bacterial spot of tomato. Phytopathology 95: 519-527.
- Yeam I, Kang BC, Lindeman W, Frantz JD, Faber N, Jahn MM. 2005. Allele-specific CAPS markers based on point mutations in resistance alleles at the *pvr1* locus encoding eIF4E in Capsicum. Theor. Appl. Genet. 112: 178-186.
- Young ND, Tanksley SD. 1989. RFLP analysis of the size of chromosomal segments retained around the Tm-2 locus of tomato during backcross breeding. Theor. Appl. Genet. 77: 353-359.
- Zamir DI, Ekstein-Michelson I, Zakay Y, Navot N, Zeidan M, Sarfatti M, Eshed Y, Harel E, Pleban T, van-Oss H, Kedar N, Rabinowitch HD, Czosnek H 1994. Mapping and introgression of a *Tomato yellow leaf curl virus* tolerance gene, *Ty-1*. Theor. Appl. Genet. 88: 141-146.
- Zhang C, Liu L, Wang X, Vossen J, Li G, Li T, Zheng Z, Gao J, Guo Y, Visser RG, Li J, Bai Y, Du Y. 2014. The *Ph-3* gene from *Solanum pimpinellifolium* encodes CC-NBS-LRR protein conferring resistance to *Phytophthora infestans*. Theor. Appl. Genet. 127: 1353-1364.
- Zhang C, Liu L, Zheng Z, Sun Y, Zhou L, Yang Y, Cheng F, Zhang Z, Wang X, Huang S, Xie B, Du Y, Bai Y, Li J. 2013. Fine mapping of the *Ph-3* gene conferring resistance to late blight (*Phytophthora infestans*) in tomato. Theor. Appl. Genet. 126: 2643-2653.