

Received 1 July 2004  
Accepted 17 September 2004

**GENETIC FACTORS ENCODING RESISTANCE TO LATE BLIGHT  
CAUSED BY *Phytophthora infestans* (MONT.) DE BARY ON THE  
POTATO GENETIC MAP**

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**Abstract:** Late blight, a potato disease caused by *Phytophthora infestans* (Mont.) de Bary, is of great economic significance, and has been the subject of numerous research projects aimed at both introducing resistance to the disease into potato cultivars, and at unravelling the mechanisms and genes underlying this resistance. This report is on publications about mapping the resistance to *P. infestans* encoded by major resistance genes or polygenes, introduced into the potato from different sources. Applied methods for resistance evaluation, methods for revealing DNA polymorphisms and for the construction of genetic maps are described and compared, as are results obtained by independent authors working in this field.

**Key Words:** Mapping, *Phytophthora infestans*, Potato, Resistance, R-genes, QTL

**INTRODUCTION**

*Phytophthora infestans* (Mont.) de Bary threatens the cultivation of the potato plant all over the world. In the right environmental conditions, this organism can cause greater losses in potato production than any other potato disease [1]. Alternatively, it can result in high input increase due to the costs of intensive

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Abbreviations used: AFLP - Amplified Fragment Length Polymorphism; AUDPC - Area Under Disease Progress Curve; CAPS - Cleaved Amplified Polymorphic Sequences; CC - Coiled Coil; CP - cDNA Potato; EBN - Endosperm Balance Number; GP - Genomic Potato; HR - Hypersensitive Reaction; InDel - Insertion/Deletion; LRR - Leucine Rich Repeat; NBS - Nucleotide Binding Site; PCR - Polymerase Chain Reaction; PR - Pathogenesis Related; RAPD - Random Amplified Polymorphic DNA; RFLP - Restriction Fragment Length Polymorphism; RGL - Resistance Gene-Like; SNP - Single Nucleotide Polymorphism; SSCP - Single Strand Conformational Polymorphism; SSR - Simple Sequence Repeat; STS - Sequence Tagged Site; QTL - Quantitative Trait Locus; TG - Tomato Genomic.

chemical control. In the 1840s, late blight epidemics on the potato crop in Ireland caused a tragedy known as the Great Irish Famine [2, 3]. Since then, phytopathologists have focused much attention and research on *P. infestans*, and potato breeders have undertaken breeding programs in order to produce resistant cultivars of potato [4]. Resistance to *P. infestans* became one of first goals of science-based potato breeding and the most important one [1].

Plant resistance to pathogens consists of recognition of the attacking organism and induction of various defence responses, such as reinforcement of cell walls, programmed cell death (hypersensitive reaction), and production of active oxygen species and other antimicrobial substances (phytoalexins, pathogenesis-related (PR) proteins). Pathogen challenge can also induce systemic acquired resistance, protecting the plant against subsequent attacks of the same or another pathogen species [5]. At the genetic level, resistance can be determined by single genes (vertical resistance) or quantitative trait loci (horizontal resistance) [5].

Both types of resistance have been used in breeding potatoes resistant to late blight. Vertical resistance, also called race-specific resistance, is based on "gene-for-gene" interaction, where the products of pathogen avirulence genes interact directly or indirectly with the products of the plant's major resistance genes (R-genes) [6, 7]. As a result, the hypersensitive reaction (HR) is switched on and infected cells together with adjacent ones undergo programmed cell death, which can prevent further growth of biotrophic or hemibiotrophic pathogens like *P. infestans* [8]. Four possible biochemical interpretations of the "gene-for-gene" model exist. The classical receptor-ligand model predicts that direct interaction between an Avr protein and a matching R-protein elicits the defence response. In the co-receptor model, the Avr protein first binds to the co-receptor, which interacts with the R-protein and initiates the defence reaction [9]. Recently, the guard model has gained more acceptance. According to it, R-proteins physically associate with the cellular targets of Avr gene products (called also effectors) and guard them from pathogen influence. Either the binding of the R-protein with a target protein can happen constitutively, but disengage upon the effector binding to its target, resulting in an active R-protein and starting the defence reaction, or the interaction between target and effector can change the target's conformation, enhancing the affinity of the complex to the R-protein, leading to R-protein binding and triggering the resistance [8, 10]. This model is supported by the existing, albeit scarce evidence for direct Avr-R interactions and by evolutionary analyses of R-gene sequences. R-genes are not as fast-evolving and polymorphic as should be assumed for defence receptors. Some of them seem to be ancient in evolutionary terms. This data indicates that the frequencies of R-gene occurrence in the natural plant population are balanced by frequency-dependent selection [6; for a detailed description of the model see: 6, 8, 10]. The fourth model takes into account the fact that some Avr genes are predicted to encode proteases; it further suggests that proteolytically processed host proteins trigger plant defence mechanisms by interaction with R-genes [9].

The second type of resistance is called horizontal or field resistance and, by contrast to the first type, it is polygenic. This kind of resistance involves

lowering the effectiveness of infection, slowing down the rate of colonisation of host tissues and hampering the sporulation of the oomycete. Field resistance is believed to be more durable than vertical resistance and is not race specific; hence, it cannot be overcome easily by the fast-evolving *P. infestans* races [11]. In the beginning of the 20<sup>th</sup> century, 11 R-genes conferring resistance to *P. infestans* were discovered in the wild species *Solanum demissum*, and breeders started applying them in potato cultivars [12, 13]. The inefficiency of these genes was demonstrated as early as the late 1940s in Central Mexico [13]. However, various major resistance genes are still being investigated and used in breeding, e.g. the R-gene from *S. bulbocastanum* [14] or *S. berthaultii* [15]. Field resistance is being given increasing importance in breeding programs [12]; this has stimulated research on the genetic nature of this kind of resistance. Until recently, quantitative traits such as field resistance to late blight were described in statistical terms, by population means and variances, heritabilities, etc. Nowadays, thanks to analysis of molecular markers and linking molecular markers to phenotypic values, it is possible to detect Quantitative Trait Loci (QTL) [19]. The QTL for resistance to *P. infestans* have been mapped in several diploid potato populations [20] and two tetraploid populations [21, 22].

### MAJOR RESISTANCE GENES

Major resistance genes encode resistance which is simply inherited in accordance with Mendel's laws. The first R-gene conferring resistance to *P. infestans* (*R1*) was located on the potato genetic map in 1992 by Leonards-Schippers [23]. Since then, nine R-genes, summarized in Tab. 1, have been mapped, and two of them have been cloned [16-18].

Tab. 1. Summary of R-gene mapping studies.

Name of gene	Chrom.	Mapping population; number of individuals; ploidy	Source of resistance	Ref.
R1	V	H79.1506/1xH80.696/4; 97; 2x	<i>S. demissum</i>	23
R2	IV	BET95-4200xDJ93-6707-10; 86; 4x	<i>S. demissum</i>	24
R3	XI	Esc.42x87-1031-29; 54; 2x	<i>S. demissum</i>	25, 26
R3a, R3b		SH83-92-488xRH89-039-16; 1748; 2x		
R6	XI	J92-6442-8x87-1024-2;85; 2x	<i>S. demissum</i>	27
R7	XI	BE93-4053-6x87-1024-2; 96; 2x	<i>S. demissum</i>	27
RB	VIII	BC <sub>2</sub> : 1K6, 1K27, LB1;173; 2x	<i>S. bulbo-</i>	14, 18
Rpi-blb1,		8005-8x8006-9; 42; 2x	<i>castanum</i>	17,
R <sub>ber</sub>	X	BCT; 146; 2x BCB; 141; 2x	<i>S. berthaultii</i>	15
Rpi1	VII	BC <sub>1</sub> ;115; 2x	<i>S. pinnati-</i> <i>sectum</i>	28

The R-genes originating from *S. demissum* (*R1*, *R2*, *R3a*, *R3b*, *R6*, and *R7*) have been applied in potato breeding programs, and *P. infestans* races compatible to those genes have been identified. Moreover, isolates able to overcome the resistance conferred by those genes are commonly present in *P. infestans* populations world-wide [29-32]. *P. infestans* isolates overcoming major genes newly introduced to the potato gene pool from two other wild species, *S. bulbocastanum* and *S. berthaultii* (*RB*, *R<sub>ber</sub>*) have not been detected so far [14, 15, 17], which indicates that these genes may be very useful for breeding purposes. The gene *Rpi1* discovered in *S. pinnatisectum* (a diploid species with Endosperm Balance Number 1 (1 EBN)) has not been transferred to the *S. tuberosum* genome due to the crossing barrier between these two species; nevertheless, this gene can also be effective against late blight, since no compatible isolate of *P. infestans* has yet been described.

Projects on mapping the R-genes usually share a common scheme consisting of: (i) choosing and crossing individuals, of which one is bearing one copy of the R-gene (is heterozygous), and the other is susceptible; (ii) phenotypically assessing resistance in the progeny, in this case usually done using a qualitative method (+/-) with the expected ratio of resistance to susceptible individuals 1:1; (iii) creating a genetic map of the investigated population using molecular markers; and (iv) finding the markers cosegregating with the resistance, i.e. finding the location of the resistance gene on the genetic map.

Resistant parents of populations used to map major resistance genes to *P. infestans* were: dihaploids obtained from potato cultivars harbouring *S. demissum* R-genes [23, 25-27], a tetraploid clone [24], an F<sub>1</sub> individual from the cross between the *S. berthaultii* and *S. tuberosum* dihaploid [15], an F<sub>2</sub> individual from the backcross of the somatic hybrid between *S. bulbocastanum* and *S. tuberosum* to *S. tuberosum* [14], or a resistant F<sub>1</sub> individual from the cross between *S. pinnatisectum* and *S. cardiophyllum* [28].

Phenotypic assessment of resistance to *P. infestans* in research on major resistance genes, is usually performed in laboratory conditions, on detached leaflets [24, 25, 27], leaves [28], whole plants grown in the greenhouse [14], *in vitro* plantlets [26], or discs cut out of the leaves [23]. Concerning gene *R<sub>ber</sub>*, the resistance of the investigated population was tested using a field test over the course of two subsequent years, because besides the R-gene, there are QTL influencing the resistance to *P. infestans*, [15]. In all the above cases, resistance was scored in +/- mode, where "+" means that the plant is resistant and has the R-gene, and "-" means a susceptible plant without the gene. Laboratory methods, even not very sensitive and rather qualitative, seem to be sufficient to observe the effect of the R-gene, which is supposed to be discrete and to clearly divide the population into two distinct classes, fitting to the 1:1 ratio, when the population is diploid and the resistant parent heterozygous.

The next stage of the mapping study is the construction of the genetic linkage map on the basis of molecular markers. The first ever applied for this purpose and thus far the most frequently used method is detection of Restriction Fragments Length Polymorphism (RFLP) [20, 33]. As with all other DNA-based

markers, RFLP permit the detection of: point mutations, which are neutral from an evolutionary point of view (Single Nucleotide Polymorphism, SNP); insertions; deletions (InDel); and inversions of DNA fragments [20]. RFLP reveal those DNA changes that concern restriction sites recognised by a given endonuclease, the length of fragments between the restriction sites and the sequence that is binding to the probe. Widely used and reliable, the RFLP markers became anchor markers that enable the alignment of different maps constructed in independent studies and locating genetic factors conferring resistances to various pathogens on the common functional map [20]. Moreover, common RFLP markers permitted the alignment of potato maps with molecular maps of tomato, tobacco and pepper, revealing syntenic resistance regions in these related *Solanaceae* genomes [20].

Tab. 2. A summary of the methods used in R-gene mapping studies.

Name of gene	Chrom.	Phenotypic resistance assessment	Type of molecular markers	Anchor markers close to R-gene	Ref.
R1	V	leaf disc assay	RFLP	GP21, GP179	23
R2	IV	detached leaflet test	AFLP		24
R3	XI	detached leaflet test	RFLP,	TG105(a),	25, 26
R3a, R3b		<i>in vitro</i> plantlet test	AFLP, STS	GP185, GP250, TG26,	
R6	XI	detached leaflet test	RFLP	GP185, GP250	27
R7	XI	detached leaflet test	RFLP	GP185, GP250	27
RB	VIII	whole plant test	RFLP,	TG513, CT64,	14, 18
Rpi-blb1		detached leaf test	RAPD, STS	CP53	17
R <sub>ber</sub>	X	field test	RFLP	TG63	15
Rpi1	VII	detached leaf test	RFLP	TG20A, CP56	28

The majority of potato R-genes acting against *P. infestans* (*R1*, *R3*, *R6*, *R7*, *R<sub>ber</sub>*, *Rpi1*, *RB*) were mapped using RFLP markers [14, 15, 23, 25, 27, 28]. Gene *R2* was located on the genetic map constructed of Amplified Fragments Length Polymorphism (AFLP) markers [24]. AFLP markers give the advantage of producing numerous bands; i.e. given similar input, they yield a denser map than RFLP markers. The disadvantages of AFLP are the uneven distribution of these markers in the genome and the difficulties in aligning the newly constructed map with the previous ones. AFLP markers were also used to increase map density in the neighbourhood of *R3*, which lead to the conclusion that *R3* resistance is conferred by two closely linked R-genes (*R3a* and *R3b*) with distinct specificities [26]. Another type of markers, Random Amplified Polymorphic DNA (RAPD) markers, was used to map the *RB* gene, together with RFLP markers [14]. Recently, more and more potato DNA sequences are available, and therefore, sequence-specific PCR-based (Sequence Tagged Site, STS) markers are gaining importance, including RFLP anchor markers converted into PCR-based ones [14, 16-18, 26]. Map construction is usually done on

commercially available software such as MAP MAKER [14, 28], MAP MANAGER [15, 28] or JOIN MAP [24], or software written by E. Ritter [23]. Tab. 2 shows methods used in mapping R-genes for *P. infestans*.

R-genes conferring resistance to different races of the pathogen or even to different pathogens tend to cluster on the genetic map. This observation is in accordance with the model for gene evolution, where members of gene families originate from common ancestors by local gene duplication and subsequent diversification [20]. *R3a*, *R3b*, *R6* and *R7* form a cluster of genes conferring resistance to different races of *P. infestans* in the distal segment of chromosome XI [25-27]. Another gene cluster can be found on chromosome V, where next to gene *R1*, R-genes for resistance to *Potato virus X* (*Rx2*, *Nb*) are located [20].

On the basis of their position, two major resistance genes for *P. infestans* have been cloned. The first one was *R1* [16], and then, two independent research groups cloned R-genes from *S. bulbocastanum*, *RB*, introduced into the *S. tuberosum* gene pool via somatic hybridisation [14, 18], and *Rpi-blb1*, in an intraspecific *S. bulbocastanum* cross [17]. The coding sequences of the *RB* and *Rpi-blb1* genes are identical. However, the flanking sequences and intron of these two genes have single nucleotide polymorphisms and insertions, leading to the conclusion that *RB* and *Rpi-blb1* are allelic, although functionally equivalent [17]. The *R1* gene belongs to the R-gene family that have leucine-rich repeats (LRR), a nucleotide binding site (NBS) and a leucine zipper, whereas *RB/Rpi-blb1* has a coiled coil (CC) domain in addition to LRR and NBS domains. Both *R1* and *RB/Rpi-blb1* have been verified by complementation analysis in potato, and *Rpi-blb1* has also been shown to function in tomato [16-18].

## QUANTITATIVE TRAIT LOCI

Quantitative resistance is assumed to be controlled by many genes on the basis of the mode of its inheritance. The distribution of this kind of resistance in the progenital population fits to the normal curve. All the involved genes act together in the plant's defence, and therefore, each gene might be ineffective if expressed alone. Every plant has a certain level of quantitative resistance, which responds rather unspecifically to different pathogens. This type of resistance does not confer complete resistance as qualitative resistance does, but rather slows down the progress of the disease and it can vary under different environmental conditions, unlike the qualitative resistance [22]. Genes underlying quantitative resistance to *P. infestans* in the potato plant are not known, although regions linked to this trait have been mapped in several mapping studies. Sources of mapped quantitative resistance, methods for resistance evaluation and genotyping, as well as results obtained in those studies are reported on below.

Exploited sources of resistance and short descriptions of the mapping populations are shown in Tab. 3 in chronological order. A number of wild *Solanum* species were used, and mapping studies were performed, both at the

diploid [15, 34-39] and tetraploid [21, 22] levels. The number of individuals in populations varied from 67 [37] to 401 [38].

A reliable and accurate phenotypic assessment of resistance is crucial for QTL studies. In most of the cases, a field trial is the method of choice for this purpose, as it reflects the situation occurring in nature and allows precise quantitative measurements of the progress of the disease. Data collected at weekly intervals enable the calculation of the area under the disease progress curve (AUDPC), which is the most widely used estimation of quantitative resistance response [15, 22, 34-37]. A field test scored on a 1-9 scale was also used [36], as well as a laboratory leaf disc assay [38, 39] and a whole plant test [21].

Tab. 3. Populations used to map QTL for resistance to late blight.

Year of publication	Sources of resistance	Ploidy of populations	Number of populations	Number of individuals	Ref.
1994	<i>S. spegazzini</i>	2x	1	197	39
1998	<i>S. demissum</i>	4x	1	94	21
	<i>S. tuberosum ssp. andigena</i>				
1999	<i>S. kurtzianum</i>	2x	1	113	34
	<i>S. vernei</i>				
	<i>S. tarijense</i>				
	<i>S. stenotomum</i>				
1999	<i>S. chacoense</i>	2x	5	401	38
	<i>S. kurtzianum</i>				
	<i>S. vernei</i>				
	<i>S. stenotomum</i>				
2000	<i>S. microdontum</i>	2x	6	368	35
2000	<i>S. berthaultii</i>	2x	2	287	15
2001	<i>S. phureja</i>	2x	1	246	36
2003	<i>S. phureja</i>	2x	1	67	37
	<i>S. vernei</i>				
2004		4x	2	179	22

Besides foliage resistance, some authors also investigated the resistance of tubers in a laboratory test [34, 38]. There is a strong association between quantitative resistance to *P. infestans* and late maturity of the potato [40, 41]; therefore, some authors include maturity testing in research on QTL for late blight resistance [22, 34, 37, 38]. Since quantitative traits are strongly influenced by the environment, it is essential to repeat testing in subsequent years or different locations to distinguish the environmental component of variation from the genetic one. Field assessments of foliage resistance were repeated over three years [22, 34, 37], two years [15, 35], only once [38] or in four locations [36]. Maturity testing was done over four years [22], three years [22, 34], two years [37] or once [38]. Tuber resistance tests were performed once [38] or three times [34].

Genetic linkage maps of the quantitative populations were constructed, similarly to maps from mapping studies of R-genes, on the basis of RFLP [15, 34, 35, 37-39], AFLP [21, 34-37], STS [22, 38], RAPD [36], Cleaved Amplified Polymorphic Sequences (CAPS) [22, 34-36], Simple Sequence Repeat (SSR) [34-36], and Single Strand Conformational Polymorphism (SSCP) [22] markers. Authors usually combine more than one marker type in order to improve map density. The next step is map assembly by software and statistical analysis of marker linkage to the trait. The marker-trait relationship is usually investigated using ANOVA, the Kruskal-Wallis test, the Mann-Whitney U-test or the t-test, depending on the trait distribution in the progeny. Results obtained by different authors are summarized in Tab. 4. The number of QTL for resistance to *P. infestans* detected in different studies varies from one [21] to twelve [38]. The same region on chromosome V harbours the QTL for resistance revealed in seven independent studies [22, 34-39] and QTL for maturity, according to all the papers searching for QTL for maturity (Tab. 4).

Tab. 4. QTL for late blight resistance located in independent mapping studies.

Ref.	Chromosome											
	I	II	III	IV	V	VI	VII	VIII	IX	X	XI	XII
15			R				R	R			R	
21								R				
22			R	RM	RM	M		RM	RM		RM	RM
34	RM	RTM	R	RM	RTM	RM	RM	RM	RT		R	RT
35				R	R					R		
36			R		R		R	R			R	R
37			R		RM							
38	R	R	R	R	RTM	R	R	R	R	R	R	R
39		R	R	R	R	R	R		R		R	R

R: QTL for foliage resistance to late blight; T: QTL for tuber resistance; M: QTL for maturity.

Remarkably, three major resistance genes have been mapped to the same region (*R1* conferring resistance to *P. infestans* and two PVX resistance genes: *Rx2* and *Nb*), as well as two QTL for resistance to *Globodera pallida* and one QTL for *G. pallida* and *G. rostochiensis*, supporting the hypothesis about the existence of resistance hot spot in this region [20]. The region on chromosome XII showed a significant effect on the resistance to late blight in three studies [22, 38, 39], and two R-genes were also mapped to this region: *Rx1* conferring resistance to PVX and *Gpa2*, a resistance gene against *G. pallida* [20]. On chromosome IX, a resistance QTL for late blight was detected in four mapping studies [22, 34, 37, 39]. Generally, different authors detect some overlapping regions. However, even within one mapping project, the detected QTL usually differ depending on the phenotypic data set; i.e. phenotypic data obtained in different years result in detecting different QTL [22, 34, 36, 38]. The strength of the QTL effect is usually described by the percentage of variance explained by the QTL ( $R^2$ ). The

strongest QTL for late blight resistance were detected on chromosome XII, explaining 43% of variance [33], on chromosome V – 41% [37] or 20.8% [34] or 15.8% [38] or 8.8% [22], on chromosome III – 36% [15] or 25% [37] or 19.1% [38], on chromosome VIII – 31.6% [21], on chromosome X – 31% [35], on chromosome IV – 30% [35], on chromosome II – 20.7% [38].

The genes controlling quantitative resistance to *P. infestans* have yet to be fully detailed. Candidate genes can belong to the Resistance Gene-Like (RGL) genes or genes involved in plant defence. RGLs were mapped to the regions of the potato genome that are known to host genes controlling qualitative and quantitative resistance to *P. infestans* [42], as were SNPs or InDels, tightly linked or located within NBS/LRR-type genes [43]. Defence genes were also found in regions of late blight QTL, among them genes encoding enzymes: phenylalanine ammonium lyase, chalcone isomerase, chalcone synthase, osmotin, and *P. infestans*-induced cytochrome P450 [44].

A new approach in the field of *P. infestans* resistance is association study, where associations between DNA markers, foliage and tuber resistance to late blight and maturity have been investigated in a gene bank collection of 600 potato cultivars, and where a highly significant association with these quantitative characteristics has been detected by PCR markers on chromosome V [45].

The search for new sources of resistance and the mapping of such newly introduced resistance, both qualitative and quantitative, is still ongoing. The first reports have been published about resistance to late blight originating from different accessions of species: *S. phureja* [46-48], *S. verrucosum* and *S. microdontum* [47, 48], and *S. brachistotrichum*, *S. mochiquense*, *S. okadae*, and *S. neorossi* [[www.sainsbury-laboratory.ac.uk/jonathan-jones/lateblight.htm](http://www.sainsbury-laboratory.ac.uk/jonathan-jones/lateblight.htm)].

In the Plant Breeding and Acclimatization Institute, Młochów Research Centre, a major resistance gene originating from *S. phureja* and QTL from *S. verrucosum* and *S. microdontum* have been identified. In a current research project, the resistance of mapping populations to late blight has been assessed over the course of five years using three laboratory methods (detached leaflet, tuber slice and whole tuber method), and vegetation length has been estimated in a field test. Mapping has been performed using PCR-based methods (RAPD, STS, CAPS and SSCP) [47, 48].

The functional map of potato resistance to late blight is still being enriched with major new genes and QTL, and the map density is increasing thanks to new types of molecular markers. New goals are emerging for resistance research: designing functional markers for resistance, effective on different genetic backgrounds, and linking natural variation at the DNA level with the phenotypic effect on resistance.

**Acknowledgements.** This work was supported by State Committee for Scientific Research, grant No. PBZ/KBN/029/P06/2000. I would like to thank Renata Lebecka, Waldemar Marczewski and Ewa Zimnoch-Guzowska for their comments on the manuscript.

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