Quantitative Resistance to Biotrophic Filamentous Plant Pathogens: Concepts, Misconceptions, and Mechanisms

Rients E. Niks,[1] Xiaoquan Qi,[2] and Thierry C. Marcel[3]

[1]Laboratory of Plant Breeding, Wageningen University and Research Centre, 6700 AJ Wageningen, The Netherlands; email: rients.niks@wur.nl

[2]Key Laboratory of Plant Molecular Physiology, Institute of Botany, Chinese Academy of Sciences, Haidan, Beijing 100093, China; email: xqi@ibcas.ac.cn

[3]INRA, UMR1290 BIOGER, F-78850 Thiverval-Grignon, France; AgroParisTech, UMR1290 BIOGER, F-78850 Thiverval-Grignon, France; email: thierry.marcel@versailles.inra.fr

Annu. Rev. Phytopathol. 2015. 53:445–70

First published online as a Review in Advance on June 5, 2015

The *Annual Review of Phytopathology* is online at phyto.annualreviews.org

This article's doi: 10.1146/annurev-phyto-080614-115928

Keywords

partial resistance, effector targets, durability, basal resistance, mechanisms

Abstract

Quantitative resistance (QR) refers to a resistance that is phenotypically incomplete and is based on the joined effect of several genes, each contributing quantitatively to the level of plant defense. Often, QR remains durably effective, which is the primary driver behind the interest in it. The various terms that are used to refer to QR, such as field resistance, adult plant resistance, and basal resistance, reflect the many properties attributed to it. In this article, we discuss aspects connected to those attributions, in particular the hypothesis that much of the QR to biotrophic filamentous pathogens is basal resistance, i.e., poor suppression of PAMP-triggered defense by effectors. We discuss what role effectors play in suppressing defense or improving access to nutrients. Based on the functions of the few plant proteins identified as involved in QR, vesicle trafficking and protein/metabolite transportation are likely to be common physiological processes relevant to QR.

INTRODUCTION

QR: quantitative resistance

Plant-pathosystem: plant species–pathogen species (or forma specialis) combination

Plants or plant populations exposed to a certain pathogen or pest organism often differ in degree of infestation or infection in quantitative ways. Such differences may be due to environmental or plant development stage differences between plots or to differences in inherited levels of plant defense. Several cultural measures may be applied to reduce the development of foliar diseases, but they have their limitations (60). The most reliable and environmentally friendly way to protect crops is the growth of cultivars with genetic resistance against their attackers. Breeding for adequate levels of resistance is indeed one of the most important goals in crop breeding. More and more breeders are recognizing the use of quantitative resistance (QR) as a valuable approach to protect crops. In case the level of resistance achieved in a particular plant-pathosystem is not sufficient in some seasons or regions to protect the crop sufficiently, QR is still useful because of the reduction in required pesticide applications (e.g., 81).

Screening a panel of accessions of a crop species against propagules of a pathogenic organism (inoculum) nearly always reveals diversity in quality and quantity of infection. Some plants may seem to be not infected at all (immunity), others show at most some flecks but no reproduction of pathogens (full resistance), and again others show various levels of infections and pathogen reproduction.

Two recent reviews, by Zhang et al. (135) and by Poland et al. (100), discuss the genetic and molecular basis of qualitative and quantitative resistances to biotrophic and necrotrophic pathogens, and a review by St. Clair (117) discusses particularly the quantitative aspect of resistance. In these reviews, it is pointed out that resistance to pathogens with a necrotrophic lifestyle generally has a molecular and mechanistic basis quite distinct from that of resistance to pathogens with a (hemi-)biotrophic lifestyle. In this article, we focus on QR to biotrophic filamentous pathogens that tend to be specialized to one or a few closely related plant species. For this resistance, several terms are popularly used in the literature, and they seem to be used as synonyms (**Table 1**). Before discussing the limited knowledge on the genetic basis and resistance mechanisms, we discuss some characteristics commonly attributed to QR.

TERMINOLOGY AND PERCEPTIONS

The Quantitative Aspects of Quantitative Resistance

The epithet quantitative is used to indicate two distinct and not strictly associated aspects of the resistance. One aspect is the phenotypic phenomenon that the resistance is incomplete, i.e.,

Table 1 Terms used to refer to quantitative types of resistance and their relative popularity in scientific literature

Search term	Number of papers found in a literature search[a]
Partial resistance	376
Quantitative resistance	135
Field resistance	195
Adult plant resistance	156
Polygenic resistance	22
Slow rusting/mildewing/blighting	59
Basal resistance[b]	41

[a]Results of a search in Web of Science™ August 18, 2014, using "search term" in title of papers for the arbitrary period 1980–2014 and refined to the categories Plant Sciences, Agronomy, and Horticulture.
[b]Refined to the categories Plant Sciences, Agronomy.

allowing some reproduction by the pathogen and therefore some epidemic progress. This notion is also expressed in the terms partial resistance and slow rusting/mildewing/blighting (**Table 1**). The antonym is qualitative, i.e., resistance that completely impedes reproduction of the pathogen. Actually, a partially resistant phenotype may be considered fully susceptible until an even more susceptible accession of the host species is identified. For example, the barley cultivar Golden Promise seems to be highly susceptible to *Puccinia hordei* (55) but was, at seedling stage, a shade less susceptible (and hence quantitatively resistant!) to this pathogen than the extremely susceptible line SusPtrit (129). Full susceptibility, therefore, is an undesirable qualification, because we never know whether some plant genotypes exist that are even more susceptible.

The second aspect to which the terms quantitative and qualitative may refer is the mode of inheritance. We recognize, of course, that segregation of genes follows Mendelian principles irrespective of the size of their effect on phenotype. However, according to general convention, only when the phenotypic effect of a gene is large enough to follow its segregation in a progeny do we consider it Mendelian and qualitative. Thus, qualitative refers to an inheritance that is based on one or two major genes that segregate according to discrete phenotypic classes according to Mendelian principles. Monogenic (one gene) inheritance is in itself not sufficient to qualify a resistance as qualitative. For example, Yeo et al. (129) detected for the 5% prolongation of the latency period (LP) of *P. hordei* in Golden Promise only one relatively weak-effect quantitative trait locus (QTL). Strictly speaking, this resistance in Golden Promise is monogenic, but the effect is so weak that a QTL mapping approach is required to detect its presence, and the effect is too small to follow its segregation in progeny. Therefore, it is not a major gene.

When considering mode of inheritance, quantitative refers to a resistance that is based on several genes, each contributing a small proportion of the resistance level. This notion is implied by the term polygenic resistance. We point out that polygenic would not rule out that some plant accessions may have only one significant minor-effect gene contributing to the trait (see the example of barley line Golden Promise/*P. hordei* referred to above). The trait is still quantitative in that case.

For the phenotypic as well as the genetic aspect, we should keep in mind that it is easy to find cases that are not readily classified into qualitative and quantitative. Genes with a large-effect QTL may in some environments, genetic backgrounds, plant development stages, or to some pathogen isolates behave Mendelian (qualitative). In others, we need QTL mapping to identify them, and they may behave as a minor-effect gene. Good examples are *Lr34* of wheat against leaf rust, stripe rust, and powdery mildew (64, 106) and *Rphq4/Rph20* of barley against barley leaf rust (49, 103).

Resistance that is quantitative according to its phenotypic nature may have a qualitative inheritance and vice versa. **Figure 1** shows the four categories of the qualitative/quantitative nature of resistance. Numerous *R*-genes have been described that inherit in a Mendelian fashion (so they are major genes) but do not fully impede replication of the pathogen. Examples are the *Lr34* gene in wheat to leaf rust, stripe rust, and powdery mildew (64), *Rph9.z*, in cultivar Trumpf to barley leaf rust and the *MlLa* gene in barley to powdery mildew (120). These genes give at the adult plant stage a large enough effect to establish them as major genes (following Mendelian inheritance rules) and to grant them their own gene symbols. Such genes, therefore, have a qualitative inheritance, but their effect on infection parameters is quantitative (**Figure 1*c***). There are also cases where resistance is complete but has a quantitative inheritance, i.e., has no Mendelian inheritance. The most typical examples are certain cases of nonhost resistance (**Figure 1*b***). The comparison of susceptible host accessions with nonhost accessions in infection experiments indicates a clear and qualitative difference in phenotype, the host typically being infected and the nonhost usually being immune. Inheritance studies indicate that the nonhost resistance of *Lactuca saligna* to the lettuce downy mildew *Bremia lactucae* (133) and of barley to several heterologous grass and cereal

Latency period (LP): period elapsing from the moment of inoculation to the moment of sporulation

Quantitative trait locus (QTL): the statistically most probable chromosomal region in which one or more genes that affect a quantitative trait are located

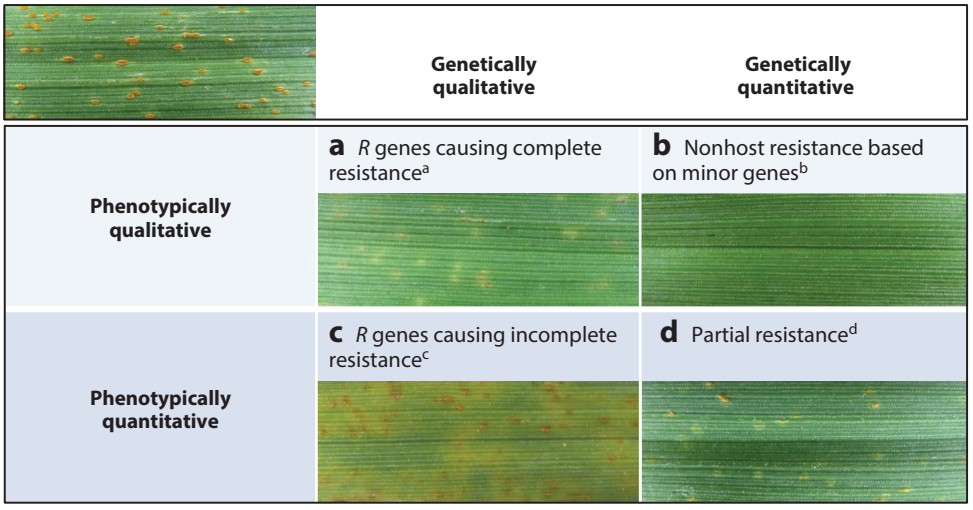

Figure 1

Four categories of qualitative/quantitative nature of resistance, split-up for phenotypic and genetic aspects of resistance. Each category is illustrated with an example of rust fungus (*Puccinia*) on barley. In the left top corner for sake of comparison, the susceptible barley accession L94 infected by *Puccinia hordei* isolate 1.2.1. (*a*) Cv Cebada Capa showing complete resistance conferred by one major gene, *Rph7g*, to avirulent isolate 1.2.1. of *P. hordei*. (*b*) Cv Vada showing complete (nonhost) resistance to an isolate of the rye grass stem rust fungus *Puccinia graminis* f. sp. *lolii*. This resistance is based on the combined effect of at least three quantitative resistance genes. (*c*) Cv Trumpf showing incomplete resistance conferred by one major gene, *Rph9.z*, to avirulent isolate Israel 202 of *P. hordei*. Some sporulation occurs, despite the hypersensitive reaction. (*d*) Cv Vada showing high level of partial resistance to *P. hordei* isolate 1.2.1., reducing infection number and decreasing development rate (see time-lapse movie). This resistance is conferred by several quantitative resistance genes.
[a]Niks & Kuiper 1983.
[b]Jafary et al. 2006.
[c]Franckowiak et al. 1997.
[d]Qi et al. 1998.

Puccinia rust fungi (51) and to heterologous powdery mildew fungi (2) is due to the combined effect of several genes with quantitative effect.

The quantitative aspect of partial resistance refers, according to the definition by Parlevliet (89), to the phenotypic aspect. Parlevliet (89) defines partial resistance as a type of resistance that retards epidemic development in the field, although plants show a susceptible (nonhypersensitive) infection type (89). The definition does not contain the notion that the inheritance should be polygenic, although the experience is that partial resistance normally is. The recessive nonhypersensitive *mlo* resistance of barley to the powdery mildew fungus *Blumeria graminis* f. sp. *hordei* (*Bgh*) actually complies with the definition of partial resistance but is monogenically rather than quantitatively inherited. In this article, we focus on resistances that are based on multiple genes, each conferring a relatively small reduction of the infection level (**Figure 1*d***).

***Blumeria graminis* f. sp. *hordei* (*Bgh*):** causes powdery mildew on barley

Quantitative Resistance Can Be Better Assessed in Adult Plants

The terms field resistance and adult plant resistance were coined because of the many examples of QR that are much more obvious in polycyclic field situations than in seedling tests in the

Video 1

Seedling leaves of three barley genotypes infected by isolate 1.2.1 of *Puccinia hordei*, the barley leaf rust fungus, showing the difference in rate of pustule development in a monocyclic test. Times (in days and hours) after inoculation are indicated.
Genotypes are extremely susceptible (L94), partially resistant (Vada), and extremely high partially resistant (17-5-16). The pale flecks are immature infections, and the orange pustules are mature sporulating reproduction organs of the fungus (uredinia).
Day 7, 17:00: Almost all pustules on L94 are mature, whereas only the first pustules on Vada are mature.
Day 9, 2:00: Almost all pustules on Vada are mature, and on 17-5-16 the first mature pustule has just appeared. Vada shows approximately 50% fewer mature pustules than L94.
Day 12, 9:00: The final number of mature pustules on 17-5-16 is 12, which is much less than on Vada and L94.
To view the video, access this article on the Annual Reviews website at **http://www.annualreviews.org**.

greenhouse or climate room. The relative ease of detection of some QRs in field situations may be due to:

1. The polycyclic character of the epidemic. QR leads to a decrease in progress of the epidemic and is therefore also called rate-reducing resistance. Susceptible accessions of a crop may show great differences in severity in polycyclic epidemic situations, e.g., pea to the *Uromyces pisi* rust fungus (10), garlic to the rust fungus *Puccinia allii* (35), and barley to the barley leaf rust fungus (*P. hordei*) (90). A difference in LP of only approximately 30 h (approximately 25% prolongation) at the seedling stage between partially resistant Vada and susceptible L94 of *P. hordei* may correspond to a contrast in disease severity in a polygenic field test in isolated field plots similar to 1 pustule per tiller on Vada versus 25% leaf area infected on L94 (92, 93) (see **Video 1**; access the online version of this article at **http://www.annualreviews.org** to view the time-lapse video).
2. Lower and more fluctuating temperatures, especially during the night, in the field than in greenhouses. In a current study (Y.J. Wang and X. Qi, unpublished data), the barley QR gene *Rphq4* against *P. hordei* had a greater effect at low and fluctuating temperatures than under rather constant 20°C greenhouse conditions.
3. Plant development stage–dependent gene expression. Evaluation of QTL-near-isogenic lines (NILs) for resistance to *P. hordei* at development stages ranging from seedling to adult plants indicated that some genes have a plant development stage–specific effect (128). Genes that are effective only or particularly at adult plant stages may belong to the nonhypersensitive type (*Rph20* = *Rphq4*) (49, 103) as well as to the hypersensitive type of resistance (out of many examples, the *Lr22a* and *Lr22b* genes in wheat against wheat leaf rust, caused by *Puccinia triticina*) (30).

Polycyclic: involving several cycles of pathogen reproduction during the season or during a test

Phenotypic screens in seedlings may reveal effects of so-called adult plant resistance genes if seedlings are submitted to low temperature and to very homogeneous administration of inoculum, e.g., *Lr34* (106), and if very detailed observations are performed. Successful phenotyping for minor differences in QR depends on precise inoculation methods, such as settling towers (18, 33, 79, 110), and on appropriate observation criteria in monocyclic tests. To detect differences in LP and infection frequency (**Video 1**), careful and laborious observations are required in order to map QTLs with small-sized to medium-sized effects.

Monocyclic: involving only one cycle of pathogen reproduction during the season or during a test

MAS: marker-assisted selection

Transgressive segregation: occurrence in segregating progeny of individuals with much higher and lower values than the parents, indicating that parents have complementary + and − genes

Phenotypic recurrent selection: strategy in which, in multiple subsequent cycles, various selected parents are randomly intercrossed to produce bulk offspring, segregating for many trait genes to accumulate desirable genes

Is It Hard to Select for Quantitative Resistance?

It is generally argued that it is hard to select for QR. Such opinions are in turn an argument for mapping genes that confer QR to enable marker-assisted selection (MAS). Selection on the basis of molecular markers is much less biased than selection for minor differences in infection level. Indeed, molecular markers are usually an unbiased selection criterion because they can be read at high throughput and with a minimum of errors. Of course, care should be taken to select QR genes on the basis of flanking markers to prevent dissociation of the marker allele from the resistance allele due to genetic recombination. The more difficult the phenotyping (because of low heritability, i.e., the variation for a trait among plants or populations is more due to variation in nongenetic factors, such as small variation in inoculum deposition, than to variation in genes) the more needed MAS is, but at the same time, the more challenging it is to establish the associations between markers and the effective alleles of QTLs. St. Clair (117) pointed out that phenotypic selection may be more cost effective than MAS for improvement of a particular quantitative trait, so MAS may not be warranted. Just on the basis of phenotypic selection, great increases in the resistance level of barley to powdery mildew (3) and to barley leaf rust (91) were achieved. For partial resistance, this resulted in a nearly completely resistant line 17-5-16 (**Video 1**) (91). In well-studied plant-pathosystems, such as barley-barley leaf rust and wheat-wheat stripe rust, abundant minor genes for partial or QR have been found with resistance alleles from different parents (14, 74, 101, 131) so that transgressive segregation is commonly observed (1, 3, 13, 56, 104, 127). This explains why phenotypic recurrent selection is a very useful strategy (94). Commercial breeders repeat cycles of intercrossing plant genotypes and selection against the highest levels of susceptibility, thereby increasing the level of partial resistance in their general germplasm. This may explain why the level of partial resistance of commercial West-European barley to *P. hordei* around the year 2000 was higher than that of commercial barley cultivars developed in the late 1970s (86, 92).

If certain quantitative genes are introduced by MAS into a large number of cultivars, the focus will be on a few particular marker-defined resistance genes rather than on many anonymous and diverse genes. Consequently, there might be a greater selective advantage for variants of the pathogen to which those particular marker-defined genes are not effective or less effective. Thus, MAS may lead to less genetic diversity and lower durability of the resistance if only a few major-effect QTLs are too often used in breeding programs.

Quantitative Resistance Is Durably Effective

The most important argument for shifting attention from the *R*-gene-based resistance to QR is the supposed durability of the latter (see sidebar How to Define Durability).

Durability of QR has been claimed frequently, but experimental evidence for the hypothesis that quantitative disease resistance is more durable than qualitative resistance remains scarce (117). Experiences vary among plant-pathosystems. The high level of partial resistance of barley cultivar

HOW TO DEFINE DURABILITY

Durability of a resistance is defined by Johnson (54) in an often-cited article as resistance that remains effective when used in a large growing area over a long period of time in environments favorable to disease development (e.g., 66). Johnson (54, p. 567) circumscribed the long period as "while a cultivar possessing it is widely cultivated" or "while cultivars containing it are widely used." The latter specification (cultivars in plural) is the more appropriate because newly introduced *R*-gene(s) are usually also deployed in consecutively released and grown cultivars, and so the *R*-gene's effectiveness should preferably be longer than the commercial lifetime of the first cultivar carrying it. Therefore, we disagree with the assumption by Leach et al. (66) that the time requirement for durability for some vegetable crops with a high variety turnover may be less than that needed for cereals. It is the *R*-gene (combination) rather than the variety that is the relevant unit to be considered for durability.

Vada against barley leaf rust in western Europe appears to have remained high for decades (86), but in the potato-late blight (caused by *Phytophthora infestans*) plant-pathosystem, local isolates developed aggressiveness specifically to locally grown potato cultivars (5). Adaptation of pathogen populations to QR by means of serial passage and selection experiments has been demonstrated for various plant-pathosystems, including wheat-wheat leaf rust and barley-barley powdery mildew (reviewed in 80).

QR that lasts over time usually results from the accumulated effect of several minor-effect genes. It is much more difficult to ascertain whether single (minor) genes are durably effective or not. Certain minor-effect genes were shown in individual studies to be isolate specific (e.g., 6, 7, 15, 41, 46, 58, 73, 102, 130). Nevertheless, it is hard to ascertain whether isolates to which a certain minor gene is not effective (anymore) have a sufficient selective advantage to substantially increase the proportion of the virulent genotype in the pathogen population.

McDonald & Linde (75) discerned pathogens with low and pathogens with high evolutionary potential. Pathogens with high evolutionary potential and hence greatest risk of breaking down resistance genes have a mixed reproduction system, a high potential for genotype flow, large effective population sizes, and high mutation rates. Pathogens we are concerned with in this article belong to the category with the highest evolutionary potential. In such plant-pathosystems, the higher durability of genes for QR has been explained by several arguments:

1. A pathogen variant that overcomes a particular QR gene gains only a marginal advantage and hence will not increase tremendously in frequency in the pathogen population. This would limit the selective advantage of this pathogen variant.
2. The fitness gain for such a pathogen variant is also limited if the particular defeated gene is present in only a relatively small proportion of the crop acreage. This would further reduce the selective advantage of the pathogen variant.
3. There is a wide diversity in resistance genes with similar, overlapping, or different defense functions within the plant-pathosystem that contribute to higher levels of QR. Each of those plant defense factors needs to be addressed by a particular pathogenicity factor in the pathogen. Thus, a pathogen able to suppress a certain defense gene may not defeat all QR in that particular host genotype, or the QR in other genotypes, unless those other genotypes share that same gene for QR. This principle would essentially result in some minor gene–for–minor gene interactions, where pathogenicity genes of minor effect in the pathogen correspond to resistance genes of minor effect in the host (46, 84, 95, 100).
4. It has been argued that the durability of a plant resistance gene is a function of the amount of fitness penalty imposed on the pathogen (66, 75). This assumption has always been

discussed in the context of R/Avr major gene resistance. Many avirulence genes encode fitness factors promoting infection. Genes associated with a fitness penalty in pathogens because of overcoming a part of QR have not been described (66).

Pathogen-associated molecular pattern (PAMP): a pathogen-specific biochemical compound, often indispensable for the microbial lifestyle, that elicits plant defense

Microbe-associated molecular pattern (MAMP): a microbe-specific biochemical compound, often indispensable for the microbial lifestyle, that elicits plant defense

PAMP-triggered immunity (PTI): plant defense that relies on the recognition of PAMPs or MAMPs by pattern recognition receptors

Effectors: proteins secreted by pathogens into host apoplast or host cells to enhance infection

Can Durability Be Explained by the Need for Gain-of-Function Mutations?

It is obvious that the larger the effect of a resistance gene, the easier it is to monitor the durability of its effect. A very informative example is the *mlo* gene in barley against powdery mildew (*Bgh*). This gene seems to violate all conditions that would promote durability. It has a very large effect, allowing less than 1% of the *Bgh* infection units to establish a haustorium in barley epidermal cells compared with the rate on *Mlo* allele–carrying barley (59). The *mlo* resistance has been applied in so many spring barley cultivars that from 2004 to 2006 approximately 50% of spring barley acreage in central and western Europe was estimated to be *mlo* barley (**http://www.crpmb.org/mlo/#mlo-varieties**). Furthermore, *Bgh* belongs to the pathogen species considered to have the highest evolutionary potential (75). Therefore, in the past 40 years since the introduction of this resistance into spring barley, there should have been a tremendous advantage and ample opportunity for *Bgh* variants to arise and to take over the original *Bgh* population. However, there is no evidence for breakdown of the *mlo* resistance. This suggests that the arguments in the previous section are not the only explanations for durability. Indeed, McDonald & Linde (75, p. 359) mention *mlo* as a case where "the resistance gene itself plays a key role in durability." This may be interpreted as a case where overcoming the *mlo* resistance by the powdery mildew fungus requires an improbable or even impossible adaptation, i.e., a particular gain-of-function mutation of one or several genes.

Surprisingly, the gain-of-function mutation requirement seems to be neglected as a possibly decisively important aspect that may promote the durability of QR genes. Such a gain-of-function mutation is statistically much harder to realize than loss-of-function mutations. Although McDonald & Linde (75) mention difference in mutation rate as a relevant factor, they connect this with the type of pathogen (viruses and bacteria versus other classes of pathogen) and with the occurrence of transposable elements, but they do not point out the obvious difference in rate between required loss-of-function mutations and gain-of-function mutations.

Quantitative Resistance and Basal Resistance

In recent literature, it has become more and more usual to use the epithet basal as more or less an equivalent of quantitative (e.g., 1, 138). Basal resistance was originally defined as defense that inhibits pathogen spread after successful infection and onset of disease (22). It is an induced defense and therefore does not include constitutive mechanisms based on morphology or aspects such as cuticle properties (50). Basal resistance is inferred when plant mutants are identified that are more susceptible to virulent pathogens than the wild type (22), such as the enhanced disease susceptibility (*eds*) mutants (44). Mutant genes identified several basal defense pathways that are activated through conserved pathogen- or microbe-associated molecular patterns (PAMPs/MAMPs), which are molecular sequences or structures in any pathogen-derived molecule that are perceived via direct interaction with a host defense receptor (50, 71). PAMPs/MAMPs elicit an induced immunity, PAMP-triggered immunity (PTI). This immunity is depicted in the zigzag model (57) as being incomplete. Therefore, it differs from the term immunity as used in plant resistance screens, in which immunity refers to the absence of symptoms. In compatible plant-pathosystems, effectors that target specific regulatory components of the basal defense system may suppress basal defense components (26, 50) or may improve access to nutrients (36) to variable degrees, depending on

the compatibility between effector and plant target (84). Such effectors may be recognized by an NB-LRR (nucleotide binding–leucine rich repeat) receptor in the plant and trigger a defense response called elicitor-triggered immunity (ETI) (57). The definition of basal resistance was later circumscribed as resistance that is activated by virulent pathogens on susceptible hosts (57), i.e., host plants in which effectors suppress, to some extent, PAMP-triggered defense. Such a (partial) suppression of PTI by effectors is called effector-triggered susceptibility (ETS). The part of PTI that is not suppressed by the effector complement of a pathogen is called basal resistance. Because ETI may be quantitative as well, Jones & Dangl (57) considered the best definition of basal resistance to be PTI plus weak ETI minus ETS. If the effectors of a pathogen are ineffective on a certain plant species, PTI is not suppressed and no infection takes place (25, 57). Thus, nonhost and basal resistance represent the same defense mechanisms. Nonhost resistance may represent complete failure of the pathogen to suppress PTI and QR a partial failure to suppress PTI (50, 84).

Elicitor-triggered immunity (ETI): plant defense triggered by recognition of an effector by a plant receptor

Effector-triggered susceptibility (ETS): the enhanced infection of a plant due to the action of effectors

The definition of basal resistance is therefore based on a hypothetical concept. For the large majority of plant-pathosystems where QR has been reported, it remains unproven whether this concept applies. Authors referring to a QR in their plant-pathosystem as basal resistance imply that they assume the resistance is due to incomplete ETS (or incompletely suppressed PTI) rather than based on constitutive defense components.

MECHANISMS UNDERLYING QUANTITATIVE RESISTANCE

Methods to Discover Genes Underlying Quantitative Resistance

Defense of plants to pathogens is usually considered multilayered. This implies that defense mechanisms are very diverse and can interfere with any of the subsequent development stages of the pathogen, i.e., spore deposition, spore germination, stoma penetration, cell wall penetration, colonization, and spore production and release (reviewed in 85). QR can be characterized at microscopic levels, where cell wall penetration and subsequent haustorium formation usually turn out to be the most critical development stages in which plant defense interferes (85, 107, 113). In monocyclic disease screens, epidemiological parameters such as LP, lesion growth, infection frequency, and sporulation rate are commonly used, and depending on the plant-pathosystem, one or more of these components are good predictors of relative severity levels in polycyclic field screens. Distinct resistance components, such as LP and infection frequency, may be due to the very same defense factor, such as hampered haustorium formation (82).

In many plant-pathosystems, genetic factors contributing to QR have been mapped to QTLs by using either biparental mapping populations or, less frequently, collections of cultivars for association mapping. The picture emerges that there is a great abundance in minor-effect genes, located all over the genome, with each parental line contributing a different set of such genes (see section Is It Hard to Select for Quantitative Resistance?). Some QTLs with rather large effects may be chosen to be fine mapped and may eventually be cloned. This approach has met with relatively little success. Up to now, only four genes underlying QR to filamentous biotrophic pathogens have been reported (see below). Such cloning is the ultimate key to understanding the mechanisms underlying QR.

Other approaches are available to suggest candidate genes to explain QR. Colocalization of QTLs for QR implicated certain gene families such as peroxidases in barley (45, 111) and mutant forms of *mlo* genes and a pectate lyase–like protein, PMR6, in cucumber (109). For example, colocalization of expression QTLs with a genetically mapped QTL implied that a phospholipid hydroperoxide glutathione peroxidase (*HvPHGPx*) is a candidate for a QR gene in barley to

P. hordei (17). In general, this gene candidacy should be based on convergent evidence, ideally combining results from transcript profiling, genetic mapping, association genetics, and transient gene silencing or transient enhanced gene expression (28), as occurred with *WIR1* genes in QR of barley to barley powdery mildew. These genes are highly expressed in pathogen-attacked plants, but their relevance for plant defense is unknown (28).

Role of Defense Genes and Effectors in Quantitative Resistance

There are several arguments that support the hypothesis that much QR is due to variation in defense genes. Variants may lead to higher QR because they are expressed at higher levels or with more effective timing. Other defense gene variants may be more difficult to manipulate by effectors. These arguments are presented and discussed below.

Defense genes contribute to quantitative resistance. A simple hypothesis on the molecular basis of QR is to presume that plant genotypes are likely to have allelic variation of defense-related genes, leading to variations in expression patterns and intensities and modes of defense reactions. Some allelic variants may be more effective in defense than others, or may be expressed at higher levels or with more effective timing, causing QR variation between accessions of a plant species. QR of rice to the rice blast fungal pathogen *Magnaporthe oryzae*, for example, has been found to be highly correlated with the expression level of defense-related genes before infection and only weakly with the induction of such genes in infected tissue (126). The authors conclude that constitutive expression of defense-related genes is likely to be responsible for a large part of QR to blast in rice. They identified two positive regulators, HSF23 and CaMBP, that strongly increase preformed defense, and they identified one negative regulator, OB-fold (47). Because induction by PAMPs or MAMPs is not involved, this QR would not represent basal resistance sensu Jones & Dangl (57).

Natural selection seems to favor the most effective defense and the highest levels of expression of such genes, unless there are negative trade-offs. Interesting trade-offs have been reported for defense-related genes in barley, where near-isogenic lines with strong resistance to powdery mildew due to *mlo* had increased susceptibility to *Ramularia* leaf spot (76) and rice blast (53). In *Arabidopsis thaliana*, knockout lines of *At*AGD5 showed higher penetration rates than wild-type plants to the nonadapted powdery mildew pathogen *Erysiphe pisi* but decreased sporulation rates to the downy mildew pathogen *Hyaloperonospora arabidopsidis* (108).

Effectors can target plant defense genes. Biotrophic pathogens are under pressure to interfere with immune responses or to reprogram host metabolism in favor of pathogens' growth and reproduction. To this end, they deliver an arsenal of effectors into the apoplast and cytoplasm (26, 43, 50, 87). Many of these effectors are supposed to function to suppress PTI responses (25). Niks & Marcel (84) hypothesized that the molecular mechanism by which effectors specifically interact with their target in the plant is based on recognition or lack thereof of motifs in the target genes, their regulatory regions, or gene products, which results in altered expression levels of those genes or altered function efficiency of the gene products (**Figure 2**). In this scenario, the structural or sequence variations in the effector's plant targets are necessary to explain variation in QR. This hypothesis is consistent with the finding that QR may be isolate specific and based on minor gene–for–minor gene interactions (46, 95), which would justify considering QR as basal resistance. Consequently, plant targets of pathogen effectors are relevant candidate genes to contribute to QR, and the identification of those targets may help to unravel its genetic basis and mechanisms. The following examples provide evidence of the functional link between the genes

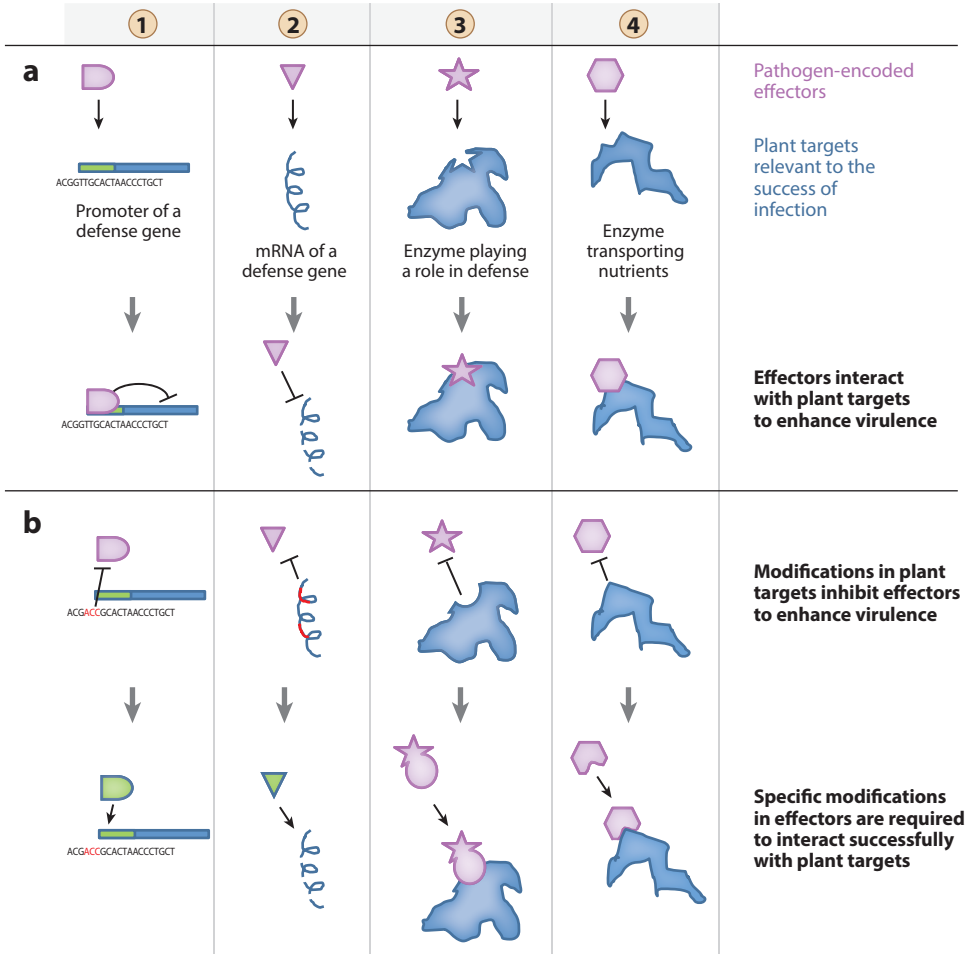

Figure 2

(*a*) Schematic representation of hypothetical suppression of plant defense and enhanced nutrient supply by effector-target interaction. Four hypothetical effectors: ① interacting with some promoter of a plant defense gene, ② splicing some transcript of a defense gene, ③ interacting with a defense protein, and ④ interacting with nutrient transporter. Effectors 1 to 3 suppress some aspect of the defense, enhancing virulence of the pathogen, effector 4 manipulates nutrient transport to the pathogen's benefit. (*b*) Hypothetical co-evolution, in which plants may modify ① a promoter sequence, ② a sequence in the coding region, or ③,④ a protein structure involved in plant defense or nutrient transport to evade manipulation by an effector but that does not affect the function of the plant protein; the pathogen effector needs a very particular adaptation to restore capacity to manipulate plant defense ①, ②, ③ and nutrient supply ④. Abbreviation: mRNA, messenger RNA.

involved in plant defense and the genes targeted by pathogens' effectors, and how these genes could explain QR. In **Table 2**, we present examples of targets of effectors from fungal and oomycete pathogens illustrative of the broad range of mechanisms used by filamentous pathogens to promote infection. In particular, effectors may interfere with gene families known to be involved in PTI, such as pathogenesis-related proteins (PRs), e.g., the PR-9 (peroxidases) and PR-17 families; genes involved in plant-immunity signaling, e.g., the MAP3Ks; and in plant immunity response, e.g., the papain-like cysteine proteases (PLCPs) and the catalases. Prehaustorial or penetration resistance

Table 2 Several effector targets from fungal and oomycete pathogens with information on their method of identification, function, and diversity

Effector target	Target function	Host plant	Effector name	Effector function	Pathogen species	Target identification method(s)	Target role in defense	Functional characterization method(s)	Target diversity	Reference(s)
Chitin (pathogen target)	Major structural component of fungal cell walls	Tomato	Avr4	Chitin-binding lectin that protects fungal cell walls against hydrolysis by plant chitinases	*Cladosporium fulvum*	Affinity precipitation assay	Fungal PAMP-triggering host immunity	Not relevant	Not relevant	122, 123
Chitin (pathogen target)	Major structural component of fungal cell walls	Tomato	Ecp6	Sequesters chitin oligosaccharides that are released from the cell walls of invading hyphae	*C. fulvum*	Affinity precipitation assay	Fungal PAMP-triggering host immunity	Not relevant	Not relevant	24
RCR3/PIP1	Papain-like cysteine proteases (PLCPs)	Tomato	Avr2	Inhibits several Cys proteases required for plant basal defense	*C. fulvum*	Protease activity profiling, coimmuno-precipitation	RCR3 plays a positive role in defense and is essential for the function of the tomato resistance gene *Cf-2*	Isogenic tomato mutant	RCR3 and PIP1 are under strong diversifying selection; RCR3 is under additional adaptive selection	105, 112, 115, 125
C14	PLCP	Potato	EPIC1/ EPIC2B[a]	Bind and inhibit proteases secreted in the apoplast	*Phytophthora infestans*	Protease activity profiling, coimmuno-precipitation	C14 plays a positive role in plant immunity	Stable RNAi and transient overexpression in tobacco	Under conservative selection in wild tomato species but diversifying selection in wild potato species	61, 115
C14	PLCP	Potato	Avrblb2	Neutralizes the secreted host defense proteases by preventing their secretion into the apoplast	*P. infestans*	In planta coimmuno-precipitation	C14 plays a positive role in plant immunity	(see above)	(see above)	12

CMPG1	U-box E3 ligase, required for infestin1 (INF1)-triggered cell death (ICD)	Potato	Avr3a	Stabilizes the plant E3 ligase CMPG1 to prevent PCD	*P. infestans*	Y2H screen	CMPG1 plays a dual role in positively contributing to PAMP-triggered immunity but also in facilitating the necrotrophic phase of *P. infestans* infection	VIGS in tobacco	ND	11, 42
MAPKKKε	Positive regulator of cell death	Tobacco	PexRD2	Suppresses plant immunity–related signaling	*P. infestans*	Y2H screen	MAPKKKε plays a positive role in plant immunity	VIGS in tobacco	ND	63
NbCAT1/ GmCAT1	Catalases	Tobacco, soy bean	PsCRN63/ PsCRN115	PsCRN63/PsCR115 interact in opposing manners to regulate H_2O_2 homeostasis and PCD	*Phytophthora sojae*	In planta coimmunoprecipitation	Catalases positively regulate plant resistance to *Phytophthora* pathogens	VIGS in tobacco	ND	132
APIP6	RING E3 ubiquitin ligase	Rice	AvrPiz-t	Suppresses BAX-induced PCD; suppresses flg22- and chitin-induced generation of ROS	*Magnaporthe oryzae*	Y2H screen	APIP6 plays a positive role in plant immunity	Stable RNAi in rice	ND	88
POX12	Class III peroxidase of the plant heme-dependent peroxidase superfamily	Maize	Pep1	Inhibitor of plant peroxidase activity	*Ustilago maydis*	Transcriptional study, bimolecular fluorescence complementation (BiFC)	POX12 activity is required for penetration resistance	VIGS in maize	ND	48

(*Continued*)

Table 2 (*Continued*)

Effector target	Target function	Host plant	Effector name	Effector function	Pathogen species	Target identification method(s)	Target role in defense	Functional characterization method(s)	Target diversity	Reference(s)
*Zm*TTK1	Uncharacterized protein kinase controlling the activation of genes in the anthocyanin biosynthesis pathway	Maize	Tin2	Differentially perturbs anthocyanin and lignin biosynthesis	*U. maydis*	Y2H screen	ND	ND	ND	118
PR17c	Sustains the fungus at sites of secondary penetration	Barley	CSEP0055	Hamper penetration resistance	*Blumeria graminis* f. sp. *hordei*	Y2H screen	PR17c plays a positive role in plant immunity	TIGS and transient overexpression in barley	ND	134
*Hv*ARF-GAP/ *Hv*UBC	ADP-ribosylation factor GTPase-activating protein/ Ubiquitin-conjugating enzyme	Barley	BEC4	Interfere with host vesicle trafficking	*B. graminis* f. sp. *hordei*	Y2H screen	*At*AGD5 (*Arabidopsis thaliana* ortholog of *Hv*ARF-GAP) plays a positive role in defense to *Erysiphe pisi* but a negative role in defense to *Hyaloperonospora arabidopsidis*	*A. thaliana* T-DNA lines	ND	108

[a] RCR3 is also a target of EPIC1/EPIC2B, and PIP1 is a target of EPIC2B (119).

Abbreviations: ND, not determined; PCD, programmed cell death; ROS, reactive oxygen species; TIGS, transient induced gene silencing; VIGS, virus-induced gene silencing; Y2H, yeast two-hybrid.

mechanisms have repeatedly been associated with QR to biotrophic fungal pathogens such as cereal rusts and powdery mildews (19, 82). In this context, it is interesting that several of the identified effector targets are involved in preventing cell penetration by the fungus. For example, the barley PR17c protein localizes to papillae in response to *Bgh* infection and restricts the fungus at sites of secondary penetration. The *Bgh* effector CSEP0055 interacts with PR17c to effectively suppress this resistance (134). Host vesicle trafficking is also an important process required for the entry of *Bgh* into barley epidermal cells (20). The *Bgh* effector BEC4 targets the barley *Hv*ARF-GAP and *Hv*UBC proteins to interfere with host vesicle trafficking and most likely restricts host cell entry and haustorium formation (108). The maize peroxidase POX12 belongs to the class III peroxidases of the plant heme-dependent peroxidase superfamily. POX12 is targeted by the fungal effector protein PEP1 during the biotrophic interaction *Ustilago maydis* (corn smut)–maize (48). The PEP1 protein is essential for fungal penetration of plant cell walls and functions as an inhibitor of apoplastic plant peroxidases. Peroxidases are important components of basal defense responses including the PAMP-triggered oxidative burst (96), and class III peroxidases have been genetically associated with QTLs for quantitative resistance of barley to fungi from the *Puccinia* and *Blumeria* genus (45, 111).

As additional evidence for the importance of effector-targeted genes to explain QR, a quantitative role in plant defense has been demonstrated for most of the effector-targeted genes listed in **Table 2**, whether through gene-silencing techniques aiming to induce RNA interference (RNAi) in plants (e.g., POX12 and PR17c) or through inoculating plant mutants predicted to encode nonfunctional protein variants of the genes of interest (e.g., *At*AGD5, which is orthologous to the barley gene *Hv*ARF-GAP).

Furthermore, effectors may not only attenuate defense reactions in plants but also enhance accessibility of nutrients and hence speed up colonization of plant tissue. An interesting example from bacteria is the transcription activator-like (TAL) effector *PthXo1* of *Xanthomonas oryzae* pv. *oryzae* that binds to the promoter region of the *Os*SWEET11 gene in rice to activate transcription of the gene. SWEET proteins transport glucose and sucrose across cell membranes. In rice mutants that have lost the TAL effector–binding element of the *Os*SWEET11 promoter, sugar supply becomes limiting to the pathogen and plants are phenotypically resistant (16). Because the mRNA levels of some SWEET family members are also elevated in powdery mildew–infected *Arabidopsis* (16), manipulation of sugar transport by effectors may also be part of the infection strategy of fungal pathogens.

Sequence variations in effector-targeted genes. Conceptual papers on PTI and ETI usually emphasize that the warfare between pathogens and plants involves basal resistance, and once this basal resistance is insufficient, making the plant species a host to the pathogen, the plant may recognize effectors through specific NB-LRR resistance proteins, leading to ETI (e.g., 26, 43, 57). It is generally recognized that the pathogen's capacity to suppress PTI depends on the plant species it attacks [one aspect to explain nonhost resistance (50, 57)], but very little attention is given to the possibility that within host species, plants differ in the ease by which effectors of a certain invading pathogen species or strain can suppress PTI.

If differences in QR between host accessions are due to differences in the degree to which the pathogen can suppress PTI, such differences in QR should result from variation in the effector targets among those host accessions. The tomato PLCPs RCR3 and PIP1 are targeted by several effectors from *Cladosporium fulvum* and are under strong diversifying selection, which is in agreement with the selection pressure exerted by the effectors on the sequence of those genes (112). A particular variant residue close to the substrate-binding groove of RCR3 affected its inhibition by the effector AVR2 and consequently conferred an adaptive advantage to this variant

(112). Another targeted PLCP, C14, is also under diversifying selection in wild potato species but under conservative selection in wild tomato species, indicating that potato pathogens are likely to exert a stronger selection pressure on this gene than tomato pathogens (61). Fabro et al. (34) identified HaRxLs candidate effectors of *H. arabidopsidis* that suppress callose deposition and increase susceptibility to *Pseudomonas syringae* pv. *tomato* DC3000. Many effectors did not confer enhanced virulence on all host accessions, suggesting that host targets had diversified and some target variants could evade interaction with the corresponding effectors.

Dong et al. (27) compared the capacity of *P. infestans* EPIC1 and *Phytophthora mirabilis* PmEPIC1 effectors to suppress their target PLCP, RCR3, from potato and tomato. RCR3 was inhibited by EPIC1, but was not at all or was much less inhibited by the PmEPIC1 from the nonadapted *P. mirabilis*. Conversely, the PmEPIC1 effector was more effective in inhibiting MRP2, which is an RCR3-like protease in *Mirabilis jalapa*, than the EPIC1 of *P. infestans*. *M. jalapa* is a nonhost to *P. infestans*. A single amino acid polymorphism in the host protease and a reciprocal single amino acid change in the pathogen effectors underpin this ecological diversification. This example strongly supports the hypothesis that adaptive sequence variations in effector targets may cause quantitative variations in resistance phenotypes.

Role of Susceptibility Genes in Quantitative Resistance

Plants have not only positive but also negative regulators of defense. Susceptibility genes (*S* genes) are dominant genes whose impairment leads to recessive resistance (97). Such recessive resistance genes have already been implicated in QR to filamentous pathogens; for example, several recessive QTLs control partial resistance to *Fusarium oxysporum* f. sp. *melonis* in melon (99), and the recessive QTL qSB11^{HJX74} confers resistance to the sheath blight disease caused by *Rhizoctonia solani* in rice (137). One of the few cloned genes for a resistance QTL is the recessive resistance gene *pi21* against rice blast (39; see also Cloned Genes for Quantitative Resistance, section below).

Another well-known recessive resistance gene is *mlo*, which confers a resistance that meets the definition of partial resistance (see section Resistance is Quantitative). Recessive *mlo* confers near-complete resistance to barley against *Bgh*. Interestingly, the tomato ortholog *Slmlo1* confers complete resistance to tomato against the powdery mildew *Oidium neolycopersici* (8, 9) but only reduces the susceptibility of tomato to the powdery mildew *Leveillula taurica* (136). The *Mlo* genes have approximately seven transmembrane domains and are located in the plasma membrane with an extracellular amino terminus and an intracellular carboxy terminus with a calmodulin-binding domain (62).

Schouten et al. (109) identified candidate *S* genes in cucumber, including *Mlo* homologs, for susceptibility to powdery mildew (caused *by Podosphaera fusca*) and downy mildew (caused by *Pseudoperonospora cubensis*) that may explain QTLs for recessively inherited resistance. Furthermore, the *A. thaliana MLO2* gene, a functional ortholog of barley *Mlo*, is required for the virulence function of the *P. syringae* effector *HopZ2* (67), supporting a role for effector-targeted genes in QR. It seems likely, therefore, that allelic differences in *S* genes may explain part of the QR of plants to biotrophic pathogens.

Cloned Genes for Quantitative Resistance

Recently, at least four genes for QR to biotrophic filamentous pathogens have been cloned, shedding light on the molecular mechanisms of this type of resistance.

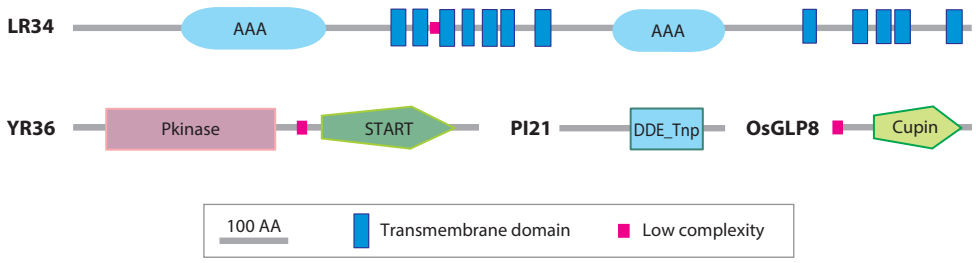

Figure 3

Functional domains of proteins involved in quantitative resistance. The protein secondary structure was predicted by using the Normal mode of SMART (**http://smart.embl-heidelberg.de/**). The PFAM (a database of protein families and domains) database for known structure and transmembrane domain prediction was used. Abbreviations: AA, amino acid; AAA, a variety of cellular activities associated with the ATPases; DDE-Tnp, DDE superfamily endonuclease; OsGLP, *Oryza sativa* germin-like protein; P Kinase, protein domain kinase; SMART, Simple Modular Architecture Research Tool; START, steroidogenic acute regulatory protein-related lipid transfer domain.

Lr34 resistance in wheat. The wheat gene *Lr34*, previously known as *LrT2* (29, 31), for QR to leaf rust (*P. triticina*) (32, 64), cosegregates with the adult plant resistance locus *Yr18* against wheat stripe rust (*Puccinia striiformis* f. sp. *tritici*) (*Pst*) (77, 114) and *Pm38* against powdery mildew (*Blumeria graminis* f. sp. *tritici*) (116). In certain genetic backgrounds, *Lr34* is also effective against stem rust (*Puccinia graminis* f. sp. *tritici*) (31). *Lr34/Yr18/Pm38* was mapped on chromosome 7D. Map-based cloning of this locus determined that a gene encoding an ATP-binding cassette (ABC) transporter is responsible for the QR to different pathogens. This ABC transporter gene is expressed at a very low level at the seedling stage but a much higher level at the adult plant stage before and after leaf tip necrosis, which agrees with the observation that *Lr34* confers higher resistance at the adult plant stage than at the seedling stage. Expression of *Lr34* was not induced by inoculation of wheat leaf rust, and there was no visible difference in expression between resistant and susceptible plants (64).

Wheat LR34 is an ABC transporter that belongs to the pleiotropic drug resistance subfamily, which includes also the cloning penetration-deficient gene 3 (*PEN3*) in *Arabidopsis* (64). The protein has two AAA (a variety of cellular activities associated with the ATPases) domains and two regions with hydrophobic transmembrane domains (**Figure 3**). LR34 may have a similar function as the *Arabidopsis* PEN3, which transports toxic compounds into the plant apoplast at the interaction sites with pathogens (68, 69). LR34 of the resistant cultivar Chinese Spring has a deletion of a phenylalanine residue compared with that of the susceptible French winter wheat cultivar Renan and a residual change from histidine to tyrosine in Renan. The amino acid deletion and substitution are located at the first transmembrane domain connecting the two nucleotide-binding domains. It is suspected that these changes could alter the structure and substrate specificity of LR34. Obviously, more precise functional studies of LR34 are required. The *Lr34* haplotype of Chinese Spring also occurs in Australian cultivar H45, but this cultivar is highly susceptible to *P. triticina* and *Pst*. However, H45 recovered its resistance to *Pst* when it was crossed with Avocet, which is also susceptible to *Pst*. This implies that the *Lr34* haplotype of Chinese Spring may interact with an unknown factor(s) to confer resistance (65).

***Puccinia striiformis* f. sp. *tritici* (*Pst*):** causes stripe rust on wheat

Yr36 resistance in wheat. *Yr36* is a temperature-dependent gene (38) that confers race-nonspecific partial resistance of wheat to stripe rust *Pst* at the adult plant (121) and seedling

stages (38) at relatively high temperature (approximately 25–35°C). *Yr36* was mapped on chromosome 6B in the tetraploid wheat *Triticum turgidum*. The cloned candidate gene was validated by analysis of mutants that were identified from a TILLING (targeting-induced local lesions in genomes) population of 1,536 mutagenized lines, and its function was confirmed through stable transformation of the gene into a susceptible wheat variety. Six alternative transcript variants were identified for *Yr36*. Transcript WKS1.1 encodes a protein with an N-terminal kinase domain and a predicted steroidogenic acute regulatory protein-related lipid transfer domain (START) at the C terminus; the other five transcripts lack exon 11 and encode proteins with truncated START domains. At high temperature, the functional transcript WKS1.1 is upregulated whereas the nonfunctional versions of WKS1.2 to WKS1.6 are downregulated. Transcript WKS1.1 was induced to higher levels during the first 3 days after inoculation of wheat stripe rust at high temperature but not at low temperature (38).

The YR36 protein contains both kinase and START domains (**Figure 3**). Studies in humans showed that proteins having the START domain are involved in lipid trafficking and sensing. The START domain proteins change their conformations when they bind with sterols and other small molecules (4). It is hypothesized that the START domain of YR36 has the ability to bind lipids from *Pst* at high temperature and to change its conformation, which may cause the kinase domain to initiate a signaling cascade leading to the observed programmed cell death (38). The kinase domain of YR36 has high similarity to several *Arabidopsis* cell wall–associated kinase (WAK)-like kinases and belongs to the non-arginine-aspartate (non-RD) kinases. This type of kinase is normally involved in the early steps of the innate immune response (23). Proteins containing both the kinase and START domains are not found in organisms other than wheat, and WKS1 was identified only in some wild tetraploid wheat accessions from Israel, Lebanon, and Syria. It was absent from all modern commercial varieties of pasta and bread wheat except from five hexaploid wheat cultivars (38).

Pi21 resistance in rice. In rice, many genes for QR to rice blast (*Magnaporthe oryzae*) have been mapped. *Pi21* mapped on rice chromosome 4, and its recessive allele *pi21* confers QR to rice blast (39). *Pi21* was fine mapped to gene *Os04g0401000* in a 1,705 bp DNA region. This gene encodes a protein containing a heavy metal–transport/detoxification protein domain in the N-terminal region (40). Two of the seven nucleotide polymorphisms in the 1,705 bp region among the resistant cultivar (Owarihatamochi) and the two susceptible cultivars (Aichiasahi and Kasalath) locate in the open reading frame of the candidate gene. Transfer by transformation of the resistance allele *pi21* from Owarihatamochi into susceptible cultivar Aichiasahi did not confer resistance, whereas transformation of the susceptibility allele *Pi21* (from Aichiasahi) into a NIL carrying *pi21* increased susceptibility to rice blast (40), suggesting that the resistance allele *pi21* carries a loss-of-function mutation. Silencing the expression of *Pi21* increases the resistance, indicating that the susceptibility allele *Pi21* suppresses the resistance and is therefore an *S* gene (see section Evidence for Susceptibility Genes). Transcript expression of *Pi21* responds to the inoculation of rice blast during 3 to 6 h; expression of pathogenesis-related genes is higher in the line carrying *pi21* than in the line carrying *Pi21*.

Rice PI21 is a small protein containing a transposase DDE_Tnp domain (**Figure 3**). It is predicted that this protein contains a heavy metal–transport/detoxification protein domain in the N-terminal region (40). The susceptible cultivars have the functional protein promoting infection, whereas cultivars and near-isogenic lines with two deletions of 18 and 48 bp in the coding sequence decrease infection by the rice blast fungus. This haplotype was found only in *japonica* rice cultivars. The deleted 18- and 48-bp sequences encode a motif sequence, PxxPxxP, that may be the core motif for protein-protein interaction in multicellular organisms (98).

***Oryza sativa* germin-like protein resistance in rice.** Another minor gene for QR to rice blast was also effective against rice sheath blight, which is caused by *Rhizoctonia solani* (72). This QTL colocalized with a cluster of 12 highly conserved oxalate oxidase-like genes known as germin-like protein (GLP)–based defense response genes. Transgenic plants in which RNAi silenced one or more of the GLP genes were more susceptible to *M. oryzae* and *R. solani*. Interestingly, the susceptibility level increased with the number of silenced GLP genes. This indicates that the GLP genes enhance disease resistance as a complex locus in which each gene contributes a small effect (72). GLPs belong to the functionally diverse cupin superfamily (**Figure 3**) and may be involved in plant defense responses. In barley, for example, functional analysis of GLPs indicated a complex role for GLPs in basal resistance to the barley powdery mildew fungus *Bgh*. Transient overexpression of four members of the GLP family enhanced resistance against *Bgh*, transient silencing of two other members also enhanced resistance, and transient silencing of a seventh member resulted in supersusceptibility (138). GLPs possess N-terminal secretory signals, suggesting a role in cell wall function or in defense against invading pathogens (138). The hypothetical function of the GLP proteins in disease resistance involves the production of superoxide dismutase, which generates hydrogen peroxide (H_2O_2) that might be involved in cell wall defense, in hypersensitive cell death, in signaling in systemic acquired resistance, and in the induction of defense-response gene expression (72).

Conclusions to be drawn from the cloned genes for quantitative resistance. Interestingly, all cloned genes for QR differ from the previously cloned *R*-genes for major-effect race-specific qualitative resistance and also differ from each other. The picture seems rather complex. The recently cloned gene *Rhg1* for QR of soybean to the cyst nematode *Heterodera glycines* illustrates that inheritance can even be more complex because it is based on the copy number of a set of three different genetically linked genes. The genes encode an amino acid transporter, an α-SNAP protein, and a protein with a WI12 (wound-inducible protein 12) region (21).

Single genes, multiple homologous genes, or multiple copies of multiple genes have been reported to be involved in QR. Transcripts of these genes may be inducible upon inoculation of pathogens or constitutively expressed. Two out of the four genes cloned thus far are effective against more than one pathogen. Of the four proteins for QR, one (LR34) is a transmembrane protein, and the other three are located outside of the cell membrane. Based on the functions of the limited number of the identified proteins, vesicle trafficking and protein/metabolite transportation are likely to be common physiological processes involved in QR.

Is a Unified Concept of Mechanisms for Quantitative Resistance to Biotrophic Filamentous Pathogens Possible?

From all the accumulated evidence, a myriad of strategies and options is clearly available for plants to defend themselves against biotrophic pathogens. Even though generalizations may not be warranted, it is possible to list some of the options that plants have in the coevolution with their pathogens, assuming a plant-pathosystem in which strong mutual selection pressure exists between the two partners. For each step, one or two references are given as examples of evidence.

1. Plants may adjust morphologically or phenologically to make it more difficult for the pathogen to reach susceptible plant tissue, germinate spores, or penetrate stomata (reviewed in 85).
2. Plants may increase the production of antimicrobial compounds, either constitutively or through perception of PAMPs (126), or develop more effective variants of those compounds.

The pathogen has to deal with many plant functions to infect and reproduce. If the pathogen is able to suppress only a fraction of the defense functions, the remaining effective functions will determine the level of QR of the plant.

3. Plants may evade the suppression (*a*) by evolving decoy targets of effectors (124); (*b*) by diversifying the target motif to prevent the effector from manipulating the plant gene expression to its benefit (34) (**Figure 2*b***); (*c*) by expanding and diversifying the number of members in the gene family, so that with its effector arsenal, the pathogen may not succeed in suppressing the activity of all the genes redundantly involved in the same function, as for the approximately 150 class III peroxidase genes (70); or (*d*) by developing NB-LRR receptors that initiate programmed cell death upon direct or indirect recognition of the cognate effector (78).
4. Pathogens may restore their original pathogenicity level on the host by adapting their effector arsenal, which involves a particular gain-of-function mutation (in options *a*–*c*, above) (**Figure 2*b***), or drop the particular cognate effector (loss-of-function mutation) to prevent the plant from initiating the programmed cell death response (option *d*, above).

Further studies are now required to link naturally occurring sequence variation in the plant genes targeted by pathogen effectors with phenotypic variation for the level of QR between plant genotypes. In the coming years, as more and more genes involved in basal defense pathways are expected to be identified, it will be of great interest to find out whether similar genes are found following positional cloning of resistance QTLs and whether expression of such genes may be differentially modified by pathogen effector variants.

DISCLOSURE STATEMENT

The authors are not aware of any affiliations, memberships, funding, or financial holdings that might be perceived as affecting the objectivity of this article.

ACKNOWLEDGMENTS

This work is supported by funds from the Ministry of Science and Technology (grant no. 2011CB100700) and the National Natural Science Foundation (grant no. 31471756) of China. We thank Johan Bucher and Anton Vels (WUR) for their help in preparing **Video 1**. We acknowledge the help of Freddy Yeo in preparing part of the text of this article.

LITERATURE CITED

1. Aghnoum R, Marcel TC, Johrde A, Pecchioni N, Schweizer P, Niks RE. 2010. Basal resistance of barley to barley powdery mildew: connecting QTLs and candidate genes. *Mol. Plant-Microbe Interact.* 23:91–102
2. Aghnoum R, Niks RE. 2010. Specificity and levels of nonhost resistance of barley to nonadapted *Blumeria graminis* forms. *New Phytol.* 185:275–84
3. Aghnoum R, Niks RE. 2011. Transgressive segregation for very low and high levels of basal resistance to powdery mildew in barley. *J. Plant Physiol.* 168:45–50
4. Alpy F, Tomasetto C. 2005. Give lipids a START: the StAR-related lipid transfer (START) domain in mammals. *J. Cell Sci.* 118:2791–801
5. Andrivon D, Pilet F, Montarry J, Hafidi M, Corbière R, et al. 2007. Adaptation of *Phytophthora infestans* to partial resistance in potato: evidence from French and Moroccan populations. *Phytopathology* 97:338–43
6. Arru L, Francia E, Pecchioni N. 2003. Isolate-specific QTLs of resistance to leaf stripe (*Pyrenophora graminea*) in the "Steptoe" × "Morex" spring barley cross. *Theor. Appl. Genet.* 106:668–75

7. Azzimonti G, Marcel TC, Robert OPS, Lannou C, Paillard S, Goyeau H. 2014. Diversity, specificity and impacts on field epidemics of QTLs involved in components of quantitative resistance in the wheat leaf rust pathosystem. *Mol. Breed.* 34:549–67
8. Bai Y, Pavan S, Zheng Z, Zappel NF, Reinstädler A, et al. 2008. Naturally occurring broad-spectrum powdery mildew resistance in a central american tomato accession is caused by loss of *Mlo* function. *Mol. Plant-Microbe Interact.* 21:30–39
9. Bai Y, van der Hulst R, Bonnema G, Marcel TC, Meijer-Dekens F, et al. 2005. Tomato defense to *Oidium neolycopersici*: dominant *Ol* genes confer isolate-dependent resistance via a different mechanism than recessive *ol-2*. *Mol. Plant-Microbe Interact.* 18:354–62
10. Barilli E, Sillero JC, Fernández-Aparicio M, Rubiales D. 2009. Identification of resistance to *Uromyces pisi* (Pers.) Wint. in *Pisum* spp. germplasm. *Field Crops Res.* 114:198–203
11. Bos JIB, Armstrong MR, Gilroy EM, Boevink PC, Hein I, et al. 2010. *Phytophthora infestans* effector AVR3a is essential for virulence and manipulates plant immunity by stabilizing host E3 ligase CMPG1. *PNAS* 107:9909–14
12. Bozkurt TO, Schornack S, Win J, Shindo T, Ilyas M, et al. 2011. *Phytophthora infestans* effector AVRblb2 prevents secretion of a plant immune protease at the haustorial interface. *PNAS* 108:20832–37
13. Broers LHM, Jacobs T. 1989. The inheritance of host plant effect on latency period of wheat leaf rust in spring wheat. II. Number of segregating factors and evidence for transgressive segregation in F3 and F5 generations. *Euphytica* 44:207–14
14. Cao XH, Zhou JH, Gong XP, Zhao GY, Jia JZ, et al. 2012. Identification and validation of a major quantitative trait locus for slow-rusting resistance to stripe rust in wheat. *J. Integr. Plant Biol.* 54:330–44
15. Chen H, Wang S, Xing Y, Xu C, Hayes PM, et al. 2003. Comparative analyses of genomic locations and pathotype specificities of loci for quantitative resistance to *Pyricularia grisea* in rice and barley. *PNAS* 100:2544–49
16. Chen LQ, Hou BH, Lalonde S, Takanaga H, Hartung ML, et al. 2010. Sugar transporters for intercellular exchange and nutrition of pathogens. *Nature* 468:527–32
17. Chen XW, Hackett CA, Niks RE, Hedley PE, Booth C, et al. 2010. An eQTL analysis of partial resistance to *Puccinia hordei* in barley. *PLOS ONE* 5:e8598
18. Chowdhury ABMNU, Bremer GB, Salt DW, Miller P, Ford MG. 2003. A method of delivering *Blumeria graminis* f. sp. *hordei* spores for laboratory experiments. *Crop Prot.* 22:917–22
19. Collins NC, Niks RE, Schulze-Lefert P. 2007. Resistance to cereal rusts at the plant cell wall—what can we learn from other host-pathogen systems? *Aust. J. Agric. Res.* 58:476–89
20. Collins NC, Thordal-Christensen H, Lipka V, Bau S, Kombrink E, et al. 2003. SNARE-protein-mediated disease resistance at the plant cell wall. *Nature* 425:973–77
21. Cook DE, Lee TG, Guo X, Melito S, Wang K, et al. 2012. Copy number variation of multiple genes at *Rhg1* mediates nematode resistance in soybean. *Science* 338:1206–9
22. Dangl JL, Jones JDG. 2001. Plant pathogens and integrated defence responses to infection. *Nature* 411:826–33
23. Dardick C, Ronald P. 2006. Plant and animal pathogen recognition receptors signal through non-RD kinases. *PLOS Pathog.* 2:e2
24. de Jonge R, van Esse HP, Kombrink A, Shinya T, Desaki Y, et al. 2010. Conserved fungal LysM effector *Ecp6* prevents chitin-triggered immunity in plants. *Science* 329:953–55
25. Dodds PN, Rathjen JP. 2010. Plant immunity: towards an integrated view of plant-pathogen interactions. *Nat. Rev. Genet.* 11:539–48
26. Doehlemann G, Hemetsberger C. 2013. Apoplastic immunity and its suppression by filamentous plant pathogens. *New Phytol.* 198:1001–16
27. Dong S, Stam R, Cano LM, Song J, Sklenar J, et al. 2014. Effector specialization in a lineage of the Irish potato famine pathogen. *Science* 343:552–55
28. Douchkov D, Johrde A, Nowara D, Himmelbach A, Lueck S, et al. 2011. Convergent evidence for a role of WIR1 proteins during the interaction of barley with the powdery mildew fungus *Blumeria graminis*. *J. Plant Physiol.* 168:20–29
29. Dyck PL. 1977. Genetics of leaf rust reaction in three introductions of common wheat. *Can. J. Genet. Cytol.* 19:711–16

30. Dyck PL. 1979. Identification of the gene for adult plant leaf rust resistance in Thatcher. *Can. J. Plant Sci.* 59:499–501
31. Dyck PL. 1987. The association of a gene for leaf rust resistance with the chromosome 7D suppressor of stem rust resistance in common wheat. *Genome* 29:467–69
32. Dyck PL, Samborski DJ, Anderson RG. 1966. Inheritance of adult-plant leaf rust resistance derived from the common wheat varieties Exchange and Frontana. *Can. J. Genet. Cytol.* 8:665–71
33. Eyal Z, Clifford BC, Caldwell RM. 1968. A settling tower for quantitative inoculation of leaf blades of mature small grain plants with urediospores. *Phytopathology* 58:530–31
34. Fabro G, Steinbrenner J, Coates M, Ishaque N, Baxter L, et al. 2011. Multiple candidate effectors from the oomycete pathogen *Hyaloperonospora arabidopsidis* suppress host plant immunity. *PLOS Pathog.* 7:e1002348
35. Fernández-Aparicio M, Barilli E, Mansilla F, Rubiales D. 2011. Identification and characterisation of resistance against rust (*Puccinia allii*) in garlic (*Allium* sp.) germplasm. *Ann. Appl. Biol.* 159:93–98
36. Fernandez J, Wilson RA. 2012. Why no feeding frenzy? Mechanisms of nutrient acquisition and utilization during infection by the rice blast fungus *Magnaporthe oryzae*. *Mol. Plant-Microbe Interact.* 25:1286–93
37. Franckowiak JD, Jin Y, Steffenson BJ. 1997. Recommended allele symbols for leaf rust resistance genes in barley. *Barley Genet. Newsl.* 27:36–44
38. Fu D, Uauy C, Distelfeld A, Blechl A, Epstein L, et al. 2009. A kinase-START gene confers temperature-dependent resistance to wheat stripe rust. *Science* 323:1357–60
39. Fukuoka S, Okuno K. 2001. QTL analysis and mapping of *pi21*, a recessive gene for field resistance to rice blast in Japanese upland rice. *Theor. Appl. Genet.* 103:185–90
40. Fukuoka S, Saka N, Koga H, Ono K, Shimizu T, et al. 2009. Loss of function of a proline-containing protein confers durable disease resistance in rice. *Science* 325:998–1001
41. Geffroy V, Sevignac M, De Oliveira JCF, Fouilloux G, Skroch P, et al. 2000. Inheritance of partial resistance against *Colletotrichum lindemuthianum* in *Phaseolus vulgaris* and co-localization of quantitative trait loci with genes involved in specific resistance. *Mol. Plant-Microbe Interact.* 13:287–96
42. Gilroy EM, Taylor RM, Hein I, Boevink P, Sadanandom A, et al. 2011. CMPG1-dependent cell death follows perception of diverse pathogen elicitors at the host plasma membrane and is suppressed by *Phytophthora infestans* RXLR effector AVR3a. *New Phytol.* 190:653–66
43. Giraldo MC, Valent B. 2013. Filamentous plant pathogen effectors in action. *Nat. Rev. Microbiol.* 11:800–14
44. Glazebrook J. 2001. Genes controlling expression of defense responses in Arabidopsis—2001 status. *Curr. Opin. Plant Biol.* 4:301–8
45. González AM, Marcel TC, Kohutova Z, Stam P, van der Linden CG, et al. 2010. Peroxidase profiling reveals genetic linkage between peroxidase gene clusters and basal host and non-host resistance to rusts and mildew in barley. *PLOS ONE* 5:e10495
46. González AM, Marcel TC, Niks RE. 2012. Evidence for a minor gene–for–minor gene interaction explaining nonhypersensitive polygenic partial disease resistance. *Phytopathology* 102:1086–93
47. Grand X, Espinoza R, Michel C, Cros S, Chalvon V, et al. 2012. Identification of positive and negative regulators of disease resistance to rice blast fungus using constitutive gene expression patterns. *Plant Biotechnol. J.* 10:840–50
48. Hemetsberger C, Herrberger C, Zechmann B, Hillmer M, Doehlemann G. 2012. The *Ustilago maydis* effector Pep1 suppresses plant immunity by inhibition of host peroxidase activity. *PLOS Pathog.* 8:e1002684
49. Hickey LT, Lawson W, Platz GJ, Dieters M, Franckowiak J. 2012. Origin of leaf rust adult plant resistance gene *Rph20* in barley. *Genome* 55:396–99
50. Ingle RA, Carstens M, Denby KJ. 2006. PAMP recognition and the plant-pathogen arms race. *BioEssays* 28:880–89
51. Jafary H, Albertazzi G, Marcel TC, Niks RE. 2008. High diversity of genes for nonhost resistance of barley to heterologous rust fungi. *Genetics* 178:2327–39
52. Jafary H, Szabo LJ, Niks RE. 2006. Innate nonhost immunity in barley to different heterologous rust fungi is controlled by sets of resistance genes with different and overlapping specificities. *Mol. Plant-Microbe Interact.* 19:1270–79

53. Jarosch B, Kogel KH, Schaffrath U. 1999. The ambivalence of the barley *Mlo* locus: mutations conferring resistance against powdery mildew (*Blumeria graminis* f. sp. *hordei*) enhance susceptibility to the rice blast fungus *Magnaporthe grisea*. *Mol. Plant–Microbe Interact.* 12:508–14
54. Johnson R. 1981. Durable resistance: definition of, genetic control, and attainment in plant breeding. *Phytopathology* 71:567–68
55. Johnston PA, Niks RE, Meiyalaghan V, Blanchet E, Pickering RA. 2013. *Rph22*: mapping of a novel leaf rust resistance gene introgressed from the non-host *Hordeum bulbosum* L. into cultivated barley (*Hordeum vulgare* L.). *Theor. Appl. Genet.* 126:1613–25
56. Jones IT. 1983. Transgressive segregation for enhanced level of adult plant resistance to mildew in the oat cross Mostyn × Maldwyn. *Euphytica* 32:499–503
57. Jones JDG, Dangl JL. 2006. The plant immune system. *Nature* 444:323–29
58. Jorge V, Dowkiw A, Faivre-Rampant P, Bastien C. 2005. Genetic architecture of qualitative and quantitative *Melampsora larici-populina* leaf rust resistance in hybrid poplar: genetic mapping and QTL detection. *New Phytol.* 167:113–27
59. Jørgensen JH, Mortensen K. 1977. Primary infection by *Erysiphe graminis* f. sp. *hordei* of barley mutants with resistance genes in the *ml-o* locus. *Phytopathology* 67:678–85
60. Jørgensen LN, Hovmøller MS, Hansen JG, Lassen P, Clark B, et al. 2014. IPM strategies and their dilemmas including an introduction to **www.eurowheat.org**. *J. Integr. Agric.* 13:265–81
61. Kaschani F, Shabab M, Bozkurt T, Shindo T, Schornack S, et al. 2010. An effector-targeted protease contributes to defense against *Phytophthora infestans* and is under diversifying selection in natural hosts. *Plant Physiol.* 154:1794–804
62. Kim MC, Panstruga R, Elliott C, Muller J, Devoto A, et al. 2002. Calmodulin interacts with MLO protein to regulate defence against mildew in barley. *Nature* 416:447–51
63. King SRF, McLellan H, Boevink PC, Armstrong MR, Bukharova T, et al. 2014. *Phytophthora infestans* RXLR effector PexRD2 interacts with host MAPKKKε to suppress plant immune signaling. *Plant Cell* 26:1345–59
64. Krattinger SG, Lagudah ES, Spielmeyer W, Singh RP, Huerta-Espino J, et al. 2009. A putative ABC transporter confers durable resistance to multiple fungal pathogens in wheat. *Science* 323:1360–63
65. Lagudah ES. 2011. Molecular genetics of race non-specific rust resistance in wheat. *Euphytica* 179:81–91
66. Leach JE, Cruz CMV, Bai JF, Leung H. 2001. Pathogen fitness penalty as a predictor of durability of disease resistance genes. *Annu. Rev. Phytopathol.* 39:187–224
67. Lewis J, Wan J, Ford R, Gong Y, Fung P, et al. 2012. Quantitative interactor screening with next-generation sequencing (QIS-Seq) identifies *Arabidopsis thaliana* MLO2 as a target of the *Pseudomonas syringae* type III effector HopZ2. *BMC Genomics* 13:8
68. Lipka U, Fuchs R, Lipka V. 2008. *Arabidopsis* non-host resistance to powdery mildews. *Curr. Opin. Plant Biol.* 11:404–11
69. Lipka U, Fuchs R, Kuhns C, Petutsching E, Lipka V. 2010. Live and let die—Arabidopsis nonhost resistance to powdery mildews. *Eur. J. Cell Biol.* 89:194–99
70. Lüthje S, Meisrimler C-N, Hopff D, Möller B. 2011. Phylogeny, topology, structure and functions of membrane-bound class III peroxidases in vascular plants. *Phytochemistry* 72:1124–35
71. Mackey D, McFall AJ. 2006. MAMPs and MIMPs: proposed classifications for inducers of innate immunity. *Mol. Microbiol.* 61:1365–71
72. Manosalva PM, Davidson RM, Liu B, Zhu X, Hulbert SH, et al. 2009. A germin-like protein gene family functions as a complex quantitative trait locus conferring broad-spectrum disease resistance in rice. *Plant Physiol.* 149:286–96
73. Marcel TC, Gorguet B, Truong TAM, Kohutova Z, Vels A, Niks RE. 2008. Isolate specificity of quantitative trait loci for partial resistance of barley to *Puccinia hordei* confirmed in mapping populations and near-isogenic lines. *New Phytol.* 177:743–55
74. Marcel TC, Varshney R, Barbieri M, Jafary H, de Kock M, et al. 2007. A high-density consensus map of barley to compare the distribution of QTLs for partial resistance to *Puccinia hordei* and of defence gene homologues. *Theor. Appl. Genet.* 114:487–500
75. McDonald BA, Linde C. 2002. Pathogen population genetics, evolutionary potential, and durable resistance. *Annu. Rev. Phytopathol.* 40:349–79

76. McGrann GRD, Stavrinides A, Russell J, Corbitt MM, Booth A, et al. 2014. A trade off between *mlo* resistance to powdery mildew and increased susceptibility of barley to a newly important disease, *Ramularia* leaf spot. *J. Exp. Bot.* 65:1025–37
77. McIntosh RA. 1992. Close genetic linkage of genes conferring adult-plant resistance to leaf rust and stripe rust in wheat. *Plant Pathol.* 41:523–27
78. Michelmore RW, Christopoulou M, Caldwell KS. 2013. Impacts of resistance gene genetics, function, and evolution on a durable future. *Annu. Rev. Phytopathol.* 51:291–319
79. Miclot AS, Wiedemann-Merdinoglu S, Duchêne E, Merdinoglu D, Mestre P. 2012. A standardised method for the quantitative analysis of resistance to grapevine powdery mildew. *Eur. J. Plant Pathol.* 133:483–95
80. Mundt CC. 2014. Durable resistance: a key to sustainable management of pathogens and pests. *Infect. Genet. Evol.* 27:446–55
81. Naerstad R, Hermansen A, Bjor T. 2007. Exploiting host resistance to reduce the use of fungicides to control potato late blight. *Plant Pathol.* 56:156–66
82. Niks RE. 1986. Failure of haustorial development as a factor in slow growth and development of *Puccinia hordei* in partially resistant barley seedlings. *Physiol. Mol. Plant Pathol.* 28:309–22
83. Niks RE, Kuiper HJ. 1983. Histology of the relation between minor and major genes for resistance of barley to leaf rust. *Phytopa-thology* 73:55–59
84. Niks RE, Marcel TC. 2009. Nonhost and basal resistance: how to explain specificity? *New Phytol.* 182:817–28
85. Niks RE, Rubiales D. 2002. Potentially durable resistance mechanisms in plants to specialised fungal pathogens. *Euphytica* 124:201–16
86. Niks RE, Walther U, Jaiser U, Martínez F, Rubiales D, et al. 2000. Resistance against barley leaf rust (*Puccinia hordei*) in West-European spring barley germplasm. *Agronomie* 20:769–82
87. Ökmen B, Doehlemann G. 2014. Inside plant: biotrophic strategies to modulate host immunity and metabolism. *Curr. Opin. Plant Biol.* 20:19–25
88. Park C-H, Chen S, Shirsekar G, Zhou B, Khang CH, et al. 2012. The *Magnaporthe oryzae* effector AvrPiz-t targets the RING E3 ubiquitin ligase APIP6 to suppress pathogen-associated molecular pattern–triggered immunity in rice. *Plant Cell* 24:4748–62
89. Parlevliet JE. 1978. Race-specific aspects of polygenic resistance of barley to leaf rust, *Puccinia hordei*. *Neth. J. Plant Pathol.* 84:121–26
90. Parlevliet JE. 1979. Components of resistance that reduce the rate of epidemic development. *Annu. Rev. Phytopathol.* 17:203–22
91. Parlevliet JE, Leijn M, van Ommeren A. 1985. Accumulating polygenes for partial resistance in barley to barley leaf rust, *Puccinia hordei*. II. Field evaluation. *Euphytica* 34:15–20
92. Parlevliet JE, Lindhout WH, van Ommeren A, Kuiper HJ. 1980. Level of partial resistance to leaf rust *Puccinia hordei*, in West-European barley and how to select for it. *Euphytica* 29:1–8
93. Parlevliet JE, van Ommeren A. 1975. Partial resistance of barley to leaf rust, *Puccinia hordei*. II. Relationship between field trials, micro plot tests and latent period. *Euphytica* 24:293–303
94. Parlevliet JE, van Ommeren A. 1988. Accumulation of partial resistance in barley to barley leaf rust and powdery mildew through recurrent selection against susceptibility. *Euphytica* 37:261–74
95. Parlevliet JE, Zadoks JC. 1977. The integrated concept of disease resistance: a new view including horizontal and vertical resistance in plants. *Euphytica* 26:5–21
96. Passardi F, Cosio C, Penel C, Dunand C. 2005. Peroxidases have more functions than a Swiss army knife. *Plant Cell Rep.* 24:255–65
97. Pavan S, Jacobsen E, Visser RGF, Bai Y. 2010. Loss of susceptibility as a novel breeding strategy for durable and broad-spectrum resistance. *Mol. Breed.* 25:1–12
98. Pawson T. 1995. Protein modules and signalling networks. *Nature* 373:573–80
99. Perchepied L, Dogimont C, Pitrat M. 2005. Strain-specific and recessive QTLs involved in the control of partial resistance to *Fusarium oxysporum* f. sp. *melonis* race 1.2 in a recombinant inbred line population of melon. *Theor. Appl. Genet.* 111:65–74
100. Poland JA, Balint-Kurti PJ, Wisser RJ, Pratt RC, Nelson RJ. 2009. Shades of gray: the world of quantitative disease resistance. *Trends Plant Sci.* 14:21–29

101. Qi X, Fufa F, Niks RE, Lindhout P, Stam P. 2000. The evidence for abundance of QTLs for partial resistance to *Puccinia hordei* on the barley genome. *Mol. Breed.* 6:1–9
102. Qi X, Jiang GL, Chen WQ, Niks RE, Stam P, et al. 1999. Isolate-specific QTLs for partial resistance to *Puccinia hordei* in barley. *Theor. Appl. Genet.* 99:877–84
103. Qi X, Niks RE, Stam P, Lindhout P. 1998. Identification of QTLs for partial resistance to leaf rust (*Puccinia hordei*) in barley. *Theor. Appl. Genet.* 96:1205–15
104. Roderick HW, Jones IT. 1991. The evaluation of adult plant resistance to powdery mildew (*Erysiphe graminis* f. sp. *avenae*) in transgressive lines of oats. *Euphytica* 53:143–49
105. Rooney HCE, van't Klooster JW, van der Hoorn RAL, Joosten MHAJ, Jones JDG, et al. 2005. *Cladosporium* Avr2 inhibits tomato Rcr3 protease required for *Cf-2*-dependent disease resistance. *Science* 308:1783–86
106. Rubiales D, Niks RE. 1995. Characterization of *Lr34*, a major gene conferring nonhypersensitive resistance to wheat leaf rust. *Plant Dis.* 79:1208–12
107. Rubiales D, Fondevilla S, Chen W, Gentzbittel L, Higgins TJV, et al. 2015. Achievements and challenges in legume breeding for pest and disease resistance. *Crit. Rev. Plant Sci.* 34:195–236
108. Schmidt SM, Kuhn H, Micali C, Liller C, Kwaaitaal M, Panstruga R. 2014. Interaction of a *Blumeria graminis* f. sp. *hordei* effector candidate with a barley ARF-GAP suggests that host vesicle trafficking is a fungal pathogenicity target. *Mol. Plant Pathol.* 15:535–49
109. Schouten HJ, Krauskopf J, Visser RGF, Bai YL. 2014. Identification of candidate genes required for susceptibility to powdery or downy mildew in cucumber. *Euphytica* 200:475–86
110. Schwarzbach E. 2004. *Efficient low cost methods in epidemiology of airborne pathogens*. Presented at Int. Cereal Rusts Powdery Mildews Conf., 11th, Norwich, UK
111. Schweizer P, Stein N. 2011. Large-scale data integration reveals colocalization of gene functional groups with Meta-QTL for multiple disease resistance in barley. *Mol. Plant-Microbe Interact.* 24:1492–501
112. Shabab M, Shindo T, Gu C, Kaschani F, Pansuriya T, et al. 2008. Fungal effector protein AVR2 targets diversifying defense-related Cys proteases of tomato. *Plant Cell* 20:1169–83
113. Sillero JC, Rubiales D. 2002. Histological characterization of the resistance of faba bean to faba bean rust. *Phytopathology* 92:294–99
114. Singh RP. 1992. Genetic association of leaf rust resistance gene *Lr34* with adult plant resistance to stripe rust in bread wheat. *Genetics* 82:835–38
115. Song J, Win J, Tian M, Schornack S, Kaschani F, et al. 2009. Apoplastic effectors secreted by two unrelated eukaryotic plant pathogens target the tomato defense protease Rcr3. *PNAS* 106:1654–59
116. Spielmeyer W, McIntosh RA, Kolmer J, Lagudah ES. 2005. Powdery mildew resistance and *Lr34/Yr18* genes for durable resistance to leaf and stripe rust cosegregate at a locus on the short arm of chromosome 7D of wheat. *Theor. Appl. Genet.* 111:731–35
117. St. Clair DA. 2010. Quantitative disease resistance and quantitative resistance loci in breeding. *Annu. Rev. Phytopathol.* 48:247–68
118. Tanaka S, Brefort T, Neidig N, Djamei A, Kahnt J, et al. 2014. A secreted *Ustilago maydis* effector promotes virulence by targeting anthocyanin biosynthesis in maize. *eLife* 3:e01355
119. Tian M, Win J, Song J, van der Hoorn R, van der Knaap E, Kamoun S. 2007. A *Phytophthora infestans* cystatin-like protein targets a novel tomato papain-like apoplastic protease. *Plant Physiol.* 143:364–77
120. Torp J, Jensen HP, Jørgensen JH. 1978. Powdery mildew resistance genes in 106 Northwest European spring barley varieties. *Kgl. Vet. Landbohøjsk. Årsskr.* 1978:75–102
121. Uauy C, Brevis JC, Chen X, Khan I, Jackson L, et al. 2005. High-temperature adult-plant (HTAP) stripe rust resistance gene *Yr36* from *Triticum turgidum* ssp. *dicoccoides* is closely linked to the grain protein content locus Gpc-B1. *Trends Microbiol.* 112:97–105
122. van den Burg HA, Harrison SJ, Joosten MHAJ, Vervoort J, De Wit PJGM. 2006. *Cladosporium fulvum* Avr4 protects fungal cell walls against hydrolysis by plant chitinases accumulating during infection. *Mol. Plant-Microbe Interact.* 19:1420–30
123. van den Burg HA, Westerink N, Francoijs K-J, Roth R, Woestenenk E, et al. 2003. Natural disulfide bond-disrupted mutants of AVR4 of the tomato pathogen *Cladosporium fulvum* are sensitive to proteolysis, circumvent *Cf-4*-mediated resistance, but retain their chitin binding ability. *J. Biol. Chem.* 278:27340–46

124. van der Hoorn RAL, Kamoun S. 2008. From guard to decoy: a new model for perception of plant pathogen effectors. *Plant Cell* 20:2009–17
125. van Esse HP, van't Klooster JW, Bolton MD, Yadeta KA, van Baarlen P, et al. 2008. The *Cladosporium fulvum* virulence protein Avr2 inhibits host proteases required for basal defense. *Plant Cell* 20:1948–63
126. Vergne E, Grand X, Ballini E, Chalvon V, Saindrenan P, et al. 2010. Preformed expression of defense is a hallmark of partial resistance to rice blast fungal pathogen *Magnaporthe oryzae*. *BMC Plant Biol.* 10:206
127. Wallwork H, Johnson R. 1984. Transgressive segregation for resistance to yellow rust in wheat. *Euphytica* 33:123–32
128. Wang L, Wang Y, Marcel TC, Niks RE, Qi X. 2010. The phenotypic expression of QTLs for partial resistance to barley leaf rust during plant development. *Theor. Appl. Genet.* 121:857–64
129. Yeo FKS, Hensel G, Vozábová T, Martin-Sanz A, Marcel TC, et al. 2014. Golden SusPtrit: a genetically well transformable barley line for studies on the resistance to rust fungi. *Theor. Appl. Genet.* 127:325–37
130. Zahirul IT, Talukdar ZI, Tharreau D, Price AH. 2004. Quantitative trait loci analysis suggests that partial resistance to rice blast is mostly determined by race-specific interactions. *New Phytol.* 162:197–209
131. Zhan J, Fitt BDL, Pinnschmidt HO, Oxley SJP, Newton AC. 2008. Resistance, epidemiology and sustainable management of *Rhynchosporium secalis* populations on barley. *Plant Pathol.* 57:1–14
132. Zhang M, Li Q, Liu T, Liu L, Shen D, et al. 2015. Two cytoplasmic effectors of *Phytophthora sojae* regulate plant cell death via interactions with plant catalases. *Plant Physiol.* 167:164–75
133. Zhang NW, Pelgrom K, Niks RE, Visser RGF, Jeuken MJW. 2009. Three combined quantitative trait loci from nonhost *Lactuca saligna* are sufficient to provide complete resistance of lettuce against *Bremia lactucae*. *Mol. Plant-Microbe Interact.* 22:1160–68
134. Zhang W-J, Pedersen C, Kwaaitaal M, Gregersen PL, Mørch SM, et al. 2012. Interaction of barley powdery mildew effector candidate CSEP0055 with the defence protein PR17c. *Mol. Plant Pathol.* 13:1110–19
135. Zhang Y, Lubberstedt T, Xu ML. 2013. The genetic and molecular basis of plant resistance to pathogens. *J. Genet. Genomics* 40:23–35
136. Zheng Z, Nonomura T, Appiano M, Pavan S, Matsuda Y, et al. 2013. Loss of function in *Mlo* orthologs reduces susceptibility of pepper and tomato to powdery mildew disease caused by *Leveillula taurica*. *PLOS ONE* 8:e70723
137. Zhu YJ, Zuo SM, Chen ZX, Chen XG, Li G, et al. 2014. Identification of two major rice sheath blight resistance QTLs, qSB1-1(HJX74) and qSB11(HJX74), in field trials using chromosome segment substitution lines. *Plant Dis.* 98:1112–21
138. Zimmermann G, Baumlein H, Mock H, Himmelbach A, Schweizer P. 2006. The multigene family encoding germin-like proteins of barley: regulation and function in basal host resistance. *Plant Physiol.* 142:181–92

Annual Review of Phytopathology

Volume 53, 2015

Contents

Errata

An online log of corrections to *Annual Review of Phytopathology* articles may be found at http://www.annualreviews.org/errata/phyto