Yield penalties of disease resistance in crops

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Recently, there have been rapid developments in understanding the costs of disease and pest resistance in model plants and their ecological relevance in wild plants. In crop plants, however, much (although not all) of our current understanding of costs of resistance must be inferred from research on model species. To determine the true costs of resistance in crops and the likely benefit of resistance genes in new cultivars, however, other aspects of the plant's phenotype must be studied alongside resistance.

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Abbreviations

Avr	avirulence
GFG	gene-for-gene
IR	induced resistance
PR	partial resistance
PT	pathogenicity target
QTL	quantitative trait locus
R	resistance
TGW	thousand-grain weight

Introduction

Disease resistance is often assumed to be costly. Indeed, many traits that are associated with resistance to pathogens and herbivores reduce plant fitness, although others do not [1]. Research on costs of resistance is currently enjoying a surge of interest. This is particularly true of studies of the mechanisms underlying costs in model organisms, such as *Arabidopsis*, and their ecological significance in wild plants. Although crops have not been completely neglected, it is fair to describe research in this area as sporadic. There has long been evidence that disease resistance may affect crop performance [2], but several of the most informative experiments were done a decade or two ago and have not been properly followed up. In this review, therefore, although I cover research progress in the past year, I also attempt to identify critical areas where our knowledge or understanding is most seriously lacking.

I focus particularly on yield, the single most important indicator of crop performance. In a breeding programme, many factors must be weighed against one another, and disease resistance is rarely the most important. In the UK, for example, the key targets for wheat breeding are yield, quality and standing power, in that order. Disease resistance as a whole is no higher than fourth in a breeder's list of priorities, whereas resistance to any one disease is simply one of several factors that must be considered when deciding whether or not to market a cultivar. If resistance has a substantial cost, therefore, it has commercial significance because it may hinder the more important objective of increasing yield.

Two useful, general reviews on costs of resistance have been written by Purrington [3], who focuses on the mechanisms of costs, and Bergelsen and Purrington [1], who comprehensively review research published before 1995 on costs of resistance to pathogens, herbivores and herbicides. Bergelsen and Purrington [1] emphasise studies in which the genetic background was controlled so that the effects of resistance (*R*) genes could be distinguished from those of other genes. They include meta-analyses of the influence of several factors on the ability of experiments to detect costs of resistance. Some caution should be exercised in this respect, because the unit of analysis was the research paper. Hence, four papers that reported a cost associated with the *mlo* gene in barley for resistance to powdery mildew (*Blumeria graminis* [syn. *Erysiphe graminis*] f. sp. *hordei*) [4–7] were treated as four separate data supporting the hypothesis that resistance is costly. In contrast, three papers in which no cost was associated with any of ten or more gene-for-gene (GFG) resistances to barley powdery mildew [5,8,9] were treated as just three data against that hypothesis.

Linkage or pleiotrophy?

A direct effect of an *R* gene on yield implies an underlying mechanistic relationship. However, genes that are linked to an *R* gene may also affect yield and hence hamper the selection of commercially successful resistant cultivars. Such linkage is especially likely to create problems when the *R* gene has been introgressed from a wild relative of the crop. Under these circumstances, there is little recombination between the introgressed segment and the homoeologous segment in the crop species. It is generally only worthwhile for a breeder to analyse such a linkage and to try to break it when the yield penalty in the absence of the target pathogen or pest is commercially significant.

Wild-relative species are especially important in the breeding of wheat. In wheat, recombinants have been found in which the *Pch1* gene for resistance to eyespot (*Tapesia* spp., a stem-base disease) from the wild grass *Aegilops ventricosa* is no longer linked to a gene for reduced yield [10]. On the other hand, linkage between yield depression and the *Lr9 R* gene from *Aegilops umbellulata*, which confers resistance to wheat brown rust (also known as leaf rust [*Puccinia triticina*, syn. *Puccinia recondita* f. sp. *tritici*]), has not been broken [11]. Other *R* genes on introgressed segments that are associated with reduced yield are *Wsm1* for resistance to wheat streak mosaic virus from *Thinopyrum intermedium*, which is associated with a mean yield reduction of

21% [12•], and three genes for stem rust (*Puccinia graminis* f. sp. *tritici*) resistance, notably *Sr26* from *Agropyron elongatum*, which has a 9% yield penalty [13]. Introgressed segments do not always incur a yield penalty. Another *T. intermedium* translocation, carrying resistance to barley yellow dwarf virus, conferred no significant reduction in grain yield, plant biomass or grain size (measured by thousand-grain weight [TGW]), of uninfected plants [14•]. Indeed, the 1RS chromosome arm from rye, which carries several disease resistance genes, is associated with increased yield even in the absence of disease [15]. Not all *R* genes that are linked to reduced yield have been introgressed from related wild species. In combination with other *Lr* genes, *Lr34* from Frontana and other South American cultivars has provided durable resistance to brown rust of wheat but was associated with a reduction in grain yield of 6%, as well as with significant reductions in most of the yield components analysed [16]. In winter barley, the gene *ym4* from the Croatian landrace Ragusa confers resistance to barley mild mosaic virus (BaMMV) and strain 1 of barley yellow mosaic virus (BaYMV-1). *ym4* was associated with an average reduction in grain yield of 2% across eight trials [17]. It is not yet possible to determine, either in the case of *Lr34* or in that of *ym4*, if the yield penalty is a direct effect of the *R* gene or an indirect cost of linked genes.

Transgenic plants may be used to distinguish the effects of linkage and pleiotropy and so to improve understanding of the mechanisms underlying costs of resistance [1]. Ideally, more than one insertion of a transgene should be used in such experiments in case the site of insertion has an effect on yield because of linkage to deleterious genes. Using this approach, Magg *et al.* [18•] showed that two insertions of the *CryIA(b)* gene, encoding an insecticidal toxin from *Bacillus thuringiensis*, had no significant effect on grain yield, grain dry matter or plant height in the absence of larvae of the European corn borer (*Ostrinia nubilalis*).

Costs of disease escape

A second indirect cost that is important in breeding concerns disease escape. Plant architecture and rate of development that are optimal for yield and agronomic performance may increase disease by promoting the spread of infection or the development of symptoms. A breeder therefore needs to balance the advantages of modifying these characters so as to escape disease against any reduction in yield or performance. The angle, length and separation of wheat leaves affect the net rate of short-distance dispersal of the splash-borne conidia of *Mycosphaerella graminicola*, which causes septoria tritici blotch. Long leaves that are close together tend to allow spores to be dispersed successfully between leaves and so increase disease [19]. Most UK breeders, however, prefer to select wheat lines that have short stems, which stay standing in wind and rain, and long leaves, which maximise the interception of sunlight. The date of crop maturity may also affect disease escape. Earlier emergence of flag leaves increases the number of septoria on upper leaves on any particular date, because there is more time for the fungus to develop and cause symptoms. When a breeding programme includes material with a wide range of maturity dates, selecting plants for resistance simply on the basis of septoria scores may be misleading because the plants with least septoria are likely to be the slowest to mature. A more effective approach is to regress disease scores on maturity dates. Plants with a large negative residual from the regression can be regarded as relatively resistant, allowing early maturity and septoria-resistance to be selected simultaneously [20].

Induced resistance

When a plant is attacked by a pest or a pathogen, it induces defences that involve the modification of cell walls, the killing of cells that contain or surround the pathogen and the induction of defence genes. It has long been known that the induction of such defences may be costly [2]. For example, in a pioneering experiment, barley that was heavily infected with an avirulent genotype of *B. graminis* f. sp. *hordei* had 7% lower grain yield, 4% smaller grains and 4% less protein per kg of grain than uninoculated control plants [21]. Nevertheless, this early evidence for costs of induced resistance (IR) seems to have had remarkably little impact on thinking about disease resistance until quite recently [22•,23••]. The great majority of recent papers on costs of IR concern wild plants, a notable exception being that by Heil *et al.* [24] who showed that application of the defence elicitor benzothiadiazole (BTH) in the absence of fungal pathogens reduced plant biomass, the number of ears and the number of grains. These effects of BTH were most pronounced when nitrogen availability was limited. As the types of cost identified in reviews by Heil [22•] and by Heil and Baldwin [23••] are as relevant to crops as they are to wild plants or to model systems such as *Arabidopsis*, insights from research on wild and model plants should be broadly applicable to crops. This does not, however, negate the need for research on crops. For example, costs may be increased by stressful conditions, such as low soil fertility or the presence of competitors [22•,23••,24]. Experiments are needed to test the extent to which the burgeoning fundamental knowledge in this area is applicable to agriculture.

A particularly interesting class of IR-related costs concerns trade-offs between resistances to different types of pest or pathogen. There is now considerable evidence that resistance to certain pathogens induced by salicylic acid limits or even reduces the expression of resistance to other pathogens and pests induced by jasmonic acid or ethene, and *vice versa*. These trade-offs are reviewed by Felton and Korth [25].

Gene-for-gene resistance

The best-understood form of constitutive plant disease resistance is that following the GFG relationship. GFG resistances have been widely used in breeding, although they tend not to be durable because pathogens adapt to them rapidly by mutation of the avirulence (*Avr*) genes matching the *R* genes. New specificities of GFG *R* genes

are generated by variation in the number and sequence of leucine-rich repeats that they encode [26]. It is difficult to imagine how such polymorphism could involve costs of any significant kind, and the limited data available are consistent with this view. In tests of three sets of near-isogenic lines of barley, those with *R* genes against powdery mildew were compared to susceptible controls [5,8,9]. In two of these studies [5,8], the control was a single line, the recurrent susceptible parent, so comparisons of different lines with the control were confounded with each other. Nevertheless, no cost of *R* alleles was apparent in either of these studies [5,8]. In the third study [9], however, ten pairs of lines, either with a particular *R* gene or without it, were developed in cv. Manchuria. In pairwise comparisons, the *R* gene had no effect on grain yield, TGW or other agronomic characters. In a fourth experiment on barley powdery mildew, two *R* genes, *Mla9* and *Mlk1*, segregated in a doubled-haploid population. Once again, neither gene was associated with differences in grain yield or other yield components [27]. In a synthetic population of the outbreeding crop species rye, two GFG *R* genes that are effective against powdery mildew, *Rm1* and *rm2*, segregated, although neither had a significant effect on fitness [28].

Nevertheless, gene expression data suggest that a cost may be associated with the number of GFG *R* genes that are involved in resistance to a particular pathogen. Overexpression of either *Prf* [29] or *Pto* [30] in tomato, which are both required for an effective response to the bacterium *Pseudomonas syringae* pv. *tomato* carrying the *avrPto* gene, causes constitutive activation of defence responses. A similar effect was produced by overexpression of *RPS2*, which is involved in resistance to *Pseudomonas syringae* in *Arabidopsis* [31]. Although overexpression of *R* genes leads to enhanced resistance to a wide range of pathogens [29,30], constitutive induction of defence genes is likely to be costly [22•,23••]. Consequently, if each GFG *R* gene independently induces a certain level of defence (which is yet to be tested when *R* genes are not over-expressed), there might be a marginal cost of each additional *R* gene. The number of such genes would be determined by a balance between that cost and the need to fight pathogens.

The R alleles that are observed in nature or in breeding material may be those that are associated with the lowest costs, such that other alleles have been eliminated by natural selection. Four mutant or recombinant alleles of the *rp1* locus of maize, which controls GFG resistance to the rust *Puccinia sorghi*, confer necrotic phenotypes in the absence of the fungus [32]. If these lesion-mimic phenotypes reduce grain yield, as one would expect when green leaf area is reduced, these *rp1* alleles would be replaced in natural populations by other genes that are similarly effective against rust but are less costly to the plant.

van der Biezen and Jones [33] proposed a new model of the function of GFG *R* genes that has a bearing on costs of resistance [34•]. The model, which has been developed by Dangl and Jones [35•], involves a tripartite interaction between a pathogen Avr factor (which is also involved in pathogenicity), a host pathogenicity target (PT; to which Avr binds) and the R protein (which binds to the PT–Avr complex and thereby induces an effective defence response). Such an interaction has been detected in *Arabidopsis*, in which the RIN4 protein binds to both RPM1, the product of a GFG *R* gene, and to two different *Avr* gene products that elicit resistance in *RPM1* plants, AvrB and AvrRpm1 [36••]. The model postulates that R 'guards' PT by monitoring the binding of Avr but it relies on several hypotheses that have not yet been fully tested. For example, it hypothesises that *Avr* genes encode pathogenicity factors, although this has been demonstrated for only a small minority of the genes cloned to date [37•], and that mutations in *Avr* genes are costly in terms of pathogen fitness, even though less is known about virulence costs than about the costs of plant resistance. At the risk of piling hypothesis upon hypothesis, a further prediction is that PT proteins (as they are targets of pathogenicity [Avr] proteins) may have significant functions in plant defence or physiology (some data supporting this are given in [34•]). Consequently, a mutation in a *PT* gene that caused loss of binding of Avr to PT might be costly if it also caused loss of the normal activity of the PT protein. In contrast, a mutation in the leucine-rich repeat of the R protein that caused increased binding to the PT–Avr complex is unlikely to affect fitness, so providing the plant with low-cost surveillance for pathogens.

Partial resistance

An important goal of plant breeding is durable resistance that remains effective for a long time over a large area while being exposed to the pathogen. Resistance that is polygenic, race-non-specific and partial in its effect against the disease is often durable. In contrast, the monogenic, race-specific, complete resistance controlled by GFG relationships is often short lived. These are two extremes of many genetic models of resistance [38]. Nevertheless, Vanderplank [39] suggested that partial (i.e. 'horizontal') resistance (PR) may be eroded over many generations either if it is masked by effective GFG (i.e. 'vertical') resistance (the Vertifolia Effect) or if plants are not exposed to the disease [39], implying that PR is costly. Studies that lend some support to this idea include two presented by Vanderplank himself [39]: first, the apparent loss of PR to late blight (*Phytophthora infestans*) in the presence of effective GFG resistance in the breeding programme from which the potato cv. Vertifolia was produced, and second, the loss of PR to rust caused by *Puccinia polysora* in African and Asian landraces of maize. If PR does indeed incur a long-term cost, this should be of great concern to breeders because it implies that this useful form of durable resistance is liable to be lost if it is not actively and continuously selected. Nevertheless, Vanderplank's hypothesis has not been critically tested and, in general, the relevant data could be interpreted in several ways. For example, was resistance lost in maize

following its introduction into Africa and Asia or gained in American maize? It is true that it is more difficult to study many genes with small effects than one gene with a large effect, but this area of research surely deserves greater attention in the future.

A possible cost of PR may be inferred from data that suggest that one aspect of PR may be greater inducibility of defences in response to pathogen infection. Lines of tomato and cabbage with high resistance to *Alternaria solani* (early blight) and *Xanthomonas campestris* pv. *campestris*, respectively, accumulate higher levels of defence proteins faster than more susceptible lines [40•]. In *Arabidopsis*, the *ISR1* locus controls both IR and basal resistance to *Pseudomonas syringae* pv. *tomato* [41]. Critical experiments that relate resistance, defence induction and costs have not yet been carried out, but it is possible that there may be a trade-off between high PR to disease and a high cost of inducing that resistance [22•,23••].

Case study: the *mlo* gene of barley

The crop gene that has been most extensively studied from the point of view of yield and other costs is *mlo* in barley, which has provided excellent, durable resistance to powdery mildew and has been used widely in breeding, especially in Europe [42]. The wildtype allele, *Mlo*, is a negative regulator of defences against powdery mildew, including cell death, so loss of Mlo activity confers resistance to mildew and deregulated leaf cell death [43]. Since the early days of research on this gene, plants carrying the *mlo* mildew resistance allele have been found to suffer from spontaneous necrotic flecking, which is apparently not associated with mildew infection [6,44].

mlo mildew resistance has long been associated with reduced grain yield [4–7]. In the most informative study of the association between *mlo* resistance and yield [6], doubled-haploid progeny of crosses between three *mlo* mutant lines and susceptible cultivars were grown in trials in which foliar diseases, including mildew, were controlled with fungicides. *mlo* (mildew-resistant) lines had an average yield that was 4.2% lower than that of *Mlo* (mildew-susceptible) lines. They also had 5.4% lower TGW and a much higher level of necrotic leaf spotting. It was concluded that the yield loss that was associated with *mlo* was probably caused by the spotting which, in turn, was a pleiotropic effect of *mlo*. It is unlikely that the yield reduction was caused by genes that are linked to *mlo* because similar costs were associated with three independent *mlo* mutations in different cultivars. Furthermore, necrotic spotting has been associated with every *mlo* allele tested [4–6]. By contrast, a quantitative trait locus (QTL) that decreased yield mapped close to but not at the *mlo11* gene in cv. Derkado [45,46•]. In different analyses of the same data, grain number per stem [45] and TGW [46•] were identified as the main yield components affected. In both studies, however, more than one QTL controlling yield mapped to chromosome 4, on which *mlo* is located, which greatly increases the difficulty of mapping QTLs accurately [46•,47]. The conclusion that yield reduction is a pleiotropic effect of *mlo* should therefore be regarded as sound [6]. As there is genetic variation in yield among the *mlo* lines of the various crosses studied [6,7,45,46•], the detrimental effect of *mlo* mildew resistance on yield can be alleviated by recombining genes elsewhere in the genome by the normal process of plant breeding.

Another, superficially quite different, trade-off of *mlo* mildew resistance is that it increases the susceptibility of barley plants to facultative pathogens, including *Magnaporthe grisea*, which causes blast [48], and *Cochliobolus sativus*, which causes spot blotch [49•]. The initial, surprising discovery was that plants with *mlo* resistance to mildew were susceptible to blast. Specifically, they had massive growth of *M. grisea* in the mesophyll, large blast lesions and high levels of disease on the leaf. The increased susceptibility was consistent for three *mlo* alleles and so is probably a pleiotropic effect of *mlo* [48]. *mlo* plants not only had higher levels of spot blotch caused by *C. sativus* but were also more susceptible to a culture filtrate containing a fungal toxin [49•]. This is consistent with the Mlo protein functioning partly as an antagonist of cell death, so that reduced Mlo activity leads both to spontaneous cell death, especially in the mesophyll, and to increased cell death when the plant is challenged by a toxin. Survival of host cells may restrict the growth of necrotrophic fungi, which are able to feed from dead cells. Indeed, in *Arabidopsis thaliana*, growth of *Botrytis cinerea* and *Sclerotia sclerotiorum* is promoted by the hypersensitive response [50]. There is evidently a trade-off between resistance to biotrophic fungi, such as *B. graminis*, which may involve death of host cells, and resistance to necrotrophs, which is enhanced when host cells are kept alive.

Are trade-offs between *mlo* resistance to mildew and susceptibility to facultative fungi significant in agriculture? Spot blotch is a significant disease of barley in hotter climates [49•], where mildew is generally insignificant, whereas the main economic significance of blast is on rice rather than barley. *mlo* has been used most extensively in northern Europe, where mildew is important. Although the necrotic spotting associated with *mlo* may be linked to susceptibility to *C. sativus* [49•], there is no evidence as yet for a similar link with facultative diseases that are important in northern Europe, such as scald (*Rhynchosporium secalis*) or net blotch (*Drechslera teres*).

A third trade-off of *mlo* is in decreasing susceptibility to the arbuscular mycorrhizal fungus *Glomus mossae*, as measured by the amount of root cortex colonised and the abundance of mycorrhizal arbuscules [51]. As only one mutant allele, *mlo5*, was tested in this work, however, we cannot be certain that reduced mycorrhizal colonisation was caused by *mlo5* itself rather than by another gene. Clearly, the pleiotropic effects of *mlo* mean that the true value of this gene for plant breeding must be assessed in the context of

the phenotype of the whole plant, including yield and yield components, as well as its responses to different kinds of microorganism.

Conclusions: putting it all together

A breeder must consider many factors when deciding whether or not to market a cultivar. By contrast, in the academic world, different people study agronomic properties and disease; and most often, different people study different diseases or at least different classes of disease. The lack of follow-up from key experiments done in the 1980s [6,10,21] has lead to a lack of integrated understanding of the effect of disease resistance on crop performance in the absence of disease. This may be substantially the result of this sub-division of research subjects. For example, if resistance is indeed costly, a breeder's most effective strategy may not be to select for excellent resistance (if that means sacrificing yield or quality) but to select for at least moderate resistance while eliminating very susceptible lines, which might not only become heavily diseased themselves but also spread inoculum to other cultivars. The entire genotype of a cultivar rather than any single gene, no matter how important, determines its value to farmers and consumers, and therefore its commercial success or failure. It's time to put the pieces back together again and to study responses to disease as part of the biology of the whole plant.

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References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

- • of special interest
- •• of outstanding interest

1. Bergelsen J, Purrington CB: **Surveying patterns in the cost of resistance in plants.** *Am Nat* 1996, **148**:536-558.

2. Smedegaard-Petersen V, Tolstrup K: **The limiting effect of disease resistance on yield.** *Annu Rev Phytopathol* 1985, **23**:475-490.

3. Purrington CB: **Costs of resistance.** *Curr Opin Plant Biol* 2000, **3**:305-308.

4. Schwarzbach E: **The pleiotropic effects of the *ml-o* gene and their implications in breeding.** In *Barley Genetics III*. Edited by Gaul H. Munich: Karl Thiemig; 1976:440-445.

5. Kølster P, Munk L, Stølen O, Løhde J: **Near-isogenic barley lines with genes for resistance to powdery mildew.** *Crop Sci* 1986, **26**:903-907.

6. Kjær B, Jensen HP, Jensen J, Jørgensen JH: **Associations between three *ml-o* powdery mildew resistance genes and agronomic traits in barley.** *Euphytica* 1990, **46**:185-193.

7. Bjørnstad Å, Aastveit K: **Pleiotropic effects on the *ml-o* mildew resistance gene in barley in different genetical backgrounds.** *Euphytica* 1990, **46**:217-226.

8. Kølster P, Stølen O: **Barley isolates with genes for resistance to *Erysiphe graminis* f. sp. *hordei* in the recurrent parent 'Siri'.** *Crop Sci* 1987, **98**:79-82.

9. Jørgensen JH, Jensen HP: **Effect of "unnecessary" powdery mildew resistance genes on agronomic properties of spring barley.** *Norsk Landbruksforsking* 1990, **(suppl 9)**:125-130.

10. Worland AJ, Law CN, Li WM: **The location of genes depressing yield associated with the transfer of eyespot resistance from *Aegilops ventricosa*.** *Annual Report of the AFRC Institute of Plant Science Research, John Innes Institute and Sainsbury Laboratory 1989*. Norwich, UK: IPSR and John Innes Institute; 1990:7-8.

11. Ortelli S, Winzeler H, Winzeler M, Fried PM, Nösberger J: **Leaf rust resistance gene *Lr9* and winter wheat yield reduction: I. yield and yield components.** *Crop Sci* 1996, **36**:1590-1595.

12. • Sharp GL, Martin JM, Lanning SP, Blake NK, Brey CW, Sivamani E, Qu R, Talbert LE: **Field evaluation of transgenic and classical sources of *wheat streak mosaic virus* resistance.** *Crop Sci* 2002, **42**:105-110.

Despite the title, transgenic approaches to controlling wheat streak mosaic virus did not reduce disease symptoms. A non-transgenic *R* gene, *Wsm1*, was associated with a large yield penalty.

13. Latter BDH, McIntosh RA, Ellison FW, Brennan PS, Fisher J, Hollamby GJ, Rathjen AJ, Wilson RE: **Grains yields of near-isogenic lines with added genes for stem rust resistance.** *Proceedings of the 7th International Wheat Genetics Symposium*: 1998 July 13–19; Cambridge, UK. Edited by Miller TE, Koebner RMD. Cambridge, UK: Institute for Plant Science Research. 1988:901-906.

14. • Ayala L, van Ginkel M, Khairallah M, Keller B, Henry M: **Expression of *Thinopyrum intermedium*-derived *barley yellow dwarf virus* resistance in elite bread wheat backgrounds.** *Phytopathol* 2001, **91**:55-62.

The authors describe an interesting exception to the tendency for introgression of wild grass DNA into wheat to cause a yield penalty. A translocation carrying a gene that confers resistance against barley yellow dwarf virus had no significant effect on wheat performance in the absence of disease.

15. Villareal RL, Bañuelos O, Mujeeb-Kazi A, Rajaram S: **Agronomic performance of chromosomes 1B and T1BL.1RS near-isolines in the spring bread wheat Seri M82.** *Euphytica* 1998, **103**:195-202.

16. Singh RP, Huerta-Espino J: **Effect of leaf rust resistance gene *Lr34* on grain yield and agronomic traits of spring wheat.** *Crop Sci* 1997, **37**:390-395.

17. Le Gouis J, Jestin L, Ordon F, de Froidmont D, Béghin D, Joseph J-L, Froidmont F: **Agronomic comparison of two sets of SSD barley lines differing for the *ym4* resistance gene against barley mosaic viruses.** *Agronomie* 1999, **19**:125-131.

18. • Magg T, Melchinger AE, Klein D, Bohn M: **Comparison of *Bt* maize hybrids with their non-transgenic counterparts and commercial varieties for resistance to European corn borer and for agronomic traits.** *Plant Breeding* 2001, **120**:397-403.

A study of the effects of *Bt*-toxin transgenes on agronomic performance. Two insertions of the gene were investigated, neither of which had any significant effect on grain yield or quality in the absence of corn borer larvae.

19. Lovell DJ, Parker SR, Hunter T, Royle DJ, Coker RR: **Influence of crop growth and structure on the risk of epidemics by *Mycosphaerella graminicola* (*Septoria tritici*) in winter wheat.** *Plant Pathol* 1997, **46**:126-138.

20. Van Beuningen LT, Kohli MM: **Deviation from the regression of infection on heading and height as a measure of resistance to *Septoria tritici* blotch in wheat.** *Plant Disease* 1990, **74**:488-493.

21. Smedegaard-Petersen V, Stølen O: **Effect of energy-requiring defense reactions on yield and grain quality in a powdery mildew-resistant barley cultivar.** *Phytopathol* 1981, **71**:396-399.

22. • Heil M: **The ecological concept of costs of induced systemic resistance (ISR).** *Eur J Plant Pathol* 2001, **107**:137-146.

A review of rapidly advancing research on the costs of induced resistance. This review discusses all forms of induced resistance, not just those triggered by jasmonate and ethene.

23. •• Heil M, Baldwin IT: **Fitness costs of induced resistance: emerging experimental support for a slippery concept.** *Trends Plant Sci* 2002, **7**:61-67.

A second review on the costs of induced resistance. This review includes a particularly useful discussion of experimental approaches to investigating the effects of resistance on fitness and the mechanisms underlying fitness costs.

24. Heil M, Hilpert A, Kaiser W, Linsenmair KE: **Reduced growth and seed set following chemical induction of pathogen defence: does systemic acquired resistance (SAR) incur allocation costs?** *J Ecol* 2000, **88**:645-654.

25. Felton GW, Korth KL: **Trade-offs between pathogen and herbivore resistance.** *Curr Opin Plant Biol* 2000, **3**:309-314.

26. Ellis J, Dodds P, Pryor T: **The generation of plant disease resistance specificities.** *Trends Plant Sci* 2000, **5**:373-379.

27. Kjær B, Haahr V, Jensen J: **Associations between 23 quantitative traits and 10 genetic markers in a barley cross.** *Plant Breeding* 1991, **106**:261-274.

28. Welz HG, Miedaner T, Geiger HH: **Two unnecessary powdery mildew resistance genes in a synthetic rye population are neutral on fitness.** *Euphytica* 1995, **81**:163-170.

29. Oldroyd GED, Staskawicz BJ: **Genetically engineered broad-spectrum disease resistance in tomato.** *Proc Natl Acad Sci USA* 1998, **95**:10300-10305.

30. Tang XY, Xie MT, Kim YJ, Zhou JM, Klessig DF, Martin GB: **Overexpression of *Pto* activates defense responses and confers broad resistance.** *Plant Cell* 1999, **11**:15-29.

31. Tao Y, Yuan FH, Leister RT, Ausubel FM, Katagiri F: **Mutational analysis of the *Arabidopsis* nucleotide binding site–leucine-rich repeat resistance gene *RPS2*.** *Plant Cell* 2000, **12**:2541-2554.

32. Hu GS, Richter TE, Hulbert SH, Pryor T: **Disease lesion mimicry caused by mutations in the rust resistance gene *rp1*.** *Plant Cell* 1996, **8**:1367-1376.

33. van der Biezen EA, Jones JDG: **Plant disease-resistance proteins and the gene-for-gene concept.** *Trends Biochem Sci* 1998, **23**:454-456.

34. • van der Hoorn RAL, de Wit PJGM, Joosten MHAJ: **Balancing selection favors guarding resistance proteins.** *Trends Plant Sci* 2002, **7**:67-71.
This review discusses fitness costs that are associated with the 'guarding' hypothesis [33], which postulates a tripartite interaction between an avirulence/pathogenicity factor from the pathogen and resistance and pathogenicity (or virulence) target factors in the host. The authors argue that natural selection may favour *R*-gene products that bind to the PT–Avr complex rather than to Avr alone. This is because mutations in Avr that might prevent the binding of R but not affect the pathogenicity activity of Avr are thought to be more likely in the latter case than the former.

35. • Dangl JL, Jones JDG: **Plant pathogens and integrated defence responses to infection.** *Nature* 2001, **411**:826-833.
This is a broad review of the genetics and molecular biology of plant disease, and is particularly concerned with parallels between responses to infection in plants and animals. A section that is particularly relevant to this paper develops the 'guarding' hypothesis [33] and makes several testable predictions from that model.

36. •• Mackey D, Holt BF, Wiig A, Dangl JL: **RIN4 interacts with *Pseudomonas syringae* type III effector molecules and is required for RPM1-mediated resistance in *Arabidopsis*.** *Cell* 2002, **108**:743-754.
This is the first paper to provide substantial support for the 'guarding' hypothesis of R–Avr interaction [33]. RIN4 is the first putative PT protein to be shown to bind both an *R* gene product, RPM1, and an *Avr* gene product (in this case two such products, AvrB and AvrRpm1, which are structurally unrelated). This is consistent with a model in which RPM1 'guards' RIN4, in a way that has yet to be determined, so that an effective defence response is induced upon binding of either Avr protein to RIN4. The complex interactions involved, in which each factor is associated with potential fitness costs [34•], should certainly stimulate new research on plant–pathogen coevolution.

37. • Luderer R, Joosten MHAJ: **Avirulence proteins of plant pathogens: determinants of victory and defeat.** *Mol Plant Pathol* 2001, **2**:355-364.
This paper reviews data on avirulence genes that are relevant to the 'guarding' hypothesis [33]. This hypothesis postulates a tripartite interaction between a avirulence/pathogenicity factor from the pathogen, host resistance and virulence target factors. It covers cloned avirulence genes in fungi, bacteria and viruses for which the matching *R* gene has been cloned.

38. Johnson R: **A critical analysis of durable resistance.** *Annu Rev Phytopathol* 1984, **22**:309-330.

39. Vanderplank JE: *Disease Resistance in Plants.* London, UK: Academic Press. 1984.

40. • Tuzun S: **The relationship between pathogen-induced systemic resistance (ISR) and multigenic (horizontal) resistance in plants.** *Eur J Plant Pathol* 2001, **107**:85-93.
The findings that are reviewed suggest that there may be a correlation between partial resistance to disease and either the constitutive level of production of defence proteins or the rate at which defence responses are induced following infection. 'ISR' in the title includes all forms of induced resistance.

41. Ton J, Pieterse CMJ, van Loon LC: **Identification of a locus in *Arabidopsis* controlling both the expression of rhizobacteria-mediated induced systemic resistance (ISR) and basal resistance against *Pseudomonas syringae* pv. *tomato*.** *Mol Plant Microbe Interact* 1999, **12**:911-918.

42. Jørgensen JH: **Discovery, characterisation and exploitation of MLO powdery mildew resistance in barley.** *Euphytica* 1992, **63**:141-152.

43. Buschges R, Hollricher K, Panstruga R, Simons G, Wolter M, Frijters A, van Daelen R, van der Lee T, Diergaarde P, Groenendijk J *et al.*: **The barley *mlo* gene: a novel control element of plant pathogen resistance.** *Cell* 1997, **88**:695-705.

44. Peterhansel C, Freialdenhoven A, Kurth J, Kolsch R, Schulze-Lefert P: **Interaction analyses of genes required for resistance responses to powdery mildew in barley reveal distinct pathways leading to leaf cell death.** *Plant Cell* 1997, **9**:1397-1409.

45. Thomas WTB, Baird E, Fuller JD, Lawrence P, Young GR, Russell J, Ramsey L, Waugh R, Powell W: **Identification of a QTL decreasing yield in barley linked to Mlo powdery mildew resistance.** *Mol Breeding* 1998, **4**:381-393.

46 • Hackett CA, Meyer RC, Thomas WTB: **Multi-trait QTL mapping in barley using multivariate regression.** *Genet Res* 2001, **77**:95-106.
The latest of several papers to show that the *mlo* mildew resistance gene in barley is associated with a reduction in grain yield. See also [6] in particular, as well as [4,5,7,45].

47. Jansen RC: **Complex plant traits: time for polygenic analysis.** *Trends Plant Sci* 1996, **1**:89-94.

48. Jarosch B, Kogel K-H, Schaffrath U: **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* 1999, **12**:508-514.

49. • Kumar J, Hückelhoven R, Beckhove U, Nagarajan S, Kogel K-H: **A compromised Mlo pathway affects the response of barley to the necrotrophic fungus *Bipolaris sorokiniana* (teleomorph: *Cochliobolus sativus*) and its toxins.** *Phytopathol* 2001, **91**:127-133.
The second of two papers to show that the mlo mildew-resistance gene in barley increases susceptibility to hemibiotrophic [48] or (in this paper) necrotrophic pathogens. Quantitative data show the increased susceptibility of mlo plants to a toxic *C. sativus* culture filtrate. However, the paper does not provide information on susceptibility to the *C. sativus* fungus itself.

50. Govrin EM, Levine A: **The hypersensitive response facilitates plant infection by the necrotrophic pathogen *Botrytis cinerea*.** *Curr Biol* 2000, **10**:751-757.

51. Ruiz-Lozano JM, Gianinazzi S, Gianinazzi-Pearson V: **Genes involved in resistance to powdery mildew in barley differentially modulate root colonization by the mycorrhizal fungus *Glomus mossae*.** *Mycorrhiza* 1999, **9**:237-240.