Minireview

The fitness costs to plants of resistance to pathogens

Jeremy J Burdon and Peter H Thrall

Address: Division of Plant Industry, CSIRO, PO Box 1600, Canberra, ACT 2601, Australia.

Correspondence: Jeremy J Burdon. E-mail: jeremy.burdon@csiro.au

Published: 14 August 2003

Genome ***Biology*** 2003, **4:**227

The electronic version of this article is the complete one and can be found online at http://genomebiology.com/2003/4/9/227

Abstract

It has long been predicted that genes giving resistance to pathogens impose a cost on the fitness of plants. A new study has shown this to be true for one resistance gene in *Arabidopsis*. This raises intriguing theoretical and practical questions about how generally the results apply and how such costs are controlled in plants carrying resistance genes to several different pathogens.

In plant-pathogen interactions, there are two broad types of genetically determined resistance to infection in host plants: quantitative (representing the combined effect of many minor genes), and qualitative resistance, which is controlled by major genes (single genes with large effects). Beginning with Harold Flor's elegant work in the 1940s and 1950s, it has been repeatedly shown that in systems characterized by qualitative host resistance, the associated pathogens have corresponding major genes that determine virulence (the ability to infect a given host genotype). As a consequence, such systems are typically referred to as 'gene-for-gene' interactions. The central assumption is that each resistance (*R*) gene in the host interacts specifically with a corresponding avirulence (*Av*) gene in the parasite, with resistance being dominant to susceptibility and avirulence dominant to virulence [1,2]. For resistance to occur, both genes for resistance in the host, as well as the corresponding *Av* genes in the pathogen, must be present. Ever since Flor first outlined the gene-for-gene hypothesis, the evolutionary outcome of these reciprocal interactions between pathogens and their host plants has attracted considerable theoretical attention.

Mathematical modeling has been an important tool for developing a better understanding of the factors that influence the evolution of host resistance and pathogen virulence. From the late 1950s onwards, the gene-for-gene hypothesis stimulated a series of deterministic models exploring how the frequencies of *R* and *Av* genes change over time in plant populations [3-5]. For simplicity, these models assumed infinitely large populations with global, rather than distance-dependent, host and pathogen dispersal (i.e. no spatial structure). Of particular interest were the conditions under which pathogen 'superraces' (strains that could overcome all *R* genes present in a host population) might evolve in mixtures of plant varieties like those used in agriculture [6-8].

A consistent feature of all these single population gene-for-gene models has been the assumption that there are reproductive fitness costs associated with host resistance and pathogen virulence genes. In these models, this is a requirement for maintaining persistent polymorphisms in resistance and virulence genes, as are typically observed in nature [9]. Without such costs, selection in these models results in the evolution of ever-increasing virulence in the pathogen, and a corresponding increase in host resistance. Once a pathogen isolate evolves that can overcome all resistance genes in the host population, however, resistance becomes selectively neutral (i.e. there is no advantage to having such genes) and drifts to fixation, while in the pathogen population the 'superrace' moves to total domination.

Other recent models that use an alternative 'matching allele' formulation allow the long-term persistence of polymorphisms without costs [10]. In this type of model, successful infection of a given host individual by a pathogen requires an exact match between their respective resistance and virulence genotypes. This formulation automatically results in cycling of *R* and *Av* gene frequencies in the population, as

there is strong selection against the most frequent alleles of each type of gene. As there is little empirical support for this alternative genetic scenario, however, the significance of such models for understanding the evolutionary dynamics of plant-pathogen interactions is unclear.

Measuring fitness costs

Despite the controversy about whether fitness costs of resistance are necessary for the maintenance of resistance and avirulence gene polymorphisms, many attempts have been made to measure resistance and/or virulence costs. Nearly all the comparisons that have been made between resistant and susceptible or virulent and avirulent lines of host and pathogen, respectively, leave open the strong possibility that, individually, the results observed may be generated by pleiotropic effects of other linked genes [11]. When considered in a meta-analysis, however, approximately half of 88 studies gleaned from the herbivore-plant, pathogen-plant and herbicide literature showed some evidence of lower fitness associated with resistance [12]. The question of fitness costs associated with virulence and resistance has thus continued to remain contentious.

A seminal article by Tian *et al.* [13] has now produced convincing evidence that at least one resistance gene with a major phenotypic effect of the type typically associated with the gene-for-gene hypothesis imposes a fitness penalty on *Arabidopsis thaliana*. By inserting the *RPM1* gene - encoding resistance to the bacterial pathogen *Pseudomonas syringae* - between two *lox* sites in a susceptible ecotype (variety) of *A. thaliana*, and subsequently inducing recombinational excision of the *RPM1* gene, these authors [13] constructed a series of four independent pairs of truly isogenic lines that differed solely by the presence or absence of *RPM1* [13]. Using a variety of checks, the 'normal' functioning of the $RPM1^+$ gene was then confirmed, as was the insertion of the transgene into a non-coding region of the genome. The impact of the presence of *RPM1* was then determined by growing the four matching $RPM1^+$ and $RPM1^-$ lines in a replicated field trial. Plants carrying the resistance gene had a lower shoot biomass and fewer siliques (seed pods) and, most significantly, showed an average decrease in seed production of 9% relative to the matching susceptible $RPM1^-$ lines [13].

Attempts to measure fitness costs associated with pathogen virulence have had a history of uneven success, but a recent study of the fecundity of a range of isolates of the rust pathogen *Melampsora lini* taken from natural populations of its host *Linum marginale* (native Australian flax) [14] found that the number of *M. lini* spores produced by individual pustules on the plant was negatively correlated with the virulence of the pathogen, suggesting that increased virulence lowered spore production. Of particular interest was the finding that such a cost could at least partly account for the patterns of virulence observed in natural populations of *M. lini* and *L. marginale*: pathogens that are broadly virulent (that is, that can infect hosts with various different *R* genes) are dominant in host populations that are highly resistant, whereas avirulent pathogens are more frequent in susceptible host populations. In combination, these two studies [13,14] provide the best existing evidence for the occurrence of fitness costs.

The consequences of fitness costs

The documentation of a fitness cost of resistance that can clearly be attributed to the resistance gene *RPM1* itself [13] raises significant research opportunities and questions. One is whether fitness costs are associated with all resistance genes, and if so, whether the magnitude of the cost differs between different resistance genes. Flowing from this is the equally important question (particularly from the point of view of the practical use of resistance genes) of how fitness costs associated with different resistance genes interact with each other.

A common feature of most of the host-pathogen associations studied in detail is that, as has been documented in *Arabidopsis*, many different resistance genes or alleles can be found. In natural situations, individual host plants may often carry one or two *R* genes against a given pathogen species. In addition, though, the same individual may carry many more resistance genes, corresponding to the range of pathogens typically confronted by that plant species. If each of these alleles carries a fitness cost, how are resistance/susceptibility polymorphisms maintained in environments in which epidemics of disease are typically patchy in space and time and in which a plant population may therefore not encounter a particular pathogen for many generations [9]? This question is thrown into particularly sharp focus in agricultural situations, in which plant breeders routinely use major resistance genes to protect crops but rarely, if ever, deliberately remove resistances that cease to be effective as the pathogen evolves in response to their use. Indeed, in many modern wheat varieties, as many as four to six different genes for resistance to stem rust (*Puccinia graminis* f.sp. *tritici*) are present, with at best only one or two providing effective resistance against the current pathogen population [15]. At the same time, these varieties also typically carry resistance genes that are effective against other rusts (such as leaf rust, *P. triticina* or stripe rust, *P. striiformis*), not to mention a range of other pathogens for which major resistance genes exist (such as powdery mildew, *Blumeria graminis* and loose smut, *Ustilago nuda*).

In such situations, the fitness costs, if they were to exist for each gene, clearly cannot operate in a simple additive or multiplicative fashion. Even taken only additively, the costs suggested by the Tian *et al.* study in *Arabidopsis* [13] rapidly become prohibitive. This paradox was recognized by these authors [13], who noted the possibility that because of its

ancient history [16], the *RPM1* gene may not be typical of the large numbers of resistance gene loci that are spread across the *Arabidopsis* genome. The ancient *RPM1* polymorphism consists of either the active gene or a complete gene deletion [16], whereas most resistance polymorphisms involve considerably smaller changes. Even if fitness costs were closer to the mean 3.5% measured in a broad review of the literature [12], however, rather than the 9% found by Tian *et al*. [13], they would still be highly visible to plant breeders attempting to combine multiple resistances against one or more pathogens.

Solving this riddle will lead to a significant improvement in our understanding of the evolutionary processes involved in the interplay of host resistance and pathogen virulence genes. Clearly, a first step in this process is to measure the fitness costs associated with a range of genes conferring resistance to other pathogens in *Arabidopsis* and other host species. In essence, we now need to know how representative the *RPM1* gene is and how fitness costs associated with different resistance genes are combined. If the *RPM1* effect is an exception, then how - in biochemical terms - it contributes to loss of fitness remains an interesting question.

In a somewhat ironic development, the predictions of the early deterministic models that were one of the main driving forces behind the search for evidence of fitness costs have now been shown to reflect an unrealistic view of the world. Indeed, when evolutionary interactions are considered in a spatially realistic context (for example, meta-populations comprising multiple interacting populations and distance-dependent dispersal), theoretical work involving simulation models has shown that genetic polymorphisms in either host resistance or pathogen virulence genes can persist without the necessity of assuming differential fitness effects [17,18]. In general, it may well be that the occurrence of fitness costs simply reinforces the patterns of host and pathogen variation that are a consequence of host-pathogen interactions occurring in spatially and temporally heterogeneous environments.

Regardless of how the question of costs in host-pathogen interactions is ultimately resolved, the Tian *et al*. study [13] provides an elegant demonstration of just how the enormous power of genetic engineering is starting to open up a new level of sophistication in the type and precision of the questions that can be asked in developmental and evolutionary biology, ecology and plant breeding.

Acknowledgements

Jeff Ellis kindly provided critical comments on an earlier version of this manuscript.

References

1. Flor HH: **The complementary genic systems in flax and flax rust.** *Adv Genet* 1956, **8:**29-54.
2. Flor HH: **Current status of the gene-for-gene concept.** *Annu Rev Phytopathol* 1971, **9:**275-296.
3. Mode CJ: **A mathematical model for the co-evolution of obligate parasites and their hosts.** *Evolution* 1958, **12:**158-165.
4. Person C: **Genetic polymorphism in parasitic systems.** *Nature* 1966, **212:**266-267.
5. Jayakar SD: **A mathematical model for interaction of gene frequencies in a parasite and its host.** *Theor Popul Biol* 1970, **1:**140-164.
6. Groth JV: **Multilines and "super races": a simple model.** *Phytopathol* 1976, **66:**937-939.
7. Leonard KJ: **Selection pressures and plant pathogens.** *Ann New York Acad Sci* 1977, **287:**207-222.
8. Marshall DR, Pryor AJ: **Multiline varieties and disease control. I. The "dirty crop" approach with each component carrying a unique single resistance gene.** *Theor Appl Genet* 1978, **71:**177-184.
9. Burdon JJ, Thrall PH: **Spatial and temporal patterns in coevolving plant and pathogen associations.** *Am Nat* 1999, **153:**S15-S33.
10. Gandon S, Capowiez Y, Dubois Y, Michalakis Y, Olivieri I: **Local adaptation and gene-for-gene coevolution in a metapopulation model.** *Proc R Soc Lond B Biol Sci* 1996, **263:**1003-1009.
11. Brown JKM: **Yield penalties of disease resistance in crops.** *Curr Opin Plant Biol* 2002, **5:**339-344.
12. Bergelson J, Purrington CB: **Surveying patterns in the cost of resistance in plants.** *Am Nat* 1996, **148:**536-558.
13. Tian D, Traw MB, Chen JQ, Kreitman M, Bergelson J: **Fitness costs of *R*-gene-mediated resistance in *Arabidopsis thaliana*.** *Nature* 2003, **423:**74-76.
14. Thrall PH, Burdon JJ: **Evolution of virulence in a plant host-pathogen metapopulation.** *Science* 2003, **299:**1735-1737.
15. Luig NH: **A survey of virulence genes in wheat stem rust, *Puccinia graminis* f. sp. *tritici*.** *Adv Plant Breeding* 1983, **11:**1-198.
16. Stahl EA, Dwyer G, Mauricio R, Kreitman M, Bergelson J: **Dynamics of disease resistance polymorphism at the *Rpm1* locus of *Arabidopsis*.** *Nature* 1999, **400:**667-671.
17. Frank SA: **Coevolutionary genetics of plants and pathogens.** *Evol Ecol* 1993, **7:**45-75.
18. Antonovics J, Thrall PH, Jarosz AM: **Genetics and the spatial ecology of species interactions: the *Silene-Ustilago* system.** In *Spatial ecology: the role of space in population dynamics and interspecific interactions*. Edited by Tilman D, Kareiva P. Princeton, NJ: Princeton University Press; 1997:158-180.