responsible for the earlier Pre-Classic abandonment of cities that occurred between about 150 and 250 A.D. These periods of drought are probably the result of climatic conditions that prevented the ITCZ and its associated rainfall from penetrating as far north as normal. Given the perspective of our long time series, it would appear that the droughts we have highlighted were the most severe to affect this region in the first millennium A.D. The intervals of peak drought were brief, each lasting between ~3 and 9 years, but they occurred during an extended period of reduced overall precipitation that may have already pushed the Maya system to the verge of collapse.

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Evolution of Virulence in a Plant Host-Pathogen Metapopulation

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In a wild plant–pathogen system, host resistance and pathogen virulence varied markedly among local populations. Broadly virulent pathogens occurred more frequently in highly resistant host populations, whereas avirulent pathogens dominated susceptible populations. Experimental inoculations indicated a negative trade-off between spore production and virulence. The nonrandom spatial distribution of pathogens, maintained through time despite high pathogen mobility, implies that selection favors virulent strains of *Melampsora lini* in resistant *Linum marginale* populations and avirulent strains in susceptible populations. These results are consistent with gene-for-gene models of host-pathogen coevolution that require trade-offs to prevent pathogen virulence increasing until host resistance becomes selectively neutral.

Infectious disease has a major influence on the demography of human, plant, and animal populations. It is generally accepted that variation in host resistance is of central importance to patterns of disease incidence and prevalence (*1*). High variability has been reported for several host loci (e.g., major histocompatibility complex and/or human leukocyte antigens) linked to disease (*1*, *2*), consistent with the selective forces imposed by pathogens (*3*). At the population level, there are indications that pathogen diversity can determine the dynamics of epidemics (e.g., the slow spread of HIV in some regions may be linked to low genetic variation in particular viral groups) (*4*). Some work has revealed negative relationships between general measures of host diversity and disease incidence (*5*–*7*). More specifically, work on the genetically well-studied *Linum-Melampsora* plant-pathogen system has shown negative correlations between population resistance diversity and disease prevalence (*8*). However, with a few notable exceptions (*9*, *10*), remarkably little effort has been directed at investigating causal links between host population genetic structure and disease dynamics. This is particularly surprising, given the potential for such variation to affect pathogen evolution and the emergence of new diseases (*11*, *12*).

Most mathematical models of the dynamics of host-pathogen coevolution, and indeed much of our current thinking about genetic interactions between hosts and parasites, have been shaped by the gene-for-gene paradigm. Essentially, this hypothesis states that for each host resistance gene, there is a corresponding avirulence gene in the pathogen with which it interacts. For a resistant reaction to occur (i.e., infection does not take place, as the host recognizes the presence of the pathogen), both the specific resistance gene in the host and the avirulence gene in the pathogen must be present. In this context, virulence is defined as the ability of a pathogen to overcome a given host resistance gene. At the population level, virulence can be thought of as the average ability of a pathogen population to overcome the diversity of resistance genes present in the corresponding host population. The gene-for-gene concept is derived from work on cultivated flax and an associated rust pathogen (*13*) but has since been shown to occur in many other systems involving interactions of plants with fungi, viruses, and some insects (*14*).

One such wild gene-for-gene interaction occurs between *L. marginale*, an herbaceous perennial endemic to southern Australia, and its host-specific rust pathogen, *M. lini*. To date, 17 separate alleles conferring resistance to a wide range of pathogen isolates have been detected in this interaction (*15*). During the growing season, generations of the pathogen follow one another in quick succession, leading to local epidemics. On the Kiandra Plain, the phenology of the host results in distinct crashes in pathogen numbers as plants die back to underground rootstocks at the end of the summer.

M. lini is an aerially dispersed rust pathogen that produces large numbers of urediospores that, like most other rust pathogens, may be dispersed large distances. For example, the appearance of a novel pathotype (distinguished by pathogenic and molecular markers) in the Kiandra area is believed to have resulted from a migration event of >100 km (*16*). In field experiments assessing pathogen extinction and recolonization in small populations of *L.*

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marginale, several instances of recolonization over distances of 80 m or more were recorded (*17*). In contrast, the seeds of *Linum marginale* have no specialized dispersal mechanisms, being distributed from open capsules by a simple "pepper-pot" shaker mechanism. Moreover, *L. marginale* populations in the Kiandra region are known to be tight inbreeders (*18*), thereby ruling out significant gene-flow through pollen dispersal.

Here we use the *Linum-Melampsora* interaction (*19*, *20*) to demonstrate the links among genetic diversity, host resistance, and the evolution of pathogen virulence and aggressiveness (defined here as pathogen fecundity—the number of spores produced per pustule) in a natural system. Previous work on a metapopulation occurring on the Kiandra Plain, Kosciuszko National Park, Australia, detected considerable differentiation, within and among populations, in resistance to local isolates of *M. lini* (*19*). Despite often marked differences between closely adjacent host populations, there was clear evidence of a nonrandom spatial distribution of resistance, with nearby populations sharing more resistance phenotypes than more distant ones. Subsequent cross-inoculation studies demonstrated strong local adaptation by *M. lini* to its host populations (*20*). This finding matched theoretical expectations for pathogens that disperse more broadly than their hosts (*21*, *22*).

Using the dataset generated for the local adaptation study, we have investigated the relationship between average host resistance and average pathogen virulence in these same populations (*23*). The results indicate a very tight evolutionary link between the resistance and virulence of associated host-pathogen population pairs, such that the virulence of a given pathogen population increases directly with the mean resistance of plant populations (Fig. 1). However, given that susceptible and resistant host populations are often closely adjacent in the Kiandra metapopulation (as close as 300 m) and that pathogen populations are highly variable and relatively mobile (*16*), this raises an important question: Why don't highly virulent pathotypes dominate susceptible host populations (Fig. 2), as might be expected from theory? This conundrum is illustrated by clear evidence that over prolonged periods of time virulent pathotypes may dominate highly diverse and resistant host populations, whereas the same pathotypes may be only intermittently present in nearby susceptible populations [Fig. 3 (*24*)].

The most likely explanation for this apparent paradox is that aggressiveness (i.e., greater spore production and transmission potential), mediated by among-pathotype competition, is favored over virulence in susceptible host populations, whereas the ability to infect multiple host genotypes (greater virulence) is favored in resistant populations. Part of this explanation rests on the assumption of a negative relationship between virulence and aggressiveness (i.e., there is a cost to carrying extra virulence genes).

Using the set of *M. lini* isolates from the local adaptation study (*20*), we examined the relationship between spore production and the number of *L. marginale* resistance genes that a given pathogen isolate could overcome (*23*). The results show a triangular relationship between average spore production and virulence such that pathotypes able to overcome few resistance genes exhibit a wide range of per pustule spore production values, whereas more virulent pathotypes able to attack a greater proportion of resistance genes show reduced levels of spore production (Fig. 4). Evidence for a trade-off between virulence and aggressiveness has been found among different pathotypes of *Erysiphe graminis* attacking mixtures of three differentially resistant barley lines (*25*). However, those results could not be set in an evolutionary context.

Although the most fit pathotypes in susceptible populations are predicted to show high aggressiveness and low virulence (with the converse for resistant host populations), less fit types may still be able to invade susceptible host populations as long as their rate of spread exceeds invasion thresholds. Although equilibrium predictions from single population models imply that the pathogen with the highest reproductive rate (R0) will eventually come to dominate, this is not necessarily what will be observed in natural situations. In wild host–pathogen metapopulations, where dynamics are highly stochastic with frequent pathogen extinction followed by reinvasion by the same or different patho-

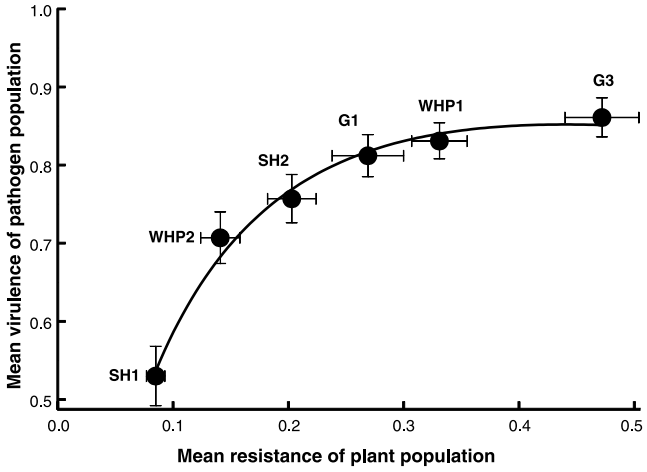

Fig. 1. Relationship between mean plant population resistance (fraction of pathogens against which resistance was observed) and mean virulence of the associated pathogen populations (fraction of hosts which could be attacked). The best fit for the relationship was given by a second-order power function ($y = a\,x^{[b\,+\,c\,\ln(x)]}$), where x and y represent mean resistance and virulence, respectively [for calculation of mean resistance and virulence values, see (*22*)].

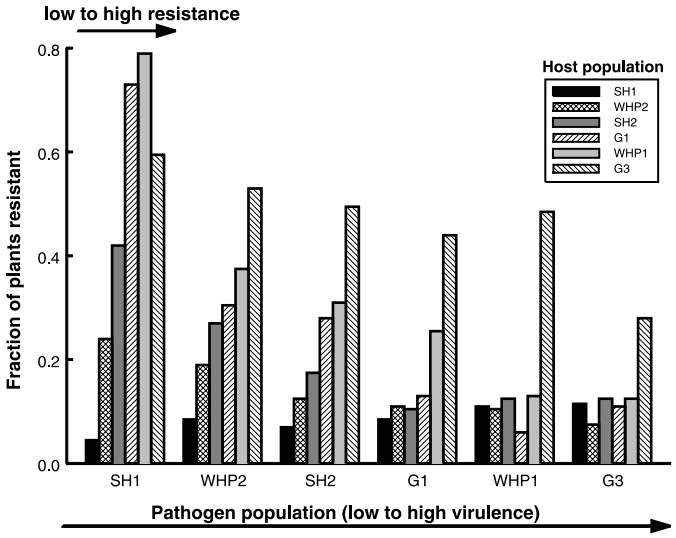

Fig. 2. The fraction of plants in each host population resistant to attack by the 10 isolates representing each pathogen population. Pathogen populations are arranged along the x axis in increasing order of average virulence from left to right. Within each pathogen population, host populations are arranged from left to right in increasing order of average resistance. Although glasshouse inoculations showed that highly virulent pathogen populations (e.g., G3) were able to infect nearly all the hosts encountered in the metapopulation, these pathogens do not constitute a major proportion of the pathogens found in susceptible host populations (e.g., as indicated in the figure, pathogen population SH1 shows low virulence against a majority of plants from more resistant host populations). In fact, one G3 isolate was able to infect all 120 plant lines across the six populations in greenhouse trials, yet this pathotype did not appear in any other population.

types in subsequent years, considerable variability can be maintained for far longer than in single populations. The effective host population size for any given pathotype is a "moving target" that is at least partly determined by the interaction of specific resistance and virulence genes. This means that the threshold for pathogen invasion will vary among populations, among pathogen isolates, and even temporally within populations as resistance and virulence coevolve.

Although partial isolation among local populations can maintain high host and pathogen variability without assuming resistance or virulence costs (*26*), this does not explain the failure of highly virulent pathotypes to dominate the system. Our results indicate that a trade-off between virulence and aggressiveness is likely to be a central causal factor in explaining these patterns. Indeed, further support for this idea comes from an earlier study where we compared host and pathogen variation in populations of two ecotypes of *L. marginale* occurring in distinctly different environments and varying significantly in overall susceptibility (*19*). As in the present study, the results showed that populations of the more resistant ecotype were dominated by more virulent *M. lini* pathotypes. This suggests that although the underlying resistance structure may have been generated by different mechanisms, the associated pathogen populations have followed similar evolutionary trajectories in response to differences in the selective environment generated by the hosts.

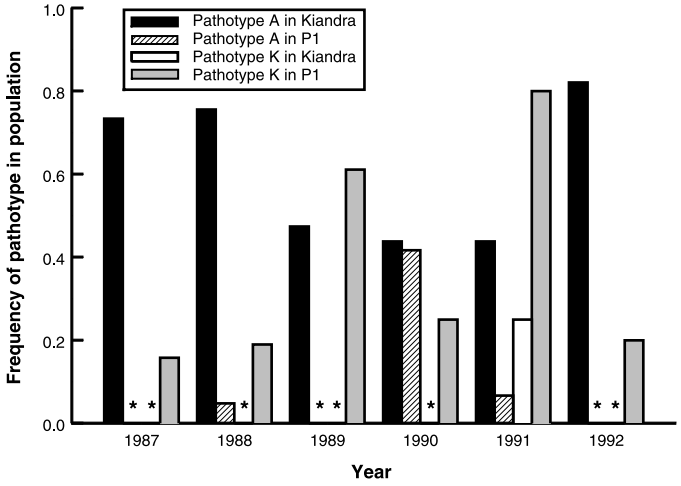

Fig. 3. Frequency of virulent (A) and avirulent (K) pathotypes of *M. lini* in resistant (Kiandra) and susceptible (P1) populations of the host plant *L. marginale* over six consecutive years. The two host populations were 300 m apart—the resistant population was composed of at least 13 different resistance phenotypes with <5% of individuals fully susceptible to a set of eight local pathotypes, whereas the susceptible population was composed of two phenotypes with >80% of individuals susceptible to the same set of pathotypes. Pathotype K was capable of attacking only one host line in a set of 11 differentially resistant lines, whereas pathotype A was able to attack four (this pathotype was virulent on both resistance phenotypes present in P1, as well as all 13 phenotypes present in Kiandra). Asterisks denote the absence of a particular pathotype in a given year rather than missing data.

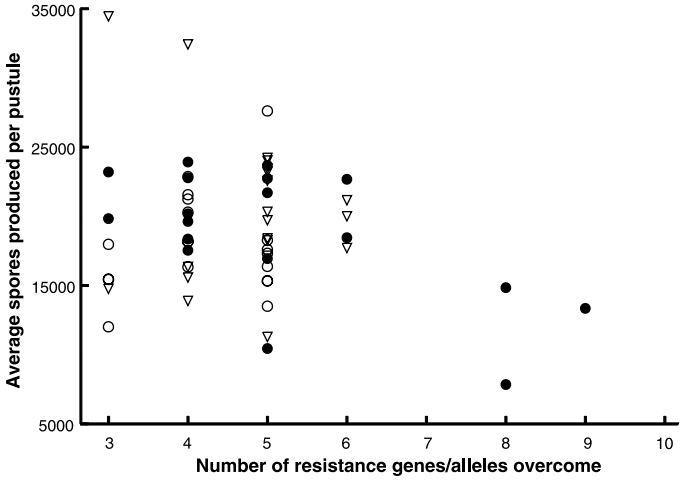

Fig. 4. Relationship between the number of resistance genes overcome by individual *M. lini* isolates and their average per-pustule spore production (4 hemocytometer counts for each of 10 pustules per pathogen isolate; 57 of 60 pathogen isolates were successful). Linear regressions showed significant negative relationships between maximum spore production values and infectivity ($r^2 = 0.99$, $P < 0.001$), and between the range of per-pustule spore production values and infectivity ($r^2 = 0.69$, $P = 0.05$), but no relationship between minimum spore production values and infectivity, confirming the triangular relationship. Isolates from the two most susceptible *L. marginale* populations (SH1, WHP2) are represented by open circles, those from populations showing intermediate resistance (SH2, G1) by triangles, and isolates from the most resistant populations (WHP1, G3) by filled circles.

The strength of the positive relationship between host resistance and pathogen virulence in the *Linum-Melampsora* interaction underscores the potential for host variation to determine evolutionary trajectories of pathogen populations. Clearly, host populations harboring many resistance alleles [often correlated with average resistance (*8*, *19*)] may favor the evolution of very different pathogen populations to those evolving in low diversity host populations. Trade-offs between virulence and aggressiveness, such as shown here, play a further important role in generating local adaptation in gene-for-gene systems by impeding the emergence and evolution of highly virulent pathotypes capable of attacking all host genotypes. This observation goes to the heart of a major evolutionary issue in plant and animal host-parasite systems regarding the balance of selection favoring virulence versus aggressiveness, as well as its implications for among-host disease transmission (*25*, *27*, *28*).

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Supporting Online Material
www.sciencemag.org/cgi/content/full/299/5613/1735/DC1
Materials and Methods

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