

The Role of Gene-for-Gene Interactions in the Determination of Host Species Specificity

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Accepted for publication 1 October 1990 (submitted for electronic processing).

All plants are "nonhosts" for the majority of potentially pathogenic microorganisms. The resistance that accounts for this nonhost status has been called basic resistance (8), nonhost resistance (5), general resistance (10), or broad resistance (17). Against fungi, studies suggest that this resistance, herein called basic or nonhost resistance, is multi-component, genetically complex, and parasite-nonspecific, and it involves constitutive and induced defenses that may or may not be the same as those that protect resistant genotypes of an otherwise susceptible host species (5,6,7). In contrast, host-genotype (cultivar) resistance toward fungi is commonly parasite-specific, is often expressed later in the infection process than basic resistance, and, from the results of classical genetical studies, may be controlled by single plant genes that are matched by single genes for avirulence in the parasite (1,2), resulting in a "gene-for-gene" interaction. For bacteria, the distinction between host and nonhost resistance is less clear because there are fewer features of infection on which to base such distinction, and because bacteria are not amenable to the same genetic studies as eukaryotic organisms. Nevertheless, differences in bacterial growth patterns and plant responses have been shown between host and "true" nonhost plants (i.e., species resistant to all biotypes of the bacterial species in question [7]) (3,20). Moreover, gene-for-gene interactions between a bacterium biotype and its host species have been demonstrated by transformation studies that show that cultivar-specific avirulence may be transferred to a virulent race by a single gene (21).

The most common mechanistic interpretation of gene-for-gene systems involving both fungi and bacteria, and for which there is direct evidence in one bacterial system (11), is that the gene for avirulence controls the production of an elicitor, the recognition of which is controlled by the gene for resistance in the plant (10). Studies of resistance to rust fungi have led to the concept that race-specific, gene-for-gene resistance is superimposed on the "basic compatibility" (2) between parasite and host species achieved when the former has evolved the pathogenicity factors necessary to overcome the basic resistance of the latter (6). This model will be called the basic compatibility model of specificity. The alternative hypothesis, that gene-for-gene interactions govern both species and cultivar specificity, necessitates the assumption that every plant has parasite-specific resistance genes for all potential pathogens, even those with which it has not come in contact during its evolutionary history. As pointed out before (6,24,26), this scenario seems highly unlikely. Nevertheless, data exist that have been interpreted as suggesting that host species specificity may be controlled by gene-for-gene systems similar to those controlling race-cultivar interactions and may even involve the same genes. For example, many single genes that confer race-specific resistance in crop plants have been introduced from noncultivated "nonhost" relatives (12), suggesting that nonhost plants have single genes for resistance that act in a race-specific manner. More recent data suggest that a weeping lovegrass strain of the fungus *Magnaporthe grisea* may contain a gene (*Avr1-M201*) that determines specific avirulence on rice cultivar M201 when introduced into strains of the fungus pathogenic on rice (23). For bacteria, a gene from a tomato strain of *Xanthomonas campestris vesicatoria* confers cultivar-specific avirulence towards bean when introduced into *X. campestris phaseoli* (25); the tomato

pathogen, *Pseudomonas syringae tomato*, contains a gene identical to *avrA* that controls the avirulence of *Pseudomonas syringae glycinea* in specific cultivars of its soybean host (13). *P. syringae tomato* also contains a gene (*avrD*) (14) that controls the production of an elicitor of necrosis active only in certain cultivars of soybean (11) and that appears to have a recessive homologue in the soybean pathovar (15). From the *P. syringae* studies, Kobayashi, et al (13) conclude that "avirulence genes may function in host-range determination at levels above race-cultivar specificity." Similarly, the fact that new genes for resistance may be revealed by hybrids of *forma speciales* of rust fungi (9,16) has led to the conclusion that "there is evidence that nonhost resistance, at least to *forma speciales*, rests on an extremely high allele frequency of effective major genes for resistance, rather than on a complex of genes that play a part in a general defense system" (16). Such a conclusion has been recently reinforced by genetic evidence of a gene-for-gene relationship between *Erysiphe graminis* f. sp. *agropyri* and *Triticum* spp. (22).

Despite the apparent strength of this evidence supporting a role for gene-for-gene interactions in determining host species specificity, there are other interpretations of the data. This letter discusses these interpretations and proposes that all the observations described above are predicted by the basic compatibility model of specificity.

The existence of genes in parasites that condition specific avirulence toward nonhost cultivars. All of the data indicating that pathogens contain genes that determine specific avirulence in nonhost plants involve bacteria and fungi with related biotypes (*forma speciales* or *pathovars*) for which the "nonhost" plant is a susceptible host. Assuming that these biotypes share a common ancestor, the process by which avirulence genes may arise is shown in Fig. 1. It is assumed from the basic compatibility model that the ancestral parasite has a host species range controlled by species specificity (*SSP*) genes; these govern the production of pathogenicity factors necessary to establish basic compatibility in host species. The parasite also has other genes (*AVRA*, *AVRB*, *AVRC*, *AVRD*) that do not control species specificity. If the parasite species is polymorphic for certain pathogenicity factors, then it may contain genotypes with different (and overlapping) host specificities. Processes such as competitive exclusion or host speciation and agricultural practices (4) may then drive the evolution of biotypes with more restricted and nonoverlapping host ranges. Fig. 1 shows two such biotypes that differ in *SSP* genes such that biotype 1 can only attack plant species 1 and biotype 2 can only attack species 2. Nevertheless, because of their common genetic background, both of these biotypes share a number of genes (e.g., the *AVR* genes) that control a variety of activities, related and unrelated to pathogenesis. Some of these may be potential avirulence genes following Person and Mayo's argument (18) that, before the evolution of a gene-for-gene interaction, genes for avirulence are genes controlling characters other than avirulence.

The basic compatibility model predicts that a gene-for-gene interaction evolves only as a response to selection pressure by the pathogen exerted after basic compatibility (or partial basic compatibility) (8) is attained. This selection pressure results in the evolution of parasite-specific forms of resistance that are activated by specific parasite molecules (e.g. elicitors). The genes that control the production of these molecules automatically become avirulence genes and the plant genes controlling the recog-

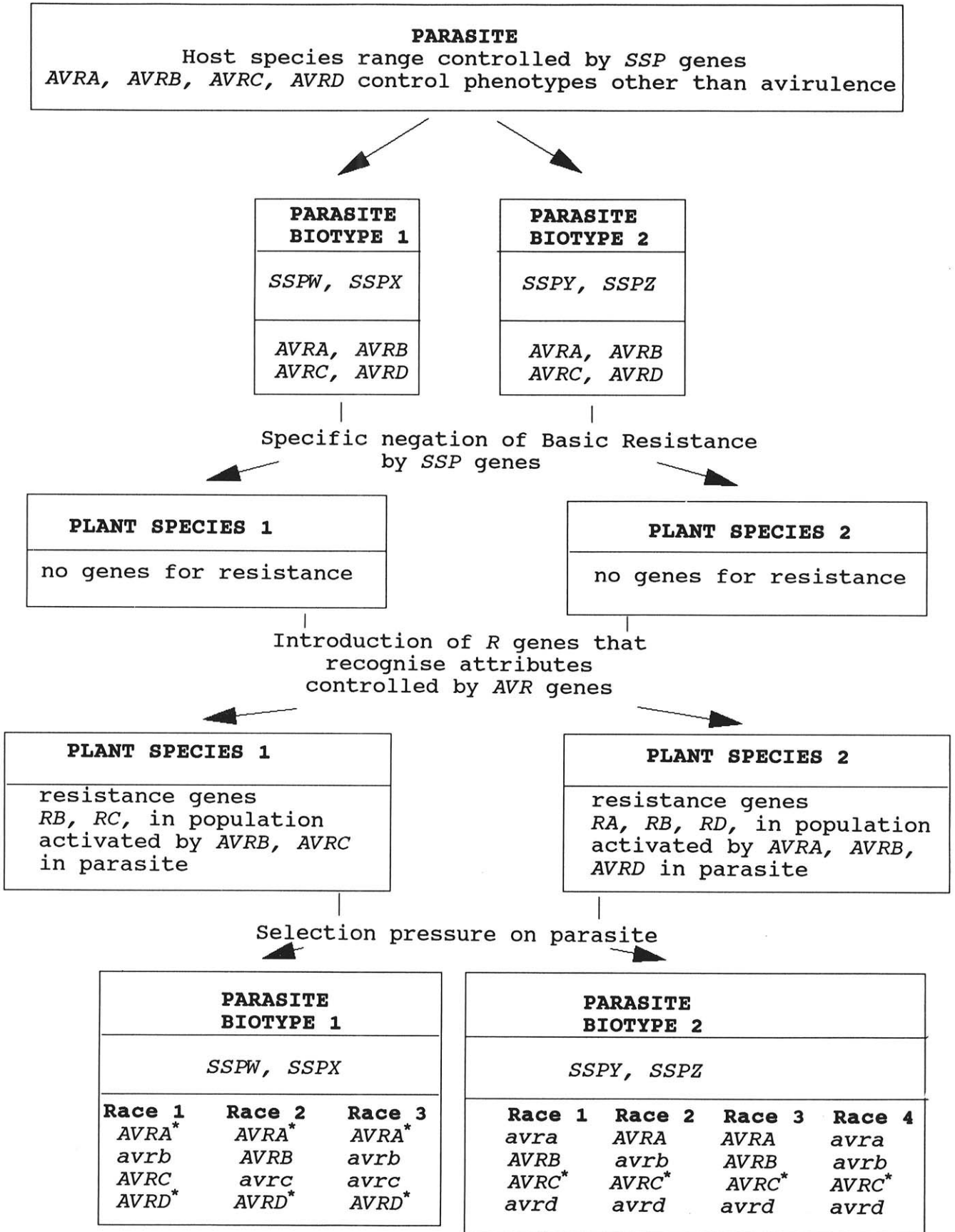


Fig. 1. Hypothetical model to illustrate the evolution of genes for resistance in the plant and of genes for avirulence in two biotypes of a parasite. Plant species 1 is a host for parasite biotype 1 but a nonhost for parasite biotype 2; plant species 2 is a host for parasite biotype 2 but a nonhost for parasite biotype 1. The host species range of each biotype is controlled by species specificity (*SSP*) genes. *AVR* genes initially control phenotypes other than avirulence before gaining their avirulence gene function. Parasite-specific resistance in host genotypes is controlled by *R* genes. (*) indicates avirulence genes for which there is a corresponding resistance gene in the nonhost species but not in the host species.

tion of each molecule are now genes for resistance. Pryor (19) has pointed out that plants generate new resistance phenotypes with unusually high frequencies, and suggests that resistance genes may arise from predesignated, hypervariable regions of the plant genome. Whether resistance genes share sequence homology across plant species remains to be determined, but it is possible that only certain types of molecules can cause their expression or interact with their products to induce resistance responses. If so, it is likely that, as shown in Fig. 1, resistance controlled by genes that develop independently in the two plant species may be elicited by molecules present in both of the two parasite biotypes. In Fig. 1, plant species 1 is shown to evolve resistance genes *RB* and *RC* to recognize the features controlled by the *AVRB* and *AVRC* genes in parasite biotype 1; plant species 2 is shown to evolve genes *RA*, *RB*, and *RD* to recognize features controlled by *AVRA*, *AVRB*, and *AVRD* genes in biotype 2. As a result, biotype 1 has genes (*AVRA*, *AVRD*) that do not control an avirulence phenotype in host species 1 but will do so in the "nonhost" species 2. Similarly, biotype 2 has a gene (*AVRC*) that does not control avirulence in host species 2 but will do so in nonhost species 1. If, as happens with rust fungi (5), basic resistance is expressed before parasite-specific resistance at each encounter site between plant and parasite, these *AVR* genes will be irrelevant in determining host species specificity; such specificity will be determined by the *SSP* genes that differ between the two biotypes. It should be noted that *AVR* and *SSP* genes have fundamentally different functions in the host-pathogen interaction. The *SSP* genes either govern the presence of molecules (e.g., enzymes that degrade phytoalexins, suppressors of defense responses) that actively negate basic resistance mechanisms in the host species, or control the absence of molecules that would otherwise trigger such defenses. In contrast, the *AVR* genes continue to have the function that they had before the evolution of the gene-for-gene interaction, at the same time producing molecules (or causing molecules to be produced) that act as cultivar-specific elicitors of resistance responses. While it is possible that, by chance, a *SSP* gene could also function as an *AVR* gene if the molecule that it produces is capable of being recognised by a resistance gene or its product, there is no inherent reason why it should do so.

Fig. 1 assumes that under the selection pressure exerted on the two biotypes by resistance in their respective hosts, new parasite races appear that have modified avirulence genes (*avr* genes) such that the defense mechanisms controlled by corresponding genes for resistance are not activated. The races of biotype 2 shown, although differing in other avirulence genes, all share *avrD*. Thus, the presence of *RD* in plant species 2 is undetectable unless *AVRD* is introduced into the parasite biotype 2 genome from biotype 1. This is the analogous situation to the revelation of a previously unknown gene for resistance found in soybean when the *avrD* gene from *Pseudomonas syringae tomato* was transferred into *Pseudomonas syringae glycinea* (13). Hybrids between parasite biotypes 1 and 2 would likely result in progeny poorly adapted to either plant species because of the reassortment of pathogenicity factors controlled by *SSP* genes; however, it is conceivable that, for example, a hybrid strain might have the pathogenicity factors necessary to infect plant species 2 but have the *AVRD* gene to reveal the presence of resistance gene *RD* in the plant. These predictions mirror reported results of studies on hybrids of rust or powdery mildew fungi (9,16).

The existence of genes governing parasite-specific resistance in nonhost plants. Fig. 1 also predicts that, for example, if *RC* from plant species 1 was introduced into species 2, all races of parasite biotype 2 would have an avirulence gene to activate it; such a situation would be analogous to the common practice of introducing a new gene for resistance into a crop plant from a wild relative. The existence of *RC*, however, depends on the existence of a biotype related to the pathogen of interest that has exerted sufficient selection pressure on the wild relative to favor a parasite-specific gene for resistance. The prediction from the hypothesis underlying Fig. 1 is that in plant species unrelated to the crop plant that are not hosts to a close relative of the

pathogen in question, resistance genes specific for this pathogen should not exist.

Apparent gene-for-gene relationships in *forma speciales*-genus interactions. The apparent gene-for-gene relationship shown by Tosa (22) for *Erysiphe graminis* f. sp. *agropyri* and *Triticum* spp. can also be explained by processes similar to those shown in Fig. 1 if it is assumed that the genes for resistance in the *Triticum* spp. arose in response to races of *E. graminis* f. sp. *tritici* that share *AVR* genes with *E. graminis* f. sp. *agropyri*. If this interpretation is correct, known races of *E. graminis* f. sp. *tritici* must contain *avr* genes to match the resistance genes in *Triticum* towards *E. graminis* f. sp. *agropyri*. However, there is also an alternative explanation of the data. As discussed before (7), related plants may share certain basic resistance mechanisms, and related pathogens may share the same pathogenicity factors. For example, the *Agropyron* host for *E. graminis* f. sp. *agropyri* may have basic resistance mechanisms **A**, **B**, **C**, and **D**, whereas a *Triticum* sp. may have resistance mechanisms **A**, **B**, **C**, and **E** (note that the letters refer to processes, not genes). Both *forma speciales* of *E. graminis* may share genes *SSPA*, *SSPB*, and *SSPC* that negate mechanisms **A**, **B**, and **C**, but *E. graminis* f. sp. *agropyri* may lack *SSPE*. While most features of basic resistance are likely to be multigenically controlled, and some may be constitutive, there is no reason why individual inducible components should not be under the control of single genes. Also, although responses associated with basic resistance may be parasite-nonspecific, there is no reason why the production of an elicitor in a given microorganism may not be governed by a single gene. Therefore, in the case under consideration, the apparent gene-for-gene interaction may represent an inducible, single-gene-controlled, residual (8) component of basic resistance (mechanism **E**) that is induced by a single-gene-controlled fungal elicitor when gene *SSPE* is absent. Unlike a gene for resistance that arose in response to selection pressure by a given pathogen and, therefore, should be parasite-specific, this plant gene should be activated by the activities of a number of potential pathogens.

Conclusions. The model discussed here predicts a complex molecular and physiological web of host-parasite interactions that is the result of millions of years of evolution and coevolution between plants and parasites. Unravelling this web will be difficult, but some of the model's predictions are testable, and related parasites with different host ranges make good investigative tools, because they may differ only in a few factors crucial for determining their different host specificities (7). However, the results will provide a misleading impression of the simplicity of the determination of host species specificity unless their place in the complex continuum of plant-parasite interactions is recognized. Even in the determination of race-cultivar specificity, Barrett (1) has argued that gene-for-gene systems are "but a small subset of a range of possible interactions between host and parasite." In summary, there are many pitfalls in data interpretation when individual components of the web of plant-parasite interactions are dissected from the entire system.

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