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When virulence originates from non-agricultural hosts: New insights into plant breeding

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ABSTRACT

Monogenic plant resistance breakdown is a model for testing evolution in action in pathogens. As a rule, plant pathologists argue that virulence – the allele that allows pathogens to overcome resistance – is due to a new mutation at the avirulence locus within the native/endemic population that infects susceptible crops. In this article, we develop an alternative and neglected scenario where a given virulence pre-exists in a non-agricultural host and might be accidentally released or introduced on the matching resistant cultivar in the field. The main difference between the two scenarios is the divergence time expected between the avirulent and the virulent populations. As a consequence, population genetic approaches such as genome scans and Approximate Bayesian Computation methods allow explicit testing of the two scenarios by timing the divergence. This review then explores the fundamental implications of this alternative scenario for plant breeding, including the invasion of virulence or the evolution of more aggressive hybrids, and proposes concrete solutions to achieve a sustainable resistance.

1. Introduction

A major question in evolutionary biology is how species can escape extinction through rapid adaptation to anthropogenic changes. Most examples of such an adaptive evolution in action involve the recurrent breakdown of monogenic plant resistance that recognizes pathogen effectors. Since Flor proposed his gene-for-gene hypothesis and conclusions based on empirical evidence (Flor, 1942, 1955, 1971), plant breeders have been fascinated by the detection of qualitative resistance genes and their introgression in agronomic species (i.e., the introduction of resistance genes by the repeated backcrossing of an interspecific hybrid with the crop species). In its simplest form, a single host qualitative resistance protein is sufficient to trigger immunity toward all pathogen populations that possess the matching avirulence (*Avr*) protein (Jones and Dangl, 2006). With few exceptions (Kolmer, 2003; Kolmer et al., 2008; Lyngkjær et al., 2000), such resistance genes generally break down soon after dispersal in the agroecosystem as a result of the emergence of a virulent population (see McDonald and Linde, 2002; Parlevliet, 2002). Examples in the literature involve a wide diversity of pathogens such as viruses (Qiu and Moyer, 1999), bacteria (Li et al., 1999), *Oomycota* (Peressotti et al., 2010) and fungi (Bayles et al., 2000; de Vallavieille-Pope et al., 2012; Guérin and Le Cam, 2004; McIntosh and Brown, 1997). Generally speaking, the durability of released resistance genes is insufficiently long to satisfy Johnson's definition of a durable resistance: a 'resistance that remains effective during its prolonged and widespread use in an environment favorable to the disease' (Johnson, 1984; Johnson and Law, 1975).

As a consequence, the time until the emergence of a new virulence is classically interpreted as a direct measure of the pathogen's adaptability. Plant pathogens are often seen as quickly evolving organisms, so that any new adaptation is able to easily occur in just a few generations after an environmental change (McDonald and Linde, 2002). Even if such an adaptive dynamic is often observed in viruses, can it be generalized to other plant pathogens such as bacteria or fungi? In fact, the few verbal and theoretical models of qualitative resistance that were developed mainly focused on only two evolutionary forces: mutation and natural selection. In other words, these models primarily dealt with the time needed for a new advantageous mutation to appear and to be fixed by selection. The more explicit theoretical models published to date have focused on the spread of a new adaptive mutation that confers virulence (Bourget et al., 2013; Fabre et al., 2009) and the way to manage the virulent genepool in order to delay the full breakdown of the resistance. For example, an interesting strategy involves a mixture of susceptible and resistant cultivars in the same field (Fabre et al., 2012; Sapoukhina et al., 2009) or a mixture of moderately resistant hosts (i.e., carrying Quantitative Trait Loci

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(QTL)) with highly resistant cultivars (Sapoukhina et al., 2013). However, the nature of these latter models remains largely deterministic, with the only stochastic parameter being the time of appearance of the new mutation to virulence.

In addition to mutation and selection, up until now, models have poorly incorporated other more stochastic evolutionary forces such as migration, recombination and genetic drift (REX Consortium, 2010). As a consequence, the effect of these stochastic parameters does not radically influence the output associated with their models, i.e., the time before the resistance is overcome. However, taking these latter forces into consideration should be relevant for a good understanding of pathogen evolutionary dynamics. For example, pathogens are known to produce large numbers of progenies (Alexopoulos et al., 1996; Andrivon et al., 2007), which favors the action of selection vs. genetic drift. However, these organisms also experience periodical bursts and founder effects that could dramatically decrease the effective size and then decrease any adaptive potential. In addition, regular production of sexual propagules (McDonald and Linde, 2002) and spreading over long distances (spores or human-aided dispersal) (Brown and Hovmøller, 2002; Wingen et al., 2013) enhance the potential for recombination and gene flow, respectively. In this article, we put forward an alternative evolutionary view of virulence emergence that focuses on standing variations in structured populations rather than rapid adaptations to resistances in the host population. As previously proposed by Burdon and Thrall (2008), connections between populations that infect non-agricultural hosts and crops can lead to the emergence of virulence through migration to the local population. Consequently, secondary contacts, i.e., gene flow and recombination between two potentially divergent populations, could possibly produce hybrid swarms where virulence could spread and compensate for its fitness cost. In addition, we highlight the fact that genetic exchanges between diverging populations could even lead to the evolution of a more aggressive population over a short period of time. This review aims to (i) explain, in detail, two alternative scenarios of emergence of virulence leading to resistance breakdown, (ii) describe how these scenarios can be explicitly tested, and (iii) highlight the importance of deciphering the mode of emergence to achieve durable resistance.

2. Evolutionary emergence of pathogens: two scenarios

In natural ecosystems, hosts and pathogens are engaged in a never-ending struggle. Hosts evolve by escaping pathogen infection and pathogens by bypassing host defenses. The terminology of war has been intensively used to describe this antagonistic co-evolution conflict. The literature in plant pathology generally opposes two main scenarios, the 'arms race', i.e., recurrent selective sweeps of new resistant and virulent alleles in hosts and pathogens, respectively (Kaltz and Shykoff, 1998), and 'trench warfare', i.e., long-term maintenance of standing polymorphism at host-pathogen recognition loci through balancing selection (Brown and Tellier, 2011; Tellier and Brown, 2011).

The first scenario, involving co-evolution, is not applicable in agroecosystems as is since host evolution is determined by the recent introgression of resistance genes from exotic (i.e., non-local) cultivars or species. This scenario, however, represents the emergence of virulence that involves a new adaptive mutation (a selective sweep) from avirulence to virulence within the agroecosystem. The second scenario instead involves the migration of a pre-existing virulent strain from a native ecosystem to the agroecosystem (Burdon and Thrall, 2008). The latter takes connectivity between non-agricultural hosts and crops that has been neglected in the plant pathogen literature into consideration (Burdon and Thrall, 2008; Jones, 2009). As we point out at the end of this section, the crucial difference between these two alternative scenarios is the divergence time between the avirulent and the virulent population.

2.1. First scenario: a new adaptive mutation from avirulence to virulence

Rapid evolutionary changes from avirulence to virulence are usually attributed to loss-of-function mutations at the *Avr* locus within the agroecosystem. Overcoming a resistance is described as a consequence of the spread of a new virulent mutant that invades resistant cultivars from infected susceptible ones (A, Fig. 1). Cloning of *Avr* genes indicates that molecular events leading to loss-of-function at the *Avr* locus are multiple: non-synonymous point mutations (Catanzariti et al., 2006; Joosten et al., 1997; Stergiopoulos et al., 2007), insertions of transposable elements (TE) (Fudal et al., 2009) or complete deletions of the *Avr* gene (Catanzariti et al., 2006; Chuma et al., 2011; Fudal et al., 2009; Gout et al., 2007; Orbach et al., 2000; Stergiopoulos et al., 2007). Plant pathogen studies have highlighted that one or two substitutions may be sufficient to break down the resistance (Fudal et al., 2009), and particularly in viruses (Ayme et al., 2006; Harrison, 2002; Lecoq et al., 2004). In fungal and oomycete pathogens, genomic regions with low gene density resulting from the mobility of TE are rapidly evolving (Ma et al., 2010; Raffaele and Kamoun, 2012). These TE-rich regions are particularly subjected to repeat-induced point (RIP) mutations, a process that inactivates duplicated genes through the accumulation of massive point mutations. Given the abundance of candidate effector genes in TE-rich regions (Rouxel et al., 2011), RIP might result in new functional alleles with premature stop codons or non-synonymous substitutions (Coleman et al., 2009; Fudal et al., 2009; Van de Wouw et al., 2010).

Given that mutations in an avirulence gene enable evasion of recognition by the plant resistance gene, the gain of virulence results in an increased fitness on resistant host genotypes. However, it is generally assumed that a fitness cost on susceptible hosts explains why virulence does not invade susceptible crops (Van der Plank, 1963). Empirical examples of this evolutionary trade-off between virulence and fitness have been widely reported (Vera Cruz et al., 2000; Leach et al., 2001; Thrall and Burdon, 2003; Huang et al., 2006; Montarry et al., 2010), but examples of mutated avirulence genes without any fitness defect also exist in the literature (Gassmann et al., 2000; Kunkeaw et al., 2010; Leach et al., 2001; Peressotti et al., 2010). Under this 'mutation-to-virulence' scenario, QTL are expected to be more durable because these resistances are assumed to induce less selective pressures on pathogen populations (Parlevliet, 2002). However, this view surmises that adaptation is only limited by the time required for adaptive mutations to occur and, therefore, that no standing genetic variations are already available at these loci.

2.2. Second scenario: migration from pre-existing virulent populations

Recombination allows multiple beneficial mutations to be simultaneously introgressed in the same genetic background and deleterious mutations to be purged (Felsenstein, 1974). The importance of recombination in plant pathogens has been quite neglected (Burdon and Thrall, 2008; but see Monteil et al., 2013). If recombination occurs, favorable mutations present in different individuals can ultimately be combined in the same genome. These mutations are not necessarily recent. Recombination can mix old polymorphisms in genomes and redistribute new genotypes in the adaptive landscape, thus leading to the discovery of new optimal adaptive peaks (Barton, 2010; Karasov et al., 2010). In eukaryotic pathogens, adaptation by recombination may occur when

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