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Chapter 1

A PERSONAL PERSPECTIVE OF THE LAST 40 YEARS OF PLANT PATHOLOGY: EMERGING THEMES, PARADIGM SHIFTS AND FUTURE PROMISE

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Abstract: The last 40 years of experimental research have resulted in a remarkable increase in our understanding of plant disease resistance to microbial pathogens, with a recent surge of clarity primarily provided by the application of molecular genetics to pathogen interactions with *Arabidopsis thaliana*. Research foci have changed over time with the availability of new techniques and the ability to identify genes, proteins, signalling systems and defensive biochemicals involved in plant resistance. In hindsight, early concepts were generally simplistic. Although some have been supported by subsequent data, others, such as the basis for the gene-for-gene phenomenon, have changed dramatically and it is now clear that plant–microbe interactions are sophisticated and complex. Much is left to discover: the role of the hypersensitive response is still enigmatic, the interplay of recognition events and defensive factors that control host or non-host resistance is still not clear and the number of well-studied pathosystems is still few. The future promises more attention to the spatial organisation of disease resistance at the cellular level, and new insights into the evolution of disease resistance and pathogen pathogenicity. Particularly urgent is the need for unequivocal data to prove which plant genes and processes involved in disease resistance are primarily responsible for the restriction of pathogen growth. Disappointingly, our considerable progress in understanding plant–microbe interactions in the last 40 years has not translated into comparable progress in developing novel, widespread and effective methods of disease control in the field, and this remains a significant challenge for the future.

Keywords: disease resistance; gene-for-gene hypothesis; host resistance; hypersensitive response; non-host resistance; resistance genes

1.1 Introduction

There is an often-quoted saying, of controversial origin and meaning, that states, 'May you live in interesting times'. Since entering the field of plant pathology as a graduate student in 1966, I believe that I have lived in very interesting times, both inside and out of academia. In 1966, the genetic code had only just been cracked and the field of 'physiological plant pathology' was in its infancy. In 1967, my PhD supervisor, Professor R.K.S. Wood, summarised virtually all that was known at the time about microbial infection and plant disease resistance in a 570-page book (Wood, 1967) – something that would be impossible to do today. When the book was being written, it was recognised that pathogens could produce disease-promoting substances, such as cell wall-degrading enzymes or toxins, that diseased plants had altered metabolism and that there was a variety of preformed structures and compounds that potentially could protect plants against pathogen attack. The more dynamic interactions between plant and pathogen were only just beginning to be appreciated with the discovery that plants actively produced low-molecular-weight antimicrobial compounds (phytoalexins) in response to infection (Cruickshank, 1963) and, subsequently, with the revelation that microorganisms might combat these compounds by producing phytoalexin-degrading enzymes (e.g. Higgins and Millar, 1970). Although there had been a number of earlier light microscopical investigations of diseased plants, in the 1960s, electron microscopy began to be applied to plant pathology, revealing new information almost daily about structural changes occurring at the plant–parasite interface, particularly with respect to fungal parasites (Bracker, 1967). It was an exciting time during the next two decades as more researchers became interested in the mechanisms of plant disease resistance, and models to explain host–parasite specificity were constructed and extensively debated as new biochemical, genetical and structural data were revealed (e.g. Hadwiger and Schwochau, 1969; Albersheim and Anderson-Prouty, 1975).

In hindsight, many of the early concepts of host–parasite specificity were simplistic, and there was a degree of arrogance in the assertions that some new technique or equipment would provide complete insight into how plant and pathogen were interacting. The progression of information and concepts since 1966 has been fascinating, and this review is a personal perspective of how concepts, paradigms and research focus have changed over the last 40 years in our search for an understanding of plant disease resistance. I have concentrated on three intertwined topics that, to me, best illustrate the often-tortuous route by which we have arrived at our current state of knowledge.

1.2 The hypersensitive response

The term 'hypersensitive' was first applied by Stakman (1915) to describe resistant cereals that responded to rust fungal infection with a rapid, but

limited, death of cells at the infection site. The subsequent realisation that an apparently similar rapid cell death was a common expression of plant disease resistance, both in resistant genotypes of host species and in non-host plants, led to its designation as the 'hypersensitive response' (HR). Whether the HR was a cause or consequence of disease resistance became a matter of hot debate (Heath, 1976). For biotrophic cellular pathogens or viruses, which require a living cell for growth, plant cell death at the infection site seemed a reasonable mechanism of disease resistance, but it was less obvious why the HR should be associated with resistance to non-biotrophic pathogens that were capable of growing in dead tissue. This conundrum seemed partially solved with the discovery that the HR appeared to be universally accompanied by antifungal phytoalexin accumulation at the infection site and that dead cells released molecules that elicited the synthesis of phytoalexins in their living neighbours (Hargreaves and Bailey, 1978). However, the picture became clouded again with the gradual appreciation that plants possess a multiplicity of inducible defensive factors in addition to phytoalexins, including other toxic molecules and a variety of antimicrobial proteins collectively known as pathogenesis-related (PR) proteins (van Loon and van Strien, 1999). The revelation that so many anti-microbial factors were associated with the HR and that these factors could be elicited by pathogen molecules in the absence of cell death, again raised the question of what actually caused the cessation of pathogen growth during the HR and what was the significance of the cell death part of the response.

The 1990s saw the beginning of what, in my opinion, has been an incredibly illuminating period in the field of plant–pathogen interactions, when hard data from molecular genetics began to replace the circumstantial evidence and hypothetical models prevalent in the previous decades. Hope for increased understanding of the HR came with the initial cloning of 'resistance (*R*) genes' that govern the expression of the HR during cultivar resistance in host plant species (Dangl, 1995) and the use of *Arabidopsis thaliana* mutants to reveal the existence of different defence signalling pathways, of which the salicylic acid-dependent pathway seemed most commonly associated with *R* gene-mediated resistance and the HR (Glazebrook, 2005). *Arabidopsis* mutants clearly demonstrated that different signalling pathways were differentially induced by different microbial pathogens (Thomma *et al.*, 2001) and that the *Arabidopsis* phytoalexin camalexin did, indeed, detrimentally influence pathogen growth *in planta*. However, the phytoalexin did not affect all pathogens tested and may not act alone (Thomma *et al.*, 1999). Interestingly, of those tested, the only pathogens affected by the phytoalexin were necrotrophs, which were not triggering an HR and for which there are no known gene-for-gene relationships with the plant (Glazebrook, 2005).

With such studies came the first widespread acceptance that the details of each plant–microbe interaction are likely to be unique with respect to the plant responses that are elicited and effects they have on the pathogen – a

conclusion that had been argued before on theoretical grounds (Heath, 1981a) and that has been further strengthened by subsequent molecular data (Jones and Dangl, 2006). Nevertheless, the current paucity of plant mutants with defects in the expression of specific defences means that there are still few, if any, examples of the HR where the factor(s) causing cessation of pathogen growth is unequivocally known.

Interest in the actual process of HR-associated cell death blossomed about a decade ago when a 'hot topic' in mammalian research was a form of programmed cell death (PCD) known as *apoptosis*. In the search for analogous processes in plants, it was realised that hypersensitive cell death, long known to be an active process requiring plant metabolism (Tomiyama, 1971), was a likely candidate. This idea was strengthened by the demonstration of a hallmark of apoptosis, the cleavage of plant nuclear DNA into oligonucleosomal fragments, during some examples of the HR (e.g. Ryerson and Heath, 1996). Since the constant association of defensive compounds with the HR makes it difficult to investigate the actual death process in isolation from defence responses, some of the more illuminating investigations of hypersensitive cell death have involved cytological studies using regular light microscopy (e.g. Tomiyama, 1971) and, more recently, computer-enhanced light microscopy and cytochemical techniques applicable to living cells. These techniques, often coupled with the use of pharmacological agents, have revealed that hypersensitive cell death generally requires an intact actin cytoskeleton and ion fluxes, and often involves the generation of reactive oxygen species (ROS) (Heath, 2000a). The discovery of the importance of ROS in plant–pathogen interactions, as in animal defence systems, was arguably another milestone in our understanding of how plants respond to potential pathogens. In the mid-1990s, a variety of studies suggested that plant cells respond to mechanical perturbations (Yahraus *et al.*, 1995) and pathogens or pathogen products with an 'oxidative burst' (Baker and Orlandi, 1995) that may have a signalling role in plant disease resistance (Lamb and Dixon, 1997). A direct role for ROS in hypersensitive cell death is suggested by the fact that a mutation in an *Arabidopsis* gene that limits photo-oxidative damage causes the HR to spread *Peronospora parasitica* (Mateo *et al.*, 2004). However, cytochemical and pharmacological studies do not support a direct role of ROS in all examples of the HR, correlating with the fact that video microscopy of living cells during the death process shows very distinct differences between different plant–microbe interactions in the speed in which the cell dies and the manner with which the various cell components are dismantled (Christopher-Kozjan and Heath, 2003).

With the increased interest in searching for plant parallels with animal apoptosis came more studies on other forms of plant PCD. Unlike the HR, developmental PCD is not associated with the accumulation of defence compounds and seems to have different cytological events accompanying cell death (Heath, 1998). If it is correct that cells are dismantled in different ways in different HRs and that these processes differ from those of other types of

plant PDCs, this adds yet another level of complexity to the HR and to the phenomenon of PCD in flowering plants.

Despite all we know about the HR, we have yet to answer the fundamental question of why cell death is needed to resist attack by cellular pathogens. The question is even more pertinent now that there are examples of experimental separation of this death from defence gene induction and disease resistance (Heath, 2000a) as well as data to suggest that hypersensitive cell death and defence gene activation during the HR may involve separate signalling pathways (Zhou *et al.*, 1998). One possibility worth exploring is that the primary role of cell death in the HR is to generate signals that trigger defence responses in local and distant non-infected tissue (Heath, 2000a).

1.3 The gene-for-gene hypothesis

The gene-for-gene hypothesis was proposed by Flor as a result of his studies, in the first half of the twentieth century, on the inheritance of pathogenicity in different races of the flax rust fungus, *Melampsora lini*, to cultivars of flax differing in genes for resistance. He suggested that 'for each gene that conditions reaction in the host there is a corresponding gene in the parasite that conditions pathogenicity' (Flor, 1971). With subsequent demonstrations that resistance in the plant and avirulence in the pathogen are usually dominant, the gene-for-gene hypothesis morphed into implying that for every gene for resistance in the host there is a corresponding gene for avirulence in the pathogen. In my opinion, few other concepts in plant disease resistance have had such a fundamental effect on the field of plant pathology and few have changed so dramatically with the advent of molecular genetics.

As well as being of enormous practical significance to plant breeders, the gene-for-gene hypothesis has dominated research into the basis of plant disease resistance, despite the fact that the number of systems clearly demonstrated to have gene-for-gene relationships is relatively small and these are predominantly diseases caused by pathogens that require living plant cells for their survival. The comparative ease of working with resistance that was genetically easily manipulated and that could be clearly distinguished from susceptibility by the common presence of the HR attracted researchers away from more genetically complex disease systems that showed only quantitative differences between resistance and susceptibility and involved preformed as well as inducible defences (see examples in Heath, 2000c).

The initial explanation for gene-for-gene relationships at the physiological level was that the gene for avirulence in the pathogen coded for an elicitor that directly interacted with the product of the corresponding gene for resistance in the plant, somehow causing an HR. However, trying to reconcile the available genetic data with the available knowledge of the regulation of gene expression and with the plethora of defence responses known to

accompany the HR proved problematic. Indeed, Ellingboe (1982) argued that failure to find ratios of avirulence (*Avr*) genes in the pathogen to *R* genes in the host other than 1:1 eliminated a role for phytoalexins in resistance since they were the end products of complex biochemical pathways controlled by many genes. However, he rightly advocated the need to identify the products of *Avr* and *R* genes as well as the use of mutants to provide proof of the role of specific defences in resistance.

The search in the 1970s for pathogen molecules that triggered phytoalexin production in a race-specific manner, as might be expected of an *Avr* gene product, had some success (Keen, 1975). However, most tested pathogen products were 'non-specific elicitors' that triggered responses in both resistant and susceptible plants, instead of being 'specific elicitors' that would trigger responses only in plants with specific *R* genes. It was not until 1984 that the first bacterial *Avr* gene was cloned (Staskawicz *et al.*, 1984) and some years later before one was cloned from a fungus (van Kan *et al.*, 1991) or a virus (Culver and Dawson, 1991). As more *Avr* genes were cloned, it became clear that *Avr* genes from different fungi or bacteria have little homology and some appear to be involved in pathogenicity, in accordance with the earlier argument by Person and Mayo (1974) that these genes had other functions prior to their products being co-opted as resistance-inducing recognition factors. However, even by the end of the twentieth century, relatively few specific elicitor molecules had been characterised, and not all had been proven to be products of *Avr* genes (Heath, 2000a) although most, but not all (Ji *et al.*, 1998), were proteins or peptides. For bacterial pathogens, we now know that the difficulty in isolating specific elicitors was due to the fact that bacterial *Avr* proteins generally are not secreted in culture but are delivered directly into the plant cell (Dangl and Jones, 2001).

The first *R* gene product to be identified was an anomaly in that it coded for an enzyme that degraded the host-selective toxin that acted as a pathogenicity factor for the nectrotrophic fungus, *Cochliobolus carbonum* race 1 (Meeley *et al.*, 1992). This pathosystem does not follow the normal pattern for those involving host-selective toxins, whereby pathogenicity in the pathogen is dominant and resistance in the plant is recessive. Thus, it acts as a reminder that much of our information, even today, applies to a limited number of experimentally manipulatable pathosystems, and there are probably exceptions to every rule.

Once a more typical *R* gene was cloned (Martin *et al.*, 1993), cloning of others progressed rapidly, many from *Arabidopsis* (Dangl and Jones, 2001). By 2001, five classes of *R* genes were recognised and there were data to show that, depending on the pathosystem, *Avr* gene products may or may not bind directly to *R* gene products (Dangl and Jones, 2001). With the concurrent demonstration that *R* gene activation results in the deployment of signalling pathways that lead to the expression of PR proteins, it finally became clear that there are more plant genes involved in 'gene-for-gene' resistance than the *R* gene itself.

It could be argued that for more than 20 years, 'tunnel vision' among researchers due to their focus on the apparent gene-for-gene relationship governing resistance of specific genotypes of host plants to specific genotypes of the pathogen had been a major obstacle in reconciling genetic and physiological information on disease resistance within host species. It is now apparent that the reason why classical genetic studies did not reveal the myriad of genes now known to be involved in the expression of *R* gene-controlled resistance is a lack of natural variation in these genes within the plant population and/or a degree of redundancy within defensive responses. The revelation of the true complexity of gene-for-gene interactions had to await the development, in other disciplines, of techniques used in modern molecular genetics and the discovery of the incredible usefulness of the weed plant, *Arabidopsis*.

1.4 Host versus non-host resistance

When I first started working on non-host resistance in the 1970s, the term was not in common usage. Many physiological or cytological studies of disease resistance did not make clear distinctions between the gene-for-gene resistance seen in host species towards different genotypes of a specific pathogen, the resistance of an otherwise susceptible plant species to forms of its pathogen that are adapted to other plants or 'true' non-host resistance in which all genotypes of a plant species are resistant to all genotypes of the pathogen species. Several times I was told that studying non-host resistance was a waste of time because it could not be investigated by classical genetics, that this resistance was uninteresting because it was caused by passive physical or chemical barriers or that it was just a manifestation of the plant 'not being a suitable host' for the pathogen. However, within a decade it was more widely appreciated that non-host resistance was of considerable significance since every plant is a non-host to the majority of plant parasites it encounters. Moreover, the narrow host range of most pathogens implies that non-host resistance is difficult to overcome – a desirable feature when breeding for resistance. A suggested explanation for this durability of non-host resistance came from data indicating that this resistance was non-specific, multicomponent and often involved both preformed and inducible defences (Heath, 1981a,b), a conclusion that still seems viable today (Lipka *et al.*, 2005; Jones and Dangl, 2006).

In the mid-1970s, it was suggested from genetic considerations that the gene-for-gene resistance seen in interactions between a specific pathogen genotype and a specific host genotype must be superimposed on a 'basic compatibility' between these pathogens and their host plant species (Person and Mayo, 1974; Ellingboe, 1976). However, it was only with increased information on non-host resistance that it became apparent that this basic compatibility required each species of pathogen to evolve traits to specifically

overcome the non-host defences of its host (Heath, 1981a). For biotrophic fungal pathogens and some bacteria, we now know that these traits include the ability to specifically suppress certain defence responses by mechanisms that differ between pathosystems (Heath, 2002; Abramovitch and Martin, 2004; Glazebrook, 2005; Fujikawa *et al.*, 2006; Jones and Dangl, 2006).

With an increasing interest in non-host resistance came the debate on whether inducible components of this resistance were simply the result of multiple *Avr–R* gene interactions or were elicited by non-specific recognition events involving non-specific elicitors. Extensions of these questions were whether *R* genes were involved in host resistance that was not dependent on the pathogen's genotype (race–non-specific resistance) and whether *R* genes could be exploited in breeding for a disease resistance that was as durable as non-host resistance (Johnson, 1984). Within the last decade, this debate has resurfaced with the concept that non-host plants respond to potential pathogens via the perception of generic microbial products (non-specific elicitors) by transmembrane 'pattern recognition receptors' (Jones and Dangl, 2006), and the potentially contrary suggestion that there may be pathogen-specific recognition in some examples of non-host resistance in which a single pathogen molecule and/or single pathogen gene is all that needed for the elicitation of a defensive response (usually a visible HR) (Heath, 2001). These different data-based conceptions of non-host resistance, together with evidence that certain *R* genes may stimulate a basal (i.e. non-host type) defence pathway (Xiao *et al.*, 2005), suggest that there is considerable diversity in, and cross-talk between, the molecular events that occur in host or non-host disease resistance.

Despite an overlap in molecular events that may occur in non-host and host resistance, the former is commonly expressed earlier after pathogen contact than the latter. As a result, the HR may be pre-empted by earlier defence responses in some examples of non-host resistance to bacteria (e.g. Soylu *et al.*, 2005) and pre-penetration resistance to fungi (e.g. Mellersh *et al.*, 2002; Lipka *et al.*, 2005). However, if a fungus does manage to reach the cell lumen in a non-host, the cell usually dies. Interestingly, video microscopy of living cells coupled with pharmacological studies suggests that the process of this non-host hypersensitive cell death is not the same as that exhibited by the same plant when it is acting as a resistant host (Christopher-Kozjan and Heath, 2003). Also significant is evidence that there is some signalling commonality in the cell death triggered by a variety of *R* genes (Muskett *et al.*, 2002; Gabriels *et al.*, 2007). It is an intriguing idea that *R* genes commonly trigger a different hypersensitive cell death from that evolved to non-specifically defend plants against microbial invaders.

1.5 Future promise

During the last 40 years, we have learned an enormous amount about how plants defend themselves against pathogen attack. In addition to the

features discussed above, we now know that localised defence responses may prime the rest of the plant to exhibit increased resistance to further invasion (Kuć, 1982), a phenomenon originally called induced resistance, but now generally known as systemic acquired resistance (SAR). There is also some evidence that damaged plants communicate stress to their neighbours (Baldwin and Schultz, 1983), although such studies usually involve herbivory, rather than pathogen, damage. Encouragingly, some disease resistance concepts based on deductive reasoning have not changed over the years and have been strengthened by new data, but others have changed dramatically. Time has not changed my opinion that careful cytological studies provide important, fundamental and objective information on any plant–pathogen interaction, and should be the first line of investigation. There have been, for example, cases where simple cytological observations of the manner of fungal pathogen growth, and it is time of cessation in resistant plants, could have channelled biochemical studies into more relevant time frames and would have revealed flaws in disease resistance models. Another factor that is now better appreciated is that with fungal and oomycete pathogens in particular, critical events during the infection process may be localised to a single cell, making it important to be able to distinguish these events from others that may subsequently occur in adjacent non-penetrated neighbours. Studying single cells in plants is technically difficult, although several laboratories have been successful at looking at pathogen-triggered gene expression in individual epidermal cells (Matsuda *et al.*, 1997; Mould *et al.*, 2003; Gjetting *et al.*, 2007). Such studies coupled with cytological and cytochemical investigations are beginning to suggest that significant plant–pathogen interactions may begin moments after contact between the two organisms. For example, it seems that for interactions with some biotrophic fungi, whether the plant cell is going to respond as a non-host, a susceptible host or resistant host is determined by events that happen prior to the complete penetration of the plant cell wall (Heath, 2002; Mould *et al.*, 2003). Given that there have been considerable recent advances in imaging the cell biology of plant–microbe interactions (Heath, 2000b; Koh and Somerville, 2006) and there now seems to be a wider appreciation of the value of combining cytological studies with other types of investigations, it is likely that more attention will be paid in the future to the spatial organisation of recognition events and defence responses between and within affected cells (e.g. Robatzek, 2007).

If we have learned anything from the last 40 years of plant disease resistance research, it is that the plant's interaction with potential microbial invaders is much more complex and sophisticated than originally imagined. We now know that different pathogens have different modes of infection and that different plants have different defence biochemistries, thereby requiring each pathogen to evolve specific adaptations to overcome the specific mix of physical and biochemical features of its host. As the data from studies with *Arabidopsis* mutants have confirmed, this means that the exact details of each plant–pathogen interaction will be unique – even with respect

to resistance of the same plant to the same pathogen species governed by different genes for resistance (Eulgem *et al.*, 2004). Therefore, we still have a lot to learn when one considers that disease resistance studies have focused on relatively few pathosystems, given that there are over 250 000 extant species of flowering plants and an unknown, but probably huge, number of microbial plant pathogens. However, the application of molecular genetics has also revealed commonalities in terms of signalling systems and defence gene involvement, both between plants and between different types of resistance, implying that all types of plant resistance, be it non-host, host, age-related, SAR or organ-specific, likely exploit different parts and/or combinations of the same complex web of interacting signalling systems and defensive biochemicals and processes that each plant possesses. Therefore, the uniqueness of each interaction is based on which signalling pathways are triggered or suppressed by the pathogen, the sensitivity of the pathogen to each defensive product or process and variation between plants (and/or plant parts) in whether certain defence gene expression is constitutive or has to be induced (Heath, 2000c, 2001). Attempts to fully understand even a few examples of disease resistance seem likely to keep researchers occupied for some time to come.

The recent exponential increase in our understanding of plant–microbe interactions has primarily been the result of the application of molecular genetics to pathogen interactions with *Arabidopsis*, and the result of looking for homologues of *Arabidopsis* genes in other plants (e.g. Pajerowska *et al.*, 2005). The surge in interest in non-host resistance is, in large part, due to the fact that genes involved in this process now can be revealed without having to resort to classical genetic studies involving the crossing of unrelated species. The ability to use genome arrays to monitor the expression profiles of huge numbers of genes after infection (e.g. Eulgem *et al.*, 2004) has removed much of the bias that a researcher might have in choice of plant response to examine, and has served to emphasise dramatically how responsive plants are to pathogen attack. As genome arrays for more plant species become available, other pathosystems can be examined in similar detail. With all this increased information comes the challenge of designing computational methods to manage the data and to sort what is important in disease resistance from what is secondary. For this, gene silencing and other techniques to selectively prevent or stimulate gene expression will be important. However, it is currently easier to identify the genes that are involved in disease resistance than it is to identify what happens in the plant cell after the expression of these genes, particularly when it comes to the trafficking of molecules between cellular compartments and the spatial and biochemical events that actually stop pathogen growth. I hope that this is where there will be great strides forward in the future.

For most of the last 40 years, there have been only sporadic attempts at comparing disease resistance in animals and plants, but this has changed in the last decade or so with the ability to compare genes, proteins and

signalling systems across kingdoms. As a result, emphasis has shifted to common underlying principles between animal and plant defence systems rather than their differences. In part, this explains some of the terminology changes that have recently taken place. For example, the 'basic resistance' (Heath, 1981a) in each plant that accounts for non-host resistance and for 'residual' disease resistance in susceptible plants has given rise to the term 'basal resistance' (Jones and Dangl, 2006) or 'basal immunity' (Robatzek, 2007), and non-specific plant defences are now considered part of the plant's 'innate immunity' to disease, and there are reviews on the 'plant immune system' (Jones and Dangl, 2006). At the level of receptors and signalling cascades, conservation across kingdoms of eukaryotic organisms is not unexpected, but this unifying approach can be problematic if it narrows conceptual thinking. I have already seen a change in the study of hypersensitive cell death where researchers either force their observations into what they expect to see on the basis of the process of mammalian apoptosis or channel their studies into looking for specific apoptotic features. Animal pathosystems may well provide some clues as to the nature of some plant–pathogen interactions, but we should also appreciate that plants have been genetically isolated from animals and subject to different evolutionary pressures, for over 400 million years. Even within the plant kingdom, although some genes involved in defence signalling appear to be conserved between higher plant species (e.g. Muskett *et al.*, 2002), others may have changed with time in role and function (Mcdowell and Simon, 2006). Particularly intriguing are data suggesting that plant genes involved in disease resistance also have a role in plant development (e.g. Holt *et al.*, 2002). We are just at the beginning of an exciting period where molecular tools and innovative classical genetic systems (Jafary *et al.*, 2006) are now available to determine just how plant disease resistance and pathogen pathogenicity have evolved during the evolution of higher plants.

As demonstrated by the other chapters in this volume, the distance that we have travelled from Wood's all-encompassing book in 1967 is astounding. One disappointing feature, however, is that there are very few examples where our increased knowledge of the basis of plant disease resistance has resulted in new ways of controlling plant diseases in the field that are commercially viable and in widespread use. The overexpression of defence response genes in transgenic plants has shown promise for some pathogens (e.g. Mackintosh *et al.*, 2007), but most successful has been the use of pathogen infection or other treatments to induce systemic plant resistance, although the level of disease control is not always sufficiently high for the treatments to be used alone (Walters *et al.*, 2005). It seems certain that the next 40 years will bring as many, or more, revelations on the basis of plant disease resistance as did the last, and it is to be hoped that our basic understanding of plant–microbe interactions at the molecular and cellular level can eventually be exploited to produce a significant effect on the disease resistance of our domesticated plants.

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