New Phytologist

Review

Tansley review

An evolutionary framework for host shifts – jumping ships for survival

Author for correspondence:
Marco Thines
Tel: +49 6975421833
Email: m.thines@thines-lab.eu

Received: *11 December 2018*
Accepted: *4 July 2019*

Marco Thines[1,2,3]

[1]Department of Biological Sciences, Institute of Ecology, Evolution and Diversity, Goethe University, Max-von-Laue-Str. 13, D-60486, Frankfurt am Main, Germany; [2]Senckenberg Gesellschaft für Naturforschung, Senckenberg Biodiversity and Climate Research Centre (BiK-F), Senckenberganlage 25, D-60325, Frankfurt am Main, Germany; [3]LOEWE Centre for Translational Biodiversity Genomics (TBG), Georg-Voigt-Str. 14-16, D-60325, Frankfurt am Main, Germany

Contents

New Phytologist (2019)
doi: 10.1111/nph.16092

Key words: co-phylogeny, co-speciation, host jump, macroevolution, microbiome, pathogen evolution, rapid adaptation.

Summary

Host jumping is a process by which pathogens settle in new host groups. It is a cornerstone in the evolution of pathogens, as it leads to pathogen diversification. It is unsurprising that host jumping is observed in facultative pathogens, as they can reproduce even if they kill their hosts. However, host jumps were thought to be rare in obligate biotrophic pathogens, but molecular phylogenetics has revealed that the opposite is true. Here, I review some concepts and recent findings and present several hypotheses on the matter. In short, pathogens evolve and diversify via host jumps, followed by radiation, specialisation and speciation. Host jumps are facilitated by, for example, effector innovations, stress, compatible pathogens and physiological similarities. Host jumping, subsequent establishment, and speciation takes place rapidly – within centuries and millennia rather than over millions of years. If pathogens are unable to evolve into neutral or mutualistic interactions with their hosts, they will eventually be removed from the host population, despite balancing trade-offs. Thus, generally, plant pathogens only survive in the course of evolution if they jump hosts. This is also reflected by the diversity patterns observed in many genera of plant pathogens, where it leads to a mosaic pattern of host groups over time, in which the original host group becomes increasingly obscure.

I. Host jumps are defined by a genetic differentiation of the pathogen gene pool

Host jumps are usually detected by a lack of congruence between pathogen and host phylogeny; (Roy, 2001; Staats *et al.*, 2005; Choi & Thines, 2015), that is, the branching patterns in the phylogenetic trees of hosts and pathogens are different and do not mirror the relationships in the other group. While initially it was thought that pathogens and their hosts co-evolve over longer time scales, and some early molecular phylogenies seemed to support this view

(Whitfield, 2000; Begerow *et al.*, 2004), there has been an increasing amount of evidence that host jumps are a very common phenomenon, both in facultative (Staats *et al.*, 2005; Videira *et al.*, 2017) and obligate biotrophic pathogens (Roy, 2001; Refrégier *et al.*, 2008; Choi & Thines, 2015; Escudero, 2015; McTaggart *et al.*, 2016).

There are two fundamentally different kinds of host jump: those that occur within the life cycle of a pathogen – among plant pathogens, the rust fungi are the most widely known example that falls into this category (Petersen, 1974; van der Merwe *et al.* 2004; Aime *et al.*, 2018) – and those that occur in the course of evolution (de Vienne *et al.*, 2013; Choi & Thines, 2015). As will be outlined later, both forms have a fundamentally different setting and influence the evolution of pathogens in different ways.

When considering host jumps over the course of evolution, it is difficult to differentiate between host range expansions and host jumps because the borders between those two categories are often ill-defined. The prevailing definition – that host range expansions are to species closely related to the original host, while host jumps are to distantly related hosts (Schulze-Lefert & Panstruga, 2011) – can be dismissed. Instead, any expansion of the host range by an organism that leads to isolation from the original gene pool, leading to genetic differentiation and finally speciation, should be considered a host jump (Choi & Thines, 2015), irrespective of the phylogenetic distance of the hosts. Only a colonisation of new hosts not affecting the gene pool of the pathogen species concerned should be considered a host range expansion. This is a common case with introduced hosts, where colonisation by indigenous pathogens can be highly efficient (Vági *et al.*, 2007; Telle *et al.*, 2011), or in mycorrhizal fungi, where the need for efficient defence by the plant against the fungus is lower. However, the paths of host range expansions and host jumps may converge later in evolution (Box 1, Fig. 1). At least in pathogens with a negative effect on plant fitness, host range expansions may be metastable if the new host is able to support a significant percentage of the pathogen population.

In an evolutionary setting, host jumps are likely to start with a suboptimal interaction of a pathogen with a new host and proceed by relative increases in efficiency of infection. The process of host jumping is concluded when the new host can be colonised with a similar efficiency to that of the original pathogen on the original host. During the initial phase of suboptimal interaction, either defence reactions of the new host halt the pathogen before a large quantity of spores for new infections have been formed, or the host individual is killed after a fast initial colonisation. This initially unbalanced interaction with the host will lead to a substantial reduction in fitness. It can be assumed that the vast majority of host jumps will almost immediately end with the removal of the pathogen from the newly colonised host due to the inability of the pathogen to sustain the disease cycle. Pathogens that are also able to obtain nutrients from dead plant tissue have an evolutionary advantage over obligate biotrophs at this stage, as necrotrophy is part of their pathogenic nature. They can absorb nutrients from dead tissue, enabling the formation of propagules even if the establishment of a biotrophic interaction fails. Following the same logic, it would be expected that biotrophic pathogens, which rely on a living host for efficient nutrition, are much less able to jump to new hosts. Counterintuitively, molecular phylogenies have revealed that host jumping is common in both facultative and obligate biotrophs (Voglmayr, 2003; Refrégier *et al.*, 2008; de Vienne *et al.*, 2013; Choi & Thines, 2015). While it seems that facultative biotrophs and hemibiotrophs have a selective advantage over obligate biotrophs at the initial stages of host jumping, this selective advantage may be counterbalanced by other effects in obligate biotrophs. One of these might be the strong selection pressure to genetically adapt to reduce damage to the new host, which might favour biotrophic interaction.

Box 1 The host–pathogen setup

Biotrophy: A mode of nutrition during which exploited host cells and tissues are kept alive. Obligate biotrophic pathogens fully depend on this mode of nutrition. Sometimes only specific life stages – in facultative biotrophic pathogens, often the dikaryotic stage – are obligate biotrophic, and in hemibiotrophic pathogens biotrophic nutrition is only in effect for a limited time.
Evolutionary trajectory: A foreshadowed, continuous path in evolution under given circumstances.
Host preference: The tendency of a pathogen to occur mostly on a specific host.
Host range: The species that can be affected by a given pathogen under natural conditions.
Host range expansion: A colonisation of new host species without direct influence on the gene pool of the pathogen.
Host jump: A colonisation of a new host species that leads to increasing genetic separation from the parent population until speciation is complete.
Radiation: The process by which a wide host range is narrowed down by superior fitness of adapted genotypes over generalist phenotypes; an evolutionary trajectory towards specialisation.
Speciation: The process during which groups of genotypes derived from the same parent population diverge to a degree that introgression leads to decreased fitness. Once this is the case these will be a trajectory towards strong genetic isolation, by increasingly less overlapping host ranges, effectively prohibiting gene flow, eventually leading to reproductive barriers.

II. Increasing non-host resistance along phylogenetic distance is counterbalanced by increasingly inefficient pathogen recognition

The primary mechanism of preventing host jumps is non-host resistance (Schulze-Lefert & Panstruga, 2011). Non-host resistance is usually mediated by pattern recognition receptors (Nürnberger & Lipka, 2005; Zipfel, 2014) that recognise molecular features of pathogens. In simplified terms it can be stated that non-host resistance to a certain pathogen is a function of phylogenetic distance to the host of said pathogen (Schulze-Lefert & Panstruga, 2011). This hypothesis was first formulated by Fahrenholz (1913) on the basis of his observations of lice. The rule he conceived states that the relationships between pathogens on particular hosts provide evidence for the relationships between said hosts. In other words, pathogens on related host species are more likely to be identical or closely related than those on more distantly related

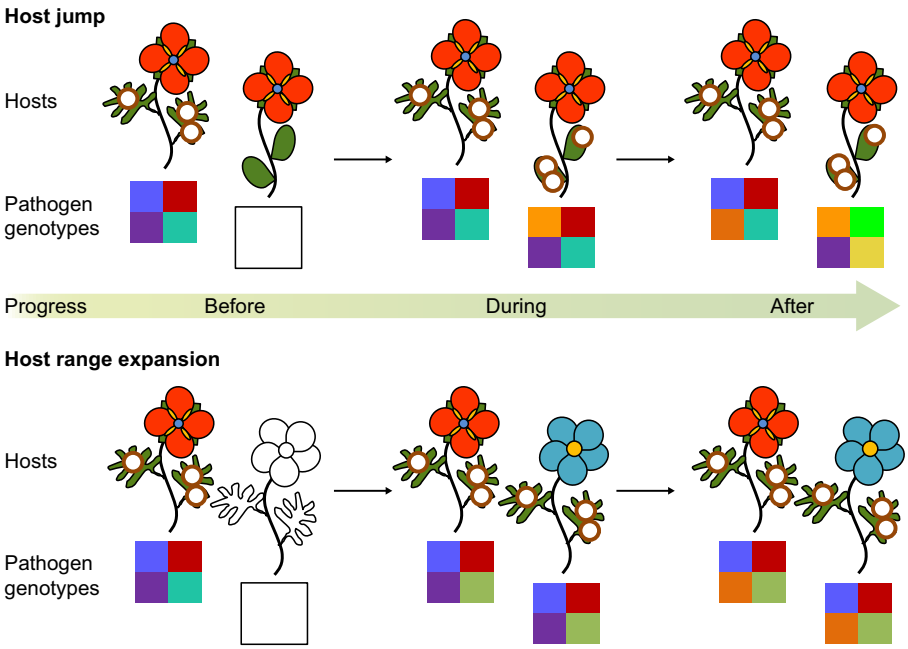

Fig. 1 A comparison of host jumps and host range expansions. In both panels the coloured squares are a schematic representation of the pathogen gene pool on each host plant over the course of time. Different colours indicate different genotypes. The plants on the left represent the original stage, those in the centre represent the initial situation after new hosts are colonised, and the plants on the right represent an advanced stage. The top row illustrates a host jump. First, only one host species is affected. Then, due to an innovation in the effector repertoire, a new host can be colonised, but the innovation is not advantageous on the original host. This leads to genetic isolation, and the gene pool and effectome diverges. The lower panel depicts a host range expansion. First, only one host is affected; the alien host is not yet present (illustrated in outline only). Then a new host comes into the same area and is colonised efficiently by the pathogen. Alternatively, the host was already present, but due to an innovation that is beneficial for the whole population, a new host can be colonised. No genetic isolation occurs, and the gene pool remains undifferentiated.

hosts. Fahrenholz deduced that the reason for this is that physiological and cell biological similarities render it easier for the pathogens to cope with the environment in a related host than in an unrelated host.

While the relationship between non-host resistance and phylogenetic distance to the host might not be as linear as assumed by Schulze-Lefert & Panstruga (2011), there are at least some trends in this direction (Fig. 2a). This is because with increasing phylogenetic distance to potential hosts, the potential effector targets will likely be increasingly divergent from the ones in the original host. Concomitantly, the percentage of pathogenicity effectors that can operate on their host target is likely to decrease. This means that the suppression of the defence reaction of the host incited by pathogen-associated molecular patterns (PAMP), leading to pattern-triggered immunity (PTI), will likely be less efficient. This might, to a certain degree, be counterbalanced by the lack of specific recognition of pathogenicity effectors that interact directly with the resistance proteins of the new host (leading to effector-triggered immunity (ETI)), for example by acting as decoy (van der Hoorn & Kamoun, 2008; Kourelis & van der Hoorn, 2018). The reason for this is that if, in a certain host, PTI is a mostly sufficient means of fighting a pathogen, it should be expected that there will be little evolutionary pressure to preserve or evolve means of effector recognition. Thus, ETI on a new host will only occur if the new pathogen targets conserved proteins that have been targeted by significant effectors of other pathogens with which the host co-evolves. Non-host resistance by ETI in species closely related to the current host is, thus, likely a vestige of the process of previous removal of a predecessor of the pathogen from that particular plant species (Fig. 2a, see also sections VI and VII of this review). This ETI will be maintained as long as the pathogen prevails on related hosts, as in this case there might be a frequent contact with the pathogen.

These considerations directly lead to an additional factor that influences the presence of non-host resistance – geographical distance (Fig. 2b). A pathogen impacting a species in a certain area might lead to the evolution and maintenance of non-host resistance in sympatric (i.e. co-occurring) species. With increasing geographical distance between the range of the current host and a potential new host, the likelihood of encounters between a pathogen and a potential host decreases. This means that selection pressure to evolve or maintain non-host resistance to a specific pathogen decreases at all levels of defence. Thus potential host species that exist in geographically isolated or distant areas and do not come into contact with the pathogen species, or even genus, will likely have a much lower degree of non-host resistance. This is probably the main reason why pathogens, when invading new areas along with their cultivated hosts for example, will jump to new hosts in that area. In line with this, hosts that are brought to new geographic areas are prone to infection by the pathogens that prevail in that area and become host to them. An example of an alien pathogen species performing host jumps is the rust fungus *Puccinia psidii* sensu lato (s.l.), which after introduction from North America to Australia colonised a variety of native Myrtaceae (Carnegie *et al.*, 2016). Examples of crops being attacked by new species are manifold and

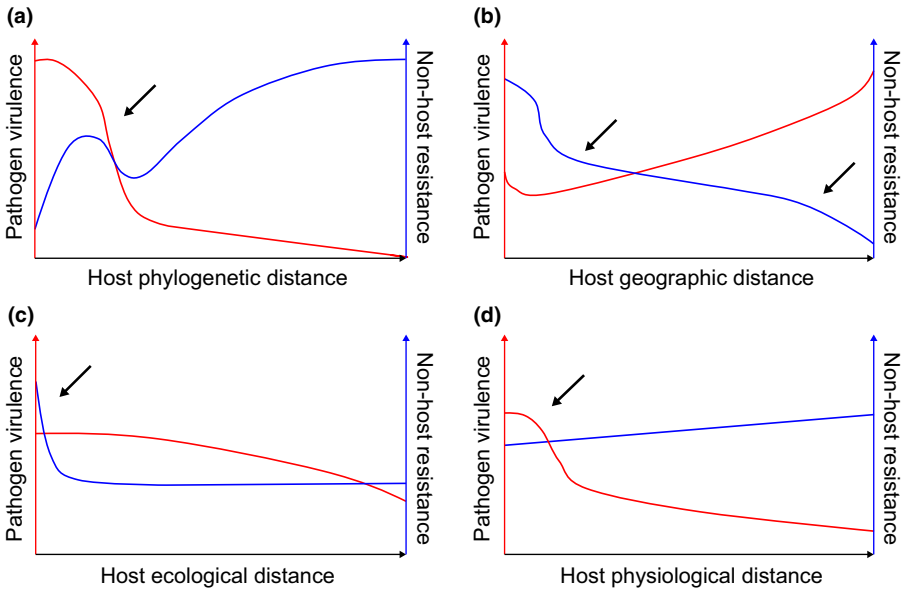

Fig. 2 Model for the dependency of non-host resistance (blue lines) and pathogen virulence (red lines) on various factors. The arrows denote important deviations from linearity. (a) Increased non-host resistance in related species as a reminiscence of the radiation step in pathogen evolution, when a huge range of hosts could still be colonised by the now more specialised pathogen. (b) Pathogen virulence in relation to geographic distance. Left arrow indicates non-overlap with the same pathogen species or species group; right arrow indicates non-overlap with the larger pathogen group concerned. (c) Increased non-host resistance in hosts with similar ecological preferences due to more frequent encounters. (d) Physiological similarities of hosts lead to a higher degree of pre-adaptation of pathogens.

the various *Peronosclerospora* species attacking maize in Asia (Kenneth, 1981; Shivas *et al.*, 2012) are a prominent example for this). This effect is likely to be stronger when there are no closely related pathogens in the natural range of the host. A good example of this is again maize – at its centre of origin, graminicolous downy mildews, including the genus *Peronosclerospora*, were originally absent (Spencer & Dick, 2002). The grass tribe to which maize belongs is therefore ill-equipped to resist parasitism by graminicolous downy mildews when grown in East Asia and Oceania, the assumed centre of origin of *Peronosclerospora* (Spencer & Dick, 2002).

Another factor that might modify the likelihood of host jumping is the likelihood of an encounter between pathogen and non-host within the same area – that is, the ecological distance between the host of a pathogen and a non-host (Fig. 2c). Hosts that frequently co-occur in the same habitat because of similar ecological preferences are more likely to be challenged by pathogens of the other host than hosts that simply co-occur in the same area. This leads to a higher likelihood of the pathogen encountering a plant in a state in which limited reproduction on it might be possible (potential reasons are outlined in section III), thus facilitating host jumps. However, the frequent encounters are also likely to provide selection pressure towards improving non-host resistance against the pathogen (Fig. 2c). A model of how various factors contribute to non-host resistance is outlined in Fig. 2.

III. Pathogens maintain effector reservoirs that are crucial for host jumps to counteract ETI

Host jumps are enabled by a variety of factors. A very important prerequisite is a mutation rate higher than that of the host, which has been generally observed in parasitic lineages (Gandon & Michalakis, 2002). A high mutation rate together with a fast cycling (and asexual reproduction, as this will make selection of somatic mutations possible) enables the pathogen to outrun the host, which is important especially in the initial phases of host jumps, but also later, when an evolutionary arms race sets in. In this context it is important to recognise that the host only needs to establish indirect recognition, for example danger-associated molecular patterns (DAMPs) sense pathogen-associated molecular patterns (PAMPs) (Zipfel, 2014; Gust *et al.*, 2017), or detect specific manipulation on one or two vital hubs targeted by the pathogen. By contrast, circumventing this recognition by manipulating defence pathways in a way that the infected plant can develop almost as if it was uninfected is likely to involve more steps, as several intertwined pathways need to be interfered with. This might be a factor explaining why filamentous pathogens usually express dozens to hundreds of effectors on their natural hosts, a topic also discussed by Thordal-Chirstensen *et al.* (2018). I speculate that it is important for pathogens to maintain not only high mutation rates, but also effector redundancy (multiple effectors targeting the same pathway or even the same target), so that effector loss as a response to recognition does not lead to a loss of pathogenicity. Along the same lines, a reservoir of effectors with only little effect on pathogenicity is likely maintained, as it contains the pre-adaptations and adaptive material that are important during arms races and host jumps. Adaptation after host jumps may also be by means of neofunctionalisation, should they by chance be interacting with a new target in the new host, as shown for Tin2 of *Ustilago maydis* by Tanaka *et al.* (2019).

All hemibiotrophic and biotrophic pathogens have evolved various means by which to maintain effector reservoirs and to rapidly adapt (Dong *et al.*, 2015; Bertazzoni *et al.*, 2018). Common to all solutions is that the duplication or deletion of one or several effectors does not have a huge impact on flanking regions of housekeeping genes. The reason for this separation of effectors and housekeeping genes is probably that regulatory changes necessary to optimise the expression of the effectors are easier to achieve if there are no housekeeping genes nearby, as co-regulation effects that could bring the cell metabolism out of balance are less likely to occur. This means that effectors often localise to 'compartments' in the genome distinct from conserved genes (Frantzeskakis *et al.*,

2019). In *Phytophthora* and powdery mildew, this is realised by the location of effectors in gene-sparse regions (Raffaele *et al.*, 2010; Spanu *et al.*, 2010; Raffaele & Kamoun, 2012; Hacquard *et al.*, 2013); in for example *Colletotrichum*, *Fusarium* and *Leptosphaeria*, this is enabled by physiologically dispensible chromosomes (Balesdent *et al.*, 2013; Vlaardingerbroek *et al.*, 2016; Plaumann *et al.*, 2018), and in *Neofusicoccum* and *Ustilago* this is made possible by clustering of virulence factors (Lanver *et al.*, 2017; Massonnet *et al.*, 2018).

The aforementioned ways in which pathogens uncouple housekeeping and virulence functions should probably be viewed as an adaptation that compensates for the reduction of saprotrophic ability ultimately leading to obligate biotrophy, as they enable a more fine-tuned deployment of virulence factors. In facultative pathogens that are still competitive saprotrophs, such as some *Pythium* species, effectors evolve in the general background of gene evolution, and the loss of pathogenicity will not impact the survival of the species significantly. The better a pathogen is adapted to its host, the more likely it is that it will be able to extract nutrients with little or no competition from other organisms. However, a more specialised adaptation is likely to lead to greater disadvantages for the pathogen species in case of the loss of virulence on a larger part of the host population. This probably drives both higher mutation rates and the evolution of plastic genome regions in pathogens to counter the evolution of resistance in the hosts.

Another way of maintaining effector reservoirs is present in dimorphic fungi, that is, fungi that have a yeast stage and a mycelium stage in their life-cycle. The strong saprotrophic performance of some yeasts of the smut fungi (Kruse *et al.*, 2017), at least in special environments, enables the retention of a species-wide pool of individuals that are sub-optimally adapted to their potential plant hosts. This might be one of the main reasons for the conservation of a yeast-like stage in most smut fungi (Sharma *et al.*, 2019). In (probably infrequent) cases of sexual reproduction, when compatible yeasts co-occur on the same host, genetically divergent lineages may hybridize. This would lead to a reshuffling of effectors, which might lead to altered host ranges. This infrequent sexual reproduction by mostly clonal or selfing lineages can also explain the large host spectrum of *Albugo candida* as a species, while single genotypes have restricted host ranges (Thines, 2014; Jouet *et al.*, 2019). In powdery mildews, host shifts by effector re-shuffling due to hybridisation have been observed (Menardo *et al.*, 2016), and in cases of overlapping hosts, hybrid-driven host jumps may not be rare (Hacquard *et al.*, 2013; Thines, 2014; McMullan *et al.*, 2015; DePotter *et al.*, 2016).

A special situation is present in the rust fungi of the class Pucciniomycetes, many of which perform an obligate host switch during their life cycle, so specific stages occur on a specific host. In the case of the rust fungi of the class Pucciniales, the hosts often belong to phylogenetically distant groups, such as angiosperms and gymnosperms or monocots and dicots (Aime *et al.*, 2018). The host switching within the life cycle in these cases is likely enabled by a strong separation of gene regulation in monokaryotic and dikaryotic hyphae (Lorrain *et al.*, 2018), which might be enabled by stage-specific transcription factors that can only be activated or deactivated in the presence or absence of a second nucleus in a hyphal compartment. By switching hosts concomitantly, the possibility of variation beyond optimal interaction is provided – sub-optimal performance on one of the two hosts may be outweighed by more successful performance on the other. As well as retaining the possibility of infrequent genetic exchange, this might also explain why there are often many different species that rely on the same monokaryon host. A model for this is *Euphorbia cyparissias*, which is parasitised by many species of *Uromyces* in their monokaryotic stage, while in their dikaryotic stage they affect phylogenetically distant species of legumes (Pfunder & Schürch, 2001). A similar mechanism might enable species of *Tuberculina* to perform inter-kingdom host jumps from plants to fungi within a single life cycle (Lutz *et al.*, 2004). Fig. 3 shows a model of the various means by which plant pathogens build and maintain a reservoir of effectors with potential new roles over the course of evolution.

IV. Host jumps are facilitated by compatible pathogens, physiological similarity and frequent contact

Apart from these general considerations, there are additional factors that need to be considered to gain insights into how pathogens perform host jumps. A notable factor that has been highlighted by the observations of Cooper *et al.* (2002) is the presence of compatible pathogens. For example, it has been observed that *Albugo laibachii* suppresses host defence in such a way that species of downy mildew (Cooper *et al.*, 2002, 2008) and *Phytophthora* (Belhaj *et al.*, 2017) are able to co-colonise *Arabidopsis thaliana*. That this process of hitchhiking is not only a laboratory curiosity but might also play a major role in nature stems from observations that, for example, *Bremia tulasnei* is very often associated with *Pustula* spp. (M. Thines, pers. obs.), while *Hyaloperonospora* sp. on *Sinapis arvensis* performs significantly better in the presence of *Albugo candida* (Fig. 4). However, there are also pathogens that rarely co-occur despite having the same host plant (e.g. *Microbotryum tragopogonis-pratensis* and *Pustula obtusata*), and such species could therefore be termed incompatible pathogens (M. Thines, pers. obs.). Plant-associated microbes interact, often forming a complex environment (Porras-Alfaro & Bayman, 2011; Vandenkoornhuyse *et al.*, 2015; Agler *et al.*, 2016; Aragón *et al.*, 2017) that is influenced to different degrees by various members of the microbiome (Agler *et al.*, 2016). Thus, one could argue that, often, compatible microbiomes rather than single organisms support host jumps in nature.

Based on recent findings (Carella *et al.*, 2018; Matei *et al.*, 2018) there is evidence for a tissue or organ specificity of non-host resistance, in line with physiological peculiarities (Miyawaki *et al.*, 2004; Bednarek *et al.*, 2005; Toruño *et al.*, 2016). Support for the hypothesised tissue specificity of non-host resistance comes from the fact that closely related pathogens on unrelated hosts often occur in similar tissues. The floricolous downy mildews provide a good example of this – all of them produce conidia in the flowers of their hosts, and many exhibit a strong preference for certain floral organs, such as the stigma (Thines & Kamoun, 2010; Thines & Kummer, 2013). Arguably, the physiology and non-host resistance

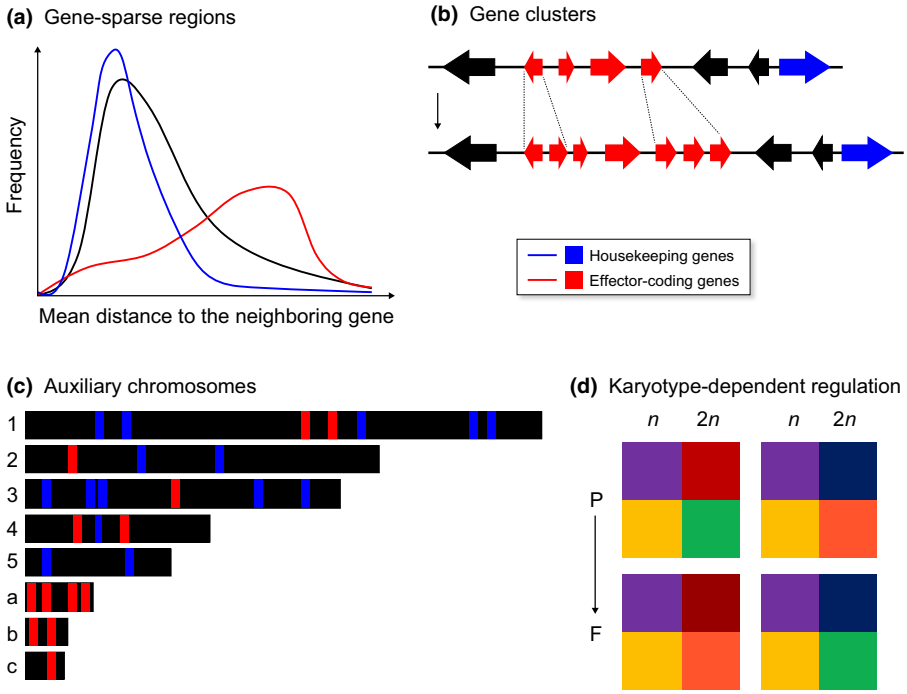

Fig. 3 Different strategies for ensuring a fast-evolving effector pool. In (a–c) effector genes are coloured red, essential housekeeping genes blue, and others black. (a) Frequency plot of the average distance of a gene to a neighbouring gene, for gene-sparse regions in which effector genes and their regulatory elements can be born and die without affecting the regulation of housekeeping genes. (b) Gene clusters in which duplications and deletions can occur without affecting neighbouring genes. (c) Auxiliary chromosomes that harbour many effector genes and no housekeeping genes and can therefore be shuffled in the population without affecting cellular functions. (d) Mosaic patterns of gene usage depending on the ploidy stage, as it is the case in rust fungi; colours code different genotypes associated with host specialisation (note the reshuffling of the 2*n*-regulated genes associated with host specificity in the offspring generation). In this case, if the subject of interest were a host switching rust, the parental generation (P) parasitises on the same host in the haplophase, but on different ones on the dikaryophase. Their offspring (F) would still parasitize the same haplophase host, but its effectome for the dikaryon host is re-shuffled, probably resulting in an altered host spectrum.

of a flower will differ from that of vegetative organs, for example, as they are a sink rather than a source of photosynthesis products (which might also be a reason why an additional sink by a pathogen is less easily recognised). So, once a proficient means of infecting floral organs has evolved, the hurdle for colonising flowers of other hosts may even be lower than for all other organs of the current host

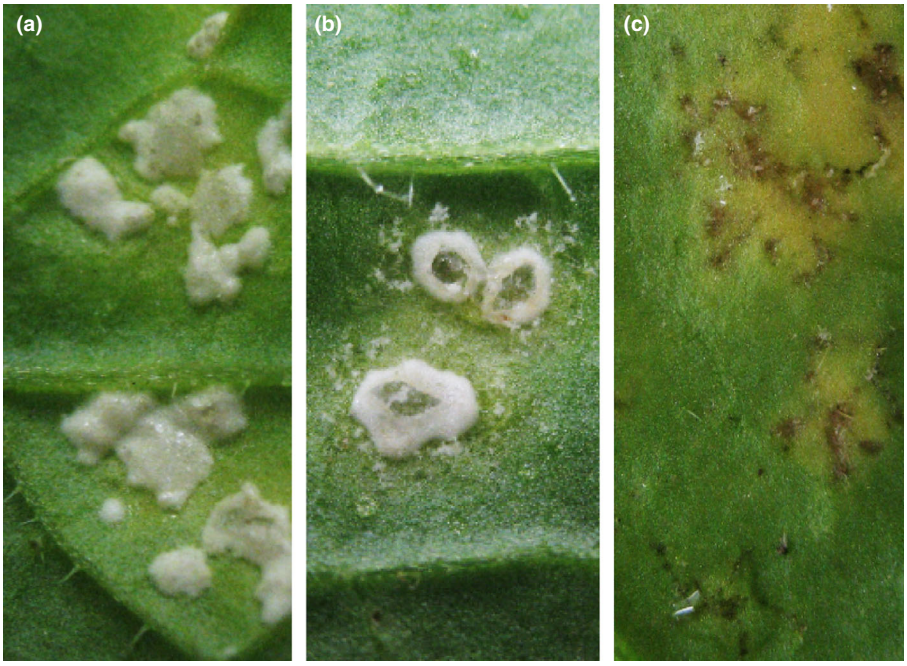

Fig. 4 Field observation of the effect of compatible pathogens as potential facilitators of host jumps. All three pictures of the same host, *Sinapis arvensis*, are from the same field. (a) Sporulation in subepidermal sori of an *Albugo candida* strain well-adapted to its host. (b) Abundant sporulation of *Hyaloperonospora brassicae* sensu lato (s.l.) near the pustules of *A. candida* (where its hyphal network is especially dense) without causing cell death. (c) *Hyaloperonospora brassicae* s.l. causing runaway cell death and with only very limited sporulation, a state that will have a very strong selection pressure for the production of more spores while simultaneously imposing a lower fitness cost on the host.

Box 2 Types of pathogenicity effectors and their significance

Apoplastic effector: An effector that exerts its function in the plant apoplast, that is the space between the cells. Usually, these effectors interact with pre-formed defence mechanisms, for example extracellular proteases.
Cytoplasmic effector: An effector that promotes disease by interacting with intracellular targets. These targets can be host RNA, DNA, protein or other complex structures, and can function in any cell compartment, including the nucleus, membrane, vesicles, mitochondria and plastids.
Core effector: An effector required for pathogenicity within a given pathogen group. Often such effectors are functionally conserved, target conserved key defence mechanisms and are a hallmark of the evolutionary success of the pathogen group concerned. An example for this is PEP1, an inhibitor of plant peroxidases which is present in all members of the Ustilaginaceae family investigated so far.
Tuning effector: An effector which enhances the pathogenicity of a few related pathogen species or even only a single pathogen species. Often such effectors are functionally variable in related species and have more specific targets, including counter-defence against specific pathogen recognition. An example of this is ATR1, a small protein known only from *Hyaloperonospora arabidopsidis* and closely related pathogens.
Auxiliary effector: An effector that only weakly promotes virulence and which therefore has only mild constraints with respect to loss, duplication and mutations. Thus, they are the seed for the evolution of new tuning and core effectors.
Effector reservoir: The majority of effectors of a pathogen. It can have largely different contents, even within different strains of the same species. Many of these effectors have only a very limited effect under normal interaction circumstances, but might be beneficial under certain conditions. This pool of effectors ensures the evolutionary flexibility of pathogens as it provides a resource for innovation. Rapid birth and death and little structural conservation are hallmarks of these effectors.

with a dense hyphal network (and this could perhaps explain why the floricolous downy mildews are able to grow in shoot vascular tissues down to the roots, as they are also carbon-sink tissues). Similarly, there has been a host jump from vines of the Cannabaceae family to vines in the Cucurbitaceae family by downy mildews of the genus *Pseudoperonospora* (Runge *et al.*, 2011; Runge & Thines, 2012). These examples give rise to the hypothesis that a similar physiology is a factor which improves pathogen virulence and the likelihood of host jumping (Fig. 2d).

It can be assumed that apart from this, the most important factor enabling successful host jumps is a contact zone created by host habitat preferences that at least partly overlap, (see also the last paragraph of section II) such that infected hosts and non-hosts frequently co-occur and there are many possibilities for the initiation of a host jump under conditions that are optimal for the pathogen. In line with this, the mostly host-species-specific pathogens of the *Hyaloperonospora arabidopsidis* species complex are all closely related but occur on largely unrelated hosts (Göker *et al.*, 2004; Thines *et al.*, 2009). However, all of the hosts are annuals or short-lived perennials that live in open habitats, and all are affected by white blister rust, which in this case might act as a bridge pathogen. While many of the hosts do not co-occur over their entire range and the white blister pathogen is not frequent everywhere, there are areas in which two of the hosts grow in the same habitat and where white blister disease is common as well (M. Thines, pers. obs.). An example host species is *Arabidopsis thaliana*, which often co-occurs with *Erophila verna* and related species on sandy soils in eastern Germany, where *A. thaliana* is also frequently parasitised by white blister rust. It is conceivable that in such a setting favourable conditions for host jumps are present, which can lead to the successful establishment of a pathogen on a new host, with intermediate steps as observed for the downy mildew pathogen of *S. arvensis* (Fig. 4).

V. Pre-adaptive innovations in core effectors trigger host jumps that lead to pronounced gene loss, diversifying selection and neofunctionalisation of effectors

In order for a host jump to occur, there must be pre-adaptations in the pathogen that is jumping hosts – the pathogen needs to be able to suppress defence reactions in the new host, at least to some degree. It is conceivable that effective manipulation of only a few hubs in plant defence pathways is sufficient to allow some colonisation. This is in line with some mutants of Arabidopsis, for which the deletion of one or few genes leads to colonisation by unadapted pathogens (Century *et al.*, 1995; Glazebrook *et al.*, 1996; Parker *et al.*, 1996; Stein *et al.*, 2006).

Effectors that contribute significantly to overall defence suppression are prone to becoming conserved after they first evolve, and have the potential to become a member of the core set of effectors that defines a certain group of pathogens. These effectors contribute significantly to the colonisation and evolutionary success of pathogen groups (Box 2, Fig. 5). An example of such a core effector is PEP1, which is required for pathogenicity in *U. maydis* (Doehlemann *et al.*, 2009) and is conserved throughout the Ustilaginaceae, a species-rich family parasitic to grass hosts (McTaggart *et al.*, 2012). It is of note that this effector is also able to exert its function – the inactivation of plant peroxidases – in distantly related plants (Hemetsberger *et al.*, 2015), which might have been an important prerequisite for the host jump from grasses to members of the dicot genus *Persicaria* of the Polygonaceae family. Thus, innovations in core effectors are likely to be a hallmark enabling diversification and radiation of plant pathogens. This also means that the advent of such an innovation – that is, the evolution of a new effector which acts upon a conserved target – can be the trigger for host jumps, radiation and diversification, as outlined in section VII.

If a host jump has occurred, the farther the host jump, the fewer effectors can be expected to find a fitting target in the new host. This means that particularly large host jumps can be expected to be associated with marked gene loss (Sharma *et al.*, 2014). Conversely, gene gain plays only a minor role in the adaptation to new hosts (Sharma *et al.*, 2014) and is probably restricted to the duplication of few effectors that are acting on structurally related plant proteins. Because most of the effectors that are still able to act upon, for example, conserved proteins of the plant defence pathways, will probably not perform optimally due to the phylogenetic distance

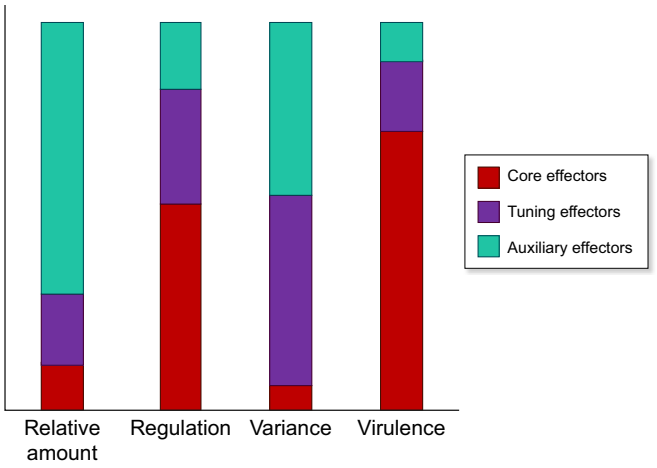

Fig. 5 Model for the relative contribution of effector types to pathogen features in a well-established pathogen. Core effectors are those conserved throughout a group of plant pathogens, while tuning effectors are those specifically adapted to interact with a particular host, for example to shut down effector-triggered immunity. The term *regulation* is meant in the sense of the strength of regulation during infection; *variance* means overall variance in the gene pool of the pathogen species.

from the original host, it is expected that there will be strong selection pressure on those effectors towards an optimised interaction, as exemplified by the dicot-affecting smut fungus *Ustilago pennsylvanica* (synonym *Melanopsichium pennsylvanicum*, Sharma *et al.*, 2014) and the *Phytophthora infestans* species cluster (Raffaele *et al.*, 2010; Dong *et al.*, 2014). In addition, some effectors will be able to interact with ontogenetically divergent, yet structurally similar, targets, which leads to neofunctionalisation of the effector (Tanaka *et al.*, 2019). A general model for the contribution of various effector categories is presented in Fig. 5.

VI. Fitness trade-offs create the evolutionary frame in which long-term survival generally requires host jumps

There is an obvious evolutionary trajectory for pathogens – especially for obligate biotrophic ones – to reduce the fitness cost for the host while still ensuring the production of enough offspring, for example in the form of spores, to ensure survival of the pathogen. This is a difficult trade-off with various metastable states. Reduction of fitness costs to the host can lead to almost asymptomatic infections in natural populations, with only rare formation of spores (Saikkonen *et al.*, 2002; Ploch & Thines, 2011), especially when vertical transmission from one generation of the host plant to the next is efficient. Fitness effects for the plants are thus reduced in such a way that they might stay close to the threshold of evolutionary insignificance. Conversely, there is always the risk of death together with the host before reproduction, or of failed colonisation of fruits and seeds under unfavourable conditions. By contrast, it might even be positive for a host to allow colonisation by pathogens with little fitness trade-offs if there are co-occurring genotypes of the host in which infections lead to a more severe fitness loss, as the former will be able to outcompete the latter in the presence of the pathogen. However, this would require a scenario of frequent co-occurrence and a minimal negative effect of the pathogen on susceptible hosts. Thus, it seems that such associations might be evolutionarily unstable in specialised pathogens. A more stable situation is reached if the pathogens provide a more general positive effect, such as the production of chemical substances that protect the host from herbivores (Carroll, 1988; Saikkonen *et al.*, 2016).

If no balancing effects are present, even a small negative impact of a pathogen on its host will lead to a selection pressure to remove the pathogen. To achieve resistance, plants must be able to perceive a manipulation by only a few effectors, or even by a single effector, which means that the cost of resistance towards a single pathogen is probably usually rather low, especially when considering that the effective guarding of a protein in a signal cascade might also provide resistance against additional pathogens that manipulate the same target (Römer *et al.*, 2009; Dodds & Rathjen, 2010; Mukhtar *et al.*, 2011; Weßling *et al.*, 2014). This means that plants susceptible to infection by a pathogen will likely suffer a stronger negative fitness effect if parasitised than resistant plants face for maintaining a resistance gene. This may also be the main reason why pathogens diversify after host jumps and radiation, as only pathogen genotypes specialised to a certain species or subspecies of the host are likely to be able to keep up with the pace of evolving resistance against the pathogen in the new host. While this evolutionary arms race leads to diversification and speciation in the pathogen, it will also render its niche smaller and smaller, and there will likely be more and more host–pathogen associations lost. As a consequence, over the course of evolution pathogens can be expected to be marginalised in such a way that they can infect fewer and fewer genotypes, so that potential hosts are more and more scattered until the pathogens are removed from host populations by chance. This is probably also one reason for the usually high dispersal potential of pathogens, which enables them to escape local populations that acquire resistance. Therefore, it seems reasonable to assume that pathogens generally have a higher dispersal ability than their hosts. An escape necessitates the production of a significant number of spores, which translates into energy drained from the host and, thus, a negative impact on host fitness. This, in turn, increases the selection pressure to remove the pathogen. A way to escape this dilemma is to jump hosts in order to avoid extinction. While there is no selection towards jumping to a new host – this happens by chance – there will be selection pressure to maintain the possibility of jumping if the boundary conditions are met, as otherwise pathogens would likely eventually face extinction over the course of evolution. A result of this is the plethora of host jump events that have been identified in various successful (in terms of species diversity and abundance) pathogen groups (Voglmayr, 2003; Vági *et al.*, 2007; Thines & Kummer, 2013; Thines, 2014; Aime *et al.*, 2018; Kruse *et al.*, 2018a).

VII. Phylogeny provides evidence for recurrent host jumping and extinction of lineages that did not jump hosts

Considering the hypotheses outlined thus far, there are a number of predictions that can be made for pathogen evolution. After a host

jump, especially if the host jump was to a geographically and phylogenetically distant host, the pathogen will not face defence reactions specifically directed against it, which means that the performance of its core effectors with respect to the suppression of plant defence is the major determinant of successful colonisation. Subsequently, there is a strong selection pressure on the pathogen to increase performance and fit to the new host environment. This will not only lead to a diversifying selection of sub-optimally interacting effectors, but also to a loss of many effectors that were needed to suppress specific defences in the previous host, as they are not needed anymore (Sharma *et al.*, 2014). This means that during these first evolutionary steps the pathogen is already prone to lose fitness on its original host, where it would be outcompeted by fully adapted strains, while backcrosses endanger its performance on the new host. Consequently, if there is no immediate gain of full virulence – which might be restricted to a few, possibly evolutionarily highly significant, host jumps – it is likely that there will be a rather quick genetic isolation of a pathogen after a host jump, leading to speciation.

Most host jumps are unlikely to be successful, because the pathogen, even if it was able to reproduce under optimal conditions (e.g. in the presence of a compatible pathogen or on an otherwise immuno-compromised host), will not find suitable conditions frequently enough to ensure survival by sustained completion of the disease cycle. If the struggle for initial survival is successful, however, the pathogen will be optimised by evolutionary pressure towards spore production and colonisation of its new host. As a consequence, if the new host is widespread, the pathogen will quickly become widespread as well, as has been observed in some pathogens invading new hosts outside their native range (Milgroom *et al.*, 1996; Gross *et al.*, 2014).

Subsequent to, or even concomitant with, the later stages of optimisation of performance on the new host, it is likely that the adaptation of the pathogen to the new host environment will often enable it to colonise other hosts related to the one it has jumped on. If the proteins the pathogen has targeted for the initial host jump are conserved throughout the phylogeny of the new host group, the pathogen might consequently be able to colonise dozens of new hosts, setting the starting point for a radiation of the pathogen. A situation like this can be seen in the oomycete genus *Pseudoperonospora*, where a host jump from hop to Cucurbitaceae has been observed (Runge *et al.*, 2011). While the source pathogen had been restricted to the genus *Humulus*, and probably only to few species within it, the species emerging from it is able to colonise a broad spectrum of species and tribes of the Cucurbitaceae family (Lebeda & Cohen, 2011), albeit with vary degrees of efficiency (Runge & Thines, 2012). Interestingly, the sister species that is parasitic to hop already has a very limited potential to infect cucurbit hosts (Runge & Thines, 2012), demonstrating the presence of pre-adaptations and highlighting their importance.

When the pathogen has fully established itself in the new hosts and infection becomes common, it will not be adapted towards minimum harm to the host – as long as the harm caused by the pathogen does not lead to a serious decline in the host population, there will be no selection pressure for this. However, there will be an onset of evolutionary pressure within both the pathogen population (to outperform co-occurring strains on particular hosts) and the populations of host species (towards removing the pathogen). This can be expected to have two different effects. First, the pressure within the pathogen population will lead to the emergence of subpopulations that are better adapted to subgroups of the new host range, for example certain host genera, ultimately leading to a specialisation of the pathogen. Second, the pressure within the host species populations will lead to the development of resistance to the pathogen; if full resistance is achieved, it will quickly spread throughout the population of the corresponding host species, leading to a selective sweep and the loss of that particular species as a host. In the initial phase, where the host range of the pathogen is still high, such losses will not have a large impact on the overall pathogen population. However, as the number of remaining hosts decreases, there will be increasing selection pressure to counter a newly evolved resistance, for example by alteration of a recognised pathogenicity effector. However, due to the many independent gene pools (host species) in which resistance can occur, the pathogen will likely only be able to sustain itself in a smaller number of hosts. The number of host species in which the pathogen can sustain itself during this period of evolution is most likely influenced by the fitness cost to the particular species, as this will determine the evolutionary pressure on the host towards resistance to the pathogen. As a result of the evolution of resistance, the initial host range will be reduced. Following this host range contraction, a specialisation of the pathogen populations towards the remaining hosts will be incited, at which time an evolutionary arms race begins. This arms race will lead to further selection pressure towards minimising fitness costs for infected hosts and towards evading recognition by the host. As different host species will exploit different possibilities for pathogen recognition, as mentioned before it will be difficult for pathogen subpopulations to maintain fitness on various hosts, leading to selection towards performance on a specific (dominant) host. Thus, genetic isolation and differentiation of the different subpopulations are likely to increase, ultimately leading to speciation. The processes outlined above can drive the diversification of pathogens, leading to the evolution of numerous specialised species, especially in pathogens with an obligate biotrophic stage. In molecular phylogenetics, the stages of radiation and subsequent speciation outlined here can be observed as a lack of resolution on the backbone of phylogenetic clades, even in multigene phylogenies, for example in various downy mildew groups (Göker *et al.*, 2004; Choi & Thines, 2015; Choi *et al.*, 2015), smut fungi (Kruse *et al.*, 2018a,b), and powdery mildews (Vági *et al.*, 2007).

It is conceivable that the contraction of host ranges will follow the relatedness of the hosts due to physiological similarities (in this case similarities of effector targets) as outlined by Fahrenholz (1913). This means that while host ranges contract, the improvement of an effector on one host might also bring about an improvement on a related host. In addition to this, the same process might also incite host shifts from one species to another related species, which would also lead to a pattern mimicking co-speciation (De Vienne *et al.*, 2007; de Vienne *et al.*, 2013; Choi & Thines, 2015). In other words, the contraction of host ranges along host phylogenetic lineages together with infrequent host jumps is a

probable explanation for the strong congruence that has been observed between host and pathogen phylogenies in some pathogen groups (e.g. in Begerow *et al.*, 2004), as outlined in Choi & Thines (2015). This can be tested using dated phylogenies. However, in the case of obligate biotrophic pathogens, estimates are often difficult due to a lack of calibration points. Therefore, dating by maximum clade age according to the associated host clade can serve as a proxy, as described by Choi & Thines (2015).

After having speciated, and having become specialised on a single host species or a small group of closely related species, the dilemma of balancing fitness costs and spreading to new host plants sets in again, removing the majority of pathogen species by the processes outlined before in this section. This also means that co-evolution over long evolutionary time scales, spanning multiple speciation events, is likely to be very rare. Thus, co-phylogenetic patterns can be expected to be a reflection of radiation and subsequent specialisation to ever smaller host spectra (Choi & Thines, 2015). Ultimately, if none of the pathogens that have evolved are able to jump to a new group of hosts, the whole pathogen group will go extinct.

The hypotheses outlined so far lead to several predictions: (1) After a successful host jump, pathogens will spread very quickly and have a high likelihood of tapping a broad range of hosts; (2) broad host range species in obligate biotrophic pathogen groups are a reflection of a recent host jump; (3) clades that diversified after a large host jump will almost always include pathogens from related hosts; (4) older clades will include an increasing number of species on distant hosts, as a reflection of new host jumps; and (5) old clades contain pathogens from a phylogenetically diverse suite of hosts, and the original host group from which its evolution began is no longer obvious. A model for host jumping over the course of evolution is given in Fig. 6.

These predicted patterns can be observed in various pathogen groups. As an example of (1), after *Phytophthora cinnamomi* was introduced to Australia, it quickly spread over the continent and affected a huge diversity of eucalypts (Shearer *et al.*, 2007). Point (2) is exemplified by *Pseudoperonospora cubensis*, which affects a wide variety of members of the Cucurbitaceae family (Runge *et al.*, 2011). It retains a very limited potential to infect hops, while at the same time its sister species, *Pseudoperonospora humuli*, shows a

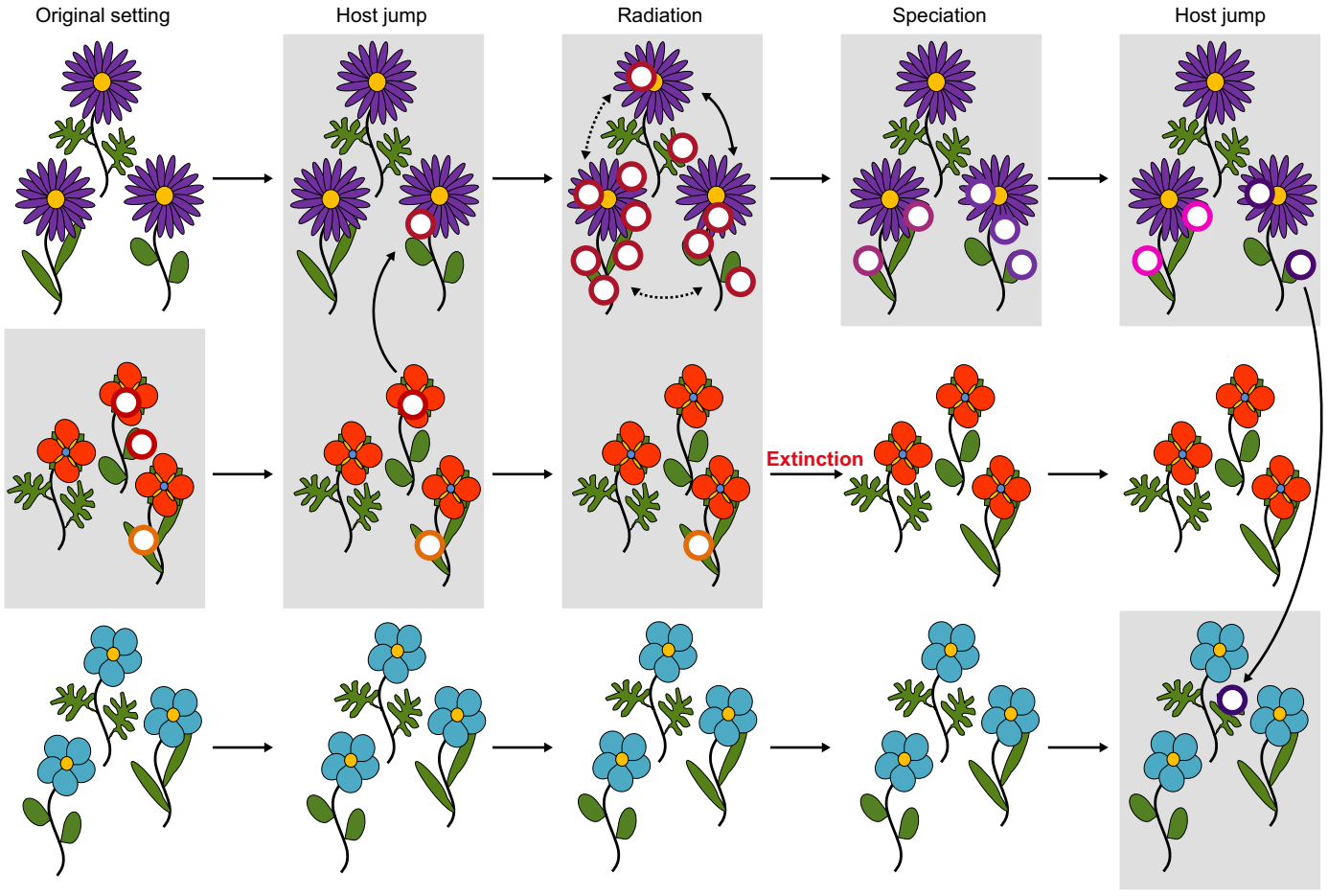

Fig. 6 Model for the fate of pathogens in the course of evolution. Hosts are symbolised by three plant groups, each with three different species that have different leaf shapes. Pathogens are symbolised by circles, for which similarity of colour indicates genetic relatedness. A pathogen jumps from one host to another because of an effector innovation, for example. If the host jump is very large, it subsequently colonises various species of the new host group until, with the onset of an evolutionary arms race, the pathogen undergoes evolutionary radiation and specialisation to a specific host, leading to speciation. Subsequently, additional host jumps occur, rendering the original host group on which the pathogen evolved more and more obscure. Host species groups affected by pathogens at a certain time-point are highlighted by grey background shading.

limited potential to colonise some Cucurbits (Runge & Thines, 2012), reflecting the fact that the host jump has occurred recently in evolutionary terms. In line with point (3), species of the oomycete genera *Bremia* and *Hyaloperonospora* and the fungal genus *Ustilago* s.l. almost exclusively infect hosts in single host families (Asteracae, Brassicaceae and Poaceae, respectively; Göker *et al.*, 2004; McTaggart *et al.*, 2012; Choi & Thines, 2015; respectively). However, in *Hyaloperonospora* host jumping to other host groups has already occurred, with evolutionarily recent host jumps to the families Capperaceae, Cistaceae, Resedaceae and Zygophallaceae (Göker *et al.*, 2004). A notable host jump to Polygonaceae has also occurred in *Ustilago* (McTaggart *et al.*, 2012; Sharma *et al.*, 2014). An example for (4) is the anther-smut genus *Microbotryum*, in which it is still apparent that the ancestral host family was the Polygonaceae, but several subsequent host jumps to a number of families, including Dipsacaceae, Asteraceae and Caryophyllaceae have resulted in a considerable expansion of the genus (Kemler *et al.*, 2009). Finally (5), there are genera such as *Peronospora* (Voglmayr, 2003), *Plasmopara* (Voglmayr *et al.*, 2004), and *Puccina* (Aime *et al.*, 2018) for which the original host group is no longer obvious and cannot be ascertained based on currently available data.

VIII. Conclusions

Host jumping is possibly the most fundamental process by which pathogen groups are able to persist over long evolutionary time scales. By jumping hosts they are escaping their extinction on a particular group of hosts that they colonised after a previous cycle of host jumping, radiation and speciation. Host jumps are enabled by effectors that are capable of efficient manipulation of key plant defence mechanisms. They usually belong to or are taken into the core effectome that is characterised by effectors conserved within pathogen lineages that act on conserved plant proteins. Factors like compatible microbiomes and a similar physiology favour host jumping. After successful host jumps, the phylogenetically and geographically farther away the new hosts are, and the more conserved the key targets are, the more likely a radiation to more distant relatives of the new host will be. After this first expansion, the onset of selection pressure to remove the pathogen will lead to a contraction of the host range and necessitate a specialisation of the pathogen, ultimately leading to genetic isolation and speciation. There is a conflict between the selection pressure associated with the need to reduce fitness costs for the host and the necessity to produce spores to spread to new host plants; ultimately, biotrophic pathogens will mostly retain a fitness cost to their hosts. Despite some balancing effects, this will in most cases finally lead to an extinction of the majority of pathogen species, which they can only escape by jumping hosts, thus closing the evolutionary cycle (Fig. 6). The hypothesis for pathogen evolution outlined here allows various predictions to be made, all of which are in line with observed patterns in the phylogeny of largely unrelated plant pathogens. This suggests that the hypothesis is valid for a wide array of plant pathogens. However, as the general considerations should also hold true for pathogens of other organisms, it could be applicable to pathogenicity in general.

Acknowledgements

MT is funded by LOEWE, under the framework of the LOEWE Centre for Translational Biodiversity Genomics. I am grateful to the Max Planck Society, who funded my initial steps into adopting a broad evolutionary research topic. This review is dedicated to Sophien Kamoun, who provided a stimulating environment in his group in Norwich while I visited him for the year 2009. During this visit I conceived and presented the basic hypotheses that culminated in this review a decade later. I am grateful to the anonymous reviewers and the editor for helping to improve the manuscript.

ORCID

Marco Thines https://orcid.org/0000-0001-7740-6875

References

Agler MT, Ruhe J, Kroll S, Morhenn C, Kim ST, Weigel D, Kemen EM. 2016. Microbial hub taxa link host and abiotic factors to plant microbiome variation. *PLoS Biology* **14**: e1002352.

Aime M, Bell C, Wilson A. 2018. Deconstructing the evolutionary complexity between rust fungi (Pucciniales) and their plant hosts. *Studies in Mycology* **89**: 143–152.

Aragón W, Reina-Pinto JJ, Serrano M. 2017. The intimate talk between plants and microorganisms at the leaf surface. *Journal of Experimental Botany* **68**: 5339–5350.

Balesdent MH, Fudal I, Ollivier B, Bally P, Grandaubert J, Eber F, Chèvre AM, Leflon M, Rouxel T. 2013. The dispensable chromosome of *Leptosphaeria maculans* shelters an effector gene conferring avirulence towards *Brassica rapa*. *New Phytologist* **198**: 887–898.

Bednarek P, Schneider B, Svatos A, Oldham NJ, Hahlbrock K. 2005. Structural complexity, differential response to infection, and tissue specificity of indolic and phenylpropanoid secondary metabolism in *Arabidopsis* roots. *Plant Physiology* **138**: 1058–1070.

Begerow D, Göker M, Lutz M, Stoll M. 2004. On the evolution of smut fungi on their hosts. In: Agerer R, Piepenbring M, Blanz P, eds. *Frontiers in basidiomycote mycology*. Eching, Germany: IHW-Verlag, 81–98.

Belhaj K, Cano LM, Prince DC, Kemen A, Yoshida K, Dagdas YF, Etherington GJ, Schoonbeek HJ, van Esse HP, Jones JD, *et al.* 2017. *Arabidopsis* late blight: infection of a nonhost plant by *Albugo laibachii* enables full colonization by *Phytophthora infestans*. *Cellular Microbiology* **19**: e12628.

Bertazzoni S, Williams A, Jones DA, Syme RA, Tan KC, Hane JK. 2018. Accessories make the outfit: accessory chromosomes and other dispensable DNA regions in plant–pathogenic fungi. *Molecular Plant–Microbe Interactions* **31**: 779–788.

Carella P, Gogleva A, Tomaselli M, Alfs C, Schornack S. 2018. *Phytophthora palmivora* establishes tissue-specific intracellular infection structures in the earliest divergent land plant lineage. *Proceedings of the National Academy of Sciences, USA* **115**: E3846–E3855.

Carnegie AJ, Kathuria A, Pegg GS, Entwistle P, Nagel M, Giblin FR. 2016. Impact of the invasive rust *Puccinia psidii* (myrtle rust) on native Myrtaceae in natural ecosystems in Australia. *Biological Invasions* **18**: 127–144.

Carroll G. 1988. Fungal endophytes in stems and leaves: from latent pathogen to mutualistic symbiont. *Ecology* **69**: 2–9.

Century KS, Holub EB, Staskawicz BJ. 1995. *NDR1*, a locus of *Arabidopsis thaliana* that is required for disease resistance to both a bacterial and a fungal pathogen. *Proceedings of the National Academy of Sciences, USA* **92**: 6597–6601.

Choi YJ, Klosterman SJ, Kummer V, Voglmayr H, Shin HD, Thines M. 2015. Multi-locus tree and species tree approaches toward resolving a complex clade of downy mildews (Straminipila, Oomycota), including pathogens of beet and spinach. *Molecular Phylogenetics and Evolution* **86**: 24–34.

Choi Y-J, Thines M. 2015. Host jumps and radiation, not co-divergence drives diversification of obligate pathogens. A case study in downy mildews and Asteraceae. *PLoS ONE* **10**: e0133655.

Cooper A, Woods-Tor A, Holub E. 2002. *Albugo candida* (white rust) suppresses resistance to downy mildew pathogens in *Arabidopsis thaliana*. *Plant Protection Science* **38**: 474–476.

Cooper AJ, Latunde-Dada AO, Woods-Tor A, Lynn J, Lucas JA, Crute IR, Holub EB. 2008. Basic compatibility of *Albugo candida* in *Arabidopsis thaliana* and *Brassica juncea* causes broad-spectrum suppression of innate immunity. *Molecular Plant–Microbe Interactions* **21**: 745–756.

DePotter JR, Seidl MF, Wood TA, Thomma BP. 2016. Interspecific hybridization impacts host range and pathogenicity of filamentous microbes. *Current Opinion in Microbiology* **32**: 7–13.

De Vienne D, Giraud T, Shykoff J. 2007. When can host shifts produce congruent host and parasite phylogenies? A simulation approach. *Journal of Evolutionary Biology* **20**: 1428–1438.

Dodds PN, Rathjen JP. 2010. Plant immunity: towards an integrated view of plant–pathogen interactions. *Nature Reviews Genetics* **11**: 539–548.

Doehlemann G, Van Der Linde K, Aßmann D, Schwammbach D, Hof A, Mohanty A, Jackson D, Kahmann R. 2009. Pep1, a secreted effector protein of *Ustilago maydis*, is required for successful invasion of plant cells. *PLoS Pathogens* **5**: e1000290.

Dong S, Raffaele S, Kamoun S. 2015. The two-speed genomes of filamentous pathogens: waltz with plants. *Current Opinion in Genetics and Development* **35**: 57–65.

Dong S, Stam R, Cano LM, Song J, Sklenar J, Yoshida K, Bozkurt TO, Oliva R, Liu Z, Tian M *et al.* 2014. Effector specialization in a lineage of the Irish potato famine pathogen. *Science* **343**: 552–555.

Escudero M. 2015. Phylogenetic congruence of parasitic smut fungi (*Anthracoidea*, Anthracoideaceae) and their host plants (*Carex*, Cyperaceae): cospeciation or host-shift speciation? *American Journal of Botany* **102**: 1108–1114.

Fahrenholz H. 1913. Ectoparasiten und Abstammungslehre. *Zoologischer Anzeiger* **41**: 371–374.

Frantzeskakis L, Kusch S, Panstruga R. 2019. The need for speed: compartmentalized genome evolution in filamentous phytopathogens. *Molecular Plant Pathology* **20**: 3–7.

Gandon S, Michalakis Y. 2002. Local adaptation, evolutionary potential and host–parasite coevolution: interactions between migration, mutation, population size and generation time. *Journal of Evolutionary Biology* **15**: 451–462.

Glazebrook J, Rogers EE, Ausubel FM. 1996. Isolation of *Arabidopsis* mutants with enhanced disease susceptibility by direct screening. *Genetics* **143**: 973–982.

Göker M, Riethmüller A, Voglmayr H, Weiss M, Oberwinkler F. 2004. Phylogeny of *Hyaloperonospora* based on nuclear ribosomal internal transcribed spacer sequences. *Mycological Progress* **3**: 83–94.

Gross A, Holdenrieder O, Pautasso M, Queloz V, Sieber TN. 2014. *Hymenoscyphus pseudoalbidus*, the causal agent of European ash dieback. *Molecular Plant Pathology* **15**: 5–21.

Gust AA, Pruitt R, Nürnberger T. 2017. Sensing danger: key to activating plant immunity. *Trends in Plant Science* **22**: 779–791.

Hacquard S, Kracher B, Maekawa T, Vernaldi S, Schulze-Lefert P, Ver Loren van Themaat E. 2013. Mosaic genome structure of the barley powdery mildew pathogen and conservation of transcriptional programs in divergent hosts. *Proceedings of the National Academy of Sciences, USA* **110**: E2219–E2228.

Hemetsberger C, Mueller AN, Matei A, Herrberger C, Hensel G, Kumlehn J, Mishra B, Sharma R, Thines M, Hückelhoven R *et al.* 2015. The fungal core effector Pep1 is conserved across smuts of dicots and monocots. *New Phytologist* **206**: 1116–1126.

Jouet A, Saunders DG, McMullan M, Ward B, Furzer O, Jupe F, *et al.* 2019. *Albugo candida* race diversity, ploidy and host-associated microbes revealed using DNA sequence capture on diseased plants in the field. *New Phytologist* **221**: 1529–1543.

van der Hoorn RA, Kamoun S. 2008. From Guard to Decoy: a new model for perception of plant pathogen effectors. *Plant Cell* **20**: 2009–2017.

Kemler M, Lutz M, Göker M, Oberwinkler F, Begerow D. 2009. Hidden diversity in the non-caryophyllaceous plant-parasitic members of *Microbotryum* (Pucciniomycotina: Microbotryales). *Systematics and Biodiversity* **7**: 297–306.

Kenneth RG. 1981. Downy mildews of graminaceous crops. In: Spencer DM, ed. *The downy mildews*. London, UK: Academic Press, 367–394.

Kourelis J, van der Hoorn RAL. 2018. Defended to the nines: 25 years of resistance gene cloning identifies nine mechanisms for R protein function. *Plant Cell* **30**: 285–299.

Kruse J, Dietrich W, Zimmermann H, Klenke F, Richter U, Richter H, Thines M. 2018a. *Ustilago* species causing leaf-stripe smut revisited. *IMA Fungus* **9**: 49–73.

Kruse J, Doehlemann G, Kemen E, Thines M. 2017. Asexual and sexual morphs of *Moesziomyces* revisited. *IMA Fungus* **8**: 117–129.

Kruse J, Piątek M, Lutz M, Thines M. 2018b. Broad host range species in specialised pathogen groups should be treated with suspicion – a case study on *Entyloma* infecting *Ranunculus*. *Persoonia* **41**: 175–201.

Lanver D, Tollot M, Schweizer G, Presti LL, Reissmann S, Ma L-S, Schuster M, Tanaka S, Liang L, Ludwig N. 2017. *Ustilago maydis* effectors and their impact on virulence. *Nature Reviews Microbiology* **15**: 409.

Lebeda A, Cohen Y. 2011. Cucurbit downy mildew (*Pseudoperonospora cubensis*)—biology, ecology, epidemiology, host–pathogen interaction and control. *European Journal of Plant Pathology* **129**: 157–192.

Lorrain C, Marchal C, Hacquard S, Delaruelle C, Petrowski J, Petre B, Hecker A, Frey P, Duplessis S. 2018. The rust fungus *Melampsora larici-populina* expresses a conserved genetic program and distinct sets of secreted protein genes during infection of its two host plants, larch and poplar. *Molecular Plant–Microbe Interactions* **31**: 695–706.

Lutz M, Bauer R, Begerow D, Oberwinkler F, Triebel D. 2004. *Tuberculina*: rust relatives attack rusts. *Mycologia* **96**: 614–626.

Massonnet M, Morales-Cruz A, Figueroa-Balderas R, Lawrence DP, Baumgartner K, Cantu D. 2018. Condition-dependent co-regulation of genomic clusters of virulence factors in the grapevine trunk pathogen *Neofusicoccum parvum*. *Molecular Plant Pathology* **19**: 21–34.

Matei A, Ernst C, Günl M, Thiele B, Altmüller J, Walbot V, Usadel B, Doehlemann G. 2018. How to make a tumour: cell type specific dissection of *Ustilago maydis*-induced tumour development in maize leaves. *New Phytologist* **217**: 1681–1695.

McMullan M, Gardiner A, Bailey K, Kemen E, Ward BJ, Cevik V, Robert-Seilaniantz A, Schultz-Larsen T, Balmuth A, Holub E. 2015. Evidence for suppression of immunity as a driver for genomic introgressions and host range expansion in races of *Albugo candida*, a generalist parasite. *eLife* **4**: e04550.

McTaggart AR, Shivas RG, Geering AD, Callaghan B, Vanky K, Scharaschkin T. 2012. Soral synapomorphies are significant for the systematics of the *Ustilago-Sporisorium-Macalpinomyces* complex (*Ustilaginaceae*). *Persoonia* **29**: 63–77.

McTaggart AR, Shivas RG, van der Nest MA, Roux J, Wingfield BD, Wingfield MJ. 2016. Host jumps shaped the diversity of extant rust fungi (Pucciniales). *New Phytologist* **209**: 1149–1158.

Menardo F, Praz CR, Wyder S, Ben-David R, Bourras S, Matsumae H, McNally KE, Parlange F, Riba A, Roffler S *et al.* 2016. Hybridization of powdery mildew strains gives rise to pathogens on novel agricultural crop species. *Nature Genetics* **48**: 201–205.

van der Merwe MM, Walker J, Ericson L, Burdon JJ. 2004. Coevolution with higher taxonomic host groups within the *Puccinia/Uromyces* rust lineage obscured by host jumps. *Mycological Research* **112**: 1387–1408.

Milgroom MG, Wang K, Zhou Y, Lipari SE, Kaneko S. 1996. Intercontinental population structure of the chestnut blight fungus, *Cryphonectria parasitica*. *Mycologia* **88**: 179–190.

Miyawaki K, Matsumoto-Kitano M, Kakimoto T. 2004. Expression of cytokinin biosynthetic isopentenyltransferase genes in *Arabidopsis*: tissue specificity and regulation by auxin, cytokinin, and nitrate. *The Plant Journal* **37**: 128–138.

Mukhtar MS, Carvunis AR, Dreze M, Epple P, Steinbrenner J, Moore J, Tasan M, Galli M, Hao T, Nishimura MT *et al.* 2011. Independently evolved virulence effectors converge onto hubs in a plant immune system network. *Science* **333**: 596–601.

Nürnberger T, Lipka V. 2005. Non-host resistance in plants: new insights into an old phenomenon. *Molecular Plant Pathology* **6**: 335–345.

Parker JE, Holub EB, Frost LN, Falk A, Gunn ND, Daniels MJ. 1996. Characterization of eds1, a mutation in Arabidopsis suppressing resistance to *Peronospora parasitica* specified by several different RPP genes. *Plant Cell* **8**: 2033–2046.

Petersen RH. 1974. The rust fungus life cycle. *The Botanical Review* **40**: 453–513.

Pfunder M, Schürch S. 2001. Sequence variation and geographic distribution of pseudoflower-forming rust fungi (*Uromyces pisi* s. lat.) on *Euphorbia cyparissias*. *Mycological Research* **105**: 57–66.

Plaumann PL, Schmidpeter J, Dahl M, Taher L, Koch C. 2018. A dispensable chromosome is required for virulence in the hemibiotrophic plant pathogen *Colletotrichum higginsianum*. *Frontiers in Microbiology* **9**: 1005.

Ploch S, Thines M. 2011. Obligate biotrophic pathogens of the genus *Albugo* are widespread as asymptomatic endophytes in natural populations of Brassicaceae. *Molecular Ecology* **20**: 3692–3699.

Porras-Alfaro A, Bayman P. 2011. Hidden fungi, emergent properties: endophytes and microbiomes. *Annual Review of Phytopathology* **49**: 291–315.

Raffaele S, Farrer RA, Cano LM, Studholme DJ, MacLean D, Thines M, Jiang RH, Zody MC, Kunjeti SG, Donofrio NM *et al.* 2010. Genome evolution following host jumps in the Irish potato famine pathogen lineage. *Science* **330**: 1540–1543.

Raffaele S, Kamoun S. 2012. Genome evolution in filamentous plant pathogens: why bigger can be better. *Nature Reviews Microbiology* **10**: 417.

Refrégier G, Le Gac M, Jabbour F, Widmer A, Shykoff JA, Yockteng R, Hood ME, Giraud T. 2008. Cophylogeny of the anther smut fungi and their caryophyllaceous hosts: prevalence of host shifts and importance of delimiting parasite species for inferring cospeciation. *BMC Evolutionary Biology* **8**: 100.

Römer P, Recht S, Lahaye T. 2009. A single plant resistance gene promoter engineered to recognize multiple TAL effectors from disparate pathogens. *Proceedings of the National Academy of Sciences, USA* **106**: 20526–20531.

Roy BA. 2001. Patterns of association between crucifers and their flower-mimic pathogens: host jumps are more common than coevolution or cospeciation. *Evolution* **55**: 41–53.

Runge F, Choi Y-J, Thines M. 2011. Phylogenetic investigations in the genus *Pseudoperonospora* reveal overlooked species and cryptic diversity in the *P. cubensis* species cluster. *European Journal of Plant Pathology* **129**: 135–146.

Runge F, Thines M. 2012. Reevaluation of the host specificity of the closely related species *Pseudoperonospora humuli* and *P. cubensis*. *Plant Disease* **96**: 55–61.

Saikkonen K, Ion D, Gyllenberg M. 2002. The persistence of vertically transmitted fungi in grass metapopulations. *Proceedings of the Royal Society of London. Series B: Biological Sciences* **269**: 1397–1403.

Saikkonen K, Young CA, Helander M, Schardl CL. 2016. Endophytic *Epichloë* species and their grass hosts: from evolution to applications. *Plant Molecular Biology* **90**: 665–675.

Schulze-Lefert P, Panstruga R. 2011. A molecular evolutionary concept connecting nonhost resistance, pathogen host range, and pathogen speciation. *Trends in Plant Science* **16**: 117–125.

Sharma R, Mishra B, Runge F, Thines M. 2014. Gene loss rather than gene gain is associated with a host jump from monocots to dicots in the smut fungus *Melanopsichium pennsylvanicum*. *Genome Biology and Evolution* **6**: 2034–2049.

Sharma R, Ökmen B, Doehlemann G, Thines M. 2019. Saprotrophic yeasts formerly classified as *Pseudozyma* have retained a large effector arsenal, including functional Pep1 orthologs. *Mycological Progress* **18**: 763–768.

Shearer B, Crane C, Barrett S, Cochrane A. 2007. *Phytophthora cinnamomi* invasion, a major threatening process to conservation of flora diversity in the south-west botanical province of Western Australia. *Australian Journal of Botany* **55**: 225–238.

Shivas R, Ryley M, Telle S, Liberato J, Thines M. 2012. *Peronosclerospora australiensis* sp. nov. and *Peronosclerospora sargae* sp. nov., two newly recognised downy mildews in northern Australia, and their biosecurity implications. *Australasian Plant Pathology* **41**: 125–130.

Spanu PD, Abbott JC, Amselem J, Burgis TA, Soanes DM, Stuber K, Ver Loren van Themaat E, Brown JK, Gurr SJ *et al.* 2010. Genome expansion and gene loss in powdery mildew fungi reveal tradeoffs in extreme parasitism. *Science* **330**: 1543–1546.

Spencer M, Dick M. 2002. Aspects of graminicolous downy mildew biology: perspectives for tropical plant pathology and Peronosporomycetes phylogeny. In: Watling R, Frankland JC, Ainsworth AM, Isaac S, Robinson CH, eds. *Tropical mycology, vol. 2, micromycetes*. Wallingford, UK: CABI Publishing, 63–81.

Staats M, van Baarlen P, van Kan JA. 2005. Molecular phylogeny of the plant pathogenic genus *Botrytis* and the evolution of host specificity. *Molecular Biology and Evolution* **22**: 333–346.

Stein M, Dittgen J, Sánchez-Rodríguez C, Hou BH, Molina A, Schulze-Lefert P, *et al.* 2006. *Arabidopsis* PEN3/PDR8, an ATP binding cassette transporter, contributes to nonhost resistance to inappropriate pathogens that enter by direct penetration. *The Plant Cell* **18**: 731–746.

Tanaka S, Schweizer G, Rossel N, Fukada F, Thines M, Kahmann R. 2019. Neofunctionalization of the secreted Tin2 effector in the fungal pathogen *Ustilago maydis*. *Nature Microbiology* **4**: 251–257.

Telle S, Shivas RG, Ryley MJ, Thines M. 2011. Molecular phylogenetic analysis of *Peronosclerospora* (Oomycetes) reveals cryptic species and genetically distinct species parasitic to maize. *European Journal of Plant Pathology* **130**: 521–528.

Thines M. 2014. Phylogeny and evolution of plant pathogenic oomycetes—a global overview. *European Journal of Plant Pathology* **138**: 431–447.

Thines M, Kamoun S. 2010. Oomycete-plant coevolution: recent advances and future prospects. *Current Opinion in Plant Biology* **13**: 427–433.

Thines M, Kummer V. 2013. Diversity and species boundaries in floricolous downy mildews. *Mycological Progress* **12**: 321–329.

Thines M, Voglmayr H, Göker M. 2009. Taxonomy and phylogeny of the downy mildews (Peronosporaceae). In: Kamoun S, Lamour K, eds. *Oomycete genetics and genomics: diversity, interactions, and research tools*. Weinheim, Germany: Wiley-VCH, 47–75.

Thordal-Chirstensen H, Birch PRJ, Spanu PD, Panstruga R. 2018. Why did filamentous plant pathogens evolve the potential to secrete hundreds of effectors to enable disease? *Molecular Plant Pathology* **19**: 781–785.

Toruño TY, Stergiopoulos I, Coaker G. 2016. Plant–pathogen effectors: cellular probes interfering with plant defenses in spatial and temporal manners. *Annual Review of Phytopathology* **54**: 419–441.

Vági P, Kovacs GM, Kiss L. 2007. Host range expansion in a powdery mildew fungus (*Golovinomyces* sp.) infecting *Arabidopsis thaliana*: *Torenia fournieri* as a new host. *European Journal of Plant Pathology* **117**: 89–93.

Vandenkoornhuyse P, Quaiser A, Duhamel M, Le Van A, Dufresne A. 2015. The importance of the microbiome of the plant holobiont. *New Phytologist* **206**: 1196–1206.

Videira S, Groenewald J, Nakashima C, Braun U, Barreto RW, de Wit PJ, Crous P. 2017. Mycosphaerellaceae – chaos or clarity? *Studies in Mycology* **87**: 257–421.

Vlaardingerbroek I, Beerens B, Schmidt SM, Cornelissen BJ, Rep M. 2016. Dispensable chromosomes in *Fusarium oxysporum* f. sp. *lycopersici*. *Molecular Plant Pathology* **17**: 1455–1466.

de Vienne DM, Refregier G, Lopez-Villavicencio M, Tellier A, Hood ME, Giraud T. 2013. Cospeciation vs host-shift speciation: methods for testing, evidence from natural associations and relation to coevolution. *New Phytologist* **198**: 347–385.

Voglmayr H. 2003. Phylogenetic relationships of *Peronospora* and related genera based on nuclear ribosomal ITS sequences. *Mycological Research* **107**: 1132–1142.

Voglmayr H, Riethmuller A, Göker M, Weiss M, Oberwinkler F. 2004. Phylogenetic relationships of *Plasmopara*, *Bremia* and other genera of downy mildew pathogens with pyriform haustoria based on Bayesian analysis of partial LSU rDNA sequence data. *Mycological Research* **108**: 1011–1024.

Weßling R, Epple P, Altmann S, He Y, Yang L, Henz SR, McDonald N, Wiley K, Bader KC, Glasser C *et al.* 2014. Convergent targeting of a common host protein-network by pathogen effectors from three kingdoms of life. *Cell Host & Microbe* **16**: 364–375.

Whitfield JB. 2000. Phylogeny of microgastroid braconid wasps, and what it tells us about polydnavirus evolution. In: Austin A, Dowton M, eds. *The Hymenoptera: evolution, biodiversity and biological control*. Collingwood, Vic., Australia: CSIRO Publishing, 97–105.

Zipfel C. 2014. Plant pattern-recognition receptors. *Trends in Immunology* **35**: 345–351.