Bacterial/Fungal Interactions: From Pathogens to Mutualistic Endosymbionts

Donald Y. Kobayashi and Jo Anne Crouch

Department of Plant Biology & Pathology, School of Environmental and Biological Sciences, Rutgers, The State University of New Jersey, New Brunswick, NJ 08901-8520; email: Kobayashi@aesop.rutgers.edu; Crouch@aesop.rutgers.edu

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Abstract

A fundamental issue in biology is the question of how bacteria initiate and maintain pathogenic relationships with eukaryotic hosts. Despite billions of years of coexistence, far less is known about bacterial/fungal interactions than the equivalent associations formed by either of these types of microorganisms with higher eukaryotes. This review highlights recent research advances in the field of bacterial/fungal interactions, and provides examples of the various forms such interactions may assume, ranging from simple antagonism and parasitism to more intimate associations of pathogenesis and endosymbiosis. Information derived from the associations of bacteria and fungi in the context of natural and agronomic ecosystems is emphasized, including interactions observed from biological control systems, endosymbiotic relationships, diseases of cultivated mushrooms, and model systems that expand our understanding of human disease. The benefits of studying these systems at the molecular level are also emphasized.

BFI: bacterial/fungal interaction

Disease: a condition of a living organism that impairs normal functioning

Symbiosis: two organisms living together in close association

Commensalism: symbiotic relationship that is beneficial to one organism and neutral to the other

Mutualism: symbiotic relationship that is beneficial to both partners

Parasitism: symbiotic relationship that is beneficial to one organism and harmful to the other organism

INTRODUCTION

An emerging area of study in the field of host/pathogen interactions involves the relationships established between bacteria and fungi or fungal-like stramenopiles. With few exceptions, the majority of characterized bacterial/fungal interactions (BFIs) are thought to be of little economic importance. Nor are many BFIs particularly well known for their impact on the environment or human health (see 110 for a review of some notable clinical exceptions). As a result, BFI studies and our understanding of these associations have lagged behind similar investigations of host/pathogen interactions in plant and animal systems. Why then is BFI research on the rise? Increasingly, scientists are recognizing the utility of BFIs to yield basic information about the molecular basis of host/pathogen interactions at the most rudimentary organismal levels. Fungi have long been appreciated for their capacity to serve as simple eukaryotic models to elucidate the mechanisms and evolution of fundamental biological processes. In addition, both partners in the BFI interface possess relatively small genomes, a trait that lends itself to comprehensive analyses of how genes function and are expressed and regulated. Thus, investigations facilitated by the genetically tractable nature of the BFI system are beginning to expand what we know about the pathogenicity process and host/pathogen interactions on a basic level.

Besides serving as model systems, BFIs are becoming known for their importance in human health, agriculture, and the environment and for their potential for advancing discovery in these areas. From an application-based perspective, the parasitism of fungi by bacteria has been used as a tool to provide biological control of plant diseases caused by fungi. Understanding BFIs may also aid in the study of plant and animal diseases, as it has been discovered in some instances that associations between bacteria and fungi significantly influence host colonization. This appears to be the case particularly with immunocompromised individuals who are susceptible to multiple infections by opportunistic pathogens, as well as toxin-producing bacterial endosymbionts of fungi. BFIs also provide information that underlies several new technological advances, ranging from improved mushroom crop production to identifying novel antibiotic compounds for human therapeutic or agricultural purposes.

The origin of bacterial life predates the appearance of eukaryotic organisms by more than two billion years. Thus for bacteria, symbiosis with eukaryotes—regardless of whether the outcome is negative, positive, or neutral for the organisms united through the interaction—is a derived lifestyle. Even today, the majority of known bacteria are still free-living organisms, surviving independently of any long-term associations with living eukaryotic cells. However, in the two billion years that bacteria and eukaryotes have shared the planet, countless symbiotic relationships between these organisms have emerged, often with profound effects on both of the associated partners. Like any form of symbiosis, BFIs are extremely variable with respect to the impact on the bacterium and fungus. Most common are reports where the bacterial partner exploits resources from the associated fungus through a parasitic or commensalist interaction, although there are intriguing examples where the fungus is able to take advantage of bacterial resources in mutualistic interactions (85, 86). In this review, we present an overview of the diversity of BFIs by providing examples from across the entire spectrum of the BFI symbiotic continuum, ranging from bacterial endosymbionts of fungi, to pathogens of yeast, to the parasitism of fungi by bacteria in natural and agricultural systems.

INTERACTION TYPES

Bacterial Endosymbionts of Fungi

Bacteria that inhabit fungi intracellularly, or endosymbiotically, have been described for more than three decades (reviewed in 14; 116). Endosymbiotic BFIs are ubiquitous and have been documented from all parts of the world (13, 42, 83, 85). To our knowledge, regardless of the impact of the association with the allied

organisms, endosymbiosis is a one-way partnership in that the single-celled bacterium is limited to the role of endosymbiont and the multicellular eukaryotic partner always acts as the host organism as the result of obvious size constraints. From a broad perspective, several reviews have been written on the subject of eukaryotic endosymbiosis, with many of these systems exceptionally well studied (10, 69, 72, 73, 89). For endosymbiotic BFIs in the fungal kingdom, however, several factors have contributed to a lack of discovery in the field, including the lack of obvious phenotypes, problems experienced when attempting to establish these organisms in pure culture (3, 11), and the overall difficulties in establishing experimentally tractable systems. Nonetheless, endosymbiotic BFIs are increasingly gaining recognition for their potential to influence agricultural systems in a significant manner, and a few model systems are providing insight into their overall lifestyle.

Although the distribution of bacterial endosymbionts includes members of all major classes in the fungal kingdom, mycorrhizal fungi are by far the most common group known to harbor endosymbiotic bacteria. Indeed, the earliest identification of endosymbiotic bacteria was made from cells of the arbuscular endomycorrhizal (AM) fungus *Gigaspora margarita*, where it was demonstrated that the endosymbiont was present within vegetative spores, germinating hyphae, and mycelia, even while the fungus was symbiotically associated with a host plant (9). AM fungi within the family Gigasporaceae, including species of *Gigaspora*, *Scutellospora*, and *Gloerella* (13), are among the best characterized fungal endosymbiont systems, although bacteria have also been observed in other AM fungi of the Glomeromycota, such as *Glomus versiforme* and *Acaulospora laevis* (reviewed in 2). Intracellular bacteria have also have been observed in ectomycorrhizal fungi including species of the ascomycete *Tuber* (3) and the basiodiomycete *Laccaria* (6, 7), as well as within nonmycorrhizal species of *Rhizopus* and other related members of the Mucoromycotina (42, 85).

Bacteria associated endosymbiotically with fungal cells have been predominantly identified as belonging to the Proteobacteria, with most characterized as either members or close relations of the genus *Burkholderia*. Originally, uncultured endosymbiotic bacterial strains associated with *Gigaspora* and *Scutellospora* species were identified as *Burkholderia* spp. (13). Subsequent application of more rigorous phylogenetic analysis indicated that although these microorganisms were closely related to *Burkholderia*, endosymbionts of AM fungi formed a clade distinct from *Burkholderia* and other affiliated genera such as *Ralstonia* and *Pandoraea*, resulting in the proposal of a new genus, "*Candidatus* Glomeribacter gigasporarum" (12). Endosymbiotic bacteria associated with *Rhizopus* are also members of the Proteobacteria, represented by two novel species of *Burkholderia* that have been found to inhabit the same fungal host species (84). In contrast, endosymbionts identified from *Laccaria bicolor* include a bacterium related to the Gram-positive genus *Paenibacillus* (7), as well as a diverse assemblage comprised primarily of α-proteobacteria (6). Alternately, members of the *Cytophaga-Flexibacter-Bacteroides* group within the *Cytophagales* were identified as the endosymbiotic bacteria inhabiting *Tuber borchii* (3, 4). Together, these findings demonstrate that partnership in endosymbiotic BFIs spans a biologically diverse taxonomic range of organisms, both with respect to the associated fungal and bacterial partners.

In general, few detectable phenotypes have ever been associated with bacterial endosymbionts of fungi as a result of the intractability of currently studied systems. There is correlative evidence suggesting that certain bacterial endosymbiont genes function to benefit the fungal host by facilitating nutrient acquisition, such as through phosphate transportation or nitrogen fixation (reviewed in 2). It remains to be demonstrated, however, whether there is a legitimate connection between these proposed endosymbiont functions and increased fitness in the host fungus (49).

AM: arbuscular endomycorrhizal

Pathogenic: capable of causing disease

A promising, relatively new approach developed for assessing endosymbiont-induced phenotypes from fungal hosts is based on establishing the fungus in culture, then curing it of the bacterial association through antibiotic treatment to demonstrate loss of phenotype, and finally reintroducing the endosymbiont into the host cells to restore the host phenotype. This strategy was used recently to identify two important phenotypes associated with bacterial endosymbionts in *Rhizopus*. In the first study, Partida-Martinez et al. (83, 85) demonstrated that the toxic compounds rhizoxin and rhizonin, attributed to the causative agent of rice seedling blight, *R. microsporus*, are produced by *Burkholderia* endosymbionts and not by the fungus. These experiments provide the first evidence of a mutalistic BFI whereby virulence of the fungal host is enhanced by the presence of endosymbionts. A second phenotype in the *Rhizopus/Burkholderia* BFI was observed when symbiont-cured *R. microsporus* was no longer able to sporulate in culture. Restoration of the cured fungal strain using a strain of the *Burkholderia* endosymbiont restored sporulation capabilities (86). Collectively, these data provide an extraordinary example of a fungal lifestyle predicated on the presence of its endosymbiont, with the fungus relying on the bacterium for host colonization, nutrient acquisition, and reproduction.

The experimental curing of fungi exemplified in the *Rhizopus/Burkholderia* interaction is mirrored in clinical studies and suggests that fungal endosymbiotic associations may also impact human health through the phenomenon of so-called hyperparasitism. In recent times, there has been a documented rise in zygomycosis, caused by the same group of fungi most commonly associated with bacterial endosymbionts (17). It has been proposed that the greater incidence of zygomycosis is an unintended side effect of increased reliance on antibacterial agents, where the initial use of antibiotics suppresses endosymbiotic bacteria in the fungal host, thus reducing production of toxin contributing to enhanced fungal virulence. Eventually, however, development of resistance to antibacterials by the endosymbiont allows for desuppression of zygomycete virulence. Whether this model holds true or not remains an open question, as work by Ibrahim et al. (42) does not support increased mucormycosis pathogenesis in fungi harboring toxin-producing endosymbionts.

Yeasts as Model Systems to Study Bacterial Pathogenesis

Numerous studies have taken advantage of genetically tractable yeast model systems to further our understanding of host/pathogen interactions and the fundamental nature of bacterial pathogenesis of fungi (reviewed in 110). In particular, research performed with the *Candida albicans* pathosystem revealed the critical role of interspecies communication in BFIs and how this process controls pathogenic capabilities and, by extension, influences the bacteria/fungal partners within third-party host organisms. Many of these investigations involve the human pathogenic yeast *C. albicans* because of the clinical implications inherent in this system, but the model organism *Saccharomyces cerevisiae* has also been the subject of BFI studies (96). Although the primary emphasis of this review is on BFIs drawn from environmental and agricultural systems, here we highlight recent results from a few representative clinical BFIs that serve to augment similar work from nonmedical research and add to what is known about the pathogenesis of fungi by bacteria.

The *Pseudomonas aeruginosa/C. albicans* BFI has provided a useful system in which to study bacterial-fungal interactions at different levels. Investigations using this system have facilitated investigations of the molecular basis for host/pathogen interactions as well as dissecting the complex communication signaling between two pathogenic organisms (39, 40, 68) and their physical interactions with each other during infection of a third-party host, as is such the case in immunocompromised humans (88). Hogan & Kolter (39) described the interaction between *P. aeruginosa* and *C. albicans* and the virulence factors involved in bacterial pathogenesis. From

this work, it was shown that the ability to colonize and kill fungal cells by *P. aeruginosa* was limited to the filamentous stage of the *C. albicans* life cycle, with the yeast stage resistant to killing. Mutant strains of the bacterium affected in various virulence traits behaved differently in their killing capacity of *C. albicans*.

Use of the same system led to the discovery that the quorum sensing (QS) molecule from *P. aeruginosa* prevents conversion of *C. albicans* from the yeast phase to the filamentous phase, which is the pathogenic form of the fungus (40). Subsequent work showed that variability in QS molecule production by *P. aeruginosa* corresponded with variation in the ability to prevent the conversion of *C. albicans* to the filamentous stage. While in the yeast form, *C. albicans* is also capable of self-regulating conversion to the filamentous stage through the production of farnesol, a yeast QS molecule that also prevents the production of QS molecules and other virulence factors in *P. aeruginosa* (24, 40).

Similar to the scenario observed with *P. aeruginosa*, in experiments exploring the interaction between *C. albicans* and the human bacterial pathogen *Acinetobacter baumannii* (88), it was demonstrated that *A. baumannii* inhibits at least two very important features of *C. albicans* pathogenicity: biofilm formation and conversion to pathogenic filamentous form. Thus, signal molecules originating from at least two bacterial species are able to influence the pathogenic behavior of *C. albicans*.

Bacterial Pathogens of Fungi in Natural Systems

There are few descriptions of naturally occurring interactions between pathogenic bacteria and fungal hosts. Willoughby's description of bacteria found within the chytrid *Karlingia rosea* provides one of the first descriptions of pathogenic bacteria intracellularly colonizing filamentous eukaryotes, which in this case is a fungus inhabiting natural systems (116). The bacterium, identified as *Pseudomonas* (*Stenotrophomonas*) *maltophilia*, was observed to colonize hyphal thalli intracellularly, which led to the development of bacteria-packed, dome-like structures originating from infected hyphae. These structures eventually lysed, releasing bacteria into the surrounding environment (115, 116). Further studies indicated the bacterial relationship was not restricted to *Karlingia*, providing evidence that other chytrid species were susceptible to *S. maltophilia* colonization (114). The *K. rosea*/*S. maltophilia* interaction clearly resembles life cycles typical of intracellular bacterial pathogens. It also represents one of the earliest descriptions for pathogenesis of fungal-like hosts that involve intracellular colonization.

QS: quorum sensing

There are a few more descriptions of bacterial parasitism of fungi that qualify as pathogenesis in natural environmental systems. De Boer et al. (27, 28) described the isolation of chitinolytic bacteria closely associated with fungal hyphae from sand dunes, a typically nutrient-sparse environment. These bacteria are capable of growth in a natural sand environment by sequestering nutrients obtained from fungi also located in the same niche (reviewed in 26). In this system, several of the bacterial strains attach to fungal hyphae and establish mycophagous relationships, demonstrating that bacteria can grow in the presence of fungi in natural systems, presumably by parasitizing nutrients from the fungi. In this particular study, chitinolytic activity appeared to be an important facilitator of the observed parasitism.

In a study involving an AM fungus in a nonendosymbiotic relationship, Roesti (101) isolated bacteria associated with spores of *Glomus* species. Microscopy indicated these bacterial isolates were associated with the hyaline layer of the spore, and signs of spore coat degradation were apparent, including pitted holes that likely represented lysed areas within the spore coat. Identified bacteria include strains belonging to the genera *Flexibacter*, *Lysobacter*, and *Pseudomonas*, all of which, not surprisingly, harbor species known to express lytic enzymes and are also associated in various forms with antagonism or pathogenesis of fungi as described in this chapter.

CLP: cyclic lipopeptide

Bacterial Diseases of Cultivated Mushrooms

The parasitism of cultivated mushroom species by bacteria has been described for nearly a century (80, 108). A number of diseases and causative agents have been described, but inconsistencies and overlaps in name use often make it difficult to gain a clear understanding of the major diseases and pathogens that cause them. In providing an overview of mushroom diseases caused by bacteria, some of these diseases can be grouped according to similarities in symptom production, whereas others are fairly distinct. Because only brown blotch caused by *Pseudomonas tolaasii* has been studied in depth to date, many of the mechanisms by which mushroom pathogens cause disease remain unresolved.

Mushroom blotch diseases are caused by a diverse group of bacteria (36, 112). Similarities in symptom production have frequently led to confusion as to the causative agent for various diseases. Blotch symptoms typically occur on basidiocarps (or caps) and occasionally on mushroom stipes. They begin initially as a lesion of discoloration, which eventually become sunken or pitted at later stages, depending on the type of blotch disease. Two blotch diseases, brown blotch and ginger blotch, have been described and can be distinguished from each other based on the color and physical nature of the damage observed on the basidiocarps. The diseases differ primarily by the color intensity of symptoms produced, which has led to some confusion presented in the literature as to the causative agents and specific diseases. Classic brown blotch symptoms are characterized by a dark brown discoloration that eventually appears as deep sunken lesions. In contrast, ginger blotch symptoms typically have a lighter, ginger-colored appearance, with lesions showing no or only mild sunken appearance (117). Because it is apparent that severity of blotch disease symptoms can vary, especially under varying environmental conditions, correct diagnosis can be difficult. Furthermore, studies have shown that differences in color can be species and strain dependent (36, 106, 112).

Based on the diverse group of bacteria capable of causing blotch disease symptoms, is it not surprising that these pathogens rely on different mechanisms to produce similar symptoms (36). As mentioned previously, among the best studied mushroom diseases is brown blotch caused by *P. tolaasii*. *P. tolaasii* produces tolaasin, a cyclic lipopeptide (CLP) toxin that is essential for disease symptom production by the bacterium. Rainey et al. (94) and Brody et al. (15) provided strong supportive evidence that tolaasin is the major contributor of symptom production in brown blotch disease. Purified toxin alone produced disease symptoms when applied to mushrooms, whereas a *P. tolaasii* mutant strain blocked in tolaasin biosynthesis was no longer capable of causing disease.

Clearly, multiple factors are involved in blotch symptom production because nontolaasin-producing bacteria are also capable of causing blotch disease. *P. reactans*, a species related to *P. tolaasii*, produces a related lipodepsipeptide compound, WLIP; however, neither the bacterium nor the toxin causes blotch symptoms at the same intensity or severity level as *P. tolaasii* or tolaasin (62).

As mentioned previously, blotch disease symptoms can be produced by a broad range of bacterial species as indicated by diversity studies conducted by Wells et al. (112) and Godfrey et al. (36). As a species, *P. tolaasii* is considered metabolically diverse (36, 74, 75, 105, 112). Furthermore, it has become apparent that CLP toxins are important contributors to blotch disease symptom production, and that these toxins can be produced by a diverse group of bacteria (29, 78). Even strains of *P. tolaasii* differ in the types of CLP molecules they produce (5). This, together with the fact that *P. tolaasii* and other blotch disease-causing fluorescent pseudomonads are readily found in soil and casing material used for mushroom propagation (36, 112), suggests blotch diseases can occur by the activity of opportunistic saprophytic bacteria.

Although diversity of causative agents is apparent, there is also distinct variation in diseases caused by the same species. *P. agaricus* is included among the bacterial species reported to be associated with causing milder blotch-like symptoms on *Agaricus* (36, 61) but also has been identified as the causative agent of yellow blotch disease of oyster mushrooms, which is characterized as yellow droplets on the surface of sporocarps (8). *P. agaricus* is also well known as the causative agent of dippy gill (35). This disease is characterized by bacterial ooze originating from gills of sporocarps and from longitudinal splits within the stipe where bacteria colonized host tissue both intercellularly and intracellularly. Unlike the brown blotch pathogen, virulence factors involved with *P. agaricus* pathogenesis have not been established.

Soft rots represent another class of mushroom diseases reported to be caused by a variety of bacterial species. Symptoms range from pitting and sticky yellowish or brownish blotches on caps to complete dissolution of mushrooms within a few days. Two different bacteria that are associated with soft rot of mushrooms have been identified. A rapid soft rot, previously referred to as cavity disease and caused by *Burkholderia gladioli* pv. *agricicola*, occurs on the sporocarp and stipe of *Agaricus* spp. (60). *Janthinobacterium agaricidamnosum* (59) was reported to cause symptoms on *Agaricus* similar to those of rapid soft rot. A third bacterium was recently reported to cause a different kind of rot in which water-soaked lesions accompanied soft rot of caps and stipes of the king oyster mushroom, *Pleurotus eryngii*. The causative agent for this disease was identified as *Pantoea* sp. (50).

Among soft rots, only *B. gladioli* pv. *agricicola* has been investigated from the interaction standpoint, in which studies indicate the involvement of a type II secretion system (T2SS), implicating secreted enzymes in rapid soft rot disease (19). Mutations within the T2SS resulted in mutant strains that did not degrade mushrooms and were significantly reduced or devoid of chitinase and protease activity compared with the wild-type parental strain. T2SS mutants were able to colonize mushroom tissue in a biofilm-like manner but were unable to degrade fungal hyphae compared with the wild-type strain. Mutants still showed antifungal activity in vitro, indicating factors associated with type II secretion are involved in mushroom degradation but not hyphal growth inhibition.

T2SS: type II secretion system

Internal stipe necrosis is a disease characterized by browning or severe necrosis of the central core tissue of the stipe, with spreading occurring outward in more severe cases (100). The disease was originally thought to be caused by a fluorescent pseudomonad, but subsequent evidence implicated the enteric bacterium *Ewinella americana* (43, 44). As with the majority of mushroom diseases, the mechanism(s) of pathogenesis remains unclear; however, chitinolytic activity has been characterized from *E. americana* (45) and attributed to a single chitinase gene (46). Although the exact role for chitinase activity in pathogenesis by *E. americana* has not been determined, stipe tissue is highly susceptible to enzymatic degradation, thus implying an important role for chitinase as a virulence factor for the disease (46).

Of all the diseases of cultivated mushrooms, determining the etiology of mummy disease has proven to be extremely problematic. Difficulty in identifying the causative agent has made it all but impossible to fulfill Koch's postulates. Mushrooms afflicted with mummy disease initially fail to reach maturity, but instead of decaying they become mummified. Schisler et al. (104) was able to reproduce disease symptoms with a single isolated strain reported as a member of the genus *Pseudomonas*. Intracellular colonization of mushroom spore cells by the bacteria was observed and confirmed in a separate study by van Zaayen & Waterreus (109). Two different bacterial species, *P. aeruginosa* and *P. fluorescens*, have been independently implicated as causative agents, but neither has been verified to date.

BACTERIAL PATHOGENS OF FUNGI IN AGRICULTURE AND IMPLICATIONS FOR THEIR USE TO CONTROL PLANT DISEASE CAUSED BY FUNGI

Introduction to Biological Control Systems

Owing largely to the efforts of plant pathologists working to harness the antagonistic properties of bacteria to biologically control fungal phytopathogens, there are many outstanding examples of bacterial pathogenesis of fungi derived from agricultural systems. Several basic mechanisms of bacteria-induced biocontrol of plant pathogenic fungi have been described in the literature (reviewed in 22, 113); however, within the context of this review, the most relevant biocontrol BFIs are those involving bacterial products that exert direct, deleterious effects on fungi. Frequently, these interactions are parasitic, a mode of symbiosis characterized by the intimate association of two dissimilar organisms where one partner increases its fitness at the expense of the second partner. Most, but not all, parasitic BFIs may also be further categorized as pathogenic, depending on whether the outcome of a parasitic association with a bacterium leads to disease in the fungal partner. Pathogenicity is a frequent outcome of parasitic interactions involving bacteria categorized as hyperparasites of fungi, particularly those exhibiting lytic activity. Other interactions, such as those that function by antibiosis, are less convincingly described as parasitic, in that the relationship between the bacterium and fungus may be fleeting, nonspecific, and conducted at a distance, rather than involving the long-term, intimate connection typically associated with symbiotic relationships. For example, there are numerous bacteria that produce antifungal compounds that cause host cell leakage or lysis, thereby releasing fungal cellular contents into the surrounding environment that the bacterium can utilize as a nutrient source. To effect this form of pathogenicity, direct contact is not required, and depending on the enzymes and metabolites released, there may be little or no specificity in the interaction.

In this section, an overview of pathogenic BFIs known through studies aimed at biocontrol of fungal pathogens of agroecosystems, including examples of specific and nonspecific interactions, is provided. Also highlighted is a BFI system where the biocontrol bacterium deploys a variety of pathogenicity mechanisms that allow it to acquire nutrients from fungi either asymbiotically, parasitically, or through combination of mechanisms associated with both lifestyles.

Antibiosis: A Simple Virulence Mechanism for Microbial Pathogenesis in Soil and Other Environmental Systems

Soil-inhabiting bacteria produce a broad range of secondary metabolites with antibiotic activity (reviewed in 37, 71, 102, 111), many of which are assumed to provide them with beneficial, competitive advantages over other microorganisms colonizing similar niches. Although the structures of secondary metabolites are diverse (for example, see 111), several bacterial antibiotics are of the nonribosomal peptide or polyketide types such as CLPs. CLPs are known to function in a variety of ways, with most displaying broad-spectrum activity against other bacteria and eukaryotic organisms such as plants, animals, and fungi (reviewed in 71). Some CLPs are known to possess antibiotic or biosurfactant activity capable of inhibiting fungal growth or lysing the zoospores of stramenopiles (reviewed in 72, 102; 31, 77, 78). Others, such as the previously mentioned toxins tolaasin and rhizoxin, are major virulence factors contributing to diseases of mushrooms and plants, respectively.

The key role that secondary metabolites play in bacterial nutrient acquisition from fungi is paralleled across ecosystem types, regardless of the particulars of any given system from which bacterial antibiotic compounds have been described (**Figure 1**). Antibiotic compounds produced by bacteria may take the form of metabolites with highly specific activity capable of

impacting only a few target organisms, such as pyoluteorin, which inhibits *Pythium* (41), or compounds displaying broad-spectrum activity, such as the CLP-type toxins. Narrowly defined, bacteria that rely on the secretion of antibiotics in order to acquire nutrients from fungi can be described as simple or opportunistic pathogens. Under these circumstances, the antibiotic functions as a virulence factor that enhances parasitism or pathogenesis of fungi. In nutrient-sparse soils, the ability to degrade any available microorganism in the general vicinity in a nondiscriminatory manner is an extremely useful property and suggests that such an environment would select for antibiotic-producing bacterial strains. This prediction is supported by data collected in a survey of CLP-producing fluorescent pseudomonads inhabiting different soil types. As many as 60% of the bacteria found in nutrient-poor sand-based soil were CLP producers, in contrast to the bacterial cohort from a rich loam-based soil, where only 6% of the bacteria secreted CLP antibiotics (78).

Lytic Bacteria: Nectrotrophic Bacterial Pathogens of Fungal Hosts

Early studies by Lockwood (63, 64) and Mitchell & Hurwitz (70) provide descriptions of fungal cell lysis attributed to soil bacteria that might be exploited for biocontrol purposes. To identify potential biocontrol-competent bacterial strains, Scher & Baker (103) devised an effective fungal baiting method to isolate bacteria parasitic to fungi. In this work, mycelial mats of *Fusarium* were buried in soil for a period of time, recovered, washed, and then plated onto media to culture any bacteria that had adhered to fungal cells. Similar strategies based upon the premise of using fungal mycelium or spores to bait and isolate potential biocontrol agents have been used successfully over the past 30 years (reviewed in 52). In one modification of the original method, fungal baiting was used in combination with an enrichment procedure. Through successive subculturing in a minimal salts medium, bacteria capable of utilizing fungal mycelia as the sole carbon source for growth were selected (51). This iterative process succeeded in isolating several bacterial strains that expressed lytic enzymes, including a strain of the proteobacterium *Lysobacter enzymogenes* (107), a species of bacteria that was found to produce a wide array of lytic enzymes and displayed potent antimicrobial activity.

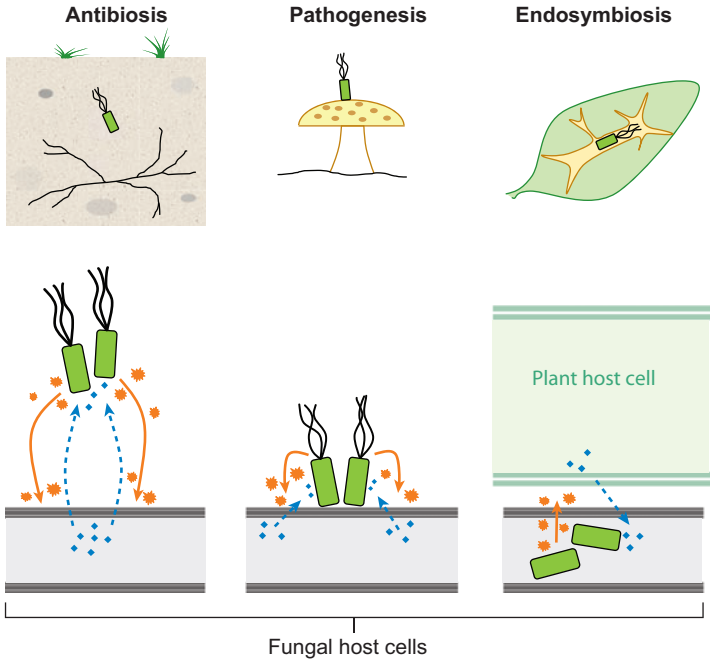

Figure 1

Antibiotic/toxin function in different modes of bacterial pathogenesis of fungal hosts. Blue diamonds depict nutrients of host origin; orange stars represent bacterial antibiotic/toxin, with arrows indicating direction of flow. Antibiosis is represented by distal soil interactions; pathogenesis is represented by mushroom disease occurring by close contact; and endosymbiosis is represented by an intracellular phytotoxin-producing bacterium.

Case Study 1: *Pseudomonas fluorescens*—A Simple, Antibiotic-Producing, Nonspecific Pathogen of Several Fungal Species

P. fluorescens strain Pf-5 provides highly effective biocontrol activity across a broad range of fungal plant pathogens through the production of several secondary metabolites. These include well-characterized antifungal compounds such as pyoluteorin, pyrrolnitrin, and 2,4-diacylphloroglucinol (reviewed in 66), as well as

several rhizoxin derivatives (65). Unlike other *P. fluorescens* strains that utilize sophisticated pathogenicity mechanisms (98), Pf-5 appears to rely mainly on the production of secondary metabolites to antagonize fungi, perhaps for the purpose of nutrient acquisition. Sequencing of the *P. fluorescens* Pf-5 genome confirmed a heavy reliance on antifungal compounds by this bacterial strain, with roughly 6% of the genome dedicated to the production of complex secondary metabolites (87).

Case Study 2: *Pseudomonas putida*—A Parasitic Pathogen of the Stramenopile *Phytophthora parasitica*

P. putida strain 06909 is capable of suppressing disease caused by *Phytophthora parasitica*. The bacterium exerts biocontrol activity by attaching to *Phythophthora* hyphae and inhibiting its growth (119). Two approaches were taken to understand the molecular basis of this interaction. In the first, a mutant *P. putida* library was used to screen for loss of the two major phenotypes. Using this approach, it was observed that mutants no longer able to colonize hyphae also lacked flagella and were nonmotile (119). During the course of this study, the researchers found that growth inhibition by *P. putida* required hyphal colonization, as well as production of the iron chelator, pyoverdine. In a second approach, in vivo expression technology (IVET) was used to identify *P. putida* genes specifically expressed during hyphal colonization (1, 56). Many of the genes identified by this method involved transport processes and metabolic pathways, including carbon catabolism and energy metabolism, providing supportive evidence that *P. putida* derives nutrients directly from *Phytophthora* during their close interaction.

Case Study 3: *Lysobacter enzymogenes*—A Broad-Host-Range Pathogen of Fungi

In recent years, the genus *Lysobacter* has emerged as a taxon of scientific interest for many reasons (reviewed in 55), although by far the most compelling work has surrounded the antibiotic and biocontrol properties of *L. enzymogenes*. Initially described as a potent antagonist of microorganisms (20), recent work shows that *L. enzymogenes* is pathogenic toward an evolutionarily diverse range of lower eukaryotic hosts, including fungi, nematodes, and bryophytes (H. Saidasan, J.A. Crouch, R.M. Reedy, B.I. Hillman, M.A. Lawton, and D.Y. Kobayashi, submitted). In these studies, *L. enzymogenes* was observed to infect each of its hosts intracellularly, with defined stages for attachment, intracellular infection, replication, and eventual release into the extracellular environment.

As its name implies, *L. enzymogenes* produces a host of lytic enzymes, such as chitinases, β-1,3-glucanases, and proteases, all of which are capable of degrading cell wall components of fungi and fungal-like stramenopiles. Several of these enzymatic compounds, along with their roles in antifungal and biocontrol activities, have been characterized at the molecular and biochemical levels (81, 82, 120). *L. enzymogenes* also makes use of a number of antibiotics, including a heat-stable antifungal factor (HSAF), a secondary metabolite structurally similar to dihydromaltophilin (120). HSAF production in *L. enzymogenes* has been characterized in-depth with demonstrated ability to inhibit ceramide synthase in *Aspergillus* (57).

Evidence to date reveals that although each of the antimicrobial traits observed from *L. enzymogenes* is capable of contributing to antagonism and biocontrol activity against fungi, there is no single trait that is solely responsible for the entire spectrum of antimicrobial activities observed (53, 54, 82). Instead, it has been determined that a single regulatory gene encoding the Clp regulator globally controls expression of several traits, including extracellular lytic enzyme production and in vitro antifungal activity. Furthermore, *L. enzymogenes* strains mutated in the *clp* regulatory gene are completely devoid of biocontrol activity against *Pythium* damping off of cucumber and *Bipolaris* leaf spot of tall fescue (53). However,

antifungal activity is not entirely eliminated in the *clp* mutant for all phytopathogens. Control of summer patch disease of Kentucky bluegrass caused by the root-colonizing fungal pathogen *Magnaporthe poae* is still possible, albeit at reduced levels compared with the wild type, even in the absence of enzyme and antibiotic production (54). These results indicate that *L. enzymogenes* must employ some other mechanism of pathogenicity not controlled by the *clp* regulator.

Genetic and genomic evidence indicate that *L. enzymogenes* employs a diverse set of mechanisms to affect pathogenicity of various organisms, including a type III secretion system (T3SS) (97; H. Saidasan, J.A. Crouch, R.M. Reedy, B.I. Hillman, M.A. Lawton, & D.Y. Kobayashi, submitted). Using a mutant strain containing a large deletion in the T3SS pathway, it has been shown that the T3SS plays an important role in the infection and induction of disease in the nematode *Caenorhabditis elegans* and the bryophyte *Physcomitrella patens*, but there is little evidence to support a similar role in fungal interactions. In contrast, *clp*-regulated traits clearly are vital for pathogenicity, as *clp* mutant strains are unable to lyse or infect fungal host cells intracellularly. Taken together, the multiplicity of pathogenicity mechanisms employed by *L. enzymogenes*, along with the ability to internalize within host cells suggests that this organism has the potential to act as a highly informative model system capable of advancing our knowledge of bacterial pathogenesis. Future research in this system will be facilitated by completion of the *L. enzymogenes* genome sequence, a project currently in progress (D.Y. Kobayashi & J. Ravel, unpublished).

MECHANISMS OF PATHOGENESIS: ARE THEY MORE COMPLEX THAN WE THINK?

In addition to lytic enzymes and antibiotics, several other virulence factors known to have important roles in bacterial pathogenesis in higher eukaryotes have been identified in BFIs. A well-characterized bacterial virulence mechanism that appears operational during pathogenesis of fungal hosts is the T4 pilus, which facilitates attachment (32, 39). Although experimental evidence outside of *P. aeruginosa* is currently lacking, it is possible that for many bacterial pathogens, attachment to fungal hosts is mediated by T4 pili; the T4 pilus is known to function in virulence of host cells, including the initial steps of attachment for bacterial infection of hosts (reviewed in 23, 79).

T3SS: type III secretion system

T4SS: type IV secretion system

One of the most sophisticated of pathogenicity mechanisms was described several years ago from *Agrobacterium tumefaciens*, where it was demonstrated that the bacterium was capable of transforming DNA into host cells using a type IV secretion system (T4SS), thereby inducing crown gall disease in plants (reviewed in 21). Subsequent research demonstrated that *A. tumefaciens* is also capable of transforming DNA into fungal hosts (30). Furthermore, T4SSs are not limited to the transfer of nucleic acids and also function in the transport of other macromolecular effectors important for pathogenesis. Although the extent to which bacteria like *Agrobacterium* utilize T4SSs to deliver effectors to fungal hosts in nature is unknown, it is possible that such transfers occur regularly and may represent a major mechanism for horizontal transfer of genetic material between bacteria and fungi.

Another important mechanism of pathogenicity has been documented from rhizosphere-inhabiting *Pseudomonas fluorescens*. Strains of these bacteria possess genes associated with a T3SS (92, 98, 99), suggesting they are involved in pathogenic interactions with eukaryotic hosts. Surveys of *P. fluorescens* showed that many, but not all, strains possess a T3SS. Mutation of the T3SS in *P. fluorescens* strain KD not only affected biocontrol activity against *Pythium ultimatum* but the mutant was no longer able to suppress activity of the host pectolytic enzyme polygalacturonase at a level comparable to the wild-type strain. Expression studies also indicated *hrpJ* gene homolog was more highly expressed in the

presence of *Pythium*, whereas the gene product was less evident during colonization of plants by *P. fluorescens*. These data demonstrate that the T3SS is functional in pathogenesis of the bacterium toward *Pythium*.

FUNGAL HOST RESPONSES TO BACTERIAL STIMULI: THE GOOD, THE BAD, AND THE UGLY

Just as there are only a small number of mycopathogenic bacterial associations described in the literature, so too are there few descriptions of fungal responses to microbial pathogens. On a very fundamental level, it is clear that host defense systems in morphologically simple multicellular organisms like fungi are not as evolved as those in higher eukaryotes. Sophisticated defense mechanisms such as acquired immunity or induced resistance, which serve to protect higher plants and animals against microbial invaders, have never been observed in fungi or filamentous stramenopiles. Nevertheless, diseases of fungi are not observed with any great frequency, suggesting they rely upon one or more mechanisms to escape the onslaught of potential pathogens.

A few representative examples of the different types of responses that have been elicited from fungi as a result of bacterial stimuli are presented here. These responses are grouped into two general categories based upon the overall impact of the interaction on the fitness of the fungus. The first is the good, which represents those interactions where an outcome beneficial to the fungal host occurs. The second is the bad, which reflects responses that occur during pathogen attack. As it will become apparent, beneficial responses to bacterial stimuli clearly involve signaling processes similar to those found in deleterious interactions; it is only the final outcome of the interaction that is altered. We also include a third category, the ugly, to describe a unique pathogen strategy that functions to suppress certain metabolic processes possibly including host defense, resulting in an altered, atypical fungal morphology.

The Good: Bacteria Promoting Hyphal Growth or Fungal Structure Development

Hyphal extension and stimulation of reproduction are two well-described physiological responses elicited in fungi by bacteria. Many of the descriptions of bacteria-induced promotion of fungal growth or development involve interactions between fungi and mycorrhiza helper bacteria (MHB), which aid mycorrhizal development between the fungus and plant host. An overview of the topic, including a comprehensive list of the various bacterial and fungal species associated with these interactions, has been provided in a recent review (34).

Two noteworthy examples of MHB-bacterial interactions highlight the considerable influence that bacteria can exert over fungal growth and structural development. Hildebrandt et al. (38) showed that *Paenibacillus validus* was able to stimulate both hyphal growth and sporulation of *Glomus intraradices* through the production of specific trisaccharides, allowing this otherwise obligate AM fungus to complete its life cycle in the absence of a plant host. In a separate study, Xavier & Germida (118) described spore-associated bacteria that were capable of inducing germination of *Glomus* spores. The nature of the bacterial stimulating factor was not determined in this work but was thought to be a result of a tropic response stemming from a nutritional stimulus provided by the bacterium. Collectively, these and other studies clearly demonstrate that bacteria are able to substitute for other forms of growth stimuli.

Bacterial stimulation of fungal physiology has also been described from nonmycorrhizal fungal systems. In one example, Rainey et al. (95) demonstrated that certain bacterial strains, especially members of *P. putida*, are capable of stimulating basidiome development from *Agaricus* mycelia, a process that typically relies on the application of a casing layer as part of mushroom cultivation practices. Although a number of factors were shown to contribute to the stimulatory effect, bacterial activity was

implicated as a major contributor to the process. Similarly, *P. putida* strains were also found capable of promoting hyphal extension in vitro (93). In a second example, endosymbiotic *Burkholderia* strains have been shown to stimulate sporulation of *Rhizopus* (86). Here the *Rhizopus* spores contained the bacterium, ensuring continued propagation of the host and the perpetuation of the bacterial association.

(Dealing with) the Bad: Host Defense Mechanisms in Response to Pathogen Attack

The presence of melanin in cell walls provides protection against many stresses encountered by fungi, including invading pathogens (reviewed in 16). Additional responses to pathogenic bacteria include active resistance to antibiotics or the production of fungal signal molecules that repress antibiotic production in bacterial antagonists (reviewed in 33). Except for these two examples, our understanding of active defense mechanisms in the fungal kingdom has seen little progress. We anticipate that as studies of fungal physiology continue to advance through the use of modern molecular methods, we will begin to see concurrent advances in our understanding of how stress responses characterized in higher eukaryotes, including programmed cell death (18, 90) and reactive oxygen species production (48), also function to protect fungi against bacterial invaders.

Fungi and bacteria often share habitats, whether they live together as free-living organisms in natural ecosystems or as intimate partners in a symbiotic relationship. Regardless of the interaction, it is inevitable that coinhabiting partners engage in some form of cross talk. Such is the case with previously mentioned immunocompromised human diseases, where opportunistic pathogens such as *C. albicans* and *P. aeruginosa* commonly coinfect a single individual. Although bacterial effects on the fungus were briefly discussed in a previous section, it is important to understand the fungal responses to bacteria as well. Both microorganisms produce QS molecules that regulate gene expression within self populations. Farnesol, the QS signal produced by *C. albicans*, represses its own filamentous hyphal growth, thereby maintaining itself in the yeast phase (40). The yeast form is also resistant to *P. aeruginosa* killing by virulence factors such as the phenazine antibiotic pyocyanin (24, 39). Farnesol also represses QS in *P. aeruginosa*, which in turn represses production of pyocyanin (24). Taken together, farnesol functions as a dual defense mechanism of *C. albicans*, not only by maintaining itself in the resistant morphological phase but also by proactively reducing antibiotic production by *P. aeruginosa*. Similar interspecies cross talk effects have been observed between *C. albicans* and species of *Acinetobacter* spp. (88) during coinfection of *C. elegans*. Filamentous growth—and by extension, virulence—of *C. albicans* was found to be inhibited by *Acinetobacter baumannii*, similar to interactions observed with *P. aeruginosa* as described above. However, the effect of farnesol on bacteria was also observed with *A. baumannii*, in which the QS molecule produced by *C. albicans* was found to directly inhibit growth of the bacterium (88).

Based on the complexity of interactions that occur between bacteria and *C. albicans*, it is clear that functional genomics-based methodology would facilitate identification of host defense responses in fungi. Such an approach was recently initiated using *L. enzymogenes* and the well-characterized filamentous fungal plant pathogen *Magnaporthe oryzae*. Microarray analysis of whole-genome expression patterns revealed hundreds of *M. oryzae* genes affected during early interaction stages with *L. enzymogenes* wild-type strain C3 compared with an avirulent strain, including genes involved in signal transduction, cell cycle, growth, and cell-cell adhesion (N. Donofrio & S. Mathioni, unpublished information). The ability to simultaneously compare the influence of virulent and avirulent bacterial strains on fungal gene expression on a genome-wide scale allows not only for detection of host responses but also potential host targets for *L. enzymogenes* virulence factors.

PCD: programmed cell death

The Ugly: Does Abnormal Polar Hyphal Growth Represent a Virulence Strategy for Bacterial Pathogens Infecting Fungal Hosts?

The antibiotics xanthobaccin and HSAF, produced by *Lysobacter* sp. SB-K88 and *L. enzymogenes* C3, respectively (76, 120), are key components of antifungal and antistramenopile activities expressed by these bacteria (47, 58). Characterization of HSAF showed that this antibiotic suppresses ceramide synthase activity during hyphal tip growth, leading to fungal developmental abnormalities (57) that result in a gnarled or curled appearance to growing hyphae (47, 58). This finding strongly suggests some antifungal compounds may possess dual functions in BFIs.

The deployment of ceramides appears to be an emerging theme in BFIs because they are known to function as signal molecules in a variety of fungal cellular processes, including programmed cell death (PCD) (91), as well as imparting innate drug resistance (25). Australifungin, an antibiotic that also disrupts ceramide synthesis in fungi (67), was recently shown to suppress PCD induction in the hyphae of *Neurospora crassa* (91). Because production of HSAF by *L. enzymogenes* similarly disrupts ceramide synthesis, this compound may likewise interfere with PCD in fungal cells, especially during host infection. Ceramide synthase activity has also been shown to increase sensitivity to a number of drugs and toxic compounds in *Schizosaccharomyces pombe* (25). Collectively, these observations suggest a plausible model for the role of HSAF production by *L. enzymogenes*, whereby the compound plays a dual role in pathogenesis: first by inducing increased host sensitivity to the antibiotics the bacterium produces, and second, through the suppression of host PCD to allow infection and intracellular colonization. Such a strategy, whereby a colonizing bacterial pathogen prevents defensive PCD in order to complete the infection cycle in living host cells, suggests that highly evolved virulence strategies may be deployed during bacterial pathogenesis of fungi, despite the relative simplicity of the organisms engaged in the interaction.

FUTURE PROSPECTS

It is expected that descriptions of bacterial pathogenesis of fungal hosts will continue to accumulate as a result of growing interest in the field, as well as the greater appreciation by the scientific community of fungi as simple model systems. In particular, the increasing availability of sequenced genomes and modern molecular methods to facilitate high-throughput studies will undoubtedly improve our understanding of host/pathogen interactions in the context of both agricultural and human health sciences. Studies by Ran et al. (96) exemplify the power of extrapolating information from a fungal model system and applying those data to provide information relevant to human health. Using the *P. aeruginosa*/*Saccharomyces cerevisiae* interaction, these researchers identified a yeast target of the bacterial toxin pyocyanin and then demonstrated the toxin had a similar effect on the homologous human gene product. Such studies represent an exciting new direction for bacterial disease control. In addition, the recognition that sophisticated cellular machinery previously associated only with bacterial pathogenesis of human hosts also functions in BFIs has initiated an exciting area of research involving effector molecules and their fungal targets, which in turn could lead to new strategies for controlling fungal pathogens of plants and cultivated mushrooms.

SUMMARY POINTS

1. Bacterial/fungal interactions are excellent model systems that are effectively used to extend our understanding of the fundamental basis of host/pathogen interactions, including bacterial virulence factors and fungal host response mechanisms.

2. Despite essential differences in life strategies, the mechanisms used by bacterial antibiotic producers, endosymbionts, and pathogens to facilitate interactions with fungal hosts are remarkably similar.
3. The net outcome of interactions between bacteria and fungi may be beneficial, neutral, or deleterious for the associated fungus.
4. Bacteria use lytic enzymes and secondary metabolites as virulence factors to attack and colonize fungal hosts. They may also employ many of the same sophisticated pathogenicity mechanisms used by bacterial pathogens to infect higher eukaryotes, including type III and type IV secretion systems.
5. Fungal host responses to bacterial infection may include complex cross talk and basal defense mechanisms such as programmed cell death.
6. A more comprehensive understanding of bacterial/fungal interactions has immediate, practical implications for the applied sciences in (*a*) the field of human health, through a greater appreciation of the interactions between coinfecting pathogens that may lead to the identification of new drugs or treatment protocols; and (*b*) the field of plant pathology, through the development of effective control strategies for mushroom diseases or through improvements in the biological control of plant diseases, which serves to minimize the use of chemicals in the environment.

DISCLOSURE STATEMENT

The authors are not aware of any affiliations, memberships, funding, or financial holdings that might be perceived as affecting the objectivity of this review.

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LITERATURE CITED

1. Ahn S-J, Yang C-H, Cooksey DA. 2007. *Pseudomonas putida* 06909 genes expressed during colonization on mycelial surfaces and phenotypic characterization of mutants. *J. Appl. Microbiol.* 103:120–32
2. Artursson V, Finlay RD, Jansson JK. 2006. Interactions between arbuscular mycorrhizal fungi and bacteria and their potential for stimulating plant growth. *Environ. Microbiol.* 8:1–10
3. Barbieri E, Potenza L, Rossi I, Sisti D, Giomaro G, et al. 2000. Phylogenetic characterization and in situ detection of a *Cytophaga-Flexibacter-Bacteroides* phylogroup bacterium in *Tuber borchii* Vittad. ectomycorrhizal mycelium. *Appl. Environ. Microbiol.* 66:5035–42
4. Barbieri E, Riccioni G, Pisano A, Sisti D, Zeppa S, et al. 2002. Competitive PCR for quantitation of a *Cytophaga-Flexibacter-Bacteroides* phylum bacterium associated with the *Tuber borchii* Vittad. mycelium. *Appl. Environ. Microbiol.* 68:6421–24
5. Bassarello C, Lazzaroni S, Bifulco G, Lo Cantore P, Iacobellis NS, et al. 2004. Tolaasins A-E, five new lipodepsipeptides produced by *Pseudomonas tolaasii*. *J. Nat. Prod.* 67:811–16

6. Bertaux J, Schmid M, Hutzler P, Hartmann A, Garbaye J, Frey-Klett P. 2005. Occurrence and distribution of endobacteria in the plant-associated mycelium of the ectomycorrhizal fungus *Laccaria bicolor* S238N. *Environ. Microbiol.* 7:1786–95
7. Bertaux J, Schmid M, Prevost-Boure NC, Churin JL, Hartmann A, et al. 2003. In situ identification of intracellular bacteria related to *Paenibacillus* spp. in the mycelium of the ectomycorrhizal fungus *Laccaria bicolor* S238N. *Appl. Environ. Microbiol.* 69:4243–48
8. Bessette AE, Kerrigan RW, Jordan DC. 1985. Yellow blotch of *Pleurotus ostreatus*. *Appl. Environ. Microbiol.* 50:1535–37
9. Bianciotto V, Bandi C, Minerdi D, Sironi M, Tichy HV, Bonfante P. 1996. An obligately endosymbiotic mycorrhizal fungus itself harbors obligately intracellular bacteria. *Appl. Environ. Microbiol.* 62:3005–10
10. Bianciotto V, Bonfante P. 2002. Arbuscular mycorrhizal fungi: a specialised niche for rhizospheric and endocellular bacteria. *Anton. Leeuw.* 81:365–71
11. Bianciotto V, Genre A, Jargeat P, Lumini E, Becard G, Bonfante P. 2004. Vertical transmission of endobacteria in the arbuscular mycorrhizal fungus *Gigaspora margarita* through generation of vegetative spores. *Appl. Environ. Microbiol.* 70:3600–8
12. Bianciotto V, Lumini E, Bonfante P, Vandamme P. 2003. '*Candidatus* Glomeribacter gigasporarum' gen. nov., sp. nov., an endosymbiont of arbuscular mycorrhizal fungi. *Int. J. Syst. Evol. Microbiol.* 53:121–24
13. Bianciotto V, Lumini E, Lanfranco L, Minerdi D, Bonfante P, Perotto S. 2000. Detection and identification of bacterial endosymbionts in arbuscular mycorrhizal fungi belonging to the family Gigasporaceae. *Appl. Environ. Microbiol.* 66:4503–9
14. Bonfante P. 2003. Plants, mycorrhizal fungi and endobacteria: a dialog among cells and genomes. *Biol. Bull.* 204:215–20
15. Brodey C, Rainey PB, Tester M, Johnstone K. 1991. Bacterial blotch disease of the cultivate mushroom is caused by an ion channel forming lipodepsipeptide toxin. *Mol. Plant-Microbe Inter.* 4:407–11
16. Butler MJ, Gardiner RB, Day AW. 2005. Degradation of melanin or inhibition of its synthesis: Are these a significant approach as a biological control of phytopathogenic fungi? *Biol. Control* 32:326–36
17. Chamilos G, Lewis RE, Kontoyiannis DP. 2007. Multidrug-resistant endosymbiotic bacteria account for the emergence of zygomycosis: A hypothesis. *Fungal Genet. Biol.* 44:88–92
18. Chen C, Dickman MB. 2005. Proline suppresses apoptosis in the fungal pathogen *Colletotrichum trifolii*. *Proc. Natl. Acad. Sci. USA* 102:3459–64
19. Chowdhury PR, Heinemann JA. 2006. The general secretory pathway of *Burkholderia gladioli* pv. agaricicola BG164R is necessary for cavity disease in white button mushrooms. *Appl. Environ. Microbiol.* 72:3558–65
20. Christensen P, Cook FD. 1978. *Lysobacter*, a new genus of nonfruiting, gliding bacteria with a high base ratio. *Int. J. Syst. Bacteriol.* 28:367–93
21. Christie PJ, Atmakuri K, Krishnamoorthy V, Jakubowski S, Cascales E. 2005. Biogenesis, architecture, and function of bacterial Type IV secretion systems. *Annu. Rev. Microbiol.* 59:451–85
22. Compant S, Duffy B, Nowak J, Clement C, Barka EA. 2005. Use of plant growth-promoting bacteria for biocontrol of plant diseases: principles, mechanisms of action, and future prospects. *Appl. Environ. Microbiol.* 71:4951–59
23. Craig L, Pique ME, Tainer JA. 2004. Type IV pilus structure and bacterial pathogenicity. *Nat. Rev. Microbiol.* 2:363–78
24. Cugini C, Calfee MW, Farrow JM, Morales DK, Pesci EC, Hogan DA. 2007. Farnesol, a common sesquiterpene, inhibits PQS production in *Pseudomonas aeruginosa*. *Mol. Microbiol.* 65:896–906
25. Dawson K, Toone WM, Jones N, Wilkinson CRM. 2008. Loss of regulators of vacuolar ATPase function and ceramide synthesis results in multidrug sensitivity in *Schizosaccharomyces pombe*. *Eukaryot. Cell* 7:926–37
26. de Boer W, Folman LB, Summerbell RC, Boddy L. 2005. Living in a fungal world: impact of fungi on soil bacterial niche development. *FEMS Microbiol. Rev.* 29:795–811
27. de Boer W, Klein Gunnewiek PJA, Kowalchuk GA, Van Veen JA. 2001. Growth of chitinolytic dune soil β-subclass proteobacteria in response to invading fungal hyphae. *Appl. Environ. Microbiol.* 67:3358–62
28. de Boer W, Klein Gunnewiek PJA, Lafeber P, Janse JD, Spit BE, Woldendorp JW. 1998. Anti-fungal properties of chitinolytic dune soil bacteria. *Soil Biol. Biochem.* 30:193–203

29. de Bruijn I, de Kock MJD, Yang M, de Waard P, van Beek TA, Raaijmakers JM. 2007. Genome-based discovery, structure prediction and functional analysis of cyclic lipopeptide antibiotics in *Pseudomonas* species. *Mol. Microbiol.* 63:417–28
30. de Groot MJA, Bundock P, Hooykaas PJJ, Beijersbergen AGM. 1998. *Agrobacterium tumefaciens*-mediated transformation of filamentous fungi. *Nat. Biotech.* 16:839–42
31. de Souza JT, de Boer M, de Waard P, van Beek TA, Raaijmakers JM. 2003. Biochemical, genetic, and zoosporicidal properties of cyclic lipopeptide surfactants produced by *Pseudomonas fluorescens*. *Appl. Environ. Microbiol.* 69:7161–72
32. Dörr J, Hurek T, Reinhold-Durek B. 1998. Type IV pili are involved in plant-microbe and fungus-microbe interactions. *Mol. Microbiol.* 30:7
33. Duffy B, Schouten A, Raaijmakers JM. 2003. Pathogen self-defense: mechanisms to counteract microbial antagonism. *Annu. Rev. Phytopathol.* 41:501–38
34. Frey-Klett P, Garbaye J, Tarkka M. 2007. The mycorrhiza helper bacteria revisited. *New Phytol.* 176:22–36
35. Gill W, Cole T. 2000. Aspects of the pathology and etiology of 'drippy gill' disease of the cultivated mushroom *Agaricus bisporus*. *Can. J. Microbiol.* 46:246–58
36. Godfrey SAC, Harrow SA, Marshall JW, Klena JD. 2001. Characterization by 16S rRNA sequence analysis of pseudomonads causing blotch disease of cultivated *Agaricus bisporus*. *Appl. Environ. Microbiol.* 67:4316–23
37. Haas D, Défago G. 2005. Biological control of soil-borne pathogens by fluorescent pseudomonads. *Nat. Rev. Microbiol.* 3:307–19
38. Hildebrandt U, Ouziad F, Marner FJ, Bothe H. 2006. The bacterium *Paenibacillus validus* stimulates growth of the arbuscular mycorrhizal fungus *Glomus intraradices* up to the formation of fertile spores. *FEMS Microbiol. Lett.* 254:258–67
39. Hogan DA, Kolter R. 2002. *Pseudomonas-Candida* interactions: an ecological role for virulence factors. *Science* 296:2229–32
40. Hogan DA, Vik A, Kolter R. 2004. A *Pseudomonas aeruginosa* quorum-sensing molecule influences *Candida albicans* morphology. *Mol. Microbiol.* 54:1212–23
41. Howell CR, Stipanovic RD. 1980. Suppression of *Pythium ultimum*-induced damping-off of cotton seedlings by *Pseudomonas fluorescens* and its antibiotic, pyoluteorin. *Phytopathology* 70:712–15
42. Ibrahim AS, Gebremariam T, Liu M, Chamilos G, Kontoyiannis DP, et al. 2008. Bacterial endosymbiosis is widely present among Zygomycetes but does not contribute to the pathogenesis of mucormycosis. *J. Infect. Dis.* 198:1083–90
43. Inglis PW, Burden JL, Peberdy JF. 1996. Evidence for the association of the enteric bacterium *Ewingella americana* with internal stipe necrosis of *Agaricus bisporus*. *Microbiology* 142:3253–60
44. Inglis PW, Peberdy JF. 1996. Isolation of *Ewingella americana* from the cultivated mushroom, *Agaricus bisporus*. *Cur. Microbiol.* 33:334–37
45. Inglis PW, Peberdy JF. 1997. Production and purification of a chitinase from *Ewingella americana*, a recently described pathogen of the mushroom, *Agaricus bisporus*. *FEMS Microbiol. Lett.* 157:189–94
46. Inglis PW, Peberdy JF, Sockett RE. 2000. Cloning of a chitinase gene from *Ewingella americana*, a pathogen of the cultivated mushroom, *Agaricus bisporus*. *Gen. Mol. Biol.* 23:685–88
47. Islam MT, Hashidoko Y, Deora A, Ito T, Tahara S. 2005. Suppression of damping-off disease in host plants by the rhizoplane bacterium *Lysobacter* sp. strain SB-K88 is linked to plant colonization and antibiosis against soilborne Peronosporomycetes. *Appl. Environ. Microbiol.* 71:3786–96
48. Jamieson DJ. 1998. Oxidative stress responses of the yeast *Saccharomyces cerevisiae*. *Yeast* 14:1511–27
49. Jargeat P, Cosseau C, Ola'h B, Jauneau A, Bonfante P, et al. 2004. Isolation, free-living capacities, and genome structure of "*Candidatus* Glomeribacter gigasporarum," the endocellular bacterium of the mycorrhizal fungus *Gigaspora margarita*. *J. Bacteriol.* 186:6876–84
50. Kim MK, Ryu JS, Lee YH. 2007. First report of *Pantoea* sp. induced soft rot disease of *Pleurotus eryngii* in Korea. *Plant Dis.* 91:109
51. Kobayashi DY, El-Barrad NE-H. 1996. Selection of bacterial antagonists using enrichment cultures for the control of summer patch disease in Kentucky bluegrass. *Curr. Microbiol.* 32:106–10

52. Kobayashi DY, Hillman BI. 2005. Fungi, bacteria, and viruses as pathogens of the fungal community. In *The Fungal Community*, ed. J Dighton, J White, P Oudemans, pp. 399–421. Boca Raton, FL: CRC Press
53. Kobayashi DY, Reedy RM, Palumbo JD, Zhou J-M, Yuen GY. 2005. A *clp* gene homologue belonging to the Crp gene family globally regulates lytic enzyme production, antimicrobial activity, and biological control activity expressed by *Lysobacter enzymogenes* strain C3. *Appl. Environ. Microbiol.* 71:261–69
54. Kobayashi DY, Yuen GY. 2005. The role of *clp*-regulated factors in antagonism against *Magnaporthe poae* and biological control of summer patch disease of Kentucky bluegrass by *Lysobacter enzymogenes* C3. *Can. J. Microbiol.* 51:719–23
55. Kobayashi DY, Yuen GY. 2007. The potential of *Lysobacter* spp. as bacterial biological control agents for plant diseases. *CAB Reviews: Persp. Agr. Vet. Sci. Nutr. Nat. Res.* 2:1–11
56. Lee SW, Glickmann E, Cooksey DA. 2001. Chromosomal locus for cadmium resistance in *Pseudomonas putida* consisting of a cadmium-transporting ATPase and a MerR family response regulator. *Appl. Environ. Microbiol.* 67:1437–44
57. Li S, Du L, Yuen G, Harris SD. 2006. Distinct ceramide synthases regulate polarized growth in the filamentous fungus *Aspergillus nidulans*. *Mol. Biol. Cell* 17:1218–27
58. Li S, Jochum CC, Yu F, Zaleta-Rivera K, Du L, et al. 2008. An antibiotic complex from *Lysobacter enzymogenes* strain C3: antimicrobial activity and role in plant disease control. *Phytopathology* 98:695–701
59. Lincoln S, Fermor T, Tindall B. 1999. *Janthinobacterium agaricidamnosum* sp. nov., a soft rot pathogen of *Agaricus bisporus*. *Int. J. Syst. Bacteriol.* 49:1577–89
60. Lincoln SP, Fermor TR, Stead DE, Sellwood JE. 1991. Bacterial soft rot of *Agaricus bitorquis*. *Plant Pathol.* 40:136–44
61. Lo Cantore P, Iacobellis NS. 2004. First report of brown discoloration of *Agaricus bisporus* caused by *Pseudomonas agarici* in southern Italy. *Phytopathol. Mediterr.* 43:35–38
62. Lo Cantore P, Lazzaroni S, Coraiola M, Dalla Serra M, Cafarchia C, et al. 2006. Biological characterization of white line-inducing principle (WLIP) produced by *Pseudomonas reactans* NCPPB1311. *Mol. Plant-Microbe Inter.* 19:1113–20
63. Lockwood JL. 1959. *Streptomyces* spp. as a cause of natural fungitoxicity in soils. *Phytopathology* 49:327–31
64. Lockwood JL. 1960. Lysis of mycelium of plant-pathogenic fungi by natural soil. *Phytopathology* 50:787–89
65. Loper JE, Henkels MD, Shaffer BT, Valeriote FA, Gross H. 2008. Isolation and identification of rhizoxin analogs from *Pseudomonas fluorescens* Pf-5 by using a genomic mining strategy. *Appl. Environ. Microbiol.* 74:3085–93
66. Loper JE, Kobayashi DY, Paulsen IT. 2007. The genomic sequence of *Pseudomonas fluorescens* Pf-5: insights into biological control. *Phytopathology* 97:233–38
67. Mandala SM, Thornton RA, Frommer BR, Curotto JE, Rozdilsky W, et al. 1995. The discovery of australifungin, a novel inhibitor of sphinganine *N*-acyltransferase from *Sporormiella australis*. Producing organism, fermentation, isolation, and biological activity. *J. Antibiot.* 48:349–56
68. McAlester G, O'Gara F, Morrissey JP. 2008. Signal-mediated interactions between *Pseudomonas aeruginosa* and *Candida albicans*. *J. Med. Microbiol.* 57:563–69
69. Minerdi D, Bianciotto V, Bonfante P. 2002. Endosymbiotic bacteria in mycorrhizal fungi: from their morphology to genomic sequences. *Plant Soil* 244:211–19
70. Mitchell R, Hurwitz E. 1965. Suppression of *Pythium debaryanum* by lytic rhizosphere bacteria. *Phytopathology* 55:156–58
71. Moffitt MC, Neilan BA. 2000. The expansion of mechanistic and organismic diversity associated with nonribosomal peptides. *FEMS Microbiol. Lett.* 191:159–67
72. Moran NA, Baumann P. 2000. Bacterial endosymbionts in animals. *Curr. Opin. Microbiol.* 3:270–75
73. Moran NA, Wernegreen JJ. 2000. Lifestyle evolution in symbiotic bacteria: insights from genomics. *Trends Ecol. Evol.* 15:321–26
74. Munsch P, Alatossava T, Marttinen N, Meyer JM, Christen R, Gardan L. 2002. *Pseudomonas costantinii* sp. nov., another causal agent of brown blotch disease, isolated from cultivated mushroom sporophores in Finland. *Int. J. Syst. Evol. Microbiol.* 52:1973–83

75. Munsch P, Geoffroy VA, Alatossava T, Meyer JM. 2000. Application of siderotyping for characterization of *Pseudomonas tolaasii* and "*Pseudomonas reactans*" isolates associated with brown blotch disease of cultivated mushrooms. *Appl. Environ. Microbiol.* 66:4834–41
76. Nakayama T, Homma Y, Hashidoko Y, Mizutani J, Tahara S. 1999. Possible role of xanthobaccins produced by *Stenotrophomonas* sp. strain SB-K88 in suppression of sugar beet damping-off disease. *Appl. Environ. Microbiol.* 65:4334–39
77. Nielsen MN, Sorensen J, Fels J, Pedersen HC. 1998. Secondary metabolite- and endochitinase-dependent antagonism toward plant-pathogenic microfungi of *Pseudomonas fluorescens* isolates from sugar beet rhizosphere. *Appl. Environ. Microbiol.* 64:3563–69
78. Nielsen TH, Sørensen D, Tobiasen C, Andersen JB, Christophersen C, et al. 2002. Antibiotic and biosurfactant properties of cyclic lipopeptides produced by fluorescent *Pseudomonas* spp. from the sugar beet rhizosphere. *Appl. Environ. Microbiol.* 68:3416–23
79. Nudleman E, Kaiser D. 2004. Pulling together with type IV pili. *J. Mol. Microbiol. Biotech.* 7:52–62
80. Paine SG. 1919. Studies in bacteriosis II: a brown blotch disease of cultivated mushrooms. *Ann. Appl. Biol.* 5:206–19
81. Palumbo JD, Sullivan RF, Kobayashi DY. 2003. Molecular characterization and expression in *Escherichia coli* of three β-1,3-glucanase genes from *Lysobacter enzymogenes* strain N4–7. *J. Bacteriol.* 185:4362–70
82. Palumbo JD, Yuen GY, Jochum CC, Tatum K, Kobayashi DY. 2005. Mutagenesis of β-1,3-glucanase genes in *Lysobacter enzymogenes* strain C3 results in reduced biological control activity towards Bipolaris leaf spot of tall fescue and Pythium damping off of sugarbeet. *Phytopathology* 95:701–7
83. Partida-Martinez LP, Flores de Looss C, Ishida K, Ishida M, Roth M, et al. 2007. Rhizonin, the first mycotoxin isolated from the Zygomycota, is not a fungal metabolite but is produced by bacterial endosymbionts. *Appl. Environ. Microbiol.* 73:793–97
84. Partida-Martinez LP, Groth I, Schmitt I, Richter W, Roth M, Hertweck C. 2007. *Burkholderia rhizoxinica* sp. nov. and *Burkholderia endofungorum* sp. nov., bacterial endosymbionts of the plant-pathogenic fungus *Rhizopus microsporus*. *Int. J. Syst. Evol. Microbiol.* 57:2583–90
85. Partida-Martinez LP, Hertweck C. 2005. Pathogenic fungus harbours endosymbiotic bacteria for toxin production. *Nature* 437:884–88
86. Partida-Martinez LP, Monajembashi S, Greulich KO, Hertweck C. 2007. Endosymbiont-dependent host reproduction maintains bacterial-fungal mutualism. *Curr. Biol.* 17:773–77
87. Paulsen IT, Press CM, Ravel J, Kobayashi DY, Myers GSA, et al. 2005. Complete genome sequence of the plant commensal *Pseudomonas fluorescens* Pf-5. *Nat. Biotech.* 23:873–78
88. Peleg AY, Tampakakis E, Fuchs BB, Eliopoulos GM, Moellering RC, Mylonakis E. 2008. Prokaryote-eukaryote interactions identified by using *Caenorhabditis elegans*. *Proc. Natl. Acad. Sci. USA* 105:14585–90
89. Perotto S, Bonfante P. 1997. Bacterial associations with mycorrhizal fungi: close and distant friends in the rhizosphere. *Trends Microbiol.* 5:496–501
90. Phillips AJ, Crowe JD, Ramsdale M. 2006. Ras pathway signaling accelerates programmed cell death in the pathogenic fungus *Candida albicans*. *Proc. Natl. Acad. Sci. USA* 103:726–31
91. Plesofsky NS, Levery SB, Castle SA, Brambl R. 2008. Stress-induced cell death is mediated by ceramide synthesis in *Neurospora crassa*. *Eukaryot. Cell* 7:2147–59
92. Preston GM, Bertrand N, Rainey PB. 2001. Type III secretion in plant growth-promoting *Pseudomonas fluorescens* SBW25. *Mol. Microbiol.* 41:999–1014
93. Rainey PB. 1991. Effect of *Pseudomonas putida* on hyphal growth of *Agaricus bisporus*. *Mycol. Res.* 95:699–704
94. Rainey PB, Brodey CL, Johnstone K. 1991. Biological properties and spectrum of activity of tolaasin, a lipodepsipeptide toxin produced by the mushroom pathogen *Pseudomonas tolaasii*. *Physiol. Mol. Plant Pathol.* 39:57–70
95. Rainey PB, Cole ALJ, Fermor TR, Wood DA. 1990. A model system for examining involvement of bacteria in basidiome initiation of *Agaricus bisporus*. *Mycol. Res.* 94:191–95
96. Ran H, Hassett DJ, Lau GW. 2003. Human targets of *Pseudomonas aeruginosa* pyocyanin. *Proc. Natl. Acad. Sci. USA* 100:14315–20
97. Reedy RM, Kobayashi DY. 2001. Evidence for a type III secretory pathway in the biocontrol bacterium *Stenotrophomonas maltophilia* strain C3. *Phytopathology* 91:S75

98. Rezzonico F, Binder C, Defago G, Moenne-Loccoz Y. 2005. The type III secretion system of biocontrol *Pseudomonas fluorescens* KD targets the phytopathogenic Chromista *Pytium ultimum* and promotes cucumber protection. *Mol. Plant-Microbe Inter.* 18:991–1001
99. Rezzonico F, Defago G, Moenne-Loccoz Y. 2004. Comparison of ATPase-encoding type III secretion system *hrcN* genes in biocontrol fluorescent pseudomonads and in phytopathogenic proteobacteria. *Appl. Environ. Microbiol.* 70:5119–31
100. Richardson PN. 1993. Stipe necrosis of cultivated mushrooms (*Agaricus bisporus*) associated with a fluorescent pseudomonad. *Plant Pathol.* 42:927–29
101. Roesti D, Ineichen K, Braissant O, Redecker D, Wiemken A, Aragno M. 2005. Bacteria associated with spores of the arbuscular mycorrhizal fungi *Glomus geosporum* and *Glomus constrictum*. *Appl. Environ. Microbiol.* 71:6673–79
102. Ron EZ, Rosenberg E. 2001. Natural roles of biosurfactants. *Environ. Microbiol.* 3:229–36
103. Scher FM, Baker R. 1980. Mechanism of biological control in a Fusarium-suppressive soil. *Phytopathology* 70:412–17
104. Schisler LC, Sinden JW, Sigel EM. 1968. Etiology of mummy disease of cultivated mushrooms. *Phytopathology* 58:944–48
105. Soler-Rivas C, Arpin N, Olivier JM, Wichers HJ. 1999. WLIP, a lipodepsipeptide of *Pseudomonas* '*reactans*', as inhibitor of the symptoms of the brown blotch disease of *Agaricus bisporus*. *J. Appl. Microbiol.* 86:635–41
106. Soler-Rivas C, Arpin N, Olivier JM, Wichers HJ. 2000. Discoloration and tyrosinase activity in Agaricus bisporus fruit bodies infected with various pathogens. *Mycol. Res.* 104:351–56
107. Sullivan RF, Holtman MA, Zylstra GJ, White JF, Kobayashi DY. 2003. Taxonomic positioning of two biological control agents for plant diseases as *Lysobacter enzymogenes* based on phylogenetic analysis of 16S rDNA, fatty acid composition and phenotypic characteristics. *J. Appl. Microbiol.* 94:1079–86
108. Tolaas AG. 1915. A bacterial disease of cultivated mushrooms. *Phytopathology* 5:51–54
109. van Zaayen A, Waterreus HAJI. 1974. Intracellular occurrence of bacteria in mummy-diseased mushrooms. *Phytopathology* 64:1474–75
110. Wargo MJ, Hogan DA. 2006. Fungal-bacterial interactions: a mixed bag of mingling microbes. *Curr. Opin. Microbiol.* 9:359–64
111. Weller DM, Raaijmakers JM, McSpadden Gardener BB, Thomashow LS. 2002. Microbial populations responsible for specific soil suppressiveness to plant pathogens. *Annu. Rev. Phytopathol.* 40:309–48
112. Wells JM, Sapers GM, Fett WF, Butterfield JE, Jones JB, et al. 1996. Postharvest discoloration of the cultivated mushroom *Agaricus bisporus* caused by *Pseudomonas tolaasii*, *P.* 'reactans', and *P.* 'gingeri'. *Phytopathology* 86:1098–104
113. Whipps JM. 2001. Microbial interactions and biocontrol in the rhizosphere. *J. Exp. Bot.* 52:487–511
114. Willoughby LG. 1983. The bacterial antagonist of *Karlingia rosea*; further observations, from Spain and Cyprus. *Nova Hedwig.* 38:113–27
115. Willoughby LG. 1983. The bacterial antagonist of *Karlingia rosea*; observations from mainland Spain. *Trans. Brit. Mycol. Soc.* 81:435–38
116. Willoughby LG. 1983. A new kind of antagonistic association, between bacteria and aquatic fungi. *Trans. Brit. Mycol. Soc.* 80:91–97
117. Wong WC, Fletcher JF, Unsworth BA, Preece TF. 1982. A note on ginger blotch, a new bacterial disease of the cultivated mushroom *Agaricus bisporus*. *J. Appl. Bacteriol.* 52:43–48
118. Xavier LJC, Germida JJ. 2003. Bacteria associated with *Glomus clarum* spores influence mycorrhizal activity. *Soil Biol. Biochem.* 35:471–78
119. Yang C, Menge J, Cooksey D. 1994. Mutations affecting hyphal colonization and pyoverdine production in pseudomonads antagonistic toward *Phytophthora parasitica*. *Appl. Environ. Microbiol.* 60:473–81
120. Yu F, Zaleta-Rivera K, Zhu X, Huffman J, Millet J, et al. 2007. Structure and biosynthesis of HSAF, a broad spectrum antimycotic with a novel mode of action. *Antimicrob. Agents Chemother.* 51:64–72

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Errata

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