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Review
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Review

Pathogenic mechanisms and control strategies of *Botrytis cinerea* causing post-harvest decay in fruits and vegetables

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Abstract

Botrytis cinerea is a significant necrotrophic plant pathogen causing devastating diseases on more than 500 plant species, especially on fresh fruits and vegetables, resulting in the economic losses ranging from $10 billion to $100 billion worldwide. This fungal pathogen invades nearly all parts of plants including stems, leaves, flowers, fruits, and seeds at both pre-harvest and post-harvest stages. Due to its wide host range and the huge economic losses that it causes, extensive investigations have been carried out to effectively control this plant pathogen. It is beneficial for exploring the pathogenic mechanisms of *B. cinerea* to provide fundamental basis for control strategies. In recent years, tremendous progress has been made in understanding these pathogenic genes and regulatory pathways, as well as the control strategies of *B. cinerea*. Here, the current knowledge will be summarized in this review.

Key words: gray mould rot; horticultural crops; pathogenesis; control technology.

Introduction

Botrytis cinerea is one of the most extensively studied necrotrophic fungal pathogens and causes gray mold rot in more than 500 plant species (Williamson *et al.*, 2007). This pathogen has a disastrous economic impact on various economically important crops including grape, strawberry, and tomato (Dean *et al.*, 2012) and is able to be present inside stems, leaves, flowers, fruits, and seeds. It may trigger obvious disease symptoms in the pre-harvest period or remain quiescent until post-harvest period (Fillinger and Elad, 2016). *Botrytis cinerea* has been reckoned as one of the most important post-harvest pathogens in fresh fruits and vegetables (Zhang *et al.*, 2014a). The annual economic losses of *B. cinerea* easily exceed $10 billion worldwide (Weiberg *et al.*, 2013). Due to its scientific and economic importance, *B. cinerea* has been classified as the second important plant pathogen (Dean *et al.*, 2012). It is difficult to control *B. cinerea* because it has broad host range, various attack modes, and both asexual and sexual stages to survive in favourable or unfavourable conditions (Fillinger and Elad, 2016). The asexual spores of *B. cinerea* are conidia, which are easily to be dispersed by wind or water, and the sexual spores of *B. cinerea* are sclerotia, which are essential for survival under adverse environment (Brandhoff *et al.*, 2017). To date, the principal means to control grey mold rot caused by *B. cinerea* remain as the application of synthetic fungicides, which may be about 8 percent of all the global fungicide market, and the annual global expenses at *Botrytis* control usually exceed €1 billion (Dean *et al.*, 2012). However, the control effects of fungicides are not satisfactory on *B. cinerea* whose genome is plasticity and prone to develop drug resistance genes. In addition, fungicides are not safe for human and environment (Droby *et al.*, 2009). Therefore, it is important to deeply understand the molecular basis of pathogenesis

of *B. cinerea* and develop new strategies to prevent grey mold rot caused by *B. cinerea* in fresh fruits. In recent years, great efforts have been put on exploring the molecular mechanisms of *B. cinerea*, since its genome information (strain B05.10) is available (Amselem *et al.*, 2011), and the functions of various genes especially those pathogenesis-related proteins are unravelled.

In this review, we mainly introduce the latest information about molecular pathogenesis of *B. cinerea*, which is beneficial for understanding the theoretical knowledge about molecular pathogenic mechanisms of the fungal pathogen, as well as current control strategies against gray mould rot in fresh fruits.

Pathogenic Mechanisms of *B. cinerea*

Roles of reactive oxygen species in pathogenesis

Reactive oxygen species (ROS) are a collective of highly reactive molecules including superoxide anion (.O^{2-}), hydroxyl radical (.OH), and certain non-radical oxidizing agents such as hydrogen peroxide (H_2O_2) and ozone (O_3) that can be converted into radicals. ROS have an ambivalent role since they damage DNA, causing lipid peroxidation and protein oxidation (Heller and Tudzynski, 2011; Qin *et al.*, 2011), but also function as diffusible second messengers (Orozco-Cárdenas *et al.*, 2001; Heller and Tudzynski, 2011). In the early stage of infection, plant hosts usually trigger oxidative burst which generate large amounts of ROS transiently to counteract the invasive pathogen (Mellersh *et al.*, 2002; Tian *et al.*, 2013). However, as a necrotrophic fungus, *B. cinerea* can exploit the oxidative burst and even contribute to it by producing its own ROS.

ROS can be generated in *B. cinerea* either as unavoidable byproducts of metabolic processes or as the major products of NADPH oxidase (NOX) (Li *et al.*, 2016). NOX is a multi-subunit complex which reduces oxygen to superoxide with the electron supplied by NADPH (Bedard *et al.*, 2007). The function of the subunits of NOX in *B. cinerea* has been extensively investigated (Siegmund *et al.*, 2013). Both the catalytic subunits BcNoxA and BcNoxB are responsible for pathogenicity and the formation of sclerotia, which allow the fungi to survive under adverse environmental conditions and are fundamental for sexual reproduction (Siegmund *et al.*, 2015). Interestingly, BcNoxA and BcNoxB were shown to play different roles in the pathogenicity of *B. cinerea* (Marschall *et al.*, 2016). BcNoxA is essential for colonizing the host tissue, whereas BcNoxB contributes to the primary infection (Segmuller *et al.*, 2008). The regulatory subunit BcNoxR has a phenotype consistent with that of *ΔbcnoxA/B* double mutant. Elimination of BcNoxR showed reduced growth rate, sporulation, and impaired virulence on French bean/tomato leaves and various fruits (Li *et al.*, 2016). Based on the comparative proteomic approach to unravel the potential downstream targets of BcNoxR, we identified a total of 49 unique proteins whose abundance changed in the deletion mutant of *bcnoxR* (*ΔbcnoxR*) and found that BcNoxR could affect the expression of proteins with various functions, such as stress response, carbohydrate metabolism, translation, and intracellular signalling. Further analysis showed that 6-phosphogluconate dehydrogenase (BcPGD), whose abundance decreased in the deletion mutant of *bcnoxR*, was responsible for growth, sporulation, and virulence of *B. cinerea* (Li *et al.*, 2016). Moreover, we observed that small GTPase BcRho3 was contributed to the regulation of mycelial growth, conidiation production, and virulence of *B. cinerea*, and deletion mutant of *bcrho3* (*Δbcrho3*) showed reduced virulence to apple, tomato fruits, and tomato leaves, and proved that the reduction in virulence of *Δbcrho3* mutant might be due to the impaired penetration ability (An *et al.*, 2015).

As signalling molecules, it is necessary for ROS to move from the place of origin to the site of action. The transformation molecules of ROS are obscure since ROS are composed of various highly reactive molecules including radicals (.O2$^-$ and .OH) and molecules (H_2O_2 and O_3), which are difficult to investigate. Among the ROS molecules, H_2O_2 is stable and suitable for investigation (Waghray *et al.*, 2005). H_2O_2 can function as both intracellular and intercellular signal molecules (Pletjushkina *et al.*, 2006; Rice, 2011). However, H_2O_2 is unable to cross the membrane lipid bilayer freely by simple diffusion, it needs to the aid of membrane lipid compositions or channel proteins to cross over plasma membranes (Seaver and Imlay, 2001). Aquaporins, which are known as efficient water channels, have been demonstrated to mediate the transportation of H_2O_2 across membranes (Bienert *et al.*, 2007; Miller *et al.*, 2010). Our studies indicated that aquaporin8 (BcAQP8) in *B. cinerea* could play a crucial role in the transmembrane transportation of ROS, and the distribution of mitochondria, which is the main source of ROS (An *et al.*, 2016). Besides to regulate ROS transportation, BcAQP8 also affects the expression of BcNoxR, the regulatory subunit of NOX. Deletion of *bcaqp8* results in decrease in growth, sporulation, and pathogenicity of *B. cinerea* (An *et al.*, 2016) (Figure 1).

Roles of extracellular proteins in pathogenesis

Plant cell wall is among the first lines of defence that an invasive pathogen encounters. They are heterogeneous structures mainly composed of polysaccharides and proteins (Kubicek *et al.*, 2014). As a necrotrophic fungus, the appressorium of *B. cinerea* was not strong enough to breach the plant cell wall (Choquer *et al.*, 2007). Therefore, it is necessary for *B. cinerea* to secrete a series of cell wall–degrading enzymes (CWDEs) to degrade the structural polysaccharides of the host cell wall. In *B. cinerea*, 1155 genes are predicted to encode enzymes to degrade, modify, or create glycosidic bonds. Among them, 275 have signal peptide sequence indicating their function in extracellular matrix (Fillinger and Elad, 2016). A variety of proteins encoded by the predicted genes were detected through comparative proteomics (Shah *et al.*, 2009; Espino *et al.*, 2010; Li *et al.*, 2012). However, only few of them have been confirmed to have

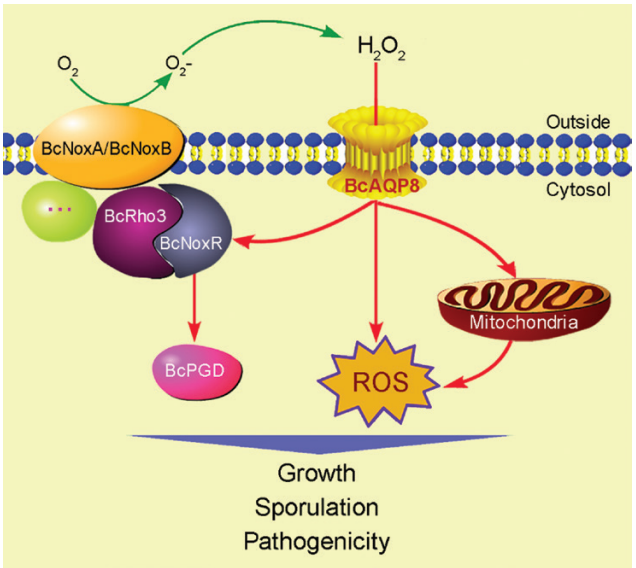

Figure 1 Model for reactive oxygen species (ROS) generation and transportation in *B. cinerea*.

function in the pathogenicity of *B. cinerea*. Two endopolygalacturonase (BcPG1 and BcPG2) are involved in the virulence of *B. cinerea*. The *Bcpg1* gene is not required for primary infection but necessary for further colonization on apple fruits, tomato fruits, and leaves (ten Have *et al.*, 1998), whereas *Bcpg2* affects both primary infection and lesion expansion on tomato and broad bean (Kars *et al.*, 2005a). The endo-β-1,4-xylanases (BcXYN11A), which degrade plant cell wall content xylan, were proven to have a pronounced effect on virulence (Brito *et al.*, 2006). Lots of the CWDEs are demonstrated to be not essential for the virulence of *B. cinerea*. Pectin methyl esterase induces the demethylesterification of cell wall components polygalacturonans (Kars *et al.*, 2005b). Cutinase has the potential to hydrolyse cutin, thus facilitating pathogen penetration through the cuticle (van Kan *et al.*, 1997). However, deletion mutants of genes of pectin methylesterase (BcPME1 and BcPME2) or cutinase (BcCUTA) exhibit no effects on the virulence of *B. cinerea* (van Kan *et al.*, 1997). Considering the high redundancy of CWDEs, these enzymes might have an overlapped function with others and contributed to the overall pathogenicity of this fungus (Kars *et al.*, 2005b).

The important roles of extracellular proteins necessitated a precise regulation mechanism. Extracellular proteins usually initiate with the process of endoplasmic reticulum (Sakaguchi, 1997), transported to the golgi compartment for further modifications (Novick and Zerial, 1997), and then transported to the membrane by secretory vesicles (Conesa *et al.*, 2001; Stenmark and Olkkonen, 2001). Rab family proteins, which belong to the Ras superfamily of small GTPase, have been extensively reported to play important roles in the secretory pathway (Novick and Zerial, 1997; Punt *et al.*, 2001; Minz-Dub *et al.*, 2013). The first identified Rab protein is SEC4 in yeast (Clement *et al.*, 1998). SEC4 has been suggested to participate in the growth and protein secretion of *Candida albicans* (Mao *et al.*, 1999). The homologue of SEC4-like Rab in *Aspergillus niger* and *Colletotrichum lindemuthianum* has also been identified, namely, srgA and CLPT1 (Dumas *et al.*, 2001). Disruption of srgA in *A. niger* resulted in reduced protein secretion and abnormal apical branching (Punt *et al.*, 2001). In contrast, deletion of CLPT1 in *C. lindemuthianum* led to a lethal phenotype (Dumas *et al.*, 2001). A mutant with a dominant-negative allele of CLPT1 was further used to investigate the function of CLPT1, and ascertained that CLPT1 was essential for secretory vesicles transportation, infectious structures formation, and pathogenicity (Siriputthaiwan *et al.*, 2005). In *B. cinerea*, BcSAS1 was determined to be a Rab/GTPase family gene. Deletion of *bcsas1* (Δ*bcsas1*) resulted in reduced virulence in apple, tomato fruits, and tomato leaves. The *Δbcsas1* mutant exhibits an accumulation of trafficking vesicles at the hyphal tips. A comparative approach was applied to investigate the secretome of Δ*bcsas1*, and the secretion of polysaccharide hydrolases and proteases were significantly depressed (Zhang *et al.*, 2014b).

Environmental Conditions Affect Pathogenicity of *B. cinerea*

Effect of ambient pH on pathogenicity

pH is a major environmental factor that affects the interaction between *B. cinerea* and its hosts. Fruits usually present a pH ranging from 3.32 to 4.39, whereas leaves, stems, and roots exhibit a higher pH ranging from 5.81 to 6.3 (Manteau *et al.*, 2003). To explore the secretome of *B. cinerea* on different host tissues, we chose pH 4 and 6 to mimic the pH values of fruits and other tissues, cultured *B. cinerea* at different pH conditions and found that distinct differences exist in the secretome of *B. cinerea*. At pH 4, most of the identified proteins were proteolysis, whereas the major proteins detected at pH 6 were CWDEs (Li *et al.*, 2012). The proteases are usually utilized by the fungi to degrade the structural plant cell or antifungal proteins secreted by the plant host (ten Have *et al.*, 2004), and CWDEs are essential for fungi to decompose plant cell wall to achieve full virulence (Kubicek *et al.*, 2014). Moreover, we found that the production of those extracellular proteins was regulated at the transcriptional level, suggesting that *B. cinerea* has the ability to fine-tune its secretome according to the predominant pH conditions to achieve successful infection, and that it might possess complicate regulatory mechanism to perceive and response to ambient pH at the transcriptional level (Li *et al.*, 2012) (Figure 2).

The most well characterized regulatory mechanism is *pal* signalling pathway (Penalva and Arst, 2002). In *Aspergillus nidulans*, several genes are involved in the *pal* signalling pathway, namely, PacC, PalA, PalB, PalC, PalF, PalH, and PalI (Penalva *et al.*, 2008). Under alkaline conditions, the pH signal is sensed and transmitted from the plasma membrane to the endosomal membrane by PalH, PalI, and PalF. When the endosomal membrane complex including PalA, PalB, and PalC receives the signal, the complex will proteolyse PacC to a protease-accessible conformation. PacC will be further processed to its active form in a pH-independent manner. Under acidic conditions, most of PacC exist in a protease-inaccessible conformation and only trace amounts of PacC are in protease-accessible conformation. PacC is a zinc finger transcription factor which will activate the alkaline-expressed genes and repress acid-expressed genes (Penalva *et al.*, 2008). PacC has also been reported in many other plant pathogens, such as *Sclerotinia sclerotiorum* (Rollins and Dickman, 2001), *Alternaria alternata* (Eshel *et al.*, 2002), *Fusarium oxysporum* (Caracuel *et al.*, 2003), *P. digitatum* (Zhang *et al.*, 2013), and *Penicillium expansum* (Barad *et al.*, 2014). In *B. cinerea*, the gene expression of *bcpacc* was significantly higher at pH 6 than that at pH 4, indicating its role in ambient pH response of *B. cinerea* (Li *et al.*, 2012). BcACP1 is a G1-family endopeptidase which only functions in acid environment. Ambient pH regulates *bcacp1* at both the transcriptional and post-translational levels; however, the pH regulation of BcACP1 was independent of the canonical PacC binding site (Rolland *et al.*, 2009), suggesting other binding site of BcPacC or even other pH signalling pathway might exist in *B. cinerea*.

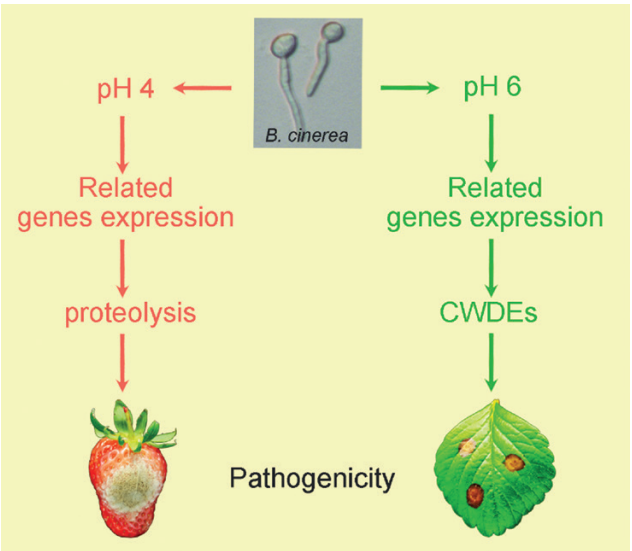

Figure 2 *Botrytis cinerea* utilize different extracellular enzymes to infect hosts according to the ambient pH conditions.

Besides adjusting an arsenal of pathogenicity factors to fit for the wide range of environment conditions, most fungi hold the potential to actively altering the local pH environment to fulfil its infection (Prusky and Yakoby, 2003; Tian *et al.*, 2016). Fungi usually achieve environmental pH changes through secreting acids or alkali. The organic acids secreted by fungi include oxalic acid, gluconic acid, citric acids, butyric acid, malate and succinate, whereas the alkali usually refers to ammonia (Vylkova, 2017). *Botrytis cinerea* has been reported to acidify the plant tissue through secreting large amounts of oxalic acid (Manteau *et al.*, 2003). Acidic pH environment can in turn regulate the activity or expression of putative pathogenicity factors, such as endopolygacturonase, laccase, and protease (ten Have *et al.*, 1998; Wubben *et al.*, 2000; Kars *et al.*, 2005a; Li *et al.*, 2012). An oxalate-deficient mutant of *B. cinerea* grew normally in vitro, but failed to produce disease symptoms (Kunz *et al.*, 2006). These results demonstrated that *B. cinerea* can modulate environmental pH conditions via utilizing OA, thus contributing to its colonization of the host tissues.

Effects of light on pathogenicity

Light is a vital environmental factor acting as energy source, signal, and stress to various living organisms. Light responsive organisms sense light to schedule their development and adjust their adaption (Rodriguez-Romero *et al.*, 2010). *Botrytis cinerea* is a light responsive strain that actively sense light conditions to fine-tune its development and pathogenicity (Zhang *et al.*, 2016). Light is an essential developmental signal for *B. cinerea* as it triggers exclusively formation of conidia, whereas constant darkness initiates the solely formation sclerotia (Fillinger and Elad, 2016). Conidia and sclerotia are two types of survival structures of *B. cinerea*. Conidia are asexual spores produced under favourable environmental conditions and contribute to rapid growth and reproduction (Brandhoff *et al.*, 2017), whereas sclerotia are sexual spores that allow for the fungi to survive adverse environmental conditions (Willetts, 1971). The balance between asexual and sexual development is tightly regulated to ensure better survival and drive adaptive responses. Extensive studies about light regulation on the development of *B. cinerea* have been conducted, especially those light responsive transcription factors. BcMADS1 is MADS-box family transcription factors that play crucial roles in regulation of various cellular functions (Shore and Sharrocks, 1995; Messenguy and Dubois, 2003). We found that deletion mutant of *bcmads1* in *B. cinerea* resulted in reduced growth rate compared with the wild type B05.10. An always conidia phenotype which lost the ability to produce sclerotia was observed, and the conidia formed by *B. cinerea* in dark was even higher than that produced in light (Zhang *et al.*, 2016). The complementation strain of *bcmads1* restored the sclerotia formation ability of *Δbcmads1*, indicating the function of BcMADS1 in light perception and in the environment fitness of this pathogen (Zhang *et al.*, 2016). Other six light-responsive transcription factors that are significantly induced when exposed to white light were termed BcLTF1-6 (Brandhoff *et al.*, 2017). BcLTF1 is a GATA transcription factor participating in the regulation of light-dependent vegetative growth and differentiation. Deletion mutants of *bcltf1* (*Δbcltf1*) lost the ability to grow under light conditions on minimal medium, and the radial growth rates have a negative correction with the exposure time to light. However, *Δbcltf1* forms more conidia upon exposed to yellow light and more sclerotia under red light than wild type (Schumacher *et al.*, 2014). BcLTF2 belongs to the C_2H_2 transcription factor family, and the overexpression of *bcltf2* is capable of switching the conidiation program on and suppressing sclerotia generation (Cohrs *et al.*, 2016). BcLTF3 is another C_2H_2 transcription factor with dual functions and represses conidiophore development but is essential for the maturation of conidia. Deletion mutant of *bcltf3* produced abundant conidiophores but failed to produce mature conidia (Brandhoff *et al.*, 2017). BcLTF4-6 are Zn2Cys6 transcription factors and exhibit no obvious roles in vegetative growth or development (Schumacher *et al.*, 2014). The expression of BcLTF2 is tightly regulated by BcLTF1, BcLTF3, BcREG1, and other proteins. (Brandhoff *et al.*, 2017). BcREG1 is a transcriptional factor previously known to be involved in the conidiogenesis and secondary metabolism in *B. cinerea* (Michielse *et al.*, 2011). In recent study, BcREG1 was re-identified as a light-responsive transcriptional regulator which influences conidia formation by repress BcLTF2-induced conidiation in the light, while active a conidiation program independent of BcLTF2 in the dark (Brandhoff *et al.*, 2017), suggesting that light is a determinant factor of generating conidia or sclerotia.

Some of the light-responsive transcriptional factors or regulators also function in the regulation of pathogenicity. We found that *Δbcmads1* showed reduced disease symptoms on apple fruit when compared with the wild type. Based on proteomic analysis, we identified the potential downstream targets of BcMADS1, and proved that 63 proteins changed abundance in *Δbcmads1*. Among them, two proteins (BcSEC14 and BcSEC31) were related to secretion and involved in the pathogenicity of *B. cinerea* (Zhang *et al.*, 2016). BcLTF1 was also demonstrated to play an important role in virulence, ROS homoeostasis, and secondary metabolism. Deletion of *bcltf1* resulted in reduced virulence on bean leaves, increased ROS accumulation, and overexpression of secondary metabolism-related genes (Schumacher *et al.*, 2014). The light-responsive transcriptional regulator BcREG1 is required for pathogenicity, and the deletion mutant of *bcreg1* is hampered in causing necrotic lesions though capable to penetrate plant tissue (Colmenares *et al.*, 2002). *Δbcreg1* mutant displayed reduced ability to produce phytotoxins such as botryane, sesquiterpenes, and polyketides, which might facilitate pathogenesis (Michielse *et al.*, 2011). It is worth noting that the pathogenesis-related light-responsive transcriptional factors or regulators also function in protein secretion or second metabolism. In filamentous fungi, velvet proteins are among the most important components coordinating light signal and secondary metabolism. Velvet proteins have been identified as a heterotrimeric velvet complex VelB/VeA/LaeA in *A. nidulans*. VeA physically interacts with VelB and bridges VelB to LaeA, a nuclear master regulator of secondary metabolism (Bayram *et al.*, 2008). In *B. cinerea*, BcVEL1/BcVEL2/BcLAE1 are, respectively, homologue to VelB/VeA/LaeA. BcVEL1 interacts with BcVEL2 and BcLAE1 to form the velvet complex (Yang *et al.*, 2013). Deletion mutants of BcVEL1, BcVEL2, or BcLAE1 present similar phenotypes such as reduced virulence and altered secondary metabolism (Schumacher *et al.*, 2015).

Control Strategies of *B. cinerea*

Due to the gigantic economic losses brought by *B. cinerea*, considerable strategies have been carried out to control *Botrytis*-incited diseases, including chemical control, resistance inducer, and biological control (Figure 3).

Chemical control

Application of synthetic fungicides to control post-harvest diseases caused by *B. cinerea* is the main method in production. There are five categories of fungicides, respectively, acting on the respiration,

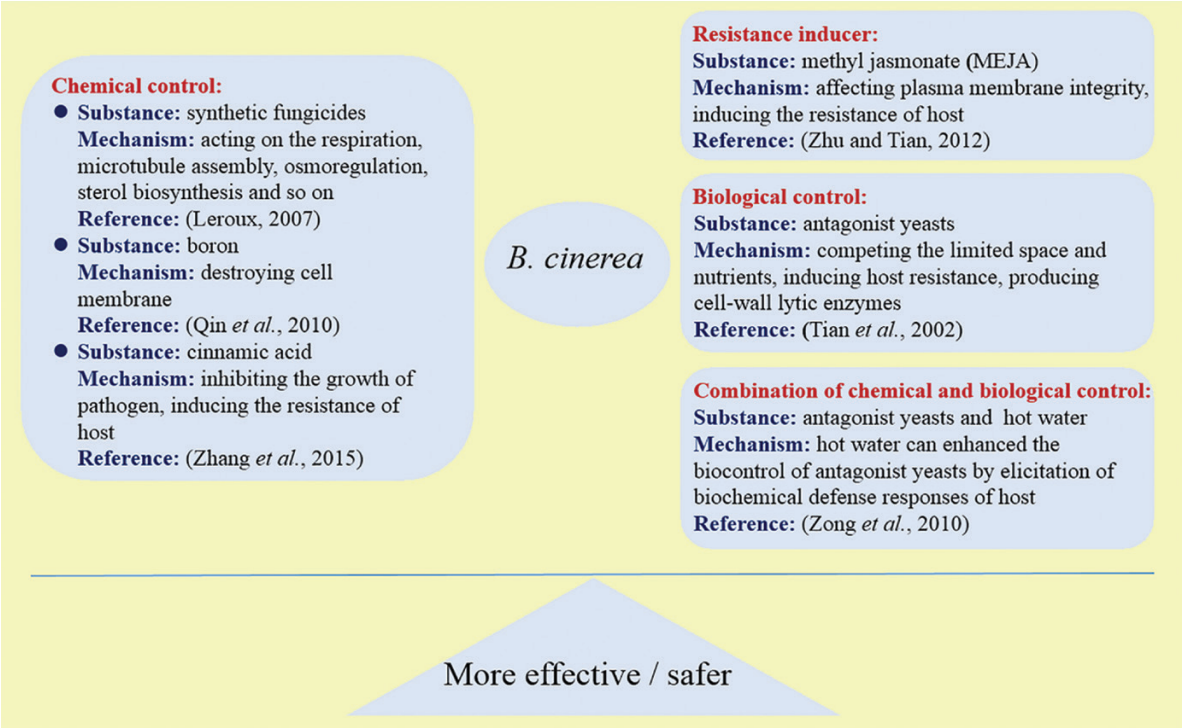

Figure 3 Control strategies of *B. cinerea*.

microtubule assembly, osmoregulation, sterol biosynthesis, and those whose effects can be reversed by methionine (Leroux, 2007). However, two main problems exist in the application of fungicides. On one hand, *Botrytis* tend to change constantly during generations as it has multinucleate conidia. Resistance strains to different categories of fungicides are frequently discovered. For example, *Botrytis* was noted to develop resistant isolates when benzimidazole fungicides were first used (Bollen and Scholten, 1971). The resistant strains to dicarboximides were also reported soon after (Katan, 1982). On the other hand, application of synthetic fungicides is expensive since the control of *B. cinerea* usually necessitates higher dose rates than other fungal pathogens. The cost at control of *Botrytis* and related species accounted for about 8 per cent of the fungicide market worldwide (Fillinger and Elad, 2016). In addition, chemical fungicides are harmful to the environment and human beings, especially their toxicological residues. Therefore, a great many of regulatory restrictions are put on the applications of botryticides (Droby *et al.*, 2009). Boron is an important plant micronutrient (Loomis and Durst, 1992) and has been shown to be effective in control of *B. cinerea* (Qin *et al.*, 2010). Boron has the potential to destroy cell membrane and result in the leakage of cytoplasmic materials from the pathogen (Qin *et al.*, 2010). The detailed antifungal mechanism of boron against *P. expansum* has been investigated by comparative proteomics. The results indicated that there were 14 proteins related to stress response and basic metabolism changed abundance after treated with borate, and among them, two proteins, catalase and glutathione S-transferase, were both down-regulated after borate treatment (Qin *et al.*, 2007). One secretory protein, namely, polygalacturonase, which contributes to virulence in various pathogens (ten Have *et al.*, 1998; Isshiki *et al.*, 2001; Oeser *et al.*, 2002; Kars *et al.*, 2005a), was also identified to be affected in the presence of borate (Qin *et al.*, 2007).

Resistance inducer

Some plant signalling molecules, such as salicylic acid (SA), jasmonic acid (JA), can induce resistant of plants against fungal pathogens (Park *et al.*, 2007; Robert-Seilaniantz *et al.*, 2011). As substitute for fungicides, they have been investigated and applied to control post-harvest diseases in fresh fruits with some success (Terry and Joyce, 2004; Yao and Tian, 2005; Romanazzi *et al.*, 2016). Our previous results indicated that SA enhanced the resistance of sweet cherry fruits against *P. expansum*, resulting in lower disease incidences and smaller lesion diameters, and revealed that antioxidant proteins, heat shock proteins, and dehydrogenases were involved in resistance response of the fruits (Chan *et al.*, 2008). Tomato fruit treated by exogenous MeJA showed higher resistance to *B. cinerea* infection, because MeJA treatment stimulated decreased catalase (CAT) and ascorbate peroxidase (APX) gene expression and enhanced ascorbate (ASC) and glutathione (GSH) content, being beneficial for scavenging excess ROS and alleviating oxidative damage of proteins (Zhu and Tian, 2012). MeJA treatment induced resistance of Chinese bayberries against fungal pathogen by priming defense responses, and up-regulated the hydrogen peroxide burst and enhanced translation levels of defence-related proteins and the contents of antimicrobial compounds (Wang *et al.*, 2014). Cinnamic acid is also proved to be effective in controlling gray mold rot caused by *B. cinerea* in table grape, its modes of the action include to inhibit the mycelial growth via damaging the plasma membrane integrity, and stimulate the resistance of fruit host by inducing the activities of proteins such as peroxidase and polyphenol oxidase (Zhang *et al.*, 2015).

Biological control

Utilizing living biological microbe agents to control post-harvest disease is a potential technology instead of chemical fungicides (Sharma *et al.*, 2009). Our previous studies indicated that a variety of

antagonistic yeasts can effectively inhibit post-harvest decay caused by *B. cinerea* in different fruits (Piano *et al.*, 1997; Fan and Tian, 2001; Tian *et al.*, 2002; Qin *et al.*, 2004). Antagonistic yeasts are more pursued since they are safer than bacteria as no toxic secondary metabolites were detected in their activities against pathogens (Tian, 2006). Their modes of action against fungal pathogens include through competing the limited space and nutrients (Janisiewicz *et al.*, 2000; Chan and Tian, 2005), inducing host resistance (Navazio *et al.*, 2007; Tian *et al.*, 2007; Hermosa *et al.*, 2012), or producing cell-wall lytic enzymes which facilitate the infection of pathogens (Yang *et al.*, 2009). However, the effect of antagonistic yeasts is not that remarkable as fungicides and usually call for the combination of fungicides or exogenous substances to gain a satisfying result (Droby *et al.*, 2009). Much work has shown that antagonistic yeasts combined with calcium chloride (An *et al.*, 2012), salicylic acid (Chan and Tian, 2006; Qin *et al.*, 2003; Zhang *et al.*, 2010), sodium bicarbonate (Yao *et al.*, 2004), silicon (Qin and Tian, 2005), boron (Cao *et al.*, 2012) and glycine betaine (Liu *et al.*, 2011) can significantly improve their biocontrol efficacy in control of post-harvest diseases in various fruits. Combination of hot water treatment with *Candida guilliermondii* or *Pichia membranaefaciens* showed a better control efficacy against *B. cinerea* in tomato fruit (Zong *et al.*, 2010).

Conclusion

Botrytis cinerea is an aggressive plant pathogen, which causes gray mould rot in fresh horticultural crops, resulting in heavy economical losses in the world. Due to the genetic variety of *B. cinerea*, resistant strains are frequently found. It is important to reveal molecular basis of pathogenicity and regulatory mechanisms of *B. cinerea*. Current understanding indicates that ROS and extracellular proteins are related to the regulation of growth, development, and virulence. The genome sequence of *B. cinerea* has been released and genetic methods such as construction of deletion mutants have been successfully used to investigate its pathogenic mechanisms. Since a few of target genes involved in pathogenicity of *B. cinerea* have been found, it is possible to develop and improve control technologies. However, more research effectors are still needed to understanding of comprehensive information about molecular pathogenic mechanisms and regulatory network to develop more precise and effective strategies for prevention and control of *B. cinerea*.

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