Dickeya Manipulates Multiple Quorum Sensing Systems to Control Virulence and Collective Behaviors

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Soft rot Pectobacteriaceae (SRP), typical of Pectobacterium and Dickeya, are a class of Gram-negative bacterial pathogens that cause devastating diseases on a wide range of crops and ornamental plants worldwide. Quorum sensing (QS) is a cell-cell communication mechanism regulating the expression of specific genes by releasing QS signal molecules associated with cell density, in most cases, involving in the vital process of virulence and infection. In recent years, several types of QS systems have been uncovered in Dickeya pathogens to control diverse biological behaviors, especially bacterial pathogenicity and transkingdom interactions. This review depicts an integral QS regulation network of Dickeya, elaborates in detail the regulation of specific QS system on different biological functions of the pathogens and hosts, aiming at providing a systematic overview of Dickeya pathogenicity and interactions with hosts, and, finally, expects the future prospective of effectively controlling the bacterial soft rot disease caused by Dickeya by quenching the key QS signal.

Keywords: soft rot Pectobacteriaceae, Dickeya, quorum sensing, regulation, virulence

INTRODUCTION

Soft rot Pectobacteriaceae (SRP) belonging to the genera Pectobacterium and Dickeya (Charkowski et al., 2012) are emerging parasitic pathogens listed in the top ten important bacterial phytopathogens in the world (Mansfield et al., 2012). In addition to causing bacterial soft rot, these pathogens also cause blackleg of potato, stalk rot of maize, and foot rot of rice, resulting in considerable economic damage to vegetable and ornamental plant production worldwide. Previously, Dickeya was grouped into the genus Erwinia containing all plant-pathogenic Enterobacteriaceae, but in 2005, it was reclassified as a new genus Dickeya (Samson et al., 2005). Currently, twelve species are included in the Dickeya genus, including Dickeya dianthicola, Dickeya dadantii, Dickeya zeae, Dickeya chrysanthemi, Dickeya paradisiaca, Dickeya solani, Dickeya aquatica, Dickeya fangzhongdai, Dickeya poaceaephila, Dickeya lacustris, Dickeya undicola, and Dickeya oryzae (Samson et al., 2005; van der Merwe et al., 2010; Brady et al., 2012; Parkinson et al., 2014; van der Wolf et al., 2014).

Diverse phenotypic differentiation and complicated pathogenic mechanisms have been revealed in different D. zeae and D. solani strains. Recent studies compared the characteristics of D. solani strains isolated from countries with different climate conditions and found higher activities of cell wall degrading enzymes (CWDEs) and virulence in Polish strains than in Finland and Israel.
strains (Golanowska et al., 2017). D. oryzae and D. zeae strains isolated from rice, banana, and ornamental clivia in China showed different types of phytoxins produced, including the zearmine I and zearmine II specific in some of the D. oryzae strains, as well as in D. solani strains (Zhou et al., 2011, 2015; Cheng et al., 2013; Hellberg et al., 2015), and another toxin produced by D. zeae banana strain MS2 but not the MS3 strain (Hu et al., 2018). Some D. zeae strains from different sources infect plant hosts in different ranges (Hu et al., 2018, 2021). Moreover, different structures of virulence factor modulating (VFM)-quorum sensing (QS) signals were implicated between D. dadantii 3937 and D. oryzae EC1 and D. zeae banana strains (Lv et al., 2019). Also, the functions of acyl-homoserine lactone (AHL) signals on the virulence of hosts are different in D. oryzae EC1 and D. zeae MS2 (Feng et al., 2019). The diversity of strains and the complexity of pathogenic mechanisms increase the difficulty of disease prevention and control in fields.

The achievement of the successful infection of Dickeya on plants depends on a complex range of virulence factors, including plant cell wall degrading enzymes (PCWDEs) (Hugouvieux-Cotte-Pattat et al., 2014), lipopolysaccharides (LPS), extracellular polysaccharide (EPS) (Condemine et al., 1992), iron carriers (Expert, 1999), pigment indigoidine, type III secretion system (T3SS) (Yang et al., 2002, 2004; Yap et al., 2005), and cell motility and adhesion associated with plants (Hussein et al., 2008; Chen et al., 2016, 2020). Motility, which is regulated by the AHL-QS signal, is a secondary virulence determinant of Dickeya, whereas pectinases in PCWDEs, which are regulated by the VFM-QS signal, are the primary virulence determinants of Dickeya, participating and dominating the macerating soft rot process of the pathogen in plant tissues. The capacity of synthesizing and secreting pectinases is modulated by complex and interconnected circuits involving multiple regulatory pathways. A recent study in our laboratory indicated that putrescine is a transkingdom communication signal modulating cell motility, biofilm formation, and virulence of D. oryzae EC1 (Shi et al., 2019). At the moment of current research, QS signals including the AHL signal, the VFM signal, and the crucial signal putrescine have been shown to participate in the intraspecific and transkingdom cell-cell communication, regulating the infection and the colonization of Dickeya toward host plants.

**N-ACYL-HOMOSERINE LACTONES-QUORUM SENSING SIGNAL REGULATES CELL MOTILITY AND BIOFILM FORMATION IN Dickeya**

Various gram-negative plant-pathogenic bacteria have been found to use a QS system dependent on the synthesis and perception of N-acyl-homoserine lactones (AHLs) as diffusible signals for coordinating QS communication. The AHL signal-mediated QS system is currently the most representative and most studied population sensing system, which is composed of two conserved categories of proteins in nearly all the sequenced Dickeya (except D. paradisiaca) (Potrykus et al., 2014) and Pectobacterium strains, ExpI (LuxI homolog) and ExpR (LuxR homolog). ExpI is a synthase in diverse Pectobacterium and Dickeya plant pathogens in charge of the synthesis of AHLs, including N-3-oxohexanoyl-homoserine lactone (3OC6-HSL), N-3-oxo-octanoyl-homoserine lactone (3OC8-HSL), N-hexanoyl-homoserine lactone (C6-HSL), and N-decanoyl-homoserine lactone (C10-HSL) in Dickeya (Nasser et al., 1998; Crépin et al., 2012; Feng et al., 2019), and N-octanoyl-homoserine lactone (C8-HSL), and N-3-oxo-decanoyl-homoserine lactone (3OC10-HSL) additionally in Pectobacterium (Crépin et al., 2012). ExpR is the AHL signal receptor and a transcriptional regulator modulating the expression of target genes.

In Pectobacterium and Dickeya bacteria, ExpR functions as a repressor in most cases, where ExpR binds to the promoter of DNA and blocks transcription in the absence of AHL, and AHL dissociates ExpR-DNA complexes to release ExpR and initiate transcription (Castang et al., 2006; Feng et al., 2019). For example, in D. oryzae EC1 and D. zeae MS2, the deletion of expI but not expR dramatically enhanced bacterial motility, aggregation, and pigment production (Hussain et al., 2008; Zhong, 2014; Feng et al., 2019). ExpR also represses its own transcription with a strong affinity for the expR regulatory region (Reverchon et al., 1998; Castang et al., 2006). Such autorepression will be relieved with the increase of AHL signal concentration. Unexpectedly, the inactivation of expI but not expR only affects the expression of pelA and pelB but does not result in visible repercussions on total pectate lyase activity in D. dadantii 3937 (Nasser et al., 1998), which also affects the expression of prtX, prtB, prtC, pelB, pelE, pelL, and some zms genes, and slightly reduces the production of pectinases and cellulases, and maceration on potato slices in D. oryzae EC1 (Hussain et al., 2008; Zhong, 2014). However, ExpR has been demonstrated to function as an activator to specifically interact with the promoters of the five major pectinase encoding genes pelA, pelB, pelC, pelD, and pelE (Nasser et al., 1998), and the expression in D. dadantii 3937 (Reverchon et al., 1998), and the addition of AHL signal dissociates ExpR-DNA complexes (Castang et al., 2006). In D. dadantii 3937, D. oryzae EC1, and D. zeae MS2, the deletion of expR has no effect on the virulence and the production of major virulence factors (Castang et al., 2006; Zhong, 2014; Feng et al., 2019).

An exception is in D. solani that the expR mutant reduced the virulence on potato tubers by 2- to 3-fold compared with the wild-type strain (Potrykus et al., 2014), suggesting a certain difference in the degree of regulation on virulence genes by this system in Dickeya depending on the strain and host plant (Potrykus et al., 2018).

In general, the ExpI–ExpR QS system plays an important role in bacterial motility, biofilm formation, and pigment production but has a limited role in the regulation of virulence traits. This system is also under the control of multiple cross-acting regulatory elements, such as cAMP-CRP and PecS in opposite manners (Figure 1A).

However, the ExpI–ExpR QS system has been shown to be quite critical in Pectobacterium species, which is involved...
in the production of PCWDEs and other virulence factors in *Pectobacterium* (Barnard and Salmond, 2007; Liu et al., 2008). There are several virulence regulators in *Pectobacterium* that act through the *Rsm* system, which plays a key role in controlling virulence, and the ExpI–ExpR QS system control occupies a vital position in the *Pectobacterium* regulatory hierarchy, with multiple downstream regulators, such as some that may operate through the ExpI–ExpR QS system control.

Some studies reveal that AHLs produced by bacteria also act as interkingdom signals which influence and reprogram plant gene expression and also interact with other microbes (Mathesius et al., 2003; Bauer and Mathesius, 2004; Schuhegger et al., 2006; Ortíz-Castro et al., 2008; von Rad et al., 2008; Schikora et al., 2011; Schenk et al., 2012).

Apart from the *luxR* genes paired with the adjacent *luxI* genes, many bacteria harbor *luxR* genes without *luxI* genes in their vicinity on the chromosome, called orphan or solo *luxR* (Hudaiberdiev et al., 2015). These solo *luxR* may respond to either internal AHL signals such as the *qscR* of *Pseudomonas aeruginosa* (Lequette et al., 2006) or exogenous signals such as the *sdiA* of *Escherichia coli* and *Salmonella enterica* (Ahmer, 2004; Hughes et al., 2010). In *D. zeae* MS2, the solo *luxR* (*pipR*) is linked to a proline iminopeptidase encoding gene *pipA* (Feng et al., 2019), similar to the solo *luxR* homologs in *Xanthomonas*, *Pseudomonas*, and *Kosakonia* (Zhang et al., 2007; Ferluga and Venturi, 2009; Coutinho et al., 2018; Mosquito et al., 2020). The expression of *pipA* is under the control of PipR, and the deletion of the *pipA*, but not *pipR*, in MS2 strain fully impaired its virulence on banana seedlings (Feng et al., 2019). In *Dickeya* genus, the *luxR*-solo systems, containing the *pipA/pipR* and the ABC-type peptide transporter genes (Feng et al., 2019), are only present in some strains including *D. parazeae* Ech586, 6 strains of *D. zeae*, 2 strains of *D. fangzhongdai*, *D. dadantii*, and *D. dianthicola*, respectively, 6 strains of *D. solani*, and *Dickeya* sp. Seccp 1600 (Table 1). Interestingly, this system is highly conserved in many *Klebsiella* strains but absent in the closely related species of *D. oryzae* (Table 1). Notably, all the host plants of *D. parazeae* and *D. zeae* harboring this *luxR*-solo system belong to monocotyledons (Table 1), suggesting that the system may be related to host specialization.

**THE Dickeya-SPECIFIC VIRULENCE FACTOR MODULATING SIGNAL REGULATES PLANT CELL WALL DEGRADING ENZYMES PRODUCTION AND VIRULENCE**

In 2013, Nasser et al. (2013) first identified the existence of a non-AHL-QS system in *D. dadantii* 3937, called the VFM system. This system is encoded by a 25-kb gene cluster, containing genes involved in the biosynthesis, transport, and induction of the VFM signal. With the exception of *D. poaceaephiila* NCPPB 569 isolated from sugarcane, which had only 46% coverage, the *vfm* gene...
cluster is extremely conserved in all *Dickeya* strains whose whole genome sequences have been sequenced (Figure 2). Notably, this gene cluster is uniquely present in *Dickeya* strains, suggesting that the VFM-QS system is an inherent, ubiquitous, and unique regulatory mechanism in *Dickeya*. In all the tested strains such as *D. dadantii* 3937, four *D. solani* strains, *D. oryzae* EC1, and *D. zeae* MS2, the VFM-QS system has been demonstrated to participate in the regulation of PCWDE production and virulence (Nasser et al., 2013; Potrykus et al., 2014, 2018; Lv et al., 2019). Furthermore, in *D. oryzae* EC1, the VFM signal also regulates pathogen swimming and swarming motility and the production of phytotoxin zeamines (Lv et al., 2019).

Although the chemical structure of the VFM signal has not been characterized yet, some characteristics of this signal can be inferred through some experimental evidence. First, the signal is an extracellular compound since it can be sensed by the VfmI histidine kinase sensor using bacterial supernatant and activates the expression of the vfmE, encoding an AraC-type family transcriptional regulator through the VfmHI two-component system (Lv et al., 2019; Figure 1B). Second, the nature of the VFM signals produced by different *Dickeya* strains might be different. A lacZ-VFM reporter, constructed based on *D. oryzae* EC1 lacZ deletion mutant, could sense the VFM signals produced by EC1, *D. zeae* MS2 and MS3, but not strain *D. dadantii* 3937, vice versa (Lv et al., 2019), suggesting that the chemical structures of the VFM signals produced by EC1 and 3937 might be different. Moreover, the VFM signal from 3937 is stable after treatment by boiling at 100°C for 3 min (Nasser et al., 2013), while that from EC1 completely loses its activity after treatment at 50°C for 30 min (Lv, 2018). Third, the VFM signal is produced at the early and middle stages of bacterial exponential growth. During the growth of *D. oryzae* EC1, the production of VFM signal was quantified, and the results showed that when the cell density is lower than OD600 at 0.5, the VFM signal increased slowly with the increase of bacterial concentration; when the cell density is over OD600 at 0.5, the signal generation rate is obviously accelerated; after OD600 at 1.2, interestingly, the signal concentration decreased sharply (Lv, 2018), suggesting that VFM signal degrading enzymes are probably present in the...
## TABLE 1 | Homologs of the luxR-solo systems (C1O30_RS14500 to C1O30_RS14535) of Dickeya zeae MS2.

| Strain               | Country                  | Host              | Coverage | Identity        |
|----------------------|--------------------------|-------------------|----------|-----------------|
| Dickeya zeae MS2     | Guangzhou                | Banana            | 100%     | 100%            |
| Dickeya zeae Ech586  | NA                       |                   | 100%     | 97.76%          |
| Dickeya zeae A586-S18-A17 | France: Durance River       | River water        | 100%     | 97.38%          |
| Dickeya zeae JZL7    | China: Guangzhou         |                   | 100%     | 96.24%          |
| Dickeya zeae Pl65    | United States: Hawaii    | Taro              | 100%     | 96.04%          |
| Dickeya zeae A5410   | United States: Hawaii    | Pineapple         | 100%     | 95.12%          |
| Dickeya zeae CE1     | China: Meizhou           |                   | 98%      | 96.48%          |
| Dickeya fangzhongdai DSM 101947T | Zhejiang | Pyrus pyrifolia    | 90%      | 72.52%          |
| Dickeya fangzhongdai ND14b | Malaysia | Waterfall         | 90%      | 72.47%          |
| Dickeya solani IFB0223 | Germany                  | Potato rhizosphere | 90%     | 72.13%          |
| Dickeya solani IFB 0099 | Poland                  |                   | 90%      | 72.13%          |
| Dickeya solani PPO 9019 | Netherlands            | Muscari           | 90%      | 72.13%          |
| Dickeya solani D50432-1 | Finland                | Potato stem       | 90%      | 72.13%          |
| Dickeya solani RNS 08.23.3.1A | France               | Potato            | 90%      | 72.13%          |
| Dickeya solani IPO 2222T | Netherlands           | Potato            | 90%      | 72.13%          |
| Dickeya dadantii DSM 18020T | Comoros               | Pelargonium capitatum | 90%     | 71.79%          |
| Dickeya dadantii 3937 | NA                      |                   | 90%      | 71.52%          |
| Dickeya dianthicola ME23 | United States:Maine     | Potato            | 86%      | 73.08%          |
| Dickeya dianthicola RNS04.9 | NA                    | Potato            | 86%      | 73.08%          |
| Dickeya sp. Secpp 1600 | Hunan                 | Radish            | 90%      | 72.51%          |
| Klebsiella oxytoca   | United Kingdom          | Human fecal       | 94%      | 79.63%          |
| Klebsiella michiganensis BD177 | NA                   | NA                | 94%      | 79.67%          |
| Klebsiella michiganensis K518, K516 | Zhejiang      | Human fecal       | 94%      | 79.67%          |
| Klebsiella oxytoca CAV1374 | United States:Virginia | Human perirectal  | 94%      | 79.67%          |
| Klebsiella michiganensis E718 | Taiwan          | Human             | 94%      | 79.67%          |
| Klebsiella michiganensis F107 | Fujian           | Human sputum      | 94%      | 79.65%          |
| Klebsiella oxytoca KONIH4, KONIH2 | United States         | Waste water       | 94%      | 79.64%          |
| Klebsiella oxytoca KONIH1 | United States         | Perirectal swab   | 94%      | 79.64%          |
| Klebsiella michiganensis C52 | Sydney             | Human clinical sample | 94%   | 79.61%          |
| Klebsiella michiganensis AR375 | NA                 | NA                | 94%      | 79.62%          |
| Klebsiella oxytoca AR_0028 | NA                   | NA                | 94%      | 79.60%          |
| Klebsiella michiganensis M1 | South Korea         | Soil              | 94%      | 79.61%          |
| Klebsiella michiganensis HKOPL1 | NA               | Panda fecal       | 94%      | 79.61%          |
| Klebsiella michiganensis KCTC 1686 | South Korea | NA                | 94%      | 79.61%          |
| Raoultella electrica DSM 102253 | Japan            | Anodic biofilm of microbial fuel cell | 94% | 79.03%          |

In addition, a pecS gene encoding a MarR family transcriptional regulator, along with the indigoidine biosynthesis gene indABC, is located upstream of the vfm gene cluster. These genes are mainly present in *Dickeya* spp. and absent in *Pectobacterium* spp. PecS functions as a repressor of the VFM system, and the deletion of pecS induces symptoms more rapidly than the wild-type strain (Hommais et al., 2008; Pédron et al., 2018), which may be attributed to the overproduction of VFM signal in the pecS mutant. PecS acts mainly in the early stages of infection, suggesting that it may prevent the vfm gene expression in the first stages of infection. Furthermore, VFM- and AHL-QS systems do not work in synergy to modulate the virulence of *Dickeya*. Previous studies have revealed that the AHL-QS system regulates the cell motility and biofilm formation of *Dickeya* spp., playing an essential role in pathogen colonization and survival in poor environmental conditions (Hussain et al., 2008; Feng et al., 2019), while the VFM-QS system is more dominant in regulating the production of diverse virulence factors and the ability to macerate plant tissue (Nasser et al., 2013; Lv et al., 2019). The interplay between these two QS systems has been studied in five *D. solani* strains at different virulence levels. The results showed that the two QS systems do not coordinate the virulence of *Dickeya* (Potrykus et al., 2018).
Apart from the PecS, Fis transcriptional regulator has been found to bind directly to the promoter region of vfmE, directly regulating the production of VFM signal and the PCWDEs (Lv et al., 2018). Recently, an organic hydroperoxide reductase regulator (OhrrR) has been identified to directly bind to the promoter regions of fis and slyA (Lv et al., 2021). The two transcriptional regulators Fis and SlyA control the production of PCWDEs in completely different pathways (Zhou et al., 2016; Lv et al., 2018).

**PUTRESCINE ACTS AS A NEW TYPE OF QUORUM SENSING AND TRANSKINGDOM COMMUNICATION SIGNAL**

Polyamines, mainly constituted by putrescine, spermine, spermidine, and cadaverine, are a group of aliphatic small polycationic molecules that can bind to RNA, DNA, nucleotide triphosphates, and other acidic substances, involved in regulating a wide variety of physiological processes within living organisms (Igarashi and Kashiwagi, 2000; Shi et al., 2019). In recent years, considerable evidence has demonstrated that in addition to core physiological functions, including translation, transcription, and chromatin remodeling, polyamines are involved in various fundamental cellular processes regulated by bacterial cells as QS signals. For instance, nonspermidine acts as an intercellular signaling molecule that activates the biofilm formation of *Vibrio cholera* via a nonspermidine sensor NspS-dependent manner, and the lack of nonspermidine biosynthetic pathway results in severely reduced biofilm formation (Griffiths et al., 1984; Karatan et al., 2005; Lee et al., 2009). Spermidine transporter-dependent signaling pathway regulates the expression of the T3SS genes of *P. aeruginosa* (Zhou et al., 2007). Putrescine has been demonstrated to be critical for biofilm formation and motility in common human pathogens. In *E. coli*, putrescine interferes with biofilm formation and surface motility (Koski and Vaara, 1991; Kurihara et al., 2011). In *Yersinia pestis*, the deficiency of putrescine synthesis enzymes can severely inhibit biofilm formation, and the exogenous addition of putrescine can effectively rescue biofilm formation (Patel et al., 2006; Wortham et al., 2010). In the urinary tract pathogen *Proteus mirabilis*, putrescine serves as an extracellular signal essential for swarming motility and invasion ability (Sturgill and Rather, 2004; Kurihara et al., 2013).

In *Dickeya* spp., only putrescine and spermidine are produced since the spermine synthase encoding gene *speA* is absent in the genomes. The previous study has shown that the deletion of the arginine decarboxylase encoding gene *speA* in *D. oryzae* EC1 impaired the synthesis of putrescine, bacterial motility, biofilm formation, and rice seed invasion ability (Shi et al., 2019). Putrescine can also act as an interkingdom communication signal transmitted through the bacterial plasma membrane by PotF and PlaP putrescine-specific transporters into the wild-type EC1 and *speA* mutant cells to activate and rescue the phenotype of bacterial motility (Shi et al., 2019; Figure 1C). In *D. zeae* MS3, the deletion of *speA*, but not *speE* (encoding spermidine synthase), decreases bacterial motility, biofilm formation, and virulence on banana seedlings and potato slices but has no effect on the production of PCWDEs (Tang, 2017), suggesting that putrescine, but not spermidine, is a conserved critical signal regulating the cell motility, biofilm formation, and virulence in *Dickeya*.

**ZEAMINES MODULATE TOXIN PRODUCTION AND TOXIN RESISTANCE IN A MANNER OF QUORUM SENSING MECHANISM**

Zeamines are polyamine phytotoxins produced by *D. oryzae* EC1, many *D. solani*, and some *Serratia* strains (Zhou et al., 2015). Zeamines are encoded by a zms gene cluster that includes 18 genes from zmsO to zmsN (Zhou et al., 2015). Among them, zmsA is a key gene responsible for the biosynthesis of zeamines (Zhou et al., 2011), and zmsK encodes a non-ribosomal peptide synthase (NRPS) catalyzing the amide bond formation by using zeamine II as a substrate to generate zeamine (Cheng et al., 2013). The mutation of zmsA and zmsK abolishes antimicrobial activity and attenuates the virulence of *D. oryzae* EC1 (Zhou et al., 2011; Cheng et al., 2013). Zeamines not only function as virulence factors in *D. oryzae* rice strains (Zhou et al., 2011; Cheng et al., 2013) but also antagonize many bacteria and fungi and even kill the nematode (Hellberg et al., 2015; Liao et al., 2015; Hu et al., 2018).

In EC1, the production of zeamines is under the control of multiple regulation pathways, such as the OhrrR–SlyA–Fis, the OhrrR–SlyA–Fis–VfmE, the Vfml–VfmH–VfmE, and the ExpS–ExpA (Zhou et al., 2016; Lv et al., 2018, 2019, 2021). Notably, an efflux pump DesABC specifically recognizes zeamines and is currently only found in many *Dickeya* spp. (Liang et al., 2019), implicating a mechanism of toxin tolerance in *Dickeya* bacteria. Surprisingly, zeamines also act as a regulator modulating the expression of desAB genes in a density-dependent manner. The exogenous addition of zeamines in a low concentration (5 µg/ml) could significantly induce the expression of desAB genes in *D. oryzae* EC1 and *D. dadantii* 3937 (Liang et al., 2019; Figure 1D), unveiling a novel and specific signaling role of zeamines in regulating microbial resistance to zeamines.

**CONCLUSION**

Quorum sensing is a “language” for microbial communication to regulate the group behavior of microbes. The vital role of QS in bacterial virulence has attracted considerable interest from researchers, making it a promising novel target for the prevention and control of QS-mediated bacterial infections (Joshi et al., 2016). Such novel disease control strategy, called quorum quenching (QQ), is distinguished from other disease biocontrol measures in that QQ disrupts signal-mediated QS by inactivating QS signal or interfering with signal production or perception,
not acting on the main growth factors of the pathogens; thus, it would not cause selective pressure on the survival of pathogens. In this study, QS systems that regulate the pathogenesis of *Dickeya* are systematically revealed which not only modulate the virulence of *Dickeya* but also affect the drug resistance and adaptability to the environment. They are differential in chemical structures, biosynthesis pathways, signal transduction pathways, and regulation mechanisms. For the widely conserved classical AHL-QS system, it mainly affects bacterial motility and biofilm formation and regulates the adaptability of *Dickeya* spp. to the surrounding environment. Except in *D. solani* strains that cause blackleg of potato disease in Western Europe, the AHL-QS system regulates the virulence of the pathogens (Potrykus et al., 2018). Given that VFM and putrescine in *Dickeya* spp. and they function as major regulatory systems modulating virulence of *Dickeya* spp., we suggest focusing on quenching these two systems for prevention and control of bacterial soft rot on crops caused by *Dickeya*.

From current research results, no obvious evidence reveals that there is a relationship between AHL and VFM systems. However, since the VFM signal actions at a relatively low cell density (OD600 below 1.2), while the AHL signal functions when the cell density is high, we think that some gene(s) may be responsible for the switching between these two QS systems. For the putrescine signal, some of the regulon overlays with those regulated by the AHL signal, but no current evidence indicates any interplay between them. The interactions between different QS systems in *Dickeya* need more in-depth investigations to draw a more accurate and clear conclusion.

**AUTHOR CONTRIBUTIONS**

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