The use of *Bacillus* spp. as bacterial biocontrol agents to control plant diseases

Adrien Anckaert, Anthony Arguelles Arias and Grégory Hoff, Gembloux Agro-Bio Tech, ULiege (University of Liège), Belgium; Maryline Calonne-Salmon and Stéphane Declerck, UCLouvain (University of Louvain-la-Neuve), Belgium; and Marc Ongena, Gembloux Agro-Bio Tech, ULiege, Belgium

1 Introduction

Biological control of plant diseases, involving the use of (micro-)organisms or compounds of biological origin, is now considered one of the most promising alternatives to the use of chemical pesticides. Sales of so-called biocontrol

agents (BCAs) are expected to reach *circa* 10% of the overall global crop protection market in the near future with an annual growth rate estimated between 15% and 20% (Parnell et al., 2016; Nishimoto, 2019; Zaki et al., 2020). Biocontrol can provide plant protection against many diseases and is environment friendly. Since it often involves several modes of action to restrict the growth of microbial pathogens, biocontrol may limit the development of resistance mechanisms in pathogens but further studies are needed to assess their durability (Geiger et al., 2010; Bardin et al., 2015; Borel, 2017; Kim et al., 2017).

BCAs may act against pathogens via a number of mechanisms: competition for space and nutrients, parasitism, antibiosis and/or by stimulating the host plant defences (Köhl et al., 2019). Biocontrol organisms are natural enemies of plant pathogens including viruses, bacteria, fungi, insects and nematodes. Non-living agents of biological origin include semiochemicals (pheromones, plant volatiles) and biochemical products mainly secreted or extracted from plants and microorganisms (Raymaekers et al., 2020).

Microbial products currently dominate the BCA market, particularly bacteria such as *Bacillus thuringiensis* which is widely used as a bio-insecticide. Selected beneficial bacteria naturally living in close association with plants, and referred to as plant growth-promoting rhizobacteria (PGPR), are also used as BCAs against plant pathogens (Savary et al., 2019). PGPRs constitute a diverse group of bacteria isolated from the rhizosphere and belonging mainly to the genera *Pseudomonas, Streptomyces, Acetobacter, Azospirillum, Paenibacillus, Serratia, Burkholderia, Herbaspirillum*, *Rhodococcus, Rhizobium* and *Bacillus* (Backer et al., 2018).

Like other PGPR, some *Bacillus* spp. can improve plant growth by nitrogen fixation, phosphate solubilization, phytohormone production or by mitigating the impact of some abiotic stress factors (Kumar et al., 2011; Saxena et al., 2020). This genus includes species that are particularly effective in controlling plant diseases, representing some of the most popular BCAs with global sales of US$ 160 million in 2016 (Chen, 2017).

Even though reduction of insect and nematode infection has also been occasionally reported (Mnif and Ghribi, 2015; Engelbrecht et al., 2018; Ruiu, 2020), the biocontrol activity of *Bacillus* species has been mainly established against plant diseases. This chapter illustrates the diversity of pathosystems in which BCA based on *Bacillus* spp. have proved effective. It describes the mechanisms underpinning this biocontrol activity via the production of a wide range of enzymes, proteins and small-size bioactive secondary metabolites (BSMs). As these BSMs are clearly involved in pathogen control, we emphasize the importance of understanding the ecological factors influencing their production. In the last part of the chapter, we highlight the potential interactions between *Bacillus* spp. and other soil microorganisms in developing consortia

of biocontrol agents combining species with synergistic activities for plant health improvement.

2 *Bacillus* spp. as biocontrol agents (BCAs)

Most of the *Bacillus* spp. reported as effective BCAs have been isolated from the rhizosphere, occasionally from the phyllosphere, and belong to the so-called *Bacillus subtilis* complex (Cawoy et al., 2011; Fan et al., 2017a). These bacteria may be very competitive in their natural niche. They form populations on plant tissues, as illustrated by *B. velezensis* FZB42, and are able to colonize roots of different monocot and dicot species (Fan et al., 2011, 2012). Root colonization ability contributes to the secretion of antimicrobial compounds and plant resistance elicitors. This metabolite secretion allows to combat a diverse range of bacteria, viruses and fungal pathogens with different lifecycles and modes of virulence (biotrophic, hemibiotrophic or necrotrophic) as illustrated via selected examples in Table 1 (Fira et al., 2018; Miljaković et al., 2020). *Bacillus* spp. biocontrol efficacy has been demonstrated in greenhouse (Fousia et al., 2016; Beris et al., 2018) and field conditions (Matzen et al., 2019; Cucu et al., 2020), as well as at the post-harvest stage for fruit diseases (Punja et al., 2016; Gava et al., 2019).

The ability of *Bacillus* spp. to antagonize Gram-negative bacteria and reduce diseases caused by these pathogens has been established mainly *in vitro* and under controlled conditions (Table 1). A single strain can act against several bacterial pathogens. For example, *B. velezensis* LS69 has been shown to display antibacterial activities against *Erwinia carotovora* and *Ralstonia solanacearum* (Liu et al., 2017). Species can counteract Gram-positive bacterial pathogens such *as Clavibacter michiganensis by B. amyloliquefaciens* S1 (Gautam et al., 2019) and *Streptomyces scabies* by *B. amyloliquefaciens* Ba01 (Lin et al., 2018).

Bacillus spp. have been shown to exhibit antagonistic activity against most economically important fungal plant pathogens (Dean et al., 2012) such as *Botrytis cinerea* (Jiang et al., 2018)*, Magnaporthe oryzae* (Rahman et al., 2015)*, Fusarium graminearum* (Ntushelo et al., 2019)*, Fusarium oxysporum* (Elanchezhiyan et al., 2018)*, Blumeria graminis* (Matzen et al., 2019)*, Zymoseptoria tritici* (Kildea et al., 2008) or *Colletotrichum acutatum* (Wang et al., 2020b). A single strain can antagonize different fungi, such as *B. velezensis* Y6 and F7 which inhibit both *F. oxysporum* and *Colletrichum gloeosporioides in vitro* (Cao et al., 2018). Antagonism of *Bacillus* strains against oomycetes such as *Pythium aphanidermatum* (Zouari et al., 2016) and *Phytophthora infestans* (Caulier et al., 2018) has also been demonstrated.

Several *Bacillus* spp. have also been reported to control diseases caused by viruses. This has been illustrated on different pathosystems including

Table 1 Selected examples of published studies showing the versatility action of *Bacillus* genus against phytopathogens with different lifecycles or distinct structural features

Pathogen group	Structural feature or lifecycles	Pathogen species	Disease	Biocontrol *Bacillus* species	Crop(s)	Experimental set-up	Reference
Bacteria	**Gram+**	*Streptomyces scabies*	Common scab	*B. amyloliquefaciens*	Potato	*In vitro*, Pot assays, Field	(Lin et al., 2018)
		Clavibacter michiganensis subsp. *michiganensis*	Bacterial canker	*B. amyloliquefaciens*	Tomato	*In vitro*, Pot assays	(Gautam et al., 2019)
	Gram-	*Rhizobium radiobacter*	Crown gall	*B. subtilis / B. amyloliquefaciens*	Tomato	*In vitro, In vivo*	(Frikha-Gargouri et al., 2017)
		Erwinia amylovora	Fire blight	*B. amyloliquefaciens*	Pear/Apple	*In vitro*, Field	(Aït Bahadou et al., 2018)
		Pseudomonas syringae	Leaf spot	*B. amyloliquefaciens / B. pumilus*	Sugar beet	*In vitro, In vivo*	(Nikolić et al., 2019)
		Xanthomonas axonopodis pv. *vesicatoria*	Bacterial leaf spot	*B. amyloliquefaciens*	Tomato/Pepper	*In vitro, In vivo*	(Medeot et al., 2020)
Fungi	**Biotrophic**	*Cladosporium fulvum*	Tomato leaf mold	*B. subtilis*	Tomato	*In vitro*, Pot assays	(Wang et al., 2018)
		Blumeria graminis	Powdery mildew	*B. velezensis*	Winter wheat/ Spring barley/ Oats/Triticale	Field, Greenhouse	(Matzen et al., 2019)
		Plasmopara halstedii	Downy mildew	*Bacillus spp.*	Sunflower	Field, Greenhouse	(Nandeeshkumar et al., 2008)
		Plasmopara viticola	Downy mildew	*B. subtilis/B. pumilus*	Grapevine	*In vitro*, Field	(Zhang et al., 2017a)
	Hemibiotrophic	*Mycosphaerella graminicola* (*Zymoseptoria tritici*)	Leaf blotch	*B. megaterium*	Winter wheat	*In vitro, In vivo*	(Kildea et al., 2008)

	Pathogen	Disease	Bacillus spp.	Crop	Condition	Reference
Necrotrophic	*Pyricularia oryzae*	Rice blast	*Bacillus* spp.	Rice	*In vitro*, Greenhouse	(Rais et al., 2016)
	Bipolaris sorokiniana	Wheat spot blotch	*B. subtilis*	Wheat	*In vitro, In vivo*	(Villa-Rodríguez et al., 2019)
	Colletotrichum acutatum	Anthracnose	*B. amyloliquefaciens*	Loquats	*In vitro, In vivo*	(Wang et al., 2020b)
	Botrytis cinerea	Gray mold	*B. velezensis*	Pepper	*In vitro*, Greenhouse	(Jiang et al., 2018)
	Fusarium oxysporum	Wilt	*B. velezensis*	Tomato	Greenhouse, Field	(Elanchezhiyan et al., 2018)
	Rhizoctonia solani	Damping-off	*B. subtilis / B. amyloliquefaciens*	Tomato	*In vitro*, Greenhouse, Field	(Solanki et al., 2015)
	Sclerotinia sclerotiorum	White mold	*B. velezensis*	Tomato	*In vivo*, Greenhouse	(Farzand et al., 2019)
Oomycete	*Pythium aphanidermatum*	Damping-off	*B. amyloliquefaciens*	Tomato	*In vivo*	(Zouari et al., 2016)
	Phytophthora infestans	Late blight	*B. subtilis*	Potato	*In vitro*, Pilot field	(Caulier et al., 2018)
Virus	Tomato yellow leaf curl virus (TYLCV)		*B. velezensis / B. amyloliquefaciens*	Tomato	*In vivo*, Pot assays	(Guo et al., 2019)
	Cucumber mosaic virus (CMV)		*B. amyloliquefaciens*	Pepper/ *Nicotiana benthamiana*	*In vivo*, Field	(Lee and Ryu, 2016)

tomato plants infected by the tomato yellow leaf curl virus counteracted by *B. amyloliquefaciens* Ba13 (Guo et al., 2019) or pepper and tobacco plants infected by the cucumber mosaic virus and controlled by *B. amyloliquefaciens* 5B6 (Lee and Ryu, 2016).

These bacilli have been commercially used as BCAs partly because of their ability to combat disease and partly because of technological advantages (Table 2). Species belonging to the so-called *B. subtilis* complex are, for example, considered GRAS ('generally regarded as safe') (Schallmey et al., 2004) and can be produced at an industrial scale. These bacteria are aerobic with relatively high growth rates, low nutritional requirements and are able to grow on various nutrient sources. They usually produce a range of enzymes (cellulases, amylases, proteases) degrading various substrates derived from naturally abundant sources such as lignocellulose, starch, proteins, hydrocarbon and biofuels (Chen et al., 2018; Elisashvili et al., 2019). This allows their cultivation in low-cost media such as plant raw materials in industrial bioreactors or in solid-state fermentation (Khardziani et al., 2017; Berikashvili et al., 2018). An important advantage of *Bacillus* spp. is their ability to form endospores which make them particularly resistant to abiotic stresses such as heat and drought (Piggot and Hilbert, 2004; Mutlu et al., 2020). The endospore allows the formulation of *Bacillus*-based products with good long-term storage due to resistance to industrial processing (lyophilization or spray drying of the spore suspensions collected from the fermentation broth) and the ability to mix endospores with appropriate additives, adjuvants or surfactants (Schisler et al., 2004; Stamenkovic-Stojanovic et al., 2019). Products can either be sprayed on aerial parts of the plants, delivered into soil or coated on seeds according to the disease targeted and farmers needs (Rahman, 2016; Toral et al., 2020).

3 The diversity of *Bacillus* spp. metabolites involved in biocontrol

The biocontrol activity of *Bacillus* species has mainly been linked to their ability to produce a wide range of chemically diverse compounds (Fig. 1). Comparative genomics has revealed that species of the *B. subtilis* group, including plant-associated clades, are particularly rich in biosynthetic gene clusters (BGCs) encoding bioactive secondary metabolites (BSMs) (Grubbs et al., 2017; Harwood et al., 2018). Up to 12% of the genome is devoted to the synthesis of those compounds (Chowdhury et al., 2015a; Molinatto et al., 2016; Liu et al., 2017; Pandin et al., 2018). Some BGCs are widespread across species in the *B. subtilis* group while others seem to be more species-specific. *B. velezensis* has the highest number of different genes coding for BSMs (Fan et al., 2018), making this species one of the most efficient and commonly used bacilli in biocontrol (Ye et al., 2018; Rabbee et al., 2019). Other species of the

B. subtilis group produce fewer BSMs in terms of diversity, for example, *B. amyloliquefaciens* and *B. subtilis* (Harwood et al., 2018; Andrić et al., 2020). Many of the commercialized strains have been registered as *B. subtilis* or *B. amyloliquefaciens*. However, according to recent re-classification based on phylogenetic analyses at the whole genome level, most of these strains actually belong to *B. velezensis* species (Dunlap et al., 2016). This is the case for the strains GBO3, MBI600, QST713, FZB42 or D747 mentioned in Table 2 (Fan et al., 2017a; Dunlap, 2019).

BSMs formed by *Bacillus* spp. originate either from classical ribosomal synthesis or from non-ribosomal synthesis involving mega-enzymatic complexes. *Bacillus* species are able to synthesize both ribosomal peptides that can be post-translationally modified (RiPPs) and non-ribosomal metabolites (Fig. 1) (Arguelles Arias et al., 2011).

Among RiPPs, *B. subtilis* and related species produce bacteriocins, including lantibiotics, (Abriouel et al., 2011; Lajis, 2020) such as plantazolicin, subtilin, ericin, mersacidin, amylolysin, subtilosin and amylocyclicin (Abriouel et al., 2011; Scholz et al., 2011, 2014; Arguelles Arias et al., 2013). Some antimicrobial peptides such as LCI peptides are also considered bacteriocin-like inhibitory substances because their structure has not been elucidated yet, or they cannot be classified in an existing group (Abriouel et al., 2011; Salazar et al., 2017).

Unlike RiPPs, non-ribosomally synthesized molecules seem to be much more conserved within the species. These molecules are synthesized by large modular enzymatic complexes (non ribsosomal peptide synthetases and polyketides synthetases) which are classified into two different types: non-ribosomal peptides (NRPs) and polyketides (PKs) (Dutta et al., 2014; Winn et al., 2016; Bozhüyük et al., 2019). These molecules are synthesized using amino acids (for NRPs) and carboxylic acids (for PKs) as building blocks (Chen et al., 2009a; Winn et al., 2016).

There are three main types of PKs produced by species of the *B. subtilis* group: bacillaene, difficidin and macrolactin (Chen et al., 2006; Caulier et al., 2019). Structural variants can often be coproduced by the same strain. For example, transcription of the difficidin operon results in the production of difficidin and its oxidized form oxydifficidin (Caulier et al., 2019). Cyclic lipopeptides (cLPs) of the iturin, surfactin, and fengycin families are the best-studied compounds among NRPs. These share amphiphilic properties due to a similar structure composed of a peptidic moiety (seven amino acids for iturins and surfactin, and ten amino acids in fengycin) linked to a fatty acid tail (ranging from 12 to 19 carbons) (Ongena and Jacques, 2008).

cLPs biosynthesis allows great structural diversity such as the incorporation of non-proteogenic amino acids or *D*-amino acids. Variants exhibiting differentiations in fatty acid chain length, branching type or amino acids

Table 2 Examples of *Bacillus*-based biocontrol agents commercialized for plant disease control (Lakshmanan et al., 2014; Fira et al., 2018; Rabbee et al., 2019; Borriss, 2020)

Product	*Bacillus* strain (species assignment)	Pathogens	Crops	Company
Amylo-X® WG	*B. amyloliquefaciens* D747	*Pseudomonas syringae, Monilinia spp, Stemphylium* spp., *Botrytis cinerea, Sclerotinia* spp., *Pezicula alba*	Vegetable cultivation, arboriculture, grapevine, mushroom, fruit trees	Certis EUROPE
DOUBLE NICKEL 55™	*B. amyloliquefaciens* D747	*Sphaerotheca fuliginea, Erysiphe cichoracearum, Phytophthora capsici; B. cinerea, Alternaria solani; Sclerotinia minor, Sclerotinia sclerotiorum, Rhizoctonia solani*	Cucumber, fruiting vegetable, grapevine, lettuce, potatoes	Certis USA, LLC
Eco-Shot	*B. amyloliquefaciens* D747	*Colletotrichum gloeosporioides, Podosphaera fuliginea, S. sclerotiorum, B. cinerea, Erysiphe polygoni, A. solani, Phyllosticta citricarpa, Cryptosporiopsis perennans*	Grape, citrus, vegetables, legumes	IHARA
Serifel®	*B. amyloliquefaciens* MBI 600	*B. cinerea, Sclerotinia* spp.	Grapes, tomato, lettuce, strawberry, mushroom, pepper, tobacco	BASF, Germany
Integral® Pro (SUBTILEX®)	*B. amyloliquefaciens* MBI 600	*Phoma* spp.	Rapeseed, *Brassicaceae*	BASF, Germany
FZB24®liquide	*B. amyloliquefaciens / velezensis* FZB42	*Rhizoctonia* spp., *Oidium* spp., *B. cinerea, Sclerotinia* spp, *Bremia* spp., *Fusarium* spp.	Potatoes, lettuce	Bayer Crop Science/ ABITEP
Taegro®	*B. amyloliquefaciens* FZB42	*Oidium* spp., *B. cinerea, Sclerotinia* spp., *Bremia* spp.	Strawberry, chicory, cucumber, lettuce, corn, salad, grapevine	Syngenta

Product	Bacillus strain	Target pathogens	Crops	Company
EcoGuard™ BIOFUNGICIDE	*B. licheniformis SB3086*	*Sclerotinia homoeocarpa, Pyricularia grisea, P. oryzae, Gloeocercospora sorghi, Puccinia graminis, Alternaria spp., Typhula spp., Microdochium nivale, Drechslera poae, Puccinia spp., Uramyces spp., Calletatrichum graminicola*	Turf, ornamental plants	Novozymes Biologicals, Inc.
Sonata®	*B. pumilus QST 2808*	*Oidium spp.*	Vegetable cultivation, tobacco, grapevine, fruit bush	Bayer Crop Science, previously AgraQuest
Ballad®	*B. pumilus QST 2808*	*Alternaria brassicae, oidium spp., Rhizoctonia oryzae, Xanthomonas spp., Puccinia sorghi, Erysiphe graminis, Puccinia spp., Xanthomonas spp., Sphaerotheca spp., Pseudomonas syringe, Cercospora spp.*	Oil seed crops, cereal grains, grass seed, sweet corn	Bayer Crop Science, previously AgraQuest
BSF4®	*B. subtilis BSF4*	*Erwinia amylovora, B. cinerea*	Pear, apple, strawberry, tomato, ornamental plants, lettuce	Agribiotec, Italy
Cease®	*B. subtilis QST 713*	*Peronospora belbahrii, B. cinerea, E. cichoracearum*	Ornamental plant, tomato, lettuce, celery, strawberry, tropical fruit, cannabis	BioWorks®
BIOBAC® WP	*B. subtilis BSY 1336*	*B. cinerea, Sclerotinia spp, Leveillula tarurica*	Tomato, grapevine, cherry, strawberry, pepper	Kuanghwa Chemical Co. Ltd., Taiwan
BACSTAR®	*B. subtilis D747*	*E. amylovora, B. cinerea, P. capsici*	Apple, pears, citrus, grapes, kiwifruit, strawberry, lettuce, onions, ornamental plant, turf	Certis USA, LLC

(Continued)

Table 2 Examples of *Bacillus*-based biocontrol agents commercialized for plant disease control (Lakshmanan et al., 2014; Fira et al., 2018; Rabbee et al., 2019; Borriss, 2020) (*Continued*)

| Product	*Bacillus* strain (species assignment)	Pathogens	Crops	Company
Companion®	*B. subtilis* GB03	*Sclerotinia* spp., *Rhizoctonia* spp., *Fusarium* spp.,*Aspergillus* spp.	Pod vegetable, cotton, peanuts, soybean, wheat, barley, corn, strawberry, grapes, tomatoes	Growth Products Ltd., USA
Kodiak ™	*B. subtilis* GB03	*Rhizoctonia* spp., *Fusarium* spp., *Alternaria* spp., *Aspergillus* spp.	Seed treatment , cotton, soybean, wheat, barley,	Bayer Crop Science, previously Gustafsson LLC
Serenade® ASO	*B. subtilis* QST 713	*B. cinerea, Oidium* spp., *Golovinomyces cichoracearum, Podosphaera* spp.	Fruit bush, vegetable cultivation, tomato, pepper	Bayer Crop Science, previously AgraQuest
Serenade® SOIL	*B. subtilis* QST 713	*Fusarium oxysporum, Pythium* spp., *Rhizoctonia* spp.	Root vegetables, bulb vegetables, leafy vegetables, *Brassicaceae,* fruiting vegetable, cucurbits	Bayer Crop Science, previously AgraQuest
Serenade® OPTI	*B. subtilis* QST 713	*Botrytis cinerea, Sclerotinia* spp., *G. cichoracearum, Podosphaera* spp., *Albugo candida, Oidium* spp., *Phytophthora* spp., *Peronospora* spp., *E. amylovora*	Stone fruits, garden beet, tomatoes, arboriculture, vegetable cultivation, fruit bush	Bayer Crop Science, previously AgraQuest
Serenade® MAX	*B. subtilis* QST 713	*B. cinerea, Oidium* spp., *Colletotrichum* spp., *Glomerella* spp.	Avocado, banana, mushroom, cucumber, ornamental plant, arboriculture, lettuce, melon, tomato, grapes	Bayer Crop Science, previously AgraQuest
Rhapsody®	*B. subtilis* QST713	*B. cinerea, Sclerotinia* spp., *Rhizoctonia* spp., *Fusarium* spp., *Pythium* spp., *Oidium* spp., *Monilinia* spp.	Vegetable cultivation, grapevine, fruit bush, ornamental plant, potatoes	Bayer Crop Science, previously AgraQuest
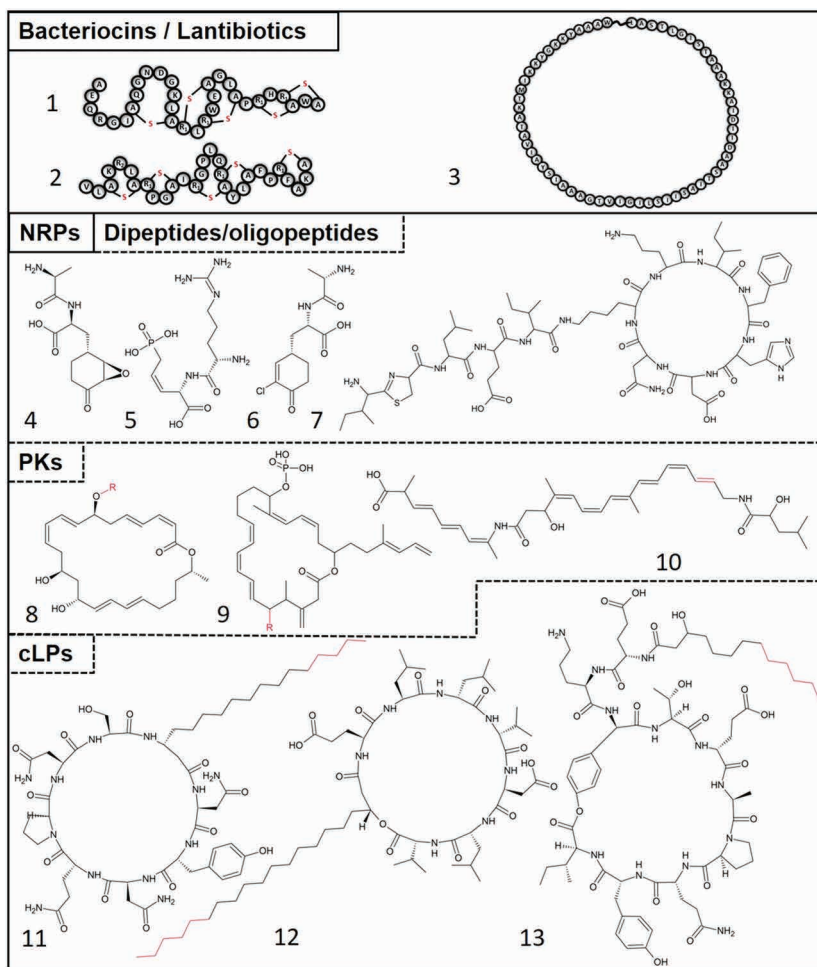
Figure 1 Overview of bioactive secondary metabolites (BSMs) produced by the *Bacillus subtilis* complex. The antimicrobial compounds can be synthesized by the classical ribosomal synthesis, such as the lantibiotics amylolysin (1, R1: aminobutyrate) or ericin A (2, R2: 2,3-didehydroalanine) and the cyclic bacteriocins amylocyclicin (**3**). Besides, some are produced by a non-ribosomal biosynthesis, the non-ribosomal peptides (NRPs), as the unusual peptides (dipeptides and oligopeptides), the cyclic lipopeptides (cLPs), and the polyketides (PKs). The dipeptides and oligopeptides include bacilysin (4), rhizocticin (5), chlorotetain (6), and bacitracin (7). The three main polyketides are synthetized by this genus, macrolactin (8, macrolactin A, R: H or $COCH_2COOH$ or $COCH_2CH_2COOH$), difficidin (9, R: H or OH for oxydifficidin) and bacillaene (10, unsaturated or bacillaene glycosylated or dihydrobacillaene glycosylated). Likewise, the three main families of cLPs produced by *Bacillus* sp. are iturin (11, iturin A, C13 to C17), surfactin (12, surfactin, C12 to C16) and fengycin (13, fengycin A, C14 to C19).

substitution can also be coproduced by the same strain. Surfactin is the only cLP that can be found in all species of the *B. subtilis* group. Some lipopeptides such as lichenysin or pumilacidin are specific to the producing species (*B. licheniformis* and *B. pumilus*, respectively). This structural diversity is also present in the iturin family, regrouping peptidic variants such as bacillomycin, iturin and mycosubtilin, or in the fengycin family that includes fengycin A, fengycin B and plipastatin (Ongena and Jacques, 2008; Raaijmakers et al., 2010; Caulier et al., 2019). Unlike surfactin, these two cLPs families are not produced by all members of the *B. subtilis* group and structural variants do not seem to be linked to the species (Andrić et al., 2020).

Several oligopeptides are known to be produced by non-ribosomal synthesis pathways, including bacilysin, chlorotetain, bacitracin and rhizocticin. These are not synthetized by the NRPS machinery and *de facto* are referred to as unusual peptides (Konz et al., 1997; Ming and Epperson, 2002; Rajavel et al., 2009).

4 *Bacillus* spp. biocontrol mechanisms: root colonization

The effectiveness of *Bacillus* spp. as a BCA relies on three main mechanisms that are (i) establishment on plant tissues, mainly roots, that prevent or reduce colonization of pathogens via competition, (ii) antibiosis towards microbial pathogens, (iii) induction of systemic resistance in the host plant.

Various approaches (comparative studies of strains with very different patterns, specific knock-out mutants, tests of purified molecules) have been used to understand the roles of the molecules involved in these mechanisms (Fig. 2).

4.1 Chemotaxis

Plant roots that provide physical support and nutrients via exudates are colonized by a plethora of microbes. As with other members of this root-associated microbiome, a successful *Bacillus* spp.-plant association is based on a fine-tuned molecular 'dialogue'. This is driven by root exudates, the composition which varies according to plant genotype and growth stage (Van Overbeek and Van Elsas, 2008; Zhang et al., 2013; Sasse et al., 2018). The proximity of the root is first sensed by the bacterium which moves towards root tissues via chemotaxis (Yssel et al., 2011; Sourjik and Wingreen, 2012). *B. velezensis* FZB42, for example, is attracted by root exudates of maize which act as a chemoattractant and facilitate motility and biofilm formation (Jin et al., 2019).

The presence of pathogens modifies root exudates, increasing their attractiveness for *Bacillus* spp. In cucumber plants infected by *F. oxysporum*

f. sp. *cucumerinum,* the proportion of chemoattractant compounds (citric acid and fumaric acid) is higher compared to non-infected plants, resulting in enhanced root colonization by *B. velezensis* SQR9 (Liu et al., 2014b, 2020). Better colonization of *B. velezensis* 32 on *Rhizobium radiobacter*-infected tomato roots has also been reported compared to uninfected seedlings, correlated with changes in root exudate composition (Abdallah et al., 2020). *Arabidopsis thaliana* foliar infection by *Pseudomonas syringae* also induced root secretion of L-malic acid*,* attracting *B. subtilis* FB17 and stimulating biofilm formation (Rudrappa et al., 2008). So far, up to ten specific chemoreceptors/chemoattractants of root exudate compounds, such as amino acids, organic acids or sugars, have been characterized in *B. subtilis* NCIB 3610 and *B. velezensis* SQR9 (Tan et al., 2013; Zhang et al., 2013; Allard-Massicotte et al., 2016; Feng et al., 2019).

4.2 Motility and biofilm formation

Biofilm formation capacity is widely distributed through the *Bacillus* genus. Biofilms can be defined as a multicellular community encased within an extracellular matrix of self-produced polymers such as exopolysaccharides and proteins (e.g. TasA or Bsla) (Vlamakis et al., 2013; Pandin et al., 2017). Exopolysaccharides promote mobility and nutrient capture. This form of communal life constitutes a divergent lifestyle of planktonic cells in which metabolism remodelling occurs through a complex regulatory network (Kearns et al., 2005; Pisithkul et al., 2019). Biofilms are composed of heterogeneous subpopulations organized through this regulator network. Different communities of cells are present in the same biofilm, including matrix-producing cells, surfactin-producing cells, flagellated motile cells and sporulated cells.

Biofilms provide a strong ecological advantage for *Bacillus* spp., promoting migration (Vlamakis et al., 2013; Flemming et al., 2016). They allow *Bacillus* spp. to colonize and survive on the surface of plant roots. *Bacillus* spp. have been shown to form biofilms on plant roots, for example, *B. velezensis* FZB42 on *Zea mays*, *A. thaliana* and *Lemna minor* plantlets (Fan et al., 2011). The plant stimulates biofilm formation both through root exudates and the presence of polysaccharides derived from the plant cell wall which act as signal molecules. Maize and cucumber root exudates, or individual exudate compounds such as glucose, fructose, citric acid, malic acid and fumaric acid, have been shown to stimulate biofilm formation in *B. velezensis SQR9* and in *B. velezensis* S3-1 (Zhang et al., 2015; Jin et al., 2019; Liu et al., 2020). Biofilm establishment is also triggered in the presence of pectin and arabinogalactan, two important plant polysaccharides, in *B. amyloliquefaciens* S499 and SQY 162, and *B. subtilis* NCIB 3610 (Beauregard et al., 2013; Debois et al., 2015; Wu et al., 2015a).
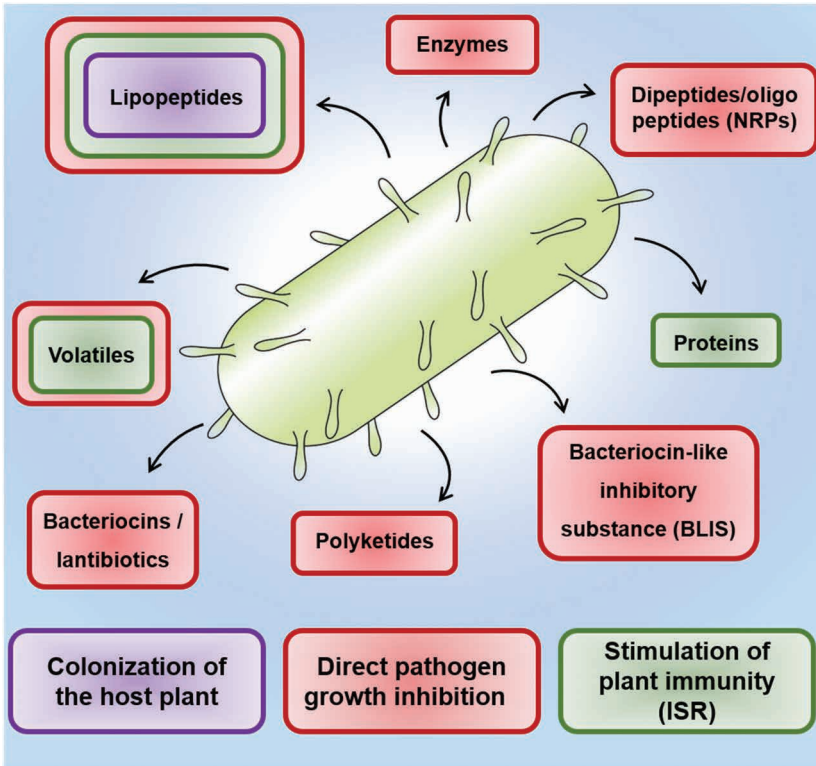
Figure 2 Implication of the different bioactive secondary metabolites (BSMs) in the three main mechanisms of plant protection: by colonization and competition for ecological niche/ substrate (in purple), by direct growth inhibition (in red) and/or as an elicitor of induced systemic resistance (ISR) (in green).

Some small-size BSMs, particularly those belonging to the lipopeptide family (especially surfactin), are essential in reducing surface tension and acting as a wetting agent. Surfactin helps to organize cells in bundles to increase biofilm surface area. When deprived of surfactin, for example, mutants of *B. subtilis* 6051 and OKB120 and *B. atrophaeus* ATCC 9372 show impaired biofilm formation (Bais et al., 2004; Aleti et al., 2016). Surfactin plays an important role in the ecological fitness of *Bacillus* spp. for root colonization, both as a surfactant and as a quorum-sensing (QS) molecule (Kearns et al., 2004; Chen et al., 2013; Aleti et al., 2016). Iturin and, to a lesser extent, fengycin have also been reported to facilitate biofilm formation. *In vitro* studies of *B. velezensis* Y6 have shown that these two lipopeptides play important roles in cell motility (Cao et al., 2018). In the case of *B. subtilis* 916, it has been suggested that bacillomycin L (a variant of the iturin family) and surfactin can synergistically contribute to biofilm formation and so to the ecological fitness of *Bacillus* spp.

(Luo et al., 2015). However, a recent study has shown that surfactin production is not required for biofilm formation by *B. subtilis* 3610 (Thérien et al., 2020). The lipopeptide arsenal of *B. subtilis* 3610 is less diverse and contains only surfactin. The involvement of surfactin in biofilm formation may be more complex than expected and could be linked to the lipopeptidome richness of each *Bacillus* species.

Biofilm lifestyle also allows *Bacillus* spp. to resist the presence of other microorganisms. Biofilms act as a fortress to block antimicrobials produced by other competitors (Flemming et al., 2016). The biofilm extracellular matrix has been shown to protect *B. subtilis* 3610 colonies from infiltration by competitors such as *Pseudomonas chlororaphis* (Molina-Santiago et al., 2019). Biofilm formation can also be boosted by the presence of other microorganisms. In *B. subtilis* ATCC6051, the expression of *sinR* and *tasA* genes involved in biofilm formation is modified in contact with the pathogen *Fusarium culmorum*, stimulating matrix multicellular production (Khezri et al., 2016). Biofilm formation also promotes the production of compounds involved in many biocontrol activities (Vlamakis et al., 2013; Pandin et al., 2019; Pisithkul et al., 2019). The biofilm extracellular matrix improves the competitiveness of *Bacillus* spp. in the rhizosphere and thus its biocontrol capability (Pandin et al., 2017). Deficiency in matrix production has been associated with a decrease in biocontrol efficacy by *B. subtilis* 3610 on tomato root against *R. solanacearum* (Chen et al., 2013) and by *B. subtilis* 6051 against *P. syringae* on *A. thaliana* (Bais et al., 2004).

5 *Bacillus* spp. biocontrol mechanisms: antagonistic activity

Bacillus spp. have great potential to control infection through direct inhibition of pathogen growth via antibiosis and/or by interfering with pathogen fitness, notably via quorum quenching (QQ). *Bacillus* spp. antimicrobial potential is related to the synthesis of different classes of metabolites, enzymes, and low-molecular-weight compounds including RiPPs, PKs, NRPs and volatiles (Fig. 2).

5.1 Enzymes

Antagonistic activities of enzymes rely on several modes of action, such as QQ or cell lysis. QQ is an important strategy in plant disease suppression by interfering with QS molecules used by most Gram-negative pathogens. As an example, lactonases, which interfere with the well-known QS molecules N-acyl–L-homoserine lactones (AHL), have been found in numerous *Bacillus* spp. and are considered as QQ enzymes (Dong et al., 2002; Chandra Kalia et al., 2011; Raafat et al., 2019). By blocking cross-talk (via degradation of AHL by QQ) of *P. syringae*, *B. cereus* INT1c reduces pathogen motility, leading to inefficient root

colonization (Ananda et al., 2019). QS interference by several *Bacillus* spp. has also been reported to decrease the hypersensitivity response of tomato plants caused by *P. syringae* due to degradation of pathogen AHLs (Jose et al., 2019).

A second enzymatic mode of action involves cell-wall-degrading enzymes. These include chitinases, which degrade chitin (a major component of fungal cell walls) and other enzymes such as chitosanases, glucanases, cellulases and lipases (Caulier et al., 2019; Miljaković et al., 2020). These lytic enzymes have been reported to reduce plant pathogen growth. Chitinase produced by *B. subtilis* ATCC1774 and *B. cereus* CRS7 decreases the growth of *Rhizoctonia solani* (Saber et al., 2015) and *B. cinerea*, respectively (Kishore and Pande, 2007). Alkaline protease purified from *B. amyloliquefaciens* SP1 and heterologously expressed in *Escherichia coli* has been reported to inhibit *F. oxysporum* growth (Guleria et al., 2016).

5.2 Bacteriocins and lantibiotics

Several RiPPs produced by *Bacillus* spp. are effective as antibacterial agents. Bacteriocins exhibit a broad spectrum of antibacterial activity acting by cell lysis, pore formation or inhibition of cell wall biosynthesis (Abriouel et al., 2011; Lajis, 2020). Bacteriocin activity has been occasionally reported against Gram-positive and Gram-negative bacterial plant pathogens. Amylocyclicin, produced by *B. velezensis* FZB42, appears to exhibit activity against *C. michiganensis*, while Bac IH7 and Bac14B inhibit the growth of *R. radiobacter* (formerly called *Agrobacterium tumefaciens*), and *Pseudomonas* spp., *E. carotovora* and *Alternaria solani* (Hammami et al., 2009, 2012; Scholz et al., 2014). LCI peptide, purified from *B. subtilis* A014 and considered as bacteriocin-like inhibitory substances, have antibacterial activities against *Xanthomonas campestris* and *R. solanacearum*. The APC2 protein, a so-called LCI-like peptide produced by *B. amyloliquefaciens* FS6, has been shown to prevent *Fusarium solani* infection (Gong et al., 2011; Fan et al., 2018; Saikia et al., 2019; Wang et al., 2020a).

5.3 Non-ribosomal metabolites

The activity of dipeptides and oligopeptides against plant pathogens has been little studied. Dipeptide bacilysin, a non-ribosomal synthesized molecule produced by *B. velezensis* FZB42, has been reported to inhibit growth of bacteria such as *Erwinia amylovora*, *Xanthomonas oryzae* and oomycete *P. infestans* (Chen et al., 2009b; Wu et al., 2015b; Caulier et al., 2018). PKs are known for their antibacterial activity. A mutant, for example, of *B. velezensis* FZB42, impaired in difficidin, has been found to inhibit *E. amylovora* (Chen et al., 2009b) and *X. oryzae* (Wu et al., 2015b) less than the wild-type strain. Purified macrolactin has also been reported to be active against *R. solanacearum* and *F.*

oxysporum (Yuan et al., 2012a). Bacillaene has been shown to protect *Bacillus* spp. cells against the degrading-enzymatic activity caused by competitors (*Streptomyces* sp. Mg1 and *Myxococcus xanthus*) (Barger et al., 2012; Müller et al., 2014, 2015). *Bacillus* PK type difficidin also shows antimicrobial activity, depending on the structure. The oxydifficidin derivative is approximately three times more active against *R. solanacearum* as compared to difficidin (Im et al., 2020) showing the importance of structural variations among *Bacillus* spp. BSMs.

The antimicrobial activity of lipopeptides is mainly related to members of the fengycin and iturin family. These two families have been reported to damage hyphae and conidia of several fungal pathogens including *F. graminearum* (Gu et al., 2017; Hanif et al., 2019) and *Monilinia fructicola* (Liu et al., 2011). The effects of lipopeptides depend on their amphiphilic nature and chemical structure. Fengycins are active against filamentous fungi such as *Rhizopus stolonifera* (Tao et al., 2011), *Magnaporthe grisea* (Zhang and Sun, 2018) or *R. solani* (Guo et al., 2014). Iturins are efficient not only against filamentous fungal pathogens such as *C. gloeosporioides* (Jin et al., 2020) and *Aspergillus flavus* (Gong et al., 2014) but also against the oomycete *P. infestans* (Wang et al., 2020c). Fengycin can also inhibit damaging mycotoxin synthesis produced by *F. graminearum* (Hanif et al., 2019). Iturins and fengycins are mainly active against fungi. However, the antibacterial activity of iturins and fengycins has also been occasionally reported against *X. campestris* and *Pectobacterium carotovorum* (Zeriouh et al., 2011) and *Xanthomonas axonopodis pv. vesicatoria* (Medeot et al., 2020) or *R. solanacearum* (Villegas-Escobar et al., 2018). Mode of actions of iturins and fengycins are still partially unknown but are most probably related to their capacity to disrupt fungal pathogens plasma membranes by forming pores, leading thus to cell death (Deleu et al., 2008; Wise et al., 2014; Zakharova et al., 2019). Small structural variations can impact bioactivity. Different homologues of bacillomycin D have thus different antimicrobial activities against the same pathogen according to the physiological stage of the fungi (Tanaka et al., 2015; Luna-Bulbarela et al., 2018). Differential activities of these variants can be viewed as a strategy by *Bacillus* spp. to increase the antibiotic spectra of one molecule family.

Surfactin has been found to have antimicrobial activity but in the 50–200 µM range, a higher concentration than in natural conditions (Jourdan et al., 2009; Raaijmakers et al., 2010; Debois et al., 2014; Liu et al., 2014a; Fan et al., 2017b; Sarwar et al., 2018). The inhibitory effect of surfactin is probably not due to direct antagonism but rather the interference with the colonization process of pathogens such as *P. syringae* (Bais et al., 2004) and *R. solanacearum* (Almoneafy et al., 2014). Even if surfactin cannot be considered as an antimicrobial molecule, it still has the ability to interact with biological membranes to induce structural modifications (Deleu et al., 2013). Its antimicrobial activity can be linked to a synergistic effect

with other cLPs. The combination of surfactin with bacillomycin D or mycosubtilin leads to more efficient control of *F. oxysporum* f. sp. *iridacearum* (Mihalache et al., 2018) and *B. cinerea* (Tanaka et al., 2015). Combining surfactin and fengycin is effective against *F. oxysporum* f. sp. *iridacearum* (Mihalache et al., 2018) and *P. infestans* (Wang et al., 2020c). Co-production of two antifungal compounds (i.e. iturins and fengycins) by *Bacillus* improves its antifungal properties since these antifungal compounds are active against different pathogens.

5.4 Volatiles

The antimicrobial activities of *Bacillus* spp. are also linked to volatiles. The most relevant group of volatiles are volatile organic compounds (VOCs) including alcohol, aldehydes, ketones, hydrocarbons, acids and terpenes. The majority of VOCs are derived from *Bacillus* spp. metabolic pathways such as 2-nonanone produced by β-oxidation of fatty acid (Korpi et al., 2009; Fincheira et al., 2017). Some of these metabolites have been reported to affect motility and biofilm formation of bacterial pathogens (Raza et al., 2016) and/or decrease fungal spore germination and growth (Yuan et al., 2012b). Antimicrobial activities of VOCs have been extensively studied (Caulier et al., 2019; Kai, 2020), including against fungal pathogens such as *Sclerotinia sclerotiorum* (Lim et al., 2017), *B. cinerea* (Jiang et al., 2018), *A. solani* (Zhang et al., 2020) or *M. fructicola* (Liu et al., 2018a). VOCs synthesized by *Bacillus* spp. also display antimicrobial activity against *R. solanacearum* such as 2-nonanone and 2-undecanone (Raza et al., 2016).

The BSM arsenal of *Bacillus* species such as *B. velezensis* includes many antimicrobials with broad-spectrum activity. However, recent studies strongly suggest no marked and durable effect of these bacteria on the microbiome of the treated crop (Correa et al., 2009; Chowdhury et al., 2013; Kröber et al., 2014; Qiao et al., 2017). Those bacilli thus provide protection to their host plant but have no detrimental effect on the microbiome, which is of prime interest for future application as BCAs.

6 *Bacillus* spp. biocontrol mechanisms: induced-systemic resistance

Bacillus spp. can protect plants by triggering an immune response which is systemically expressed in all organs of the host plant called induced systemic resistance (ISR) (Yu et al., 2017; Ranf, 2018; Schellenberger et al., 2019). ISR involves activation of a latent defence process called priming and characterized by activation of defence responses only after infection. Priming provides an enhanced level of protection and a faster/stronger activation of defences by the whole plant (Pieterse et al., 2014). ISR activated by *Bacillus*

spp. protects plants against a broad spectrum of pathogens (Köhl et al., 2019; Miljaković et al., 2020). ISR can, *de facto*, complement resistance induced by pathogen attack such as recognition of pathogen- or microbial-associated molecular patterns (PAMPs or MAMPs, respectively) (Van Wees et al., 2000). *Bacillus* spp. are not generally a source of MAMPs, even though some *Bacillus* spp. can trigger ISR in host plants (Vanthana et al., 2019; Rajamanickam and Nakkeeran, 2020). BSM induction of ISR by *Bacillus* spp. involves different types of metabolites, degradation products due to bacterial activity or secreted molecules and volatiles (Pršić and Ongena, 2020). However, the molecular mechanisms driving recognition of these elicitors of *Bacillus* spp., especially for BSMs, are poorly understood.

    Bacillus spp. can produce some protein elicitors of plant defence. The AMEP 412 protein in the *Bacillus* genus triggers ISR in tobacco against *P. syringae* pv. *Tomato* (Shen et al., 2019). The PeBA1 protein from *B. amyloliquefaciens* NC6 induces resistance in tobacco against infection by *B. cinerea* and by the tobacco mosaic virus (Wang et al., 2016).

    cLPs are key ISR elicitors in a range of pathosystems. Surfactin and, to a lesser extent, iturin or fengycin, are powerful inducers of plant systemic resistance (Crouzet et al., 2020). Application of surfactin at the root level decreases disease severity due to the necrotrophic fungus *B. cinerea* on bean, tomato and *A. thaliana* leaves (Ongena et al., 2007; Debois et al., 2015). A comparative analysis using different *Bacillus* strains revealed a strong correlation between the amounts of surfactin and its ability to trigger defence immunity in a plant (Cawoy et al., 2014). Studies with *B. velezensis* FZB42 surfactin deficient mutant demonstrated the importance of this lipopeptide in the induction of plant defences in lettuce against *R. solani* (Chowdhury et al., 2015b). ISR activation by surfactin has been reported for several other pathosystems such as melon/*Podosphaera fusca* (García-Gutiérrez et al., 2013) and wheat/*Z. tritici* (Le Mire et al., 2018). Several iturin variants have also been shown to trigger ISR in different pathosystems, such as strawberry/*C. gloeosporioides* (Yamamoto et al., 2015), chili pepper/*Phytophthora capsica* (Park et al., 2016) or wheat/ *Z. tritici* (Mejri et al., 2018). The iturin variant mycosubtilin has been reported to induce an immune response in grapevine against *B. cinerea* (Farace et al., 2015). Fengycin has been shown to trigger ISR in tomato against *B. cinerea* (Ongena et al., 2007), and more recently in grapevine and in tomato against *Plasmopara viticola* and *S. sclerotiorum*, respectively (Farzand et al., 2019; Li et al., 2019).

    Lipopeptide activity has been shown to be plant and even organ-dependent (Pršić and Ongena, 2020). Surfactin is more efficient on dicots than on monocots (Ongena et al., 2007; Rahman et al., 2015; Mejri et al., 2018). Iturin treatment is more efficient when applied on leaves rather than roots (Han et al., 2015; Yamamoto et al., 2015). Iturin and surfactin have been shown to trigger

an immune response by interacting with plant membrane lipids, but the precise mechanism remains unclear (Henry et al., 2011; Deleu et al., 2013; Fiedler and Heerklotz, 2015; Balleza et al., 2019). It appears that surfactin activity is related to plant plasma membrane composition and is also affected by lipopeptide structure. Structural changes in fatty acid chain length (long chains are more efficient), as well as the substitution in the peptidic cycle, modulate their ability to trigger ISR (Jourdan et al., 2009; Kawagoe et al., 2015).

Volatiles produced by *Bacillus* are also involved in the induction of plant immunity. Exposure of roots of *A. thaliana* seedlings to VOC mixtures, produced by *B. subtilis* GBO3 or by *B. amyloliquefaciens* IN937a, resulted in fewer lesions from the pathogen *E. carotovora* subsp. *carotovora* due to immune resistance induction (Ryu et al., 2004). The majority of cases showing VOCs as inducers of systemic resistance relate to acetoin and 2,3-butanediol (Ryu et al., 2004; Rudrappa et al., 2010; Peng et al., 2019). Commercially available compounds such as 3-pentanol are involved in the induced resistance in pepper plants against *X. axonopodis* pv. *vesicatoria* (Choi et al., 2014).

7 Factors influencing the production of bioactive secondary metabolites: cellular regulation

The conditions under which optimal production of BSMs is achieved by *Bacillus* spp. are still poorly understood and studied in a restricted number of metabolites. Evidence for efficient *in situ* production of these metabolites by *Bacillus* spp. inoculants mainly concerns lipopeptides. Surfactin and/or iturin have been recovered in biologically relevant quantities from cucumber roots inoculated with *B. velezensis* strain QST713 (Kinsella et al., 2009) and from the tomato rhizosphere after treatment with *B. subtilis* BGS3 (Ongena et al., 2007; Nihorimbere et al., 2009) and strain RB14-C (Asaka and Shoda, 1996). Surfactin synthesis *ad planta* by *B. velezensis* FZB42 has been demonstrated in Lemna plantlets (Fan et al., 2011) and in lettuce together with fengycin and bacillomycin (Chowdhury et al., 2015b). Fengycins and iturins have also been detected on leaves and in fruits, illustrating that these plant tissues may also support cLP biosynthesis (Touré et al., 2004; Romero et al., 2007; Zeriouh et al., 2011, 2014; Debois et al., 2015). This limited research on the production of BSMs under natural conditions reflects the inherent difficulties in detecting and quantifying these small-size compounds in complex environments like soil. These molecules can be chemically unstable, degraded by other (micro)organisms or adsorbed on the surface or within soil particles. Whether BSMs accumulate to biologically efficient concentrations in the rhizosphere is, therefore, still a matter of debate. However, it is crucial to measure such concentrations in order to better understand the real impact of these molecules in eliciting plant defences and/or in the direct biocontrol of pathogens.

Recent studies mainly on *B. subtilis* suggest that regulation of the expression of BGCs at the cellular level is quite complex, at least for NRP/PK products. It involves a range of pleiotropic regulators or transcription factors driving developmental processes such as QS, biofilm formation or sporulation. Natural conditions are also far from *in vitro* cultural conditions in artificial media. Root-associated bacteria feed almost exclusively on plant exudates, cross-communicate with other organisms (with positive or negative outcomes) and have to face multiple abiotic factors in the soil. Production of BSMs may, therefore, also be modulated by multiple ecological parameters.

The regulation of lipopeptides biosynthesis at the cellular level has been quite well studied. Two QS regulatory systems; that is, ComQXPA (Lopez et al., 2009) and Rap-Phr (Auchtung et al., 2006), are key players in surfactin regulation. Phosphorylated ComA is required to initiate *srfA* gene transcription, while the Rap phosphatases dephosphorylate ComA act as repressors. Additional transcription factors such as Spx (Zhang et al., 2006) or codY (Coutte et al., 2015) interfere with the role of ComA (Han et al., 2015) and others, such as ClpX/P, (Nakano et al., 2000) display a chaperone activity to facilitate ComA DNA binding. DegU, another master regulator, has also been shown to have a positive effect on surfactin production (Ogura, 2001). The AbrB/Abh system seems to affect lipopeptide synthesis in a more specific manner depending on the physiology of the cell (Zhi et al., 2017).

Environmental factors such as phosphate limitation or oxidative stress also have an impact on surfactin regulation via transcription factors such as PhoP and PerR (Ogura, 2001; Hayashi et al., 2005). The regulation of iturin and fengycin shares some regulators with surfactin. DegU, ComA, AbrB and GlnR, which are involved in glutamine synthesis (Koumoutsi et al., 2007; Zhang et al., 2017b; Xu et al., 2020), regulate iturin biosynthesis together with YczE, presumably acting at the post-transcriptional level (Koumoutsi et al., 2007; Dang et al., 2019). DegQ, PhoP and AbrB drive fengycin synthesis (Wang et al., 2015; Lu et al., 2016; Guo et al., 2018). Two extra-factors LutR and SinR, both involved in cellular mechanisms, are also positive regulators (İrigül-Sönmez et al., 2014).

The regulation of lantibiotics is determined by cell density. They act as autoinducing peptides via a typical two-component regulatory system composed of a sensor (histidine kinase) and a response regulator (LanRK) present in their operon (Kleerebezem et al., 2004; Schmitz et al., 2006).

The complexity of BSM regulation in *Bacillus* spp. is illustrated in the case of the dipeptide bacilysin. It involves several pleiotropic regulators depending on the physiological state of the cells in culture. In *B. subtilis*, bacilysin biosynthesis is under the control of the ComQXPA and PhrC QS system (Yazgan et al., 2001; Yazgan Karata et al., 2003). ComA binds directly to the promoter region of the *bac* operon and initiates a basal expression of this BGC (Köroğlu et al., 2011). The LutR regulon and the two interconnected regulators (DegU and DegQ) also

regulate bacilysin synthesis (Köroğlu et al., 2008; Mariappan et al., 2012). ComA may also act indirectly on bacilysin production by influencing DegU through DegQ activation. AbrB acts as a repressor of *bac* during the exponential growth phase, but its negative regulatory effect is silenced by Spo0A (Köroğlu et al., 2011). The other transcription factors CodY and ScoC also negatively regulate bacilysin production by binding directly to the promoter region.

Less information is available regarding PKS regulation. In *B. subtilis,* expression of the *bae* operon, which is the only PK cluster conserved among species of the *B. subtilis* complex (Fan et al., 2018), is under the control of several transcriptional regulators. Full expression of this operon requires ComA, DegU, the ScoC regulon and CodY, which binds multiple sites in the cluster (Belitsky and Sonenshein, 2013; Vargas-Bautista et al., 2014). The *dfn* and *mln* operons, responsible for the synthesis of the two other PKs (difficidin and macrolactin, respectively) are only present within the *B. velezensis* species, explaining the low number of studies dealing with their regulatory pathways. The antiterminator LoaP, encoded by a gene positioned directly upstream of the *dfn* operon, has been shown to regulate the transcriptional readthrough of termination sites located within the *dfn* and *mln* operons in *B. velezensis* (Goodson et al., 2017). Upon *loaP* deletion, the production of both difficidin and macrolactin is abolished, but bacillaene synthesis is fully conserved (Goodson et al., 2017). Difficidin production is also impaired in mutants not expressing the DegU regulator (Mariappan et al., 2012).

8 Factors influencing the production of bioactive secondary metabolites: biofilm formation

Agitated liquid cultures are commonly used to assess the effect of a given factor on secondary metabolite synthesis. However, the physiology of planktonic cells, when undergoing fast 'latence-exponential-stationary' growth typically observed in batch cultivation, does not reflect the physiology of bacteria developing in the close vicinity of roots. PGPR form biofilm-structured multicellular communities at the surface of roots in nutritionally limited conditions very different from the optimized laboratory conditions. The inoculated strain establishes on plant tissues as biofilm-structured patches. Biofilm formation is associated with the diversification of the cell community into sub-populations with distinct roles and activities (metabolically active vegetative cells, matrix producers, cannibals and spores). This formation results in phenotypic heterogeneity that may influence the synthesis of secondary metabolites (Nihorimbere et al., 2009).

The effect of biofilm formation on the pattern of lipopeptides produced by *B. amyloliquefaciens* has been assessed by growing the bacterium in static liquid cultures conducted in wells of microtiter plates. In these conditions, cells

readily aggregate to form pellicles at the liquid-air interface. LC-MS profiling of the secreted lipopeptides revealed clear differences compared to agitated cultures with enhanced production of surfactin production but not iturins and fengycins. The proportions of the three lipopeptide families were similar to those secreted after root colonization and clearly differed from planktonic cells secreting much higher amounts of iturins and fengycins (Nihorimbere et al., 2012; Debois et al., 2014). The formation of biofilm is accompanied by metabolic changes under the control of regulators such as SpoOA. These transcriptional modifications may also influence the production of BSMs like the *bacABCDEF* and *sbo-alb* operons coding, respectively, for bacilysin and subtilosin A that are up-regulated during biofilm formation (Pisithkul et al., 2019). The production of other BSMs under biofilm conditions has not yet been investigated.

The formation, organization and functioning of this complex multi-cellular structure have been extensively studied in *B. subtilis* and related species but almost exclusively *in vitro* by forming macrocolonies on gelified media or as pellicles developing at the air-liquid interface. However, biofilm formation on plant tissues is very different compared to an inert surface, taking into account interactions with the host. In natural conditions, *Bacillus* cells evolve in the middle of other microbes and interactions with other microbial species can modulate motility and biofilm formation (Andrić et al., 2020) (see below). Biofilm formation and functionality have been poorly investigated *in planta*, including all these biotic parameters that may interfere with this process. There is a need to develop new cultivation methods in the lab to mimic biofilm formation by bacterial cells colonizing roots or influenced by plant factors. This initially requires gnotobiotic conditions where the bacterium and the plant interact under controlled physico-chemical settings such as temperature and pH. Population diversification and phenotypic heterogeneity should be studied using fluorescent transcriptional reporters designed to highlight the phenotype of interest using confocal laser-scanning or other microscopy techniques. The use of flow cytometry on microbial cells extracted from biofilm structures may also provide a dynamic view of the microbial population of interest.

9 Factors influencing the production of bioactive secondary metabolites: abiotic factors

The potential of BCAs such as *Bacillus* spp. to produce BSMs has been, in most cases, evaluated *in vitro* using optimal growth conditions for key parameters such as temperature, pH and oxygen availability. However, these conditions fluctuate in soil and may significantly influence BSMs production *in planta*. Research so far has mainly focused on the impact of these abiotic factors on lipopeptide production.

Oxygen depletion is common in the rhizosphere due to consumption by roots and microbes (Dubern and Bloemberg, 2006). Under oxygen-starvation conditions, surfactin production remains unchanged, suggesting that a low oxygen level is not detrimental for surfactin synthesis in the rhizosphere (Nihorimbere et al., 2009, 2012). A positive effect of O_2 limitation has even been reported for surfactin production but under bioreactor conditions (Yeh et al., 2006; Yi et al., 2017). In contrast, expression of iturin and fengycin operons is O_2-dependent (Guez et al., 2008; Nihorimbere et al., 2012; Rangarajan et al., 2015).

Temperature stress is a key factor affecting basal and secondary metabolism production in microbes, significantly affecting the survival and effectiveness of plant-associated microbes used as microbial inoculants. Little is known about the effects of low or fluctuating temperature on the production of BSMs by *Bacillus* spp. Several studies have reported an increase in lipopeptide production with decreasing temperatures (Fickers et al., 2008; Pertot et al., 2013; Pereira Monteiro et al., 2016; Chen et al., 2019). Growth at low temperatures (15°C) led to a marked increase in surfactin production in comparison to high temperatures (>35°C) (Pertot et al., 2013). Low temperatures may affect the expression of ComK and further down-regulate genes coding for the RapF and RapH repressors of surfactin gene expression (Budde et al., 2006; Jacques, 2011). Enhanced production at low temperature may also rely on post-transcriptional events, such as NRPS protein turn-over or modifications in the lipopeptide export process (Fickers et al., 2008). Data from *in planta* assays performed in greenhouses have also suggested that enhanced surfactin production at low temperature may counter-balance the reduced growth of *B. amyloliquefaciens* S499 on roots, maintaining its ISR triggering potential under cold conditions (Pertot et al., 2013). The effect of cold/heat on the production of other *Bacillus* spp. lipopeptides has been little investigated but enhanced iturin synthesis by lowering the temperature from 37 to 25°C has been observed (Ohno et al., 1995; Jacques et al., 1999; Fickers et al., 2008). The consequences of temperature fluctuations on cLP production seem to vary between strains. Results obtained for surfactin in *B. velezensis* S499 and FZB42 could not be confirmed for *B. velezensis* QST713 (Pertot et al., 2013). It has also been shown that increased temperature can cause a higher production of surfactin in *B. velezensis* FJAT-46737 (Chen et al., 2020). Further investigation covering a wider range of temperatures and evaluating the impact on the whole secreted metabolome is required to better appreciate its impact on the production of BSMs.

The effect of pH on BSMs production is poorly documented. Surfactin production has been reported to be inhibited at pH 5 (Yi et al., 2017). Efficient synthesis of lipopeptides is favoured in mild-acidic to neutral environments, which is often the case for rhizosphere due to multiple processes related notably to plant exudation and root/microflora activity (Cosby et al., 1998; Akpa et al., 2001; Hinsinger et al., 2009; Wang et al., 2020a).

10 Factors influencing the production of bioactive secondary metabolites: biotic factors

10.1 Interactions with the host plant

Root exudates are primarily used as nutrients by plant-associated bacteria to sustain growth but may also stimulate flagella motility, chemotaxis and biofilm formation. They are, therefore, essential for rhizosphere establishment (Kierul et al., 2015; Pandin et al., 2017). The chemical nature of these exudates also influences the production of BSMs.

cLPs production is impacted both qualitatively and quantitatively by changes in exudate components. Carbon (C) sources in root exudates support *B. amyloliquefaciens* S499 growth. Surfactin secretion (but not iturin or fengycin) has been shown to be significantly higher in the presence of organic acids as compared to sugars (Nihorimbere et al., 2012). The relative proportions of different homologues may vary in relation to carbon sources. The synthesis of C_{15} surfactins is promoted in the presence of organic and amino acids compared to sugars.

In response to maize root exudates, the expression of genes involved in the synthesis of bacillaene, difficidin, macrolactin, fengycin and surfactin was up-regulated in *B. velezensis* FZB42 and in *B. velezensis* SQR9 (Fan et al., 2012; Zhang et al., 2015). Root exudates of *Eruca sativa* (rocket salad) have been shown to induce *pks* operon expression, responsible for bacillaene synthesis in *B. subtilis*, allowing the bacterium to attack other root-associated bacteria (Ogran et al., 2019). In *B. velezensis* SQR9, comparative proteomic analysis revealed that PKs, fengycin and surfactin were overproduced upon colonization of cucumber roots (Qiu et al., 2014).

Physical contact with the root surface and, more specifically, perception of plant polymers may initiate processes such as biofilm formation in *Bacillus* species. It has been shown that polymers of the plant cell wall (xylan, pectin) also act as cues for triggering the synthesis of surfactin (Beauregard et al., 2013; Debois et al., 2015; Wu et al., 2015a). The *srfAA* gene is induced when *Bacillus* spp. are placed in contact with rice seedlings (Xie et al., 2015). As surfactin is involved in swarming motility and biofilm formation, improved production may contribute to spread on root tissues and aggregation in biofilm-related multicellular communities.

10.2 Interactions with microbial pathogens

Bacillus spp. have to compete with other microorganisms in the rhizosphere. *Bacillus* spp. thus have to adapt and improve their ecological fitness by modulating BSM production in response to fungal and bacterial competitors. The presence of chitin or S-glucan has been found to increase the production of fungal cell wall

degrading enzymes such as chitinase and glucanases by *B. subtilis* JF419701, (Alamri, 2015). It has been shown that co-cultures between plant beneficial bacilli and oomycetes or fungi (including *P. aphanidermatum*, *F. oxysporum* or *S. sclerotiorum*) increase iturin and fengycin production, both known for their antifungal properties (Cawoy et al., 2015; Farzand et al., 2020). Fengycin synthesis by *B. velezensis* S499 has also been reported to be upregulated in the presence of *Rhizomucor variabilis*, suggesting that the bacterium is able to perceive some molecular trigger(s) emitted by the pathogen (Zihalirwa Kulimushi et al., 2017).

In addition to these two antifungal cLPs, surfactin production has also been induced when *Bacillus* spp. are confronted to *Phytophthora parasitica*, *R. solani*, *F. solani*, *S. sclerotiorum*, *R. stolonifera, Fusarium sambucinum and Trichoderma aggressivum* (Chowdhury et al., 2013; DeFilippi et al., 2018; Pandin et al., 2019). Surfactin overproduction could promote competition for nutrients and space (Molina-Santiago et al., 2019; Andrić et al., 2020). Surfactin is involved in QS, stimulates biofilm formation, and contributes to plant root colonization (Kinsinger et al., 2003; Lopez et al., 2009; Raaijmakers et al., 2010). The isoform profile of cLPs changes depending on the competitor pathogen (Cao et al., 2018; DeFilippi et al., 2018). This suggests that bacteria modulate BSM synthesis depending on signals emitted by specific fungal pathogens (Frey-Klett et al., 2011).

Variation in BSM production in response to bacterial competitors has been poorly studied and mostly limited to transcriptional analyses. Expression of genes belonging to iturin, fengycin and surfactin operons has been shown to be up-regulated in the presence of *R. solanacearum* (Almoneafy et al., 2014; Cao et al., 2018). Expression of lipopeptide operons and bacilysin in *B. velezensis* BK7 has been reported to be significantly upregulated in the presence of *Pseudomonas fuscovaginae* (Kakar et al., 2014). Bacterial competitors also stimulate *B. subtilis* motility and biofilm formation, but the causal link between overproduction of biofilm in the presence of some competitors and surfactin production has not yet been demonstrated (Grau et al., 2015; van Gestel et al., 2015; Liu et al., 2018c).

11 Interactions of *Bacillus* spp. with other beneficial microorganisms and their use in biocontrol

Interactions between *Bacillus* spp. and other microorganisms do not always lead to competition and antagonism but may be compatible and result in synergistic effects. The application of *Bacillus* spp. with other beneficial microbes has thus emerged as a promising biocontrol strategy.

Synergistic effects in protecting plants against pathogens and promoting growth have been reported using combinations of *Bacillus* spp. with *Trichoderma* species (Wu et al., 2018; Karuppiah et al., 2019; Izquierdo-García et al., 2020), another BCA acting via competition, mycoparasitism, antibiosis

and triggering of ISR (Vinale et al., 2008; Ghorbanpour et al., 2018). Higher production of BSMs, as well as cryptic compounds (depending on specific conditions), has also been reported in liquid co-cultivation of *B. subtilis* 22 and *Trichoderma atroviride* SG3403 as compared with the two microorganisms cultivated individually (Li et al., 2020).

Arbuscular mycorrhizal (AM) fungi are also key microorganisms in soil, forming symbiotic associations with more than 70% of vascular plant species (Brundrett and Tedersoo, 2018). They improve plant nutrition (mainly phosphorus and nitrogen) and water uptake. Plants forming associations with these soil fungi have been found to resist biotic and abiotic stresses better (Bonfante and Genre, 2010; Plouznikoff et al., 2016; Mathieu et al., 2018), partly due to the ability of AM fungi to induce ISR (Gallou et al., 2011, 2012; Fiorilli et al., 2018; Deja-Sikora et al., 2020). Some synergies and improved functionality of PGPR-AM fungi consortia have been reported for plant growth and health (Armada et al., 2018; Zhang et al., 2018; Yadav et al., 2020). Co-inoculation of *B. subtilis* or *B. amyloliquefaciens* with AM fungi did not affect fungal growth but improved resistance to biotic and abiotic stresses due to more efficient nutrient supply in *Artemisia annua* L., *Allium sativum* L. and *Triticum aestivum* L. (Awasthi et al., 2011; Agnolucci et al., 2019; Rashad et al., 2020; Yadav et al., 2020). Metabolism markers such as succinate dehydrogenase and alkaline phosphatase showed a positive impact of *Bacillus* spp. on AM fungi metabolism (Vivas et al., 2003). However, there remains a lack of data demonstrating enhanced biocontrol activity of formulations combining bacilli and AM fungi.

Co-inoculation of *Bacillus* spp. with bacteria belonging to the *Pseudomonas* or *Streptomyces* genera is also promising. These BCA species are competitors, producing antimicrobials affecting *Bacillus* growth. Antagonistic interactions have been reported between *Pseudomonas protegens* PF-5 and *B. subtilis* NCIB3610 (Powers et al., 2015; Molina-Santiago et al., 2019) or between *Streptomyces* sp. MG1 and *B. subtilis* 3610 (Barger et al., 2012; Traxler and Kolter, 2015). However, co-inoculation of *B. licheniformis* B642 and the beneficial *Pseudomonas fluorescens* strain FAP2 may have beneficial effects on the host plant (Ansari and Ahmad, 2019). The combination of these two genera enhanced resistance against *X. campestris* pv. *campestris* compared to their use individually (Mishra and Arora, 2012). The combination of *B. subtilis* GBO3 with *P. fluorescens* CECT 5398 has been shown to improve the control of *F. oxysporum* and *R. solani* in tomato and pepper (Domenech et al., 2006). However, the molecular basis underpinning synergistic effects still remains to be deciphered.

Combining strains belonging to the *Bacillus* genus can also enhance disease suppression. The combination of *B. amyloliquefaciens, B. sphaericus, B. pumilus* strains or of *B. altitudinis and B. velezensis* strains exhibited higher levels of biocontrol against *X. axonopodis* pv. *vesicatoria*, *P. syringae* pv. *tomato*

and *R. solanacearum* on tomato but also against *Pythium ultimum* and cucumber mosaic virus on cucumber compared single bacteria (Jetiyanon and Kloepper, 2002; Liu et al., 2018b). Studies in greenhouses have demonstrated that a mixture of *Bacillus* species (*B. pumilus* and *B. amyloliquefaciens*) significantly improved control of *P. capsici* on squash compared to individual strains (Zhang et al., 2010).

Some products combining other PGPR species with *Bacillus* spp. have been commercialized as BCAs. Products include LS213 by Gustafson Inc. (combining *B. subtilis* strain GB03 and *B. amyloliquefaciens* strain IN937a), Bio Protector by Bacto Agro Culture Care Pvt Ltd (2 strains of *Trichoderma*, *Ps. fluorescens* and *B. subtilis*) or BioYield™ by Bayer Crop Science (*B. amyloliquefaciens* GB99 + *B. subtilis GB12*), though most are described as biofertilizers or biostimulants (Domenech et al., 2006; Woo et al., 2014; Le Mire et al., 2016; Borriss, 2020).

Further research is needed to better understand the molecular dialogue existing between *Bacillus* and other BCAs to evaluate factors that inhibit or enhance synergistic interactions. Interaction-mediated variations in colony morphology, motility, biofilm formation, or sporulation illustrate how soil bacilli can protect themselves from antimicrobials emitted by bacterial competitors. The effect on these developmental processes could be coupled with significant modulation in the production of specific BSMs. These BSMs would then act as antimicrobials or in promoting cooperative interspecies communication processes which do not affect growth (Bleich et al., 2015; Liu et al., 2018c). This understanding would help design combinations of *Bacillus* with other microbes for more efficient biocontrol products.

12 Conclusions and future trends

The potential of some *Bacillus* species to control plant diseases caused by a range of pathogens has been amply demonstrated from lab to field, and selected isolates have been successfully commercialized. However, as for other microorganisms, the success of *Bacillus*-based products has been hampered by their highly variable or poor performance across agro-ecological environments and host plant species. There is a need to optimize/adapt their production and formulation (addition of prebiotics) at an industrial scale. It is also crucial to improve our basic knowledge of the processes influencing the expression of biocontrol traits and their persistence in plants following application in the field.

The biocontrol potential of *Bacillus* species mostly relies on their capacity to synthesize a wide range of BSMs involved in the three processes underpinning biocontrol. Some BSMs viewed as 'specialized' metabolites having a single main function may actually play multiple roles. As illustrated for surfactin, many BSMs may be multifunctional and act as signals or antimicrobials depending on the concentration. It is necessary to combine

approaches such as loss/gain of functions of mutants and the effect of purified BSMs to clearly identify bioactivities, depending on the concentration and the type of microbial pathogen (for antagonism) or plant genotype (for ISR). Better characterization of the molecular mechanisms of key bioactivities compounds acting individually or in combination is required if we want to understand why they inhibit some pathogens but not others or why they can stimulate immunity in some plants but not others. There is a need to combine carefully designed biotests with other approaches such as experimental and *in silico* biophysics to investigate effects on cellular membranes (depending on lipid composition) and thus on the target organism (Deleu et al., 2014; Balleza et al., 2019).

As they can be affected by abiotic factors and multitrophic interactions, we also need to improve our knowledge on the timing, amount and diversity of BSMs when produced *in planta* under natural conditions. This would help to understand whether these BSMs act as signals at sub-inhibitory concentrations or if they can play antimicrobial functions upon reaching threshold amounts at least locally around the plant tissues. It will also help in determining to what extent effects differ according to plant species, age and physico-chemical conditions. We need to develop new *ex vivo* approaches and exploit technologies like imaging mass spectrometry to spatiotemporally resolve the dynamics of production of those small molecules produced upon colonization or during microbial interspecies interactions (Debois et al., 2014; Boughton et al., 2016; Spraker et al., 2020).

Integrating all those data is necessary to predict the pathosystems against which these bacilli would work as BCAs. This will benefit the practical use of *Bacillus*-based products as sprays to treat aerial parts of the plants or as soil inoculants to protect seedlings from attack by soil-borne microbial pathogens. Even if results are promising (Parnell et al., 2016; Meng and Hao, 2017), prophylactic applications such as soil drenching or seed coating to protect crops in the first stage of their development remain a major challenge for large-scale biocontrol, notably for cereals.

B. velezensis is among the best candidate species for the development of biocontrol agents. Several products with different strains of this species are already on the market (Table 2) but all these strains are genetically close and have a similar arsenal of bioactive metabolites. Soil represents an un-tapped reservoir from which new *Bacillus* species/strains forming unknown but highly active compounds can be isolated, based on rationally designed screening procedures (Köhl et al., 2019).

Another attractive alternative is the development of products with *Bacillus* spp. metabolites as active ingredients (Glare et al., 2012; Heimpel and Mills, 2017). Lipopeptides are naturally formed in high amounts by species such as *B. subtilis* and *B. velezensis* and optimization of their production in bioreactors

at pilot scale has been thoroughly investigated (Rangarajan et al., 2015; Motta Dos Santos et al., 2016; Brück et al., 2019). There are methods available for extraction and (semi-)purification, allowing cost-effective processes to obtain bio-sourced products with reasonable purity and good stability (Coutte et al., 2017). If formulated metabolites are developed, their (eco-)toxicological risks need to be carefully assessed in relation to doses used to treat crops and stability in the environment.

13 Funding

14 Where to look for further information

The International Organisation for biological and integrated control (IOBC) is a very active society headed by (academic)experts in the field who organizes symposia, workshops, and congresses on all aspects of the biocontrol science. The website https://www.iobc-wprs.org/ also provides valuable information on integrated production and integrated pest management.

For more information about the biocontrol industry and a comprehensive view of biocontrol technologies are used (or being developed) as alternatives to control pests and diseases effectively in an environmental friendly way in agriculture, forestry: https://ibma-global.org/

15 References

Abdallah, D. B., Krier, F., Jacques, P., Tounsi, S. and Frikha-Gargouri, O. (2020). *Agrobacterium tumefaciens* C58 presence affects Bacillus velezensis 32a ecological fitness in the tomato rhizosphere, *Environ. Sci. Pollut. Res. Int.* 27(22), 28429–28437. doi: 10.1007/s11356-020-09124-1.

Abriouel, H., Franz, C. M. A. P., Omar, N. and Gálvez, A. (2011) Diversity and applications of *Bacillus bacteriocins*, *FEMS Microbiol. Rev.* 35(1), 201–232. doi: 10.1111/j.1574-6976.2010.00244.x.

Agnolucci, M., Avio, L., Pepe, A., Turrini, A., Cristani, C., Bonini, P., Cirino, V., Colosimo, F., Ruzzi, M. and Giovannetti, M. (2019). Bacteria associated with a commercial

mycorrhizal inoculum: community composition and multifunctional activity as assessed by illumina sequencing and culture-dependent tools, *Front. Plant Sci.* 9(1956), 1–13. doi: 10.3389/fpls.2018.01956.

Ait Bahadou, S., Ouijja, A., Karfach, A., Tahiri, A. and Lahlali, R. (2018). New potential bacterial antagonists for the biocontrol of fire blight disease (*Erwinia amylovora*) in Morocco, *Microb. Pathog.* 117, 7–15. doi: 10.1016/j.micpath.2018.02.011.

Akpa, E., Jacques, P., Wathelet, B., Paquot, M., Fuchs, R., Budzikiewicz, H. and Thonart, P. (2001). Influence of culture conditions on lipopeptide production by *Bacillus subtilis*, *Appl. Biochem. Biotechnol.* 91–93, 551–561. doi: 10.1385/ABAB:91-93:1-9:551.

Alamri, S. A. (2015). Enhancing the efficiency of the bioagent *Bacillus subtilis* JF419701 against soil-borne phytopathogens by increasing the productivity of fungal cell wall degrading enzymes, *Arch. Phytopathol. Plant Prot.* 48(2), 159–170. doi: 10.1080/03235408.2014.884671.

Aleti, G., Lehner, S., Bacher, M., Compant, S., Nikolic, B., Plesko, M., Schuhmacher, R., Sessitsch, A. and Brader, G. (2016). Surfactin variants mediate species-specific biofilm formation and root colonization in Bacillus, *Environ. Microbiol.* 18(8), 2634–2645. doi: 10.1111/1462-2920.13405.

Allard-Massicotte, R., Tessier, L., Lécuyer, F., Lakshmanan, V., Lucier, J. F., Garneau, D., Caudwell, L., Vlamakis, H., Bais, H. P. and Beauregard, P. B. (2016). *Bacillus subtilis* early colonization of *Arabidopsis thaliana* roots involves multiple chemotaxis receptors, *mBio* 7(6), 1–10. doi: 10.1128/mBio.01664-16.

Almoneafy, A. A., Kakar, K. U., Nawaz, Z., Li, B., Saand, M. A., Chun-lan, Y. and Xie, G.-L. (2014). Tomato plant growth promotion and antibacterial related-mechanisms of four rhizobacterial Bacillus strains against *Ralstonia solanacearum*, *Symbiosis* 63(2), 59–70. doi: 10.1007/s13199-014-0288-9.

Ananda, M., Rusmana, I. and Akhdiya, A. (2019). Quorum quenching of *Bacillus cereus* INT1c against *Pseudomonas syringae*, *J. Phys. Conf. Ser.* 1277(012010), 1–9. doi: 10.1088/1742-6596/1277/1/012010.

Andrić, S., Meyer, T. and Ongena, M. (2020). Bacillus responses to plant-associated fungal and bacterial communities, *Front. Microbiol.* 11(1350), 1350. doi: 10.3389/fmicb.2020.01350.

Ansari, F. A. and Ahmad, I. (2019). Fluorescent Pseudomonas -FAP2 and *Bacillus licheniformis* interact positively in biofilm mode enhancing plant growth and photosynthetic attributes, *Sci. Rep.* 9(1), 4547. doi: 10.1038/s41598-019-40864-4.

Arguelles Arias, A., Craig, M. and Fickers, P. (2011). Gram-positive antibiotic biosynthetic clusters: a review, In: Mendez-Vilas, (ed) *Science Against Microbial Pathogens: Communicating Current Research and Technological Advances*, 977–986.

Arguelles Arias, A., Ongena, M., Devreese, B., Terrak, M., Joris, B. and Fickers, P. (2013). Characterization of amylolysin, a novel lantibiotic from *Bacillus amyloliquefaciens* GA1, *Plos One* 8(12), e83037. doi: 10.1371/journal.pone.0083037.

Armada, E., Leite, M. F. A., Medina, A., Azcón, R. and Kuramae, E. E. (2018). Native bacteria promote plant growth under drought stress condition without impacting the rhizomicrobiome, *FEMS Microbiol. Ecol.* 94(7), 1–13. doi: 10.1093/femsec/fiy092.

Asaka, O. and Shoda, M. (1996). Biocontrol of *Rhizoctonia solani* damping-off of tomato with *Bacillus subtilis* RB14, *Appl. Environ. Microbiol.* 62(11), 4081–4085. doi: 10.1128/AEM.62.11.4081-4085.1996.

AQ: Please provide the publisher details for ref. "Arguelles Arias et al. (2011)".

Auchtung, J. M., Lee, C. A. and Grossman, A. D. (2006). Modulation of the ComA-dependent quorum response in *Bacillus subtilis* by multiple rap proteins and phr peptides, *J. Bacteriol.* 188(14), 5273–5285. doi: 10.1128/JB.00300-06.

Awasthi, A., Bharti, N., Nair, P., Singh, R., Shukla, A. K., Gupta, M. M., Darokar, M. P. and Kalra, A. (2011). Synergistic effect of Glomus mosseae and nitrogen fixing *Bacillus subtilis* strain Daz26 on artemisinin content in *Artemisia annua* L., *Appl. Soil Ecol.* 49(1), 125–130. doi: 10.1016/j.apsoil.2011.06.005.

Backer, R., Rokem, J. S., Ilangumaran, G., Lamont, J., Praslickova, D., Ricci, E., Subramanian, S. and Smith, D. L. (2018). Plant growth-promoting rhizobacteria: context, mechanisms of action, and roadmap to commercialization of biostimulants for sustainable agriculture, *Front. Plant Sci.* 9(1473), 1473. doi: 10.3389/fpls.2018.01473.

Bais, H. P., Fall, R. and Vivanco, J. M. (2004). Biocontrol of *Bacillus subtilis* against infection of Arabidopsis roots by *Pseudomonas syringae* is facilitated by biofilm formation and surfactin production, *Plant Physiol.* 134(1), 307–319. doi: 10.1104/pp.103.028712.

Balleza, D., Alessandrini, A. and Beltrán García, M. J. (2019). Role of lipid composition, physicochemical interactions, and membrane mechanics in the molecular actions of microbial cyclic lipopeptides, *J. Membr. Biol.* 252(2–3), 131–157. doi: 10.1007/s00232-019-00067-4.

Bardin, M., Ajouz, S., Comby, M., Lopez-Ferber, M., Graillot, B., Siegwart, M. and Nicot, P. C. (2015). Is the efficacy of biological control against plant diseases likely to be more durable than that of chemical pesticides?, *Front. Plant Sci.* 6(566), 566. doi: 10.3389/fpls.2015.00566.

Barger, S. R., Hoefler, B. C., Cubillos-Ruiz, A., Russell, W. K., Russell, D. H. and Straight, P. D. (2012). Imaging secondary metabolism of Streptomyces sp. Mg1 during cellular lysis and colony degradation of competing *Bacillus subtilis*, *Antonie Leeuwenhoek* 102(3), 435–445. doi: 10.1007/s10482-012-9769-0.

Beauregard, P. B., Chai, Y., Vlamakis, H., Losick, R. and Kolter, R. (2013). Bacillus biofilm induction by plant polysaccharides, *Proc. Natl. Acad. Sci. U. S. A.* 110(17), E1621–E1630. doi: 10.1073/pnas.1218984110.

Belitsky, B. R. and Sonenshein, A. L. (2013). Genome-wide identification of *Bacillus subtilis* CodY-binding sites at single-nucleotide resolution, *Proc. Natl. Acad. Sci. U. S. A.* 110(17), 7026–7031. doi: 10.1073/pnas.1300428110.

Berikashvili, V., Sokhadze, K., Kachlishvili, E., Elisashvili, V. and Chikindas, M. L. (2018). *Bacillus amyloliquefaciens* spore production under solid-state fermentation of lignocellulosic residues, *Probiotics Antimicrob. Proteins* 10(4), 755–761. doi: 10.1007/s12602-017-9371-x.

Beris, D., Theologidis, I., Skandalis, N. and Vassilakos, N. (2018). *Bacillus amyloliquefaciens* strain MBI600 induces salicylic acid dependent resistance in tomato plants against Tomato spotted wilt virus and Potato virus Y, *Sci. Rep.* 8(1), 10320. doi: 10.1038/s41598-018-28677-3.

Bleich, R., Watrous, J. D., Dorrestein, P. C., Bowers, A. A. and Shank, E. A. (2015). Thiopeptide antibiotics stimulate biofilm formation in *Bacillus subtilis*, *Proc. Natl. Acad. Sci. U. S. A.* 112(10), 3086–3091. doi: 10.1073/pnas.1414272112.

Bonfante, P. and Genre, A. (2010). Mechanisms underlying beneficial plant–fungus interactions in mycorrhizal symbiosis, *Nat. Commun.* 1(48), 48. doi: 10.1038/ncomms1046.

Borel, B. (2017). CRISPR, microbes and more are joining the war against crop killers, *Nature* 543(7645), 302–304. doi: 10.1038/543302a.

Borriss, R. (2020). Phytostimulation and biocontrol by the plant-associated *Bacillus amyloliquefaciens* FZB42: an update. In: Kumar, M., Kumar, V. and Prasad, R. (eds) *Phyto-Microbiome in Stress Regulation. Environmental and Microbial Biotechnology*. Springer, Singapore, 1–20. doi: 10.1007/978-981-15-2576-6_1.

Boughton, B. A., Thinagaran, D., Sarabia, D., Bacic, A. and Roessner, U. (2016). Mass spectrometry imaging for plant biology: a review, *Phytochem. Rev.* 15(3), 445–488. doi: 10.1007/s11101-015-9440-2.

Bozhüyük, K. A., Micklefield, J. and Wilkinson, B. (2019). Engineering enzymatic assembly lines to produce new antibiotics, *Curr. Opin. Microbiol.* 51, 88–96. doi: 10.1016/j.mib.2019.10.007.

Brück, H. L., Delvigne, F., Dhulster, P., Jacques, P. and Coutte, F. (2019). Molecular strategies for adapting *Bacillus subtilis* 168 biosurfactant production to biofilm cultivation mode, *Bioresour. Technol.* 293, 1–8. doi: 10.1016/j.biortech.2019.122090.

Brundrett, M. C. and Tedersoo, L. (2018). Evolutionary history of mycorrhizal symbioses and global host plant diversity, *New Phytol.* 220(4), 1108–1115. doi: 10.1111/nph.14976.

Budde, I., Steil, L., Scharf, C., Völker, U. and Bremer, E. (2006). Adaptation of *Bacillus subtilis* to growth at low temperature: a combined transcriptomic and proteomic appraisal, *Microbiology (Reading)* 152(3), 831–853. doi: 10.1099/mic.0.28530-0.

Cao, Y., Pi, H., Chandrangsu, P., Li, Y., Wang, Y., Zhou, H., Xiong, H., Helmann, J. D. and Cai, Y. (2018). Antagonism of two plant-growth promoting *Bacillus velezensis* isolates against *Ralstonia solanacearum* and *Fusarium oxysporum*, *Sci. Rep.* 8(1), 4360. doi: 10.1038/s41598-018-22782-z.

Caulier, S., Gillis, A., Colau, G., Licciardi, F., Liépin, M., Desoignies, N., Modrie, P., Legrève, A., Mahillon, J. and Bragard, C. (2018). Versatile antagonistic activities of soil-borne *Bacillus* spp. and *Pseudomonas* spp. against *Phytophthora infestans* and other potato pathogens, *Front. Microbiol.* 9(143), 143. doi: 10.3389/fmicb.2018.00143.

Caulier, S., Nannan, C., Gillis, A., Licciardi, F., Bragard, C. and Mahillon, J. (2019). Overview of the antimicrobial compounds produced by members of the *Bacillus subtilis* group, *Front. Microbiol.* 10(302), 302. doi: 10.3389/fmicb.2019.00302.

Cawoy, H., Bettiol, W., Fickers, P. and Ongena, M. (2011). Bacillus-based biological control of plant diseases. In: *Pesticides in the Modern World–Pesticides Use and Management*. InTechOpen, London. doi: 10.5772/17184.

Cawoy, H., Debois, D., Franzil, L., De Pauw, E., Thonart, P. and Ongena, M. (2015). Lipopeptides as main ingredients for inhibition of fungal phytopathogens by *Bacillus subtilis*/amyloliquefaciens, *Microb. Biotechnol.* 8(2), 281–295. doi: 10.1111/1751-7915.12238.

Cawoy, H., Mariutto, M., Henry, G., Fisher, C., Vasilyeva, N., Thonart, P., Dommes, J. and Ongena, M. (2014). Plant defense stimulation by natural isolates of Bacillus depends on efficient surfactin production, *Mol. Plant Microbe Interact.* 27(2), 87–100. doi: 10.1094/MPMI-09-13-0262-R.

Chandra Kalia, V., Raju, S. C. and Purohit, H. J. (2011). Genomic analysis reveals versatile organisms for quorum quenching enzymes: acyl-homoserine lactone-acylase and -Lactonase, *Open Microbiol. J.* 3, 1–13. doi: 10.2174/1874285801105010001.

Chen, J. (2017). *Global Markets for Biopesticides*. BCC Research, Wellesley.

Chen, L., Gu, W., Xu, H. Y., Yang, G. L., Shan, X. F., Chen, G., Kang, Y. H., Wang, C. F. and Qian, A. D. (2018). Comparative genome analysis of *Bacillus velezensis* reveals a

potential for degrading lignocellulosic biomass, *3 Biotech* 8(5), 253. doi: 10.1007/s13205-018-1270-7.

Chen, M., Wang, J., Liu, B., Zhu, Y., Xiao, R., Yang, W., Ge, C. and Chen, Z. (2020). Biocontrol of tomato bacterial wilt by the new strain *Bacillus velezensis* FJAT-46737 and its lipopeptides, *BMC Microbiol.* 20(1), 160. doi: 10.1186/s12866-020-01851-2.

Chen, M. C., Wang, J. P., Zhu, Y. J., Liu, B., Yang, W. J. and Ruan, C. Q. (2019). Antibacterial activity against *Ralstonia solanacearum* of the lipopeptides secreted from the *Bacillus amyloliquefaciens* strain FJAT-2349, *J. Appl. Microbiol.* 126(5), 1519–1529. doi: 10.1111/jam.14213.

Chen, X. H., Koumoutsi, A., Scholz, R., Schneider, K., Vater, J., Süssmuth, R., Piel, J. and Borriss, R. (2009a). Genome analysis of *Bacillus amyloliquefaciens* FZB42 reveals its potential for biocontrol of plant pathogens, *J. Biotechnol.* 140(1–2), 27–37. doi: 10.1016/j.jbiotec.2008.10.011.

Chen, X. H., Scholz, R., Borriss, M., Junge, H., Mögel, G., Kunz, S. and Borriss, R. (2009b). Difficidin and bacilysin produced by plant-associated *Bacillus amyloliquefaciens* are efficient in controlling fire blight disease, *J. Biotechnol.* 140(1–2), 38–44. doi: 10.1016/j.jbiotec.2008.10.015.

Chen, X. H., Vater, J., Piel, J., Franke, P., Scholz, R., Schneider, K., Koumoutsi, A., Hitzeroth, G., Grammel, N., Strittmatter, A. W., Gottschalk, G., Süssmuth, R. D. and Borriss, R. (2006). Structural and functional characterization of three polyketide synthase gene clusters in *Bacillus amyloliquefaciens* FZB 42, *J. Bacteriol.* 188(11), 4024–4036. doi: 10.1128/JB.00052-06.

Chen, Y., Yan, F., Chai, Y., Liu, H., Kolter, R., Losick, R. and Guo, J. H. (2013). Biocontrol of tomato wilt disease by Bacillus subtilis isolates from natural environments depends on conserved genes mediating biofilm formation, *Environ. Microbiol.* 15(3), 848–864. doi: 10.1111/j.1462-2920.2012.02860.x.

Choi, H. K., Song, G. C., Yi, H. S. and Ryu, C. M. (2014). Field evaluation of the bacterial volatile derivative 3-pentanol in priming for induced resistance in pepper, *J. Chem. Ecol.* 40(8), 882–892. doi: 10.1007/s10886-014-0488-z.

Chowdhury, S. P., Dietel, K., Rändler, M., Schmid, M., Junge, H., Borriss, R., Hartmann, A. and Grosch, R. (2013). Effects of *Bacillus amyloliquefaciens* FZB42 on lettuce growth and health under pathogen pressure and its impact on the rhizosphere bacterial community, *Plos One* 8(7), e68818. doi: 10.1371/journal.pone.0068818.

Chowdhury, S. P., Hartmann, A., Gao, X. and Borriss, R. (2015a). Biocontrol mechanism by root-associated *Bacillus amyloliquefaciens* FZB42—a review, *Front. Microbiol.* 6(780), 780. doi: 10.3389/fmicb.2015.00780.

Chowdhury, S. P., Uhl, J., Grosch, R., Alquéres, S., Pittroff, S., Dietel, K., Schmitt-Kopplin, P., Borriss, R. and Hartmann, A. (2015b). Cyclic lipopeptides of *Bacillus amyloliquefaciens* subsp. plantarum colonizing the lettuce rhizosphere enhance plant defense responses toward the bottom rot pathogen *Rhizoctonia solani*, *Mol. Plant Microbe Interact.* 28(9), 984–995. doi: 10.1094/MPMI-03-15-0066-R.

Correa, O. S., Montecchia, M. S., Berti, M. F., Fernández Ferrari, M. C., Pucheu, N. L., Kerber, N. L. and García, A. F. (2009). *Bacillus amyloliquefaciens* BNM122, a potential microbial biocontrol agent applied on soybean seeds, causes a minor impact on rhizosphere and soil microbial communities, *Appl. Soil Ecol.* 41(2), 185–194. doi: 10.1016/j.apsoil.2008.10.007.

Cosby, W. M., Vollenbroich, D., Lee, O. H. and Zuber, P. (1998). Altered srf expression in *Bacillus subtilis* resulting from changes in culture pH Is dependent on the Spo0K

oligopeptide permease and the ComQX system of extracellular control, *J. Bacteriol.* 180(6), 1438–1445. doi: 10.1128/JB.180.6.1438-1445.1998.

Coutte, F., Lecouturier, D., Dimitrov, K., Guez, J. S., Delvigne, F., Dhulster, P. and Jacques, P. (2017). Microbial lipopeptide production and purification bioprocesses, current progress and future challenges, *Biotechnol. J.* 12(7), 1–10. doi: 10.1002/biot.201600566(28636078).

Coutte, F., Niehren, J., Dhali, D., John, M., Versari, C. and Jacques, P. (2015). Modeling leucine's metabolic pathway and knockout prediction improving the production of surfactin, a biosurfactant from *Bacillus subtilis*, *Biotechnol. J.* 10(8), 1216–1234. doi: 10.1002/biot.201400541.

Crouzet, J., Arguelles-Arias, A., Dhondt-Cordelier, S., Cordelier, S., Pršić, J., Hoff, G., Mazeyrat-Gourbeyre, F., Baillieul, F., Clément, C., Ongena, M. and Dorey, S. (2020). Biosurfactants in plant protection against diseases: rhamnolipids and lipopeptides case study, *Front. Bioeng. Biotechnol.* 8(1014), 1014. doi: 10.3389/fbioe.2020.01014.

Cucu, M. A., Gilardi, G., Pugliese, M., Gullino, M. L. and Garibaldi, A. (2020). An assessment of the modulation of the population dynamics of pathogenic *Fusarium oxysporum* f. sp. *lycopersici* in the tomato rhizosphere by means of the application of *Bacillus subtilis* QST 713, *Trichoderma* sp. TW2 and two composts, *Biol. Control* 142, 1–10. doi: 10.1016/j.biocontrol.2019.104158.

Dang, Y., Zhao, F., Liu, X., Fan, X., Huang, R., Gao, W., Wang, S. and Yang, C. (2019). Enhanced production of antifungal lipopeptide iturin A by *Bacillus amyloliquefaciens* LL3 through metabolic engineering and culture conditions optimization, *Microb. Cell Fact.* 18(1), 68. doi: 10.1186/s12934-019-1121-1.

Dean, R., Van Kan, J. A. L., Pretorius, Z. A., Hammond-Kosack, K. E., Di Pierto, A., Spanu, P. D., Rudd, J. J., Dickman, M., Kahmann, R., Ellis, J. and Foster, G. D. (2012). The Top 10 fungal pathogens in molecular plant pathology, *Mol. Plant Pathol.* 13(4), 414–430. doi: 10.1111/j.1364-3703.2011.00783.x.

Debois, D., Fernandez, O., Franzil, L., Jourdan, E., de Brogniez, A., Willems, L., Clément, C., Dorey, S., De Pauw, E. and Ongena, M. (2015). Plant polysaccharides initiate underground crosstalk with bacilli by inducing synthesis of the immunogenic lipopeptide surfactin, *Environ. Microbiol. Rep.* 7(3), 570–582. doi: 10.1111/1758-2229.12286.

Debois, D., Jourdan, E., Smargiasso, N., Thonart, P., De Pauw, E. and Ongena, M. (2014). Spatiotemporal monitoring of the antibiome secreted by Bacillus biofilms on plant roots using MALDI mass spectrometry imaging, *Anal. Chem.* 86(9), 4431–4438. doi: 10.1021/ac500290s.

DeFilippi, S., Groulx, E., Megalla, M., Mohamed, R. and Avis, T. J. (2018). Fungal competitors affect production of antimicrobial lipopeptides in *Bacillus subtilis* Strain B9–5, *J. Chem. Ecol.* 44(4), 374–383. doi: 10.1007/s10886-018-0938-0.

Deja-Sikora, E., Kowalczyk, A., Trejgell, A., Szmidt-Jaworska, A., Baum, C., Mercy, L. and Hrynkiewicz, K. (2020). Arbuscular mycorrhiza changes the impact of potato virus Y on growth and stress tolerance of *Solanum tuberosum* L. in vitro, *Front. Microbiol.* 10(2971), 1–12. doi: 10.3389/fmicb.2019.02971.

Deleu, M., Crowet, J. M., Nasir, M. N. and Lins, L. (2014). Complementary biophysical tools to investigate lipid specificity in the interaction between bioactive molecules and the plasma membrane: a review, *Biochim. Biophys. Acta* 1838(12), 3171–3190. doi: 10.1016/j.bbamem.2014.08.023.

Deleu, M., Lorent, J., Lins, L., Brasseur, R., Braun, N., El Kirat, K., Nylander, T., Dufrêne, Y. F. and Mingeot-Leclercq, M. P. (2013). Effects of surfactin on membrane models displaying lipid phase separation, *Biochim. Biophys. Acta* 1828(2), 801–815. doi: 10.1016/j.bbamem.2012.11.007.

Deleu, M., Paquot, M. and Nylander, T. (2008). Effect of fengycin, a lipopeptide produced by *Bacillus subtilis*, on model biomembranes, *Biophys. J.* 94(7), 2667–2679. doi: 10.1529/biophysj.107.114090.

Domenech, J., Reddy, M. S., Kloepper, J. W., Ramos, B. and Gutierrez-Mañero, J. (2006). Combined application of the biological product LS213 with Bacillus, Pseudomonas or Chryseobacterium for growth promotion and biological control of soil-borne diseases in pepper and tomato, *BioControl* 51(2), 245–258. doi: 10.1007/s10526-005-2940-z.

Dong, Y. H., Gusti, A. R., Zhang, Q., Xu, J. L. and Zhang, L. H. (2002). Identification of quorum-quenching N-acyl homoserine lactonases from *Bacillus* species, *Appl. Environ. Microbiol.* 68(4), 1754–1759. doi: 10.1128/AEM.68.4.1754-1759.2002.

Dubern, J. F. and Bloemberg, G. V. (2006). Influence of environmental conditions on putisolvins I and II production in *Pseudomonas putida* strain PCL1445, *FEMS Microbiol. Lett.* 263(2), 169–175. doi: 10.1111/j.1574-6968.2006.00406.x.

Dunlap, C. A. (2019). Taxonomy of registered Bacillus spp. strains used as plant pathogen antagonists, *Biol. Control* 134, 82–86. doi: 10.1016/j.biocontrol.2019.04.011.

Dunlap, C. A., Kim, S. J., Kwon, S. W. and Rooney, A. P. (2016). *Bacillus velezensis* is not a later heterotypic synonym of *Bacillus amyloliquefaciens*; *Bacillus methylotrophicus*, *Bacillus amyloliquefaciens* subsp. *plantarum* and "*Bacillus oryzicola*" are later heterotypic synonym, *Int. J. Syst. Evol. Microbiol.* 66(3), 1212–1217. doi: 10.1099/ijsem.0.000858.

Dutta, S., Whicher, J. R., Hansen, D. A., Hale, W. A., Chemler, J. A., Congdon, G. R., Narayan, A. R. H., Håkansson, K., Sherman, D. H., Smith, J. L. and Skiniotis, G. (2014). Structure of a modular polyketide synthase, *Nature* 510(7506), 512–517. doi: 10.1038/nature13423.

Elanchezhiyan, K., Keerthana, U., Nagendran, K., Prabhukarthikeyan, S. R., Prabakar, K., Raguchander, T. and Karthikeyan, G. (2018). Multifaceted benefits of *Bacillus amyloliquefaciens* strain FBZ24 in the management of wilt disease in tomato caused by *Fusarium oxysporum* f. sp. *lycopersici*, *Physiol. Mol. Plant Pathol.* 103, 92–101. doi: 10.1016/j.pmpp.2018.05.008.

Elisashvili, V., Kachlishvili, E. and Chikindas, M. L. (2019). Recent advances in the physiology of spore formation for Bacillus probiotic production, *Probiotics Antimicrob. Proteins* 11(3), 731–747. doi: 10.1007/s12602-018-9492-x.

Engelbrecht, G., Horak, I., Jansen van Rensburg, P. J. and Claassens, S. (2018). Bacillus-based bionematicides: development, modes of action and commercialisation, *Biocontrol Sci. Technol.* 28(7), 629–653. doi: 10.1080/09583157.2018.1469000.

Fan, B., Blom, J., Klenk, H. P. and Borriss, R. (2017a). *Bacillus amyloliquefaciens*, *Bacillus velezensis*, and *Bacillus siamensis* form an "operational group *B. amyloliquefaciens*" within the *B. subtilis* species complex, *Front. Microbiol.* 8(22), 22. doi: 10.3389/fmicb.2017.00022.

Fan, B., Borriss, R., Bleiss, W. and Wu, X. (2012). Gram-positive rhizobacterium *Bacillus amyloliquefaciens* FZB42 colonizes three types of plants in different patterns, *J. Microbiol.* 50(1), 38–44. doi: 10.1007/s12275-012-1439-4.

Fan, B., Chen, X. H., Budiharjo, A., Bleiss, W., Vater, J. and Borriss, R. (2011). Efficient colonization of plant roots by the plant growth promoting bacterium *Bacillus amyloliquefaciens* FZB42, engineered to express green fluorescent protein, *J. Biotechnol.* 151(4), 303–311. doi: 10.1016/j.jbiotec.2010.12.022.

Fan, B., Wang, C., Song, X., Ding, X., Wu, L., Wu, H., Gao, X. and Borriss, R. (2018). *Bacillus velezensis* FZB42 in 2018: the gram-positive model strain for plant growth promotion and biocontrol, *Front. Microbiol.* 9(2491), 2491. doi: 10.3389/fmicb.2018.02491.

Fan, H., Zhang, Z., Li, Y., Zhang, X., Duan, Y. and Wang, Q. (2017b). Biocontrol of bacterial fruit blotch by *Bacillus subtilis* 9407 via surfactin-mediated antibacterial activity and colonization, *Front. Microbiol.* 8, 1–15. doi: 10.3389/fmicb.2017.01973.

Farace, G., Fernandez, O., Jacquens, L., Coutte, F., Krier, F., Jacques, P., Clément, C., Barka, E. A., Jacquard, C. and Dorey, S. (2015). Cyclic lipopeptides from *Bacillus subtilis* activate distinct patterns of defence responses in grapevine, *Mol. Plant Pathol.* 16(2), 177–187. doi: 10.1111/mpp.12170.

Farzand, A., Moosa, A., Zubair, M., Khan, A. R., Ayaz, M., Massawe, V. C. and Gao, X. (2020). Transcriptional profiling of diffusible lipopeptides and fungal virulence genes during *Bacillus amyloliquefaciens* EZ1509-mediated suppression of *Sclerotinia sclerotiorum*, *Phytopathology*® 110(2), 317–326. doi: 10.1094/PHYTO-05-19-0156-R.

Farzand, A., Moosa, A., Zubair, M., Khan, A. R., Massawe, V. C., Tahir, H. A. S., Sheikh, T. M. M., Ayaz, M. and Gao, X. (2019). Suppression of *Sclerotinia sclerotiorum* by the induction of systemic resistance and regulation of antioxidant pathways in tomato using fengycin produced by *Bacillus amyloliquefaciens* FZB42, *Biomolecules* 9(10), 1–17. doi: 10.3390/biom9100613.

Feng, H., Zhang, N., Fu, R., Liu, Y., Krell, T., Du, W., Shao, J., Shen, Q. and Zhang, R. (2019). Recognition of dominant attractants by key chemoreceptors mediates recruitment of plant growth-promoting rhizobacteria, *Environ. Microbiol.* 21(1), 402–415. doi: 10.1111/1462-2920.14472.

Fickers, P., Leclère, V., Guez, J. S., Béchet, M., Coucheney, F., Joris, B. and Jacques, P. (2008). Temperature dependence of mycosubtilin homologue production in *Bacillus subtilis* ATCC6633, *Res. Microbiol.* 159(6), 449–457. doi: 10.1016/j.resmic.2008.05.004.

Fiedler, S. and Heerklotz, H. (2015). Vesicle leakage reflects the target selectivity of antimicrobial lipopeptides from *Bacillus subtilis*, *Biophys. J.* 109(10), 2079–2089. doi: 10.1016/j.bpj.2015.09.021.

Fincheira, P., Parra, L., Mutis, A., Parada, M. and Quiroz, A. (2017). Volatiles emitted by *Bacillus* sp. BCT9 act as growth modulating agents on Lactuca sativa seedlings, *Microbiol. Res.* 203, 47–56. doi: 10.1016/j.micres.2017.06.007.

Fiorilli, V., Vannini, C., Ortolani, F., Garcia-Seco, D., Chiapello, M., Novero, M., Domingo, G., Terzi, V., Morcia, C., Bagnaresi, P., Moulin, L., Bracale, M. and Bonfante, P. (2018). Omics approaches revealed how arbuscular mycorrhizal symbiosis enhances yield and resistance to leaf pathogen in wheat, *Sci. Rep.* 8(1), 9625. doi: 10.1038/s41598-018-27622-8.

Fira, D., Dimkić, I., Berić, T., Lozo, J. and Stanković, S. (2018). Biological control of plant pathogens by *Bacillus* species, *J. Biotechnol.* 285, 44–55. doi: 10.1016/j.jbiotec.2018.07.044.

Flemming, H. C., Wingender, J., Szewzyk, U., Steinberg, P., Rice, S. A. and Kjelleberg, S. (2016). Biofilms: an emergent form of bacterial life, *Nat. Rev. Microbiol.* 14(9), 563–575. doi: 10.1038/nrmicro.2016.94.

Fousia, S., Paplomatas, E. J. and Tjamos, S. E. (2016). *Bacillus subtilis* QST 713 confers protection to tomato plants against *Pseudomonas syringae* pv tomato and induces plant defence-related genes, *J. Phytopathol.* 164(4), 264–270. doi: 10.1111/jph.12455.

Frey-Klett, P., Burlinson, P., Deveau, A., Barret, M., Tarkka, M. and Sarniguet, A. (2011). Bacterial-fungal interactions: hyphens between agricultural, clinical, environmental, and food microbiologists, *Microbiol. Mol. Biol. Rev.* 75(4), 583–609. doi: 10.1128/MMBR.00020-11.

Frikha-Gargouri, O., Ben Abdallah, D., Bhar, I. and Tounsi, S. (2017). Antibiosis and bmyB gene presence as prevalent traits for the selection of efficient Bacillus biocontrol agents against crown gall disease, *Front. Plant Sci.* 8(1363), 1363. doi: 10.3389/fpls.2017.01363.

Gallou, A., Declerck, S. and Cranenbrouck, S. (2012). Transcriptional regulation of defence genes and involvement of the WRKY transcription factor in arbuscular mycorrhizal potato root colonization, *Funct. Integr. Genomics* 12(1), 183–198. doi: 10.1007/s10142-011-0241-4.

Gallou, A., Lucero Mosquera, H. P., Cranenbrouck, S., Suárez, J. P. and Declerck, S. (2011). Mycorrhiza induced resistance in potato plantlets challenged by *Phytophthora infestans*, *Physiol. Mol. Plant Pathol.* 76(1), 20–26. doi: 10.1016/j.pmpp.2011.06.005.

García-Gutiérrez, L., Zeriouh, H., Romero, D., Cubero, J., de Vicente, A. and Pérez-García, A. (2013). The antagonistic strain *Bacillus subtilis* UMAF6639 also confers protection to melon plants against cucurbit powdery mildew by activation of jasmonate- and salicylic acid-dependent defence responses, *Microb. Biotechnol.* 6(3), 264–274. doi: 10.1111/1751-7915.12028.

Gautam, S., Chauhan, A., Sharma, R., Sehgal, R. and Shirkot, C. K. (2019). Potential of *Bacillus amyloliquefaciens* for biocontrol of bacterial canker of tomato incited by *Clavibacter michiganensis* ssp. *michiganensis*, *Microb. Pathog.* 130, 196–203. doi: 10.1016/j.micpath.2019.03.006.

Gava, C. A. T., Alves, Í. L. S. and Duarte, N. C. (2019). Timing the application of *Bacillus subtilis* QST 713 in the integrated management of the postharvest decay of mango fruits, *Crop Prot.* 121, 51–56. doi: 10.1016/j.cropro.2019.03.013.

Geiger, F., Bengtsson, J., Berendse, F., Weisser, W. W., Emmerson, M., Morales, M. B., Ceryngier, P., Liira, J., Tscharntke, T., Winqvist, C., Eggers, S., Bommarco, R., Pärt, T., Bretagnolle, V., Plantegenest, M., Clement, L. W., Dennis, C., Palmer, C., Oñate, J. J., Guerrero, I., Hawro, V., Aavik, T., Thies, C., Flohre, A., Hänke, S., Fischer, C., Goedhart, P. W. and Inchausti, P. (2010). Persistent negative effects of pesticides on biodiversity and biological control potential on European farmland, *Basic Appl. Ecol.* 11(2), 97–105. doi: 10.1016/j.baae.2009.12.001.

van Gestel, J., Vlamakis, H. and Kolter, R. (2015). From cell differentiation to cell collectives: *Bacillus subtilis* uses division of labor to migrate, *PLOS Biol.* 13(4), e1002141. doi: 10.1371/journal.pbio.1002141.

Ghorbanpour, M., Omidvari, M., Abbaszadeh-Dahaji, P., Omidvar, R. and Kariman, K. (2018). Mechanisms underlying the protective effects of beneficial fungi against plant diseases, *Biol. Control* 117, 147–157. doi: 10.1016/j.biocontrol.2017.11.006.

Glare, T., Caradus, J., Gelernter, W., Jackson, T., Keyhani, N., Köhl, J., Marrone, P., Morin, L. and Stewart, A. (2012). Have biopesticides come of age?, *Trends Biotechnol.* 30(5), 250–258. doi: 10.1016/j.tibtech.2012.01.003.

Gong, Q., Zhang, C., Lu, F., Zhao, H., Bie, X. and Lu, Z. (2014). Identification of bacillomycin D from *Bacillus subtilis* fmbJ and its inhibition effects against *Aspergillus flavus*, *Food Control* 36(1), 8–14. doi: 10.1016/j.foodcont.2013.07.034.

Gong, W., Wang, J., Chen, Z., Xia, B. and Lu, G. (2011). Solution structure of LCI, a novel antimicrobial peptide from *Bacillus subtilis*, *Biochemistry* 50(18), 3621–3627. doi: 10.1021/bi200123w.

Goodson, J. R., Klupt, S., Zhang, C., Straight, P. and Winkler, W. C. (2017). LoaP is a broadly conserved antiterminator protein that regulates antibiotic gene clusters in *Bacillus amyloliquefaciens*, *Nat. Microbiol.* 2(17003), 17003. doi: 10.1038/nmicrobiol.2017.3.

Grau, R. R., de Oña, P., Kunert, M., Leñini, C., Gallegos-Monterrosa, R., Mhatre, E., Vileta, D., Donato, V., Hölscher, T., Boland, W., Kuipers, O. P. and Kovács, Á. T. (2015). A duo of potassium-responsive histidine kinases govern the multicellular destiny of *Bacillus subtilis*, *mBio* 6(4), e00581. doi: 10.1128/mBio.00581-15.

Grubbs, K. J., Bleich, R. M., Santa Maria, K. C., Allen, S. E., Farag, S., AgBiome Team, Shank, E. A. and Bowers, A. A. (2017). Large-scale bioinformatics analysis of Bacillus genomes uncovers conserved roles of natural products in bacterial physiology, *mSystems* 2(6), 1–18. doi: 10.1128/mSystems.00040-17.

Gu, Q., Yang, Y., Yuan, Q., Shi, G., Wu, L., Lou, Z., Huo, R., Wu, H., Borriss, R. and Gao, X. (2017). Bacillomycin D produced by *Bacillus amyloliquefaciens* is involved in the antagonistic interaction with the plant-pathogenic fungus *Fusarium graminearum*, *Appl. Environ. Microbiol.* 83(19), 1075–1092. doi: 10.1128/AEM.01075-17.

Guez, J. S., Müller, C. H., Danze, P. M., Büchs, J. and Jacques, P. (2008). Respiration activity monitoring system (RAMOS), an efficient tool to study the influence of the oxygen transfer rate on the synthesis of lipopeptide by *Bacillus subtilis* ATCC6633, *J. Biotechnol.* 134(1–2), 121–126. doi: 10.1016/j.jbiotec.2008.01.003.

Guleria, S., Walia, A., Chauhan, A. and Shirkot, C. K. (2016). Molecular characterization of alkaline protease of *Bacillus amyloliquefaciens* SP1 involved in biocontrol of *Fusarium oxysporum*, *Int. J. Food Microbiol.* 232, 134–143. doi: 10.1016/j.ijfoodmicro.2016.05.030.

Guo, Q., Dong, W., Li, S., Lu, X., Wang, P., Zhang, X., Wang, Y. and Ma, P. (2014). Fengycin produced by *Bacillus subtilis* NCD-2 plays a major role in biocontrol of cotton seedling damping-off disease, *Microbiol. Res.* 169(7–8), 533–540. doi: 10.1016/j.micres.2013.12.001.

Guo, Q., Dong, L., Wang, P., Li, S., Zhao, W., Lu, X., Zhang, X. and Ma, P. (2018). The PhoR/PhoP two-component system regulates fengycin production in *Bacillus subtilis* NCD-2 under low-phosphate conditions, *J. Integr. Agric.* 17(1), 149–157. doi: 10.1016/S2095-3119(17)61669-1.

Guo, Q., Li, Y., Lou, Y., Shi, M., Jiang, Y., Zhou, J., Sun, Y., Xue, Q. and Lai, H. (2019). *Bacillus amyloliquefaciens* Ba13 induces plant systemic resistance and improves rhizosphere microecology against tomato yellow leaf curl virus disease, *Appl. Soil Ecol.* 137, 154–166. doi: 10.1016/j.apsoil.2019.01.015.

Hammami, I., Jaouadi, B., Bacha, A. Ben, Rebai, A., Bejar, S., Nesme, X. and Rhouma, A. (2012). *Bacillus subtilis* bacteriocin Bac 14B with a broad inhibitory spectrum:

purification, amino acid sequence analysis, and physicochemical characterization, *Biotechnol. Bioprocess Eng.* 17, 41–49. doi: 10.1007/s12257-010-0401-8.

Hammami, I., Rhouma, A., Jaouadi, B., Rebai, A. and Nesme, X. (2009). Optimization and biochemical characterization of a bacteriocin from a newly isolated *Bacillus subtilis* strain 14B for biocontrol of *Agrobacterium* spp. *strains*, *Lett. Appl. Microbiol.* 48(2), 253–260. doi: 10.1111/j.1472-765X.2008.02524.x.

Han, Q., Wu, F., Wang, X., Qi, H., Shi, L., Ren, A., Liu, Q., Zhao, M. and Tang, C. (2015). The bacterial lipopeptide iturins induce *Verticillium dahliae* cell death by affecting fungal signalling pathways and mediate plant defence responses involved in pathogen-associated molecular pattern-triggered immunity, *Environ. Microbiol.* 17(4), 1166–1188. doi: 10.1111/1462-2920.12538.

Hanif, A., Zhang, F., Li, P., Li, C., Xu, Y., Zubair, M., Zhang, M., Jia, D., Zhao, X., Liang, J., Majid, T., Yan, J., Farzand, A., Wu, H., Gu, Q. and Gao, X. (2019). Fengycin produced by *Bacillus amyloliquefaciens* FZB42 inhibits *Fusarium graminearum* growth and mycotoxins biosynthesis, *Toxins (Basel)* 11(5), 1–11. doi: 10.3390/toxins11050295.

Harwood, C. R., Mouillon, J. M., Pohl, S. and Arnau, J. (2018). Secondary metabolite production and the safety of industrially important members of the *Bacillus subtilis* group, *FEMS Microbiol. Rev.* 42(6), 721–738. doi: 10.1093/femsre/fuy028.

Hayashi, K., Ohsawa, T., Kobayashi, K., Ogasawara, N. and Ogura, M. (2005). The H_2O_2 stress-responsive regulator PerR positively regulates srfA expression in *Bacillus subtilis*, *J. Bacteriol.* 187(19), 6659–6667. doi: 10.1128/JB.187.19.6659-6667.2005.

Heimpel, G. E. and Mills, N. J. (2017). *Biological Control: Ecology and Applications*. Cambridge University Press, Cambridge. doi: 10.1017/9781139029117.

Henry, G., Deleu, M., Jourdan, E., Thonart, P. and Ongena, M. (2011). The bacterial lipopeptide surfactin targets the lipid fraction of the plant plasma membrane to trigger immune-related defence responses, *Cell. Microbiol.* 13(11), 1824–1837. doi: 10.1111/j.1462-5822.2011.01664.x.

Hinsinger, P., Bengough, A. G., Vetterlein, D. and Young, I. M. (2009). Rhizosphere: biophysics, biogeochemistry and ecological relevance, *Plant Soil* 321(1–2), 117–152. doi: 10.1007/s11104-008-9885-9.

Im, S. M., Yu, N. H., Joen, H. W., Kim, S. O., Park, H. W., Park, A. R. and Kim, J. C. (2020). Biological control of tomato bacterial wilt by oxydifficidin and difficidin-producing *Bacillus methylotrophicus* DR-08, *Pestic. Biochem. Physiol.* 163, 130–137. doi: 10.1016/j.pestbp.2019.11.007.

İrigül-Sönmez, Ö., Köroğlu, T. E., Öztürk, B., Kovács, Á. T., Kuipers, O. P. and Yazgan-Karataş, A. (2014). In *Bacillus subtilis* LutR is part of the global complex regulatory network governing the adaptation to the transition from exponential growth to stationary phase, *Microbiology (Reading)* 160(2), 243–260. doi: 10.1099/mic.0.064675-0.

Izquierdo-García, L. F., González-Almario, A., Cotes, A. M. and Moreno-Velandia, C. A. (2020). *Trichoderma virens* Gl006 and *Bacillus velezensis* Bs006: a compatible interaction controlling *Fusarium wilt* of cape gooseberry, *Sci. Rep.* 10(1), 6857. doi: 10.1038/s41598-020-63689-y.

Jacques, P. (2011). Surfactin and other lipopeptides from *Bacillus* spp. In: Soberón-Chávez, G. (ed) *Biosurfactants. Microbiology Monographs*, vol 20. Springer, Berlin, Heidelberg, 57–91. doi: 10.1007/978-3-642-14490-5_3.

Jacques, P., Hbid, C., Destain, J., Razafindralambo, H., Paquot, M., De Pauw, E. and Thonart, P. (1999). Optimization of biosurfactant lipopeptide production from *Bacillus subtilis*

S499 by Plackett-Burman design, *Appl. Biochem. Biotechnol.* 77(1–3), 223–234. doi: 10.1385/ABAB:77:1-3:223.

Jetiyanon, K. and Kloepper, J. W. (2002). Mixtures of plant growth-promoting rhizobacteria for induction of systemic resistance against multiple plant diseases, *Biol. Control* 24(3), 285–291. doi: 10.1016/S1049-9644(02)00022-1.

Jiang, C.-H., Liao, M.-J., Wang, H.-K., Zheng, M.-Z., Xu, J.-J. and Guo, J.-H. (2018). Bacillus velezensis, a potential and efficient biocontrol agent in control of pepper gray mold caused by *Botrytis cinerea*, *Biol. Control* 126, 147–157. doi: 10.1016/j.biocontrol.2018.07.017.

Jin, P., Wang, H., Tan, Z., Xuan, Z., Dahar, G. Y., Li, Q. X., Miao, W. and Liu, W. (2020). Antifungal mechanism of bacillomycin D from *Bacillus velezensis* HN-2 against *Colletotrichum gloeosporioides* Penz, *Pestic. Biochem. Physiol.* 163, 102–107. doi: 10.1016/j.pestbp.2019.11.004.

Jin, Y., Zhu, H., Luo, S., Yang, W., Zhang, L., Li, S., Jin, Q., Cao, Q., Sun, S. and Xiao, M. (2019). Role of maize root exudates in promotion of colonization of *Bacillus velezensis* Strain S3-1 in rhizosphere soil and root tissue, *Curr. Microbiol.* 76(7), 855–862. doi: 10.1007/s00284-019-01699-4.

Jose, P. A., Krishnamoorthy, R., Kwon, S.-W., Janahiraman, V., Senthilkumar, M., Gopal, N. O., Kumutha, K. and Anandham, R. (2019). Interference in quorum sensing and virulence of the phytopathogen *Pseudomonas syringae* pv. *passiflorae* by *Bacillus* and *Variovorax* species, *BioControl* 64(4), 423–433. doi: 10.1007/s10526-019-09932-6.

Jourdan, E., Henry, G., Duby, F., Dommes, J., Barthélemy, J. P., Thonart, P. and Ongena, M. (2009). Insights into the defense-related events occurring in plant cells following perception of surfactin-type lipopeptide from *Bacillus subtilis*, *Mol. Plant Microbe Interact.* 22(4), 456–468. doi: 10.1094/MPMI-22-4-0456.

Kai, M. (2020). Diversity and distribution of volatile secondary metabolites throughout *Bacillus subtilis* isolates, *Front. Microbiol.* 11(559), 559. doi: 10.3389/fmicb.2020.00559.

Kakar, K. U., Duan, Y. -P., Nawaz, Z., Sun, G., Almoneafy, A. A., Hassan, M. A., Elshakh, A., Li, B. and Xie, G. L. (2014). A novel rhizobacterium Bk7 for biological control of brown sheath rot of rice caused by *Pseudomonas fuscovaginae* and its mode of action, *Eur. J. Plant Pathol.* 138(4), 819–834. doi: 10.1007/s10658-013-0356-7.

Karuppiah, V., Sun, J., Li, T., Vallikkannu, M. and Chen, J. (2019). Co-cultivation of *Trichoderma asperellum* GDFS1009 and *Bacillus amyloliquefaciens* 1841 causes differential gene expression and improvement in the wheat growth and biocontrol activity, *Front. Microbiol.* 10(1068), 1068. doi: 10.3389/fmicb.2019.01068.

Kawagoe, Y., Shiraishi, S., Kondo, H., Yamamoto, S., Aoki, Y. and Suzuki, S. (2015). Cyclic lipopeptide iturin A structure-dependently induces defense response in Arabidopsis plants by activating SA and JA signaling pathways, *Biochem. Biophys. Res. Commun.* 460(4), 1015–1020. doi: 10.1016/j.bbrc.2015.03.143.

Kearns, D. B., Chu, F., Branda, S. S., Kolter, R. and Losick, R. (2005). A master regulator for biofilm formation by *Bacillus subtilis*, *Mol. Microbiol.* 55(3), 739–749. doi: 10.1111/j.1365-2958.2004.04440.x.

Kearns, D. B., Chu, F., Rudner, R. and Losick, R. (2004). Genes governing swarming in *Bacillus subtilis* and evidence for a phase variation mechanism controlling surface motility, *Mol. Microbiol.* 52(2), 357–369. doi: 10.1111/j.1365-2958.2004.03996.x.

Khardziani, T., Kachlishvili, E., Sokhadze, K., Elisashvili, V., Weeks, R., Chikindas, M. L. and Chistyakov, V. (2017). Elucidation of *Bacillus subtilis* KATMIRA 1933 potential

for spore production in submerged fermentation of plant raw materials, *Probiotics Antimicrob. Proteins* 9(4), 435–443. doi: 10.1007/s12602-017-9303-9.

Khezri, M., Jouzani, G. S. and Ahmadzadeh, M. (2016). *Fusarium culmorum* affects expression of biofilm formation key genes in *Bacillus subtilis*, *Braz. J. Microbiol.* 47(1), 47–54. doi: 10.1016/j.bjm.2015.11.019.

Kierul, K., Voigt, B., Albrecht, D., Chen, X. H., Carvalhais, L. C. and Borriss, R. (2015). Influence of root exudates on the extracellular proteome of the plant growth-promoting bacterium *Bacillus amyloliquefaciens* FZB42, *Microbiology (Reading)* 161(1), 131–147. doi: 10.1099/mic.0.083576-0.

Kildea, S., Ransbotyn, V., Khan, M. R., Fagan, B., Leonard, G., Mullins, E. and Doohan, F. M. (2008). *Bacillus megaterium* shows potential for the biocontrol of *Septoria tritici* blotch of wheat, *Biol. Control* 47(1), 37–45. doi: 10.1016/j.biocontrol.2008.07.001.

Kim, K. H., Kabir, E. and Jahan, S. A. (2017). Exposure to pesticides and the associated human health effects, *Sci. Total Environ.* 575, 525–535. doi: 10.1016/j.scitotenv.2016.09.009.

Kinsella, K., Schulthess, C. P., Morris, T. F. and Stuart, J. D. (2009). Rapid quantification of *Bacillus subtilis* antibiotics in the rhizosphere, *Soil Biol. Biochem.* 41(2), 374–379. doi: 10.1016/j.soilbio.2008.11.019.

Kinsinger, R. F., Shirk, M. C. and Fall, R. (2003). Rapid surface motility in *Bacillus subtilis* is dependent on extracellular surfactin and potassium ion, *J. Bacteriol.* 185(18), 5627–5631. doi: 10.1128/JB.185.18.5627-5631.2003.

Kishore, G. K. and Pande, S. (2007). Chitin-supplemented foliar application of chitinolytic *Bacillus cereus* reduces severity of Botrytis gray mold disease in chickpea under controlled conditions, *Lett. Appl. Microbiol.* 44(1), 98–105. doi: 10.1111/j.1472-765X.2006.02022.x.

Kleerebezem, M., Bongers, R., Rutten, G., Vos, W. M. and Kuipers, O. P. (2004) Autoregulation of subtilin biosynthesis in *Bacillus subtilis*: the role of the spa-box in subtilin-responsive promoters, *Peptides* 25(9), 1415–1424. doi: 10.1016/j.peptides.2003.11.025.

Köhl, J., Kolnaar, R. and Ravensberg, W. J. (2019). Mode of action of microbial biological control agents against plant diseases: relevance beyond efficacy, *Front. Plant Sci.* 10(845), 845. doi: 10.3389/fpls.2019.00845.

Konz, D., Klens, A., Schörgendorfer, K. and Marahiel, M. A. (1997). The bacitracin biosynthesis operon of *Bacillus licheniformis* ATCC 10716: molecular characterization of three multi-modular peptide synthetases, *Chem. Biol.* 4(12), 927–937. doi: 10.1016/S1074-5521(97)90301-X.

Köroğlu, T. E., Kurt-Gür, G., Ünlü, E. C. and Yazgan-Karataş, A. (2008). The novel gene yvfI in *Bacillus subtilis* is essential for bacilysin biosynthesis, *Antonie Leeuwenhoek* 94(3), 471–479. doi: 10.1007/s10482-008-9265-8.

Köroğlu, T. E., Öğülür, I., Mutlu, S., Yazgan-Karataş, A. and Özcengiz, G. (2011). Global regulatory systems operating in bacilysin biosynthesis in *Bacillus subtilis*, *J. Mol. Microbiol. Biotechnol.* 20(3), 144–155. doi: 10.1159/000328639.

Korpi, A., Järnberg, J. and Pasanen, A. L. (2009). Microbial volatile organic compounds, *Crit. Rev. Toxicol.* 39(2), 139–193. doi: 10.1080/10408440802291497.

Koumoutsi, A., Chen, X. H., Vater, J. and Borriss, R. (2007). DegU and YczE positively regulate the synthesis of bacillomycin D by *Bacillus amyloliquefaciens* strain FZB42, *Appl. Environ. Microbiol.* 73(21), 6953–6964. doi: 10.1128/AEM.00565-07.

Kröber, M., Wibberg, D., Grosch, R., Eikmeyer, F., Verwaaijen, B., Chowdhury, S. P., Hartmann, A., Pühler, A. and Schlüter, A. (2014). Effect of the strain *Bacillus*

amyloliquefaciens FZB42 on the microbial community in the rhizosphere of lettuce under field conditions analyzed by whole metagenome sequencing, *Front. Microbiol.* 5(252), 252. doi: 10.3389/fmicb.2014.00252.

Kumar, A., Prakash, A. and Johri, B. N. (2011). Bacillus as PGPR in crop ecosystem. In: Maheshwari, D. (ed) *Bacteria in Agrobiology: Crop Ecosystems*. Springer, Berlin, Heidelberg, 37–60. doi: 10.1007/978-3-642-18357-7.

Lajis, A. F. B. (2020). Biomanufacturing process for the production of bacteriocins from Bacillaceae family, *Bioresour. Bioprocess.* 7(1), 1–26. doi: 10.1186/s40643-020-0295-z.

Lakshmanan, V., Selvaraj, G. and Bais, H. P. (2014). Functional soil microbiome: belowground solutions to an aboveground problem, *Plant Physiol.* 166(2), 689–700. doi: 10.1104/pp.114.245811.

Lee, G. H. and Ryu, C. M. (2016). Spraying of leaf-colonizing *Bacillus amyloliquefaciens* protects pepper from Cucumber mosaic virus, *Plant Dis.* 100(10), 2099–2105. doi: 10.1094/PDIS-03-16-0314-RE.

Li, T., Tang, J., Karuppiah, V., Li, Y., Xu, N. and Chen, J. (2020). Co-culture of *Trichoderma atroviride* SG3403 and *Bacillus subtilis* 22 improves the production of antifungal secondary metabolites, *Biol. Control* 140, 1–8. doi: 10.1016/j.biocontrol.2019.104122.

Li, Y., Héloir, M. C., Zhang, X., Geissler, M., Trouvelot, S., Jacquens, L., Henkel, M., Su, X., Fang, X., Wang, Q. and Adrian, M. (2019). Surfactin and fengycin contribute to the protection of a *Bacillus subtilis* strain against grape downy mildew by both direct effect and defence stimulation, *Mol. Plant Pathol.* 20(8), 1037–1050. doi: 10.1111/mpp.12809.

Lim, S. M., Yoon, M. Y., Choi, G. J., Choi, Y. H., Jang, K. S., Shin, T. S., Park, H. W., Yu, N. H., Kim, Y. H. and Kim, J. C. (2017). Diffusible and volatile antifungal compounds produced by an antagonistic *Bacillus velezensis* G341 against various phytopathogenic fungi, *Plant Pathol. J.* 33(5), 488–498. doi: 10.5423/PPJ.OA.04.2017.0073.

Lin, C., Tsai, C. H., Chen, P. Y., Wu, C. Y., Chang, Y. L., Yang, Y. L. and Chen, Y. L. (2018). Biological control of potato common scab by *Bacillus amyloliquefaciens* Ba01, *Plos One* 13(4), e0196520. doi: 10.1371/journal.pone.0196520.

Liu, C., Yin, X., Wang, Q., Peng, Y., Ma, Y., Liu, P. and Shi, J. (2018a). Antagonistic activities of volatiles produced by two Bacillus strains against *Monilinia fructicola* in peach fruit, *J. Sci. Food Agric.* 98(15), 5756–5763. doi: 10.1002/jsfa.9125.

Liu, G., Kong, Y., Fan, Y., Geng, C., Peng, D. and Sun, M. (2017). Whole-genome sequencing of *Bacillus velezensis* LS69, a strain with a broad inhibitory spectrum against pathogenic bacteria, *J. Biotechnol.* 249, 20–24. doi: 10.1016/j.jbiotec.2017.03.018.

Liu, J., Hagberg, I., Novitsky, L., Hadj-Moussa, H. and Avis, T. J. (2014a). Interaction of antimicrobial cyclic lipopeptides from *Bacillus subtilis* influences their effect on spore germination and membrane permeability in fungal plant pathogens, *Fungal Biol.* 118(11), 855–861. doi: 10.1016/j.funbio.2014.07.004.

Liu, J., Zhou, T., He, D., Li, X. Z., Wu, H., Liu, W. and Gao, X. (2011). Functions of lipopeptides bacillomycin D and fengycin in antagonism of *Bacillus amyloliquefaciens* C06 towards *Monilinia fructicola*, *J. Mol. Microbiol. Biotechnol.* 20(1), 43–52. doi: 10.1159/000323501.

Liu, K., Mclnroy, J. A., Hu, C. H. and Kloepper, J. W. (2018b). Mixtures of plant-growth-promoting rhizobacteria enhance biological control of multiple plant diseases and plant-growth promotion in the presence of pathogens, *Plant Dis.* 102(1), 67–72. doi: 10.1094/PDIS-04-17-0478-RE.

Liu, Y., Feng, H., Fu, R., Zhang, N., Du, W., Shen, Q. and Zhang, R. (2020). Induced root-secreted D-galactose functions as a chemoattractant and enhances the biofilm formation of *Bacillus velezensis* SQR9 in an McpA-dependent manner, *Appl. Microbiol. Biotechnol.* 104(2), 785–797. doi: 10.1007/s00253-019-10265-8.

Liu, Y., Kyle, S. and Straight, P. D. (2018c). Antibiotic stimulation of a *Bacillus subtilis* migratory response, *mSphere* 3(1), 1–13. doi: 10.1128/mSphere.00586-17.

Liu, Y., Zhang, N., Qiu, M., Feng, H., Vivanco, J. M., Shen, Q. and Zhang, R. (2014b). Enhanced rhizosphere colonization of beneficial *Bacillus amyloliquefaciens* SQR9 by pathogen infection, *FEMS Microbiol. Lett.* 353(1), 49–56. doi: 10.1111/1574-6968.12406.

Lopez, D., Vlamakis, H., Losick, R. and Kolter, R. (2009). Paracrine signaling in a bacterium, *Genes Dev.* 23(14), 1631–1638. doi: 10.1101/gad.1813709.

Lu, H., Qian, S., Muhammad, U., Jiang, X., Han, J. and Lu, Z. (2016). Effect of fructose on promoting fengycin biosynthesis in *Bacillus amyloliquefaciens* fmb-60, *J. Appl. Microbiol.* 121(6), 1653–1664. doi: 10.1111/jam.13291.

Luna-Bulbarela, A., Tinoco-Valencia, R., Corzo, G., Kazuma, K., Konno, K., Galindo, E. and Serrano-Carreón, L. (2018). Effects of bacillomycin D homologues produced by *Bacillus amyloliquefaciens* 83 on growth and viability of *Colletotrichum gloeosporioides* at different physiological stages, *Biol. Control* 127, 145–154. doi: 10.1016/j.biocontrol.2018.08.004.

Luo, C., Zhou, H., Zou, J., Wang, X., Zhang, R., Xiang, Y. and Chen, Z. (2015). *Bacillomycin* L and surfactin contribute synergistically to the phenotypic features of *Bacillus subtilis* 916 and the biocontrol of rice sheath blight induced by *Rhizoctonia solani*, *Appl. Microbiol. Biotechnol.* 99(4), 1897–1910. doi: 10.1007/s00253-014-6195-4.

Mariappan, A., Makarewicz, O., Chen, X. H. and Borriss, R. (2012). Two-component response regulator DegU controls the expression of bacilysin in plant-growth-promoting bacterium *Bacillus amyloliquefaciens* FZB42, *J. Mol. Microbiol. Biotechnol.* 22(2), 114–125. doi: 10.1159/000338804.

Mathieu, S., Cusant, L., Roux, C. and Corradi, N. (2018). Arbuscular mycorrhizal fungi: intraspecific diversity and pangenomes, *New Phytol.* 220(4), 1129–1134. doi: 10.1111/nph.15275.

Matzen, N., Heick, T. M. and Jørgensen, L. N. (2019). Control of powdery mildew (*Blumeria graminis* spp.) in cereals by Serenade®ASO (*Bacillus amyloliquefaciens* (former subtilis) strain QST 713), *Biol. Control* 139, 1–8. doi: 10.1016/j.biocontrol.2019.104067.

Medeot, D. B., Fernandez, M., Morales, G. M. and Jofré, E. (2020). Fengycins from *Bacillus amyloliquefaciens* MEP218 exhibit antibacterial activity by producing alterations on the cell surface of the pathogens *Xanthomonas axonopodis* pv. *vesicatoria* and *Pseudomonas aeruginosa* PA01, *Front. Microbiol.* 10(3107), 1–12. doi: 10.3389/fmicb.2019.03107.

Mejri, S., Siah, A., Coutte, F., Magnin-Robert, M., Randoux, B., Tisserant, B., Krier, F., Jacques, P., Reignault, P. and Halama, P. (2018). Biocontrol of the wheat pathogen *Zymoseptoria tritici* using cyclic lipopeptides from *Bacillus subtilis*, *Environ. Sci. Pollut. Res. Int.* 25(30), 29822–29833. doi: 10.1007/s11356-017-9241-9.

Meng, Q. and Hao, J. J. (2017). Optimizing the application of *Bacillus velezensis* BAC03 in controlling the disease caused by *Streptomyces scabies*, *BioControl* 62(4), 535–544. doi: 10.1007/s10526-017-9799-7.

Mihalache, G., Balaes, T., Gostin, I., Stefan, M., Coutte, F. and Krier, F. (2018). Lipopeptides produced by *Bacillus subtilis* as new biocontrol products against fusariosis in

ornamental plants, *Environ. Sci. Pollut. Res. Int.* 25(30), 29784–29793. doi: 10.1007/s11356-017-9162-7.

Miljaković, D., Marinković, J. and Balešević-Tubić, S. (2020). The significance of Bacillus spp. in disease suppression and growth promotion of field and vegetable crops, *Microorganisms* 8(7), 1–19. doi: 10.3390/microorganisms8071037.

Ming, L. J. and Epperson, J. D. (2002). Metal binding and structure–activity relationship of the metalloantibiotic peptide bacitracin, *J. Inorg. Biochem.* 91(1), 46–58. doi: 10.1016/S0162-0134(02)00464-6.

Le Mire, G., Nguyen, M. L., Fassotte, B., Du Jardin, P., Verheggen, F., Delaplace, P. and Haissam Jijakli, M. (2016). Implementing plant biostimulants and biocontrol strategies in the agroecological management of cultivated ecosystems: a review, *Biotechnol. Agron. Soc. Environ.* 20 (Suppl.1), 299–313. doi: 10.25518/1780-4507.12717.

Le Mire, G., Siah, A., Brisset, M.-N., Gaucher, M., Deleu, M. and Jijakli, M. (2018). Surfactin protects wheat against *Zymoseptoria tritici* and activates both salicylic acid- and jasmonic acid-dependent defense responses, *Agriculture* 8(1), 1–14. doi: 10.3390/agriculture8010011.

Mishra, S. and Arora, N. K. (2012). Evaluation of rhizospheric Pseudomonas and Bacillus as biocontrol tool for *Xanthomonas campestris* pv *campestris*, *World J. Microbiol. Biotechnol.* 28(2), 693–702. doi: 10.1007/s11274-011-0865-5.

Mnif, I. and Ghribi, D. (2015). Potential of bacterial derived biopesticides in pest management, *Crop Prot.* 77, 52–64. doi: 10.1016/j.cropro.2015.07.017.

Molina-Santiago, C., Pearson, J. R., Navarro, Y., Berlanga-Clavero, M. V., Caraballo-Rodriguez, A. M., Petras, D., García-Martín, M. L., Lamon, G., Haberstein, B., Cazorla, F. M., de Vicente, A., Loquet, A., Dorrestein, P. C. and Romero, D. (2019). The extracellular matrix protects *Bacillus subtilis* colonies from Pseudomonas invasion and modulates plant co-colonization, *Nat. Commun.* 10(1), 1919. doi: 10.1038/s41467-019-09944-x.

Molinatto, G., Puopolo, G., Sonego, P., Moretto, M., Engelen, K., Viti, C., Ongena, M. and Pertot, I. (2016). Complete genome sequence of *Bacillus amyloliquefaciens* subsp. plantarum S499, a rhizobacterium that triggers plant defences and inhibits fungal phytopathogens, *J. Biotechnol.* 238, 56–59. doi: 10.1016/j.jbiotec.2016.09.013.

Motta Dos Santos, L. F., Coutte, F., Ravallec, R., Dhulster, P., Tournier-Couturier, L. and Jacques, P. (2016). An improvement of surfactin production by *B. subtilis* BBG131 using design of experiments in microbioreactors and continuous process in bubbleless membrane bioreactor, *Bioresour. Technol.* 218, 944–952. doi: 10.1016/j.biortech.2016.07.053.

Müller, S., Strack, S. N., Hoefler, B. C., Straight, P. D., Kearns, D. B. and Kirby, J. R. (2014). Bacillaene and sporulation protect *Bacillus subtilis* from predation by *Myxococcus xanthus*, *Appl. Environ. Microbiol.* 80(18), 5603–5610. doi: 10.1128/AEM.01621-14.

Müller, S., Strack, S. N., Ryan, S. E., Kearns, D. B. and Kirby, J. R. (2015). Predation by *Myxococcus xanthus* induces *Bacillus subtilis* to form spore-filled megastructures, *Appl. Environ. Microbiol.* 81(1), 203–210. doi: 10.1128/AEM.02448-14.

Mutlu, A., Kaspar, C., Becker, N. and Bischofs, I. B. (2020). A spore quality–quantity tradeoff favors diverse sporulation strategies in *Bacillus subtilis*, *ISME J.* 14(11), 2703–2714. doi: 10.1038/s41396-020-0721-4.

Nakano, M. M., Zhu, Y., Liu, J., Reyes, D. Y., Yoshikawa, H. and Zuber, P. (2000). Mutations conferring amino acid residue substitutions in the carboxy-terminal domain of

RNA polymerase α can suppress clpX and clpP with respect to developmentally regulated transcription in *Bacillus subtilis*, *Mol. Microbiol.* 37(4), 869–884. doi: 10.1046/j.1365-2958.2000.02052.x.

Nandeeshkumar, P., Ramachandrakini, K., Prakash, H. S., Niranjana, S. R. and Shekar Shetty, H. (2008). Induction of resistance against downy mildew on sunflower by rhizobacteria, *J. Plant Interact.* 3(4), 255–262. doi: 10.1080/17429140802245697.

Nihorimbere, V., Cawoy, H., Seyer, A., Brunelle, A., Thonart, P. and Ongena, M. (2012). Impact of rhizosphere factors on cyclic lipopeptide signature from the plant beneficial strain *Bacillus amyloliquefaciens* S499, *FEMS Microbiol. Ecol.* 79(1), 176–191. doi: 10.1111/j.1574-6941.2011.01208.x.

Nihorimbere, V., Fickers, P., Thonart, P. and Ongena, M. (2009). Ecological fitness of *Bacillus subtilis* BGS3 regarding production of the surfactin lipopeptide in the rhizosphere, *Environ. Microbiol. Rep.* 1(2), 124–130. doi: 10.1111/j.1758-2229.2009.00017.x.

Nikolić, I., Berić, T., Dimkić, I., Popović, T., Lozo, J., Fira, D. and Stanković, S. (2019). Biological control of *Pseudomonas syringae* pv. *aptataon* sugar beet with *Bacillus pumilus* SS-10.7 and *Bacillus amyloliquefaciens* (SS-12.6 and SS-38.4) strains, *J. Appl. Microbiol.* 126(1), 165–176. doi: 10.1111/jam.14070.

Nishimoto, R. (2019). Global trends in the crop protection industry, *J. Pestic. Sci.* 44(3), 141–147. doi: 10.1584/jpestics.D19-101.

Ntushelo, K., Ledwaba, L. K., Rauwane, M. E., Adebo, O. A. and Njobeh, P. B. (2019). The mode of action of *Bacillus* species against *Fusarium graminearum*, tools for investigation, and future prospects, *Toxins (Basel)* 11(10), 1–14. doi: 10.3390/toxins11100606.

Ogran, A., Yardeni, E. H., Keren-Paz, A., Bucher, T., Jain, R., Gilhar, O. and Kolodkin-Gal, I. (2019). The plant host induces antibiotic production to select the most-beneficial colonizers, *Appl. Environ. Microbiol.* 85(13), 1–15. doi: 10.1128/AEM.00512-19.

Ogura, M. (2001). DNA microarray analysis of *Bacillus subtilis* DegU, ComA and PhoP regulons: an approach to comprehensive analysis of *B.subtilis* two-component regulatory systems, *Nucleic Acids Res.* 29(18), 3804–3813. doi: 10.1093/nar/29.18.3804.

Ohno, A., Ano, T. and Shoda, M. (1995). Effect of temperature on production of lipopeptide antibiotics, iturin A and surfactin by a dual producer, *Bacillus subtilis* RB14, in solid-state fermentation, *J. Ferment. Bioeng.* 80(5), 517–519. doi: 10.1016/0922-338X(96)80930-5.

Ongena, M. and Jacques, P. (2008). *Bacillus lipopeptides*: versatile weapons for plant disease biocontrol, *Trends Microbiol.* 16(3), 115–125. doi: 10.1016/j.tim.2007.12.009.

Ongena, M., Jourdan, E., Adam, A., Paquot, M., Brans, A., Joris, B., Arpigny, J. L. and Thonart, P. (2007). Surfactin and fengycin lipopeptides of *Bacillus subtilis* as elicitors of induced systemic resistance in plants, *Environ. Microbiol.* 9(4), 1084–1090. doi: 10.1111/j.1462-2920.2006.01202.x.

Van Overbeek, L. and Van Elsas, J. D. (2008). Effects of plant genotype and growth stage on the structure of bacterial communities associated with potato (*Solanum tuberosum* L.), *FEMS Microbiol. Ecol.* 64(2), 283–296. doi: 10.1111/j.1574-6941.2008.00469.x.

Pandin, C., Le Coq, D., Canette, A., Aymerich, S. and Briandet, R. (2017). Should the biofilm mode of life be taken into consideration for microbial biocontrol agents?, *Microb. Biotechnol.* 10(4), 719–734. doi: 10.1111/1751-7915.12693.

Pandin, C., Le Coq, D., Deschamps, J., Védie, R., Rousseau, T., Aymerich, S. and Briandet, R. (2018). Complete genome sequence of *Bacillus velezensis* QST713: a biocontrol

agent that protects *Agaricus bisporus* crops against the green mould disease, *J. Biotechnol.* 278, 10–19. doi: 10.1016/j.jbiotec.2018.04.014.

Pandin, C., Darsonval, M., Mayeur, C., Le Coq, D., Aymerich, S. and Briandet, R. (2019). Biofilm formation and synthesis of antimicrobial compounds by the biocontrol agent *Bacillus velezensis* QST713 in an agaricus bisporus compost micromodel, *Appl. Environ. Microbiol.* 85(12), 1–13. doi: 10.1128/AEM.00327-19.

Park, K., Park, Y.-S., Ahamed, J., Dutta, S., Ryu, H., Lee, S.-H., Balaraju, K., Manir, M. and Moon, S.-S. (2016). Elicitation of induced systemic resistance of chili pepper by iturin A analogs derived from *Bacillus vallismortis* EXTN-1, *Can. J. Plant Sci.* 96(4), 564–570. doi: 10.1139/cjps-2015-0199.

Parnell, J. J., Berka, R., Young, H. A., Sturino, J. M., Kang, Y., Barnhart, D. M. and DiLeo, M. V. (2016). From the lab to the farm: an industrial perspective of plant beneficial microorganisms, *Front. Plant Sci.* 7(1110), 1110. doi: 10.3389/fpls.2016.01110.

Peng, G., Zhao, X., Li, Y., Wang, R., Huang, Y. and Qi, G. (2019). Engineering *Bacillus velezensis* with high production of acetoin primes strong induced systemic resistance in *Arabidopsis thaliana*, *Microbiol. Res.* 227, 1–12. doi: 10.1016/j.micres.2019.126297.

Pereira Monteiro, F., Henrique Vasconcelos de Medeiros, F., Ongena, M., Franzil, L., Estevao de Souza, P. and Teodoro de Souza, J. (2016). Effect of temperature, pH and substrate composition on production of lipopeptides by *Bacillus amyloliquefaciens* 629, *African. J. Microbiol. Res.* 10(36), 1506–1512. doi: 10.5897/AJMR2016.8222.

Pertot, I., Puopolo, G., Hosni, T., Pedrotti, L., Jourdan, E. and Ongena, M. (2013). Limited impact of abiotic stress on surfactin production in planta and on disease resistance induced by *Bacillus amyloliquefaciens* S499 in tomato and bean, *FEMS Microbiol. Ecol.* 86(3), 505–519. doi: 10.1111/1574-6941.12177.

Pieterse, C. M. J., Zamioudis, C., Berendsen, R. L., Weller, D. M., Van Wees, S. C. M. and Bakker, P. A. H. M. (2014). Induced systemic resistance by beneficial microbes, *Annu. Rev. Phytopathol.* 52(1), 347–375. doi: 10.1146/annurev-phyto-082712-102340.

Piggot, P. J. and Hilbert, D. W. (2004). Sporulation of *Bacillus subtilis*, *Curr. Opin. Microbiol.* 7(6), 579–586. doi: 10.1016/j.mib.2004.10.001.

Pisithkul, T., Schroeder, J. W., Trujillo, E. A., Yeesin, P., Stevenson, D. M., Chaiamarit, T., Coon, J. J., Wang, J. D. and Amador-Noguez, D. (2019). Metabolic remodeling during biofilm development of *Bacillus subtilis*, *mBio* 10(3), 1–32. doi: 10.1128/mBio.00623-19.

Plouznikoff, K., Declerck, S. and Calonne-Salmon, M. (2016). Mitigating abiotic stresses in crop plants by arbuscular mycorrhizal fungi. In: Vos, C. and Kazan, K. (eds) *Belowground Defence Strategies in Plants. Signaling and Communication in Plants*. Springer, Cham, 341–400. doi: 10.1007/978-3-319-42319-7_15.

Powers, M. J., Sanabria-Valentín, E., Bowers, A. A. and Shank, E. A. (2015). Inhibition of cell differentiation in *Bacillus subtilis* by *Pseudomonas protegens*, *J. Bacteriol.* 197(13), 2129–2138. doi: 10.1128/JB.02535-14.

Pršić, J. and Ongena, M. (2020). Elicitors of plant immunity triggered by beneficial bacteria, *Front. Plant Sci.* 11, 1–12. doi: 10.3389/fpls.2020.594530.

Punja, Z. K., Rodriguez, G. and Tirajoh, A. (2016). Effects of *Bacillus subtilis* strain QST 713 and storage temperatures on post-harvest disease development on greenhouse tomatoes, *Crop Prot.* 84, 98–104. doi: 10.1016/j.cropro.2016.02.011.

Qiao, J., Yu, X., Liang, X., Liu, Y., Borriss, R. and Liu, Y. (2017). Addition of plant-growth-promoting *Bacillus subtilis* PTS-394 on tomato rhizosphere has no durable impact

on composition of root microbiome, *BMC Microbiol.* 17(1), 131. doi: 10.1186/s12866-017-1039-x.

Qiu, M., Xu, Z., Li, X., Li, Q., Zhang, N., Shen, Q. and Zhang, R. (2014). Comparative proteomics analysis of *Bacillus amyloliquefaciens* SQR9 revealed the key proteins involved in in situ root colonization, *J. Proteome Res.* 13(12), 5581–5591. doi: 10.1021/pr500565m.

Raafat, M. M., Ali-Tammam, M. and Ali, A. E. (2019). Quorum quenching activity of *Bacillus cereus* isolate 30b confers antipathogenic effects in *Pseudomonas aeruginosa*, *Infect. Drug Resist.* 12, 1583–1596. doi: 10.2147/IDR.S182889.

Raaijmakers, J. M., De Bruijn, I., Nybroe, O. and Ongena, M. (2010). Natural functions of lipopeptides from Bacillus and Pseudomonas : more than surfactants and antibiotics, *FEMS Microbiol. Rev.* 34(6), 1037–1062. doi: 10.1111/j.1574-6976.2010.00221.x.

Rabbee, M. F., Ali, M. S., Choi, J., Hwang, B. S., Jeong, S. C. and Baek, K. H. (2019). *Bacillus velezensis*: a valuable member of bioactive molecules within plant microbiomes, *Molecules* 24(6), 1–13. doi: 10.3390/molecules24061046.

Rahman, A., Uddin, W. and Wenner, N. G. (2015). Induced systemic resistance responses in perennial ryegrass against *Magnaporthe oryzae* elicited by semi-purified surfactin lipopeptides and live cells of *Bacillus amyloliquefaciens*, *Mol. Plant Pathol.* 16(6), 546–558. doi: 10.1111/mpp.12209.

Rahman, M. (2016). *Bacillus* spp.: a promising biocontrol agent of root, foliar, and postharvest diseases of plants. In: Islam, M., Rahman, M., Pandey, P., Jha, C. and Aeron, A. (eds) *Bacilli and Agrobiotechnology*. Springer, Cham, 113–141. doi: 10.1007/978-3-319-44409-3_6.

Rais, A., Shakeel, M., Hafeez, F. Y. and Hassan, M. N. (2016). Plant growth promoting rhizobacteria suppress blast disease caused by *Pyricularia oryzae* and increase grain yield of rice, *BioControl* 61(6), 769–780. doi: 10.1007/s10526-016-9763-y.

Rajamanickam, S. and Nakkeeran, S. (2020). Flagellin of *Bacillus amyloliquefaciens* works as a resistance inducer against groundnut bud necrosis virus in chilli (*Capsicum annuum* L.), *Arch. Virol.* 165(7), 1585–1597. doi: 10.1007/s00705-020-04645-z.

Rajavel, M., Mitra, A. and Gopal, B. (2009). Role of *Bacillus subtilis* BacB in the synthesis of bacilysin, *J. Biol. Chem.* 284(46), 31882–31892. doi: 10.1074/jbc.M109.014522.

Ranf, S. (2018). Pattern recognition receptors–versatile genetic tools for engineering broad-spectrum disease resistance in crops, *Agronomy* 8(8), 1–13. doi: 10.3390/agronomy8080134.

Rangarajan, V., Dhanarajan, G. and Sen, R. (2015). Bioprocess design for selective enhancement of fengycin production by a marine isolate *Bacillus megaterium*, *Biochem. Eng. J.* 99, 147–155. doi: 10.1016/j.bej.2015.03.016.

Rashad, Y. M., Abbas, M. A., Soliman, H. M., Abdel-Fattah, G. G. and Abdel-Fattah, G. M. (2020). Synergy between endophytic *Bacillus amyloliquefaciens* GGA and arbuscular mycorrhizal fungi induces plant defense responses against white rot of garlic and improves host plant growth, *Phytopathol. Mediterr.* 59(1), 169–186. doi: 10.14601/Phyto-11019.

Raymaekers, K., Ponet, L., Holtappels, D., Berckmans, B. and Cammue, B. P. A. (2020). Screening for novel biocontrol agents applicable in plant disease management–a review, *Biol. Control* 144, 1–18. doi: 10.1016/j.biocontrol.2020.104240.

Raza, W., Ling, N., Yang, L., Huang, Q. and Shen, Q. (2016). Response of tomato wilt pathogen *Ralstonia solanacearum* to the volatile organic compounds produced by a biocontrol strain *Bacillus amyloliquefaciens* SQR-9, *Sci. Rep.* 6, 24856. doi: 10.1038/srep24856.

Romero, D., de Vicente, A., Rakotoaly, R. H., Dufour, S. E., Veening, J. W., Arrebola, E., Cazorla, F. M., Kuipers, O. P., Paquot, M. and Pérez-García, A. (2007). The Iturin and fengycin families of lipopeptides are key factors in antagonism of *Bacillus subtilis* toward *Podosphaera fusca*, *Mol. Plant Microbe Interact.* 20(4), 430–440. doi: 10.1094/MPMI-20-4-0430.

Rudrappa, T., Biedrzycki, M. L., Kunjeti, S. G., Donofrio, N. M., Czymmek, K. J., Paré, P. W. and Bais, H. P. (2010). The rhizobacterial elicitor acetoin induces systemic resistance in *Arabidopsis thaliana*, *Commun. Integr. Biol.* 3(2), 130–138. doi: 10.4161/cib.3.2.10584.

Rudrappa, T., Czymmek, K. J., Paré, P. W. and Bais, H. P. (2008). Root-secreted malic acid recruits beneficial soil bacteria, *Plant Physiol.* 148(3), 1547–1556. doi: 10.1104/pp.108.127613.

Ruiu, L. (2020). Plant-growth-promoting bacteria (PGPB) against insects and other agricultural pests, *Agronomy* 10(6), 1–12. doi: 10.3390/agronomy10060861.

Ryu, C. M., Farag, M. A., Hu, C. H., Reddy, M. S., Kloepper, J. W. and Paré, P. W. (2004). Bacterial volatiles induce systemic resistance in Arabidopsis, *Plant Physiol.* 134(3), 1017–1026. doi: 10.1104/pp.103.026583.

Saber, W. I. A., Ghoneem, K. M., Al-Askar, A. A., Rashad, Y. M., Ali, A. A. and Rashad, E. M. (2015). Chitinase production by *Bacillus subtilis* ATCC 11774 and its effect on biocontrol of Rhizoctonia diseases of potato, *Acta Biol. Hung.* 66(4), 436–448. doi: 10.1556/018.66.2015.4.8.

Saikia, K., Belwal, V. K., Datta, D. and Chaudhary, N. (2019). Aromatic-rich C-terminal region of LCI is a potent antimicrobial peptide in itself, *Biochem. Biophys. Res. Commun.* 519(2), 372–377. doi: 10.1016/j.bbrc.2019.09.013.

Salazar, F., Ortiz, A. and Sansinenea, E. (2017). Characterisation of two novel bacteriocin-like substances produced by *Bacillus amyloliquefaciens* ELI149 with broad-spectrum antimicrobial activity, *J. Glob. Antimicrob. Resist.* 11, 177–182. doi: 10.1016/j.jgar.2017.08.008.

Sarwar, A., Hassan, M. N., Imran, M., Iqbal, M., Majeed, S., Brader, G., Sessitsch, A. and Hafeez, F. Y. (2018). Biocontrol activity of surfactin A purified from Bacillus NH-100 and NH-217 against rice bakanae disease, *Microbiol. Res.* 209, 1–13. doi: 10.1016/j.micres.2018.01.006.

Sasse, J., Martinoia, E. and Northen, T. (2018). Feed your friends: do plant exudates shape the root microbiome?, *Trends Plant Sci.* 23(1), 25–41. doi: 10.1016/j.tplants.2017.09.003.

Savary, S., Willocquet, L., Pethybridge, S. J., Esker, P., McRoberts, N. and Nelson, A. (2019). The global burden of pathogens and pests on major food crops, *Nat. Ecol. Evol.* 3(3), 430–439. doi: 10.1038/s41559-018-0793-y.

Saxena, A. K., Kumar, M., Chakdar, H., Anuroopa, N. and Bagyaraj, D. J. (2020). *Bacillus* species in soil as a natural resource for plant health and nutrition, *J. Appl. Microbiol.* 128(6), 1583–1594. doi: 10.1111/jam.14506.

Schallmey, M., Singh, A. and Ward, O. P. (2004). Developments in the use of *Bacillus* species for industrial production, *Can. J. Microbiol.* 50(1), 1–17. doi: 10.1139/w03-076.

Schellenberger, R., Touchard, M., Clément, C., Baillieul, F., Cordelier, S., Crouzet, J. and Dorey, S. (2019). Apoplastic invasion patterns triggering plant immunity: plasma membrane sensing at the frontline, *Mol. Plant Pathol.* 20(11), 1602–1616. doi: 10.1111/mpp.12857.

Schisler, D. A., Slininger, P. J., Behle, R. W. and Jackson, M. A. (2004). Formulation of *Bacillus* spp. for biological control of plant diseases, *Phytopathology*® 94(11), 1267–1271. doi: 10.1094/PHYTO.2004.94.11.1267.

Schmitz, S., Hoffmann, A., Szekat, C., Rudd, B. and Bierbaum, G. (2006). The lantibiotic mersacidin is an autoinducing peptide, *Appl. Environ. Microbiol.* 72(11), 7270–7277. doi: 10.1128/AEM.00723-06.

Scholz, R., Molohon, K. J., Nachtigall, J., Vater, J., Markley, A. L., Sussmuth, R. D., Mitchell, D. A. and Borriss, R. (2011). Plantazolicin, a novel microcin B17/Streptolysin S-like natural product from *Bacillus amyloliquefaciens* FZB42, *J. Bacteriol.* 193(1), 215–224. doi: 10.1128/JB.00784-10.

Scholz, R., Vater, J., Budiharjo, A., Wang, Z., He, Y., Dietel, K., Schwecke, T., Herfort, S., Lasch, P. and Borriss, R. (2014). Amylocyclicin, a novel circular bacteriocin produced by *Bacillus amyloliquefaciens* FZB42, *J. Bacteriol.* 196(10), 1842–1852. doi: 10.1128/JB.01474-14.

Shen, Y., Li, J., Xiang, J., Wang, J., Yin, K. and Liu, Q. (2019). Isolation and identification of a novel protein elicitor from a *Bacillus subtilis* strain BU412, *AMB Express* 9(1), 117. doi: 10.1186/s13568-019-0822-5.

Solanki, M. K., Singh, R. K., Srivastava, S., Kumar, S., Kashyap, P. L. and Srivastava, A. K. (2015). Characterization of antagonistic-potential of two Bacillus strains and their biocontrol activity against *Rhizoctonia solani* in tomato, *J. Basic Microbiol.* 55(1), 82–90. doi: 10.1002/jobm.201300528.

Sourjik, V. and Wingreen, N. S. (2012). Responding to chemical gradients: bacterial chemotaxis, *Curr. Opin. Cell Biol.* 24(2), 262–268. doi: 10.1016/j.ceb.2011.11.008.

Spraker, J. E., Luu, G. T. and Sanchez, L. M. (2020). Imaging mass spectrometry for natural products discovery: a review of ionization methods, *Nat. Prod. Rep.* 37(2), 150–162. doi: 10.1039/C9NP00038K.

Stamenkovic-Stojanovic, S., Karabegovic, I., Beskoski, V., Nikolic, N. and Lazic, M. (2019). Bacillus based microbial formulations: optimization of the production process, *Hem. Ind.* 73(3), 169–182. doi: 10.2298/HEMIND190214014S.

Tan, S., Yang, C., Mei, X., Shen, S., Raza, W., Shen, Q. and Xu, Y. (2013). The effect of organic acids from tomato root exudates on rhizosphere colonization of *Bacillus amyloliquefaciens* T-5, *Appl. Soil Ecol.* 64, 15–22. doi: 10.1016/j.apsoil.2012.10.011.

Tanaka, K., Amaki, Y., Ishihara, A. and Nakajima, H. (2015). Synergistic effects of [Ile 7] surfactin homologues with bacillomycin D in suppression of gray mold disease by *Bacillus amyloliquefaciens* biocontrol strain SD-32, *J. Agric. Food Chem.* 63(22), 5344–5353. doi: 10.1021/acs.jafc.5b01198.

Tao, Y., Bie, X. M., Lv, F. X., Zhao, H. Z. and Lu, Z. X. (2011). Antifungal activity and mechanism of fengycin in the presence and absence of commercial surfactin against *Rhizopus stolonifer*, *J. Microbiol.* 49(1), 146–150. doi: 10.1007/s12275-011-0171-9.

Thérien, M., Kieveswalter, H. T., Auria, E., Charron-Lamoureux, V., Wibowo, M., Maróti, G., Kovács, Á. T. and Beauregard, P. B. (2020). Surfactin production is not essential for pellicle and root-associated biofilm development of *Bacillus subtilis*, *Biofilm* 2, 1–7. doi: 10.1016/j.bioflm.2020.100021.

Toral, L., Rodríguez, M., Béjar, V. and Sampedro, I. (2020). Crop protection against *Botrytis cinerea* by Rhizhosphere biological control agent *Bacillus velezensis* XT1, *Microorganisms* 8(7), 1–17. doi: 10.3390/microorganisms8070992.

Touré, Y., Ongena, M., Jacques, P., Guiro, A. and Thonart, P. (2004). Role of lipopeptides produced by *Bacillus subtilis* GA1 in the reduction of grey mould disease

caused by *Botrytis cinerea* on apple, *J. Appl. Microbiol.* 96(5), 1151–1160. doi: 10.1111/j.1365-2672.2004.02252.x.

Traxler, M. F. and Kolter, R. (2015). Natural products in soil microbe interactions and evolution, *Nat. Prod. Rep.* 32(7), 956–970. doi: 10.1039/C5NP00013K.

Vanthana, M., Nakkeeran, S., Malathi, V. G., Renukadevi, P. and Vinodkumar, S. (2019). Induction of in planta resistance by flagellin (Flg) and elongation factor-TU (EF-Tu) of *Bacillus amyloliquefaciens*(VB7) against groundnut bud necrosis virus in tomato, *Microb. Pathog.* 137, 1–11. doi: 10.1016/j.micpath.2019.103757.

Vargas-Bautista, C., Rahlwes, K. and Straight, P. (2014). Bacterial competition reveals differential regulation of the pks genes by *Bacillus subtilis*, *J. Bacteriol.* 196(4), 717–728. doi: 10.1128/JB.01022-13.

Villa-Rodríguez, E., Parra-Cota, F., Castro-Longoria, E., López-Cervantes, J. and de los Santos-Villalobos, S. (2019). Bacillus subtilis TE3: a promising biological control agent against *Bipolaris sorokiniana*, the causal agent of spot blotch in wheat (Triticum turgidum L. subsp. durum), *Biol. Control* 132, 135–143. doi: 10.1016/j.biocontrol.2019.02.012.

Villegas-Escobar, V., González-Jaramillo, L. M., Ramírez, M., Moncada, R. N., Sierra-Zapata, L., Orduz, S. and Romero-Tabarez, M. (2018). Lipopeptides from *Bacillus* sp. EA-CB0959: active metabolites responsible for in vitro and in vivo control of *Ralstonia solanacearum*, *Biol. Control* 125, 20–28. doi: 10.1016/j.biocontrol.2018.06.005.

Vinale, F., Sivasithamparam, K., Ghisalberti, E. L., Marra, R., Woo, S. L. and Lorito, M. (2008). Trichoderma-plant-pathogen interactions, *Soil Biol. Biochem.* 40(1), 1–10. doi: 10.1016/j.soilbio.2007.07.002.

Vivas, A., Marulanda, A., Gómez, M., Barea, J. M. and Azcón, R. (2003). Physiological characteristics (SDH and ALP activities) of arbuscular mycorrhizal colonization as affected by *Bacillus thuringiensis* inoculation under two phosphorus levels, *Soil Biol. Biochem.* 35(7), 987–996. doi: 10.1016/S0038-0717(03)00161-5.

Vlamakis, H., Chai, Y., Beauregard, P., Losick, R. and Kolter, R. (2013). Sticking together: building a biofilm the *Bacillus subtilis* way, *Nat. Rev. Microbiol.* 11(3), 157–168. doi: 10.1038/nrmicro2960.

Wang, H., Shi, Y., Wang, D., Yao, Z., Wang, Y., Liu, J., Zhang, S. and Wang, A. (2018). A biocontrol strain of *Bacillus subtilis* WXCDD105 used to control tomato *Botrytis cinerea* and *Cladosporium fulvum* Cooke and promote the growth of seedlings, *Int. J. Mol. Sci.* 19(5), 1–17. doi: 10.3390/ijms19051371.

Wang, N., Liu, M., Guo, L., Yang, X. and Qiu, D. (2016). A novel protein elicitor (PeBA1) from *Bacillus amyloliquefaciens* NC6 induces systemic resistance in tobacco, *Int. J. Biol. Sci.* 12(6), 757–767. doi: 10.7150/ijbs.14333.

Wang, P., Guo, Q., Ma, Y., Li, S., Lu, X., Zhang, X. and Ma, P. (2015). DegQ regulates the production of fengycins and biofilm formation of the biocontrol agent *Bacillus subtilis* NCD-2, *Microbiol. Res.* 178, 42–50. doi: 10.1016/j.micres.2015.06.006.

Wang, R., Liang, X., Long, Z., Wang, X., Yang, L., Lu, B. and Gao, J. (2020a). An LCI-like protein APC 2 protects ginseng root from *Fusarium solani* infection, *J. Appl. Microbiol.* 130(1), 165–178. doi: 10.1111/jam.14771.

Wang, X., Yuan, Z., Shi, Y., Cai, F., Zhao, J., Wang, J. and Wang, Y. (2020b). *Bacillus amyloliquefaciens* HG01 induces resistance in loquats against anthracnose rot caused by *Colletotrichum acutatum*, *Postharvest Biol. Technol.* 160, 1–7. doi: 10.1016/j.postharvbio.2019.111034.

Wang, Y., Zhang, C., Liang, J., Wang, L., Gao, W., Jiang, J. and Chang, R. (2020c). Surfactin and fengycin B extracted from *Bacillus pumilus* W-7 provide protection against potato late blight via distinct and synergistic mechanisms, *Appl. Microbiol. Biotechnol.* 104(17), 7467–7481. doi: 10.1007/s00253-020-10773-y.

Van Wees, S. C. M., De Swart, E. A. M., Van Pelt, J. A., Van Loon, L. C. and Pieterse, C. M. J. (2000). Enhancement of induced disease resistance by simultaneous activation of salicylate- and jasmonate-dependent defense pathways in *Arabidopsis thaliana*, *Proc. Natl. Acad. Sci. U. S. A.* 97(15), 8711–8716. doi: 10.1073/pnas.130425197.

Winn, M., Fyans, J. K., Zhuo, Y. and Micklefield, J. (2016). Recent advances in engineering nonribosomal peptide assembly lines, *Nat. Prod. Rep.* 33(2), 317–347. doi: 10.1039/C5NP00099H.

Wise, C., Falardeau, J., Hagberg, I. and Avis, T. J. (2014). Cellular lipid composition affects sensitivity of plant pathogens to fengycin, an antifungal compound produced by *Bacillus subtilis* strain CU12, *Phytopathology®* 104(10), 1036–1041. doi: 10.1094/PHYTO-12-13-0336-R.

Woo, S. L., Ruocco, M., Vinale, F., Nigro, M., Marra, R., Lombardi, N., Pascale, A., Lanzuise, S., Manganiello, G. and Lorito, M. (2014). Trichoderma-based products and their widespread use in agriculture, *TOMYCJ* 8(1), 71–126. doi: 10.2174/1874437001408010071.

Wu, K., Fang, Z., Guo, R., Pan, B., Shi, W., Yuan, S., Guan, H., Gong, M., Shen, B. and Shen, Q. (2015a). Pectin enhances bio-control efficacy by inducing colonization and secretion of secondary metabolites by *Bacillus amyloliquefaciens* SQY 162 in the rhizosphere of tobacco, *Plos One* 10(5), e0127418. doi: 10.1371/journal.pone.0127418.

Wu, L., Wu, H., Chen, L., Yu, X., Borriss, R. and Gao, X. (2015b). Difficidin and bacilysin from *Bacillus amyloliquefaciens* FZB42 have antibacterial activity against *Xanthomonas oryzae* rice pathogens, *Sci. Rep.* 5, 12975. doi: 10.1038/srep12975.

Wu, Q., Ni, M., Dou, K., Tang, J., Ren, J., Yu, C. and Chen, J. (2018). Co-culture of *Bacillus amyloliquefaciens* accC11060 and *Trichoderma asperellum* GDFS1009 enhanced pathogen-inhibition and amino acid yield, *Microb. Cell Fact.* 17(1), 155. doi: 10.1186/s12934-018-1004-x.

Xie, S., Wu, H., Chen, L., Zang, H., Xie, Y. and Gao, X. (2015). Transcriptome profiling of *Bacillus subtilis* OKB105 in response to rice seedlings, *BMC Microbiol.* 15(21), 21. doi: 10.1186/s12866-015-0353-4.

Xu, Y., Cai, D., Zhang, H., Gao, L., Yang, Y., Gao, J., Li, Y., Yang, C., Ji, Z., Yu, J. and Chen, S. (2020). Enhanced production of iturin A in *Bacillus amyloliquefaciens* by genetic engineering and medium optimization, *Process Biochem.* 90, 50–57. doi: 10.1016/j.procbio.2019.11.017.

Yadav, R., Ror, P., Rathore, P. and Ramakrishna, W. (2020). Bacteria from native soil in combination with arbuscular mycorrhizal fungi augment wheat yield and biofortification, *Plant Physiol. Biochem.* 150, 222–233. doi: 10.1016/j.plaphy.2020.02.039.

Yamamoto, S., Shiraishi, S. and Suzuki, S. (2015). Are cyclic lipopeptides produced by *Bacillus amyloliquefaciens* S13-3 responsible for the plant defence response in strawberry against *Colletotrichum gloeosporioides*?, *Lett. Appl. Microbiol.* 60(4), 379–386. doi: 10.1111/lam.12382.

Yazgan, A., Özcengiz, G. and Marahiel, M. A. (2001). Tn10 insertional mutations of *Bacillus subtilis* that block the biosynthesis of bacilysin, *Biochim. Biophys. Acta* 1518(1–2), 87–94. doi: 10.1016/S0167-4781(01)00182-8.

Yazgan Karata, A., Çetin, S. and Özcengiz, G. (2003). The effects of insertional mutations in comQ, comP, srfA, spo0H, spo0A and abrB genes on bacilysin biosynthesis in *Bacillus subtilis*, *Biochim. Biophys. Acta Gene Struct. Expr.* 1626(1–3), 51–56. doi: 10.1016/S0167-4781(03)00037-X.

Ye, M., Tang, X., Yang, R., Zhang, H., Li, F., Tao, F., Li, F. and Wang, Z. (2018). Characteristics and application of a novel species of Bacillus: *Bacillus velezensis*, *ACS Chem. Biol.* 13(3), 500–505. doi: 10.1021/acschembio.7b00874.

Yeh, M.-S., Wei, Y.-H. and Chang, J.-S. (2006). Bioreactor design for enhanced carrier-assisted surfactin production with *Bacillus subtilis*, *Process Biochem.* 41(8), 1799–1805. doi: 10.1016/j.procbio.2006.03.027.

Yi, G., Liu, Q., Lin, J., Wang, W., Huang, H. and Li, S. (2017). Repeated batch fermentation for surfactin production with immobilized *Bacillus subtilis* BS-37: two-stage pH control and foam fractionation, *J. Chem. Technol. Biotechnol.* 92(3), 530–535. doi: 10.1002/jctb.5028.

Yssel, A., Reva, O. and Tastan Bishop, O. (2011). Comparative structural bioinformatics analysis of *Bacillus amyloliquefaciens* chemotaxis proteins within *Bacillus subtilis* group, *Appl. Microbiol. Biotechnol.* 92(5), 997–1008. doi: 10.1007/s00253-011-3582-y.

Yu, X., Feng, B., He, P. and Shan, L. (2017). From chaos to harmony: responses and signaling upon microbial pattern recognition, *Annu. Rev. Phytopathol.* 55(1), 109–137. doi: 10.1146/annurev-phyto-080516-035649.

Yuan, J., Li, B., Zhang, N., Waseem, R., Shen, Q. and Huang, Q. (2012a). Production of bacillomycin- and macrolactin-type antibiotics by *Bacillus amyloliquefaciens* NJN-6 for suppressing soilborne plant pathogens, *J. Agric. Food Chem.* 60(12), 2976–2981. doi: 10.1021/jf204868z.

Yuan, J., Raza, W., Shen, Q. and Huang, Q. (2012b). Antifungal activity of *Bacillus amyloliquefaciens* NJN-6 volatile compounds against *Fusarium oxysporum* f. sp. *cubense*, *Appl. Environ. Microbiol.* 78(16), 5942–5944. doi: 10.1128/AEM.01357-12.

Zakharova, A. A., Efimova, S. S., Malev, V. V. and Ostroumova, O. S. (2019). Fengycin induces ion channels in lipid bilayers mimicking target fungal cell membranes, *Sci. Rep.* 9(1), 16034. doi: 10.1038/s41598-019-52551-5.

Zaki, O., Weekers, F., Thonart, P., Tesch, E., Kuenemann, P. and Jacques, P. (2020). Limiting factors of mycopesticide development, *Biol. Control* 144, 1–12. doi: 10.1016/j.biocontrol.2020.104220.

Zeriouh, H., Romero, D., García-Gutiérrez, L., Cazorla, F. M., de Vicente, A. and Pérez-García, A. (2011). The Iturin-like lipopeptides are essential components in the biological control arsenal of *Bacillus subtilis* against bacterial diseases of cucurbits, *Mol. Plant Microbe Interact.* 24(12), 1540–1552. doi: 10.1094/MPMI-06-11-0162.

Zeriouh, H., de Vicente, A., Pérez-García, A. and Romero, D. (2014). Surfactin triggers biofilm formation of *Bacillus subtilis* in melon phylloplane and contributes to the biocontrol activity, *Environ. Microbiol.* 16(7), 2196–2211. doi: 10.1111/1462-2920.12271.

Zhang, D., Yu, S., Yang, Y., Zhang, J., Zhao, D., Pan, Y., Fan, S., Yang, Z. and Zhu, J. (2020). Antifungal effects of volatiles produced by *Bacillus subtilis* against *Alternaria solani* in potato, *Front. Microbiol.* 11(1196), 1196. doi: 10.3389/fmicb.2020.01196.

Zhang, L., Feng, G. and Declerck, S. (2018). Signal beyond nutrient, fructose, exuded by an arbuscular mycorrhizal fungus triggers phytate mineralization by a phosphate solubilizing bacterium, *ISME J.* 12(10), 2339–2351. doi: 10.1038/s41396-018-0171-4.

Zhang, L. and Sun, C. (2018). Fengycins, cyclic lipopeptides from marine *Bacillus subtilis* strains, kill the plant-pathogenic fungus *Magnaporthe grisea* by inducing reactive oxygen species production and chromatin condensation, *Appl. Environ. Microbiol.* 84(18), 1–17. doi: 10.1128/AEM.00445-18.

Zhang, N., Wang, D., Liu, Y., Li, S., Shen, Q. and Zhang, R. (2013). Effects of different plant root exudates and their organic acid components on chemotaxis, biofilm formation and colonization by beneficial rhizosphere-associated bacterial strains, *Plant Soil* 374(1–2), 689–700. doi: 10.1007/s11104-013-1915-6.

Zhang, N., Yang, D., Wang, D., Miao, Y., Shao, J., Zhou, X., Xu, Z., Li, Q., Feng, H., Li, S., Shen, Q. and Zhang, R. (2015). Whole transcriptomic analysis of the plant-beneficial rhizobacterium *Bacillus amyloliquefaciens* SQR9 during enhanced biofilm formation regulated by maize root exudates, *BMC Genomics* 16(685), 685. doi: 10.1186/s12864-015-1825-5.

Zhang, S., White, T. L., Martinez, M. C., McInroy, J. A., Kloepper, J. W. and Klassen, W. (2010). Evaluation of plant growth-promoting rhizobacteria for control of Phytophthora blight on squash under greenhouse conditions, *Biol. Control* 53(1), 129–135. doi: 10.1016/j.biocontrol.2009.10.015.

Zhang, X., Zhou, Y., Li, Y., Fu, X. and Wang, Q. (2017a). Screening and characterization of endophytic Bacillus for biocontrol of grapevine downy mildew, *Crop Prot.* 96, 173–179. doi: 10.1016/j.cropro.2017.02.018.

Zhang, Y., Nakano, S., Choi, S. Y. and Zuber, P. (2006). Mutational analysis of the *Bacillus subtilis* RNA polymerase α C-terminal domain supports the interference model of Spx-dependent repression, *J. Bacteriol.* 188(12), 4300–4311. doi: 10.1128/JB.00220-06.

Zhang, Z., Ding, Z. T., Zhong, J., Zhou, J. Y., Shu, D., Luo, D., Yang, J. and Tan, H. (2017b). Improvement of iturin A production in *Bacillus subtilis* ZK0 by overexpression of the comA and sigA genes, *Lett. Appl. Microbiol.* 64(6), 452–458. doi: 10.1111/lam.12739.

Zhi, Y., Wu, Q. and Xu, Y. (2017). Genome and transcriptome analysis of surfactin biosynthesis in *Bacillus amyloliquefaciens* MT45, *Sci. Rep.* 7, 40976. doi: 10.1038/srep40976.

Zihalirwa Kulimushi, P., Argüelles Arias, A., Franzil, L., Steels, S. and Ongena, M. (2017). Stimulation of fengycin-type antifungal lipopeptides in *Bacillus amyloliquefaciens* in the presence of the maize fungal pathogen *Rhizomucor variabilis*, *Front. Microbiol.* 8(850), 850. doi: 10.3389/fmicb.2017.00850.

Zouari, I., Jlaiel, L., Tounsi, S. and Trigui, M. (2016). Biocontrol activity of the endophytic *Bacillus amyloliquefaciens* strain CEIZ-11 against *Pythium aphanidermatum* and purification of its bioactive compounds, *Biol. Control* 100, 54–62. doi: 10.1016/j.biocontrol.2016.05.012.