marine drugs

MDPI

Review

Saline Environments as a Source of Potential Quorum Sensing Disruptors to Control Bacterial Infections: A Review

Marta Torres [1,2,3], Yves Dessaux [3,*] and Inmaculada Llamas [1,2,*]

[1] Department of Microbiology, Faculty of Pharmacy, University of Granada, 18071 Granada, Spain; mtorres@ugr.es
[2] Institute of Biotechnology, Biomedical Research Center (CIBM), University of Granada, 18100 Granada, Spain
[3] Institute for Integrative Biology of the Cell (I2BC), CEA/CNRS/University Paris-Sud, University Paris-Saclay, 91198 Gif-sur-Yvette, France
* Correspondence: yves.dessaux@i2bc.paris-saclay.fr (Y.D.); illamas@ugr.es (I.L.)

Received: 27 February 2019; Accepted: 20 March 2019; Published: 25 March 2019

Abstract: Saline environments, such as marine and hypersaline habitats, are widely distributed around the world. They include sea waters, saline lakes, solar salterns, or hypersaline soils. The bacteria that live in these habitats produce and develop unique bioactive molecules and physiological pathways to cope with the stress conditions generated by these environments. They have been described to produce compounds with properties that differ from those found in non-saline habitats. In the last decades, the ability to disrupt quorum-sensing (QS) intercellular communication systems has been identified in many marine organisms, including bacteria. The two main mechanisms of QS interference, i.e., quorum sensing inhibition (QSI) and quorum quenching (QQ), appear to be a more frequent phenomenon in marine aquatic environments than in soils. However, data concerning bacteria from hypersaline habitats is scarce. Salt-tolerant QSI compounds and QQ enzymes may be of interest to interfere with QS-regulated bacterial functions, including virulence, in sectors such as aquaculture or agriculture where salinity is a serious environmental issue. This review provides a global overview of the main works related to QS interruption in saline environments as well as the derived biotechnological applications.

Keywords: quorum sensing; QSI; quorum quenching; QQ; marine habitat; saline environment; hypersaline habitat; marine pathogens; plant pathogens; *Vibrio*

1. Introduction

Many bacterial species have developed sophisticated cell concentration-dependent gene expression mechanisms. These are collectively called quorum sensing (QS), a term that was first introduced by Fuqua et al. in 1994 [1]. This phenomenon involves the synthesis, release and detection of signal molecules known as autoinducers, the concentration of which mirrors that of the bacterial population. Once a threshold signal concentration, i.e., a threshold bacterial concentration is reached, the presence of the signal is perceived by the emitting bacteria which in turn induce the QS-regulated biological response in a synchronous way (reviews: [2–4]). The first instance of QS-regulation was found in the *Vibrionaceae Photobacterium fischeri* (now *Aliivibrio fischeri*; [5]), where it regulates light emission (bioluminescence) by the bacteria in dedicated organs of marine animals [6,7]. The biological role of this symbiotic interaction is not fully understood, though it has been proposed that light production may attract some marine organisms including zooplankton ([8], review: [9]).

Multiple QS signals have been identified in bacteria. The most common ones are *N*-acylhomoserine lactones (AHLs) produced by numerous *Proteobacteria*; oligopeptides produced by *Firmicutes,* and furanosylborate diester (AI-2) produced by both *Proteobacteria* and *Firmicutes* (reviews: [2–4,10–12]). Other signals, such as 3-hydroxypalmitate (3OH-PAME; [13]), diketopiperazines (DKP; [14]), quinolones (PQS; [15]), diffusible signal factors (DSF; [16]), or resorcinol derivatives [17] have been detected in a limited number of proteobacterial species.

QS is ubiquitous in the bacterial world. It regulates different cellular functions that generally permit the adaptation of the bacteria to its environment, most often by gaining a better access to resources. For instance, QS-regulated functions include the production of antibiotics that allow the emitting bacteria to outcompete other microbes, or exoenzymes and toxins that permit bacteria to take advantage of the metabolites and tissues of other organisms that they parasite. QS-regulated functions also include the production of exopolysaccharides, the control of swarming motility or biofilm formation, the conjugal transfer of plasmids, etc. (a nonlimitative list; reviews: [2–4,12,18,19]). In plant and animal pathogens, some of the above QS-regulated functions are therefore determinants of the bacterial virulence or virulence-associated traits.

2. Quorum Sensing in Bacteria of Aquacultural Importance

The genera *Vibrio*, *Edwardsiella*, *Aeromonas*, *Pseudomonas*, and *Yersinia* encompass species that are pathogens of marine organisms [20–24]. Numerous studies have focused on Vibrio species that are ubiquitous in marine and estuarine ecosystems, including aquaculture farms. Some of these species, such as *V. harveyi*, *V. campbellii*, or *V. alginolyticus* are the main causative agents of diseases in marine animals that generate a high mortality rate worldwide [25–30].

In *Vibrio*, QS depends on at least three major signal classes: AHLs [7], AI-2 (4,5-dihydroxy-2,3-pentanedione and its boron-containing derivatives; [31,32]), and 3-hydroxytridecan-4-one (or CAI-1), the latter compound being a key regulator of pathogenicity in *V. cholerae* [33,34]. In *V. harveyi* and *V. campbellii*, the three QS signals can also be produced [10] but in these species CAI-1 slightly differs from that of *V. cholerae* as being (*Z*)-3-aminoundec-2-en-4-one [35]. This triple signalization pathway involves three different sensing systems (LuxN, Lux Q, and CqsS). Schematically (Figure 1), each of them consists of a membrane-bound histidine-kinase sensor protein that, in the absence of QS signal, activates by phosphorylation via the phosphorelay protein LuxU, the common response receptor LuxO (Figure 1, left panel). LuxO activates the transcription of sRNAs that mostly target the mRNA resulting from the transcription of *luxR*. LuxR is the main QS regulator of the transcription of QS-regulated genes. In the presence of the QS signals (Figure 1, right panel), the histidine kinases become phosphatases, a feature that eventually leads to the dephosphorylation of LuxO thus authorizing the production of LuxR and the expression of the QS-regulated genes (reviews: [10,36,37]). In *Vibrio* spp., QS-regulated genes encode the synthesis of biofilm, exoenzymes, and pigments [22,24,38–43], some being, as indicated earlier, virulence factors. For instance, the QS-controlled traits in *Vibrio campbellii* include the synthesis of siderophores that efficiently chelate iron, and that of metalloprotease, and chitinase A that can degrade the tissue of the host [30,44,45]. In *V. anguillarum* QS controls the production of metalloprotease, siderophore and biofilm [38,46] while in *V. owensii*, *V. mediterranei*, and *V. corallilyticus* QS regulates the production of exoenzymes and the swarming ability (Table 1) [47].

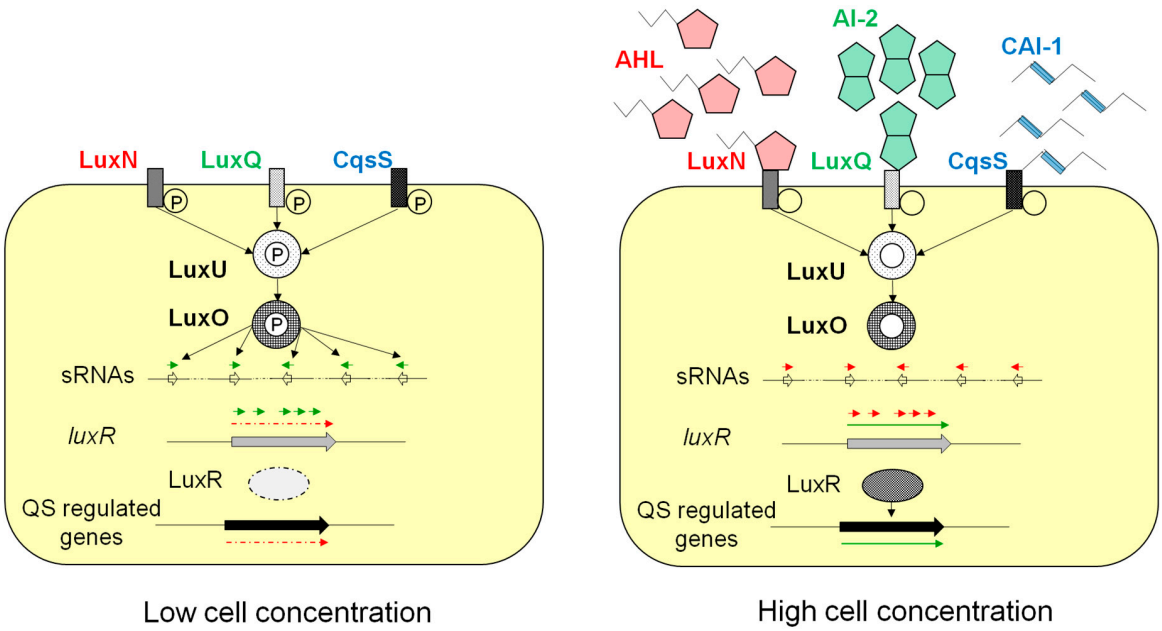

Figure 1. The three parallel quorum-sensing (QS) signaling pathways of *Vibrio harveyi*. The three types of QS signals (AHL, AI-2, and CAI-1) as well as the regulatory process are described below in the text. Legends: sRNAs stands for bacterial small RNAs. The circles linked to LuxN, LuxQ, CqsS, LuxU, and LuxO indicate the phosphorylation status of the proteins (P, phosphorylated; no letter, dephosphorylated). Bold arrows symbolize genes; thin arrows represent RNAs, either sRNAs or mRNAs. Red lines indicate nontranscribed RNAs; green lines, transcribed RNAs. Figure is adapted from [48].

3. Inhibition of Quorum Sensing Mechanisms

In the last decades (see for instance: [49–53]), research has focused on one promising strategy based on the inhibition of the expression of virulence genes that are regulated by QS mechanisms (reviews: [54,55]) in proteobacteria of marine and agricultural importance (Table 1). This strategy has been termed antivirulence (reviews: [56,57]) since it aims at "disarming" the pathogens rather than killing them, thereby preventing disease induction in their host. Given that QS-regulated genes are generally not essential for the bacteria, antivirulence approaches apply less selective pressure on the pathogens and attenuate bacterial infections without decreasing growth, in contrast to antibiotics (review: [58]). Therefore, in principle, the inhibition of the cell-to-cell communication system would not lead to the development of resistance in bacteria. However, several authors have suggested that some bacteria could originate resistance mechanisms to compounds that interfere with QS [59–63]. This could be achieved by enhanced effluxes of signal molecules or modifications on the receptor-binding site of the LuxR-type regulator, or through the generation of spontaneous mutants that stop controlling their virulence via signal molecules and become resistant to QS interference [64,65]. However, even if resistances might happen, some authors suggested that this does not imply that it will spread [66]. Moreover, the resistance rates could be much lower than what has been observed for conventional antimicrobials (reviews: [66–69]).

Many organisms, including bacteria [70–74], yeasts [75–77], fungi [78,79], and marine and terrestrial plants [80–83] and animals [84–86] have developed the ability to disrupt AHL-based QS systems through various mechanisms (reviews: [54,55,87,88]). The first mechanism described is based on the production of molecules that act as antagonists of signals and interfere with the detection of signal molecules by their cognate transcriptional regulator (Figure 2). These molecules were termed quorum sensing inhibitors (QSIs; [80,89]). Another mechanism, known as quorum quenching (QQ; [72]), consists of the enzymatic inactivation of AHL signal molecules that abolishes bacterial QS-regulated functions (Figure 2). Nowadays, three main groups of QQ enzymes have been described

based on the involved enzymatic activity. These are: (i), the AHL acylases [90] that catalyze the hydrolytic cleavage of an amide bond between the acyl chain and the homoserine lactone ring; (ii), the AHL lactonases [71] that open the lactone ring in the AHL molecule to form *N*-acylhomoserine as a product; and (iii), the AHL oxidoreductases [91] that modify the AHLs by oxidizing or reducing the acyl chain without degrading the compound (reviews: [55,92]). The biological roles of QSI production and QQ enzymes are multiple: they range from the fine tuning of QS regulated function to resistance to antimicrobial compounds, and from the recycling of QS signals to the establishment of sophisticated "decision mechanisms" (review: [55]).

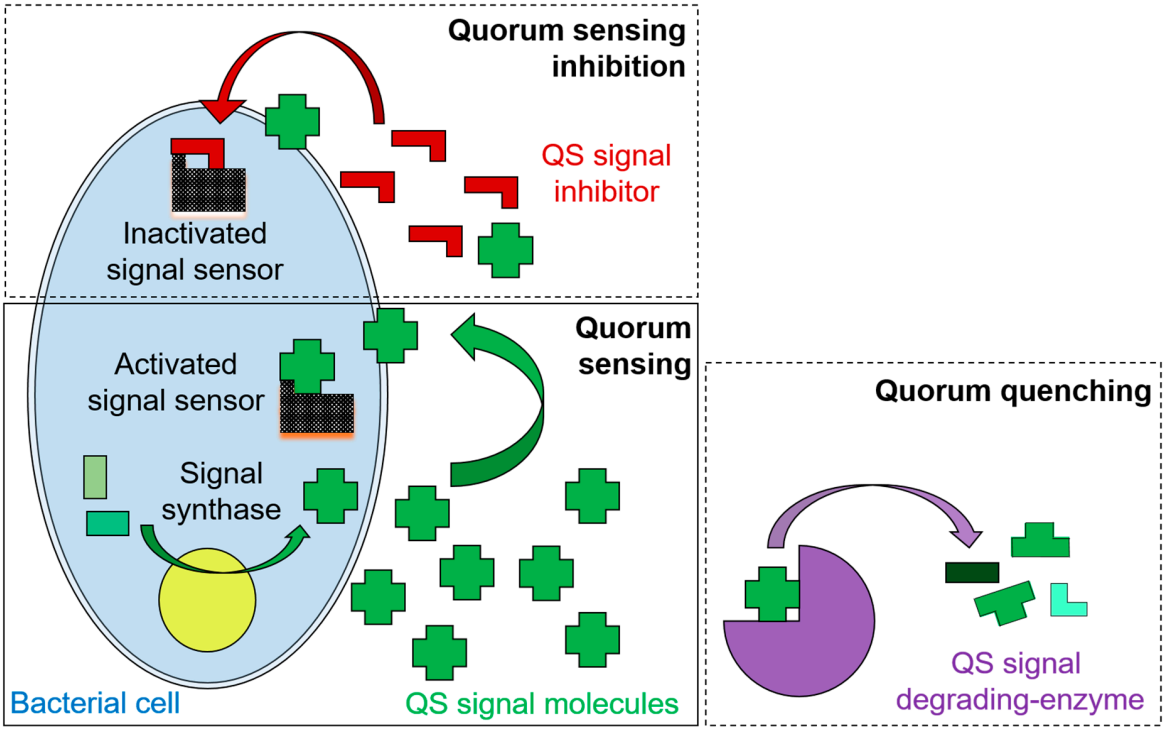

Figure 2. Schematic representation of a quorum sensing (QS) system and its interruption mechanisms: quorum quenching (QQ) and QS inhibition (QSI). The QS signals (green crosses) are synthesized by a synthase from the metabolic pool of the bacterial cell. They diffuse out of the cell and their presence is sensed by a bacterial sensor protein once a threshold cell, hence signal concentration, is reached (lower left panel). QS signals can however be degraded by enzymatic activity (lower right panel), preventing their detection by the bacterial cells. The presence of QS inhibitors (red L-shape figures, upper left panel) inactivate the sensors, hindering the detection of the QS signals. Both mechanisms (QQ and QSI) lead to a reduced or abolished expression of QS regulated genes.

Various technical approaches were used to identify QSIs and QQ organisms and compounds that interfere with AHL signaling. Mass screenings of chemical or natural compounds libraries were instrumental to the identification of several QSIs (reviews: [93,94]), such as hordenine (*N*,*N*-dimethyltyramine) or the human hormone estrone and its structural relatives estriol and estradiol [95]. The primary structures of the molecules are not closely related to that of AHLs, but their spatial structures bear sufficient similarity to allow their recognition by LuxR-like regulators. A tetrazole with a 12-carbon alkyl tail, as well as *N*-nonyl-3-oxo-3-phenyl-propionamide [96] and several other AHL structural analogues [97] were also characterized in the same way. In plants, QSIs were identified either serendipitously [80] or by random tests in plants [83,98], including medicinal plants [99,100]. Drug design strategies such as protein ligand docking have also been implemented to generate molecules with putative or existing QSIs activity [101,102]. On the other hand, QQ microorganisms were identified mostly via targeted approaches. These later were based on the

ability of organisms to degrade AHL signals in culture followed by the identification of the enzymatic activity [70,91,103–106]. Considering that a large part of the microbiome of natural and complex environment such as soil is still uncultivable, several authors successfully developed metagenomics strategies to identify genes encoding novel enzymes with AHL-degradation ability [97,107–115].

Most of the interference work targeted AHL signalization. However, several studies (review: [94]) also aimed at finding QSIs or QQ enzymes/organisms interfering with signals other than AHLs, as exemplified by the isolation of microorganisms that degrade 3-OH-PAME [116], PQS [117], and DSF [118]. Recently, an AI-2 degrading enzyme was identified via a metagenomic approach [113]. Another one was detected in an *Acinetobacter lactucae* strain isolated from activated sludge, and found to reduce biofouling in a membrane bioreactor [119]. A more comprehensive examination of the studies that aimed at AI-2 signaling can be read below in the section "Interference in marine environments".

Table 1. Virulence-associated QS and QQ/QSI disruptors in proteobacteria of marine and agricultural importance.

Bacterium	QS Signal Molecules		QS-Regulated Phenotypes	References	Possible QS Disruptors		References
	AHLs	Others			QQ Enzymes	QSI Compounds	
Of marine importance							
Aeromonas hydrophila	C4-HSL, C6-HSL	AI-2	Production of extracellular protease and biofilm formation	[120–122]	AiiA lactonase	Vanillin, plant extracts and caffeine	[123–127]
Aeromonas salmonicida	C4-HSL, C6-HSL, 3OC6-HSL, C10-HSL	AI-2	Production of extracellular protease	[120,121,128]	-	Sulphur-containing AHL-analogues	[129]
Aliivibrio fischeri	3OC6-HSL, C8-HSL	AI-2	Bioluminescence	[130]	-	-	-
Aliivibrio salmonicida	C6-HSL, 3OC6-HSL	AI-2	Biolumenescence and biofilm	[32,40]	-	-	-
Edwarsiella tarda	C4-HSL, C6-HSL, 3OC6-HSL, C7-HSL	AI-2	Production of extracellular protein	[39,131,132]	Aii20J lactonase	Small peptides	[133,134]
Vibrio alginolyticus	3OHC4-HSL, 3OC10-HSL, 3OHC14-HSL	AI-2	Biofilm formation	[42,135]	-	-	-
Vibrio anguillarum	C6-HSL, 3OC10-HSL, 3OHC10-HSL	AI-2, CAI-1	Biofilm formation, Production of metalloprotease and pigments	[46]	Aac-like acylase	Furanones; cinnamaldehyde analogs	[41,104,136,137]
Vibrio campbelli	3OHC4-HSL	AI-2, CAI-1	Production of metalloprotease, siderophores and chitinase A	[30,44,45,138,139]		Furanones	[140]
Vibrio corallilyticus	C4-HSL 3OH,C10-HSL	AI-2	Control of motility, production of hemolysin, caseinase, amylase and alkaline phosphatase	[47,141]	HqiA lactonase, QuiP-like acylase, AiiA lactonase, AttM lactonase	-	[47,105]
Vibrio harveyi	3OHC4-HSL	AI-2, CAI-1	Bioluminescence, type III secretion system, extracellular toxin, metalloprotease and siderophore	[48,142,143]	AiiA lactonase	Furanones; 2,6-di-*tert*-butyl-4-methylphenol; cinnamaldehyde analogs; pyrogallol and analogs, AI-2 analogs	[137,140,144–149]

Table 1. *Cont.*

Bacterium	QS Signal Molecules		QS-Regulated Phenotypes	References	Possible QS Disruptors		References
	AHLs	Others			QQ Enzymes	QSI Compounds	
Vibrio mediterranei	C4-HSL, C6-HSL, 3OHC12-HSL 3OC13-HSL	AI-2	Control of motility, production of DNAse, and chitinase	[22,47]	HqiA lactonase, Aac-like acylase, AiiA lactonase, AttM lactonase	-	[47,104,150]
Vibrio owensii	C12-HSL, 3OHC12-HSL	-	Control of motility, production of hemolysin, amylase, DNAse, chitinase and phosphatase	[47]	HqiA lactonase, AiiA lactonase, AttM lactonase	-	[47]
Vibrio vulnificus	C4-HSL, 3OC6-HSL 3OHC6-HSL	AI-2	Production of metalloprotease, exoprotease and hemolysin	[36,151]	-	2,6-di-*tert*-butyl-4-methylphenol; cinnamaldehyde analogs	[137,144]
Of agricultural importance							
Agrobacterium tumefaciens	3OC8-HSL, 3OHC8-HSL		Virulence plasmid conjugation	[152–154]	AttM (BlcC) lactonase, AiiB lactonase	Floridoside, betonicine, isethionic acid, thiolactones, dimethyl disulfide, hordenine, estrone	[95,155–160]
Burkholderia glumae	C6-HSL, C8-HSL	-	Production of the phytotoxin toxoflavin and lipase, biogenesis of flagella, control of internal osmolarity	[161–164]	AiiA lactonase	AHL- analog J8-C8 (d)	[165,166]
Dickeya dadantii	C6-HSL, 3OC6-HSL	-	Partial control of pectate lyase synthesis, control of motility and cell aggregation	[167,168]	AiiA lactonase	-	[169,170]
Dickeya solani	C6-HSL (a), C8-HSL	Unknown (Vfm system)	Partial control of the production of macerating exoenzymes	[171,172]	-	-	-
Erwinia amylovora	3OC6-HSL, 3OHC6-HSL	AI-2	Possible partial control of virulence	[173–175]	-	-	-
Pantoea stewartii	3OC6-HSL		Production of exopolysaccharide Bacterial adhesion and biofilm formation	[176,177]	AiiO lactonase	-	[178]

Table 1. *Cont.*

Bacterium	QS Signal Molecules		QS-Regulated Phenotypes	References	Possible QS Disruptors		References
	AHLs	Others			QQ Enzymes	QSI Compounds	
Pectobacterium atrosepticum	3OC6-HSL, C8-HSL, 3OC8-HSL, C10-HSL		Production and secretion of macerating exoenzymes, production of harpin, control of motility	[179–182]	AttM (BlcC) lactonase, AiiB lactonase, AiiA lactonase, QsdA lactonase	*N*,*N*′-alkylated imidazolium-derivatives	[183–185]
Pectobacterium carotovorum	C6-HSL, 3OC6-HSL, 3OC8-HSL	AI-2 (b)	Production of macerating exoenzymes and antibiotics	[186–190]	HqiA lactonase, QuiP-like acylase, AiiA lactonase, AhlD lactonase, QsdA lactonase, QlcA lactonase, QsdB amidohydrolase, unidentified oxidoreductase	Furanones, dimethyl disulfide	[70,74,91,103,105, 108,112,115,159, 191,192]
Ralstonia solanacearum	C6-HSL (c), C8-HSL	3OH-PAME	Production of exopolysaccharide I and macerating exoenzymes	[13]	β-hydroxy-palmitate methyl ester hydrolase	-	[116]
Xanthomonas campestris	-	DSF (cis-11-methyl-2-dodecenoic acid)	Production of exopolysaccharide and exoenzymes	[16]	Degradation of DSF by unidentified bacterial activities	-	[118]
Xyllela fastidiosa	-	Xf-DSF (12-methyl-tetradecanoic acid)	Adhesin production, biofilm stability, insect transmission, production of outer membrane vesicules and attachment to plant vessel cells	[193–195]	-	-	-

(a) AHLs are not the main signals regulating virulence; (b) AHLs are the main signals regulating virulence; (c) AHL functions are unknown but AHLs do not regulate virulence; (d) This compound inhibits AHL synthesis and not AHL detection.

4. Saline Environments as an Important Source of Bioactive Molecules

The categories proposed by Kushner and Kamekura [196] are the most accepted by scientists when classifying microorganisms on the basis of their optimal growth rates at different salinities. Thus, microbes fall into the four following categories: extreme halophiles, which grow best in media with 15–30% w/v NaCl (2.5–5.2 M); moderate halophiles, that grow optimally in media containing 3 to 15% w/v NaCl (0.5–2.5 M); slight halophiles, that include most marine microorganisms and grow optimally in media with 1–3% w/v NaCl (0.2–0.5 M); and non-halophilic, with optimal growth in media with less than 1% w/v NaCl (0.2 M). Non-halophilic microorganisms that are able to tolerate (but do not require) high concentrations of salts are called halotolerant [196].

Saline habitats are widely distributed around the world and are represented by marine environments, saline and hypersaline lakes, solar salterns or hypersaline soils (>0.2% w/v salts), amongst others. Microorganisms that inhabit those environments are mainly halophiles, although a high amount of halotolerant organisms are also present. All of these microorganisms are adapted to grow in the presence of a high ionic content (mainly NaCl) and often to withstand other environmental stress factors such as low oxygen availability, alkaline pH values, low or high temperatures, presence of toxic compounds, etc. (reviews: [197,198]).

These specific physiochemical characteristics of saline environments may induce halophiles to synthesize unique molecules and physiological pathways to cope with the stress conditions that characterize these habitats. In fact, halophiles have been reported to produce bioactive molecules with properties that differ from those found in non-saline habitats (reviews: [199–202]). Indeed, hypersaline environments have demonstrated to be a valuable source of microorganisms that produce a number of novel compounds such as exopolysaccharides [203,204] and enzymes, such as alpha-amylases [205], endoglucanases [206], or lipases [207] that exhibit unique properties and promising perspectives for biotechnological exploitation.

In the same way as saline and hypersaline environments, the marine environment, based on its huge microbial biodiversity, is also considered as an important resource of novel bioactive compounds, including secondary metabolites used for pharmaceutical and biotechnological applications (reviews: [202,208,209]) and anti-QS substances (reviews: [114,202,210,211]) amongst other molecules.

5. Quorum Sensing Interference in Marine Environments

All the above data demonstrate that the ability to disrupt QS systems by different mechanisms occur in many organisms. Possibly, these phenomena could be more frequent in the marine environment than in the soil. In a study performed in bare soil and in a tobacco rhizosphere, the percentage of AHL-degrading bacteria was ca. 2 to 3% [212]. Similar ratios of QS-interfering bacteria were reported for a set of soil bacteria (5%; [70]) and bacterial isolates from a wheat rhizosphere (7%; [213]). This percentage reached 14% for dense microbial communities from marine surfaces and 28% for strains from surface oceanic samples [214]; it increased up to 84% in bacterial strains isolated from ocean at 2000 m depth [215]. Interestingly, the proportion of AHL degraders dropped as did the salinity of the water. In estuarine water (with less salt concentration than seawater), such proportion was found to be as low as 2% [111], a value comparable to that found in soil environments.

Mechanisms of QS interference, QSI and QQ, have been investigated in numerous marine organisms (reviews: [216–218]): micro-algae [219], macro-algae [80], invertebrates [220], fungi [221], and marine bacteria [214]. With respect to microorganisms, numerous data on QSI and QQ have been obtained from marine bacterial strains isolated from specific habitats such as aquaculture tank seawater [104,106], sediments [214,222], sponges [220,223,224], cnidarians [105], seagrass [225], and marine algae [226]. Some authors have also studied the occurrence of QQ and QSI in metagenomes obtained from diverse seawater samples from different depths and sampling places [111,114,215].

QSI occurrence was first described in the red marine alga *Delisea pulchra* that produces halogenated furanones (Figure 3) which interfere with AHL signaling and protect both shrimp and fish from

vibriosis [80,136]. Since then, other furanones have been identified in marine organisms, such as plakofuranolactones which were isolated in the marine sponge *Plakortis* cf. *lita* [224]. Furanones, however, may exhibit some toxicity towards some marine organisms [140]. As a consequence, efforts were made to develop less toxic furanone derivatives retaining QSI activity [227]. QSIs of AHL molecules have been described also in the marine bacteria *Rhizobium* sp. [228], *Halobacillus salinus* [210], *Oceanobacillus* sp. [229], *Rheinheimera aquimaris* [230], and *Streptomyces* sp. [231]. Recently, 2,6-di-*tert*-butyl-4-methylphenol, a novel QSI compound isolated from the marine cyanobacteria *Chroococcus turgidus*, proved to be very effective for the control of the virulence-associated traits of *Vibrio* spp. [144] (Figure 3). Interestingly, some AHLs could also be regarded as QSIs in some specific marine systems, such as the Mediterranean sea strain *Pseudoalteromonas ulvae* [232].

QSIs were also searched for the interference of AI-2 signal communication (Figure 3). Patulin and penicillic acid, which are known as QSIs, were successfully tested on AI-2 signaling in *Halomonas pacifica* and *Marinobacter hydrocarbonoclasticus* [233]. Screening based on classical methods, e.g., bioluminescence inhibition of *Vibrio harveyi*, was used also to identify QSIs such as pyrogallol and boronic acids [145,234]. Metagenomic library screening led to the identification of adenine analogues which affect biofilm formation, decrease pigment and protease production in *V. anguillarum* and protect *Artemia* sp. from *V. harveyi*-induced mortality [235]. Drug design approaches were also implemented to identify putative AI-2 QSIs [236,237] while computer-assisted docking experiments permitted the identification of seven polycyclic compounds that drastically reduce bioluminescence in *V. harveyi* without originating cell toxicity [238–240].

The second antivirulence mechanism, i.e., QQ, appears to be an important process in the seawater [111]. Although QQ of AI-2-type molecules has recently been reported [113], most studies have focused on the degradation of AHLs. Indeed, QQ enzymes having AHL signals as substrates have been described in many marine species, such as *Alteromonas stellipolaris, A. genovensis, Pseudoalteromonas paragorgicola, P. tetraodonis, P. carrageenovora, P. atlantica, P. distincta* [104]; *P. flavipulchra* [241]; *A. marina, Thalassomonas agariperforans, Paracoccus homiensis* [106]; *Muricauda olearia* [242]; *Tenacibaculum maritimum* [243]; *Roseovarius aestuarii, Rhodococcus erythropolis, Salinicola salarius* [214]; *Ruegeria mobilis* [244]; *Stenotrophomonas maltophilia* [105]; *Maribacter ulvicola, Olleya marilimosa* [111]; *Planococcus* sp. [245] and *Bacillus* sp. [246].

Genes encoding AHL degradation enzymes are also abundant in marine metagenomic collections. Interestingly, searches for QQ enzymes in such collections revealed that acylases might be more abundant than lactonases [111,215], in agreement with the results obtained for cultivable bacteria. For instance, acylases have been described in *Alteromonas stellipolaris* [104], *Pseudomonas flavipulchra* [241], *Shewanella sp.* [247], *Oceanobacillus sp.* [214], *Stenotrophomonas maltophilia* [105] and *Anabaena* sp. [248]. On the other hand, lactonases have been identified only in some species such as *Ruegeria mobilis* [244], *Muricauda olearia* [242], *Planococcus* sp. [245] and *Tenacibaculum* sp. [249]. This comes in contrast with the situation in terrestrial environments, where AHL lactonases were more frequently isolated. Soils are generally less alkaline than seawater, the average pH of which being 8.2. At this pH value, AHLs undergo a moderate chemical lactonolysis [83,250,251] but whether this can be related to the more frequent detection of acylases activity in marine samples remains unclear.

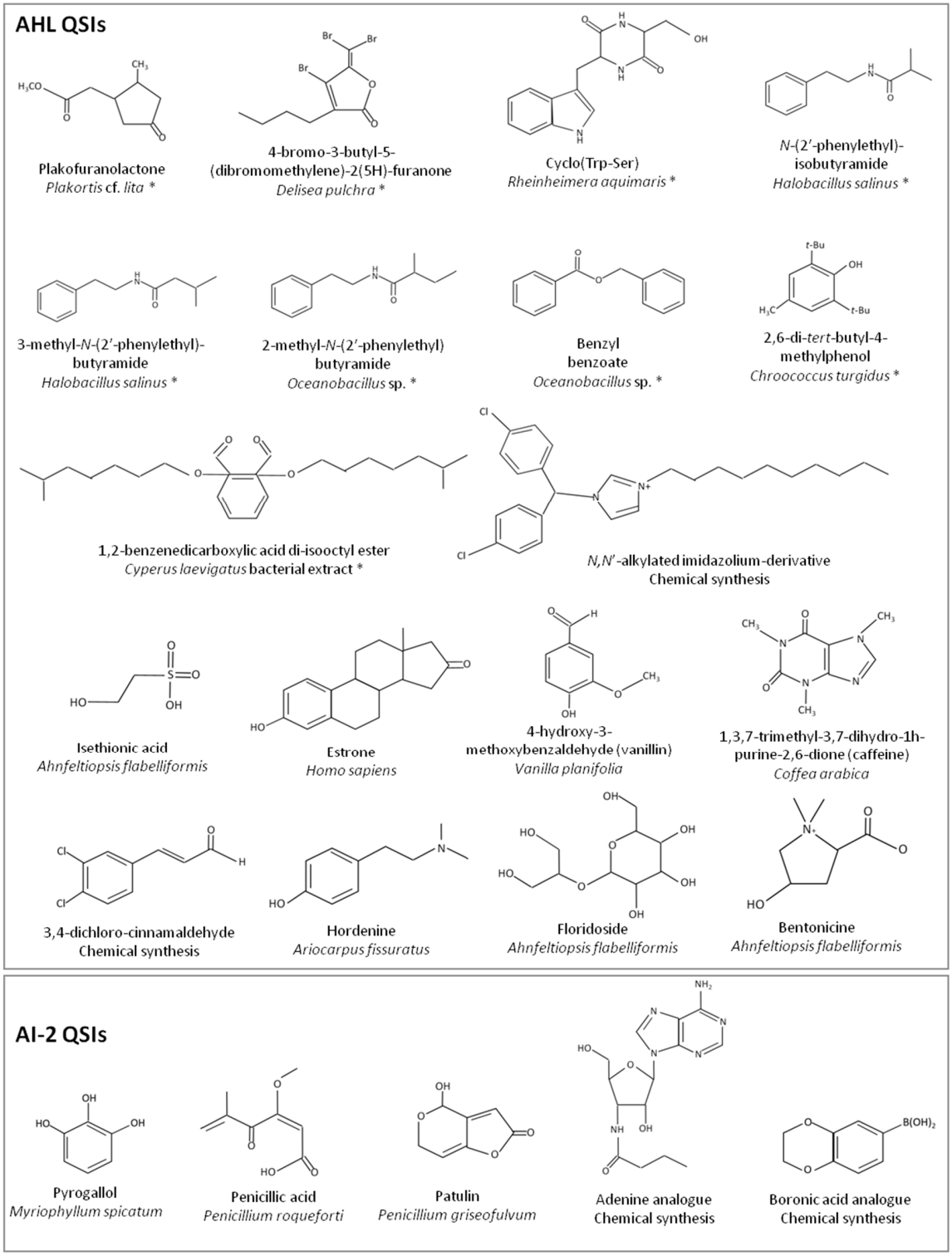

Figure 3. Chemical structures of some quorum sensing inhibitors (QSIs) and their origin. QSI compounds of marine origin are marked with an asterisk.

6. Quorum Sensing Interference in Saline and Hypersaline Environments

Although QS inhibition has proved to be a frequent mechanism in marine aquatic environments, little is known about this phenomenon in saline and hypersaline habitats. However, a growing interest exists in the identification of novel bioactive compounds, enzymes and bacteria from extreme environments, including QQ enzymes [252], since they generally have characteristics and

phenotypes—and, therefore, biotechnological applications—that differ from those retrieved in bacteria isolated from less harsh habitats (reviews: [253,254]).

The studies related to QS in saline and hypersaline habitats are also scare. The first report of QS communication systems in halophilic bacteria was conducted by Llamas et al. in 2005 [255], who described the AHL synthesis in the exopolysaccharide-producing species of *Halomonas* isolated from hypersaline soils in Spain and Morocco. Afterwards, AHL production has also been reported in 43 additional bacterial species belonging to the family *Halomonadaceae*, as well as the identification and characterization of the QS gene system *hanI/hanR* [256]. However, the role of QS in these bacteria has not yet been elucidated, although recently, it has been suggested that it could be related to exopolysaccharide production in the species *Halomonas smyrnensis* [257]. Regarding the other types of QS signal molecules, AI-2 production has been described in the halophilic bacteria *Halobacillus halophilus* [258], and production of DKP-type molecules has been characterized in the extremely halophilic archaeon *Haloterrigena hispanica* [259–261].

In relation with QS inhibition, several QSI compounds have been identified in hypersaline cyanobacterial mat in Oman [262]. More recently, the QSI compound 1,2-benzenedicarboxylic acid di-isooctyl ester that is active on the inhibition of AHL signaling in *Pseudomonas aeruginosa*, has been characterized in extracts of the bacteria isolated from the root system of smooth flatsedge (*Cyperus laevigatus*) growing in a wet saline coastal soil in India [263]. Regarding QQ enzymes, a novel AHL lactonase was identified in a metagenomic library constructed from a hypersaline soil in Spain [115]. Its expression on three aquaculture-related pathogenic *Vibrio* spp. reduce their virulence in brine shrimps (*Artemia salina*) and Manila clams (*Venerupis philippinarum*) [47]. This overall limited information can be explained by the difficulty to study QS and QQ in halophilic bacteria, since their salt requirements can inhibit the biosensors used for the detection of AHLs [255].

7. Applications in Aquaculture and Other Industries

To date, bacterial diseases are an important cause of mortality, causing considerable economic losses in commercial aquaculture and agriculture (reviews: [264–266]). Classically, antibiotics have been used in many countries to prevent and control bacteria outbreaks. However, resistances are rapidly spreading, posing a substantial problem [267–270]. Since the use of antibiotics for disease treatments and as growth promoters have been prohibited in Europe and tightly regulated in other countries, global efforts are needed in order to explore novel strategies to control bacterial pathogens and to overcome the disadvantages of antibiotics.

QS inhibition mechanisms have been reported to boast numerous biotechnological applications, which have become of great interest as alternative to other treatments. In the last decades, QQ and QSI approaches have been tested in aquaculture, agriculture, wastewater treatment, medicine and food packaging, amongst others, as reflected by the increasing number of patents within the field (reviews: [88,271,272]).

In the aquaculture sector, different studies have proved the potential value of QQ to fight bacterial infections by incorporating the AHL-degrading bacteria or QQ enzymes in the rearing water or by bioencapsulating them in the feed stock [47,104,125,133,273–275]. Here also, several patent applications have been registered (reviews: [88,271,272]). To date, the use of AHL-degrading marine bacteria and their purified QQ enzymes has proved to be successful in reducing or eliminating the virulence of pathogenic bacteria against fish, crustaceans, mollusks, and corals. For instance, cultures from the intestinal tract of healthy shrimp and fish enriched in QQ enzymes increase the survival rate of turbot larvae (*Scophthalmus maximus*) [275] and of giant freshwater prawns (*Macrobrachium rosenbergii*) [274]. Another example is the addition of an AHL-degrading *Alteromonas stellipolaris* strain to the rearing water, which reduces the virulence of *Vibrio mediterranei* upon the coral *Oculina patagonica* [104], or the protection of the fish *Danio rerio* and *Carassius auratus* from *Aeromonas hydrophila* infection by the addition of an AHL-degrading *Bacillus* sp. strain [124,125,273]. In the same way, the use of the purified QQ enzyme of an AHL-degrading marine strain of *Bacillus licheniformis* reduces shrimp

(*Penaeus indicus*) and common carp (*Cyprinus carpio*) intestinal colonization and mortality by *Vibrio parahaemolyticus* [123,276]. Finally, addition of an AHL-degrading *B. thuringiensis* strain has proved to protect rainbow trout (*Oncorthynchus mykiss*) from *Yersinia ruckeri* infection [277].

Another important application of QS disruption is the prevention of biofouling. Formation of biofilms on ships and in wastewater treatment facilities are in many occasions regulated by QS mechanisms, and they cause significant economic losses [278,279]. Nowadays, different QQ enzymes have been immobilized in nanoparticles, nanofibers, nanotubes, entrapping sheets, and other types of inorganic devices, successfully reducing or preventing biofouling [178,280–286]. This novel treatment is presented as a promising alternative in the cleaning process of filtering systems in the wastewater treatment plants and in the maintenance of ships, entailing a considerable reduction in the frequency and cost of such processes [69,287].

Last, QSIs and mostly QQ organisms isolated from marine and saline environments could also be used in the future in agriculture since many bacterial phytopathogens that induce economic losses control their virulence or virulence associated functions through QS (Table 1) (reviews: [288,289]). This is the case for instance of *Pectobacterium carotovorum* [186,188,290] (review: [291]), *P. atrosepticum* [179,180], *Erwinia amylovora* [173] (review: [292]), *Burkholderia glumae* (review: [293]), *Ralstonia solanacearum* (review: [294]), and *Agrobacterium tumefaciens* (review: [19]) that regulate motility, plasmid transfer, and the synthesis of macerating exoenzymes, amongst others, through such intercellular communication systems. To date, promising results have been obtained using different compounds or bacterial strains to quench QS-regulated virulence function in *in vivo* assays in plants, for instance, in tomato (*Solanum lycopersicum;* [295,296]) or potato (*Solanum tuberosum*; [70,71,74,115,183,297]). With global changes arising, the world may face a raise of seawater level (review: [298]), generating an increased salinity of underground water and arable areas especially in low lands or fertile river deltas [299,300] even in temperate regions (review: [301]). While researchers and breeders have started to generate important crop cultivars with increased tolerance to salt [302] (review: [303]) the existence of salt tolerant AHL-degrading bacteria may become an asset to control phytopathogens in a context of increasing food demand and increasing world population.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Fuqua, W.C.; Winans, S.C.; Greenberg, E.P. Quorum sensing in bacteria: The LuxR-LuxI family of cell density-responsive transcriptional regulators. *J. Bacteriol.* **1994**, *176*, 269–275. [CrossRef] [PubMed]
2. Papenfort, K.; Bassler, B.L. Quorum sensing signal-response systems in Gram-negative bacteria. *Nat. Rev. Microbiol.* **2016**, *14*, 576–588. [CrossRef]
3. Whiteley, M.; Diggle, S.P.; Greenberg, E.P. Progress in and promise of bacterial quorum sensing research. *Nature* **2017**, *551*, 313–320. [CrossRef] [PubMed]
4. Abisado, R.G.; Benomar, S.; Klaus, J.R.; Dandekar, A.A.; Chandler, J.R. Bacterial quorum sensing and microbial community interactions. *MBio* **2018**, *9*. [CrossRef] [PubMed]
5. Urbanczyk, H.; Ast, J.C.; Higgins, M.J.; Carson, J.; Dunlap, P.V. Reclassification of *Vibrio fischeri*, *Vibrio logei*, *Vibrio salmonicida* and *Vibrio wodanis* as *Aliivibrio fischeri* gen. nov., comb. nov., *Aliivibrio logei* comb. nov., *Aliivibrio salmonicida* comb. nov. and *Aliivibrio wodanis* comb. nov. *Int. J. Syst. Evol. Microbiol.* **2007**, *57*, 2823–2829. [CrossRef]
6. Eberhard, A. Inhibition and activation of bacterial luciferase synthesis. *J. Bacteriol.* **1972**, *109*, 1101–1105.
7. Eberhard, A.; Burlingame, A.L.; Eberhard, C.; Kenyon, G.L.; Nealson, K.H.; Oppenheimer, N.J. Structural identification of autoinducer of *Photobacterium fischeri* luciferase. *Biochemistry* **1981**, *20*, 2444–2449. [CrossRef]
8. Zarubin, M.; Belkin, S.; Ionescu, M.; Genin, A. Bacterial bioluminescence as a lure for marine zooplankton and fish. *Proc. Natl. Acad. Sci. USA* **2012**, *109*, 853–857. [CrossRef]
9. Dunn, A.K. *Vibrio fischeri* metabolism. *Adv. Microb. Physiol.* **2012**, *61*, 37–68. [CrossRef]
10. Ng, W.W.L.; Bassler, B.B.L. Bacterial quorum-sensing network architectures. *Annu. Rev. Genet.* **2009**, *43*, 197–222. [CrossRef]

11. Parker, C.T.; Sperandio, V. Cell-to-cell signalling during pathogenesis. *Cell. Microbiol.* **2009**, *11*, 363–369. [CrossRef] [PubMed]
12. Banerjee, G.; Ray, A.K. The talking language in some major Gram-negative bacteria. *Arch. Microbiol.* **2016**, *198*, 489–499. [CrossRef]
13. Flavier, A.B.; Clough, S.J.; Schell, M.A.; Denny, T.P. Identification of 3-hydroxypalmitic acid methyl ester as a novel autoregulator controlling virulence in *Ralstonia solanacearum*. *Mol. Microbiol.* **1997**, *26*, 251–259. [CrossRef] [PubMed]
14. Holden, M.T.G.; Chhabra, S.R.; De Nys, R.; Stead, P.; Bainton, N.J.; Hill, P.J.; Manefield, M.; Kumar, N.; Labatte, M.; England, D.; et al. Quorum-sensing cross talk: isolation and chemical characterization of cyclic dipeptides from *Pseudomonas aeruginosa* and other Gram-negative bacteria. *Mol. Microbiol.* **1999**, *33*, 1254–1266. [CrossRef]
15. Deziel, E.; Lepine, F.; Milot, S.; He, J.; Mindrinos, M.N.; Tompkins, R.G.; Rahme, L.G. Analysis of *Pseudomonas aeruginosa* 4-hydroxy-2-alkylquinolines (HAQs) reveals a role for 4-hydroxy-2-heptylquinoline in cell-to-cell communication. *Proc. Natl. Acad. Sci. USA* **2004**, *101*, 1339–1344. [CrossRef]
16. Barber, C.E.; Tang, J.L.; Feng, J.X.; Pan, M.Q.; Wilson, T.J.; Slater, H.; Dow, J.M.; Williams, P.; Daniels, M.J. A novel regulatory system required for pathogenicity of *Xanthomonas campestris* is mediated by a small diffusible signal molecule. *Mol. Microbiol.* **1997**, *24*, 555–566. [CrossRef] [PubMed]
17. Brameyer, S.; Kresovic, D.; Bode, H.B.; Heermann, R. Dialkylresorcinols as bacterial signaling molecules. *Proc. Natl. Acad. Sci. USA* **2015**, *112*, 572–577. [CrossRef]
18. Gospodarek, E.; Bogiel, T.; Zalas-Wiecek, P. Communication between microorganisms as a basis for production of virulence factors. *Polish J. Microbiol.* **2009**, *58*, 191–198.
19. Dessaux, Y.; Faure, D. Quorum sensing and quorum quenching in *Agrobacterium*: A "go/no go system"? *Genes (Basel)* **2018**, *9*, 210. [CrossRef]
20. García-Aljaro, C.; Vargas-Cespedes, G.J.; Blanch, A.R. Detection of acylated homoserine lactones produced by *Vibrio* spp. and related species isolated from water and aquatic organisms. *J. Appl. Microbiol.* **2011**, *112*, 383–389. [CrossRef]
21. Rasmussen, B.B.; Nielsen, K.F.; MacHado, H.; Melchiorsen, J.; Gram, L.; Sonnenschein, E.C. Global and phylogenetic distribution of quorum sensing signals, acyl homoserine lactones, in the family of *Vibrionaceae*. *Mar. Drugs* **2014**, *12*, 5527–5546. [CrossRef]
22. Yang, Q.; Han, Y.; Zhang, X.H. Detection of quorum sensing signal molecules in the family *Vibrionaceae*. *J. Appl. Microbiol.* **2011**, *110*, 1438–1448. [CrossRef] [PubMed]
23. Li, J.; Kuang, W.; Long, L.; Zhang, S. Production of quorum-sensing signals by bacteria in the coral mucus layer. *Coral Reefs* **2017**, *36*, 1235–1241. [CrossRef]
24. Liu, J.; Fu, K.; Wu, C.; Qin, K.; Li, F.; Zhou, L. "In-group" communication in marine *Vibrio*: A review of n-acyl homoserine lactones-driven quorum sensing. *Front. Cell. Infect. Microbiol.* **2018**, *8*. [CrossRef] [PubMed]
25. Chen, F.R.; Liu, P.C.; Lee, K.K. Lethal attribute of serine protease secreted by *Vibrio alginolyticus* strains in Kuruma prawn *Penaeus japonicus*. *Z. Naturforsch. C* **2000**, *55*, 94–99. [CrossRef] [PubMed]
26. Prado, S.; Dubert, J.; Barja, J.L. Characterization of pathogenic vibrios isolated from bivalve hatcheries in Galicia, NW Atlantic coast of Spain. Description of *Vibrio tubiashii* subsp. *europaensis* subsp. nov. *Syst. Appl. Microbiol.* **2015**, *38*, 26–29. [CrossRef] [PubMed]
27. Gómez-León, J.; Villamil, L.; Lemos, M.L.; Novoa, B.; Figueras, A. Isolation of *Vibrio alginolyticus* and *Vibrio splendidus* from aquacultured carpet shell clam (*Ruditapes decussatus*) larvae associated with mass mortalities. *Appl. Environ. Microbiol.* **2005**, *71*, 98–104. [CrossRef] [PubMed]
28. Rojas, R.; Miranda, C.D.; Santander, J.; Romero, J. First report of *Vibrio tubiashii* associated with a massive larval mortality event in a commercial hatchery of scallop *Argopecten purpuratus* in Chile. *Front. Microbiol.* **2016**, *7*, 1–13. [CrossRef]
29. Dubert, J.; Barja, J.L.; Romalde, J.L. New insights into pathogenic vibrios affecting bivalves in hatcheries: present and future prospects. *Front. Microbiol.* **2017**, *8*, 1–16. [CrossRef]
30. Ruwandeepika, H.A.D.; Defoirdt, T.; Bhowmick, P.P.; Karunasagar, I.; Karunasagar, I.; Bossier, P. In vitro and in vivo expression of virulence genes in *Vibrio* isolates belonging to the Harveyi clade in relation to their virulence towards gnotobiotic brine shrimp (*Artemia franciscana*). *Environ. Microbiol.* **2011**, *13*, 506–517. [CrossRef]

31. Bassler, B.B.L.; Wright, M.; Silverman, M.M.R. Multiple signalling systems controlling expression of luminescence in *Vibrio harveyi*: Sequence and function of genes encoding a second sensory pathway. *Mol. Microbiol.* **1994**, *13*, 273–286. [CrossRef] [PubMed]
32. Chen, X.; Schauder, S.; Potier, N.; Van Dorsselaer, A.; Pelczer, I.; Bassler, B.L.; Hughson, F.M. Structural identification of a bacterial quorum-sensing signal containing boron. *Nature* **2002**, *415*, 545–549. [CrossRef] [PubMed]
33. Miller, M.B.; Skorupski, K.; Lenz, D.H.; Taylor, R.K.; Bassler, B.L. Parallel quorum sensing systems converge to regulate virulence in *Vibrio cholerae*. *Cell* **2002**, *110*, 303–314. [CrossRef]
34. Higgins, D.A.; Pomianek, M.E.; Kraml, C.M.; Taylor, R.K.; Semmelhack, M.F.; Bassler, B.L. The major *Vibrio cholerae* autoinducer and its role in virulence factor production. *Nature* **2007**, *450*, 883–886. [CrossRef] [PubMed]
35. Ng, W.L.; Perez, L.J.; Wei, Y.; Kraml, C.; Semmelhack, M.F.; Bassler, B.L. Signal production and detection specificity in *Vibrio* CqsA/CqsS quorum-sensing systems. *Mol. Microbiol.* **2011**, *79*, 1407–1417. [CrossRef]
36. Milton, D.L. Quorum sensing in vibrios: Complexity for diversification. *Int. J. Med. Microbiol.* **2006**, *296*, 61–71. [CrossRef]
37. Defoirdt, T. Quorum-sensing systems as targets for antivirulence therapy. *Trends Microbiol.* **2018**, *26*, 313–328. [CrossRef]
38. Croxatto, A.; Pride, J.; Hardman, A.; Williams, P.; Cámara, M.; Milton, D. A distinctive dual-channel quorum sensing system operates in *Vibrio anguillarum*. *Mol. Microbiol.* **2004**, *52*, 1677–1689. [CrossRef]
39. Morohoshi, T.; Inaba, T.; Kato, N.; Kanai, K.; Ikeda, T. Identification of quorum-sensing signal molecules and the LuxRI homologs in fish pathogen *Edwardsiella tarda*. *J. Biosci. Bioeng.* **2004**, *98*, 274–281. [CrossRef]
40. Bruhn, J.B.; Dalsgaard, I.; Nielsen, K.F.; Buchholtz, C.; Larsen, J.L.; Gram, L. Quorum sensing signal molecules (acylated homoserine lactones) in Gram-negative fish pathogenic bacteria. *Dis. Aquat. Organ.* **2005**, *65*, 43–52. [CrossRef]
41. Defoirdt, T.; Bossier, P.; Sorgeloos, P.; Verstraete, W. The impact of mutations in the quorum sensing systems of *Aeromonas hydrophila*, *Vibrio anguillarum* and *Vibrio harveyi* on their virulence towards gnotobiotically cultured *Artemia franciscana*. *Environ. Microbiol.* **2005**, *7*, 1239–1247. [CrossRef] [PubMed]
42. Liu, J.; Fu, K.; Wang, Y.; Wu, C.; Li, F.; Shi, L.; Ge, Y.; Zhou, L. Detection of diverse *N*-acyl-homoserine lactones in *Vibrio alginolyticus* and regulation of biofilm formation by *N*-(3-oxodecanoyl) homoserine lactone in vitro. *Front. Microbiol.* **2017**, *8*, 1–15. [CrossRef]
43. Li, X.; Dierckens, K.; Bossier, P.; Defoirdt, T. The impact of quorum sensing on the virulence of *Vibrio anguillarum* towards gnotobiotic sea bass (*Dicentrarchus labrax*) larvae. *Aquac. Res.* **2018**, *49*, 3686–3689. [CrossRef]
44. Defoirdt, T.; Verstraete, W.; Bossier, P. Luminescence, virulence and quorum sensing signal production by pathogenic *Vibrio campbellii* and *Vibrio harveyi* isolates. *J. Appl. Microbiol.* **2008**, *104*, 1480–1487. [CrossRef] [PubMed]
45. Lilley, B.N.; Bassler, B.L. Regulation of quorum sensing in *Vibrio harveyi* by LuxO and sigma-54. *Mol. Microbiol.* **2000**, *36*, 940–954. [CrossRef]
46. Milton, D.L.; Hardman, A.; Camara, M.; Chhabra, S.R.; Bycroft, B.W.; Stewart, G.S.A.B.; Williams, P. Quorum sensing in *Vibrio anguillarum*: characterization of the *vanI/vanR* locus and identification of the autoinducer *N*-(3-oxodecanoyl)-L-homoserine lactone. *J. Bacteriol.* **1997**, *179*, 3004–3012. [CrossRef] [PubMed]
47. Torres, M.; Reina, J.C.; Fuentes-Monteverde, J.C.; Fernandez, G.; Rodrıguez, J.; Llamas, I. AHL-lactonase expression in three marine emerging pathogenic *Vibrio* spp. reduces virulence and mortality in brine shrimp (*Artemia salina*) and Manila clam (*Venerupis philippinarum*). *PLoS ONE* **2018**, *13*, e0195176. [CrossRef] [PubMed]
48. Defoirdt, T.; Boon, N.; Sorgeloos, P.; Verstraete, W.; Bossier, P. Quorum sensing and quorum quenching in *Vibrio harveyi*: Lessons learned from in vivo work. *ISME J.* **2008**, *2*, 19–26. [CrossRef]
49. Finch, R. Quorum sensing: A novel target for anti-infective therapy. *J. Antimicrob. Chemother.* **1998**, *42*, 569–571. [CrossRef] [PubMed]
50. Zhang, L.H.H. Quorum quenching and proactive host defense. *Trends Plant Sci.* **2003**, *8*, 238–244. [CrossRef]
51. Dong, Y.; Zhang, L. Quorum sensing and quorum-quenching enzymes. *J. Microbiol.* **2005**, *43*, 101–109. [PubMed]

52. Czajkowski, R.; Jafra, S. Quenching of acyl-homoserine lactone-dependent quorum sensing by enzymatic disruption of signal molecules. *Acta Biochim. Pol.* **2009**, *56*, 1–16. [CrossRef]
53. Uroz, S.; Dessaux, Y.; Oger, P. Quorum sensing and quorum quenching: The yin and yang of bacterial communication. *ChemBioChem* **2009**, *10*, 205–216. [CrossRef] [PubMed]
54. Hong, K.W.; Koh, C.L.; Sam, C.K.; Yin, W.F.; Chan, K.G. Quorum quenching revisited: From signal decays to signalling confusion. *Sensors* **2012**, *12*, 4661–4696. [CrossRef] [PubMed]
55. Grandclément, C.; Tannières, M.; Moréra, S.; Dessaux, Y.; Faure, D. Quorum quenching: role in nature and applied developments. *FEMS Microbiol. Rev.* **2016**, *40*, 86–116. [CrossRef] [PubMed]
56. Cegelski, L.; Marshall, G.R.; Eldridge, G.R.; Hultgren, S.J. The biology and future prospects of antivirulence therapies. *Nat. Rev. Microbiol.* **2008**, *6*, 17–27. [CrossRef]
57. Zucca, M.; Scutera, S.; Savoia, D. New antimicrobial frontiers. *Mini Rev. Med. Chem.* **2011**, *11*, 888–900. [CrossRef]
58. Rasko, D.A.; Sperandio, V. Anti-virulence strategies to combat bacteria-mediated disease. *Nat. Rev. Drug Discov.* **2010**, *9*, 117–128. [CrossRef]
59. Defoirdt, T.; Boon, N.; Bossier, P. Can bacteria evolve resistance to quorum sensing disruption? *PLoS Pathog.* **2010**, *6*, 1–6. [CrossRef] [PubMed]
60. García-Contreras, R.; Maeda, T.; Wood, T.K. Resistance to quorum-quenching compounds. *Appl. Environ. Microbiol.* **2013**, *79*, 6840–6846. [CrossRef]
61. García-Contreras, R.; Maeda, T.; Wood, T.K. Can resistance against quorum-sensing interference be selected? *ISME J.* **2016**, 1–7. [CrossRef]
62. Kalia, V.C. Quorum sensing inhibitors: An overview. *Biotechnol. Adv.* **2013**, *31*, 224–245. [CrossRef]
63. Kalia, V.C.; Wood, T.K.; Kumar, P. Evolution of resistance to quorum-sensing inhibitors. *Microb. Ecol.* **2014**, *68*, 13–23. [CrossRef] [PubMed]
64. Sandoz, K.M.; Mitzimberg, S.M.; Schuster, M. Social cheating in *Pseudomonas aeruginosa* quorum sensing. *Proc. Natl. Acad. Sci. USA* **2007**, *104*, 15876–15881. [CrossRef] [PubMed]
65. Maeda, T.; García-Contreras, R.; Pu, M.; Sheng, L.; Garcia, L.R.; Tomás, M.; Wood, T.K. Quorum quenching quandary: resistance to antivirulence compounds. *ISME J.* **2012**, *6*, 493–501. [CrossRef] [PubMed]
66. Mellbye, B.; Schuster, M. The sociomicrobiology of antivirulence drug resistance: A proof of concept. *MBio* **2011**, *2*, e00131-11. [CrossRef] [PubMed]
67. Defoirdt, T.; Sorgeloos, P.; Bossier, P. Alternatives to antibiotics for the control of bacterial disease in aquaculture. *Curr. Opin. Microbiol.* **2011**, *14*, 251–258. [CrossRef] [PubMed]
68. Rémy, B.; Plener, L.; Elias, M.; Daudé, D.; Chabrière, E. Des enzymes pour bloquer la communication bactérienne, une alternative aux antibiotiques? *Ann. Pharm. Françaises* **2016**, *74*, 413–420. [CrossRef]
69. Bzdrenga, J.; Daudé, D.; Rémy, B.; Jacquet, P.; Plener, L.; Elias, M.; Chabrière, E. Biotechnological applications of quorum quenching enzymes. *Chem. Biol. Interact.* **2017**, *1*, 1–12. [CrossRef] [PubMed]
70. Dong, Y.H.H.; Xu, J.L.; Li, X.Z.; Zhang, L.H. AiiA, an enzyme that inactivates the acylhomoserine lactone quorum-sensing signal and attenuates the virulence of *Erwinia carotovora*. *Proc. Natl. Acad. Sci. USA* **2000**, *97*, 3526–3531. [CrossRef]
71. Dong, Y.H.; Wang, L.H.; Xu, J.L.; Zhang, H.B.; Zhang, X.F.; Zhang, L.H. Quenching quorum-sensing-dependent bacterial infection by an *N*-acyl homoserine lactonase. *Nature* **2001**, *411*, 813–817. [CrossRef] [PubMed]
72. Dong, Y.; Gusti, A.; Zhang, Q.; Xu, J.; Zhang, L. Identification of quorum-quenching *N*-acyl homoserine lactonases from *Bacillus* species. *Appl. Environ. Microbiol.* **2002**, *68*, 1754–1759. [CrossRef] [PubMed]
73. Leadbetter, J.R.; Greenberg, E.P. Metabolism of acyl-homoserine lactone quorum-sensing signals by *Variovorax paradoxus*. *J. Bacteriol.* **2000**, *182*, 6921–6926. [CrossRef]
74. Uroz, S.; D'Angelo-Picard, C.; Carlier, A.; Elasri, M.; Sicot, C.; Petit, A.; Oger, P.; Faure, D.; Dessaux, Y. Novel bacteria degrading *N*-acylhomoserine lactones and their use as quenchers of quorum-sensing-regulated functions of plant-pathogenic bacteria. *Microbiology* **2003**, *149*, 1981–1989. [CrossRef]
75. Hornby, J.M.; Jensen, E.C.; Lisec, A.D.; Tasto, J.J.; Jahnke, B.; Shoemaker, R.; Dussault, P.; Nickerson, K.W. Quorum sensing in the dimorphic fungus *Candida albicans* is mediated by farnesol. *Appl. Environ. Microbiol.* **2001**, *67*, 2982–2992. [CrossRef]

76. Wong, C.S.; Koh, C.L.; Sam, C.K.; Chen, J.; Chong, Y.; Yin, W.F.; Chan, K.G. Degradation of bacterial quorum sensing signaling molecules by the microscopic yeast *Trichosporon loubieri* isolated from tropical wetland waters. *Sensors* **2013**, *13*, 12943–12957. [CrossRef]
77. Leguina, A.C.d.V.; Nieto, C.; Pajot, H.F.; Bertini, E.V.; Mac Cormack, W.; Castellanos de Figueroa, L.I.; Nieto-Peñalver, C.G. Inactivation of bacterial quorum sensing signals *N*-acyl homoserine lactones is widespread in yeasts. *Fungal Biol.* **2018**, *122*, 52–62. [CrossRef] [PubMed]
78. Rasmussen, T.B.; Skindersoe, M.E.; Bjarnsholt, T.; Phipps, R.K.; Christensen, K.B.; Jensen, P.O.; Andersen, J.B.; Koch, B.; Larsen, T.O.; Hentzer, M.; et al. Identity and effects of quorum-sensing inhibitors produced by *Penicillium* species. *Microbiology* **2016**, *151*, 1325–1340. [CrossRef]
79. Uroz, S.; Heinonsalo, J. Degradation of *N*-acyl homoserine lactone quorum sensing signal molecules by forest root-associated fungi. *FEMS Microbiol. Ecol.* **2008**, *65*, 271–278. [CrossRef] [PubMed]
80. Givskov, M.; de Nys, R.; Manefield, M.; Gram, L.; Maximilien, R.; Eberl, L.; Molin, S.; Steinberg, P.D.; Kjelleberg, S. Eukaryotic interference with homoserine lactone-mediated prokaryotic signalling. *J. Bact.* **1996**, *178*, 6618–6622. [CrossRef]
81. Teplitski, M.; Robinson, J.B.; Bauer, W.D. Plants secrete substances that mimic bacterial *N*-acyl homoserine lactone signal activities and affect population density-dependent behaviors in associated bacteria. *Mol. Plant-Microbe Interact.* **2000**, *13*, 637–648. [CrossRef] [PubMed]
82. Huber, B.; Eberl, L.; Feucht, W.; Polster, J. Influence of polyphenols on bacterial biofilm formation and quorum sensing. *Z. Naturforsch. C* **2003**, *58*, 879–884. [CrossRef] [PubMed]
83. Delalande, L.; Faure, D.; Raffoux, A.A.; Uroz, S.S.; D'Angelo-Picard, C.; Elasri, M.; Carlier, A.A.; Berruyer, R.; Petit, A.; Williams, P.; et al. *N*-hexanoyl-l-homoserine lactone, a mediator of bacterial quorum-sensing regulation, exhibits plant-dependent stability and may be inactivated by germinating *Lotus corniculatus* seedlings. *FEMS Microbiol. Ecol.* **2005**, *52*, 13–20. [CrossRef] [PubMed]
84. Draganov, D.I.; Teiber, J.F.; Speelman, A.; Osawa, Y.; Sunahara, R.; La Du, B.N. Human paraoxonases (PON1, PON2 and PON3) are lactonases with overlapping and distinct substrate specificities. *J. Lipid Res.* **2005**, *46*, 1239–1247. [CrossRef]
85. Yang, F.; Wang, L.H.; Wang, J.; Dong, Y.H.; Hu, J.Y.; Zhang, L.H. Quorum quenching enzyme activity is widely conserved in the sera of mammalian species. *FEBS Lett.* **2005**, *579*, 3713–3717. [CrossRef] [PubMed]
86. Park, J.; Kaufmann, G.F.; Bowen, J.P.; Arbiser, J.L.; Janda, K.D. Solenopsin A, a venom alkaloid from the fire ant *Solenopsis invicta*, inhibits quorum-sensing signaling in *Pseudomonas aeruginosa*. *J. Infect. Dis.* **2008**, *198*, 1198–1201. [CrossRef]
87. Kalia, V.C.; Purohit, H.J. Quenching the quorum sensing system: Potential antibacterial drug targets. *Crit. Rev. Microbiol.* **2011**, *37*, 121–140. [CrossRef]
88. Bhardwaj, A.K.; Vinothkumar, K.; Rajpara, N. Bacterial quorum sensing inhibitors: Attractive alternatives for control of infectious pathogens showing multiple drug resistance. *Recent Pat. Antiinfect. Drug Discov.* **2013**, *8*, 68–83. [CrossRef]
89. Manefield, M.; de Nys, R.; Naresh, K.; Roger, R.; Givskov, M.; Peter, S.; Kjelleberg, S. Evidence that halogenated furanones from *Delisea pulchra* inhibit acylated homoserine lactone (AHL)-mediated gene expression by displacing the AHL signal from its receptor protein. *Microbiology* **1999**, *145*, 283–291. [CrossRef]
90. Lin, Y.H.; Xu, J.L.; Hu, J.; Wang, L.H.; Ong, S.L.; Leadbetter, J.R.; Zhang, L.H. Acyl-homoserine lactone acylase from *Ralstonia strain* XJ12B represents a novel and potent class of quorum-quenching enzymes. *Mol. Microbiol.* **2003**, *47*, 849–860. [CrossRef] [PubMed]
91. Uroz, S.; Chhabra, S.R.; Cámara, M.; Williams, P.; Oger, P.; Dessaux, Y. N-acylhomoserine lactone quorum-sensing molecules are modified and degraded by *Rhodococcus erythropolis* W2 by both amidolytic and novel oxidoreductase activities. *Microbiology* **2005**, *151*, 3313–3322. [CrossRef]
92. Fetzner, S. Quorum quenching enzymes. *J. Biotechnol.* **2015**, *201*, 2–14. [CrossRef]
93. Stevens, A.M.; Queneau, Y.; Soulere, L.; von Bodman, S.; Doutheau, A. Mechanisms and synthetic modulators of AHL-dependent gene regulation. *Chem. Rev.* **2011**, *111*, 4–27. [CrossRef] [PubMed]
94. LaSarre, B.; Federle, M.J. Exploiting quorum sensing to confuse bacterial pathogens. *Microbiol. Mol. Biol. Rev.* **2013**, *77*, 73–111. [CrossRef]
95. Beury-Cirou, A.; Tannières, M.; Minard, C.; Soulère, L.; Rasamiravaka, T.; Dodd, R.H.; Queneau, Y.; Dessaux, Y.; Guillou, C.; Vandeputte, O.M.; et al. At a supra-physiological concentration, human sexual hormones act as quorum-sensing inhibitors. *PLoS ONE* **2013**, *8*, e83564. [CrossRef]

96. Muh, U.; Schuster, M.; Heim, R.; Singh, A.; Olson, E.R.; Greenberg, E.P. Novel *Pseudomonas aeruginosa* quorum-sensing inhibitors identified in an ultra-high-throughput screen. *Antimicrob. Agents Chemother.* **2006**, *50*, 3674–3679. [CrossRef]
97. Borlee, B.R.; Geske, G.D.; Blackwell, H.E.; Handelsman, J. Identification of synthetic inducers and inhibitors of the quorum-sensing regulator lasR in *Pseudomonas aeruginosa* by high-throughput screening. *Appl. Environ. Microbiol.* **2010**, *76*, 8255–8258. [CrossRef] [PubMed]
98. Götz, C.; Fekete, A.; Gebefuegi, I.; Forczek, S.T.; Fuksová, K.; Li, X.; Englmann, M.; Gryndler, M.; Hartmann, A.; Matucha, M.; et al. Uptake, degradation and chiral discrimination of *N*-acyl-D/L-homoserine lactones by barley (*Hordeum vulgare*) and yam bean (*Pachyrhizus erosus*) plants. *Anal. Bioanal. Chem.* **2007**, *389*, 1447–1457. [CrossRef] [PubMed]
99. Adonizio, A.L.; Downum, K.; Bennett, B.C.; Mathee, K. Anti-quorum sensing activity of medicinal plants in southern Florida. *J. Ethnopharmacol.* **2006**, *105*, 427–435. [CrossRef] [PubMed]
100. Bouyahya, A.; Dakka, N.; Et-Touys, A.; Abrini, J.; Bakri, Y. Medicinal plant products targeting quorum sensing for combating bacterial infections. *Asian Pac. J. Trop. Med.* **2017**, *10*, 729–743. [CrossRef] [PubMed]
101. Ahumedo, M.; Díaz, A.; Vivas-Reyes, R. Theoretical and structural analysis of the active site of the transcriptional regulators LasR and TraR, using molecular docking methodology for identifying potential analogues of acyl homoserine lactones (AHLs) with anti-quorum sensing activity. *Eur. J. Med. Chem.* **2010**, *45*, 608–615. [CrossRef] [PubMed]
102. Soulère, L.; Sabbah, M.; Fontaine, F.; Queneau, Y.; Doutheau, A. LuxR-dependent quorum sensing: Computer aided discovery of new inhibitors structurally unrelated to *N*-acylhomoserine lactones. *Bioorg. Med. Chem. Lett.* **2010**, *20*, 4355–4358. [CrossRef] [PubMed]
103. Uroz, S.; Oger, P.M.; Chapelle, E.; Adeline, M.T.; Faure, D.; Dessaux, Y. A *Rhodococcus qsdA*-encoded enzyme defines a novel class of large-spectrum quorum-quenching lactonases. *Appl. Environ. Microbiol.* **2008**, *74*, 1357–1366. [CrossRef] [PubMed]
104. Torres, M.; Rubio-Portillo, E.; Antón, J.; Ramos-Esplá, A.A.; Quesada, E.; Llamas, I. Selection of the *N*-acylhomoserine lactone-degrading bacterium *Alteromonas stellipolaris* PQQ-42 and of its potential for biocontrol in aquaculture. *Front. Microbiol.* **2016**, *7*, 646. [CrossRef] [PubMed]
105. Reina, J.C.; Torres, M.; Llamas, I. *Stenotrophomonas maltophilia* AHL-degrading strains isolated from marine invertebrate microbiota attenuate the virulence of *Pectobacterium carotovorum* and *Vibrio corallilyticus*. *Mar. Biotechnol.* **2019**. [CrossRef] [PubMed]
106. Torres, M.; Romero, M.; Prado, S.; Dubert, J.; Tahrioui, A.; Otero, A.; Llamas, I. *N*-acylhomoserine lactone-degrading bacteria isolated from hatchery bivalve larval cultures. *Microbiol. Res.* **2013**, *168*, 547–554. [CrossRef] [PubMed]
107. Williamson, L.L.; Borlee, B.R.; Schloss, P.D.; Guan, C.; Allen, H.K.; Handelsman, J. Intracellular screen to identify metagenomic clones that induce or inhibit a quorum-sensing biosensor. *Appl. Environ. Microbiol.* **2005**, *71*, 6335–6344. [CrossRef]
108. Riaz, K.; Elmerich, C.; Moreira, D.; Raffoux, A.; Dessaux, Y.; Faure, D. A metagenomic analysis of soil bacteria extends the diversity of quorum-quenching lactonases. *Environ. Microbiol.* **2008**, *10*, 560–570. [CrossRef]
109. Bijtenhoorn, P.; Schipper, C.; Hornung, C.; Quitschau, M.; Grond, S.; Weiland, N.; Streit, W.R. BpiB05, a novel metagenome-derived hydrolase acting on *N*-acylhomoserine lactones. *J. Biotechnol.* **2011**, *155*, 86–94. [CrossRef] [PubMed]
110. Schipper, C.; Hornung, C.; Bijtenhoorn, P.; Quitschau, M.; Grond, S.; Streit, W.R. Metagenome-derived clones encoding two novel lactonase family proteins involved in biofilm inhibition in *Pseudomonas aeruginosa*. *Appl. Environ. Microbiol.* **2009**, *75*, 224–233. [CrossRef]
111. Romero, M.; Martin-Cuadrado, A.; Otero, A. Determination of whether quorum quenching is a common activity in marine bacteria by analysis of cultivable bacteria and metagenomic sequences. *Appl. Environ. Microbiol.* **2012**, *78*, 6345–6348. [CrossRef]
112. Tannières, M.; Beury-Cirou, A.; Vigouroux, A.; Mondy, S.; Pellissier, F.; Dessaux, Y.; Faure, D. A Metagenomic study highlights phylogenetic proximity of quorum-quenching and xenobiotic-degrading amidases of the AS-family. *PLoS ONE* **2013**, *8*, e65473. [CrossRef]
113. Weiland-Bräuer, N.; Kisch, M.J.; Pinnow, N.; Liese, A.; Schmitz, R.A. Highly effective inhibition of biofilm formation by the first metagenome-derived AI-2 quenching enzyme. *Front. Microbiol.* **2016**, *7*. [CrossRef]

114. Yaniv, K.; Golberg, K.; Kramarsky-Winter, E.; Marks, R.; Pushkarev, A.; Béjà, O.; Kushmaro, A. Functional marine metagenomic screening for anti-quorum sensing and anti-biofilm activity. *Biofouling* **2017**, *33*, 1–13. [CrossRef]
115. Torres, M.; Uroz, S.; Salto, R.; Fauchery, L.; Quesada, E.; Llamas, I. HqiA, a novel quorum-quenching enzyme which expands the AHL lactonase family. *Sci. Rep.* **2017**, *7*, 943. [CrossRef]
116. Shinohara, M.; Nakajima, N.; Uehara, Y. Purification and characterization of a novel esterase (β-hydroxypalmitate methyl ester hydrolase) and prevention of the expression of virulence by *Ralstonia solanacearum*. *J. Appl. Microbiol.* **2007**, *103*, 152–162. [CrossRef]
117. Pustelny, C.; Albers, A.; Büldt-Karentzopoulos, K.; Parschat, K.; Chhabra, S.R.; Cámara, M.; Williams, P.; Fetzner, S. Dioxygenase-mediated quenching of quinolone-dependent quorum sensing in *Pseudomonas aeruginosa*. *Chem. Biol.* **2009**, *16*, 1259–1267. [CrossRef] [PubMed]
118. Newman, K.L.; Chatterjee, S.; Ho, K.A.; Lindow, S.E. Virulence of plant pathogenic bacteria attenuated by degradation of fatty acid cell-to-cell signaling Factors. *Mol. Plant-Microbe Interact.* **2008**, *21*, 326–334. [CrossRef] [PubMed]
119. Lee, K.; Kim, Y.W.; Lee, S.; Lee, S.H.; Nahm, C.H.; Kwon, H.; Park, P.K.; Choo, K.H.; Koyuncu, I.; Drews, A.; et al. Stopping autoinducer-2 chatter by means of an indigenous bacterium (*Acinetobacter* sp. DKY-1): a new antibiofouling strategy in a membrane bioreactor for wastewater treatment. *Environ. Sci. Technol.* **2018**, *52*, 6237–6245. [CrossRef]
120. Swift, S.; Lynch, M.J.; Fish, L.; Kirke, D.F.; Tomás, J.M.; Stewart, G.S.A.B.; Williams, P.; Tomas, J.M.; Stewart, G.S.A.B.; Williams, P. Quorum sensing-dependent regulation and blockade of exoprotease production in *Aeromonas hydrophila*. *Infect. Immun.* **1999**, *67*, 5192–5199.
121. Swift, S.; Karlyshev, A.V.; Fish, L.; Durant, E.L.; Winson, M.K.; Chhabra, S.R.; Williams, P.; Macintyre, S.; Stewart, G.S. Quorum sensing in *Aeromonas hydrophila* and *Aeromonas salmonicida*: identification of the LuxRI homologs AhyRI and AsaRI and their cognate *N*-acylhomoserine lactone signal molecules. *J. Bacteriol.* **1997**, *179*, 5271–5281. [CrossRef]
122. Lynch, M.J.; Swift, S.; Kirke, D.F.; Keevil, C.W.; Dodd, C.E.R.; Williams, P. The regulation of biofilm development by quorum sensing in *Aeromonas hydrophila*. *Environ. Microbiol.* **2002**, *4*, 18–28. [CrossRef]
123. Chen, R.; Zhou, Z.; Cao, Y.; Bai, Y.; Yao, B. High yield expression of an AHL-lactonase from *Bacillus* sp. B546 in *Pichia pastoris* and its application to reduce *Aeromonas hydrophila* mortality in aquaculture. *Microb. Cell Fact.* **2010**, *9*, 39. [CrossRef]
124. Cao, Y.; He, S.; Zhou, Z.; Zhang, M.; Mao, W.; Zhang, H.; Yaoa, B. Orally administered thermostable *N*-acyl homoserine lactonase from *Bacillus* sp. strain AI96 attenuates *Aeromonas hydrophila* infection in zebrafish. *Appl. Environ. Microbiol.* **2012**, *78*, 1899–1908. [CrossRef]
125. Zhou, S.; Zhang, A.; Yin, H.; Chu, W. Bacillus sp. QSI-1 Modulate quorum sensing signals reduce *Aeromonas hydrophila* level and alter gut microbial community structure in fish. *Front. Cell. Infect. Microbiol.* **2016**, *6*, 1–8. [CrossRef]
126. Ponnusamy, K.; Paul, D.; Kweon, J.H. Inhibition of quorum sensing mechanism and *Aeromonas hydrophila* biofilm formation by vanillin. *Environ. Eng. Sci.* **2009**, *26*, 1359–1363. [CrossRef]
127. Husain, F.M.; Ahmad, I.; Khan, M.S.; Al-Shabib, N.A. *Trigonella foenum*-graceum (seed) extract interferes with quorum sensing regulated traits and biofilm formation in the strains of *Pseudomonas aeruginosa* and *Aeromonas hydrophila*. *Evid.-Based Complement. Altern. Med.* **2015**, *2015*, 1–10. [CrossRef]
128. Meng, L.; Du, Y.; Liu, P.; Li, X.; Liu, Y. Involvement of LuxS in *Aeromonas salmonicida* metabolism, virulence and infection in Atlantic salmon (*Salmo salar* L.). *Fish Shellfish Immunol.* **2017**, *64*, 260–269. [CrossRef]
129. Rasch, M.; Kastbjerg, V.; Bruhn, J.; Dalsgaard, I.; Givskov, M.; Gram, L. Quorum sensing signals are produced by *Aeromonas salmonicida* and quorum sensing inhibitors can reduce production of a potential virulence factor. *Dis. Aquat. Organ.* **2007**, *78*, 105–113. [CrossRef]
130. Lupp, C.; Ruby, E.G. Vibrio fischeri uses two quorum-sensing systems for the regulation of early and late colonization. *J. Bacteriol.* **2005**, *187*, 3620–3629. [CrossRef]
131. Han, Y.; Li, X.; Qi, Z.; Zhang, X.H.; Bossier, P. Detection of different quorum-sensing signal molecules in a virulent *Edwardsiella* tarda strain LTB-4. *J. Appl. Microbiol.* **2010**, *108*, 139–147. [CrossRef]
132. Zhang, M.; Sun, K.; Sun, L. Regulation of autoinducer 2 production and *luxS* expression in a pathogenic *Edwardsiella tarda* strain. *Microbiology* **2008**, *154*, 2060–2069. [CrossRef]

133. Romero, M.; Muras, A.; Mayer, C.; Buján, N.; Magariños, B.; Otero, A. In vitro quenching of fish pathogen *Edwardsiella tarda* AHL production using marine bacterium *Tenacibaculum* sp. strain 20-J cell extracts. *Dis. Aquat. Organ.* **2014**, *108*, 217–225. [CrossRef] [PubMed]
134. Zhang, M.; Jiao, X.D.; Hu, Y.H.; Sun, L. Attenuation of *Edwardsiella tarda* virulence by small peptides that interfere with *luxS*/autoinducer type 2 quorum sensing. *Appl. Environ. Microbiol.* **2009**, *75*, 3882–3890. [CrossRef]
135. Ye, J.; Ma, Y.; Liu, Q.; Zhao, D.L.; Wang, Q.Y.; Zhang, Y.X. Regulation of *Vibrio alginolyticus* virulence by the LuxS quorum-sensing system. *J. Fish Dis.* **2008**, *31*, 161–169. [CrossRef] [PubMed]
136. Rasch, M.; Buch, C.; Austin, B.; Slierendrecht, W.; Ekmann, K.; Larsen, J.; Johansen, C.; Riedel, K.; Eberl, L.; Givskov, M.; et al. An inhibitor of bacterial quorum sensing reduces mortalities caused by vibriosis rainbow trout (*Oncorthynchus inmykiss*, Walbaum). *Syst. Appl. Microbiol.* **2004**, *27*, 350–359. [CrossRef]
137. Brackman, G.; Celen, S.; Hillaert, U.; Van Calenbergh, S.; Cos, P.; Maes, L.; Nelis, H.J.; Coenye, T. Structure-activity relationship of cinnamaldehyde analogs as inhibitors of AI-2 based quorum sensing and their effect on virulence of *Vibrio* spp. *PLoS ONE* **2011**, *6*, e16084. [CrossRef]
138. Haldar, S.; Chatterjee, S.; Sugimoto, N.; Das, S.; Chowdhury, N.; Hinenoya, A.; Asakura, M.; Yamasaki, S. Identification of *Vibrio campbellii* isolated from diseased farm-shrimps from south India and establishment of its pathogenic potential in an *Artemia* model. *Microbiology* **2011**, *157*, 179–188. [CrossRef]
139. Noor, N.M.; Defoirdt, T.; Alipiah, N.; Karim, M.; Daud, H.; Natrah, I. Quorum sensing is required for full virulence of *Vibrio campbellii* towards tiger grouper (*Epinephelus fuscoguttatus*) larvae. *J. Fish Dis.* **2019**. [CrossRef]
140. Defoirdt, T.; Crab, R.; Wood, T.K.; Sorgeloos, P.; Verstraete, W.; Bossier, P. Quorum sensing-disrupting brominated furanones protect the gnotobiotic brine shrimp *Artemia franciscana* from pathogenic *Vibrio harveyi*, *Vibrio campbellii* and *Vibrio parahaemolyticus* isolates. *Appl. Environ. Microbiol.* **2006**, *72*, 6419–6423. [CrossRef]
141. Tait, K.; Hutchison, Z.; Thompson, F.L.; Munn, C.B. Quorum sensing signal production and inhibition by coral-associated vibrios. *Environ. Microbiol. Rep.* **2010**, *2*, 145–150. [CrossRef]
142. Bassler, B.L.; Wright, M.; Showalter, R.E.; Silverman, M.R. Intercellular signalling in *Vibrio harveyi*: Sequence and function of genes regulating expression of luminescence. *Mol. Microbiol.* **1993**, *9*, 773–786. [CrossRef] [PubMed]
143. Cao, J.G.; Meighen, E.A. Purification and structural identification of an autoinducer for the luminescence system of *Vibrio harveyi*. *J. Biol. Chem.* **1989**, *264*, 21670–21676.
144. Santhakumari, S.; Jayakumar, R.; Logalakshmi, R.; Prabhu, N.M.; Abdul Nazar, A.K.; Karutha Pandian, S.; Veera Ravi, A. In vitro and in vivo effect of 2,6-di-*tert*-butyl-4-methylphenol as an antibiofilm agent against quorum sensing mediated biofilm formation of *Vibrio* spp. *Int. J. Food Microbiol.* **2018**, *281*, 60–71. [CrossRef]
145. Ni, N.; Choudhary, G.; Li, M.; Wang, B. Pyrogallol and its analogs can antagonize bacterial quorum sensing in *Vibrio harveyi*. *Bioorg. Med. Chem. Lett.* **2008**, *18*, 1567–1572. [CrossRef]
146. Henke, J.M.; Bassler, B.L. Quorum sensing regulates type III secretion in *Vibrio harveyi* and *Vibrio parahaemolyticus*. *J. Bacteriol.* **2004**, *186*, 3794–3805. [CrossRef]
147. Bai, F.; Han, Y.; Chen, J.; Zhang, X.H. Disruption of quorum sensing in *Vibrio harveyi* by the AiiA protein of *Bacillus thuringiensis*. *Aquaculture* **2008**, *274*, 36–40. [CrossRef]
148. Pande, G.S.J.; Scheie, A.A.; Benneche, T.; Wille, M.; Sorgeloos, P.; Bossier, P.; Defoirdt, T. Quorum sensing-disrupting compounds protect larvae of the giant freshwater prawn *Macrobrachium rosenbergii* from *Vibrio harveyi* infection. *Aquaculture* **2013**, *406–407*, 121–124. [CrossRef]
149. Lowery, C.A.; Abe, T.; Park, J.; Eubanks, L.M.; Sawada, D.; Kaufmann, G.F.; Janda, K.D. Revisiting AI-2 quorum sensing inhibitors: Direct comparison of alkyl-DPD analogues and a natural product fimbrolide. *J. Am. Chem. Soc.* **2009**, *131*, 15584–15585. [CrossRef]
150. Torres, M.; Hong, K.W.; Chong, T.M.; Reina, J.C.; Chan, K.G.; Dessaux, Y.; Llamas, I. Genomic analyses of two *Alteromonas stellipolaris* strains reveal traits with potential biotechnological applications. *Sci. Rep.* **2019**, *9*, 1215. [CrossRef]
151. Valiente, E.; Bruhn, J.B.; Nielsen, K.F.; Larsen, J.L.; Roig, F.J.; Gram, L.; Amaro, C. *Vibrio vulnificus* produces quorum sensing signals of the AHL-class: Research article. *FEMS Microbiol. Ecol.* **2009**, *69*, 16–26. [CrossRef]
152. Piper, K.R.; von Bodman, S.B.; Farrand, S.K. Conjugation factor of *Agrobacterium tumefaciens* regulates Ti plasmid transfer by autoinduction. *Nature* **1993**, *362*, 448–450. [CrossRef]

153. Zhang, L.; Murphy, P.J.; Kerr, A.; Tate, M.E. *Agrobacterium* conjugation and gene regulation by *N*-acyl-L-homoserine lactones. *Nature* **1993**, *362*, 446–448. [CrossRef]
154. Mhedbi-Hajri, N.; Yahiaoui, N.; Mondy, S.; Hue, N.; Pélissier, F.; Faure, D.; Dessaux, Y. Transcriptome analysis revealed that a quorum sensing system regulates the transfer of the pAt megaplasmid in *Agrobacterium tumefaciens*. *BMC Genom.* **2016**, *17*, 661. [CrossRef]
155. Zhang, X.H.; Wang, L.; Zhang, L.H. Genetic control of quorum-sensing signal turnover in Agrobacterium tumefaciens. *Proc. Natl. Acad. Sci. USA* **2002**, *99*, 4638–4643. [CrossRef]
156. Carlier, A.; Chevrot, R.; Dessaux, Y.; Faure, D. The assimilation of γ-butyrolactone in *Agrobacterium tumefaciens* C58 interferes with the accumulation of the *N*-acyl-homoserine lactone signal. *Mol. Plant-Microbe Interact.* **2004**, *17*, 951–957. [CrossRef]
157. Haudecoeur, E.; Tannières, M.; Cirou, A.; Raffoux, A.; Dessaux, Y.; Faure, D. Different regulation and roles of lactonases AiiB and AttM in *Agrobacterium tumefaciens* C58. *Mol. Plant-Microbe Interact.* **2009**, *22*, 529–537. [CrossRef]
158. McInnis, C.E.; Blackwell, H.E. Thiolactone modulators of quorum sensing revealed through library design and screening. *Bioorg. Med. Chem.* **2011**, *19*, 4820–4828. [CrossRef]
159. Chernin, L.; Toklikishvili, N.; Ovadis, M.; Kim, S.; Ben-Ari, J.; Khmel, I.; Vainstein, A. Quorum-sensing quenching by rhizobacterial volatiles. *Environ. Microbiol. Rep.* **2011**, *3*, 698–704. [CrossRef]
160. Liu, H.B.; Koh, K.P.; Kim, J.S.; Seo, Y.; Park, S. The effects of betonicine, floridoside, and isethionic acid from the red alga *Ahnfeltiopsis flabelliformis* on quorum-sensing activity. *Biotechnol. Bioprocess Eng.* **2008**, *13*, 458–463. [CrossRef]
161. Kim, J.; Kim, J.G.; Kang, Y.; Jang, J.Y.; Jog, G.J.; Lim, J.Y.; Kim, S.; Suga, H.; Nagamatsu, T.; Hwang, I. Quorum sensing and the LysR-type transcriptional activator ToxR regulate toxoflavin biosynthesis and transport in *Burkholderia glumae*. *Mol. Microbiol.* **2004**, *54*, 921–934. [CrossRef]
162. Kim, J.; Kang, Y.; Choi, O.; Jeong, Y.; Jeong, J.E.; Lim, J.Y.; Kim, M.; Moon, J.S.; Suga, H.; Hwang, I. Regulation of polar flagellum genes is mediated by quorum sensing and FlhDC in *Burkholderia glumae*. *Mol. Microbiol.* **2007**, *64*, 165–179. [CrossRef]
163. Devescovi, G.; Bigirimana, J.; Degrassi, G.; Cabrio, L.; LiPuma, J.J.; Kim, J.; Hwang, I.; Venturi, V. Involvement of a quorum-sensing-regulated lipase secreted by a clinical isolate of *Burkholderia glumae* in severe disease symptoms in rice. *Appl. Environ. Microbiol.* **2007**, *73*, 4950–4958. [CrossRef]
164. Kang, Y.; Goo, E.; Kim, J.; Hwang, I. Critical role of quorum sensing-dependent glutamate metabolism in homeostatic osmolality and outer membrane vesiculation in *Burkholderia glumae*. *Sci. Rep.* **2017**, *7*, 44195. [CrossRef]
165. Cho, H.S.; Park, S.Y.; Ryu, C.M.; Kim, J.F.; Kim, J.G.; Park, S.H. Interference of quorum sensing and virulence of the rice pathogen *Burkholderia glumae* by an engineered endophytic bacterium. *FEMS Microbiol. Ecol.* **2007**, *60*, 14–23. [CrossRef]
166. Chung, J.; Goo, E.; Yu, S.; Choi, O.; Lee, J.; Kim, J.; Kim, H.; Igarashi, J.; Suga, H.; Moon, J.S.; et al. Small-molecule inhibitor binding to an *N*-acyl-homoserine lactone synthase. *Proc. Natl. Acad. Sci. USA* **2011**, *108*, 12089–12094. [CrossRef]
167. Nasser, W.; Bouillant, M.L.; Salmond, G.; Reverchon, S. Characterization of the *Erwinia chrysanthemi expI-expR* locus directing the synthesis of two *N*-acyl-homoserine lactone signal molecules. *Mol. Microbiol.* **1998**, *29*, 1391–1405. [CrossRef]
168. Hussain, M.B.B.M.; Zhang, H.B.; Xu, J.L.; Liu, Q.; Jiang, Z.; Zhang, L.H. The acyl-homoserine lactone-type quorum-sensing system modulates cell motility and virulence of *Erwinia chrysanthemi* pv. *zeae*. *J. Bacteriol.* **2008**, *190*, 1045–1053. [CrossRef]
169. Hosseinzadeh, S.; Shams-Bakhsh, M.; Yamchi, A. A comparative study on effect of two different *aiiA* genes on pathogenicity factors of *Dickeya chrysanthemi* pv. chrysanthemi. *Arch. Phytopathol. Plant Prot.* **2013**, *46*, 1468–1479. [CrossRef]
170. Hosseinzadeh, S.; Shams-Bakhsh, M.; Sadeghizadeh, M. Attenuation and quantitation of virulence gene expression in quorum-quenched *Dickeya chrysanthemi*. *Arch. Microbiol.* **2017**, *199*, 51–61. [CrossRef]
171. Nasser, W.; Dorel, C.; Wawrzyniak, J.; Van Gijsegem, F.; Groleau, M.C.; Déziel, E.; Reverchon, S. Vfm a new quorum sensing system controls the virulence of *Dickeya dadantii*. *Environ. Microbiol.* **2013**, *15*, 865–880. [CrossRef]

172. Potrykus, M.; Golanowska, M.; Hugouvieux-Cotte-Pattat, N.; Lojkowska, E. Regulators involved in *Dickeya solani* virulence, genetic conservation and functional variability. *Mol. Plant-Microbe Interact.* **2015**, *2015*, 5–16. [CrossRef]
173. Venturi, V.; Venuti, C.; Devescovi, G.; Lucchese, C.; Friscina, A.; Degrassi, G.; Aguilar, C.; Mazzucchi, U. The plant pathogen *Erwinia amylovora* produces acyl-homoserine lactone signal molecules in vitro and *in planta*. *FEMS Microbiol. Lett.* **2004**, *241*, 179–183. [CrossRef]
174. Gao, Y.; Song, J.; Hu, B.; Zhang, L.; Liu, Q.; Liu, F. The *luxS* gene is involved in AI-2 production, pathogenicity, and some phenotypes in *Erwinia amylovora*. *Curr. Microbiol.* **2009**, *58*, 1–10. [CrossRef]
175. Molina, L.; Rezzonico, F.; Defago, G.; Duffy, B. Autoinduction in *Erwinia amylovora*: Evidence of an acyl-homoserine lactone signal in the fire blight pathogen. *J. Bacteriol.* **2005**, *187*, 3206–3213. [CrossRef] [PubMed]
176. von Bodman, S.B.; Majerczak, D.R.; Coplin, D.L. A negative regulator mediates quorum-sensing control of exopolysaccharide production in *Pantoea stewartii* subsp. *stewartii*. *Proc. Natl. Acad. Sci. USA* **1998**, *95*, 7687–7692. [CrossRef] [PubMed]
177. Koutsoudis, M.D.; Tsaltas, D.; Minogue, T.D.; von Bodman, S.B. Quorum-sensing regulation governs bacterial adhesion, biofilm development, and host colonization in *Pantoea stewartii* subspecies *stewartii*. *Proc. Natl. Acad. Sci. USA* **2006**, *103*, 5983–5988. [CrossRef]
178. Oh, H.S.H.; Tan, C.H.; Low, J.H.J.; Rzechowicz, M.; Siddiqui, M.M.F.; Winters, H.; Kjelleberg, S.; Fane, A.G.; Rice, S.A. Quorum quenching bacteria can be used to inhibit the biofouling of reverse osmosis membranes. *Water Res.* **2017**, *112*, 29–37. [CrossRef] [PubMed]
179. Smadja, B.; Latour, X.; Faure, D.; Chevalier, S.; Dessaux, Y.; Orange, N. Involvement of *N*-acylhomoserine lactones throughout plant infection by *Erwinia carotovora* subsp. atroseptica (Pectobacterium atrospecticum). *Mol. Plant. Microbe. Interact.* **2004**, *17*, 1269–1278. [CrossRef]
180. Liu, H.; Coulthurst, S.J.; Pritchard, L.; Hedley, P.E.; Ravensdale, M.; Humphris, S.; Burr, T.; Takle, G.; Brurberg, M.B.; Birch, P.R.J.; et al. Quorum sensing coordinates brute force and stealth modes of infection in the plant pathogen *Pectobacterium atrosepticum*. *PLoS Pathog.* **2008**, *4*, e1000093. [CrossRef]
181. Monson, R.; Burr, T.; Carlton, T.; Liu, H.; Hedley, P.; Toth, I.; Salmond, G.P.C. Identification of genes in the VirR regulon of *Pectobacterium atrosepticum* and characterization of their roles in quorum sensing-dependent virulence. *Environ. Microbiol.* **2013**, *15*, 687–701. [CrossRef] [PubMed]
182. Bowden, S.D.; Hale, N.; Chung, J.C.S.; Hodgkinson, J.T.; Spring, D.R.; Welch, M. Surface swarming motility by *Pectobacterium atrosepticum* is a latent phenotype that requires O antigen and is regulated by quorum sensing. *Microbiology* **2013**, *159*, 2375–2385. [CrossRef]
183. Barbey, C.; Crepin, A.; Bergeau, D.; Ouchiha, A.; Mijouin, L.; Taupin, L.; Orange, N.; Feuilloley, M.; Dufour, A.; Burini, J.F.; et al. *In planta* biocontrol of *Pectobacterium atrosepticum* by *Rhodococcus erythropolis* involves silencing of pathogen communication by the *Rhodococcal* gamma-lactone catabolic pathway. *PLoS ONE* **2013**, *8*. [CrossRef]
184. Carlier, A.; Uroz, S.; Smadja, B.; Fray, R.; Latour, X.; Dessaux, Y.; Faure, D. The Ti plasmid of *Agrobacterium tumefaciens* harbors an *attM*-paralogous gene, *aiiB*, also encoding *N*-acyl homoserine lactonase activity. *Appl. Environ. Microbiol.* **2003**, *69*, 4989–4993. [CrossRef] [PubMed]
185. Raoul des Essarts, Y.; Sabbah, M.; Comte, A.; Soulère, L.; Queneau, Y.; Dessaux, Y.; Hélias, V.; Faure, D.; des Essarts, Y.; Sabbah, M.; et al. *N,N'*-alkylated imidazolium-derivatives act as quorum-sensing inhibitors targeting the *Pectobacterium atrosepticum*-induced symptoms on potato tubers. *Int. J. Mol. Sci.* **2013**, *14*, 19976–19986. [CrossRef] [PubMed]
186. Mukherjee, A.; Cui, Y.; Liu, Y.; Dumenyo, C.K.; Chatterjee, A.K. Global regulation in *Erwinia* species by *Erwinia carotovora rsmA*, a homologue of *Escherichia coli csrA*: Repression of secondary metabolites, pathogenicity and hypersensitive reaction. *Microbiology* **1996**, *142*, 427–434. [CrossRef]
187. Cui, Y.; Chatterjee, A.; Liu, Y.; Dumenyo, C.K.; Chatterjee, A.K. Identification of a global repressor gene, *rsmA*, of *Erwinia carotovora* subsp. *carotovora* that controls extracellular enzymes, *N*-(3-oxohexanoyl)-L-homoserine lactone, and pathogenicity in soft-rotting *Erwinia* spp. *J. Bacteriol.* **1995**, *177*, 5108–5115. [CrossRef]
188. Liu, Y.; Cui, Y.; Mukherjee, A.; Chatterjee, A.K. Characterization of a novel RNA regulator of *Erwinia carotovora* ssp. *carotovora* that controls production of extracellular enzymes and secondary metabolites. *Mol. Microbiol.* **1998**, *29*, 219–234. [CrossRef] [PubMed]

189. Coulthurst, S.J.; Lilley, K.; Salmond, G. Genetic and proteomic analysis of the role of *luxS* in the enteric phytopathogen, *Erwinia carotovora*. *Mol. Plant Pathol.* **2006**, *7*, 31–45. [CrossRef] [PubMed]
190. Laasik, E.; Andresen, L.; Mäe, A. Type II quorum sensing regulates virulence in *Erwinia carotovora* ssp. *carotovora*. *FEMS Microbiol. Lett.* **2006**, *258*, 227–234. [CrossRef] [PubMed]
191. Manefield, M.; Welch, M.; Givskov, M.; Salmond, G.P.C.; Kjelleberg, S. Halogenated furanones from the red alga, *Delisea pulchra*, inhibit carbapenem antibiotic synthesis and exoenzyme virulence factor production in the phytopathogen *Erwinia carotovora*. *FEMS Microbiol. Lett.* **2001**, *205*, 131–138. [CrossRef] [PubMed]
192. Park, S.; Lee, S.; Oh, T.; Oh, J.; Koo, B.; Yum, D.; Lee, J. AhlD, an *N*-acylhomoserine lactonase in *Arthrobacter* sp., and predicted homologues in other bacteria. *Microbiology* **2003**, *149*, 1541–1550. [CrossRef] [PubMed]
193. Colnaghi Simionato, A.V.; da Silva, D.S.; Lambais, M.R.; Carrilho, E. Characterization of a putative *Xylella fastidiosa* diffusible signal factor by HRGC-EI-MS. *J. Mass Spectrom.* **2007**, *42*, 1375–1381. [CrossRef]
194. Chatterjee, S.; Wistrom, C.; Lindow, S.E. A cell-cell signaling sensor is required for virulence and insect transmission of *Xylella fastidiosa*. *Proc. Natl. Acad. Sci. USA* **2008**, *105*, 2670–2675. [CrossRef]
195. Ionescu, M.; Zaini, P.A.; Baccari, C.; Tran, S.; da Silva, A.M.; Lindow, S.E. *Xylella fastidiosa* outer membrane vesicles modulate plant colonization by blocking attachment to surfaces. *Proc. Natl. Acad. Sci. USA* **2014**, *111*, E3910–E3918. [CrossRef]
196. Kushner, D.; Kamekura, M. Physiology of halophilic bacteria. In *Halophilic Bacteria*; Rodriguez-Valera, F., Ed.; CRC Press: Boca Raton, FL, USA, 1988; Volume 1, pp. 109–138.
197. Oren, A. Diversity of halophilic microorganisms: Environments, phylogeny, physiology, and applications. *J. Ind. Microbiol. Biotechnol.* **2002**, *28*, 56–63. [CrossRef]
198. Ventosa, A. Unusual microorganisms from unusual habitats: Hypersaline environments. In *Prokaryotic Diversity-Mechanism and Significance*; Logan, N.A., Lappin-Scott, H.M., Oyston, P.C.F., Eds.; Cambridge University Press: Cambridge, UK, 2006; pp. 223–252.
199. Margesin, R.; Schinner, F. Potential of halotolerant and halophilic microorganisms for biotechnology. *Extremophiles* **2001**, *5*, 73–83. [CrossRef]
200. Bhatnagar, I.; Kim, S.K. Immense essence of excellence: Marine microbial bioactive compounds. *Mar. Drugs* **2010**, *8*, 2673–2701. [CrossRef] [PubMed]
201. Trincone, A. Marine biocatalysts: Enzymatic features and applications. *Mar. Drugs* **2011**, *9*, 478–499. [CrossRef]
202. Hamza, F.; Zinjarde, S. Marine biodiversity as a resource for bioactive molecules as inhibitors of microbial quorum sensing phenotypes. In *Biotechnological Applications of Quorum Sensing Inhibitors*; Springer: Singapore, 2018; pp. 329–350.
203. Llamas, I.; Amjres, H.; Mata, J.A.; Quesada, E.; Béjar, V. The Potential biotechnological applications of the exopolysaccharide produced by the halophilic bacterium *Halomonas almeriensis*. *Molecules* **2012**, *17*, 7103–7120. [CrossRef] [PubMed]
204. Radchenkova, N.; Boyadzhieva, I.; Atanasova, N.; Poli, A.; Finore, I.; Di Donato, P.; Nicolaus, B.; Panchev, I.; Kuncheva, M.; Kambourova, M. Extracellular polymer substance synthesized by a halophilic bacterium *Chromohalobacter canadensis* 28. *Appl. Microbiol. Biotechnol.* **2018**, *102*, 4937–4949. [CrossRef]
205. Chang, J.; Lee, Y.S.; Fang, S.J.; Park, I.H.; Choi, Y.L. Recombinant expression and characterization of an organic-solvent-tolerant α-amylase from *Exiguobacterium* sp. DAU5. *Appl. Biochem. Biotechnol.* **2013**, *169*, 1870–1883. [CrossRef]
206. Scapin, S.M.N.; Souza, F.H.M.; Zanphorlin, L.M.; de Almeida, T.S.; Sade, Y.B.; Cardoso, A.M.; Pinheiro, G.L.; Murakami, M.T. Structure and function of a novel GH8 endoglucanase from the bacterial cellulose synthase complex of *Raoultella ornithinolytica*. *PLoS ONE* **2017**, *12*, e0176550. [CrossRef]
207. Li, X.; Qian, P.; Wu, S.G.; Yu, H.Y. Characterization of an organic solvent-tolerant lipase from *Idiomarina* sp. W33 and its application for biodiesel production using Jatropha oil. *Extremophiles* **2014**, *18*, 171–178. [CrossRef]
208. Houssen, W.E.; Jaspars, M. Isolation of Marine Natural Products. *Methods Mol. Biol.* **2012**, *864*, 367–392. [CrossRef]
209. Nikapitiya, C. Bioactive secondary metabolites from marine microbes for drug discovery. *Adv. Food Nutr. Res.* **2012**, *65*, 363–387. [CrossRef]

210. Teasdale, M.E.; Liu, J.; Wallace, J.; Akhlaghi, F.; Rowley, D.C. Secondary metabolites produced by the marine bacterium *Halobacillus salinus* that inhibit quorum sensing-controlled phenotypes in Gram-negative bacteria. *Appl. Environ. Microbiol.* **2009**, *75*, 567–572. [CrossRef]
211. Teasdale, M.E.; Donovan, K.A.; Forschner-Dancause, S.R.; Rowley, D.C. Gram-positive marine bacteria as a potential resource for the discovery of quorum sensing inhibitors. *Mar. Biotechnol.* **2011**, *13*, 722–732. [CrossRef]
212. D'Angelo-Picard, C.; Faure, D.; Penot, I.; Dessaux, Y. Diversity of *N*-acyl homoserine lactone-producing and -degrading bacteria in soil and tobacco rhizosphere. *Environ. Microbiol.* **2005**, *7*, 1796–1808. [CrossRef]
213. Pierson, E.A.; Wood, D.; Cannon, J.; Blachere, F.; Leland, S. Interpopulation signaling via *N*-acyl-homoserine lactones among bacteria in the wheat rhizosphere. *Mol. Plant-Microbe Interact.* **1998**, *11*, 1078–1084. [CrossRef]
214. Romero, M.; Martin-Cuadrado, A.B.; Roca-Rivada, A.; Cabello, A.M.; Otero, A. Quorum quenching in cultivable bacteria from dense marine coastal microbial communities. *FEMS Microbiol. Ecol.* **2011**, *75*, 205–217. [CrossRef]
215. Muras, A.; López-Pérez, M.; Mayer, C.; Parga, A.; Amaro-Blanco, J.; Otero, A. High prevalence of quorum-sensing and quorum-quenching activity among cultivable bacteria and metagenomic sequences in the Mediterranean sea. *Genes (Basel)* **2018**, *9*, 100. [CrossRef]
216. Natrah, F.; Defoirdt, T.; Sorgeloos, P.; Bossier, P. Disruption of bacterial cell-to-cell communication by marine organisms and its relevance to aquaculture. *Mar. Biotechnol.* **2011**, *13*, 109–126. [CrossRef]
217. Saurav, K.; Costantino, V.; Venturi, V.; Steindler, L. Quorum sensing inhibitors from the sea discovered using bacterial *N*-acyl-homoserine lactone-based biosensors. *Mar. Drugs* **2017**, *15*, 53. [CrossRef]
218. Chen, J.; Wang, B.; Lu, Y.; Guo, Y.; Sun, J.; Wei, B.; Zhang, H.; Wang, H. Quorum sensing inhibitors from marine microorganisms and their synthetic derivatives. *Mar. Drugs* **2019**, *17*, 80. [CrossRef]
219. Natrah, F.M.I.; Kenmegne, M.M.; Wiyoto, W.; Sorgeloos, P.; Bossier, P.; Defoirdt, T. Effects of micro-algae commonly used in aquaculture on acyl-homoserine lactone quorum sensing. *Aquaculture* **2011**, *317*, 53–57. [CrossRef]
220. Saurav, K.; Bar-Shalom, R.; Haber, M.; Burgsdorf, I.; Oliviero, G.; Costantino, V.; Morgenstern, D.; Steindler, L. In search of alternative antibiotic drugs: Quorum-quenching activity in sponges and their bacterial isolates. *Front. Microbiol.* **2016**, *7*, 1–18. [CrossRef]
221. Martín-Rodríguez, A.; Reyes, F.; Martín, J.; Pérez-Yépez, J.; León-Barrios, M.; Couttolenc, A.; Espinoza, C.; Trigos, Á.; Martín, V.; Norte, M.; et al. Inhibition of bacterial quorum sensing by extracts from aquatic fungi: First report from marine endophytes. *Mar. Drugs* **2014**, *12*, 5503–5526. [CrossRef]
222. Rehman, Z.U.; Leiknes, T. Quorum-quenching bacteria isolated from Red sea sediments reduce biofilm formation by *Pseudomonas aeruginosa*. *Front. Microbiol.* **2018**, *9*. [CrossRef]
223. Gutiérrez-Barranquero, J.A.; Reen, F.J.; Parages, M.L.; McCarthy, R.; Dobson, A.D.W.; O'Gara, F. Disruption of *N*-acyl-homoserine lactone-specific signalling and virulence in clinical pathogens by marine sponge bacteria. *Microb. Biotechnol.* **2017**. [CrossRef]
224. Costantino, V.; Della Sala, G.; Saurav, K.; Teta, R.; Bar-Shalom, R.; Mangoni, A.; Steindler, L. Plakofuranolactone as a quorum quenching agent from the Indonesian sponge Plakortis cf. lita. *Mar. Drugs* **2017**, *15*, 59. [CrossRef]
225. Blanchet, E.; Prado, S.; Stien, D.; Oliveira da Silva, J.; Ferandin, Y.; Batailler, N.; Intertaglia, L.; Escargueil, A.; Lami, R. Quorum sensing and quorum quenching in the Mediterranean seagrass *Posidonia oceanica* microbiota. *Front. Mar. Sci.* **2017**, *4*. [CrossRef]
226. Pande, G.S.J.; Natrah, F.M.I.; Flandez, A.V.B.; Kumar, U.; Niu, Y.; Bossier, P.; Defoirdt, T. Isolation of AHL-degrading bacteria from micro-algal cultures and their impact on algal growth and on virulence of *Vibrio campbellii* to prawn larvae. *Appl. Microbiol. Biotechnol.* **2015**, *99*, 10805–10813. [CrossRef]
227. Defoirdt, T.; Benneche, T.; Brackman, G.; Coenye, T.; Sorgeloos, P.; Scheie, A.A. A Quorum sensing-disrupting brominated thiophenone with a promising therapeutic potential to treat luminescent vibriosis. *PLoS ONE* **2012**, *7*, e41788. [CrossRef]
228. Chang, H.; Zhou, J.; Zhu, X.; Yu, S.; Chen, L.; Jin, H.; Cai, Z. Strain identification and quorum sensing inhibition characterization of marine-derived *Rhizobium* sp. NAO1. *R. Soc. Open Sci.* **2017**, *4*, 170025. [CrossRef]
229. Chen, X.; Chen, J.; Yan, Y.; Chen, S.; Xu, X.; Zhang, H.; Wang, H. Quorum sensing inhibitors from marine bacteria *Oceanobacillus* sp. XC22919. *Nat. Prod. Res.* **2018**, 1–5. [CrossRef]

230. Sun, S.; Dai, X.; Sun, J.; Bu, X.; Weng, C.; Li, H.; Zhu, H. A diketopiperazine factor from *Rheinheimera aquimaris* QSI02 exhibits anti-quorum sensing activity. *Sci. Rep.* **2016**, *6*, 39637. [CrossRef]
231. Miao, L.; Xu, J.; Yao, Z.; Jiang, Y.; Zhou, H.; Jiang, W.; Dong, K. The anti-quorum sensing activity and bioactive substance of a marine derived *Streptomyces*. *Biotechnol. Biotechnol. Equip.* **2017**, *31*, 1007–1015. [CrossRef]
232. Mireille Ayé, A.; Bonnin-Jusserand, M.; Brian-Jaisson, F.; Ortalo-Magné, A.; Culioli, G.; Koffi Nevry, R.; Rabah, N.; Blache, Y.; Molmeret, M. Modulation of violacein production and phenotypes associated with biofilm by exogenous quorum sensing *N*-acylhomoserine lactones in the marine bacterium *Pseudoalteromonas ulvae* TC14. *Microbiology* **2015**, *161*, 2039–2051. [CrossRef]
233. Liaqat, I.; Bachmann, R.T.; Edyvean, R.G.J. Type 2 quorum sensing monitoring, inhibition and biofilm formation in marine microrganisms. *Curr. Microbiol.* **2014**, *68*, 342–351. [CrossRef]
234. Ni, N.; Chou, H.T.; Wang, J.; Li, M.; Lu, C.D.; Tai, P.C.; Wang, B. Identification of boronic acids as antagonists of bacterial quorum sensing in *Vibrio harveyi*. *Biochem. Biophys. Res. Commun.* **2008**, *369*, 590–594. [CrossRef]
235. Brackman, G.; Celen, S.; Baruah, K.; Bossier, P.; Van Calenberg, S.; Nelis, H.J.; Coenye, T.; Van Calenbergh, S.; Nelis, H.J.; Coenye, T. AI-2 quorum-sensing inhibitors affect the starvation response and reduce virulence in several *Vibrio* species, most likely by interfering with LuxPQ. *Microbiology* **2009**, *155*, 4114–4122. [CrossRef]
236. Shen, G.; Rajan, R.; Zhu, J.; Bell, C.E.; Pei, D. Design and synthesis of substrate and intermediate analogue inhibitors of S-ribosylhomocysteinase. *J. Med. Chem.* **2006**, *49*, 3003–3011. [CrossRef]
237. Malladi, V.L.A.; Sobczak, A.J.; Meyer, T.M.; Pei, D.; Wnuk, S.F. Inhibition of LuxS by S-ribosylhomocysteine analogues containing a [4-aza]ribose ring. *Bioorg. Med. Chem.* **2011**, *19*, 5507–5519. [CrossRef]
238. Li, M.; Ni, N.; Chou, H.T.; Lu, C.D.; Tai, P.C.; Wang, B. Structure-based discovery and experimental verification of novel AI-2 quorum sensing inhibitors against *Vibrio harveyi*. *ChemMedChem* **2008**, *3*, 1242–1249. [CrossRef]
239. Zhu, P.; Peng, H.; Ni, N.; Wang, B.; Li, M. Novel AI-2 quorum sensing inhibitors in *Vibrio harveyi* identified through structure-based virtual screening. *Bioorg. Med. Chem. Lett.* **2012**, *22*, 6413–6417. [CrossRef]
240. Jiang, T.; Zhu, P.; Du, L.; Li, M. Identification of AI-2 quorum sensing inhibitors in *Vibrio harveyi* through structure-based virtual screening. *Methods Mol. Biol.* **2018**, *1673*, 353–362. [CrossRef]
241. Liu, N.; Yu, M.; Zhao, Y.; Cheng, J.; An, K.; Zhang, X.H. PfmA, a novel quorum-quenching *N*-acylhomoserine lactone acylase from *Pseudoalteromonas flavipulchra*. *Microbiology* **2017**, *163*, 1389–1398. [CrossRef]
242. Tang, K.; Su, Y.; Brackman, G.; Cui, F.; Zhang, Y.; Shi, X.; Coenye, T.; Zhang, X.H. MomL, a novel marine-derived *N*-acyl homoserine lactonase from *Muricauda olearia*. *Appl. Environ. Microbiol.* **2015**, *81*, 774–782. [CrossRef]
243. Romero, M.; Avendaño-Herrera, R.; Magariños, B.; Cámara, M.; Otero, A. Acylhomoserine lactone production and degradation by the fish pathogen *Tenacibaculum maritimum*, a member of the Cytophaga-Flavobacterium-Bacteroidetes (CFB) group. *FEMS Microbiol. Lett.* **2010**, *304*, 131–139. [CrossRef]
244. Cai, X.; Yu, M.; Shan, H.; Tian, X.; Zheng, Y.; Xue, C.; Zhang, X.H. Characterization of a novel *N*-acylhomoserine lactonase RmmL from *Ruegeria mobilis* YJ3. *Mar. Drugs* **2018**, *16*, 370. [CrossRef] [PubMed]
245. See-Too, W.S.; Convey, P.; Pearce, D.A.; Chan, K.G. Characterization of a novel *N*-acylhomoserine lactonase, AidP, from Antarctic *Planococcus* sp. *Microb. Cell Fact.* **2018**, *17*, 179. [CrossRef]
246. Zhou, S.; Xia, Y.; Zhu, C.; Chu, W. Isolation of marine *Bacillus* sp. with antagonistic and organic-substances-degrading activities and its potential application as a fish probiotic. *Mar. Drugs* **2018**, *16*, 196. [CrossRef]
247. Morohoshi, T.; Nakazawa, S.; Ebata, A.; Kato, N.; Ikeda, T. Identification and characterization of *N*-acylhomoserine lactone-acylase from the fish intestinal *Shewanella* sp. strain MIB015. *Biosci. Biotechnol. Biochem.* **2008**, *72*, 1887–1893. [CrossRef] [PubMed]
248. Romero, M.; Diggle, S.P.; Heeb, S.; Cámara, M.; Otero, A. Quorum quenching activity in *Anabaena* sp. PCC 7120: identification of AiiC, a novel AHL-acylase. *FEMS Microbiol. Lett.* **2008**, *280*, 73–80. [CrossRef] [PubMed]
249. Mayer, C.; Romero, M.; Muras, A.; Otero, A. Aii20J, a wide-spectrum thermostable *N*-acylhomoserine lactonase from the marine bacterium *Tenacibaculum* sp. 20J, can quench AHL-mediated acid resistance in *Escherichia coli*. *Appl. Microbiol. Biotechnol.* **2015**, *99*, 9523–9539. [CrossRef] [PubMed]

250. Yates, E.A.; Philipp, B.; Buckley, C.; Atkinson, S.; Chhabra, S.R.; Sockett, R.E.; Goldner, M.; Dessaux, Y.; Cámara, M.; Smith, H.; et al. *n*-acylhomoserine lactones undergo lactonolysis in a pH-, temperature-, and acyl chain length-dependent manner during growth of *Yersinia pseudotuberculosis* and *Pseudomonas aeruginosa*. *Infect. Immun.* **2002**, *70*, 5635–5646. [CrossRef]
251. Byers, J.; Lucas, C.; Salmond, G.; Welch, M. Nonenzymatic turnover of an *Erwinia carotovora* quorum-sensing signaling molecule. *J. Biotechnol.* **2002**, *184*, 1163–1171. [CrossRef]
252. Ng, F.S.W.; Wright, D.M.; Seah, S.Y.K. Characterization of a phosphotriesterase-like lactonase from *Sulfolobus solfataricus* and its immobilization for disruption of quorum sensing. *Appl. Environ. Microbiol.* **2011**, *77*, 1181–1186. [CrossRef]
253. Demirjian, D.C.; Morís-Varas, F.; Cassidy, C.S. Enzymes from extremophiles. *Curr. Opin. Chem. Biol.* **2001**, *5*, 144–151. [CrossRef]
254. Ravot, G.; Masson, J.M.; Lefèvre, F. Applications of extremophiles: The industrial screening of extremophiles for valuable biomolecules. *Methods Microbiol.* **2006**, *35*, 785–813. [CrossRef]
255. Llamas, I.; Quesada, E.; Martínez-Cánovas, M.J.; Gronquist, M.; Eberhard, A.; González, J.E. Quorum sensing in halophilic bacteria: detection of *N*-acyl-homoserine lactones in the exopolysaccharide-producing species of *Halomonas*. *Extremophiles* **2005**, *9*, 333–341. [CrossRef]
256. Tahrioui, A.; Schwab, M.; Quesada, E.; Llamas, I. Quorum sensing in some representative species of *Halomonadaceae*. *Life* **2013**, *3*, 260–275. [CrossRef]
257. Abbamondi, G.R.; Suner, S.; Cutignano, A.; Grauso, L.; Nicolaus, B.; Oner, E.T.; Tommonaro, G. Identification of *N*-hexadecanoyl-L-homoserine lactone (C16-AHL) as signal molecule in halophilic bacterium *Halomonas smyrnensis* AAD6. *Ann. Microbiol.* **2016**, *66*, 1329–1333. [CrossRef]
258. Sewald, X.; Saum, S.; Palm, P.; Pfeiffer, F.; Oesterhelt, D.; Muller, V. Autoinducer-2-producing protein LuxS, a novel salt- and chloride-induced protein in the moderately halophilic bacterium *Halobacillus halophilus*. *Appl. Environ. Microbiol.* **2007**, *73*, 371–379. [CrossRef]
259. Tommonaro, G.; Abbamondi Gennaro, R.; Toksoy Oner, R.; Nicolaus, B. Investigating the quorum sensing system in halophilic bacteria. *Halophiles* **2015**, 189–207. [CrossRef]
260. Tommonaro, G.; Abbamondi, G.R.; Iodice, C.; Tait, K.; De Rosa, S. Diketopiperazines produced by the halophilic archaeon, *Haloterrigena hispanica*, activate AHL bioreporters. *Microb. Ecol.* **2012**, *63*, 490–495. [CrossRef]
261. Montgomery, K.; Charlesworth, J.C.; LeBard, R.; Visscher, P.T.; Burns, B.P. Quorum sensing in extreme environments. *Life* **2013**, *3*, 131–148. [CrossRef]
262. Abed, R.M.M.; Dobretsov, S.; Al-Fori, M.; Gunasekera, S.P.; Sudesh, K.; Paul, V.J. Quorum-sensing inhibitory compounds from extremophilic microorganisms isolated from a hypersaline cyanobacterial mat. *J. Ind. Microbiol. Biotechnol.* **2013**, *40*, 759–772. [CrossRef]
263. Singh, V.K.; Mishra, A.; Jha, B. Anti-quorum sensing and anti-biofilm activity of delftia tsuruhatensis extract by attenuating the quorum sensing-controlled virulence factor production in *Pseudomonas aeruginosa*. *Front. Cell. Infect. Microbiol.* **2017**, *7*. [CrossRef]
264. Kannan, V.; Bastas, K.; Devi, R. Scientific and economic impact of plant pathogenic bacteria. In *Sustainable Approaches to Controlling Plant Pathogenic Bacteria*; Kannan, V.R., Bastas, K.K., Eds.; CRC Press: Boca Raton, FL, USA, 2015; pp. 369–392.
265. FAO. *The State of World Fisheries and Aquaculture: Contributing to Food Security and Nutrition for All*; FAO: Rome, Italy, 2016; ISBN 978-92-5-109185-2.
266. Martins, P.M.M.; Merfa, M.V.; Takita, M.A.; De Souza, A.A. Persistence in phytopathogenic bacteria: Do we know enough? *Front. Microbiol.* **2018**, *9*. [CrossRef]
267. Smith, P. Antimicrobial resistance in aquaculture. *Rev. Sci. Tech.* **2008**, *27*, 243–264. [CrossRef] [PubMed]
268. Akinbowale, O.L.; Peng, H.; Barton, M.D. Antimicrobial resistance in bacteria isolated from aquaculture sources in Australia. *J. Appl. Microbiol.* **2006**, *100*, 1103–1113. [CrossRef]
269. WHO. *Report of a joint FAO/OIE/WHO Expert Consulation on Antimicrobial Use in Aquaculture and Antimicrobial Resistance, Seoul, Republic of Korea*; WHO: Geneva, Switzerland, 2006; pp. 13–16.
270. Watts, J.E.M.; Schreier, H.J.; Lanska, L.; Hale, M.S. The rising tide of antimicrobial resistance in aquaculture: Sources, sinks and solutions. *Mar. Drugs* **2017**, *15*, 158. [CrossRef] [PubMed]
271. Romero, M.; Acuña, L.; Otero, A. Patents on quorum quenching: interfering with bacterial communication as a strategy to fight infections. *Recent Pat. Biotechnol.* **2012**, *6*, 2–12. [CrossRef]

272. Chen, X.; Zhang, L.; Zhang, M.; Liu, H.; Lu, P.; Lin, K. Quorum sensing inhibitors: A patent review (2014–2018). *Expert Opin. Ther. Pat.* **2018**, 1–17. [CrossRef]
273. Chu, W.; Zhou, S.; Zhu, W.; Zhuang, X. Quorum quenching bacteria *Bacillus* sp. QSI-1 protect zebrafish (*Danio rerio*) from *Aeromonas hydrophila* infection. *Sci. Rep.* **2014**, *4*, 5446. [CrossRef]
274. Nahn, D.; Cam, D.; Wille, M.; Defoirdt, T.; Bossier, P.; Sorgeloos, P. Quorum quenching bacteria protect *Macrobrachium rosenbergii* larvae from *Vibrio harveyi* infection. *J. Appl. Microbiol.* **2010**, *109*, 1007–1016. [CrossRef] [PubMed]
275. Tinh, N.T.N.; Dierckens, K.; Sorgeloos, P.; Bossier, P. A review of the functionality of probiotics in the larviculture food chain. *Mar. Biotechnol.* **2008**, *10*, 1–12. [CrossRef]
276. Vinoj, G.; Vaseeharan, B.; Thomas, S.; Spiers, A.J.; Shanthi, S. Quorum-quenching activity of the AHL-lactonase from *Bacillus licheniformis* DAHB1 inhibits *Vibrio* biofilm formation in vitro and reduces shrimp intestinal colonisation and mortality. *Mar. Biotechnol.* **2014**, *16*, 707–715. [CrossRef] [PubMed]
277. Torabi Delshad, S.; Soltanian, S.; Sharifiyazdi, H.; Haghkhah, M.; Bossier, P. Identification of *N*-acyl homoserine lactone-degrading bacteria isolated from rainbow trout (*Oncorhynchus mykiss*). *J. Appl. Microbiol.* **2018**, 1–2. [CrossRef]
278. Weerasekara, N.A.; Choo, K.H.; Lee, C.H. Biofouling control: Bacterial quorum quenching versus chlorination in membrane bioreactors. *Water Res.* **2016**, *103*, 293–301. [CrossRef] [PubMed]
279. Dobretsov, S.; Teplitski, M.; Bayer, M.; Gunasekera, S.; Proksch, P.; Paul, V. Inhibition of marine biofouling by bacterial quorum sensing inhibitors. *Biofouling* **2011**, *27*, 893–905. [CrossRef] [PubMed]
280. Yeon, K.M.; Lee, C.H.; Kim, J. Magnetic enzyme carrier for effective biofouling control in the membrane bioreactor based on enzymatic quorum quenching. *Environ. Sci. Technol.* **2009**, *43*, 7403–7409. [CrossRef] [PubMed]
281. Kim, J.H.; Choi, D.C.; Yeon, K.M.; Kim, S.R.; Lee, C.H. Enzyme-immobilized nanofiltration membrane to mitigate biofouling based on quorum quenching. *Environ. Sci. Technol.* **2011**, *45*, 1601–1607. [CrossRef]
282. Lade, H.; Paul, D.; Kweon, J.H. Quorum quenching mediated approaches for control of membrane biofouling. *Int. J. Biol. Sci.* **2014**, *10*, 550–565. [CrossRef] [PubMed]
283. Singh, B.N.; Upreti, D.K.; Singh, B.R.; Defoirdt, T.; Gupta, V.K.; De Souza, A.O.; Singh, H.B.; Barreira, J.C.; Ferreira, I.C.; Vahabi, K. Bactericidal, quorum quenching and anti-biofilm nanofactories: A new niche for nanotechnologists. *Crit. Rev. Biotechnol.* **2016**, 1–16. [CrossRef] [PubMed]
284. Nahm, C.H.; Choi, D.C.; Kwon, H.; Lee, S.H.S.; Lee, S.H.S.; Lee, K.; Choo, K.H.; Lee, J.K.; Lee, C.H.; Park, P.K. Application of quorum quenching bacteria entrapping sheets to enhance biofouling control in a membrane bioreactor with a hollow fiber module. *J. Memb. Sci.* **2017**, *526*, 264–271. [CrossRef]
285. Lee, J.; Lee, I.; Nam, J.; Hwang, D.S.; Yeon, K.M.; Kim, J. Immobilization and stabilization of acylase on carboxylated polyaniline nanofibers for highly effective antifouling application via quorum quenching. *ACS Appl. Mater. Interfaces* **2017**, *9*, 15424–15432. [CrossRef]
286. Kim, T.H.; Lee, I.; Yeon, K.M.; Kim, J. Biocatalytic membrane with acylase stabilized on intact carbon nanotubes for effective antifouling via quorum quenching. *J. Memb. Sci.* **2018**, *554*, 357–365. [CrossRef]
287. Schultz, M.P.; Bendick, J.A.; Holm, E.R.; Hertel, W.M. Economic impact of biofouling on a naval surface ship. *Biofouling* **2011**, *27*, 87–98. [CrossRef] [PubMed]
288. Mansfield, J.; Genin, S.; Magori, S.; Citovsky, V.; Sriariyanum, M.; Ronald, P.; Dow, M.; Verdier, V.; Beer, S.V.; Machado, M.A.; et al. Top 10 plant pathogenic bacteria in molecular plant pathology. *Mol. Plant Pathol.* **2012**, *13*, 614–629. [CrossRef] [PubMed]
289. Helman, Y.; Chernin, L. Silencing the mob: Disrupting quorum sensing as a means to fight plant disease. *Mol. Plant Pathol.* **2015**, *16*, 316–329. [CrossRef]
290. Pirhonen, M.; Flego, D.; Heikinheimo, R.; Palva, E.T. A small diffusible signal molecule is responsible for the global control of virulence and exoenzyme production in the plant pathogen *Erwinia carotovora*. *EMBO J.* **1993**, *12*, 2467–2476. [CrossRef]
291. Põllumaa, L.; Alamäe, T.; Mäe, A. Quorum sensing and expression of virulence in *Pectobacteria*. *Sensors* **2012**, *12*, 3327–3349. [CrossRef]
292. Piqué, N.; Miñana-Galbis, D.; Merino, S.; Tomás, J. Virulence Factors of Erwinia amylovora: A Review. *Int. J. Mol. Sci.* **2015**, *16*, 12836–12854. [CrossRef]

293. Naughton, L.M.; An, S.; Hwang, I.; Chou, S.H.; He, Y.Q.; Tang, J.L.; Ryan, R.P.; Dow, J.M. Functional and genomic insights into the pathogenesis of *Burkholderia* species to rice. *Environ. Microbiol.* **2016**, *18*, 780–790. [CrossRef]
294. Kai, K. Bacterial quorum sensing in symbiotic and pathogenic relationships with hosts. *Biosci. Biotechnol. Biochem.* **2018**, *82*, 363–371. [CrossRef] [PubMed]
295. Molina, L.; Constantinescu, F.; Michel, L.; Reimmann, C.; Duffy, B.; Défago, G. Degradation of pathogen quorum-sensing molecules by soil bacteria: A preventive and curative biological control mechanism. *FEMS Microbiol. Ecol.* **2003**, *45*, 71–81. [CrossRef]
296. Mori, Y.; Hosoi, Y.; Ishikawa, S.; Hayashi, K.; Asai, Y.; Ohnishi, H.; Shimatani, M.; Inoue, K.; Ikeda, K.; Nakayashiki, H.; et al. Ralfuranones contribute to mushroom-type biofilm formation by *Ralstonia solanacearum* strain OE1-1. *Mol. Plant Pathol.* **2018**, *19*, 975–985. [CrossRef] [PubMed]
297. Cirou, A.; Diallo, S.; Kurt, C.; Latour, X.; Faure, D. Growth promotion of quorum-quenching bacteria in the rhizosphere of *Solanum tuberosum*. *Environ. Microbiol.* **2007**, *9*, 1511–1522. [CrossRef] [PubMed]
298. Cazenave, A.; Llovel, W. Contemporary sea level rise. *Ann. Rev. Mar. Sci.* **2010**, *2*, 145–173. [CrossRef]
299. Nguyen, T.T.X.; Woodroffe, C.D. Assessing relative vulnerability to sea-level rise in the western part of the Mekong River Delta in Vietnam. *Sustain. Sci.* **2016**, *11*, 645–659. [CrossRef]
300. Hernández-Delgado, E.A. The emerging threats of climate change on tropical coastal ecosystem services, public health, local economies and livelihood sustainability of small islands: Cumulative impacts and synergies. *Mar. Pollut. Bull.* **2015**, *101*, 5–28. [CrossRef] [PubMed]
301. Daliakopoulos, I.N.; Tsanis, I.K.; Koutroulis, A.; Kourgialas, N.N.; Varouchakis, A.E.; Karatzas, G.P.; Ritsema, C.J. The threat of soil salinity: A European scale review. *Sci. Total Environ.* **2016**, *573*, 727–739. [CrossRef]
302. Takagi, H.; Tamiru, M.; Abe, A.; Yoshida, K.; Uemura, A.; Yaegashi, H.; Obara, T.; Oikawa, K.; Utsushi, H.; Kanzaki, E.; et al. MutMap accelerates breeding of a salt-tolerant rice cultivar. *Nat. Biotechnol.* **2015**, *33*, 445–449. [CrossRef] [PubMed]
303. Hanin, M.; Ebel, C.; Ngom, M.; Laplaze, L.; Masmoudi, K. New insights on plant salt tolerance mechanisms and their potential use for breeding. *Front. Plant Sci.* **2016**, *7*. [CrossRef] [PubMed]