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Communication mechanisms in extremophiles: Exploring their existence and industrial applications

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ABSTRACT

Quorum sensing plays important roles in the regulation of physiological and virulence processes in most bacteria, but its role in extremophiles is largely unknown. Comparative genomic, phylogenic, structural and signaling pathways analyses and deletion mutant studies have suggested the presence of three major quorum sensing systems (AI-1, Peptide based and AI-2) in extremophiles. Autoinducer-1(AI-1) system was found to be most prevalent (except in thermophiles where it is autoinducer-2) while peptide based system was least prevalent in extremophiles. Some unknown mechanisms of quorum sensing have also been reported which need further exploration. Quorum sensing is utilized by extremophiles for processes like cold adaptation, lowering the freezing point, biofilm formation, oxidative stress resistance and persister cell formation. Explication of quorum sensing in extreme environments may provide discernment regarding the role and functional strategies for survival of extremophiles. Here the role of quorum sensing in different classes of extremophiles and also in their survival strategies has been reviewed. Further, the applications and problems caused by quorum sensing regulated factors in extreme environments are discussed.

1. Introduction

Extremophiles are important not only because of their incredible capabilities to tolerate extreme environments but also because of their numerous applications in the fields of biotechnology and medicine besides providing industrially important enzymes (Table 1). It would be impossible to imagine the success of PCR without the immense potential of thermophilic DNA polymerases. Diminishing supply of non-renewable fossil fuels and use of high temperature during production of biofuels has made the use of thermophiles *viz*. *Thermoanaerobacterium saccharolyticum* (Olson et al., 2012), *Pyrococcus* (Keller et al., 2017) and *Aeropyrum* (Nishimura and Sako, 2009) a boon for biofuel. *Halobacterium salinarum*, a halophilic archaea, produces bacteriorhodopsin that can be used for artificial retinas and photochromic dyes (Schiraldi et al., 2002). Certain halophiles such as *Naloterrigena hispanica* and *Natronococcus occultus* possess quorum quenching properties against the nosocomical pathogen *Pseudomonas aeruginosa* (Charlesworth and Burns, 2015). Not only this, extremophiles form the base of tree of life, as many of the hyperthermophiles represent universal ancestors of all life forms on earth as shown by evolutionary and phylogenetic studies (Rampelotto, 2013). All these magnificent properties have made the study of these fascinating extremophiles one of the most exhilarating areas of research.

Despite numerous applications, there are certain industrial and health issues associated with extremophiles such as contamination of food in refrigerated environment by the psychrophile *Pseudomonas fluorescens* that also causes numerous problems in dairy industry (Eller et al., 2013). Thermophilic bacteria, *Anoxybacillus flavithermus* and *Geobacillus* spp., are major sources of contamination in the dairy industry (Kent et al., 2016). Similarly, *Alicyclobacillus*, an acidophile, can cause spoilage of juices and beverages because of their high acid content (Huang et al., 2015). Furthermore, halophiles are also the major contaminants in salted meat and fish products (Felix et al., 2016). Environmental problems are also caused by extremophiles such as deterioration of Capuchin Catacombs in Palermo, Italy due to the presence of halophilic bacteria in that environment (Pinar et al., 2014). Thermophilic biofilms are major sources of industrial problems like corrosion of pipelines by genera *Anaerobaculum* and *Methanothermobacter* (Liang et al., 2014), deterioration of paper in paper mills by *Meiothermus* sp. and *Geobacillus* sp. biofilms (Ekman, 2011).

These applications and problems caused by extremophiles demand the knowledge of communication mechanisms used by these microorganisms to fulfill their tasks, as cell to cell communication (quorum sensing) is essential for the development and survival of these

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Table 1
Applications of extremophiles in industry, health, medicine and environment.

Extremophilic class	Members	Applications	References
Acidophiles	*Acidimicrobium ferrooxidans* (strain TH3) and *Ferroplasma acidiphilum* (strain MT17)	Biomining	Okibe et al. (2003)
Thermophiles	*Sulfobacillus thermosulfidooxidans* and *Metallosphaera sp.*	Biomining Biofuel production	Tourova et al. (1994); Vera et al. (2013); de Vrije et al., 2010; Abol Fotouh et al. (2016), Correa-llanten et al. (2014); Verma et al., (2014); Gupta et al. (2012); Wang et al. (2010); Touzel et al. (2000)
	Caldicellulosiruptor saccharolyticus and *Thermotoga neopolitana*	Lipase production Superoxide dismutase production	
	Geobacillus thermoleovorans	Laccase production	
	Alicyclobacillus sp. strain CC2.	Taq polymerase production	
	Geobacillus thermocatenulatus	Restriction endonucleases (MspNI and MspNII) production	
	Thermus aquaticus	Cellulose production	
	Meiothermus ruber	Xylanases production	
	Fervidobacterium nodosum Rt17-B1		
	Thermobacillus xylanolyticus		
Halophiles	*Halobacterium salinarum*	Holography,	Charlesworth and Burns (2015); Asker and Ohta (2018); Ghanmi et al. (2016); Charlesworth and Burns (2015)
	Haloferax	artificial retinas, photochromic dyes, spatial light	
	Alexandrines	modulators, and the renewal of biochemical	
	Haloterrigena thermotolerans SS1R12,	energy	
	and *Halorubrum chaoviator* SS1R17	Canthaxanthin used as a food dye, a feed additive	
	Naloterrigena hispanica and	and cosmetic industry	
	Natronococcus occultus	Antimicrobial peptides production	
		Diketopiperazines having blood-clotting functions,	
		antimicrobial, antifungal, antiviral, and antitumor properties	
Psychrophiles	*Pseudoalteromonas haloplanktis*	Bioremediation of aromatic compounds	Parrilli et al. (2010); Dornez et al., (2011); Margesin et al. (2018); Zeng et al. (2004)
	Pseudoalteromonas haloplanktis TAH3a	Xylanase production	
	Pedobacter cryoconitis	Catalase, Protease, amylase, oxidase production	
	Flavobacterium psychrophilum	Metalloprotease production	
	Psychrobacter okhotskensis	Lipases production	
Radiation resistant	*Deinococcus radiodurans*	Bioremediation of radioactive waste	Misra et al. (2014)

microorganisms in extreme environments (de Oliveira et al., 2015; Perez-Rodriguez et al., 2015; Fazli et al., 2014; Riley et al., 2008; Johnson et al., 2005). Moreover, most bacteria rely on quorum sensing (QS) for coordinated gene expression at high cell densities which is based on the production and detection of signaling molecules called autoinducers (Miller and Bassler, 2001). The significance of QS in mesophilic pathogens is well studied where it regulates various processes such as bioluminescence, virulence, motility, cell competency and biofilm formation (Papenfort and Bassler, 2016; Montgomery et al., 2013). However the world is merely at the initial stage of exploring and analyzing QS system(s) in extremophiles.

This review aims at assessing the occurrence, type and role of QS in extremophiles and how they utilize this communication for their development and survival in extreme conditions. Though QS can only be speculated in certain cases but strong bioinformatic analysis suggests their established proven role in future.

2. Quorum sensing systems prevalent in mesophiles: a quick look

2.1. AI-1 based system

QS signaling molecules are of three major types. Autoinducer-1(AI-1) system uses acylated homoserine lactones (AHLs) as signals having *N*-acylated homoserine-lactone ring consisting of 4–18 carbon acyl chain (Galloway et al., 2011). It was first discovered in *Vibrio fischeri*, where it controls bioluminescence. This system is prevalent in Gram-negative bacteria; but has been identified in cyanobacteria (Sharif et al., 2008) and archaea (Zhang et al., 2012) as well. AHLs are produced by LuxI (AI-1 synthase) or its homologues and the receptor for these signals is LuxR (AI-1 receptor) or its homologues (cytoplasmic transcription factors) (Fig. 1). The lactone moiety is acquired from S-adenosylmethionine (SAM) while the acyl chains are obtained most commonly from the biosynthesis of fatty acids (Papenfort and Bassler, 2016). However, few exceptions are there like in the photosynthetic bacterium *Rhodopseudomonas palustris,* *p*-coumaroyl-homoserine lactone synthase (RpaI) synthesizes *p*-coumaroyl-homoserine lactone where the acyl group is drawn from plant derived *p*-coumarate (Schuster et al., 2013). Similarly, certain uncommon autoinducers are produced by *Bradyrhizobium* spp. and *Aeromonas* spp. which synthesize isovaleryl-HSL (Lindemann et al., 2011) and cinnamoyl-HSL (Ahlgren et al., 2011) respectively. All these molecules are species specific and are known to regulate various phenotypic characters such as bioluminescence in *V. harveyi* and *V. fischeri* (Sitnikov et al., 1995; Stevens et al., 1994), swarming motility in *Serratia marcescens* (Soo et al., 2008), biofilm formation in *Acinetobacter baumannii* (Bhargava et al., 2012, 2010), virulence and biofilm formation in *P. aeruginosa* (Rasamiravaka et al., 2015), swimming motility and virulence in *Acidovorax avenae* (Fan et al., 2011).

2.2. Peptide based system

Second type of signaling molecules are autoinducing peptides (AIPs), used by Gram-positive bacteria to communicate (LaSarre and Federle, 2013). These peptides are linear or cyclic in nature and are 5–34 amino acids long. These autoinducing peptides are synthesized as inactive pro-peptides and are exported by ABC transporters or general secretion mechanisms. During export, pro-peptides are processed to generate active peptides. As peptides are impermeable to biological membranes, they utilize specialized transport systems for import. Peptide based signals can be transported either by the typical two-component system comprising membrane-bound histidine kinase receptor and a cognate cytoplasmic response regulator (Ng and Bassler, 2009) or by peptide transporter complexes (Shanker and Federle, 2017). In the two component system, binding of peptide to histidine kinase receptor prompts its autophosphorylation activity, which causes ATP-driven phosphorylation of a cytoplasmic conserved histidine residue. This phosphate group is further transferred to the conserved aspartate residue of the cognate response regulator that now becomes active DNA-binding transcription factors (Fig. 2). Peptide signals are activated by cleavage. Alternatively, AIPs are transported back into the

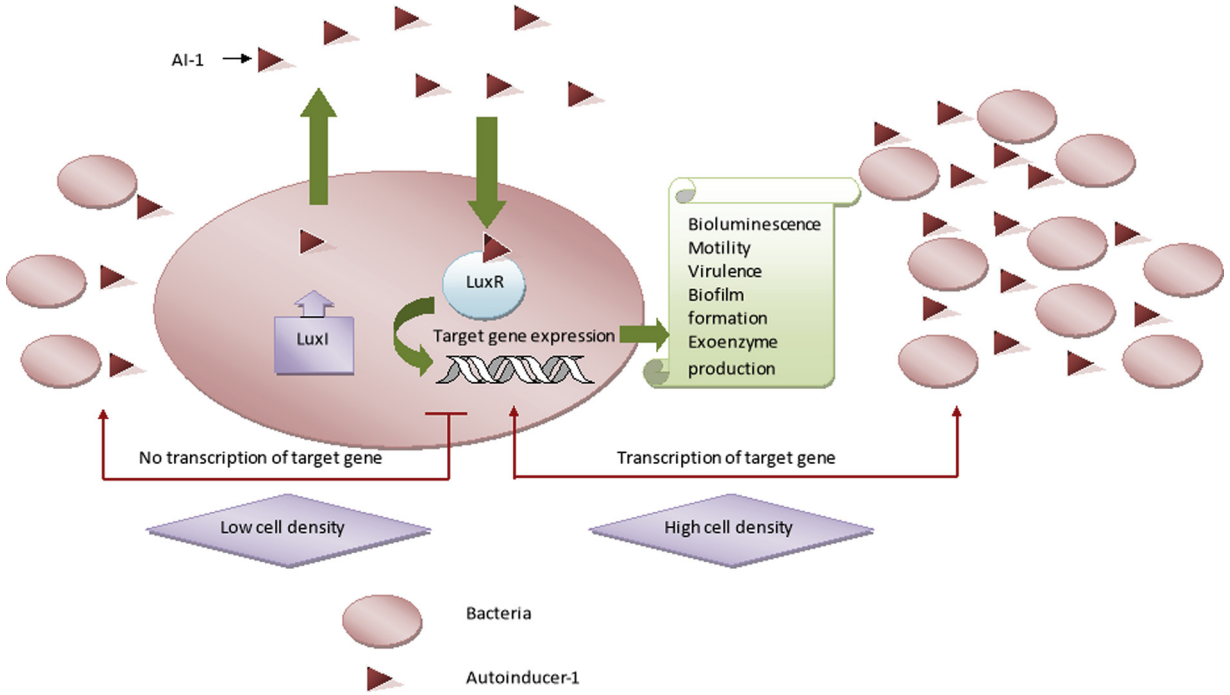

Fig. 1. Autoinducer-1 type quorum sensing. LuxI (AI-1 synthase) produces AHLs. At high cell density bacteria recognize the nearby AHLs secreted by neighbor bacteria. LuxR (transcriptional activator) receives the cognate AHLs resulting in gene expression of appropriate phenotype.

cell after sensing the threshold of AIPs in its environment detected by cytoplasmic transcription factors. This second peptide based system utilizes extracellular proteases for the secretion and maturation of propeptides. Like acylated homoserine lactones, AIPs are also species specific and regulate various important functions in bacteria such as virulence in *Staphylococcus aureus* (AIP: AIP 2) (Kim et al., 2017), competence development in *Bacillus subtilis* (AIP: ComX) (Schultz et al., 2009) and *Streptococcus pneumoniae* (AIP: CSP, Competence Stimulating Peptide) (Johnsborg and Havarstein, 2009), bacteriocin-inducing peptide IP-673 in *Lactobacillus sake* LTH673 (AIP: IP-673) (La Rosa et al., 2015) and programmed cell death in *E. coli* (AIP: EDF, Extracellular Death Factor) (Yan et al., 2015).

2.3. AI-2 based system

The third major signaling system used by bacteria is based on autoinducer-2 (AI-2), a furanosyl borate diester. This mode of QS is shared by both Gram-positive and Gram-negative bacteria (Chen et al., 2002). This molecule is produced by LuxS enzyme by recycling of S-adenosyl-homocysteine (SAH) to S-ribosyl-homocysteine (SRH) which further produces (S)-4, 5-dihydroxy-2, 3-pentanedione (DPD), the AI-2 precursor. LuxS is not only involved in QS but it has important role in

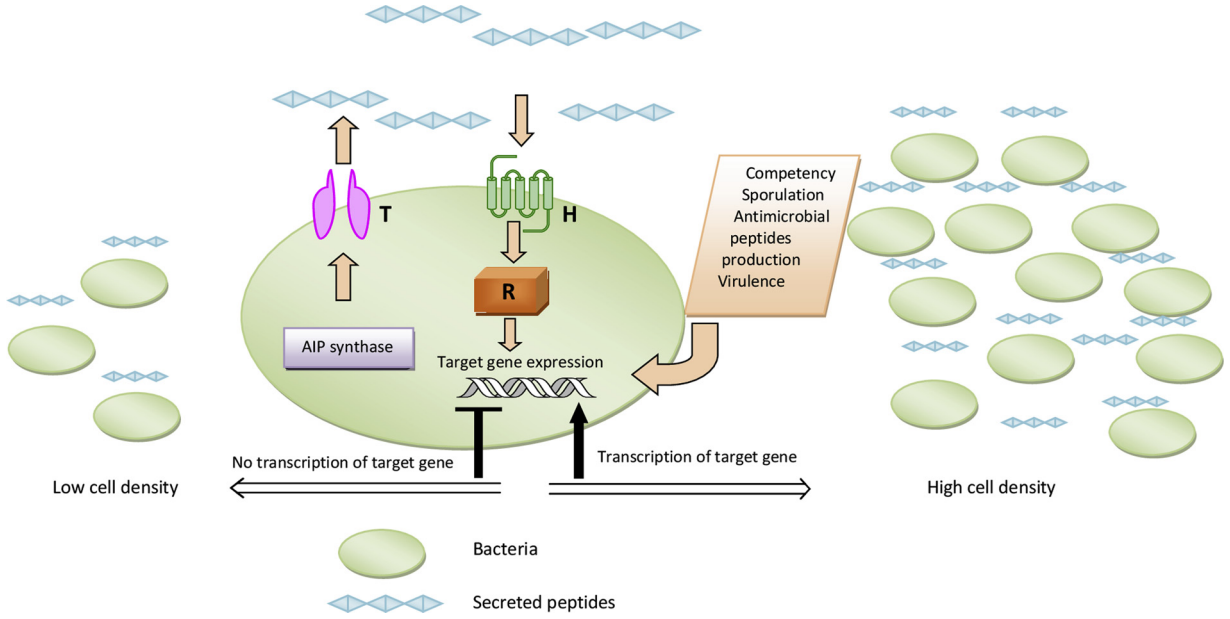

Fig. 2. Peptide based quorum sensing. AIP synthase produces autoinducing peptides that are release through the transporter **T** into the environment. At high cell density secreted peptides are recognized by two component sensor kinases **H** and this interaction causes phosphorylation of cognate response regulator **R,** thus activating it. This results in gene expression of appropriate phenotype.

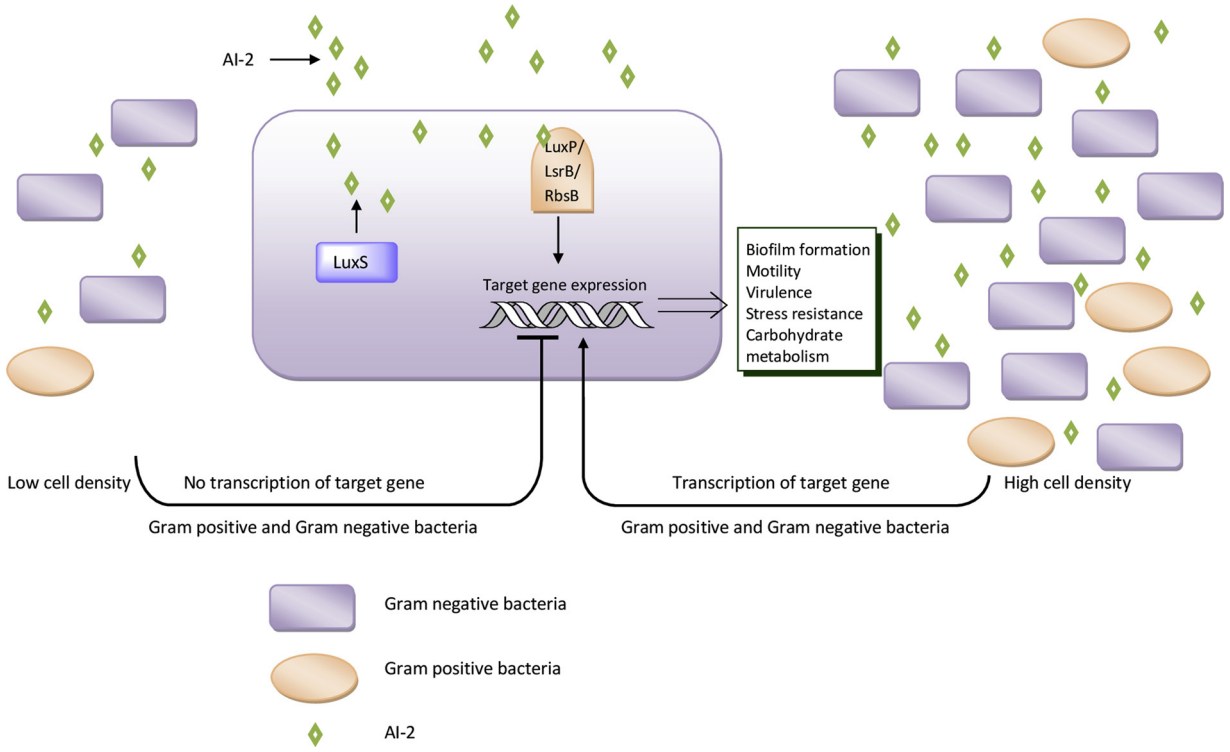

Fig. 3. Autoinducer-2 type quorum sensing. LuxS (AI-2 synthase) produces furanosyl borate diester. At high cell density bacteria recognizes the nearby AI-2 signals secreted by neighbor bacteria. LuxP or LsrB or RbsB (transcriptional activator) receives the cognate AI-2 resulting in gene expression of appropriate phenotype.

activated methyl cycle for the generation of S-adenosyl-L-methionine (SAM) that acts as major methyl group donor in cell. Thus, the presence of *luxS* in bacteria without stimulation of bioluminescence in *V. harveyi* BB170 (autoinducer-2 assay) suggests its non-QS role. Different bacterial species recognize different AI-2 DPD stereoisomer. Cyclization of DPD generates two major stereoisomers, S-DHMF (2S, 4S)-dihydroxy-2-methyldihydro-3-furanone) and R-DHMF (2R, 4S)-dihydroxy-2methyl-dihydro-3-furanone), their hydration generates others DPDs that are interconvertable and exist in equilibrium with each other in aqueous solutions thus stimulating interspecies communication. The known receptors for autoinducer-2 are: LuxP (Chen et al., 2002), LsrB (Miller et al., 2004), RbsB (James et al., 2006) that are all periplasmic proteins (Fig. 3). AI-2 is extremely important among different bacterial species as it works in both interspecies as well as in intraspecies communication. Some examples of autoinducer-2 mediated regulation are biofilm formation by *Bifidobacterium longum* (Sun et al., 2014), *Staphylococcus epidermidis* RP62A (Xue et al., 2015), virulence in *E. coli* 0152:H7 (Kim et al., 2009), motility in *Campylobacter jejuni* subsp. jejuni (Plummer et al., 2012), biofilm formation and oxidative stress in *Deinococcus radiodurans* (Lin et al., 2016).

2.4. Other quorum sensing systems

Another less common QS system is AI-3, a product of an amination of aromatic compound whose structure is unknown and is found in enteric bacteria Enterohemorrhagic *Escherichia coli* (EHEC). Mammalian hormones (epinephrine and norepinephrine) cause similar responses as AI-3 by binding to AI-3 receptor (Walters and Sperandio, 2006). Thus AI-3 is involved in inter-kingdom communication. luxS gene influences the synthesis of autoinducer-3 (AI-3), which further turns on the expression of virulence genes to colonize the large intestine (Walters and Sperandio, 2006). However it cannot induce bioluminescence in *V. harveyi*. AI-3 is chemically distinct from AI-2 as it is not furanosyl-borate diester. Moreover unlike AI-2, AI-3 can bind C-18 columns and is eluted with methanol (Sperandio et al., 2003).

Indole is another QS compound gaining interest as an intercellular signaling molecule playing role in biofilm formation, virulence, antibiotic resistance and formation of persister cells (Kim and Wood, 2010). Indole is produced from tryptophan in enteric bacteria by tryptophanase (Yanofsky et al., 1991). Supplementation of culture medium with indole results in the formation of quiescent cells in *E.coli* (Chen et al., 2015) and its accumulation in aged cultures promotes cell death (Saint-Ruf et al., 2014). Indole producing resistant bacteria defend non-resistant neighbor cells against antibiotic stress (Lee and Lee, 2010). Some other QS molecules are Diffusible Signal Factor (DSF), reported as a QS factor in *Xanthomonas campestris* (Barber et al., 1997) and *Stenotrophomonas maltophilia* (Ryan et al., 2008) and responsible for virulence and antibiotic resistance in these bacteria; DiKetoPiperazine (DKP) allows the coexistence of *Cronobacter sakazakii* and *Bacillus cereus* leading to contamination of food (Bofinger et al., 2017); *Pseudomonas* Quinolone Signal (PQS) plays a key role in regulating virulence in nosocomial pathogen *P. aeruginosa* (Reen et al., 2011); 2-Amino Acetophenone (2-AA) promotes virulence in *P. aeruginosa* (Kesarwani et al., 2011); Integrated Quorum Sensing System (IQS) is another one prevalent in *P. aeruginosa* which under phosphate depletion conditions controls the role of central las system (Lee et al., 2013); Competence Stimulating Peptide (CSP) controls competence of genetic transformation in *Streptococcus pneumoniae* (Oggioni et al., 2004); Cholera Autoinducer-1 (CAI-1) has role in production of virulence factors in *Vibrio cholerae* (Higgins et al., 2007); γ-butyrolactone regulates differentiation and antibiotic production in *Streptomyces* (Takano, 2006), Dialkylresorcinols (DARs) constitute an important virulence regulating QS system in Photorhabdus asymbiotica, sensed by the LuxR homolog PauR (Brameyer and Heermann, 2015) and Photopyrone autoinducer (PPY) QS system found in insect pathogen *Photorhabdus luminescens*, might be involved in virulence (Brachmann et al., 2013).

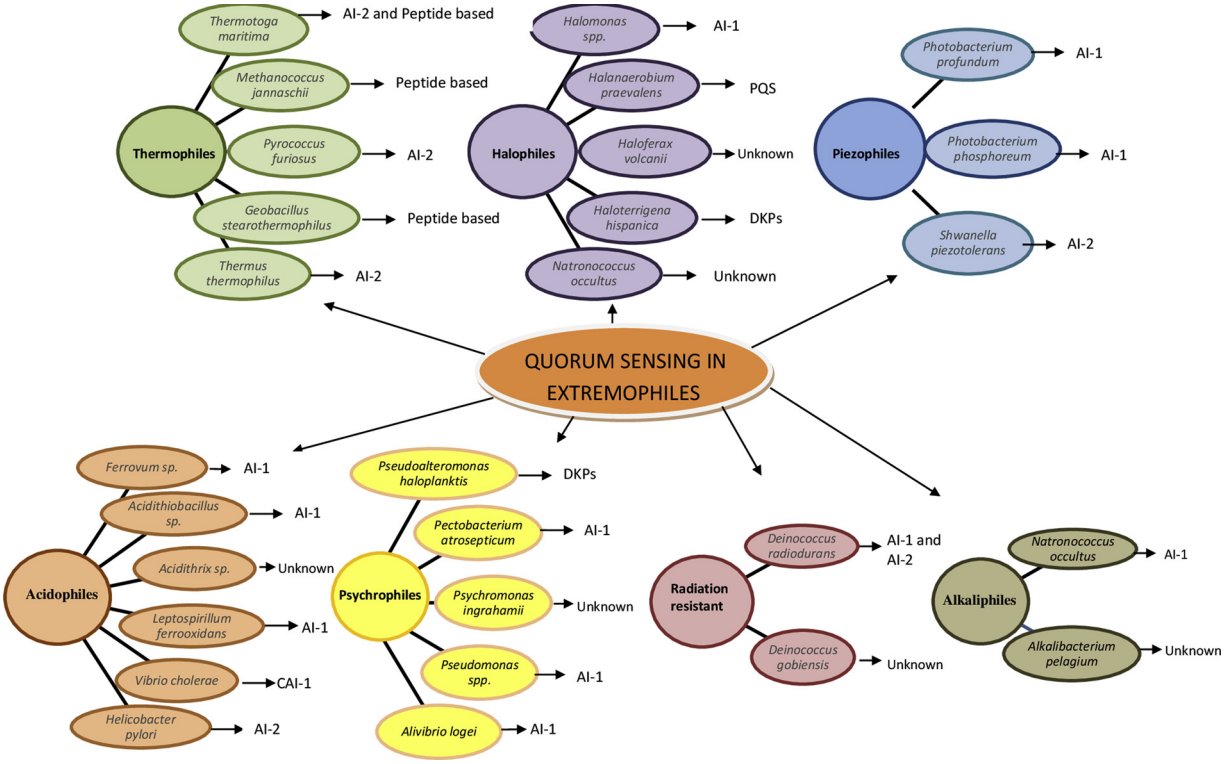

Fig. 4. Members from each extremophilic class showing evidences of quorum sensing systems.

3. Quorum sensing systems prevalent in extremophiles (Fig. 4)

3.1. Bacteria thriving at extreme temperatures

3.1.1. Thermophiles

All the three major QS systems found in mesophiles had been explored in thermophilic bacteria (Table 2,). It was observed that hydrogen produced by certain fermentative H_2 producers inhibits their own growth after sometime when these microorganisms are present in monocultures; however when they are present with methanogenic H_2 acceptors in syntrophic relationship, inhibitory hydrogen is utilized as the energy source for formation of methane. This association was observed between *Thermotoga maritima* which produces H_2 as autoinhibitory product and hydrogenotrophic methanogen *Methanococcus jannaschii*. Co-culturing *T. maritima* with *M. jannaschii* facilitated the formation of extracellular polymeric substances (EPS) in *T. maritima* during mid log phase that led to the formation of cellular aggregates and speculatively promoted the interspecies H_2 transfer. Transcriptional analysis of *T. maritima* in co-culture revealed that the gene 'TM0504' (predicted signal peptide) encoding a 43 amino acid polypeptide was up-regulated. This gene is in proximity of genes coding for permeases and ATP binding subunits (including oligopeptide ABC transporter), and these may function in the export of small peptide derived from 'TM0504'. Moreover the cleavage site of active autoinducing peptide in *S. pneumonia* and lactic acid bacteria is very similar to the GG motif of 'TM0504' (Havarstein et al., 1995). This was further proved by adding the truncated version of polypeptide from 'TM0504' to pure culture of *T. maritima* that resulted in the production of EPS within 30 min which otherwise is not visible at this point without peptide addition. This observation suggests the role of peptide based QS as the mode of interaction (Johnson et al., 2005).

Further exploration in *T. maritima* revealed the presence of AI-2 type QS. Nichols et al., (2009) demonstrated that two hyperthermophiles, *T. maritima* and *Pyrococcus furiosus,* produce AI-2 signal despite lacking the autoinducer-2 synthase, LuxS. However, both these organisms contain SAH hydrolase, another enzyme in the pathway of activated methyl cycle which catalyzes the cleavage of SAH to adenosine and homocysteine. Adenosine produced is converted to AI-2 signal as determined by *Vibrio harveyi* reporter assay. It was speculated that the AI-2 formed here might be the result of temperature dependent rearrangement of phosphorylated ribose by the action of enzyme nucleoside phosphorylase, producing ribose-1-phosphate that is converted to ribose-5-phospate by phosphosugar mutase, which would then spontaneously convert to DPD in the presence of heat. This was tested by GC–MS analysis using nucleoside phosphorylase and phosphosugar mutase of *T. maritima* that showed a peak with the similar fragmentation pattern at the same place as was observed in case of AI-2 synthesized from purified *E. coli* LuxS. Further, it was noticed that the dose response used in *V. harveyi* AI-2 assay was consistent with that of methy-3(2 H)-furanone (MHF). These results lead to the possibility that MHF is the furanone formed here. Hauck et al. (2003) suggested that MHF formed from "D-ribulose- 5- phosphate" gives rise to DPD. In this way AI-2 could be formed in *luxS*-independent manner which has the capability to stimulate bioluminescence in *V. harveyi* AI-2 assay. No phenotypic change was observed which suggested that the adenosine from SAH is involved in the production of AI-2 without the involvement of appropriate AI-2 type QS genes.

Another thermophile, *Geobacillus stearothermophilus* T-6, produced an extracellular xylanase (Xyn10 A) that formed xylo-oligosaccharides from xylan. Earlier studies by Shulami et al. (2014) suggested that the expression of *xynA* in strain T-6 occurs during stationary phase. However, higher expression was observed when growth was carried out in well aerated fermenter that allowed maintenance of logrithimic phase for more generations. The specific activity of Xyn10 A increased over 50-fold during early exponential growth, suggesting cell density dependent regulation. In order to confirm this, the high cell density *xynA* expressing culture was diluted. This resulted in decreased xylanase activity followed by increase when growth of culture was continued. Further, expression of *xynA* was observed at different cell densities which showed that the increase in expression is correlated with the increase in cell density. Quantitative measurements of *xynA*-mRNA using qRT-PCR and RNase protection assays indicated that this cell

Table 2
Prevalence of quorum sensing systems in extremophiles and their role in extreme environment.

Extremophilic class	Member	QS systems	Genes involved	Signaling molecule (Detected or predicted)	Expected role of QS	Reference
Thermophiles	*Thermotoga maritima*	Peptide based, AI-2	Unknown	TM0504 (Predicted)	EPS formation	Nichols et al. (2009); Johnson et al. (2005)
	Pyrococcus furiosus	AI-2	Unknown	AI-2 (Detected)	Unknown	Nichols et al. (2009)
	Geobacillus stearothermophilus T-6	Peptide based	Unknown	XDF (Predicted)	Enhances xylanase production	Shulami et al. (2014)
	Truepera radiovictrix DSM 17,093	AI-2	*luxS*	AI-2(Predicted)	Unknown	Rao et al. (2016)
	Thermus thermophilus HB27	AI-2	*luxS*	AI-2(Predicted)	Biofilm formation	Rao et al., 2016
	Oceanithermus profundus DSM 14977	AI-2	*luxS*	AI-2(Predicted)	Unknown	Rao et al. (2016)
	Meiothermus silvanus DSM 9946	AI-2	*luxS*	AI-2(Predicted)	Unknown	Rao et al. (2016)
	Caminibacter mediatlanticus	AI-2	*IuxS*	AI-2(Predicted)	Biofilm formation	Perez-Rodriguez et al. (2015)
Psychrophiles	*Pseudoalteromonas haloplanktis* TAC125	DKPs	*PSHAa*0159	DKPs(Predicted)	Free radical scavenging	Mitova et al. (2005)
	Pectobacterium atrosepticum	AI-1	*expIR*	3-oxo-C8-HSL, C8-HSL, 3-oxo-C6-HSL, 3-oxo-C10-HSL (Detected)	Exoenzyme synthesis	Latour et al. (2007)
	Psychromonas ingrahamii	Unknown	Ortholog of *hapR*	Unknown	Lowers the freezing point, biofilm formation	Riley et al. (2008)
	Pseudomonas fluorescens	AI-1	*mupI/mupR*	C4-HSL and 3OC8-HSL, N-(3-oxodecanoyl)homoserine lactone (Detected)	Enhances production of extracellular proteases and lipases, mupirocin biosynthesis	de Oliveira et al. (2015); Hothersall et al. (2011)
	Aliivibrio logei	AI-1	*luxIR*	AHLs mostly 3-oxo-C6-HSL (Detected)	Bioluminescence	Konopleva et al. (2016)
	Pseudomonas mandelii 6A1	AI-1	*algZR*	AHLs(Predicted)	Alginate production	Vasquez-Ponce et al. (2017)
	Pseudomonas simiae RGCB 73	AI-1	*luxIR*	AHLs(Detected)	Cold adaptation	Dharmaprakash et al. (2016)
	Pseudomonas brenneri RGCB 108	AI-1	*luxIR*	AHLs(Detected)	Cold adaptation	Dharmaprakash et al. (2016)
Radiation resistant	*Deinococcus radiodurans*	AI-1 and AI-2	*DqslR, luxS*	AHLs and AI-2 (Detected)	Regulates oxidative stress, expression of stress related genes (superoxide dismutase, catalase, Dps-1, ABC transporters and gamma radiations)	Li et al. (2017); Lin et al. (2016)
	Deinococcus gobiensis	Unknown	Homologue of *gidA* gene	Unknown	UV irradiation	Yuan et al. (2012)
Piezophiles	*Photobacterium profundum* SS9	AI-1	Putative genes *luxMN* and *ainSR*	Unknown	Unknown	Montgomery et al. (2013)
	Photobacterium phosphoreum ANT-2200	AI-1	*luxIR/ainSR* homologue	AHLs (Predicted)	Bioluminescence	Martini et al. (2013)
	Shewanella piezotolerans WP3	AI-2	*luxS*	AI-2 (Predicted)	Iron homeostasis	Nawaz et al. (2017)
Acidophiles	*Ferrovum spp.*	AI-1	*foye1 /luxR*	AHLs (Predicted)	FOYE-1	Scholtissek et al. (2017)
	Acidithiobacillus ferrooxidans	AI-1	*afeI/R, Act*	AHLs(Detected)	Sulfur and iron stress, biofilm formation	Mamani et al. (2016), Rivas et al. (2007, 2005)
	Leptospirillum ferrooxidans	AI-1	putative *mqsR /mqsA*	unknown	Biofilm formation	Moreno-Paz et al. (2010)
	Acidiphilum strain C61	Unknown	Unknown	2-phenethyamine (PEA) (Predicted)	Formation of iron snow, cell aggregation	Mori et al. (2017)
	Acidithrix strain C25	Unknown	Unknown	2-phenethyamine (PEA) (Predicted)	Formation of iron snow, cell aggregation	Mori et al. (2017)
	Vibrio cholerae	CAI-1	*hapR, cqsA /cqsR*	(S)-3-hydroxytridecan-4-one (Predicted)	Virulence and biofilm formation	March and Bently (2004); Hammer and Bassler (2003)
	Helicobacter pylori	AI-2	*luxS*	AI-2 (Detected)	Flagella gene regulation	Rader et al. (2007)
Alkaliphiles	*Natronococcus occultus*	AI-1	Unknown	AHLs like molecules (Detected)	Enhancement of protease activity	Paggi et al. (2003)
	Agromyces aurantiacus	Unknown	Unknown	Unknown	Copper biobleaching	Ramanathan and Ting, (2015)

(*continued on next page*)

Table 2 (*continued*)

Extremophilic class	Member	QS systems	Genes involved	Signaling molecule (Detected or predicted)	Expected role of QS	Reference
Halophiles	*Halanaerobium praevalens*	PQS and 4-hydroxy-1-methyl-2-quinolone	*hmqF*	PQS and 4-hydroxy-1-methyl-2-quinolone (Detected)	Biofilm formation	Monzon et al. (2016)
	Halomonas anticariensis FP35T	AI-1	*hanR/hanI*	C8-HL, C6-HL, 3-oxo-C6-HL, C4-HL (Detected)	Biosynthesis of exopolysaccharides	Tahrioui et al. (2013), 2011
	Halomonas maura	Unknown	*luxI*	AHLs (Detected)	Biosynthesis of exopolysaccharides	Tahrioui et al. (2013); Llamas et al. (2006)
	Halobacillus halophilus	AI-2	*luxS*	AI-2 (Predicted)	Motility	Sewald et al. (2007)
	Haloferax volcanii	Unknown	*fliI*	C_4 and C_6 acyl homoserine lactone (Detected)	Competence, Persister formation	Megaw and Gilmore (2017)
	Haloterrigena hispanica	DKPs	Putative *luxR*	DKPs (Predicted)	Not known	Tommonaro et al. (2012)
	Natronococcus occultus	Unknown	Unknown	Unknown	Synthesis of extracellular protease	Paggi et al. (2003)

density dependent, QS based regulation was at the transcriptional level. Xylanase density factor (XDF), a small peptide, was suggested as the QS signal (Shulami et al., 2014). Conditioned culture medium was prepared by growing strain T-6 in modified basal salt medium (mBSM) containing 1% xylose to a density of ˜0.8 OD600. The cells were removed and supernatant was filter sterilized, concentrated two-fold and boiled for 10 min. High activity of Xyn10 A was observed when this conditioned medium was added to low cell density cultures suggesting the QS functioning of heat stable XDF. Further, it was found that XDF is protease sensitive and can be absorbed on hydrophobic matrix and eluted with 20–25% acetonitrile using a C18 reverse phase HPLC column (Shulami et al., 2014). These characterstics are similar to those of Gram-positive QS peptide factors (Ibrahim et al., 2007).

Thermophilic origin of *luxS* lineage was observed in epsilonproteobacteria. Mesophilic epsilonproteobacteria are nested within the thermophilic clades and the phylogenetic analysis of LuxS sequence revealed higher amino acid identity to those found in thermophiles. This revealed an evolutionary link between thermophiles and mesophilic pathogens (Perez-Rodriguez et al., 2015). The thermophile *Caminibacter mediatlanticus* and a mesophile *Sulfurovum lithotrophicum* from deep sea hydrothermal vent produced bioluminescence in *V. harveyi* AI-2 assay and indicated that the epsilonproteobacterial lineage of the LuxS enzyme originated in high-temperature geothermal environments (Perez-Rodriguez et al., 2015). *luxS* was found to be involved in the formation of biofilm in deep sea hydrothermal vents. It was suggested that reduced sulfur is not limiting in geothermal environments, thus *de novo* synthesis of methionine is energetically inexpensive. Therefore, the role of LuxS in activated methyl cycle is not very remarkable as in other habitats. The presence of *luxS* in thermophilic bacteria from deep sea hydrothermal vent thus may be involved in AI-2 synthesis rather than methionine recycling.

Moreover, LuxS protein search in non-redundant database suggested its presence in certain members of *Deinococcus-Thermus* phylum (*Thermus thermophilus* HB27, *Truepera radiovictrix* DSM 17,093, *Oceanithermus profundus* DSM 14977, *Meiothermus silvanus* DSM 9946), but its role in these environments as well as experimental validation remain to be understood. *T. radiovictrix* was selected as the representative member of the phylum for structure analysis which suggested that N-terminal region of the protein was different from rest of the LuxS sequences from mesophilic representatives (Rao et al., 2016). Further work is required to validate the presence and role of LuxS in these thermophiles.

In an extensive study in our lab, proteomes of 106 thermophilic eubacteria and 21 thermophilic archaea were searched for the presence of QS systems (Kaur et al., 2018). Bioinformatic analysis revealed the presence of complete AI-2 system in 17 thermophilic bacteria belonging to phyla Deinococcus- Thermus and Firmicutes while 18 were having only LuxS and 16 were having only LsrB and/or RbsB. None of the archaea was found to have any existing QS system. But the possibility of novel, unknown mechanisms of communication cannot be ruled out.

3.1.2. Psychrophiles

A considerable fraction of earth is covered by sea that forms shelter for microorganisms which can survive at temperature below 15 °C. Little is known about the survival strategies and communication in these cold adaptive microbes (Table 2).

DiKetoPiperazines (DKP) are considered QS molecules that can activate LuxR utilizing quorum-sensing systems. Antarctic psychrophile *Pseudoalteromonas haloplanktis* TAC125 produced a novel DKP, cyclo-(D-pipecolinyl- L-isoleucine) and 7 other known DKPs (Mitova et al., 2005). It was reported that microbial DKPs are either the *de novo* synthesized compounds or the catabolic products of constituents of nutrient rich medium. Cyclo-(L-propyl- L-tyrosine), identified in this work, was shown previously as QS molecule (Degrassi et al., 2002), but it was also shown that the concentration of this DKP was same in both sterile medium as well as in cell free culture supernatant which suggests that it

is the component of medium used. It was presumed that the presence of DKP (cyclo-(L-propyl- L-tyrosine) in medium was not providing any wrong information regarding the cell density as the organism grew appropriately in LB medium. However, this DKP contained phenyl group and showed activity in free radical scavenging assay, so it may have antioxidant properties but requires experimental validation (Mitova et al., 2005). The exact role in QS was not discussed in this report. Other QS systems were also searched in this bacterium *viz.* AI-1, AI-2, quinolones, cyclicdipeptide and indole, but none was found. However, PSHAa0159 gene was detected which codes for putative aconitate hydratase that utilizes aconitate as iron sulfur cluster dependent signal during stationary phase (Médigue et al., 2005; Kiley and Beinert, 2003).

In general, psychrophiles are considered non-pathogenic but some are involved in causing disease in plants. *Pectobacterium atrosepticum* is a psychrotroph that causes soft rot in *Solanum tuberosum* in low temperature regions where potatoes are grown. As the thermoregulation of bacterial multiplication differs from that of exoenzyme production, it was reported that the thermoregulation of AI-1 type QS triggers exoenzyme synthesis (Latour et al., 2007).

QS also plays an important role in the survival of psychrophiles at low temperature. Cyclic di-guanylate systems are known to regulate genes for motility, biofilm formation and adhesion factors. Presence of regulators of cyclic diGMP signaling system in *Psychromonas ingrahamii* suggested that it is involved in the formation of an extracellular polysaccharide that may help lower the freezing point in surrounding area of the cell (Riley et al., 2008). Moreover, an ortholog of biofilm controlling regulator, HapR (in *V. cholerae*) is present. HapR (a homolog of LuxR in *V. cholerae*) is the master high cell density regulator that controls the genes for quorum sensing dependent biofilm formation and virulence. Detection of CAI-1 (S)-3-hyroxytridecan-4-one) and AI-2 (4, 5-dihydroxy-2, 3-pentanedione) at high cell density is correlated with the production of HapR (Papenfort et al., 2017). Papenfort et al., (2017) examined the culture fluids from a *V. cholerae* Δ*hapR* mutant that was found to be completely deficient in the production of CAI-1 and AI-2, thus suggesting the importance of *hapR* in QS. Since only *hapR* was found in *Psychromonas* and no autoinducer producer, it was concluded that the QS mechanism is unknown. Thus it is presumed that *P. ingrahamii* may form biofilm to combat cold conditions but the type of QS system was not known.

QS regulated factors may cause spoilage of milk and dairy products as AHLs are present in milk deteriorating psychrotroph *Pseudomonas* spp. High cell density of *P. fluorescens* may enhance the production of extracellular proteases and lipases that results in degradation of proteins and fats in milk products. However the role of QS has to be further validated for these preliminary findings (de Oliveira et al., 2015).

Bioluminescence in the psychrophile *Aliivibrio logei* is regulated by AI-1 type QS containing two copies of *luxR* (*luxR1* and *luxR2*). Autoinducer concentration required to activate LuxR1 was 100 times more than for the activation of LuxR2. LuxR2 was a substrate for Lon protease and required GroEL/ES chaperonin for its folding while it was not required by LuxR1 nor was it degraded by Lon. Further, combination of *luxR1* and *luxR2* products could activate pr-promoters of *A. logei lux* operon in *E. coli* without the requirement of GroEL/ES and Lon. This combination allows LuxR2 activation at high cell concentration even in the absence of GroEL/ES (Konopleva et al., 2016; Khrulnova et al., 2016).

QS mechanism utilized by certain psychrophiles can be exploited for commercially valuable products e.g. biofilm formation by *Pseudomonas mandelii* was mediated by alginate overproduction at low temperature. QS is known to mediate alginate synthesis in pseudomonads (Fazli et al., 2014) by expressing genes *algU* and *mucA*. AlgU (transcriptional activator of the alginate operon) expression was controlled by MucA which binds to AlgU to stop the alginate operon transcription. During biofilm formation by *P. mandelii*, expression of *algU* did not change at different temperatures; while the downregulation of *mucA* was reported at lower temperatures (4 and 15 °C) which resulted in increased alginate production at lower temperatures. Biofilm formation proves to be a useful strategy for survival of this Antarctic isolate at low temperatures (Vasquez-Ponce et al., 2017). However exact QS mechanism has not been explained.

Recently, genome sequences of two psychrophiles, *Pseudomonas simiae* RGCB 73 and *Pseudomonas brenneri* RGCB 108, from the Arctic were found to have more than one *luxIR* type genes producing acyl homoserine lactone molecule, thus speculating the presence of AI-1 type QS. The presence of AHL was detected by AHL reporter strains *Chromobacterium violaceum* CV026, *Escherichia coli* pJBA132, and *Pseudomonas putida* F117 pKR-C12. This information will enable to understand the survival strategy used by these psychrophiles at low temperature and the function of QS (Dharmaprakash et al., 2016).

3.2. Bacteria thriving at extreme pH

3.2.1. Acidophiles

QS mechanisms have been detected in some acidophiles (Table 2), for example *Ferrovum*, where ene-reductases (ERs), the flavin-dependent oxidoreductases, might have a role in QS mediated oxidative stress response (Toogood et al., 2010). *Ferrovum* (iron-oxidizing betaproteobacterium) was found to have a thermostable (60 °C) and pH stable ER (*F*OYE-1) with close phylogenetic relationship to that of mesophilic *Dr*OYE, *Rm*OYE, and OYE*Ro2* (Scholtissek et al., 2017). *foye-1* is present immediately downstream of *luxR* but *luxI* is lacking. Thus, *F*OYE-1 is speculated to be a part of QS mechanism by substituting LuxI (that provides the autoinducer for LuxR) with regard to its genomic neighborhood and substrate specificity. These homoserine lactones are supposed to be produced in response to transhydrogenation of the respective furanones (Scholtissek et al., 2017).

Acidithiobacillus ferrooxidans, one of the microorganisms important in acid mine draining and industrial recovery of copper and gold, has two autoinducer-1 type QS systems which respond to different environments. First one (LuxIR) is upregulated when bacteria are grown in sulfur containing medium (Rivas et al., 2005) while the second one having 'Act' as AHL synthase is upregulated when grown in iron containing medium. It has been presumed that these QS mechanisms regulate biofilm formation (Rivas et al., 2007). Further, transcriptome analysis of QS regulon in *A. ferrooxidans* revealed that the AHL synthase, *afeI,* is regulated by QS while transcriptional regulator *afeR* is not. Moreover it was observed that 4.5% genome of *A. ferrooxidans* ATCC 23270 T represents QS network, of which 42.5% was part of biofilm formation (Mamani et al., 2016). Thus it may be presumed that QS regulates biofilm formation in this bacterium.

QS systems were investigated in acidophile *Leptospirillum ferrooxidans* that is used in biomining. Genes *ygiU* and *ygiT* (homologues of *mqsR* and *mqsA* of *E.coli*) are upregulated during biofilm formation. It is known that MqsR (motility and QS regulator) is linked to biofilm formation and persister cell development (Kim and Wood, 2010; Gonzalez Barrios et al., 2006). Moreover it was observed that deletion of *mqsR* results in reduction of biofilm (Moreno-Paz et al., 2010). However no QS molecule was detected.

Mori et al. (2017) investigated the role of QS in two co-occurring bacteria, *Acidithrix str.* and *Acidiphilum str.* from iron snow (iron rich aggregates). Presence of cell free supernatant of *Acidiphilum* enhanced the amount of nucleic acid and Fe (II) oxidation by *Acidithrix*. *Acidiphilum* possesses polar flagella which prevent cell aggregation. However, addition of cell free supernatant of *Acidithrix* resulted in formation of macroscopic aggregates in *Acidiphilum* (Mori et al., 2017). This might be the result of chemical communication between these bacteria which needs further investigation of QS molecules.

Pathogenic bacteria also rely on the process of QS for pathogenesis inside human body extreme environments such as acidic stomach. *V. cholerae* survives acidic environment by the development of thick, glutinous biofilm. This is achieved by QS regulator, HapR, that inhibits

the expression of *Vibrio* polysaccharide (VPS) operon. After the bacteria come out of acidic environment of stomach, biofilm protection is not required; therefore HapR production restarts resulting in change of biofilm conformation (March and Bentley, 2004). *H. pylori* is another bacterium known to survive the acidic environment of stomach. It has AI-2 type QS responsible for flagellar gene regulation and has role in pathogenesis (Rader et al., 2007).

3.2.2. Alkaliphiles

Extracellular protease production was reported in the haloalkaliphilic archaeon *Natronococcus occultus* during late exponential and stationary phases of growth. Paggi et al. (2003) proposed that the production may be due to QS at high cell density during the late exponential phase, as when the low cell density culture was suspended in the cell free culture filtrate of late exponential phase culture, the production of extracellular protease shifted to early exponential phase. *Agrobacterium* biosensor strain was used to confirm the presence of AI-1 molecules (N-3-oxo-octanoyl- and N-3- oxodecanoyl-homoserine lactones) in this archaeon. More work is required to establish the exact role of AHLs in this archaeon or whether QS is directly linked with extracellular protease production.

Ramanathan and Ting (2015) reported the presence of QS in pure cultures of four alkaliphilic bacteria *viz. Agromyces aurantiacus*, *Alkalibacterium pelagium*, *Alkalibacterium* sp. and *Bacillus foraminis* which were used for bioleaching of copper. They hypothesized that these alkaliphilic bacteria may utilize QS for synergistic bioleaching.

3.3. Bacteria resistant to DNA damaging agents

3.3.1. Radiation/ oxidative stress resistant bacteria

QS mechanism is well characterized in radiation resistant *Deinococcus radiodurans* (Lin et al., 2016). The reason for this resistance is its remarkable ability to repair DNA damage and the presence of four to ten copies of genome. *D. radiodurans* is one of those bacteria that utilize both AI-1 and AI-2 systems for communication. AI-1 mediated QS plays a vital role during oxidative stress that is controlled by DqsI/DqsR regulatory system. Under non-stress conditions quorum quenchers (QqaR and QqlR) inhibit the DqsI/DqsR regulatory system (Lin et al., 2016). Further, it was found that the levels of AHLs were much less during non-stress conditions indicating their role only during oxidative stress.

Another mechanism controlled by AI-2 is cell death by MazEF, a type II TA (Toxin-antitoxin) system, well known for its involvement in cell death in *E. coli* under stress conditions (amino acid starvation, antibiotics, oxidative stress and high temperature) (Hazan et al., 2004). Similar mechanism was observed in *D. radiodurans* during DNA damage stress in the presence of lethal concentration of mitomycin C to save nutrients by suicide of certain cells enabling the survival of remaining population (Li et al., 2017). In *E.coli*, EDF(Extracellular Death Factor) (QS factor) is required for activation of MazF mediated cell death but not in *D. radiodurans* where AHLs may activate MazEF as AHLs are produced in the presence of lethal levels of oxidative stress (Li et al., 2017; Lin et al., 2016).

Importance of AI-2 system in *D. radiodurans* was investigated by constructing a *luxS* (dr_2387) deletion mutant (Lin et al., 2016). AI-2 regulates the expression of stress related genes coding for superoxide dismutase, catalase, DNA protection during starvation, protein- 1 (Dps-1), ATP-binding cassette (ABC) transporters and resistance to gamma radiations. AI-2 receptor in this bacterium is yet to be found to understand the complete mechanism of QS (Lin et al., 2016).

Deinococcus gobiensis is another radiation resistant bacterium that has mechanism to overcome UV irradiation. Its *gidA* gene encoding *g*lucose-*i*nhibited *c*ell *d*ivision protein A controls the regulation of QS genes in *P. aeroginosa* via RhlR dependent and RhlR independent pathways in a similar manner as QS in soil symbionts. However, the exact function of this gene is yet to be explored (Montgomery et al., 2013).

3.4. Other extremophiles

3.4.1. Piezophiles

Piezophiles/barophiles are the microorganisms capable of surviving high pressure environment such as ocean floor. Sea beneath 1000 m depth is distinguished by a high hydrostatic pressure, predominantly having coldness, darkness and shortage of organic-matter.

Photobacterium profundum is a member of the family Vibrionaceae comprising of the microorganisms (*Vibrio harveyi* and *Aliivibrio fischeri*) in which QS was first explored. Although *Photobacterium profundum* and *Vibrio harveyi* belong to the same family Vibrionaceae, still they have differences in genomes with regard to quorum sensing genes. Comparative genomic studies had been attempted by Rezzonico and Duffy (2008) for searching AI-2 signaling system in *P. profundum* and found that though LuxS homologue is present but no *luxP* (AI-2 receptor) homolog was found there, although *luxP* is prevalent in Vibrionales having AI-2 type of QS and no alternative receptor for AI-2 has been described in bacteria belonging to the Vibrionales. Therefore, *luxS* in *Photobacterium profundum* appears to have only metabolic role, suggesting that *P. profundum* may be using some unknown mechanisms of QS (Montgomery et al., 2013). However it requires experimental validation.

Likewise, the effect of pressure was observed on the growth and bioluminescence of *P. phosphoreum* isolated at the depth of 2200 m and 22 MPa pressure. Higher level of luminescence was observed at high pressure (22 MPa) in comparison to atmospheric pressure (0.1 MPa) (Rezzonico and Duffy, 2008), reason being the formation of aggregates at high pressure that keep the cells in close proximity, and higher cell densities possibly generate a QS response resulting in high bioluminescence as observed in other marine microorganisms such as *V. harveyi* (Martini et al., 2013).

QS mechanism was also reported in *Shewanella piezotolerans* that is able to survive and grow in the pressure range 0.1–50 MPa and is found at the depth of 1914 m. Genomic studies revealed the presence of a large number of small regulatory RNAs, 92% of which allied to the dominant *trans*-encoded RNAs class and remaining were *cis*-regulatory. Most of the *cis*-sRNAs were cold regulated. However, *trans*-regulatory sRNAs are assumed to be part of the mechanisms such as iron homeostasis and QS (Gottesman and Storz, 2011).

3.4.2. Halophiles

Extreme halophiles can survive at salt concentration 3.4–5.1 M. Tahrioui et al. (2013) demonstrated the presence of AI-1 type QS in 43 species of *Halomonadaceae* family using *Chromobacterium violaceum* strain CV026 and *Agrobacterium tumefaciens* NTL4 (pZLR4) dependent assays for detection of AHLs. TLC analysis suggested the presence of C8-HSL (N-octanoyl-homoserine lactone), C6-HSL (N-hexanoyl-L-homoserine lactone) and 3-oxo-C6-HSL (N-(3-oxo-hexanoyl)-L-homoserine lactone). AI-1 synthase gene was also searched using PCR primers specific to active site of *luxI*. 29 species were found to have the sequences similar to *luxI,* however 14 did not contain it. Tahrioui et al. (2013) suggested that the possible reason could be 'primer mismatching' in those 14 species. However, it could be because of the presence of alternative non-homologous enzymes for AHL production in those 14 species.

Similarly, AHLs are also produced by some members of the moderately halophilic genus *Halomonas*, viz. *H. eurihalina*, *H. maura*, *H. ventosae* and *H. anticariensis* (Llamas et al., 2006). The presence of AHLs was confirmed using *Chromobacterium violaceum* strain and *Agrobacterium tumefaciens* based assays. TLC analysis showed the presence of C8-HL, C6-HL, 3-oxo-C6-HL, C4-HL. Also, *H. anticariensis* possessed *luxR/luxI* homologues, *hanI* and *hanR,* and formed biofilms with the help of AHLs produced (Tahrioui et al., 2011). Presence of QS in these halophiles suggests its role in adaptation to a wide range of hypersaline

habitats which further needs to be evaluated.

Another QS mechanism has been reported in halophiles belonging to genus *Halanaerobium* that has great importance in oil and gas industry since it is a common habitant of oil reservoirs and shale formation. It is also present in processed water from hydraulic fracturing (Monzon et al., 2016). Anodic biofilm was formed by *H. praevalens,* found in saline oil and gas reservoirs, in a hypersaline microbial fuel cells (100 g/L NaCl) through QS by incorporation of exogenous QS signals PQS and 4-hydroxy-1-methyl-2-quinolone (found in *P. aeruginosa*) that resulted in increase in biomass and generated power density.

Chloride dependent homologue of LuxS was found in the moderately halophilic bacterium *Halobacillus halophilus* (Sewald et al., 2007). *luxS* transcription was salt dependent with maximal mRNA concentrations at 2.0 M NaCl in the growth medium and motility was chloride dependent. However the role of QS or production of AI-2 was not proved.

Evidences have shown the presence of QS in halophilic archaea such as *Haloferax volcanii, Haloterrigena hispanica* and *Natronococcus occultus. H.volcanii* was isolated from the Dead Sea, the Great Salt Lake, oceans and is naturally competent, which suggests that it may be using QS as a regulatory mechanism for competence. Bioinformatic analysis further showed significant homology with c*omA* of *S. pneumoniae* that also functions for competence. Recently, Megaw and Gilmore (2017) suggested the role of AHL induced QS in *H.volcanii* in response to stress that mediates persister formation. The AHL produced was different from that of other bacterial AHLs. QS molecule, DKP has been reported in an extremely halophilic archaeon, *H. hispanica* that activates the bioreporters of AHL (Tommonaro et al., 2012).

4. Quorum sensing dependent applications of extremophiles

Extremophiles have found their way in industry, biotechnology, biomining, health, production of electricity (Table 1) and are the best alternatives to replace the conventional enzymes used in industries from mesophiles. The efficiency of enzymes produced by mesophiles is usually improved by genetic or chemical modification or by immobilization (Mukhopadhyay and Banerjee, 2015) which makes the process lengthy as well as costly (Coker, 2016). However, extremophiles provide alternative source to be used at extreme temperature, pressure, pH and salinity. The reason for their flexibility in extremes is the presence of stable proteins and cell membranes in thermophiles, flexible cellular and antifreeze proteins in psychrophiles, presence of compatible solutes providing salt-resistance in halophiles and the capability to pump ions to keep internal pH close to neutrality in acidophiles and alkaliphiles. Applications of extremophiles can be further improved by exploration of QS mechanisms involved.

4.1. Quorum sensing as an emerging area of research

4.1.1. Development of quorum quenchers

The problems discussed in the beginning of the review that are associated with thermophilic biofilm formers lead to huge economic loses and severe environmental contamination which demands interest in developing strategies to disrupt QS in these thermophilic bacteria. In the last decade, attempts have been made to find or develop inhibitors which will control the production of autoinducers by inhibiting key enzymes involved in autoinducers biosynthesis *viz*. MTAN (5'-methylthioadenosine/S-adenosylhomo-cysteine nucleosidase), LuxS, LuxI; that will decrease the amount of AI-1 and 2 production (Guo et al., 2013).

4.1.2. Biosensors utilizing quorum sensing systems

QS is attaining importance in the development of whole cell microbial biosensors able to sense pathogenic microbes in the surroundings and diseased host (Choudhary and Schmidt-Dannert, 2010). QS phenomenon can be used to develop anti-cancer therapeutics by supplementation of cancer destructing material in engineered bacteria able to permeate the cancer cells (Choudhary and Schmidt-Dannert, 2010). One such example is the introduction of invasin gene (regulated by the AI-1 system) from *Yersinia pestis* in the genome of *E. coli*. At high concentration of AHLs, expression of invasin gene is induced which further allows *E. coli* to attach and invade cells exhibiting β1-integrin cell surface receptors (Anderson et al., 2006). Another example involves AI-1 signal 3-oxo-C12-HSL produced by *P. aeruginosa* that has the capability to inhibit proliferation and induce apoptosis in breast cancer cell lines (Li et al., 2004). However *P. aeruginosa* cannot be used directly because of its virulence in immune-compromised patients. More such QS molecules can be explored from non-pathogens for host. Extremophiles are usually non-pathogenic and their QS systems can be employed in this area. Further, synthetic homologs of autoinducers can be prepared that can act as anti-QS molecules (Oliver et al., 2009).

4.1.3. Biocontrol strategies utilizing quorum sensing systems

AHLs are essential for the pathogenicity of *E.carotovora* in tobacco plants. Transgenic tobacco plants are capable of producing AHLs thus fooling the bacteria to switching to virulent form at low cell density which makes the bacteria vulnerable to defense mechanisms of tobacco plant. This kind of biocontrol strategy can be employed if the AHLs produced by virulent bacteria are known (Mae et al., 2001). Likewise autoinducer molecules from extremophiles can be used in developing biocontrol strategy by utilizing their autoinducers in transgenic crops which can provide resistance to the crops in similar manner.

4.1.4. Industrial importance of quorum sensing systems from extremophiles

A novel psychrophile, *Pseudomonas mandelii*, was isolated from Antarctica capable of producing alginate, known to have various applications in pharmaceutical, cosmetic, textile and paper industry (Vasquez-Ponce et al., 2017; Muller et al., 2009). It is known that alginate synthesis is regulated by QS in pseudomonads (Hay et al., 2013; Bakkevig et al., 2005). Similarly, ene-reductases from acidophilic iron oxidizing bacterium *Ferrovum sp*. were found to have high stability because of which these are acquiring great importance. This thermophilic-like ene-reductase (FOYE-1) has shown involvement in QS process (Scholtissek et al., 2017). Likewise, the acidophile *A. ferrooxidans,* utilizing QS, is involved in bioleaching, biorecovery of copper and in biogeochemical cycling of iron, sulfur, heavy metals, and nutrients (Rivas et al., 2007). Similarly, 50-fold increase was noticed in extracellular xylanase (Xyn10 A) produced by a thermophile, *G. stearothermophilus* during early exponential growth, which might be because of high cell density (QS) (Shulami et al., 2014). *Halomonas maura,* known to degrade aromatic compounds and produce exoenzymes and exopolysaccharides (EPS's) and carry out denitrification, also uses QS to fulfill these processes (Tahrioui et al., 2013). QS autoinducers in *H. praevalens* enhanced power generation in a hypersaline microbial fuel cell (Tahrioui et al., 2011).

5. Conclusions

Information regarding QS in extremophiles is limited. However, bioinformatic analysis has made it possible to understand the genomes of extremophiles through which the identification of QS systems can be carried out by utilizing known QS genes/proteins as queries. In future, knowledge of QS in extremophiles can be utilized for the development of quorum quenching molecules against those extremophiles which are causing industrial problems.

Traditional QS systems are not sufficient for the complete knowledge of communication in extremophiles. In *T. maritima,* no phenotypic change was detected although the LuxS formed was able to prompt bioluminescence in *V. harveyi* AI-2 assay. Confirmation for the involvement of peptide based system was not provided in *G. stearothermophilus*. In *P. haloplanktis*, *Ferrovum* sp., *N. occultus, S. piezotolerans, H. halophilus* and certain species of *Halomonadaceae* family, role of QS was not explained despite the presence of QS genes. In *P.*

ingrahamii, *P. fluorescens*, *P. mandelii, Acidithrix* sp., *Acidiphilum* sp., *A. auranticus, A. pelagium, B. foraminis* and *D. gobiensis* the type of QS system was not described although the phenotypes regulated by QS/ regulators of signaling systems/ high cell density dependent enhancement of enzymes were observed. Experimental validation is required for the speculative bioinformatic results for the presence of QS genes in *P. profundum* and in certain thermophilic bacteria. There is a possibility of the presence of novel QS genes or systems in extremophiles which are yet to be discovered. Through the use of bioinformatics, gene knockout and cloning can reveal the possible role of QS in some extremophiles, however for others new techniques or biosensors need to be developed.

Contributors

All authors have seen and approved the final version submitted.

Conflict of interest

Authors declare no conflict of interest.

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References

Abol Fotouh, D.M., Bayoumi, R.A., Hassan, M.A., 2016. Production of thermoalkaliphilic lipase from *Geobacillus thermoleovorans* DA2 and application in leather industry. Enzyme Res. https://doi.org/10.1155/2016/9034364.

Ahlgren, N.A., Harwood, C.S., Schaefer, A.L., Giraud, E., Greenberg, E.P., 2011. Aryl-homoserine lactone quorum sensing in stem-nodulating photosynthetic bradyrhizobia. Proc. Natl. Acad. Sci. 108, 7183–7188.

Anderson, J.C., Clarke, E.J., Arkin, A.P., Voigt, C.A., 2006. Environmentally controlled invasion of cancer cells by engineered bacteria. J. Mol. Biol. 355, 619–627.

Asker, D., Ohta, Y., 2018. *Haloferax alexandrinus* sp. nov., an extremely halophilic canthaxanthin-producing archaeon from a solar saltern in Alexandria (Egypt). Int. J. Syst. Evol. Microbiol. 52, 729–738.

Bakkevig, K., Sletta, H., Gimmestad, M., Aune, R., Ertesvag, H., Degnes, K., et al., 2005. Role of the *Pseudomonas fluorescens* alginate lyase (AlgL) in clearing the periplasm of alginates not exported to the extracellular environment. J. Bacteriol. 187, 8375–8384.

Barber, C.E., Tang, J.L., Feng, J.X., Pan, M.Q., Wilson, T.J.G., Slater, H., et al., 1997. A novel regulatory system required for pathogenicity of *Xanthomonas campestris* is mediated by a small diffusible signal molecule. Mol. Microbiol. 24, 555–566.

Bhargava, N., Sharma, P., Capalash, N., 2010. Quorum sensing in Acinetobacter: an emerging pathogen. Crit. Rev. Microbiol. 36, 349–360.

Bhargava, N., Sharma, P., Capalash, N., 2012. N-acyl homoserine lactone mediated interspecies interactions between *A. baumannii* and *P. aeruginosa*. Biofouling 28, 813–822.

Bofinger, M.R., de Sousa, L.S., Fontes, J.E.N., Marsaioli, A.J., 2017. Diketopiperazines as cross-communication quorum-sensing signals between *Cronobacter sakazakii* and *Bacillus cereus*. ACS Omega 2, 1003–1008.

Brachmann, A.O., Brameyer, S., Kresovic, D., Hitkova, I., Kopp, Y., Manske, C., et al., 2013. Pyrones as bacterial signaling molecules. Nat. Chem. Biol. 9, 573–581.

Brameyer, S., Heermann, R., 2015. Specificity of signal-binding via non-AHL LuxR-type receptors. PLoS One. https://doi.org/10.1371/journal.pone.0124093.

Charlesworth, J.C., Burns, B.P., 2015. Untapped resources: biotechnological potential of peptides and secondary metabolites in archaea. Archaea. https://doi.org/10.1155/2015/282035.

Chen, X., Schauder, S., Potier, N., Van Dorsselaer, A., Pelczer, I., Bassler, B.L., et al., 2002. Structural identification of a bacterial quorum-sensing signal containing boron. Nature 415, 545–549.

Chen, C.C., Walia, R., Mukherjee, K.J., Mahalik, S., Summers, D.K., 2015. Indole generates quiescent and metabolically active *Escherichia coli* cultures. Biotechnol. J. 10, 636–646.

Choudhary, S., Schmidt-Dannert, C., 2010. Applications of quorum sensing in biotechnology. Appl. Microbiol. Biotechnol. 86, 1267–1279.

Coker, J.A., 2016. Extremophiles and biotechnology: current uses and prospects. F1000Research 5, 396.

Correa-llanten, D.N., Amenabar, M.J., Munoz, P.A., Monsalves, M.T., Castro, M.E., Blamey, J.M., 2014. Bacterium isolated from Deception Island (Antarctica) containing a thermostable superoxide dismutase enzyme. Adv. Polar Sci. 25, 92–96.

de Oliveira, G.B., Favarin, L., Luchese, R.H., McIntosh, D., 2015. Psychrotrophic bacteria in milk: how much do we really know? Braz. J. Microbiol. 46, 313–321.

de Vrije, T., Budde, M.A.W., Lips, S.J., Bakker, R.R., Mars, A.E., Claassen, P.A.M., 2010. Hydrogen production from carrot pulp by the extreme thermophiles *Caldicellulosiruptor saccharolyticus* and *Thermotoga neapolitana*. Int. J. Hydrogen Energy. 35, 13206–13213.

Degrassi, G., Aguilar, C., Bosco, M., Zahariev, S., Pongor, S., Venturi, V., 2002. Plant growth-promoting *Pseudomonas putida* WCS358 produces and secretes four cyclic dipeptides: cross-talk with quorum sensing bacterial sensors. Curr. Microbiol. 45, 250–254.

Dharmaprakash, A., Reghunathan, D., Sivakumar, K.C., Prasannakumar, M., Thomas, S., 2016. Insights into the genome sequences of an N-Acyl homoserine lactone molecule producing two *Pseudomonas* spp. isolated from the arctic. Genome Announc. 4, e00767–16.

Dornez, E., Verjans, P., Arnaut, F., Delcour, J.A., Courtin, C.M., 2011. Use of psychrophilic xylanases provides insight into the xylanase functionality in bread making. J. Agric. Food Chem. 59, 9553–9562.

Ekman, J., 2011. Bacteria Colonizing Paper Machines. Dissertation. University of Helsinki.

Eller, M.R., Salgado, R.L., Vidigal, P.M.P., Alves, M.P., Dias, R.S., De Oliveira, L.L., et al., 2013. Complete genome sequence of the *Pseudomonas fluorescens* bacteriophage UFV-P2. Genome Announc. 1, 6–12.

Fan, J., Qian, G., Chen, T., Zhao, Y., Liu, F., Walcott, R.R., et al., 2011. The acyl-homoserine lactone (AHL)-type quorum sensing system affects growth rate, swimming motility and virulence in *Acidovorax avenae*subsp. citrulli. World J. Microbiol. Biotechnol. 27, 1155–1166.

Fazli, M., Almblad, H., Rybtke, M.L., Givskov, M., Eberl, L., Tolker-Nielsen, T., 2014. Regulation of biofilm formation in *Pseudomonas* and *Burkholderia* species. Environ. Microbiol. 16, 1961–1981.

Felix, M.M., Czerner, M., Ameztoy, I., Ramirez, E., Yeannes, M.I., 2016. Investigation of *Halococcus morrhuae* in salted-ripened anchovy products. Int. Food Res. J. 23, 2668–2674.

Galloway, W.R.J.D., Hodgkinson, J.T., Bowden, S.D., Welch, M., Spring, D.R., 2011. Quorum sensing in gram-negative bacteria: small-molecule modulation of AHL and AI-2 quorum sensing pathways. Chem. Rev. 111, 28–67.

Ghanmi, F., Carre, A., Manon, M., Ines, V., Frikha, D., Ayadi, H., et al., 2016. Antagonistic interactions and production of halocin antimicrobial peptides among extremely halophilic prokaryotes isolated from the solar saltern of Sfax, Tunisia. Extremophiles 20, 363–374.

Gonzalez Barrios, A.F., Zuo, R., Hashimoto, Y., Yang, L., Bentley, W.E., Wood, T.K., 2006. Autoinducer 2 controls biofilm formation in *Escherichia coli* through a novel motility quorum-sensing regulator (MqsR, B3022). J. Bacteriol. 188, 305–316.

Gottesman, S., Storz, G., 2011. Bacterial small RNA regulators: versatile roles and rapidly evolving variations. Cold Spring Harb. Perspect. Biol. https://doi.org/10.1101/cshperspect.a003798.

Guo, M., Gamby, S., Zheng, Y., 2013. Small molecule inhibitors of AI-2 signaling in Bacteria: state-of-the-Art and future perspectives for anti-quorum sensing agents. Int. J. Mol. Sci. 14, 17694–17728.

Gupta, R., Xu, S.Y., Sharma, P., Capalash, N., 2012. Characterization of MspNI (G/GWCC) and MspNII (R/GATCY), novel thermostable Type II restriction endonucleases from *Meiothermus* sp., isoschizomers of AvaII and BstYI. Mol. Biol. Rep. 39, 5607–5614.

Hammer, B.K., Bassler, B.L., 2003. Quorum sensing controls biofilm formation in *Vibrio cholerae*. Mol. Microbiol. 50, 101–114.

Hauck, T., Landmann, C., Brühlmann, F., Schwab, W., 2003. Formation of 5-methyl-4-hydroxy-3[2H]-furanone in cytosolic extracts obtained from *Zygosaccharomyces rouxii*. J. Agric. Food Chem. Appl. Environ. Microbiol. 69, 3911–3918.

Havarstein, L., Coomaraswamy, G., Morrison, D.A., 1995. An unmodified heptadecapeptide pheromone induces competence for genetic transformation in *Streptococcus pneumoniae*. Proc. Natl. Acad. Sci. 92, 11140–11144.

Hay, I.D., Rehman, Z.U., Moradali, M.F., Wang, Y., Rehm, B.H.A., 2013. Microbial alginate production, modification and its applications. Microb. Biotechnol. 6, 637–650.

Hazan, R., Sat, B., Engelberg-Kulka, H., 2004. *Escherichia coli* mazEF-mediated cell death is triggered by various stressful conditions. J. Bacteriol. 186, 3663–3669.

Higgins, D.A., Pomianek, M.E., Kraml, C.M., Taylor, R.K., Semmelhack, M.F., Bassler, B.L., 2007. The major *Vibrio cholerae* autoinducer and its role in virulence factor production. Nature 450, 883–886.

Hothersall, J., Murphy, A.C., Iqbal, Z., Campbell, G., Stephens, E.R., Wu, J., et al., 2011. Manipulation of quorum sensing regulation in *Pseudomonas fluorescens* NCIMB 10586 to increase mupirocin production. Appl. Microbiol. Biotechnol. 90, 1017–1026.

Huang, X.C., Yuan, Y.H., Guo, C.F., Gekas, V., Yue, T.L., 2015. *Alicyclobacillus* in the fruit juice industry: spoilage, detection, and prevention/control. Food Rev. Int. 31, 91–124.

Ibrahim, M., Nicolas, P., Bessieres, P., Bolotin, A., Monnet, V., Gardan, R., 2007. A genome-wide survey of short coding sequences in streptococci. Microbiology 153, 3631–3644.

James, D., Shao, H., Lamont, R.J., Demuth, D.R., 2006. The *Actinobacillus actinomycetemcomitans* ribose binding protein RbsB interacts with cognate and heterologous autoinducer 2 signals. Infect. Immun. 74, 4021–4029.

Johnsborg, O., Havarstein, L.S., 2009. Regulation of natural genetic transformation and acquisition of transforming DNA in *Streptococcus pneumoniae*. FEMS Microbiol. Rev. 33, 627–642.

Johnson, M.R., Montera, C.I., Conners, S.B., Chou, C.J., Shockley, K.R., Kelly, R.M., 2005. Population density-dependent regulation of exopolysaccharide formation in the hyperthermophilic bacterium *Thermotoga maritima*. Mol. Microbiol. 55, 664–674.

Kaur, A., Capalash, N., Sharma, P., 2018. Quorum sensing in thermophiles: prevalence of autoinducer-2 system. BMC Microbiol. 18, 62.

Keller, M.W., Lipscomb, G.L., Nguyen, D.M., Crowley, A.T., Schut, G.J., Scott, I., et al., 2017. Ethanol production by the hyperthermophilic archaeon *Pyrococcus furiosus* by expression of bacterial bifunctional alcohol dehydrogenases. Microb. Biotechnol. 10, 1535–1545.

Kent, D.J., Chauhan, K., Boor, K.J., Wiedmann, M., Martin, N.H., 2016. Spore test parameters matter: mesophilic and thermophilic spore counts detected in raw milk and dairy powders differ significantly by test method. Dairy Sci. 99, 5180–5191.
Kesarwani, M., Hazan, R., He, J., Que, Y.A., Apidianakis, Y., Lesic, B., et al., 2011. A quorum sensing regulated small volatile molecule reduces acute virulence and promotes chronic infection phenotypes. PLoS Pathog. 7, e1002192.
Khrulnova, S.A., Baranova, A., Bazhenov, S.V., Goryanin, I.I., Konopleva, M.N., Maryshev, I.V., et al., 2016. Lux-operon of the marine psychrophilic bacterium *Aliivibrio logei*: a comparative analysis of the LuxR1/LuxR2 regulatory activity in *Escherichia coli* cells. Microbiology (United Kingdom). https://doi.org/10.1099/mic.0.000253.
Kiley, P.J., Beinert, H., 2003. The role of Fe-S proteins in sensing and regulation in bacteria. Curr. Opin. Microbiol. 6, 181–185.
Kim, Y., Wood, T.K., 2010. Toxins Hha and CspD and small RNA regulator Hfq are involved in persister cell formation through MqsR in *Escherichia coli*. Biochem. Biophys. Res. Commun. 391, 209–213.
Kim, Y., Oh, S., Park, S., Kim, S.H., 2009. Interactive transcriptome analysis of enterohemorrhagic *Escherichia coli* (EHEC) O157:H7 and intestinal epithelial HT-29 cells after bacterial attachment. Int. J. Food Microbiol. 131, 224–232.
Kim, M.K., Zhao, A., Wang, A., Brown, Z.Z., Muir, T.W., Stone, H.A., et al., 2017. Surface-attached molecules control *Staphylococcus aureus* quorum sensing and biofilm development. Nat. Microbiol. 2, 17080.
Konopleva, M.N., Khrulnova, S.A., Baranova, A., Ekimov, L.V., Bazhenov, S.V., Goryanin, I.I., et al., 2016. A combination of luxR1 and luxR2 genes activates Pr-promoters of psychrophilic *Aliivibrio logei* lux-operon independently of chaperonin GroEL/ES and protease Lon at high concentrations of autoinducer. Biochem. Biophys. Res. Commun. 473, 1158–1162.
La Rosa, S.L., Solheim, M., Diep, D.B., Nes, I.F., Brede, D.A., 2015. Bioluminescence based biosensors for quantitative detection of enterococcal peptide – pheromone activity reveal inter-strain telesensing in vivo during polymicrobial systemic infection. Sci. Rep. 5, 8339.
LaSarre, B., Federle, M.J., 2013. Exploiting quorum sensing to confuse bacterial pathogens. Microbiol. Mol. Biol. Rev. 77, 73–111.
Latour, X., Diallo, S., Chevalier, S., Morin, D., Smadja, B., Burini, J.F., et al., 2007. Thermoregulation of N-acyl homoserine lactone-based quorum sensing in the soft rot bacterium *Pectobacterium atrosepticum*. Appl. Environ. Microbiol. 73, 4078–4081.
Lee, J.H., Lee, J., 2010. Indole as an intercellular signal in microbial communities. FEMS Microbiol. Rev. 34, 426–444.
Lee, J., Wu, J., Deng, Y., Wang, J., Wang, C., Wang, J., et al., 2013. A cell-cell communication signal integrates quorum sensing and stress response. Nat. Chem. Biol. 9, 339–343.
Li, F.Q., Person, R.E., Takemaru, K.I., Williams, K., Meade-White, K., Ozsahin, A.H., et al., 2004. Lymphoid enhancer Factor-1 links two hereditary leukemia syndromes through core-binding factor α regulation of ELA2. J. Biol. Chem. 279, 2873–2884.
Li, Y.S., Pan, X.R., Cao, J.S., Song, X.N., Fang, F., Tong, Z.H., et al., 2017. Augmentation of acyl homoserine lactones-producing and -quenching bacterium into activated sludge for its granulation. Water Res. 125, 309–317.
Liang, R., Grizzle, R.S., Duncan, K.E., McInerney, M.J., Suflita, J.M., 2014. Roles of thermophilic thiosulfate-reducing bacteria and methanogenic archaea in the biocorrosion of oil pipelines. Front. Microbiol. https://doi.org/10.3389/fmicb.2014.00089.
Lin, L., Dai, S., Tian, B., Li, T., Yu, J., Liu, C., et al., 2016. DqsIR quorum sensing-mediated gene regulation of the extremophilic bacterium *Deinococcus radiodurans* in response to oxidative stress. Mol. Microbiol. 100, 527–541.
Lindemann, A., Pessi, G., Schaefer, A.L., Mattmann, M.E., Christensen, Q.H., Kessler, A., et al., 2011. Isovaleryl-homoserine lactone, an unusual branched-chain quorum-sensing signal from the soybean symbiont *Bradyrhizobium japonicum*. Proc. Natl. Acad. Sci. 108, 16765–16770.
Llamas, I., del Moral, A., Martínez-Checa, F., Arco, Y., Arias, S., Quesada, E., 2006. *Halomonas maura* is a physiologically versatile bacterium of both ecological and biotechnological interest. Antonie van Leeuwenhoek. J. Gen. Microbiol. 89, 395–403.
Mae, A., Montesano, M., Koiv, V., Tapio Palva, E., 2001. Transgenic plants producing the bacterial pheromone N-Acyl-homoserine lactone exhibit enhanced resistance to the bacterial phytopathogen *Erwinia carotovora*. Mol. Plant Microbe Interact. 14, 1035–1042.
Mamani, S., Moinier, D., Denis, Y., Soulere, L., Queneau, Y., Talla, E., et al., 2016. Insights into the quorum sensing regulon of the acidophilic *Acidithiobacillus ferrooxidans* revealed by transcriptomic in the presence of an acyl homoserine lactone superagonist analog. Front. Microbiol. 7, 1365.
March, J.C., Bentley, W.E., 2004. Quorum sensing and bacterial cross-talk in biotechnology. Curr. Opin. Biotechnol. 15, 495–502.
Margesin, R., Sproer, C., Schumann, P., Schinner, F., 2018. *Pedobacter cryoconitis* sp. nov., a facultative psychrophile from alpine glacier cryoconite. Int. J. Syst. Evol. Microbiol. 53, 1291–1296.
Martini, S., Al Ali, B., Garel, M., Nerini, D., Grossi, V., Pacton, M., et al., 2013. Effects of hydrostatic pressure on growth and luminescence of a moderately-piezophilic luminous Bacteria *Photobacterium phosphoreum* ANT-2200. PLoS One 8, e66580.
Megaw, J., Gilmore, B.F., 2017. Archaeal persisters: persister cell formation as a stress response in *Haloferax volcanii*. Front. Microbiol. https://doi.org/10.3389/fmicb.2017.01589.
Miller, M.B., Bassler, B.L., 2001. Quorum sensing in Bacteria. Annu. Rev. Microbiol. 55, 165–199.
Miller, S.T., Xavier, K.B., Campagna, S.R., Taga, M.E., Semmelhack, M.F., Bassler, B.L., et al., 2004. *Salmonella typhimurium* recognizes a chemically distinct form of the bacterial quorum-sensing signal AI-2. Mol. Cell 15, 677–687.
Misra, C.S., Mukhopadhyaya, R., Apte, S.K., 2014. Harnessing a radiation inducible promoter of *Deinococcus radiodurans* for enhanced precipitation of uranium. J. Biotechnol. 189, 88–93.
Mitova, M., Tutino, M.L., Infusini, G., Marino, G., De Rosa, S., 2005. Exocellular peptides from antarctic psychrophile *Pseudoalteromonas haloplanktis*. Mar. Biotechnol. 7, 523–531.
Montgomery, K., Charlesworth, J.C., Lebard, R., Visscher, P.T., Burns, B.P., 2013. Quorum sensing in extreme environments. Life 3, 131–148.
Monzon, O., Yang, Y., Li, Q., Alvarez, P.J.J., 2016. Quorum sensing autoinducers enhance biofilm formation and power production in a hypersaline microbial fuel cell. Biochem. Eng. J. 109, 222–227.
Moreno-Paz, M., Gomez, M.J., Arcas, A., Parro, V., 2010. Environmental transcriptome analysis reveals physiological differences between biofilm and planktonic modes of life of the iron oxidizing bacteria *Leptospirillum* spp. in their natural microbial community. BMC Genomics 11, 404.
Mori, J.F., Ueberschaar, N., Lu, S., Cooper, R.E., Pohnert, G., Kusel, K., 2017. Sticking together: inter-species aggregation of bacteria isolated from iron snow is controlled by chemical signaling. ISME J. 11, 1075–1086.
Mukhopadhyay, M., Banerjee, R., 2015. Purification and biochemical characterization of a newly produced yellow laccase from *Lentinus squarrosulus* MR13. 3Biotech 5, 227–236.
Muller, C., Bang, I.S., Velayudhan, J., Karlinsey, J., Papenfort, K., Vogel, J., et al., 2009. Acid stress activation of the σ E stress response in *Salmonella enterica* serovar Typhimurium. Mol. Microbiol. 71, 1228–1238.
Nawaz, M.Z., Jian, H., He, Y., Xiong, L., Xiao, X., Wang, F., 2017. Genome-wide detection of small regulatory RNAs in deep-sea bacterium *Shewanella piezotolerans* WP3. Front. Microbiol. 8, 1–12.
Ng, W.L., Bassler, B.L., 2009. Bacterial quorum-sensing network architectures. Annu. Rev. Genet. 43, 97–222.
Nichols, J.D., Johnson, M.R., Chou, C.J., Kelly, R.M., 2009. Temperature, not LuxS, mediates AI-2 formation in hydrothermal habitats. FEMS Microbiol. Ecol. 68, 1173–1181.
Nishimura, H., Sako, Y., 2009. Purification and characterization of the oxygen-thermostable hydrogenase from the aerobic hyperthermophilic archaeon *Aeropyrum camini*. J. Biosci. Bioeng. 108, 299–303.
Oggioni, M.R., Iannelli, F., Ricci, S., Chiavolini, D., Parigi, R., Trappetti, C., et al., 2004. Antibacterial activity of a competence-stimulating peptide in experimental sepsis caused by *Streptococcus pneumoniae*. Antimicrob. Agents Chemother. 48, 725–4732.
Okibe, N., Gericke, M., Hallberg, K.B., Johnson, D.B., 2003. Enumeration and characterization of acidophilic microorganisms isoltated from a pilot plant stirred tank bioleaching operation. J. Appl. Environ. Microbiol. 69, 1936–1943.
Oliver, C.M., Schaefer, A.L., Greenberg, E.P., Sufrin, J.R., 2009. Microwave synthesis and evaluation of phenacylhomoserine lactones as anticancer compounds that minimally activate quorum sensing pathways in *Pseudomonas aeruginosa*. J. Med. Chem. 52, 1569–1575.
Olson, D.G., McBride, J.E., Shaw, A.J., Lynd, L.R., 2012. Recent progress in consolidated bioprocessing. Curr. Opin. Biotechnol. 23, 396–405.
Paggi, R.A., Martone, C.B., Fuqua, C., De Castro, R.E., 2003. Detection of quorum sensing signals in the haloalkaliphilic archaeon *Natronococcus occultus*. FEMS Microbiol. Lett. 221, 49–52.
Papenfort, K., Bassler, B.L., 2016. Quorum sensing signal-response systems in Gram-negative bacteria. Nat. Rev. Microbiol. 14, 576–588.
Papenfort, K., Silpe, J.E., Schramma, K.R., Cong, J.P., Seyedsayamdost, M.R., Bassler, B.L., 2017. A *Vibrio cholerae* autoinducer-receptor pair that controls biofilm formation. Nat. Chem. Biol. 13 (5), 551–557.
Parrilli, E., Giuliani, M., Pezzella, C., Danchin, A., Marino, G., Tutino, M.L., 2010. PssA is required for α-amylase secretion in Antarctic *Pseudoalteromonas haloplanktis*. Microbiology 156, 211–219.
Perez-Rodriguez, I., Bolognini, M., Ricci, J., Bini, E., Vetriani, C., 2015. From deep-sea volcanoes to human pathogens: a conserved quorum-sensing signal in Epsilonproteobacteria. ISME J. 9, 1222–1234.
Pinar, G., Krakova, L., Pangallo, D., Piombino-Mascali, D., Maixner, F., Zink, A., et al., 2014. Halophilic bacteria are colonizing the exhibition areas of the Capuchin Catacombs in Palermo, Italy. Extremophiles 18, 677–691.
Plummer, P., Sahin, O., Burrough, E., Sippy, R., Mou, K., Rabenold, J., et al., 2012. Critical role of luxS in the virulence of *Campylobacter jejuni* in a guinea pig model of abortion. Infect. Immun. 80, 585–593.
Rader, B.A., Campagna, S.R., Semmelhack, M.F., Bassler, B.L., Guillemin, K., 2007. The quorum-sensing molecule autoinducer 2 regulates motility and flagellar morphogenesis in *Helicobacter pylori*. J. Bacteriol. 189, 6109–6117.
Ramanathan, T., Ting, Y.P., 2015. Selective copper bioleaching by pure and mixed cultures of alkaliphilic bacteria isolated from a fly ash landfill site. Water Air Soil Pollut. https://doi.org/10.1007/s11270-015-2641-x.
Rampelotto, P., 2013. Extremophiles and extreme environments. Life 3, 482–485.
Rao, R.M., Pasha, S.N., Sowdhamini, R., 2016. Genome-wide survey and phylogeny of S-Ribosylhomocysteinase (LuxS) enzyme in bacterial genomes. BMC Genomics 17, 742.
Rasamiravaka, T., Vandeputte, O.M., Pottier, L., Huet, J., Rabemanantsoa, C., Kiendrebeogo, M., et al., 2015. *Pseudomonas aeruginosa* biofilm formation and persistence, along with the production of quorum sensing-dependent virulence factors, are disrupted by a triterpenoid coumarate ester isolated from dalbergia trichocarpa, a tropical legume. PLoS One 10, e0132791.
Reen, F.J., Mooij, M.J., Holcombe, L.J., McSweeney, C.M., McGlacken, G.P., Morrissey, J.P., et al., 2011. The Pseudomonas quinolone signal (PQS), and its precursor HHQ, modulate interspecies and interkingdom behaviour. FEMS Microbiol. Ecol. 77, 413–428.
Rezzonico, F., Duffy, B., 2008. Lack of genomic evidence of AI-2 receptors suggests a non-quorum sensing role for luxS in most bacteria. BMC Microbiol. 8, 154.

Riley, M., Staley, J.T., Danchin, A., Zhang, T.Z., Brettin, T.S., Hauser, L.J., et al., 2008. Genomics of an extreme psychrophile, *Psychromonas ingrahamii*. BMC Genomics 9, 210.

Rivas, M., Seeger, M., Holmes, D.S., Jedlicki, E., 2005. A Lux-like quorum sensing system in the extreme acidophile *Acidithiobacillus ferrooxidans*. Biol. Res. 38, 283–297.

Rivas, M., Seeger, M., Jedlicki, E., Holmes, D.S., 2007. Second acyl homoserine lactone production system in the extreme acidophile *Acidithiobacillus ferrooxidans*. Appl. Environ. Microbiol. 73, 3225–3231.

Ryan, R.P., Fouhy, Y., Garcia, B.F., Watt, S.A., Niehaus, K., Yang, L., et al., 2008. Interspecies signalling via the Stenotrophomonas maltophilia diffusible signal factor influences biofilm formation and polymyxin tolerance in *Pseudomonas aeruginosa*. Mol. Microbiol. 68, 75–86.

Saint-Ruf, C., Garfa-Traore, M., Collin, V., Cordier, C., Franceschi, C., Matic, I., 2014. Massive diversification in aging colonies of *Escherichia coli*. J. Bacteriol. 196, 3059–3073.

Schiraldi, C., Giuliano, M., De Rosa, M., 2002. Perspectives on biotechnological applications of archaea. Archaea 1, 75–86.

Scholtissek, A., Tischler, D., Westphal, A., van Berkel, W., Paul, C., 2017. Old yellow enzyme-catalysed asymmetric hydrogenation: linking family roots with improved catalysis. Catalysts 7, 130.

Schultz, D., Wolynes, P.G., Jacob, E.B., Onuchic, J.N., 2009. Deciding fate in adverse times: sporulation and competence in *Bacillus subtilis*. Proc. Natl. Acad. Sci. 106, 21027–21034.

Schuster, M., Joseph Sexton, D., Diggle, S.P., Peter Greenberg, E., 2013. Acyl-homoserine lactone quorum sensing: from evolution to application. Annu. Rev. Microbiol. 67, 43–63.

Sewald, X., Saum, S.H., Palm, P., Pfeiffer, F., Oesterhelt, D., Muller, V., 2007. Autoinducer-2-producing protein LuxS, a novel salt- and chloride-induced protein in the moderately halophilic bacterium Halobacillus halophilus. Appl. Environ. Microbiol. 73, 371–379.

Shanker, E., Federle, M.J., 2017. Quorum sensing regulation of competence and bacteriocins in *Streptococcus pneumoniae* and mutans. Genes 8, 15.

Sharif, D.I., Gallon, J., Smith, C.J., Dudley, E., 2008. Quorum sensing in Cyanobacteria: N-octanoyl-homoserine lactone release and response, by the epilithic colonial cyanobacterium *Gloeothece* PCC6909. ISME J. 2, 1171–1182.

Shulami, S., Shenker, O., Langut, Y., Lavid, N., Gat, O., Zaide, G., et al., 2014. Multiple regulatory mechanisms control the expression of the *Geobacillus stearothermophilus* gene for extracellular xylanase. J. Biol. Chem. 289, 25957–25975.

Sitnikov, D.M., Schineller, J.B., Baldwin, T.O., 1995. Transcriptional regulation of bioluminesence genes from Vibrio fischeri. Mol. Microbiol. 17, 801–812.

Soo, P.C., Horng, Y.T., Wei, J.R., Shu, J.C., Lu, C.C., Lai, H.C., 2008. Regulation of swarming motility and flhDCSm expression by RssAB signaling in *Serratia marcescens*. J. Bacteriol. 190, 2496–2504.

Sperandio, V., Torres, A.G., Jarvis, B., Nataro, J.P., Kaper, J.B., 2003. Bacteria-host communication: the language of hormones. Proc. Natl. Acad. Sci. 100, 8951–8956.

Stevens, A.M., Dolan, K.M., Greenberg, E.P., 1994. Synergistic binding of the *Vibrio fischeri* LuxR transcriptional activator domain and RNA polymerase to the lux promoter region (autoinduction/DNA binding/luminescence/quorum sensing). Biochemistry 91, 12619–12623.

Sun, Z., He, X., Brancaccio, V.F., Yuan, J., Riedel, C.U., 2014. *Bifidobacteria* exhibit LuxS-dependent autoinducer 2 activity and biofilm formation. PLoS One. https://doi.org/10.1371/journal.pone.0088260.

Tahrioui, A., Quesada, E., Llamas, I., 2011. The hanR/hanl quorum-sensing system of *Halomonas anticariensis,* a moderately halophilic bacterium. Microbiology 157, 3378–3387.

Tahrioui, A., Schwab, M., Quesada, E., Llamas, I., 2013. Quorum sensing in some representative species of Halomonadaceae. Life 3, 260–275.

Takano, E., 2006. γ-Butyrolactones: streptomyces signalling molecules regulating antibiotic production and differentiation. Curr. Opin. Microbiol. 9, 287–294.

Tommonaro, G., Abbamondi, G.R., Iodice, C., Tait, K., De Rosa, S., 2012. Diketopiperazines produced by the halophilic archaeon, *Haloterrigena hispanica*, activate AHL bioreporters. Microb. Ecol. 63, 490–495.

Toogood, H.S., Gardiner, J.M., Scrutton, N.S., 2010. Biocatalytic reductions and chemical versatility of the old yellow enzyme family of flavoprotein oxidoreductases. Chem. Cat. Chem. 2, 892–914.

Tourova, T.P., Poltoraus, A.B., Lebedeva, I.A., Tsaplina, I.A., Bogdanova, T.I., Karavaiko, G.I., 1994. 16S ribosomal RNA (rRNA) sequence analysis and phylogenetic position of *Sulfobacillus thermosulfidooxidans*. Syst. Appl. Microbiol. 17, 509–512.

Touzel, J.P., Donohue, M.O., Debeire, P., Samain, E., Breton, C., 2000. *Thermobacillus xylanilyticus* gen. nov., a new aerobic thermophilic xylan-degrading bacterium isolated from farm soil. Int. J. Syst. Evol. Microbiol. 50, 315–320.

Vasquez-Ponce, F., Higuera-Llanten, S., Pavlov, M.S., Ramirez-Orellana, R., Marshall, S.H., Olivares-Pacheco, J., 2017. Alginate overproduction and biofilm formation by psychrotolerant *Pseudomonas mandelii* depend on temperature in Antarctic marine sediments. Electron. J. Biotechnol. 28, 27–34.

Vera, M., Schippers, A., Sand, W., 2013. Progress in bioleaching: fundamentals and mechanisms of bacterial metal sulfide oxidation-part A. Appl. Microbiol. Biotechnol. 97, 7529–7541.

Verma, A., Shirkot, P., Verma, A., 2014. Purification and characterization of thermostable laccase from thermophilic *Geobacillus thermocatenulatus* MS5 and its applications in removal of textile. J. Biosci. 2, 479–485.

Walters, M., Sperandio, V., 2006. Autoinducer 3 and epinephrine signaling in the kinetics of locus of enterocyte effacement gene expression in enterohemorrhagic *Escherichia coli*. Infect. Immun. 74, 5445–5455.

Xue, T., Ni, J., Shang, F., Chen, X., Zhang, M., 2015. Autoinducer-2 increases biofilm formation via an ica- and bhp-dependent manner in *Staphylococcus epidermidis* RP62A. Microbes Infect. 17, 345–352.

Yan, Z., Li, G., Gao, Y., Qi, Y., Zhai, M., 2015. The extracellular death factor (EDF) protects *Escherichia coli* by scavenging hydroxyl radicals induced by bactericidal antibiotics. SpringerPlus 4, 182.

Yanofsky, C., Horn, V., Gollnick, P., 1991. Physiological studies of tryptophan transport and tryptophanase operon induction in Escherichia coli. J. Bacteriol. 173, 6009–6017.

Yuan, M., Chen, M., Zhang, W., Lu, W., Wang, J., Yang, M., et al., 2012. Genome sequence and transcriptome analysis of the radioresistant bacterium *Deinococcus gobiensis:* insights into the extreme environmental adaptations. PLoS One 7, 1–11.

Zeng, X., Xiao, X., Wang, P., Wang, F., 2004. Screening and characterization of psychrotrophic lipolytic bacteria from deep-sea sediments. J. Microbiol. Biotechnol. 14, 952–958.

Zhang, G., Zhang, F., Ding, G., Li, J., Guo, X., Zhu, J., et al., 2012. Acyl homoserine lactone-based quorum sensing in a methanogenic archaeon. ISME J. 6, 1336–1344.