International Journal of Current Trends in
Pharmacobiology and Medical Sciences
Volume 1 • Number 3 (August-2016) • ISSN: 2456-2432
Journal homepage: www.ijctpms.com

Review Article

Review on Quorum Sensing and Actions of Quorum Quenching Mechanisms in Bacteria and Some Social Insects

Tsegaye Shamebo*, Ketema Bacha and Tsige Ketema

College of Natural Science, Jimma University, Jimma Ethiopia

Corresponding author.

Abstract

Quorum sensing is the phenomenon through which the release and accumulation of signaling molecules enable bacteria and social insects to communicate and coordinate with each other. Communication is the most important tool to exchange information (idea) between any living organisms. Organisms can make decision easily about their cells (population) via communication. Bacteria can regulate a diverse range of physiological activities including symbiosis, virulence, competence, drug resistance, conjugation, defense, antibiotic production, motility, biofilm formation and sporulation through Quorum sensing mechanism. The quorum sensing condition in bacteria is a population density dependent process. Besides bacteria social insects (like ants and honey bees) also use Quorum sensing in making decision about their new nesting sites. In contrast various enzymes and chemical substances have been studied for their potential to inhibit Quorum sensing pathways in bacteria. They are known as quorum-quenching molecules. The main target of these molecules is blocking the bacterial cell to cell communications (Quorum sensing) mechanisms. Since pathogens are mainly rely on cell to cell communication (Quorum sensing) to overcome the host dense and to progress their infection, quorum-quenching can play a significant role in interfering with this condition and permissive in controlling infectious diseases. Even though several studies have reported on Quorum sensing from different region of the world, there has been no such a kind of review published anywhere. Therefore, this review was aimed to provide exhaustive information on quorum sensing and the mechanisms of quorum-quenching in bacteria and social insects.

Article Info

Accepted: 30 July2016
Available Online: 25 August 2016

Keywords

AHL-acylase
AHL-lactonase
Autoinducer
Paraoxonases
Quorum quenching
Quorum sensing

Introduction

Quorum sensing is the process of cell to cell communication in bacteria and some social insects which is mediated by signaling molecules. It is a type of decision making process used by decentralized groups of bacteria to regulate their behavior. According to the local density of their population many species of bacteria use quorum sensing to coordinate their gene expression. Similarly, some social insects (like ants and honey bees) also use quorum sensing to make a collective decisions about where to nest (Britton and Sacks, 2004; Peysakhov and Regli, 2005).

Pathogenic microbes, infecting humans, animals and plants, cause economic and personal losses. Until the establishment of germ theory and identification of specific tremendous microbes as the causal agents of a wide variety of infectious diseases, mankind seemed helpless against these diseases. This landmark finding ultimately led to the discovery and development of vaccines and antibiotics (Morens et al., 2004). The invention of antibiotics in the 1920s and subsequent developments have rewritten the history of medicine, allowing treatment of infections that were once widely fatal. However, the early optimistic prediction of eradicating infectious diseases has become non-sustainable, as many pathogens have developed resistance to antibiotics. Infectious diseases continue to be the leading causes of death and illness worldwide (Livermore, 2004; Morens et al., 2004). The rapid emergence of 'superbugs' that resist most commonly used antibiotics has microbial emphasized the need for the development of new antibiotics and novel strategies against pathogens (Livermore, 2004).

Conventional antibiotics kill or stop bacterial growth by interfering with essential housekeeping functions (e.g. DNA, RNA and protein synthesis), hence inevitably imposing selection pressure that results in the emergence of antibiotic-resistant microbial pathogens. The concern`s about resistance not only call for better use and administration of conventional antibiotics, but also prompt scientists to look for new disease control strategies. At least in theory, any strategy that can effectively stop pathogenic infection, but does not impose a 'life-or-death' selection pressure, would be a promising alternative to contain infectious diseases and may help to prevent antibiotic resistance in microbial communities. One such promising strategy is the recently demonstrated quorum-quenching approach, also known as antipathogenic or signal interference or quorum sensing interference, which abolishes bacterial infection by interfering with microbial cell-to-cell communication—also known as quorum sensing (Hentzer and Givskov, 2003; Zhang and Dong, 2004).

Why does quenching microbial quorum sensing hold promises in infection control? This novel strategy results from the realization that many single-celled microbial organisms, including bacterial and fungal pathogens, can communicate with each other and act collectively in the regulation of infection-related traits, including expression of virulence genes and production of biofilms. The pathogens produce, detect and respond in a population density-dependent manner to specific small signal molecules, ranging from fatty acid derivatives to oligopeptides and furanones thus synchronizing the expression of virulence genes among family members (Whitehead et al., 2001; Zhang and Dong, 2004; Waters and Bassler , 2005). This review focuses on the principle of quorum sensing in bacteria and some social insects and the mechanisms and action of quorum quenching.

General mechanisms and key components of quorum sensing

Bacterial colonies and some Social insect are an excellent example of a decentralized system, because no individual is in charge of directing or making decisions for the colony. Several groups of social insects have been shown to use quorum sensing in a process that resembles collective decision-making (Mallon and Pratt, 2001).

Quorum sensing mechanisms in bacteria with some specific models

Quorum sensing was discovered and described over 25 years ago in two luminous marine bacterial species, *Vibrio fischeri* and *Vibrio harveyi* .In both species the enzymes responsible for light production are encoded by the luciferase structural operon *luxCDABE* (Engebrecht and Silverman, 1984) and light emission was determined to occur only at high cell-population density in response to the accumulation of secreted autoinducer signaling molecules. Until recently, only a few other cases of bacterial regulation of gene expression in response to cell-cell signaling were known. For example, antibiotic production by *Streptomyces* spp. conjugation in *Enterococcus faecalis* and fruiting body development in *Myxococcus xanthus* were also recognized to be controlled by intercellular signaling (Fig. 1). These bacterial communication systems were considered anomalous, and in general, bacteria as a whole were not believed to use cell-cell communication. Rather, the exchange of chemical signals between cells/organisms was assumed to be a trait highly characteristic of eukaryotes. The recent explosion of advances in the field of cell-cell communication in bacteria has now shown that many or most bacteria probably communicate using secreted chemical molecules to coordinate the behavior of the group.

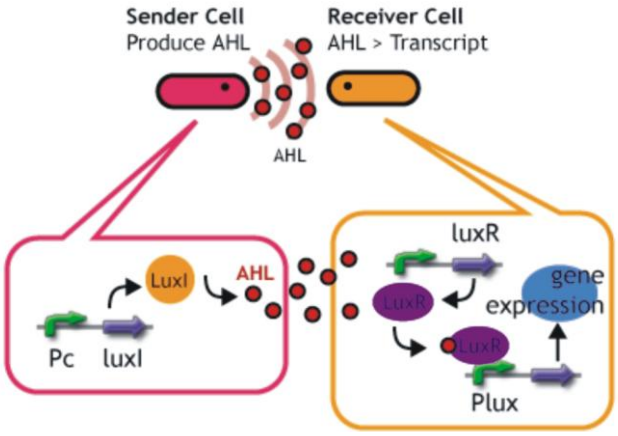

Fig. 1: Mechanisms involved in bacterial QS (Source - http://parts.mit.edu/igem07/index.php/Chiba/Communication)

Quorum sensing in Gram-positive bacteria

Gram-positive bacteria communicate using modified oligopeptides as signals and "two component"-type membrane-bound sensor histidine kinases as receptors. Signaling is mediated by a phosphorylation flow that influences the activity of a DNA-binding transcriptional regulatory protein termed as response regulator. Each gram-positive bacterium uses a signal different from that used by other bacteria and the cognate receptors are neatly sensitive to the signals' structures. Thus, as in LuxIR systems, peptide quorum sensing circuits are understood to confer intraspecies communication. Peptide signals are not diffusible across the membrane, hence signal release is mediated by dedicated oligopeptide exporters. In most cases, associated with signal release is signal processing and modification. While the biochemistry underlying these events is poorly defined, it is known that most peptide quorum-sensing signals are cleaved from larger precursor peptides, which then are modified to contain lactone and thiolactone rings, lanthionines, and isoprenyl groups (Ansaldi et al., 2002; Booth et al., 1996; Mayville et al., 1999).

Many gram-positive bacteria communicate with multiple peptides in combination with other types of quorum-sensing signals. An interesting example of peptide quorum sensing exists in *Staphylococcus aureus,* which is normally a benign human commensal but becomes a deadly pathogen upon penetration into host tissues (Tenover and Gaynes, 2000). *S. aureus* uses a biphasic strategy to cause disease: At low cell density, the bacteria express protein factors that promote attachment and colonization, whereas at high cell density, the bacteria repress these traits and initiate secretion of toxins and proteases that are presumably required for dissemination .This switch in gene expression programs is regulated by the Agr quorum-sensing system (Fig. 2). The system consists of an autoinducing peptide of *Staphylococcus aureus* (AIP) encoded by *agrD* (Ji et al.,1995) and a two-component sensor kinase-response regulator pair, AgrC and AgrA.

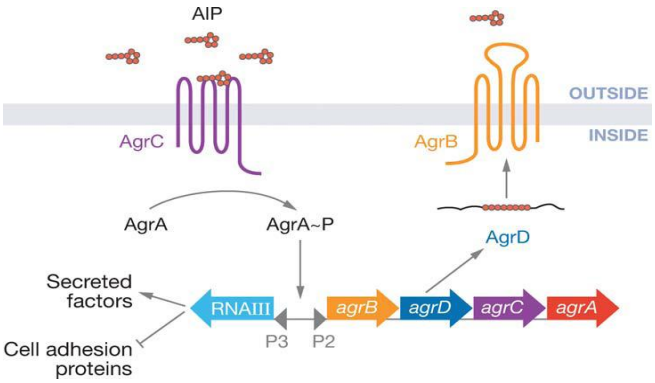

Fig. 2: Quorum sensing mechanism in Gram-positive bacteria, *Staphylococcus aureus* (Source: Dufour et al., 2002).

Quorum sensing in Gram-negative bacteria

The first described quorum-sensing system is that of the bioluminescent marine bacterium *Vibrio fischeri*, and it is considered the paradigm for quorum sensing in most gram-negative bacteria. *V. fischeri* colonizes the light organ of the Hawaiian squid *Euprymna scolopes*. In this organ, the bacteria grow to high cell density and induce the expression of genes required for bioluminescence. The squid uses the light provided by the bacteria for counter illumination to mask its shadow and avoid predation (Visick et al., 2000). The bacteria benefit because the light organ is rich in nutrients and allows proliferation in numbers unachievable in seawater.

Quorum sensing in *Vibrio fischeri* is a LuxIR signaling circuit. Red triangles indicate the autoinducer that is produced by LuxI. OM, outer membrane; IM, inner membrane proteins, LuxI and LuxR, control expression of the luciferase operon (*luxICDABE*) required for light production (Fig. 3). LuxI is the autoinducer synthase, which produces the acyl-homoserine lactone (AHL) autoinducer 3OC6 homoserine lactone (Eberhard et al., 1981; Engebrecht and Silverman, 1984) and LuxR is the cytoplasmic autoinducer receptor/DNA binding transcriptional activator. Following production, the AHL freely diffuses in and out of the cell and increases in concentration with increasing cell density (Kaplan and Greenberg, 1985). When the signal reaches a critical, threshold concentration, it is bound by LuxR and this

complex activates transcription of the operon encoding luciferase. Importantly, the LuxR-AHL complex also induces expression of *luxI* because it is encoded in the luciferase operon (Fig. 3). This regulatory configuration floods the environment with Quorum sensing: a process of cell-cell communication in bacteria. Autoinducers: small molecules secreted by bacteria that are used to measure population density AHL: acyl-homoserine lactone SAM: *S*-adenosylmethionine the signal. This creates a positive feedback loop that causes the entire population to switch into "quorum-sensing mode" and produce light.

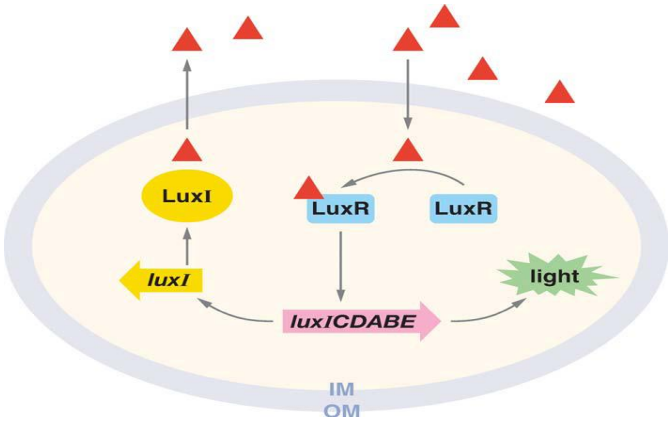

Fig. 3: Quorum Sensing mechanisms in Gram-Negative Bacteri *Vibrio fischeri* (Eberhard et al., 1981; Engebrecht and Silverman, 1984).

Quorum sensing mechanisms in *Vibrio fischeri*

Bacteria release small signal molecules (autoinducers) into the environment, and they respond once a threshold level of the signal accumulates. Various bacteria use quorum sensing to regulate diverse activities, such as luminescence, motility, protease expression, antibiotic production, and biofilm formation. Many of these activities are thought to be most effective when coordinately expressed by many bacteria (Hense et al., 2007).

Quorum sensing was first observed in *Vibrio fischeri*, a bioluminiscent bacterium that lives as a mutualistic symbiont in the photophore (or light-producing organ) of the Hawaiian bobtail squid (Kok Gan et al., 2010). When *V. fischeri* cells are free-living (or planktonic), the autoinducer is at low concentration, and, thus, cells do not luminesce. However, when they are highly concentrated in the photophore (about 10^{11} cells/ml) transcription of luciferase is induced, leading to bioluminescence. The first quorum-sensing system characterized was the *V. fischeri* LuxIR system, in which accumulation of an acyl-homoserine lactone (HSL) signal leads to the induction of luminescence. Since that time, dozens of other bacterial quorum-sensing systems have been identified, including those that utilize different signal molecules, such as oligopeptides (Antunes et al., 2007).Some bacteria have multiple systems that can be either independent or integrated. Examples of such integration include parallel systems that converge on the same regulators, or sequential ones in which one system regulates another in addition to its own target genes (Henke and Bassler, 2004).

V. fischeri has two acyl-HSL quorum-sensing systems, the AinS system and the LuxIR system, which work together in a sequential manner (Fig. 4) (Lupp and Ruby, 2004). The signal synthase AinS produces octanoyl-l-HSL (C8-HSL) which, at threshold densities achieved in culture, will interact with the receptor AinR and initiate a signaling cascade. AinR binding of C8-HSL represses LuxO, allowing translation of the master transcriptional activator LitR. With LuxO repressed, LitR is able to upregulate a number of genes, most notably luxR (Mandel et al., 2008) LuxR can interact with C8-HSL to weakly induce transcription of the luxICDABEG operon, leading to a low level of luminescence and the production of 3-oxohexanoyl-l-HSL (3OC6-HSL) by LuxI.

Once 3OC6-HSL accumulates to a sufficient concentration, it binds to LuxR, activating it and leading to an even greater induction of the LuxR regulon (Henke and Bassler, 2004). While AinS regulates a number of activities through LitR, such as rpoS expression and normal motility, examinations of mutant strains have identified activities controlled by AinS independently of LitR, such as normal persistence in the light organ, indicating that LitR controls only one branch of the AinS regulon.

The sequential nature of this system gives *V. fischeri* the ability to differentiate between, and respond to, at least three bacterial population conditions: low cell density, when neither autoinducer is sensed; intermediate cell density, when only C8-HSL is sensed; and high cell density, when both C8-HSL and 3OC6-HSL are sensed. In environments that support the growth of *V. fischeri*, this sequential arrangement also leads to temporal control over the expression of various genes.

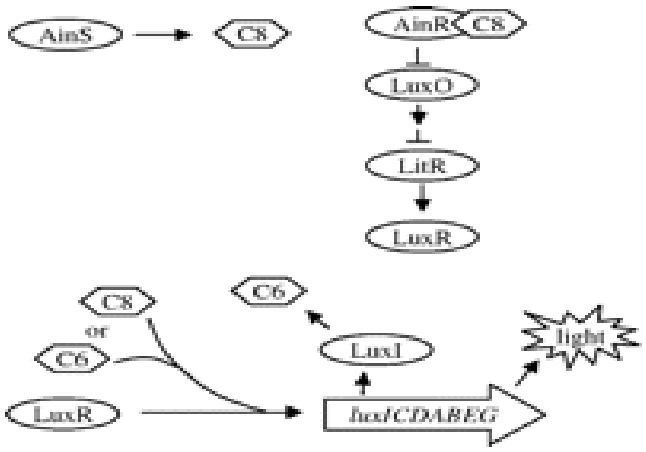

Fig. 4: Quorum sensing mechanisms in symbiotic *Vibrio fischeri* (Source: Mandel et al., 2008).

Quorum sensing mechanisms in *Escherichia coli*

In the Gram-negative bacteria *Escherichia coli*, cell division may be partially regulated by AI-2 mediated quorum sensing. This species uses AI-2, which is produced and processed by the *lsr* operon. Part of it encodes an ABC transporter, which imports AI-2 into the cells during the early stationary (latent) phase of growth. AI-2 is then phosphorylated by the LsrK kinase, and the newly produced phospho-AI-2 can be either internalized or used to suppress LsrR, a repressor of the *lsr* operon (thereby activating the operon) (Contiero et al., 2000). Transcription of the *lsr* operon is also thought to be inhibited by dihydroxyacetone phosphate (DHAP) through its competitive binding to LsrR. Glyceraldehyde 3-phosphate has also been shown to inhibit the *lsr* operon through cAMP-CAPK-mediated inhibition. This explains why, when grown with glucose, *E. coli* will lose the ability to internalize AI-2 (because of catabolite repression). When grown normally, AI-2 presence is transient (Beatty et al., 2003). *E. coli* and *Salmonella enterica* do not produce AHL signals commonly found in other Gram-negative bacteria. However, they have a receptor that detects AHLs from other bacteria and change their gene expression in accordance with the presence of other "quorate" populations of Gram-negative bacteria (Miller and Bassler, 2001).

Quorum sensing mechanisms in *Salmonella enterica*

Salmonella encodes a LuxR homolog, SdiA, but does not encode an AHL synthase. SdiA detects AHLs produced by other species of bacteria including *Aeromonas hydrophila*, *Hafnia alvei*, and *Yersinia enterocolitica*. When AHL is detected, SdiA regulates the *rck* operon on the *Salmonella* virulence plasmid (*pefI-srgD-srgA-srgB-rck-srgC*) and a single gene horizontal acquisition in the chromosome *srgE* (Ahmer, 2004). *Salmonella* does not detect AHL when passing through the gastrointestinal tracts of several animal species, suggesting that the normal microbiota does not produce AHLs. However, SdiA does become activated when *Salmonella* transits through turtles colonized with *Aeromonas hydrophila* or mice infected with *Yersinia enterocolitica*. Therefore, *Salmonella* appears to use SdiA to detect the AHL production of other pathogens rather than the normal gut flora (Michael, 2001).

Even though food microbiologists often conduct experiments using planktonic cells, which are nonadherent bacteria growing as individual cells in liquid culture, biofilms are more likely to be a concern in the food industry. Human pathogens form biofilms on food and food contact surfaces, thereby enhancing their ability to survive harsh environments, resist antimicrobial treatments, and persist in the food processing environment. Biofilms may cause persistent low-level contamination of foods, and the presence of food borne pathogens in a biofilm could cause food safety concerns. Cells in biofilms have been shown to detach and inoculate model food systems (Midelet and Carpentier, 2004).

Quorum sensing mechanisms in *Pseudomonas aeruginosa*

The opportunistic bacteria *Pseudomonas aeruginosa* use quorum sensing to coordinate the formation of biofilms, swarming motility, exopolysaccharide production, and cell aggregation (Smith et al., 2008) .These bacteria can grow within a host without harming it, until they reach a certain concentration. Then they become aggressive, develop to the point at which their numbers become sufficient to overcome the host's immune system, and form a biofilm, leading to disease within the host. Another form of gene regulation that allows the bacteria to rapidly adapt to surrounding changes is through environmental signaling. Recent studies have discovered that anaerobiosis can significantly impact the major regulatory circuit of quorum sensing. This important link between quorum sensing and anaerobiosis has a significant impact on production of virulence factors of this organism (Dyszel et al., 2010).Garlic experimentally blocks quorum sensing in *Pseudomonas aeruginosa*. It is hoped that the therapeutic enzymatic degradation of

the signaling molecules will prevent the formation of such biofilms and possibly weaken established biofilms. Disrupting the signaling process in this way is called *quorum inhibition* (Lewis Sauer et al., 2002).

Quorum sensing mechanism in *Vibrio harveyi*

Vibrio harveyi and closely related species such as *Vibrio campbellii* and *Vibrio parahaemolyticus* are amongst the most important bacterial pathogens in the intensive rearing of molluscs, finfish and especially shrimp (Austin and Zhang, 2006).

Vibrios are opportunists that only cause disease when the host organisms are immune-suppressed or otherwise physiologically stressed, with the frequency of infection often being attributable to adverse culture conditions (Alderman and Hastings, 1998). In our laboratories, adverse culture conditions are simulated in laboratory challenge tests by feeding the animals with a suboptimal diet (Defoirdt et al., 2005). In order to overcome the negative consequences of adverse culture conditions, farmers traditionally rely on the use of antibiotics. Due to the indiscriminate misuse of antibiotics in aquaculture (Cabello, 2006), vibrios are now resistant to several antibiotics and consequently, antibiotics are no longer effective in treating luminescent vibriosis (Karunasagar et al., 1994), for instance, reported mass mortality in tiger shrimp (*Penaeus monodon*) larvae caused by *V. harveyi* strains with multiple antibiotic resistance that was linked to the use of antibiotics in hatcheries. Hence, the quest for alternative methods to control infections caused by antibiotic-resistant bacteria is an important challenge for the sustainable development of aquaculture.

V. harveyi has been found to use a three-channel quorum sensing system .The first channel of this system is mediated by the harveyi autoinducer 1 (HAI-1), an acylated homoserine lactone (AHL). The second channel is mediated by the so-called autoinducer 2 (AI-2), which is a furanosyl borate diester (Chen et al., 2002). The chemical structure of the third autoinducer, called cholerae autoinducer 1 (CAI-1), is still unknown.

The autoinducers are detected at the cell surface by membrane-bound, two-component receptor proteins that feed a common phosphorylation/dephosphorylation signal transduction cascade (Taga and Bassler, 2003). Central in the signal transduction cascade is the LuxO protein. Phosphorylated LuxO indirectly inhibits production of the transcriptional regulator protein $LuxR_{Vh}$ through the action of five small regulatory RNAs (Tu and Bassler, 2007).

$LuxR_{Vh}$ directly activates the *lux* operon whereas the majority of other quorum sensing-regulated genes appears to be indirectly controlled by $LuxR_{Vh}$ (Waters and Bassler, 2007). Tu and Bassler (2007) recently proposed that the multiple small regulatory RNAs function to translate increasing autoinducer concentrations into a precise gradient of $LuxR_{Vh}$, resulting in a gradient of expression of quorum sensing-regulated target genes. In other words, the concentration of $LuxR_{Vh}$ depends on the concentration of the five small regulatory RNAs, which is determined by the phosphorylation status of LuxO. The phosphorylation status of LuxO in its turn is determined by the net result of the kinase and phosphatase activities of the three receptors and thus dependent on the concentration of the three autoinducers (Fig. 5).

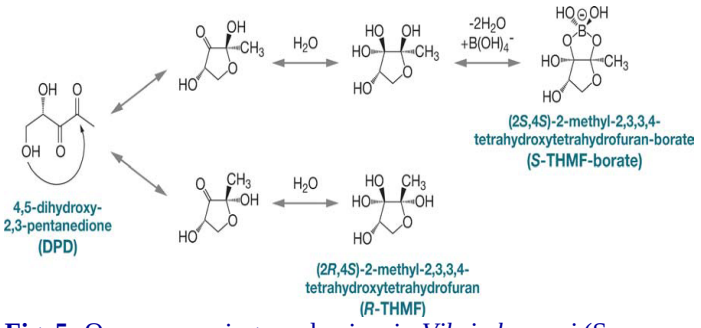

Fig. 5: Quorum sensing mechanism in *Vibrio harveyi* (Source: Miller et al., 2004).

Quorum sensing mechanism in *Agrrobacterium tumefactiens*

Agrobacterium tumefaciens is a bacterial organism which utilizes quorum sensing to signal the process of conjugation in the presence of a high-density population of bacterial cells. The function of this organism is to induce crown gall tumors within a variety of plant strains. The genes which permit the organism to exhibit this virulent quality reside on a large tumor-inducing (Ti) plasmid, shown in (Fig. 6). There exists two main regions, common to all strains, located on this plasmid which are essential for tumor-induction (Kunik et al., 2001). The first of these is the Vir region, which contains genes that are expressed in the bacterium. These genes are required for T-DNA transfer to plant cells, in addition to affecting the efficiency of this transfer. The second main region is the T region which

is transferred to the plant cell, where it, then, becomes integrated into one of the host chromosomes as T-DNA. The T-DNA encodes for the production of the plant hormones auxin and cytokinin, responsible for tumor formation, in addition to a specific amino-acid derivative called an opine (Vaudequin-Dransart et al., 1998).

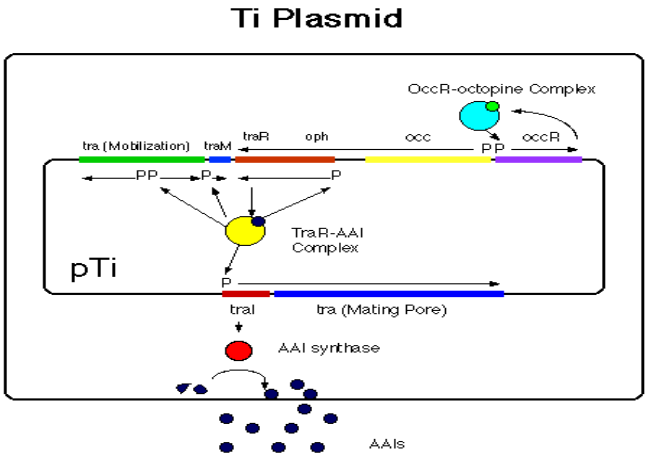

Fig. 6: Ti Plasmid from *Agrobacterium tumefaceins* (Source: Kunik et al., 2001).

Thus, the *Agrobacterium tumefaciens* infects plant cells by injecting them with the Ti plasmid. The plant cells, then secrete the opines, which are produced from the T-DNA. The opines then serve as a component of the signaling process which causes conjugation of the *A. tumefaciens* cells. This is accomplished by a Ti plasmid encoding system, within the bacterial cells, which is required in order for the bacteria to catabolize the opines, in addition to a conjugation system that transfers the Ti plasmid to bacterial recipients.

Regulation of this system is operated through a locus known as *acc* located on the Ti plasmid pTiC58. A specific example of this occurs within *Agrobacterium tumefaciens* strains which contain the pTiC58 tumor-inducing plasmid, or nopaline-type *A. tumefaciens*. This strain synthesizes the agrocinopines A and B. The *acc* locus confers utilization of and chemotaxis toward agrocinopines A and B, in addition to susceptibility to the antiagrobacterial antibiotic, agrocin 84. The *acc* locus is composed of eight genes: *accR* and *accA* through *accG*. The genes within this locus can be divided into three groups based upon function as shown in (Fig. 7): regulation of the expression of the operon, uptake of agrocinopines A and B and agrocin 84, and the metabolism of the opines and, possibly, that of agrocin 84. The first gene within the operon, *accR*, codes for a repressor, which functions to repress one of the phenotypes, forcing the cell to synthesize only one of the opines. The genes *accABCDE* are known to code for a periplasmic protein-dependent ABC-type transport system which regulates the uptake of the agrocinopines as well as the agrocin 84. The genes *accF* and *accG* encode for enzymes which catabolize the opines (Vaudequin-Dransart et al., 1998). conjugal transfer. TraM, then, modulates the system such that transfer is not induced until the cells encounter the environment of a tumor producing the conjugal opines. Thus, the system ensures that the energy-utilization process of conjugal transfer does not initiate until the conditions are favorable for the transfer process (Wood et al., 2001).

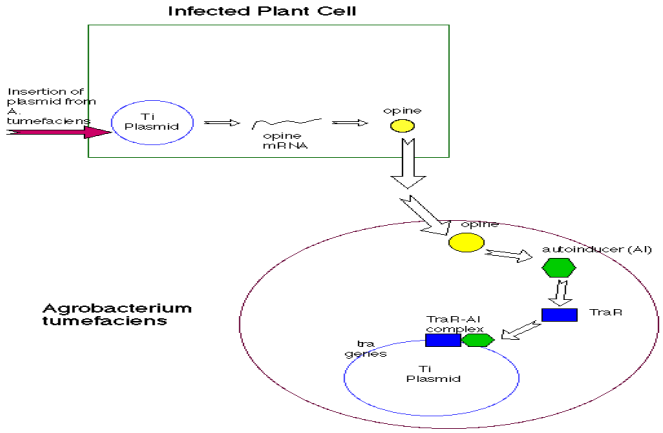

Fig. 7: Mechanism of conjugal transfer within *A. tumefaciens* by the process of quorum sensing (Source: Kunik et al., 2001).

Quorum sensing mechanism in nitrogen fixing *Rhizobacterium* species

Bacterial populations coordinately regulate gene expression by producing diffusible signal molecules. These signals, known as autoinducers, accumulate extracellularly and interact specifically with a receptor protein to affect changes not related to their own metabolism. Production of autoinducers typically occurs at specific stages of growth or in response to changes in the environment and induces a concerted response once a critical concentration has been reached. These diffusible signals frequently act to induce gene expression in response to bacterial cell density in a process often referred to as quorum sensing (Fuqua et al., 2001; Gray, 1997).

Recent publications have shown that quorum sensing plays a major role in preparing and perhaps coordinating the symbiotic nitrogen-fixing rhizobia during the establishment of their interactions with the host plant

(Wisniewski-Dye and Downie, 2002). The sybionts are known with one another by molecular croos talk which is similar to quorum sensing. In addition to the well-characterized signal molecules (flavonoids, Nod factors, and exopolysaccharides) that are involved in the nodulation process, AHLs produced by bacterial quorum sensing can now be included in the list of symbiotic signals. As discussed (Fig. 8) below, quorum sensing has recently been linked to various phenomena including nodulation efficiency, symbiosome development, exopolysaccharide production, and nitrogen fixation, all of which are important for the establishment of a successful symbiosis (Wisniewski-Dye and Downie, 2002).

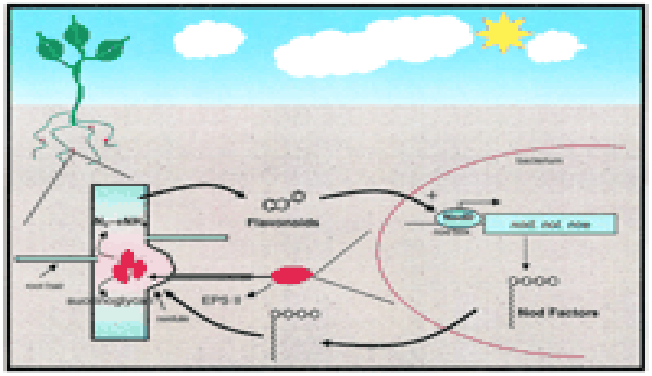

Fig. 8: Mechanisms of molecular cross talk in nitrogen fixing bacteria and the symbiotic plant (Source: Wisniewski-Dye and Downie, 2002).

Quorum sensing mechanism in some social insects

Social insect colonies are an excellent example of a decentralized system, because no individual is in charge of directing or making decisions for the colony. Several groups of social insects have been shown to use quorum sensing in a process that resembles collective decision-making (Mallon and Pratt, 2001).

Ants

Colonies of the ant (*Temnothorax albipennis*) nest in small crevices between rocks. When the rocks shift and the nest is broken open, these ants must quickly choose a new nest to move in to. During the first phase of the decision-making process, a small portion of the workers leave the destroyed nest and search for new crevices. When one of these scout ants finds a potential nest, she assesses the quality of the crevice based on a variety of factors including the size of the interior, the number of openings (based on light level), and the presence or absence of dead ants (Franks and Dornhaus et al., 2006). The worker then returns to the destroyed nest, where it will wait for a short period before recruiting other workers to follow her to the nest she found, using a process called tandem running. The waiting period is inversely related to the quality of the site; for instance, a worker that has found a poor site will wait longer than a worker that encountered a good site (Mallon and Pratt, 2001). As the new recruits visit the potential nest site and make their own assessment of its quality, the number of ants visiting the crevice increases. During this stage, ants may be visiting many different potential nests. However, because of the differences in the waiting period, the number of ants in the best nest will tend to increase at the greatest rate. Eventually, the ants in this nest will sense that the rate at which they encounter other ants has exceeded a particular threshold, indicating that the quorum number has been reached. Once the ants sense a quorum, they return to the destroyed nest and begin rapidly carrying the brood, queen, and fellow workers to the new nest. Scouts that are still tandem-running to other potential sites are also recruited to the new nest, and the entire colony moves. Thus, although no single worker may have visited and compared all of the available options, quorum sensing enables the colony as a whole to quickly make good decisions about where to move (Mallon and Pratt, 2001).

Honey bees

Honey bees (*Apis mellifera*) also use quorum sensing to make decisions about new nest sites. Large colonies reproduce through a process called budding, in which the queen leaves the hive with a portion of the workers to form a new nest elsewhere. After leaving the nest, the workers form a swarm that hangs from a branch or overhanging structure. This swarm persists during the decision-making phase until a new nest site is chosen (Mallon and Pratt, 2001; Seeley and Visscher, 2006).

The quorum sensing process in honey bees is similar to the method used by *Temnothorax* ants in several ways. A small portion of the workers leave the swarm to search out new nest sites, and each worker assesses the quality of the cavity it finds. The worker then returns to the swarm and recruits other workers to her cavity using the honey bee waggle dance. However, instead of using a time delay, the number of dance repetitions the worker performs is dependent on the quality of the site (Fig. 9). Workers that found poor nests stop dancing sooner, and can therefore be recruited to the better sites. Once the

visitors to a new site sense that a quorum number (usually 10–20 bees) has been reached, they return to the swarm and begin using a new recruitment method called piping. This vibration signal causes the swarm to take off and fly to the new nest location. In an experimental test, this decision-making process enabled honey bee swarms to choose the best nest site in four out of five trials (Seeley and Visscher, 2006).

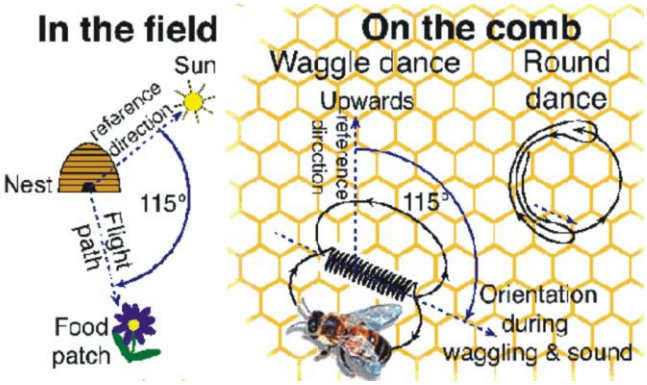

Fig. 9: QS demonstrated by honey bees (Source: www.bees.ucr.edu/dancelanguage.html)

Quorum-quenching and its mechanisms

The term "quorum quenching" was coined to describe all processes that interfere with quorum sensing (Morohoshi et al., 2005). Quorum quenching is the process of blocking or interfering the communication of bacteria (Quorum sensing). It may be achieved by degrading the signaling molecule (Waters and Bassler, 2005). Recently, a well-studied quorum quenching bacteria has been isolated and its AHL degradation kinetic has been studied by using rapid resolution liquid chromatography (RRLC).

Quorum quenching strategies do not aim to kill bacteria or limit their growth. Rather, they affect the expression of a specific function. This is an important feature because these strategies exert a more limited selective pressure for microbial survival than biocide treatments. This is a valuable trait for the development of sustainable biocontrol or therapeutic procedures in the present context of rising antibiotic resistance.

Today, about 70% of the bacteria that cause infections are resistant to at least one of the drugs most commonly used for treatment. Some organisms are resistant to all approved antibiotics and can be treated only with experimental and potentially toxic drugs. A substantial increase in resistance of bacteria that cause community-acquired infections has also been documented, especially in the *staphylococci* and *pneumococci*, which are prevalent causes of disease and mortality. In a recent study, 25% of bacterial pneumonia cases were shown to be resistant to penicillin, and an additional 25% of cases were resistant to more than one antibiotic.

Quorum sensing is crucial for virulence in many pathogenic bacteria that pose significant medical and agricultural threats. In the opportunistic bacterium *Pseudomonas aeruginosa*, quorum sensing signaling controls the expression of several hundred genes, constituting about 6% of the genome .One of these regulated processes is the production of biofilms that are associated with a variety of chronic infections (Smith and Iglewski, 2003). Biofilms consist of sessile bacterial colonies encased in polysaccharide matrices that have been shown to be resistant to antimicrobials and host immune cells; hence, treatment of infected cystic fibrosis patients and immune-compromised individuals has proven difficult (Kravchenko et al, 2006; Tateda et al., 2003). Thus, strategies to interfere with quorum sensing provide new avenues to combating bacterial diseases in humans, animals, and plants. In fact, several antagonistic approaches, such as heterologous overexpression of quorum-quenching lactonases or discovery of inhibitors against the I or R proteins using combinatorial chemistry, have recently been reported (Geske et al., 2005; Smith et al., 2003; Dong et al., 2001; Hentzer et al., 2003). Interference with quorum sensing affords the great benefit of controlling infectious bacteria without interfering with growth, thus avoiding the type of selection pressure that frequently results in development and selection of resistant bacterial strains to antibiotics when traditional antibiotic treatments are used (Rasmussen and Givskov, 2006).

Prospective and demonstrated quorum- quenching strategies

The first example of natural inhibition of AHL signal sensing involves AHLs themselves. *N*-decanoyl-HSL (C10-HSL) and *N*-(3-oxo) tetradecanoyl-HSL (3O, 14C-HSL) were reported to inhibit the production of the antibiotic pigment violacein by *Chromobacterium violaceum*, a quorum sesing-dependent function controlled by *N*-hexanoyl-HSL (C6-HSL). Similarly, the acyl length and the substitution of the acyl chain can perturb quorum sensing -regulated functions such as *V. fischeri* luminescence or conjugal transfer in *Agrobacterium tumefaciens*. Other natural compounds

are capable of interfering with quorum sensing - regulated functions in vivo. Their mode of action and chemical structure frequently remain unknown. These compounds often compete with AHL for binding to the LuxR-like receptor. This prevents quorum sensing regulation from occurring. In addition, because AHLs are involved in the conformation and stabilization of the receptor, competition can lead to an increased degradation of this peptide. One of the main classes of quorum sensing inhibitors is composed of the furanones. Some of these molecules, which are produced by the red algae *Delisea pulchra*, were shown to inhibit the formation of bacterial biofilms. Some bacterial cyclopeptides (i.e., cyclo(Ala-Val)) also perturb quorum sesing quorum sensing-regulated functions. Penicillic acid and patulin are produced by fungi and were also reported as quorum sensing inhibitors. Last, but not least, numerous quorum sensing inhibitors were also discovered in the extracts of several plants, such as *Allium sativum*, *Chlamydomonas reinhardtii*, *Fragaria vesca*, *Glycina max*, *Lycopersicum esculentum*, *Medicago truncatula*, *Oryza sativa*, *Pisum stivum*, and *Vanilla*. One of these quorum sesing inhibitors was identified as L-canavanine in *Medicago sativa*, and appears to be produced in large quantities by alfalfa and other legumes. Three main enzymatic mechanisms have been clearly described: lactone hydrolysis, amidohydrolysis and oxidoreduction (Choo and Rukayadi, 2006).

Quorum quenching in basic research and biotechnological applications

Naturally occurring quorum-quenching processes are being tested as novel antimicrobial therapies. Overexpression of *aiiA* in tobacco and potato plants confers resistance to *E. carotovora*, which requires AHL-controlled virulence factor expression to cause disease (Dong et al., 2001). Likewise, coculture of *Bacillus thuringiensis* decreased *E. carotovora*–mediated plant disease in an *aiiA*-dependent manner. Mice treated with synthetic antagonists of *S. aureus* AIP show resistance to infection (Mayville et al., 1999). Similarly, purified halogenated furanones appear to attenuate virulence of bacteria in mouse models (Hentzer et al., 2003). These and other examples predict that inhibition of quorum sensing offers an attractive alternative to traditional antibiotics because these strategies are not bactericidal and the occurrence of bacterial resistance therefore could be reduced. Likewise, approaches aimed at promoting beneficial quorum sensing associations may enhance industrial scale production of natural or engineered bacterial products.

Quorum-quenching molecules have proved to be valuable tools in addressing both the basic and the conceptional questions .Skin lesions on inoculated mice were reduced when AIP-II, the group-specific cell-to-cell communication signal produced by group-II *S. aureus*, was included in the inoculum mixture of group-I *S. aureus* bacterial cells (Mayville et al., 1999). The experiment identified the key structural features of the signals involved in activation and antagonism, and led to the design of a global inhibitor of the virulence response in *S. aureus* (Lyon et al., 2000). Since the discovery of the first quorum-quenching enzyme encoded by aiiA the prokaryotic-origin AHL-lactonases and AHL-acylases have been frequently used in investigations of the role of AHL signals owing to the convenience in cloning and expression.

More recently, the importance of AHL quorum-sensing signalling in the regulation of virulence and other physiological functions in *Burkholderia thailandensis* and *Erwinia amylovora* has been demonstrated by expression of the AHL-lactonases encoded by the *aiiA* homologues in these two pathogens, respectively (Ulrich, 2004; Molina et al., 2005).

E. carotovora infection (Dong et al., 2001) Pseudomonas aeruginosa decreases production of elastase, rhamnolipids, hydrogen cyanide and pyocyanin and inhibits bacterial swarming (Reimmann et al., 2002) *Escherichia coli* attenuates the pathogenicity of *E. carotovora* when co-inoculated *Bacillus thuringiensis* the efficiency of biocontrol against *E. carotovora* infection is dependent on AHL-lactonase *Burkholderia thailandensis* reduces the bacterial swarming and twitching motility, prevents the b-haemolysis of sheep erythrocytes (Ulrich, 2004) *Erwinia amylovora* impairs extracellular polysaccharide production and tolerance to hydrogen peroxide, and reduces the fire blight symptom on apple leaves (Molina et al., 2005) attM, aiiB *Erwinia carotovora* subsp. *atroseptica* decreases maceration in potato tubers (Carlier et al., 2003) paraoxonase PON1 *P. aeruginosa* the serum containing PON1 prevents bacterial biofilm formation in vitro (Ozer et al., 2005) AHL-acylase aiiD P. aeruginosa decreases swarming ability, elastase and pyocyanin production, and attenuates nematode paralysation (Lin et al., 2003) synthetic AIP-II mouse treated mice show resistance to

S. aureus infection (Mayville et al., 1999) 3-oxo-C12-(2 aminocyclo hexanone) *P. aeruginosa* reduces the production of virulence factors and biofilm formation (Smith et al., 2003) furanone mouse attenuates the virulence of *P. aeruginosa* in mouse models (Hentzer et al.,2003) DSF *Candida albicans* inhibits the fungal dimorphic transition that is associated with virulence (Wang et al., 2004) .

The quorum-quenching enzymes, along with other small naturally quorum-sensing inhibitors and synthetic derivatives, have been explored and evaluated as novel antimicrobial agents against different pathogens with promising results. Expression of AiiA in transgenic potato and tobacco plants conferred strong resistance to the bacterial pathogen *E. carotovora*, which required AHL quorum-sensing signals to activate the expression of virulence genes (Dong et al., 2001). Similarly, natural or recombinant AHL-lactonase producing bacterial strains, including *B. thuringiensis*, *Arthrobacter sp*. and *Pseudomonas fluorescens*, protected potato from *E. carotovora* infection when co-inoculated with the pathogen (Molina et al., 2003).

Implication of quorum sensing in host defense

The intriguing findings that the PONs from human and other mammalian species have high catalytic activities against long-chain AHL signals suggest that these quorum-quenching enzymes could be active components of mammalian innate immune systems (Ozer et al., 2005; Yang et al., 2005). However, somewhat unexpectedly, PON1-knockout mice are protected from infection by quorum sensing-dependent *P. aeruginosa* pathogen cells that were introduced intraperitoneally; in sharp contrast, wild-type mice show a high percentage of mortality (Ozer et al., 2005). Subsequent analysis showed that the transcriptional expressions of PON2 and PON3 are significantly enhanced in the PON1-deficient mice (Ozer et al., 2005). This compensation-like phenomenon may explain the enhanced resistance to *P. aeruginosa* infection in PON1-deficient mice. Moreover, it may be worthy to note that in humans, PON1 expression is limited to the liver and PON3 primarily to liver and kidney, whereas PON2 is found in most tissues including the heart, kidney, liver, lung, placenta, small intestine, spleen, stomach and testis (Ng et al., 2005). Thus, if the expression pattern of PONs in mouse is similar to that in humans, one may speculate that PON2 may be more important in defense against intraperitoneally injected pathogens than the two tissue specific members. This is the case even though PON2 and PON3 can circulate and reach different tissues through blood vessels (Ng et al., 2005). Among the three members of the PON family, PON1 is the best characterized, but very little is known about PON2 and PON3. The overlapping lactonase activity and the potential compensation mechanisms of these PONs suggest that coordinated investigation is essential to unveil the role and implications of these endogenous quorum-quenching enzymes in the host innate defense against microbial pathogens. *Pseudomonas aeruginosa* is an opportunistic pathogen. Patients with cystic fibrosis, severe burns, or immunosuppression are at particularly high risk of *P. aeruginosa* infection. In addition, the pathogen also frequently causes nosocomial bloodstream infections, which cause significant patient mortality and increased health care costs.

Plants as sources of quorum quenching substances

Cell-cell communication or “quorum sensing” between members of a population is an established phenomenon that has been described for many different bacterial species. A number of different types of quorum sensing systems have been discovered; however, a unifying theme is the synthesis of a small signal molecule, often called an autoinducer or pheromone, which activates a specific response when it accumulates to a threshold concentration within a population. A relatively new and exciting aspect of the field of quorum sensing that has received much recent attention is “quorum quenching” or interference of a quorum sensing signaling system. This occurs through either the inhibition of a quorum sensing component or the depletion of the signal itself, resulting in an attenuation of the response. In the plant pathogen *Agrobacterium tumefaciens*, an enzyme (BlcC) that destroys the bacterium's quorum sensing signal has been recently described, prompting much speculation that this enzyme is specifically involved in the quenching of the quorum sensing system. A variety of explanations for the adaptive significance of quorum quenching in the quorum sensing system of *A. tumefaciens* and implications for the bacterium's role as a plant pathogen have been suggested in the literature (Khan and Farrand, 2008). However, the role of BlcC in quorum quenching was never directly addressed. In *A. tumefaciens*, the quorum sensing system regulates Ti (tumor-inducing) plasmid conjugation. In this issue (Khan and Farrand, 2008) directly address the biological significance of BlcC by examining its effect on Ti

plasmid conjugation both in culture and in plants. Their study has implications for our understanding of the possible roles in *Agrobacterium* and other bacteria of BlcC-like enzymes, which are generally thought to function as quorum quenchers of proteobacteria. The most widespread and best-studied type of quorum sensing system in proteobacteria is the LuxR-LuxI-type system. The LuxI-type protein synthesizes a small diffusible signal molecule called an *N*-acylhomoserine lactone (AHL), while LuxR is the cytoplasmic receptor for that signal, regulating target genes in response to inducing concentrations of the cognate AHL (Wang et al., 2004). In *A. tumefaciens*, the LuxI-type protein, called TraI, synthesizes the AHL *N*-3-oxooctanoyl-L-homoserine lactone (OOHL), which is recognized with high specificity by the receptor protein

TraR. TraI, TraR, and all known quorum sensing-regulated genes in *A. tumefaciens* occur on the Ti plasmid, which is required for the formation of tumors, called crown galls, on a wide range of host plants. During the infection process, a segment of the Ti plasmid is transferred to the nucleus of host plant cells, where it directs the overproduction of phytohormones (hence, the formation of a tumor) and the production of novel compounds called opines. The infecting strain of *A. tumefaciens* carries the complement of genes, again on the Ti plasmid, that are required for the utilization of the opines as sources of carbon and nitrogen. By thus harnessing the metabolism of the host plant to produce a novel food source, the bacteria provide a specialized niche for themselves and, presumably, a competitive advantage over other plant-colonizing bacteria. What about in plants? To answer this question, those authors inoculated a mix of donors (either the wild type or *blcC* mutants) and recipients at wounds produced on the stems of tomato plants. At regular intervals postinfection, macerates of the infected plant tissue were plated onto selective medium to count donors, recipients, and transconjugants. Although an early and transient effect was observed, it disappeared by about 4 weeks post infection (tumors are visible between 2 and 3 weeks), at which point conjugation frequency was indistinguishable whether *blcC* was expressed or not. Although BlcC does appear to be expressed in plants, it does not seem to have a lasting effect or significant impact on the biological role of TraR-OOHL in the induction of Ti plasmid conjugation (Khan and Farrand, 2008). Is the early and transient effect an "accident," as those authors suggested? Prior to that study, the most compelling argument that *blcC* is not involved in quorum quenching is that it is not upregulated by AHLs and is part of an operon that confers the ability to grow on GBL but not AHLs. This also argues against a specific role of BlcC in quorum quenching of signals from other bacteria in the rhizosphere. It was shown previously that purified AiiA has a much higher level of activity on AHLs than on GBL, and thus, its role in quorum quenching is much more convincing (Wang et al., 2004). It is unfortunate that this direct comparison of substrate specificity has not been reported for BlcC, although we predict that activity would be at least similar if not higher for GBL than for HSLs. It is most likely that BlcC has been selected for the degradation of plant-released compounds such as GBL, and activity against HSLs may indeed be an "accident" with an effect minimal enough that it has not been selected against.

Conclusion

Bacteria and social insects occupying diverse niches have broadly adapted quorum sensing systems to optimize them for regulating a variety of activities. In every case quorum sensing confers on bacteria and social insects have the ability to communicate and to alter behavior in response to the presence of other bacteria and social insects. Quorum sensing allows a population of individuals to coordinate global behavior and thus act as a multi-cellular unit. Although the study of quorum sensing is only at its beginning, we are now in a position to gain fundamental insight into how bacteria and social insects build community networks. We will learn how quorum sensing allows populations to act synergistically and how quorum sensing can be used to conquer competitors. We will learn about the assortment of signals that are employed by bacteria and about the biosynthesis of these signals as well as how the information encoded in these chemical signals is processed and transduced to control gene expression.

The emergence of antibiotic resistance in microbial pathogens highlights why it is important to explore new ways to prevent and control infectious diseases. Previous work, in particular the research progress over the past decade or so, has outlined how single-celled bacterial pathogens use quorum sensing, a community genetic regulatory mechanism, to synchronize microbial activities among family members so as to gain an upper hand in microbe–microbe and pathogen–host interactions. In addition to this rapid progress in understanding quorum-sensing, novel quorum-

quenching mechanisms have been discovered that interfere effectively with microbial quorum sensing; these have been consecutively found in a wide range of organisms, including both prokaryotes and eukaryotes. These naturally occurring quorum-quenching mechanisms act by blocking the key steps of quorum sensing, such as signal generation, signal accumulation or signal reception. They have promising potential in both basic research and biotechnological applications. Quorum quenching could also be a host innate defense mechanism.

Conflict of interest statement

Authors declare that they have no conflict of interest.

Acknowledgement

The authors would like to acknowledge Jimma University, College of Natural Science, Department of Biology, for providing facilities.

References

Ahmer, B.M., 2004. Cell-to-cell signalling in *Escherichia coli* and *Salmonella enterica*. Mol. Microbiol. 52(4), 933-945.

Aldeman, D.J., Hastings, T. S., 1998. Antibiotic use in aquaculture: development of antibiotic resistance—potential for consumer health risks. Int. J. Food Sci. Technol. 33. 139-155.

Ansaldi, M., Marolt, D., Stebe, T., Mandic-Mulec, I., Dubnau, D., 2002. Specific activation of the *Bacillus* quorum-sensing systems by isoprenylated pheromone variants. Mol. Microbiol. 44, 1561-1573.

Antunes, L. C., Schaefer, A. L., Ferreira, R. B., Qin, N., Stevens, A. M., Ruby, E. G., Greenberg, E. P., 2007. Transcriptome analysis of the *Vibrio fischeri* LuxR-LuxI regulon. J. Bacteriol. 189, 8387-8391.

Austin, B., Zhang, X. H., 2006. *Vibrio harveyi*: A significant pathogen of marine vertebrates and invertebrates. Lett. Appl. Microbiol. 43, 119-124.

Beatty, C. M., Browning, D. F., Busby, S. J., Wolfe, A. J., 2003. Cyclic AMP receptor protein-dependent activation of the *Escherichia coli* acsP2 promoter by a synergistic class III mechanism. J. Bacteriol. 185, 5148-5157.

Booth, M. C., Bogie, C. P., Sahl, H.G., Siezen, R. J., Hatter, K. L., Gilmore, M. S., 1996. Structural analysis and proteolytic activation of *Enterococcus faecalis* cytolysin, a novel lantibiotic. Mol. Microbiol. 21, 1175-1184.

Britton, M., Sacks, L., 2004. The SECOAS Project—Development of a Self-Organising, Wireless Sensor Network for Environmental Monitoring (PDF). SANPA.

Cabello, F. C., 2006. Heavy use of prophylactic antibiotics in aquaculture: a growing problem for human and animal health and for the environment. Environ. Microbiol. 8, 1137-1144.

Carlier, A., Uroz, S., Smadja, B., Fray, R., Latour, X., Dessaux, Y., Faure, D., 2003. The Ti plasmid of *Agrobacterium tumefaciens* harbors an attM-paralogous gene, aiiB, also encoding N-acyl homoserine lactonase activity. Appl. Environ. Microbiol. 69, 4989-4993.

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

Choo, J. H., Rukayadi, Y., Hwang, J. K., 2006. Inhibition of bacterial quorum sensing by vanilla extract. Lett. Appl. Microbiol. 42, 637-641.

Defoirdt, T., Bossier, P., Sorgeloos, P., Verstraete, W., 2005. 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. 7, 1239-1247.

Dong, Y. H., Wang, L. H., Xu, J. L., Zhang, H. B., Zhang, X. F., Zhang, L. H., 2001. Quenching quorum sensing-dependent bacterial infection by an N-acyl homoserine lactonase. Nature. 411, 813-817.

Dufour, P., Jarraud, S., Vandenesch, F., Greenland, T., Novick, R. P., 2002. High genetic variability of the agr locus in *Staphylococcus species*. J. Bacteriol. 184, 1180-1186.

Dyszel, J. L., Smith, J. N., Lucas, D. E., 2010. *Salmonella enterica*, serovar and *S. typhimurium* can detect acyl homoserine lactone production by *Yersinia enterocolitica* in mice. J. Bacteriol. 192(1), 29-37.

Eberhard, A., Burlingame, A. L., Eberhard, C., Kenyon, G. L., Nealson, K. H., Oppenheimer, N. J., 1981. Structural identification of autoinducer of *Photobacterium fischeri* luciferase. Biochem. 20(9), 2444-2449.

Engebrecht, J., Silverman, M., 1984. Identification of genes and gene products necessary for bacterial bioluminescence. Proc. Natl. Acad. Sci. USA. 81, 4154-4158.

Franks, N. R., Dornhaus, A., 2006. Not everything that counts can be counted: ants use multiple metrics for a single nest trait. Proc. Royal Soc. B-Biol. Sci. 273(1583), 165-169.

Fuqua, C., Parsek, M. R., Greenberg, E. P., 2001. Regulation of gene expression by cell-to-cell communication. Acyl-homoserine lactone quorum sensing. Annu. Rev. Genet. 35, 439-468.

Geske, G. D., Wezeman, R. J., Siegel, A. P., Blackwell, H. E., 2005. Small molecule inhibitors of bacterial quorum sensing and biofilm formation. J. Am. Chem. Soc. 127, 12762-12763.

Gray, K. M., Garey, J. R., 2001. The evolution of bacterial LuxI and LuxR quorum sensing regulators. Microbiology. 147(Pt 8), 2379-2387.

Henke, J. M., Bassler, B. L., 2004. Three parallel quorum-sensing systems regulate gene expression in *Vibrio*

harveyi. J. Bacteriol. 186, 6902-6914.

Hense, B. A., Kuttler, C., Müller, J., Rothballer, M., Hartmann, A., Kreft, J. U., 2007. Does efficiency sensing unify diffusion and quorum sensing? Nature Rev. Microbiol. 5(3), 230-239.

Hentzer, M., Wu, H., Andersen, J. B., Riedel, K., Rasmussen, T. B., Bagge, N., Kumar, N., Schembri, M. A., Song, Z., Kristoffersen, P., 2003. Attenuation of *Pseudomonas aeruginosa* virulence by quorum sensing inhibitors. Eur. Mol. Biol. Org. J. 22, 3803-3815.

Ji, G., Beavis, R. C., Novick, R. P., 1995. Cell density control of staphylococcal virulence mediated by an octapeptide pheromone. Proc. Natl. Acad. Sci. USA. 92, 12055-12059.

Kaplan, H. B., Greenberg, E. P., 1985. Diffusion of autoinducer is involved in regulation of the *Vibrio fischeri* luminescence system. J. Bacteriol. 163, 1210-1214.

Karunasagar, I., Pai, R., Malahti, G. R., 1994. Mass mortality of *Penaeus monodon* larvae due to antibiotic-resistant *Vibrio harveyi* infection. Aquacult. 128, 203-209.

Khan, S. R., Farrand, S. K., 2008. The BlcC (AttM) lactonase of *Agrobacterium tumefaciens* does not quench the quorum sensing system that regulates Ti plasmid conjugative transfer. J. Bacteriol. 191, 1320-1329.

Kravchenko, V. V., Kaufmann, G. F., Mathison, J. C., Scott, D. A., Katz, A. Z., Wood, M. R., Brogan, A. P., Lehmann, M., Mee, J. M., Iwata, K., Pan, Q., Fearns, C., Knaus, U. G., Meijler, M. M., Janda, K. D., Ulevitch, R. J., 2006. N-(3-oxo-acyl)homoserine lactones signal cell activation through a mechanism distinct from the canonical pathogen-associated molecular pattern recognition receptor pathways. J. Biol. Chem. 281, 28822-28830.

Kunik, T., Tzfira, T., Kapulnik, Y., Gafni, Y., Dingwall, C., Citovsky, V., 2001. Genetic transformation of HeLa cells by *Agrobacterium*. Proc. Natl. Acad. Sci. USA. 98, 1871-1876.

Lewis Sauer, K., Camper, A., Ehrlich, G., Costerton, J., Davies, D., 2002. *Pseudomonas aeruginosa* displays multiple phenotypes during development as a biofilm. J. Bacteriol. 184 (4), 1140-1154.

Lin, Y. H., Xu, J. L., Hu, J., Wang, L. H., Ong, S. L., Leadbetter, J. R., Zhang, L. H., 2003. Acyl-homoserine lactone acylase from *Ralstonia* strain XJ12B represents a novel and potent class of quorum-quenching enzymes. Mol. Microbiol. 47, 849-860.

Livermore, D. M., 2004. The need for new antibiotics. Clin. Microbiol. Infect. (Suppl. 4), 1-9.

Lupp, C., Ruby, E. G., 2004. *Vibrio fischeri* LuxS and AinS: Comparative study of two signal synthases. J. Bacteriol. 186, 3873-3881.

Lyon, G. J., Mayville, P., Muir, T. W., Novick, R. P., 2000. Rational design of a global inhibitor of the virulence response in *Staphylococcus aureus,* based in part on localization of the site of inhibition to the receptor-histidine kinase, AgrC. Proc. Natl Acad. Sci. USA. 97, 13 330-13 335.

Mallon, E. B., Pratt, S. C., 2001. Individual and collective decision-making during nest site selection by the ant *Leptothorax albipennis*. Behav. Ecol. Sociobiol. 50(4), 352-359.

Mayville, P., Ji, G., Beavis, R., Yang, H., Goger, M., Novick, R. P., Muir, T. W., 1999. Structure–activity analysis of synthetic auto inducing thiolactone peptides from *Staphylococcus aureus* responsible for virulence. Proc. Natl Acad. Sci. USA. 96, 1218-1223.

Michael, B., Smith, J. N., Swift, S., Heffron, F., Ahmer, B. M., 2001. SdiA of *Salmonella enterica* is a LuxR homolog that detects mixed microbial communities. J. Bacteriol. 183(19), 5733-5742.

Midelet, G., Carpentier, B., 2004. Impact of cleaning and disinfection agents on biofilm structure and on microbial transfer to a solid model food. J. Appl. Microbiol. 97, 262-270.

Miller, M. B., Bassler, B. L., 2001. Quorum sensing in bacteria. Annu. Rev. Microbiol. 55, 165-199.

Molina, L., Constantinescu, F., Michel, L., Reimmann, C., Duffy, B., Défago, G., 2003. Degradation of pathogen quorum-sensing molecules by soil bacteria: A preventive and curative biological control mechanism. FEMS Microbiol. Ecol. 45, 71-81.

Morens, D. M., Folkers, G. K., Fauci, A. S., 2004. The challenge of emerging and re-emerging infectious diseases. Nature. 430, 242-249.

Morohoshi, T., Ebata, A., Nakazawa, S., Kato, N., Ikeda, T., 2005. N-Acyl homoserine lactone-producing or -degrading bacteria isolated from the intestinal microbial flora of ayu fish (*Plecoglossus altivelis*). Microb. Environ. 20, 264-268.

Ng, C. J., Shih, D. M., Hama, S. Y., Villa, N., Navab, M., Reddy, S. T., 2005. The paraoxonase gene family and atherosclerosis. Free Radic. Biol. Med. 38, 153-163.

Ozer, E. A., Pezzulo, A., Shih, D. M., Chun, C., Furlong, C., Lusis, A. J., Greenberg, E. P., Zabner, J., 2005. Human and murine paraoxonase 1 are host modulators of *Pseudomonas aeruginosa* quorum-sensing. FEMS Microbiol. Lett. 253, 29-37.

Peysakhov, M., Regli, W., 2005. Ant inspired server population management in a service based computing environment. Proceedings 2005 IEEE Swarm Intelligence Symposium, 2005. SIS 2005. Swarm Intelligence Symposium, Proceedings 2005 IEEE. pp.357-364.

Rasmussen, T. B., Givskov, M., 2006. Quorum-sensing inhibitors as anti-pathogenic drugs. Int. J. Med. Microbiol. 296, 149-161.

Reimmann, C., 2002. Genetically programmed autoinducer destruction reduces virulence gene expression and swarming motility in *Pseudomonas aeruginosa* PAO1. Microbiology. 148, 923-932.

Seeley, T. D., Visscher, P. K., 2006. Group decision making in honey bee swarms. Amer. Scientist. 94(3), 220-229.

Smith, K. M., Bu, Y., Suga, H., 2003. Induction and inhibition of *Pseudomonas aeruginosa* quorum sensing by synthetic autoinducer analogs. Chem. Biol. 10, 81-89.

Smith, J. N., Dyszel, J. L., Soares, J. A., Ellermeier, C. D., Altier, C., Lawhon, S. D., Adams, L. G., Konjufca, V., Curtiss, R., Slauch, J. M., Ahmer, B. M., 2008. SdiA, an N-acylhomoserine lactone receptor, becomes active during the transit of *Salmonella enterica* through the gastrointestinal tract of turtles. PLoS ON. 3(7), e2826.

Taga, M. E., Bassler, B. L., 2003. Chem communication among bacteria. Proc. Natl. Acad. Sci. USA. 100(Suppl. 2), 14549-14554.

Tateda, K., Ishii, Y., Horikawa, M., Matsumoto, T., Miyairi, S., Pechere, J. C., Standiford, T. J., Ishiguro, M., Yamaguchi, K., 2003. The *Pseudomonas aeruginosa* autoinducer N-3-oxododecanoyl homoserine lactone accelerates apoptosis in macrophages and neutrophils. Infect. Immun. 71, 5785-5793.

Tenover, F. C., Gaynes, R. P., 2000. The epidemiology of *Staphylococcus aureus* infections. In: Gram-Positive Pathogens (Eds.: Fischetti, V.A., Novick, R.P., Ferretti, J.J., Portnoy, D.A., Rood, J.J.). ASM Press, Washington, DC. pp.414-421.

Tu, K. C., Bassler, B. L., 2007. Multiple small RNAs act additively to integrate sensory information and control quorum sensing in *Vibrio harveyi.* Genes Dev. 21, 221-233.

Ulrich, R. L., 2004. Quorum quenching: enzymatic disruption of N-acylhomoserine lactone-mediated bacterial communication in *Burkholderia thailandensis*. Appl. Environ. Microbiol. 70, 6173-6180.

Vaudequin-Dransart, V., Petit, A., Chilton, W. S., Dessaux, Y., 1998. The cryptic plasmid of *Agrobacterium tumefaciens* cointegrates with the Ti plasmid and cooperates for opine degradation. Mol. Plant-microbe Interact. 11, 583-591.

Visick, K. L., Foster, J., Doino, J., McFall-Ngai, M., Ruby, E. G., 2000. *Vibrio fischeri* lux genes play an important role in colonization and development of the host light organ. J. Bacteriol. 182, 4578-4586.

Wang, L. H., Weng, L. X., Dong, Y. H., Zhang, L. H., 2004. Specificity and enzyme kinetics of the quorum quenching N-acyl homoserine lactone lactonase (AHLlactonase). J. Biol. Chem. 14, 13645-13651.

Waters, C. M., Bassler, B. L., 2005. Quorum sensing: Cell-to-cell communication in bacteria. Annu. Rev. Cell Dev. Biol. 21, 319-346.

Whitehead, N. A., Barnard, A. M., Slater, H., Simpson, N. J., Salmond, G. P., 2001. Quorum sensing in Gram-negative bacteria. FEMS Microbiol. 25, 365-404.

Wisniewski-Dye, F., Downie, J.A., 2002. Quorum-sensing in *Rhizobium*. Antonie Leeuwenhoek. 81, 397-407.

Wood, D. W., Setubal, J. C., Kaul, R., Monks, D. E., 2001. The Genome of the natural genetic engineer *Agrobacterium tumefaciens* C58. Science. 294, 2317-2323.

Yang, F., Wang, L. H., Wang, J., Dong, Y. H., Hu, J. Y., Zhang, L. H., 2005. Quorum quenching enzyme activity is widely conserved in the sera of mammalian species. FEBS Lett. 579, 3713-3717.

Zhang, L. H., Dong, Y.-H., 2004. Quorum sensing and signal interference: diverse implications. Mol. Microbiol. 53, 1563-1571.

Zhang, L. H., 2003. Quorum quenching and proactive host defense. Trends Plant Sci. 8, 238-244.

How to cite this article:
Shamebo, T., Bacha, K., Ketema, T., 2016. Review on quorum sensing and actions of quorum quenching mechanisms in bacteria and some social insects. Int. J. Curr. Trend. Pharmacobiol. Med. Sci. 1(3), 35-49.