Microbial Quorum Sensing and Its Role in Biofilm Formation

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Author's contribution
The sole author designed, analyzed and interpreted and prepared the manuscript.

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ABSTRACT

Quorum sensing is defined as the effect of fluctuation in cells density on the regulation of gene expression within the cell. Approximately all bacteria produce small molecules (auto-inducers) to control Quorum sensing. S-adenosylmethionine (SAM) is responsible for auto-inducers production in Gram-negative bacteria. Auto-inducers interaction with particular receptors provokes different behaviours that are under the control of Quorum sensing The presence of fungal Quorum sensing systems was bare eleven years before after the sighting that farnesol panels filamentation in the pathogenic polymorphic fungus Candida albicans. In the previous era, farnesol has been shown to play manifold roles in C. albicans physiology as a signalling molecule and encouragement damaging effects on host cells and other microbes. In addition to farnesol, the aromatic alcohol tyrosol was also initiated to be a C. albicans QSM regulatory growth, morphogenesis and biofilm formation. In Saccharomyces cerevisiae, two other aromatic alcohols, phenyl ethanol and tryptophol were found to be QSMs regulating morphogenesis during nitrogen starvation conditions. Moreover, population density-dependent performances that look like QS have been labelled in numerous other fungal species. Although fungal QS investigation is still in its beginning, its detection has changed our opinions about the fungal kingdom and might ultimately lead to the growth of new antifungal therapeutics.

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1. INTRODUCTION TO QUORUM SENSING

Quorum sensing is defined as the effect of fluctuation in cells density on the regulation of gene expression within the cell [1]. Quorum sensing is a way of communication between bacterial cells presents within a biofilm through chemicals produced by those bacteria. These signalling chemicals are known as auto-inducers and their production is directly linked with cell density in biofilm [2]. These auto-inducers act as a stimulant to change gene expression within cells of biofilm. Quorum sensing communication pathway is responsible for the regulation of various physiological activities in both Gram-positive and Gram-negative Bacteria [3]. Quorum sensing supports motility, virulence, conjugation, sporulation, competence, biofilm formation and antibiotic production of bacteria [4]. Lactones, acylated homoserine is the autoinducer used by Gram-negative bacteria while processed oligopeptides are autoinducers used by Gram-positive bacteria [3]. These auto-inducers are synthesized by common metabolites like fatty acids; S-adenosylmethionine and anthranilate with one signal synthetase are a battery of enzymes [5]. Quorum sensing is a mean of communication within as well as between bacterial species [6]. These auto-inducers of bacteria also provoke a specific response within the host [7,8]. In Quorum sensing different bacteria use different chemical molecules, different signal rely on the mechanism so that genes targeted by Quorum sensing also differ [9]. This change the overall behaviour of the whole community. Some scientist believes that Quorum sensing system is the early step in the evolution from unicellular to multicellular [10].

2. QUORUM SENSING IN BACTERIA AND ITS ROLE IN BIOFILM FORMATION

Approximately all bacteria produce small molecules (auto-inducers) to control Quorum sensing. S-adenosylmethionine (SAM) is responsible for auto-inducers production in Gram-negative bacteria. Auto-inducers interaction with particular receptors provokes different behaviours that are under the control of Quorum sensing [11]. Membrane-bound histidine sensor kinase or cytoplasmic transcription factors act as receptors for auto-inducers responsible for Quorum sensing [12]. When these auto-inducers are recognized by receptors the phenomena is called Autoinduction. This Autoinduction enhancer the production of auto-inducers via feed-forwarded regulatory loop mechanism. Optimized Incorporation of Auto-inducers-encoded information and ideal Quorum sensing dynamics are the consequences of different features like small regulatory RNAs and positive and negative feedback loop [13]. Quorum sensing is responsible for the formation of microbial communities. For instance, various bacterial species that belongs to human GIT tract normal flora are capable of producing auto-inducers. They can also respond to the auto-inducers produced by other bacteria. There is an enhancing proof that Quorum sensing regulates various key physiological processes in the human digestive tract and it has a strong effect on the virulence mechanism of foreign invader microbes [14].

For a long time, it was a strong belief that prokaryotes are unicellular organism and each of them exist independent. They do not show any coordination among them. There are no multicellular behavioural activities in prokaryotes [15]. Now Microbiologist knows that an unexpectedly high degree interactive multicellular behaviour of bacteria is responsible for Biofilm (cities of microbes) formation. Various bacteria regulate various group activities and the physiological process by producing, detecting and responding to small molecules through a mechanism called Quorum sensing [16]. Various bacteria need a certain level of cell density within-host body to express their virulence and to overcome the host immune system before starting an infectious disease [17]. This cell-cell communication (Quorum sensing) between bacterial cells play a key role in bacterial social activities, imitation of infectious diseases and Biofilm formation [18]. Intracellular communication within the bacterial community is regulated by production, recognition and responds to auto-inducers. The process of Quorum sensing was first discovered within marine bioluminescent bacteria Vibrio fischeri [19].

V. fischeri lives in symbiotic relation with various marine animals. In these relationships, V. fischeri provide light to these host organisms that protect them from predators, help to attract prey and matting [20]. In return, V. fischeri obtains nutrition from its host. A luciferase enzyme complex present in V. fischeri produces light.
3. BIOFILM

Biofilms are the cohesive syntrophic consortium of bacteria produced as a result of the combination of the extracellular matrix of EPS (exopolysaccharide) and proteins. It also has the ability to adhere to biotic and abiotic surfaces. Bacteria start the ability to adherence to biotic and abiotic surfaces. (exopolysaccharide) and proteins. It also has the combination of the extracellular matrix of EPS of bacteria produced as a result of the formation, spore synthesis, production of fruiting bodies, symbiotic, gene competency, pathogenesis and programmed cell death [22].

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different *C. albicans* morphological forms in biofilm structure Ramage et al. assessed the effects of farnesol on biofilm development {Ramage, 2002 #8}. They observed that in addition to its role in regulating *C. albicans* morphology, farnesol reserved biofilm formation. Moreover, they presented that the rate of the reserve was reliant on how much time the cells had to stick to before farnesol was added. Once the cells started to filament the adding of farnesol had no consequence on the expansion of biofilm structure but cells on mature biofilms replied to the isoprenoid and this effect may influence biofilm dispersal (Nickerson, 2006). Microarray analysis of biofilms unprotected to farnesol discovered that genes related to drug resistance, cell wall upkeep, cell surface hydrophobicity, iron transport and heat shock proteins were prejudiced in adding to the genes associated with hyphae formation.

5. VIRAL QUORUM SENSING

Not all viruses do quorum sensing except a few viruses like phages. Phage reproduction depends on bacterial cells and thus it is perilous for phages to control plan of reproduction to cell host cell densities {SINGH, 2017 #10} explain the regulatory mechanism controlling host cell density reliant on lysis-lysogeny verdict made by Vibrio phage that is reliant on upon a host QMS. Bacteriophages are either temperate or obligate viruses that infect bacteria. Within inside the cell infection, temperate bacteriophage can either enter the lytic or lysogenic cycle. In lytic cell releasing progeny virion upon lysis of the bacterial cell or integrate to the host bacterial genome. Under the certain conservational condition, a prophage of the integrated cell may become persuaded and enter again the lytic reproduction cycle. The lysis-lysogeny also has a vital impact on host metabolism, population dynamics, ecological processes and phage dissemination (Xue, 2015 #2). Previous studies described that temperate phages also have specific mechanisms to detect the host cell density. The first-ever experimental indication of cell density-dependent prophage induction linked to QMS was studied by () in groundwater and soil bacteria and a model system of *E. coli*. A model bacterial system was used to studies the basic molecular level regulatory mechanism. The homoserine lactone based induction mechanism was SOS independent {Hall, 2011 #3}.

Numerous studies have also revealed that phage profusion is positively associated with host density in a diversity of environments, and lytic infections are preferred under auspicious conditions supporting quick cell growth, whilst sogeny becomes more communal under situations less auspicious for growth with lower cell density. However, in some high-host-density environs, such as the ruminant gut, lysogenic replication may be preferred consequent the Piggyback-The-Winner model It is serious to examine the molecular mechanisms overdue the phage-host interfaces for better sympathetic of microbial ecology and procedures {Høyland-Kroghsbo, 2013 #4}.

Bacteria can harvest, secrete, and detect signal molecules (“autoinducer,” Al) for cell-cell communication to organize a wide range of group behaviours; a process called QS, that is cell density reliant on. recently considered a new QS circuit that comprises a cytoplasmic receptor and transcription factor, VqmA, and an Al 3,5-dimethyl pyrazin-2-ol (DPO). The authors hypothesized that phages might be capable of utilizing the host QS system for lysis-lysogeny decisions, thus took a further step and evaluated the hypothesis. collected VqmA homologs to identify DPO-binding proteins of viral origin through bioinformatics analyses. Interestingly, one such protein, VqmApag, of virophage VP882, can cause host cell lysis and cell density decline, similarly as mitomycin C (MMC) inducing lytic reproduction of VP882 phages.{Liang, 2019 #5}demonstrated that the activation of VqmApag by binding to host-produced QS Al launches the phage lytic life cycle This gives a new perspective on phage-host interaction in which phage proteins use host-signalling molecules as cues for reproductive fate (i.e., lytic-lysogeny) decisions.

6. APPLICATIONS OF QUORUM SENSING

6.1 Biosensors

An interesting application of Quorum Sensing is in the engineering of whole-cell microbial biosensors to distinguish pathogenic microbes present in the environment with diseased host organisms. Quorum Sensing has also been used to produce engineered bacteria capable of attacking cancer cells. It is probable to visualize the creation of new anti-cancer therapeutics by the addition of cancer-destructing elements to these microbial biosensors. Another function of QS and quorum quenching lies in the designing of transgenic plants that can protect themselves against general bacterial pathogens.
6.2 Pathogen Diagnostics and Therapeutics

The majority of the whole-cell QS biosensors that have been explained so far recognize Gram-negative AHLs [13] (Steindler and Venturi 2007). A standard AHL biosensor contains an AHL responsive transcriptional regulator also a cognate promoter, which directs the transcription of a reporter gene. It has been recommended that QS signals only can be used as markers for the occurrence of pathogenic bacteria in clinical and environmental samples. Thus, QS signals should not be engaged as the only inputs for microbial biosensors. However, Quorum sensing-based amplification circuits can still be used to engineer biosensing circuits to find the occurrence of pathogenic microbes in contaminated groundwater products, dairy, and meat products. Upcoming design directions will include the formation of ingestible whole-cell biosensors by launching QS-based biosensing devices into GRAS organisms such as lactic acid bacteria (Konings et al. 2000). Such diagnostic biosensors would be much useful in identifying the existence of pathogens in the gut microflora. So collecting these results bring up the exciting possibility that future QS-based microbial biosensors may not only detect pathogens but also increase a concerted reaction against them.

7. CANCER DETECTION

The *P. aeruginosa* Quorum Sensing signal 3-oxo-C12-HSL reduces proliferation also induce apoptosis breast cancer cell lines in human (Li et al. 2004).

7.1 Biocontrol

The rhizosphere is a limited region of soil that surrounds a plant’s roots and is affected by secretions from the root also soil microbes in the vicinity. Quorum sensing bacteria form a main component of the rhizosphere community. Scientists have also engaged quorum-quenching enzymes to decrease bacterial virulence against plants. This research proposes that engineering the production also the secretion of quorum-quenching enzymes into plants and plant-associated microbes can also serve as a crop protection plan. Though, QS systems also control necessary functions in useful rhizosphere bacteria, as well as biofilm formation, antibiotic production, and nitrogen fixation (Muller et al. 2009; Sanchez-Contreras et al. 2007). More research is therefore essential to understand the promising effects of quorum quenching on plant biochemical pathways. In brief, while quorum quenching is an attractive approach for biocontrol, more research is essential to demonstrate its safety and efficacy.

7.2 Prevention of Biofouling

Biofouling is the increase of bacteria, algae; also animals like protozoans and crustaceans on surfaces that prolonged contact with water. Biofouling can happen on surfaces as assorted as pipes, tanks, ship hull, membrane bioreactors, medical or dental implants, and catheters. This unwanted growth of living organisms and their secretions lead to contamination, colonization, also corrosion of machine parts expose to water and reduce machine efficiency. Incorporation of Quorum Sensing inhibitors on the device surface is a possible strategy for declining *P. aeruginosa* biofouling of surgical implants. QS inhibition may be used to give defence against many pathogens that rely on QS to start biofilm development.

7.3 Recombinant Gene Expression

Possibly one of the exciting areas for research in quorum sensing is the synthesis of recombinant gene products with metabolic engineering. Quorum sensing has been used to control gene expression and cellular growth. Brief reviews by Toniatti et al. (Toniatti C, et al 2004) discuss some of the progress in control of gene expression through the perceptions of possible gene therapy applications.

7.4 Pathogen/Pest Management

Pathogen and pest (i.e. some organism whose existence in a specific environment is undesirable) management include most of the present applications of quorum-sensing technology. Inhibition of quorum signalling is the evidence and, in practice, most appreciated application of quorum-sensing knowledge.

7.5 Quorum Sensing in Seaweeds

Explaining this title, the quorum sensing is wider spread among bacterial population then was previously thought, in Gram-positive, Gram-negative bacterial communication. Followed by this numerous researchers have concluded that in Gram-negative bacteria acyl-homoserine lactone is dependable for the cell to the cellular communication system.
In gram-positive bacteria, peptide and derivative peptide based signalling molecules appear to be the main mode of communication. Throughout high cell density, the marine bacteria can produce enzymes, surfactants, toxins, antibiotics by the chemical signal communication. Marine epibiotic bacteria are also identified to produce compounds active beside drug-resistant hospital pathogen by the cross-species induction process. Austin described in building on assays (Billaud and Austin 1990) a screening method has been developed in which marine bacteria are confront by exposing them to terrestrial bacteria before assay of antimicrobial compounds. Therefore, in current studies, it is proposed to search the abilities of seaweed epibiotic bacterial organisms to create antibacterial compounds by quorum sensing. These conclusions have important consequences for the discovery of new antimicrobial compounds from marine bacteria and might allow the growth of novel process for screening new compounds effective against multidrug-resistant bacteria.

8. CONCLUSION

In early century, the discovery of antibiotics marked the beginning of active control and prevention of infectious microbial diseases. Extensive use of antibiotics has also unavoidably resulted in the emergence of ‘superbugs’ that resist conventional antibiotics. The finding that many pathogens rely on cell-to-cell communication mechanisms, known as quorum sensing, to synchronize microbial activities essential for infection and survival in the host suggests a promising disease control strategy, i.e. quenching microbial quorum sensing or in short, quorum quenching. Work over the past few years has demonstrated that quorum-quenching mechanisms are widely conserved in many prokaryotic and eukaryotic organisms. These naturally occurring quorum-quenching mechanisms appear to play important roles in microbe-microbe and pathogen-host interactions and have been used, or served as lead compounds, in developing and formulating a new generation of antimicrobials.

An advance study of bacterial quorum sensing process can facilitate the development of novel technologies intended at interfering with bacterial communication and virulence.

The term “quorum sensing” explains the capability of a microorganism to recognize and response to diffusible signal molecules. Bacterial cells sense their inhabitant’s density by a complicated cell-to-cell communication system also triggers expression of exact genes.

COMPETING INTERESTS

Author has declared that no competing interests exist.

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