**Microbial Communication via Quorum Sensing: Influence and Alteration of Gut Ecosystem**

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**Abstract**

*Background:* The cellular communications has been found to regulate numerous microbial events and plays a crucial role in elicitating microbial diversity within the population and overall changes in the surrounding environment. The presence and role of species-specific and inter-species microorganism cell to cell communication and the intrinsic networking of communication within an organization has been recently accepted. It has now been widely accepted that the cellular communications within the microbial system plays an important role in the healthy well-being and as well as in networking.

*Objective:* The mammalian digestive tract contains rich and diverse microbiota on its length. However, extensive studies have been reported on the role and variety of microorganism communities within the gut, scanty work has been reported on QS within the commensal and pathogenic microflora of the tract, with reference to the mode of pathogenesis and infection within the GI tract. The sole patent as of today related to the role of QS in GI tract is said to be on the detection of Lactobacillus strain within the GI Tract.

*Conclusion:* The potential role for QS in GI infections and interaction with commensal microflora is also a very important strategy for the hindrance and treatment.

**INTRODUCTION**

The human body houses diverse microbiome, which live in association with their host many health benefits to the host. Studies of the human microbiome discovered a personal and age-related diversity of microbes, occupying completely different habitats like skin, mouth, exocrine gland, epithelial duct and gut [1]. The human colon harbours an extremely dense microbial community of $10^{11}$-$10^{12}$ cells per gram of gut content [2]. Though the bulk of this community thrives within the lumen, few microbes are found at intervals the protecting mucose layer that covers the animal tissue cells ($10^{5}$-$10^{6}$ cells per cc of mucus) [3]. These microbes constitute the colon ‘mucosal biofilm’ membrane. The biofilms were antecedently outlined as microbial biofilms that are distinctive to the membrane atmosphere. As against to biofilms that grow on inert surfaces, they're modulated by host inflammatory responses, and host proteins and cells contribute to the composition of the animate thing matrix [4]. There is a need to understand the interactive communication within these communities and its influence on human health owing to the ever fluctuating population dynamics between the pathogenic and non-pathogenic strains resulting in disturbances in the microbiota or dysbiosis. Alterations in the microbiota can result from exposure to various environmental factors, including diet, toxins, drugs, and pathogens. Of these, enteric pathogens have the greatest potential to cause microbial dysbiosis as seen in experimental animal models, where foodborne viral pathogens can trigger both local and systemic inflammation altering the composition of the microbiota and barrier function [5]. Another cause of dysbiosis is the frequent use of antibiotics specifically, the broad spectrum antibiotics [6].

It is currently worldwide accepted that several microorganism species use little chemical substances to interact and communicate with one another and with their host. These substances which are typically made at the organismal level and exert their effects as soon as they reach a threshold levels, permitting microorganism to detect and respond to their population according to the signal especially towards enhancing their density [7-9]. In response to the signal when the cells reach a specific density, as this microorganism communication has been involved in improving the cellular density, it been termed as assemble sensing [10]. There are various categories of microbial communication substances, such as acyl-homoserine lactones, peptides, quinolones, and α-hydroxyketones, etc [7-9,11] which are generated and utilized for communication and many more are still emerging.
Role of chemical communications

Studies on the microorganism communication have been targeted completely on laboratory-grown, pure cultures of microorganisms. However, this provides a very artificial setup, in contrast, within the hosts; microbes are normally associated with a large number of different species and are constantly exposed to various opportunities for competition and cooperation. As an example, at elevated “unnatural” concentrations, we all know that microorganism communication molecules will have antimicrobial properties. However, once antibiotics made by microbes within the setting, they’re unlikely to be gift at concentrations high enough to exert antimicrobial activity, thus it’s probable that their main biological function is to modulate microorganism organic phenomenon [1,2,13].

Indeed, chemical communication has been shown to be a vital aspect of microorganism interactions within the soil setting, and samples of communication between totally different microorganism species i.e., between microbes and plants, each in interdependence and pathologic process, exist. Within the N2-fixation-driven interdependence between bacteria genus and its legume host, several chemical signals act to mark a mutualistic relationship [14,15]. The microorganism will sense plant made small molecules; the foundation exudates containing flavonoids induce microorganism migration to the foundation surface. Here, gathering sensing happens through the assembly of acyl-homoserine lactones, culminating within the production of nodulation factors (made from lipochito-oligosacharides) by the microorganism that induce nodule formation within the plant host [14,15].

Quorum sensing and its role in pathogenicity

Quorum Sensing (QS) is the cell-to-cell communication mechanism that refers to the flexibility of microorganism to revert to chemical molecules, referred to as autoinducers (AIs), in their atmosphere in a very dose dependent fashion. The autoinducers are made from microorganism of the same species or bacteria of different genera. Once the autoinducer concentration reaches a crucial threshold, the microorganism discovers and replies to this signal by neutralizing their organic phenomenon. This development permits microorganism to act as a collective unit, i.e., a multicellular entity as against individual cells which perform individual functions.

Recent investigations have revealed that the QS sensing method is activated within the human gut via a collection of acylhomoserine lactone ( AHL) molecules, i.e. signalling molecules made by gram-negative microorganism, which has been reported in human feaces of patients suffering from GI tract diseases as well as in healthy subjects [16]. Moreover, microorganismal QS molecules probably play a crucial role in microorganism colonization on tissue layer i.e., mucosal colonization, which requires QS-mediated biofilm formation [17]. It was Casula and Cutting [18], who provided vital clues on the germination of Bacillus subtilis spores within the murine digestive tract that indicated the probability of requiring signaling peptides for QS pathway activation. Though clear proofs lacking but, it could be probably concluded that QS peptides are found within the human intestinal tract.

Gram-negative microorganism communicates via tiny molecules such as AIs. These are either acylhomoserine lactones (AHLs) or alternative molecules whose production depends on S-adenosylmethionine (SAM) as a substrate [19]. AIs are made within the cell and freely diffuse across the inner and outer membranes. Once the concentration of AIs is sufficiently high, that happens at high cell density, they bind to their respective cytoplasmic receptors that are actually the transcription factors. The AI-bound receptors regulate expression of the genes within the QS regulon (Figure 1C). In some cases of gram-negative microorganism QS, AIs has been detected by two-component histidine kinase receptors (Figure 1D).

There is proof of a probable role for the quorum sensing during the colonization phase of the pathogens when the cell number, density and communication play a crucial role in virulence. It is relatively a straightforward and easy to determine the pathogenic dose in the animal’s model and human studies. However, the LD50 dose may consists of a sub-population that really goes on to cause the morbidity, the remainder might not survive the infection process or might be removed from the gut straightforward (Figure 1; 20).

Hence, development of disease manifestation needs a minimum number of bacterium adhering to their site of action to cause the infection. Typically a brief period of proliferation is required for the bacterium to multiply till it reaches a sufficient numbers, for instance induction of aggressins. The timing and quantum of aggressin expression is highly crucial because the flourishing infectious strain has to reach a sufficient number so as to overcome the host defense before the expression of aggressin is induced. As a result, during the proliferation phase, the aggressin expression is kept to a minimum level to avoid activation of host defense system. The correlation between the onset of pathogenicity and the time regulated production of EPS by Pantoea stewartii [21] and controlled switching from an evasive phenotype to an aggressive phenotype by Staphylococcus aureus have been well documented.

The interaction of pathogens with the commensal bacterium of the gut also will be necessary to understand, particularly in the bacterium like Escherichia coli, where commensal as well as infection causing strains exist. The study of the co-operation and/or competition between this bacterium can provide useful data, and if cell to cell signaling is involved, the balance could be exploited to restore the balance favoring the commensal strain. For instance, as an example, if an infectious agent provides a signal to a barrier microorganism to disperse, permitting the infectious strain to have access to the membrane cells, blockage of this signal might provide a good protection against the pathogenicity and the disease.

As cell density increases, so do the nutritional demands created upon the environment rises and eventually new food sources are also needed. The bacteria could utilize vital amounts of energy liberating newer nutrients throughout the pathological phases and would like to be shielded in this environment. The quorum sensing could be used to influence this by coupling antibiotic synthesis with exoenzyme production, as is seen within the cases of Erwinia carotovora, Pseudomonas aeruginosa and Chromobacterium violaceum [22]. The spread of the bacte-
Figure 1 Canonical bacterial quorum-sensing (QS) circuits. Adapted from Rutherford and Bassler (2012) [20].

ria from colonies is a crucial as well as a necessary step during the colonization cycle and highlights the actual fact that colonization could be a dynamic method with several important events occurring when the adhesion of the bacterium to the tissue layer surface. The biological impact of the signals upon the gut itself may additionally be vital because the immune-modulatory and cardiovascular effects [23,24] would possibly favour colonization of the host by bacterium.

Majority of the quorum sensing mechanism reported has been with regards to the gram-positive strains. However, there is very poor literature available pertaining to the role of gut microbiota and cancer progression. There is increasing evidence pertaining to the role of QS being activated in gut associated diseases [16]. The QS-peptides many also be involved in the onset and progression of colon cancer. However, the actual mechanism of induction needs to be ascertained [25,26].

Bacteria within the gut are separated or rather compartmentalized. The inter-colony and intra-colony communication are directly or indirectly depend upon the physical properties of the signal. The strength and the type of signal, its diffusion and range, and partitioning between lipid membranes and therefore encompassing the fluid medium are some of the crucial factors. It is conceivable that gradients of a signaling molecule may be used to attract or repel bacterium, like signaling from cell associated bacteria to luminal bacteria. The interaction within the gut is further complicated by the dynamic composition of the lumen contents such as the pH, macromolecules and even the intestinal emulsifying agents.

Bacteria are also separated in time and it is as crucial for the signal to be delivered at the right place in the gut but at the same time the timing of the delivery of the target bacteria which is equally important. The LuxS derived signal of *Escherichia coli* that can be degraded within a short time after synthesis [27]. Moreover, it has been shown that a gram-positive bacteria i.e., *Bacillus* spp can readily degrade the acyl-HSL signals of gram-negative bacteria [28]. The apparent advantage of this strategy suggests that analogous activities are also present in an array of bacterial species and against various types of signals. This characteristic phenomenon is of particular importance for those bacteria which colonize the GI tract and in order the survive have entered into dormant state. Researchers are currently working on identification of various detecting techniques to understand the colonization characteristic of gram positive strains in the gastrointestinal tract [29] and simultaneously trying to understand the inhibition of gram-negative bacterial pathogens [30]. As it is now clearly evident that gram-negative QS system could be an ideal target for regulating the dysbiosis, through identifying QS inhibiting system [31] or by quenching it [32].

CONCLUSION

Heightening the impact of signal manipulation among the microbiota could be an important mechanism towards the identification of Al-regulated functions within the microorganism community and to explore feasibility of modulating the Al signaling to revive the protecting functions of the gut microbiota or to influence the microbiota-induced host responses. The identification of candidate bacteria that may seem to favor signal producers could be used as models that may enhance Al-dependent effects. The potential gain from understanding and manipulating the bacterial chemical repertoire working the bacterial community inhabiting the gut, towards the aim of modulat-
ing the composition of the microbiota to our benefit.

For a stronger appreciation of how the microbial ecology of the gut influences the health of the entire organism, it is necessary to understand as to how the bacteria in the gut to influence the dynamics of colonization and its subsequent pathogenicity. The reports so are available suggests that population cell density and cell-to-cell communication are a vital link towards the regulation of microbial activity at intervals the high cell density microorganism population of the gut. It is really a greater challenge to use this information to maintain a healthy gut microbiota.

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REFERENCES