REVIEW

Research progress on quorum sensing system and the formation and regulatory mechanism of bacterial biofilms

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ABSTRACT

This paper systematically summarizes the latest research progress of quorum sensing system and the formation and regulatory mechanism of bacterial biofilms. The role of quorum sensing system in various stages of biofilm formation is described, including initial adhesion, microcolony formation and biofilm maturation. In addition, the molecular mechanism of quorum sensing system to regulate the formation of biofilms and the biofilm prevention and control strategies for quorum sensing system are also discussed. Finally, the future development direction of quorum sensing system and bacterial biofilm research is prospected.

Key Words: Quorum sensing system, Bacterial biofilms, Signaling molecules, Gene regulation, Antimicrobial strategies

1. INTRODUCTION

The quorum sensing system (QS) is an important mechanism of intercellular communication in bacteria, which can coordinate quorum behaviors (such as the formation of biofilms, the production of virulence factors, and antibiotic resistance etc.), by secreting and sensing specific signaling molecules. Bacterial biofilms are structured colonies formed by bacteria on the surface, encapsulated in a self-produced polysaccharide matrix, which has an important biological and medical significance. The formation of biofilms significantly increases the resistance of bacteria to antibiotics and the host immune system, leading to serious problems such as chronic infections and infections associated with medical devices.

In recent years, the relationship between quorum sensing system and bacterial biofilms has attracted extensive attention. Studies have shown that quorum sensing system play a key role in all stages of biofilm formation. A better understanding of the mechanism by which the quorum sensing system regulates biofilm formation is of great significance for the development of novel antimicrobial strategies. The purpose of this article is to review the latest research progress on quorum sensing system and bacterial biofilm formation and its regulatory mechanism, and to provide a reference for the research in related fields.

2. THE BASIC CONCEPT AND THE MECHANISM OF QUORUM SENSING SYSTEM

The quorum sensing system is a communication mechanism between cells. This system allows bacteria to detect changes in quorum density based on the accumulation of signaling molecules generated by themselves, further regulate the expression of related genes, and promote the formation and dis-

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persion of biofilms.[1] The quorum sensing system is mainly composed of signaling molecules, signaling molecule synthetases and receptor proteins. Quorum sensing is a signal exchange system of bacteria. It sends corresponding signals through quorum sensing, regulates the synthesis and secretion of various signaling molecules during the formation of bacterial biofilms, regulates the adhesion and colonization, maturity and dispersion of bacteria, etc.[2]

According to the chemical structure and synthetic pathway of signaling molecules, the quorum sensing systems are mainly divided into three categories: the acylhomoserine lactone (AHL) system for Gram-negative bacteria, the oligopeptide system for Gram-positive bacteria, and the autoinduction-2 (AI-2) system shared by Gram-negative and positive bacteria. These systems are widely present in different bacteria and regulate various physiological processes. When the bacterial quorum density reaches a certain threshold, the concentration of signaling molecules increases, and after binding to the receptor proteins, they activate or inhibit the expression of specific genes, affecting the expression of different genes in bacteria, such as biofilm formation, virulence factor production, antibiotic synthesis and spore formation, etc.[3]

3. The formation process and characteristics of bacterial biofilms

Bacterial biofilms are structured colonies formed by bacteria on the surface, encapsulated in a self-produced polysaccharide matrix. The biofilm formation process can be divided into three stages: initial adhesion, microcolon formation and biofilm maturation. During the initial adhesion stage, bacteria adhere to the surface through the structures such as flagella and pili. Subsequently, the bacteria proliferate to form microcolonies and begin to secrete matrix components such as extracellular polysaccharides. Finally, the biofilm structure gradually gets mature, forming a colony with complex three-dimensional structures. There is a large category of protein pumps in bacterial membranes that can discharge antibiotics from cells. Epis inhibitors (Epis) can block antibiotic effluent. The thiaflavonoid library of effluent pump inhibitors has antimicrobial activity and inhibits effluent pumps, biofilm formation and population induction.[4]

Mature biofilms have unique structural and functional characteristics. The bacteria in the biofilms are encapsulated in a matrix composed of polysaccharides, proteins and DNA, forming a protective barrier. There is a gradient distribution of nutrients and metabolites inside the biofilms, resulting in the heterogeneity of bacteria. Bacteria have the ability to adapt to the new environment and to induce environmental changes. Bacteria adapt to environmental conditions through this mechanism, including pH, permeability, nutritional supply and population density etc. Density sensing system is one of the mechanisms that regulate bacterial survival mode by using the density of sensing quorum survival, controlling the production of bacterial biofilms and bacterial virility.[5] In addition, bacteria in biofilms exhibit different gene expression profiles and physiological characteristics from the plankton state, such as enhanced antibiotic resistance and reduced metabolic activity. These characteristics make biofilms an ideal place for bacteria to survive and reproduce in harsh environments.

4. The role of quorum sensing system in the formation of bacterial biofilms

The quorum sensing system plays an important role in all stages of bacterial biofilm formation. During the initial adhesion stage, the quorum sensing system regulates the expression of bacterial surface adhesion factors, affecting the interaction between bacteria and the surface. For instance, the LasI/LasR system for Pseudomonas aeruginosa regulates the synthesis of type IV fimbriae and flagella, promoting the initial colonization of bacteria on the surface. The oil compound linalool extracted from coriander inhibits the formation of Acinetobacter baumannii biofilm by affecting bacterial adhesion and interfering with the QS system.[6]

In the microcolony formation stage, the quorum sensing system regulates the synthesis and secretion of the extracellular matrix. The Agr system of Staphylococcus aureus affects the formation of microcolonies and the stability of biofilm structure by regulating the synthesis of polysaccharide intercellular adhesin (PIA). Photodynamic therapy can inhibit the transmission of QS signaling, after photosensitization treatment with indocycline green, the expression levels of QS system genes abaI, agrA and Iasi related to biofilm formation in Acinetobacter baumannii, Pseudomonas aeruginosa and Staphylococcus aureus were down-regulated.[7] In addition, the quorum sensing system also regulates the motility and aggregation behavior of bacteria, and promotes the formation and expansion of microcolonies.

In the biofilm maturation stage, the quorum sensing system regulates the maintenance and dispersion of the biofilm structure. The Rhl system of Pseudomonas aeruginosa regulates the synthesis of rhamnolipids, influencing the formation of biofilm channels and nutrient transport. The use of benzamide-benzimidazole compounds can inhibit the Pseudomonas aeruginosa quorum sensing regulator MvfR (PqsR), interfere with biofilm formation, and enhance biofilm sensitivity to antibiotics.[8] At the same time, the quorum sensing

system also regulates the dispersion process of the biofilm, by activating enzymes that degrade the substrate or regulating flagellar synthesis, which promotes the release of bacteria from the biofilm and achieves new colonization.

5. The molecular mechanism of the quorum sensing system to regulate bacterial biofilm formation

Quorum sensing systems regulate the expression of biofilm-related genes through complex signal transduction networks. In Pseudomonas aeruginosa, the LasI/LasR system affects the synthesis of exopolysaccharide Pel and Psl by regulating the level of c-di-GMP (second messenger). Bacteria achieve communication within and between microbiota to form biofilms through quorum sensing mechanisms. Quorum sensing inhibitors are a new generation of antibacterial agents, mainly including N-acetylhomoserine lactone (AHL) antagonists that bind to LuxR-type receptors and AHL synthesis inhibitors. The main mechanism of the former is to compete with natural AHL for binding sites and inhibit its binding, so that the LuxR homolog will not be activated and the virulence factors will not be expressed. The main mechanism of the latter is the inhibition of AHL synthesis.[9] In addition, the quorum sensing system also interacts with other regulatory systems, such as the c-di-GMP signaling system, the two-component system, and the σ factor, to form a complex regulatory network.

The cross-dialogue between quorum sensing systems and other regulatory systems plays an important role in biofilm formation. For instance, in vibrio cholerae, the quorum sensing system synergistically regulates biofilm formation with the c-di-GMP signaling system. At high cell density, the quorum sensing system inhibits the synthesis of c-di-GMP and promotes the dispersion of biofilms. At low cell density, the level of c-di-GMP is elevated, promoting the formation of biofilms. This cross-regulation allows bacteria to flexibly adjust biofilm formation and dispersion based on environmental conditions and population density.

6. Strategies for bacterial biofilm prevention and control for quorum sensing systems

The biofilm prevention and control strategies based on quorum sensing quenching mainly include enzymatic degradation of signaling molecules, competitive inhibition of signaling molecules binding to receptors, and synthesis of interfering signaling molecules. For instance, AHL lactones and AHL acylases can degrade AHL-like signaling molecules and inhibit the activation of quorum sensing systems. In addition, synthetic AHL analogues can competitively inhibit the binding of natural signaling molecules to receptors and block the quorum sensing signaling pathway.

Quorum sensing inhibitors have broad application prospects in biofilm prevention and control. AgNPs, widely used in clinical practice, by inhibiting the adhesion and movement of bacteria, activating oxidative stress response, disrupting iron homeostasis and blocking aerobic and anaerobic respiration, can affect the QS system, inhibit the expression of related genes, inhibit the formation of multidrug-resistant Acinetobacter baumannii biofilms, destroy the biofilm of Pseudomonas aeruginosa, and have anti-biofilm activity against Staphylococcus aureus and Escherichia coli.[10] The inhibitory effect of baicalin on the early and mature biofilms of Staphylococcus aureus can reduce the adhesion of Staphylococcus aureus to the vector, inhibit and clear the biofilms of Staphylococcus aureus. Baicalin has a synergistic effect with antibiotics. The combination of baicalin and ceftazidime, cefazolin, levofloxacin, vancomycin, etc., can accelerate the destruction of the biofilm structure, enhance the penetration of antibiotics and the removal of bacteria, showing a synergistic bactericidal effect, which is closely related to its interference with the bacterial quorum sensing system.[11] Essential oil inhibits biofilms through its concentration, mainly by inhibiting the expression of related genes, affecting the integrity and metabolic activity of bacterial structure in biofilm, inhibiting the synthesis of extracellular polysaccharides and extracellular proteins, and inhibiting quorum sensing to achieve anti-biofilm effects.[12] These inhibitors can be used alone or in combination with antibiotics to enhance the prevention and treatment of biofilm-associated infections. However, the clinical application of quorum sensing inhibitors still faces challenges, such as in vivo stability, toxicity and drug resistance, and other issues need to be further addressed.

7. Conclusion

Quorum sensing systems play a key role in bacterial biofilm formation and regulation. By regulating processes such as initial adhesion, microcolony formation and biofilm maturation, the quorum sensing system affects the structure and function of biofilms. By using high-throughput sequencing technology and bioinformatics tools, the gene regulatory network of quorum sensing systems in the formation of biofilms can be analyzed more deeply, and the molecular mechanism by which quorum sensing systems regulate the formation of biofilms can be deeply understood, providing a theoretical basis for the development of new antibacterial strategies. Biofilm prevention and control strategies based on quorum sensing quenching and inhibition have shown good application prospects, but the further research is still needed to

overcome the challenges in clinical application. The future research should focus on the interaction of quorum sensing systems with other regulatory networks, develop more effective quorum sensing inhibitors, and explore their potential applications in clinical and industrial settings.

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AUTHORS CONTRIBUTIONS
Xue Fu contributed to the study conception, design, data acquisition, data analysis, statistical analysis, manuscript drafting and revision; Lingfeng Wang contributed to the academic leadership and guidance, manuscript review and revision; Hang Dong, Fang Li, Ran An, Lihua Hui, Xuewei Mao and Shiyu Qin contributed to the data acquisition, data analysis, statistical analysis.

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REFERENCES

[1] Mohamad F, Alzahrani RR, Alsaadi A, et al. An explorative review on advanced approaches to overcome bacterial resistance by curbing bacterial biofilm formation. Infection and Drug Resistance. 2023; 16: 19-49. PMid:36636380. https://doi.org/10.2147/IDR.S380883

[2] Wang Y, Bianz, Wang Y. Biofilm formation and inhibition mediated by bacterial quorum sensing. Appl Microbiol Biotechnol. 2022; 106(19-20): 6365-6381. PMid:36089638. https://doi.org/10.1007/s00253-022-12150-3

[3] Wu K, Zheng YY, Wu QP, et al. Erratum to: Vibrio parahaemolyticus cqsA controls production of quorum sensing signal molecule 3-hydroxyundecan-4-one and regulates colony morphology. Journal of Microbiology. 2020; 58(1): 78. PMid:31898256. https://doi.org/10.1007/s12275-020-9721-3

[4] Duraes F, Pahneira A, Cruz B, et al. Antimicrobial activity of a library of thioxanthones and their potential as efflux pump inhibitors. Pharmaceuticals (Basel). 2021; 14(6): 572. PMid:34203998. https://doi.org/10.3390/ph14060572

[5] Reading NC, Sperandio V. Quomm sensing: the many languages of bacteria. FEMS Micmbiol Lett. 2006; 254: 1-11. PMid:16451172. https://doi.org/10.1111/j.1574-6968.2005.00001.x

[6] Alves S, Duarte A, Sousa S, et al. Study of the major essential oil compounds of Coriandrum sativum against Acinetobacter baumannii and the effect of linalool on adhesion, biofilms and quorum sensing. Biofouling. 2016; 32(2): 155-165. PMid:26901586. https://doi.org/10.1080/08927014.2015.1133810

[7] Pourhajibagher M, Mahmoudi H, Rezaei-Soufi L, et al. Potentiation effects of antimicrobial photodynamic therapy on quorum sensing genes expression: a promising treatment for multi-species bacterial biofilms in burn wound infections. Photodiagnosis Photodyn Ther. 2020; 30: 101717. PMid:32165339. https://doi.org/10.1016/j.pdpdt.2020.101717

[8] Maura D, Rahme LG. Pharmacological inhibition of the Pseudomonas aeruginosa MvfR quorum-sensing system interferes with biofilm formation and potentiates antibiotic-mediated biofilm disruption. Antimicrob Agents Chemother. 2017; 61(12): e01362-17. PMid:28923875. https://doi.org/10.1128/AAC.01362-17

[9] Styles MJ, Boursier ME, McEwan MA, et al. Autoinducer fluorophore conjugates enable FRET in LuxR proteins in vitro and in cells. Nat Chem Biol. 2022; 18(10): 1115-1124. PMid:35927585. https://doi.org/10.1038/s41589-022-01089-1

[10] Hetta HF, Al-kadmy IMS, Khazaal SS, et al. Antibiofilm and antivirulence potential of silver nanoparticles against multidrug-resistant Acinetobacter baumannii. Scientific Reports. 2021; 11(1): 10751. PMid:34031472. https://doi.org/10.1038/s41598-021-90208-4

[11] Du ZY, Huang YY, Chen Y, et al. Combination effects of baiealin with levofloxacin against biofilm-related infections. Am J Transl Res. 2019; 11(3): 1270-1281.

[12] Alrashidi AA, Noumi E, Snoussi M, et al. Chemical composition, antibacterial and anti-quorum sensing activities of Pimenta dioica L. essential oil and Its major compound (Eugenol) against foodborne pathogenic bacteria. Plants (Basel). 2022; 11(4): 540. PMid:35214872. https://doi.org/10.3390/plants11040540