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A Commentary on Screening Strategies for Quorum Sensing Inhibitors in Combating Bacterial Infections

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Commentary

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ABOUT THE STUDY

Antimicrobial Resistance (AMR) poses a severe threat to public health and requires global action. As a result of a wasteful and uncritical use of antibiotics without adequate consideration of the societal consequences caused by AMR, the effectiveness of traditional antibacterial drugs has generally declined. Much more work and concern are urgently needed for the novel strategies to result in effective antibacterial drugs and therapies to sustainably combat AMR. In this regard, a strong trend towards non-traditional approaches emerges, including diverse antivirulence approaches, phage-derived therapeutics and microbiota-modulating approaches [1]. Antivirulence approaches, including inhibition of quorum sensing, biofilm formation and adhesion, etc., act to “disarm” rather than kill bacteria, which are less vulnerable to the emergence of AMR. Between 2015 and 2019, among first-in-class antimicrobial agents approved by US FDA, a quarter of agents were Virulence Arresting Drugs (VAD) [2].

Quorum Sensing Inhibitors (QSIs), as an important class of VAD, can act by disrupting or blocking collective behaviors of bacteria coordinated by bacterial cell-cell communication to interfere with virulence production, motility, biofilm formation and drug resistance mechanisms [3,4]. The development of QSI has showed a significant impact on the discovery of anti-infective drugs against a variety of bacteria.

The recent article "Screening strategies for quorum sensing inhibitors in combating bacterial infections" by Lu et al. summarized and discussed some latest findings in strategies and methodologies for QSIs screening, offering a comprehensive guide of screening approaches of QSIs and a valuable insight into QSI discovery. These findings offer a new perspective on QSI/VAD discovery, but several key issues need to be addressed:

1. Critical challenges in QSI/VAD clinical application: It is inspiring that an increasing number of QSI/VAD have been registered for clinical use. However, QSI/VAD prescriptions based on an empirical or "trial-and-error" strategy will be wasteful. Uptake of QSI/VAD may be hampered by the lack of effective approaches to screen patients as susceptible subjects to benefit from novel QSI/VAD. Personalized genomics guided use of QSI/VAD provides a promising direction to achieve individually targeted therapies by determining the most suitable treatment based on the genomic profile of each pathogen. By enabling personalized genomics to guide the clinical use of QSI/VAD, it will assist hospitals to optimize the use of these expensive drugs and facilitate future therapeutic regime.
2. Evidence of potential impact on AMR: Although VADs exhibit no bactericidal activity, there is new evidence that resistance mutations still occur, and since VAD treatment may indirectly affect bacterial survival. It was reported that clinical strains of Pseudomonas aeruginosa rapidly developed in vitro resistance to furanone C-30, a type of QSI, due to silencing mutations in the mexR gene showing the risk of producing selective pressure and developing resistance by QSIs [5,6].
3. Repurposed drugs for developing novel QSI/VAD: Reasonable, less time-consumable and low-cost methods for discovering QSI/VAD should also be greatly considered. In recent years, approved drugs to treat non-infectious diseases have been discovered to possess potent antivirulence properties. These medications offer a promising therapeutic option due to their known safety and well-understood bioavailability profiles [7].

In an era of growing AMR, we are searching for novel strategies to combat bacterial infections. The development of QSI/VAD is promising and urgent, but more work and attention should be required for the issues discussed above for QSI/VAD discovery and antivirulence strategies.

AUTHOR CONTRIBUTIONS

LL mainly designed the study and completed this manuscript. JYW revised the manuscript and provided some help.

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