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Challenges and Limitations of Anti-quorum Sensing Therapies

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Quorum sensing (QS) is a mechanism allowing microorganisms to sense population density and synchronously control genes expression. It has been shown that QS supervises the activity of many processes important for microbial pathogenicity, e.g., sporulation, biofilm formation, and secretion of enzymes or membrane vesicles. This contributed to the concept of anti-QS therapy [also called quorum quenching (QQ)] and the opportunity of its application in fighting against various types of pathogens. In recent years, many published articles reported promising results indicating the possibility of reducing pathogenicity of tested microorganisms and their easier eradication when co-treated with antibiotics. The aim of the present article is to point to the opposite, negative side of the QQ therapy, with particular emphasis on three fundamental properties attributed to anti-QS substances: the selectivity, virulence reduction, and lack of resistance against QQ. This point of view may highlight new directions of research, which should be taken into account in the future before the widespread introduction of QQ therapies in the treatment of people.

Keywords: quorum sensing, quorum quenching, microbiota, pathogenicity, virulence, resistance

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INTRODUCTION

Quorum sensing (QS) is a mechanism allowing microorganisms to sense population density, synchronously control genes expression after reaching a critical point (a quorum) and assess the efficiency of producing diffusible extracellular effectors. This process is associated with the synthesis of extracellular autoinductive substances with a function similar to hormones produced by higher organisms (Redfield, 2002; Hense et al., 2007; Bandara et al., 2012; Hawver et al., 2016). The first scientific report, indicating the presence of hormone-like compounds in bacteria, was an article by Tomasz (1965). In the next decade, attention was drawn to the relationship between the production of a specific group of metabolites (autoinducers) and luciferase-dependent bioluminescence in bacteria of the Vibrionaceae family (Nealson et al., 1970; Greenberg et al., 1979). A breakthrough in QS research was made by Eberhard et al. (1981), who for the first time identified the structure of signaling factors involved in the microbial communication, i.e., acyl-homoserine lactones (AHLs), now often named as autoinducer-1 (AI-1). In 1994, the presence of other substances controlling bioluminescence was shown (Bassler et al., 1994). They were called autoinducer-2 (AI-2), and their structure was identified at the beginning of the twenty-first century (Chen et al., 2002). In 1995, two publications were released, in which the relationship between oligopeptides synthesis [called autoinducing peptides (AIPs)] and inter-microbial communication in Gram-positive bacteria was noticed (Havarstein et al., 1995; Ji et al., 1995). AI-1, AIPs, and AI-2 are currently the most intensively investigated compounds related to the QS activity, and their presence has been demonstrated in many bacteria belonging