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Targeting quorum sensing in bacterial pathogens: Next generation antibiotics

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Quorum sensing is a mechanism of cell-to-cell communication seen in bacteria that occurs through certain autoinducers or chemical signal molecules. The concentration of these autoinducer molecules increases with the increase in cell density. Once a certain threshold concentration is reached, these autoinducer molecules lead to the alteration of gene expression in the population. It is now known that quorum sensing is the underlying mechanism of a wide spectrum of bacterial physiological processes, such as virulence, bioluminescence, sporulation, conjugation, development of genetic competence and the synthesis of antibiotics.

Considering the implications of quorum sensing in various aspects of bacterial life processes, it is evident that inhibiting quorum sensing could have potential therapeutic applications. There are various strategies in which the quorum sensing pathways can be inhibited and they are called quorum-quenching. The compounds or molecules used to do so are called anti-quorum sensing (AQS) compounds. Strategies used in quorum-quenching include the inhibition of the synthesis of autoinducer molecules, designing analogues of autoinducer molecules or receptor analogs and antibody or enzyme-catalysed hydrolysis of autoinducer molecules.

Further, Nâ€‘acyl homoserine lactones (AHLs) are an important class of signalling molecules produced by Gram-negative bacteria which are known to govern the population density. Lactonases are the enzymes that hydrolyse either the amide linkage between lactone and acyl side chain or affect the ester bonds, thereby inhibiting the signalling molecules. Acylases and oxidoreductases are found to have quorum-quenching activities as well. The degradation of signalling molecules is also possible via antibody-mediated catalysis. Lamo Marin et al., in their studies, reported that hydrolysis of AHL is efficiently achieved by original squaric monoester monoamide hapten. Kristina M Smith and Yigong Bu reported two novel compounds, namelyN-(2-oxocyclohexyl)-3-oxo dodecanamide, which is a moderate antagonist and N-(trans-2-hydroxycyclopentyl)-3-oxo dodecanamide, which is a strong antagonist of autoinducer molecules of P. aeruginosa. Exploiting the quorum-sensing activity of bacterial pathogens can lead to the discovery of next-generation antibiotics, i.e., AQS agents, which can curb infections without a killing action.

Keywords: Quorum Sensing, Next generation antibiotics, Bacterial pathogens, Anti-quorum sensing

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