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Quorum Sensing: Utilizing Molecular Modelling to Discover Novel Inhibitors

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COLUMN ARTICLE

Quorum sensing (QS) is a bacterial communication system that enables bacterial cells to express their virulence genes [1]. In this communication system, bacterial cells produce a chemical compound (signal) that when reaches certain concentration threshold initiates production of bacterial virulence factors, which are related to bacterial pathogenicity (see Figure 1). Quorum sensing is involved in the bacterial resistance to antibiotics and biofilm formation [2]. Biofilm is a polymeric matrix includes bacterial community (homogeneous or heterogeneous community), which is strongly involved in the persistent bacterial infections. Also, biofilm could adhere to the implanted medical devices and decrease their function [2]. Accordingly, finding new QS inhibitors that stop the expression of bacterial virulence genes without killing bacterial cells would enable host immune system to eradicate that infection, which could avoid the antibiotic resistance problem.

Researchers used to test huge number of compounds to find a chemical lead compound to inhibit certain enzyme. This process is time and money consuming. Nowadays, molecular modelers use versatile computer-based (in-silico) techniques to ease the process of drug discovery. Molecular modelling, in the drug discovery process, utilizes all theoretical methods to find the best binding between the chemical compound and its receptor [3]. Also, it is used to predict the activity of certain proposed chemical compound. Molecular modelling technique could generate a search query, which could be used to screen large chemical libraries to find a compound with desired inhibition activity.

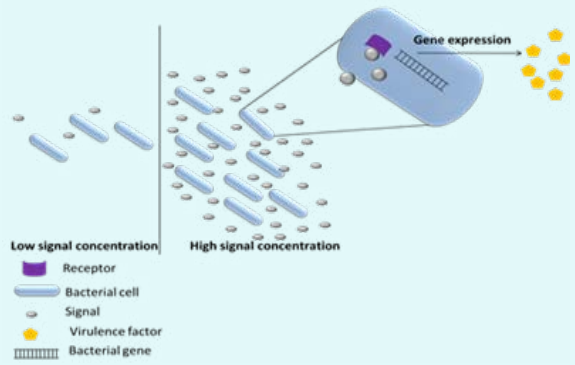

Figure 1: Representation of bacterial quorum sensing. At high signal concentration, bacterial cells start to express their virulence genes and produce virulence factors, which are involved in the bacterial pathogenicity.

Different QS inhibitors have been discovered through molecular modelling technique such as pharmacophore, quantitative structure activity relationship (QSAR) and molecular docking. For example, pharmacophore modelling was used to discover QS inhibitors in a range of Nano molar IC50, amongst others [4]. This compound, as well as other discovered QS inhibitors, could be optimized to develop anti-QS drug. In the optimization process, the researcher uses different in-silico software to improve the physicochemical properties of these inhibitors to meet the drug criteria. Also, molecular modelling could be used to propose an inhibitor with decreased toxicity and good potency. Finally, I would say that we have promising advances in the field of QS, which hopefully will produce some anti-QS drugs to help immune system to eradicate severe infections as well as to treat the persistent infections.

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