Quorum Sensing Inhibitors as Anti-Pathogenic Drugs in the Fight Against Pseudomonas aeruginosa Infections

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The increasing of antibiotic resistance among clinically P. aeruginosa strains determined researchers to find out new alternatives to antibiotic treatment. The newest strategy in therapeutics development is represented by an alternative approach which aims to target functions essential for infection, such as virulence factors required to cause host damage and disease. This approach has several potential advantages including expanding the repertoire of bacterial targets, preserving the host endogenous microbiome, and exerting less selective pressure, which may result in decreased resistance [1]. Most efforts to inhibit the regulation of virulence factors expression have focused on interfering with quorum sensing (QS). Because of the significant role of QS in the regulation of hundreds of virulence factors in P. aeruginosa, significant efforts have been made to discover compounds with inhibitory activity of QS systems, that could stay to the base of an anti-pathogenic strategy, since they will inhibit the coordinated expression of virulence determinants, without interfering with bacterial growth, being less likely to generate resistance [2]. Many studies that have shown that deletion of one or more QS genes result in reduced P. aeruginosa virulence compared with the wild-type P. aeruginosa [3].

Many groups of researchers from worldwide had focused to find out the most appropriate quorum sensing inhibitors (QSI) that could be used for the inhibition of pathogenicity and virulence of multidrug resistant P. aeruginosa strains. Of the numerous compounds able to inhibit QS a few have been tested in animal models with great success. Unfortunately, these compounds are unsuitable for human use. The halogenated furanones are unstable and the fungal compounds inhibit QS a few have been tested in animal models with great success. Unfortunately, these compounds are unsuitable for human use. The increasing of antibiotic resistance among clinically P. aeruginosa strains determined researchers to find out new alternatives to antibiotic treatment. The newest strategy in therapeutics development is represented by an alternative approach which aims to target functions essential for infection, such as virulence factors required to cause host damage and disease. This approach has several potential advantages including expanding the repertoire of bacterial targets, preserving the host endogenous microbiome, and exerting less selective pressure, which may result in decreased resistance [1]. Most efforts to inhibit the regulation of virulence factors expression have focused on interfering with quorum sensing (QS). Because of the significant role of QS in the regulation of hundreds of virulence factors in P. aeruginosa, significant efforts have been made to discover compounds with inhibitory activity of QS systems, that could stay to the base of an anti-pathogenic strategy, since they will inhibit the coordinated expression of virulence determinants, without interfering with bacterial growth, being less likely to generate resistance [2]. Many studies that have shown that deletion of one or more QS genes result in reduced P. aeruginosa virulence compared with the wild-type P. aeruginosa [3].

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In our studies we have shown that soluble molecules accumulated in the probiotic supernatant of Lactobacillus paracasei subsp. paracasei CMGB 18 culture filtrate (PCF), isolated from newborn faeces, are exhibiting inhibitory properties on P. aeruginosa strains growth, adherence to the inert substratum [17] and on QS genes expression level [7]. We have further aimed to detect and quantify the soluble molecules accumulated in PCF, and to investigate their inhibitory activity on P. aeruginosa QS genes expression level. In a recent study we have shown that real-time RT-qPCR that the sub-inhibitory concentrations of organic acids (acetic acid and lactic acid) secreted by the same probiotic strain resulted in decreased resistance [1]. Most efforts to inhibit the regulation of virulence factors expression have focused on interfering with quorum sensing (QS). Because of the significant role of QS in the regulation of hundreds of virulence factors in P. aeruginosa, significant efforts have been made to discover compounds with inhibitory activity of QS systems, that could stay to the base of an anti-pathogenic strategy, since they will inhibit the coordinated expression of virulence determinants, without interfering with bacterial growth, being less likely to generate resistance [2]. Many studies that have shown that deletion of one or more QS genes result in reduced P. aeruginosa virulence compared with the wild-type P. aeruginosa [3].

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decreased the QS genes expression in P. aeruginosa multidrug resistant strains grown in the presence of these acids comparatively with with the expression level in control strains grown in normal conditions [1]. In conclusion these metabolites (soluble molecules) secreted by probiotic strain have inhibitory activity on the QS genes expression, and could represent QSI.

At present the researchers from worldwide are interested to find out the most appropriate QSI that could be used for the inhibition of virulence of multidrug resistant P. aeruginosa strains. Whether QSIs offer new hope in the continuing battle against multi-antibiotic-resistant bacteria is not yet fully apparent but the results certainly appear promising. Not only is expression of many virulence factors down regulated by QSI compounds but the inhibitors also render biofilm bacteria more susceptible to conventional anti-microbial treatments. In spite of the enormous number of QSIs investigated until now, no one of these compounds was investigated in clinical trials in order to be used in treatment of P. aeruginosa infections.

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