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Development of a cell based high-content/high-throughput compound microarray screen for *Klebsiella pneumoniae*

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Carbapenem-resistant *K. pneumoniae* is an emerging multidrug-resistant Gram-negative bacterium causing infections associated with significant morbidity and mortality worldwide. *K. pneumoniae* has adapted and selected for carbapenemases, which are versatile β-lactamase enzymes capable of hydrolyzing carbapenems: A class of broad-spectrum antibiotics reserved for the treatment of infections caused by multidrug resistant pathogens. This has necessitated the use of Colistin and Tigecycline as last resort therapeutic option for treating infections caused by the pathogen. However, it has developed resistance against these antibiotics, thus further complicating treatment, due to limited antibiotic options. Recently, the World Health Organization (WHO) identified the carbapenem-resistant K. pneumoniae as the most important multidrug-resistant bacteria at the global level, for which there is an urgent need for new treatments. To accelerate and minimize the cost involved in drug discovery efforts, a cell-based high-content/high-throughput reverse transfection microarray screening platform will be employed to screen hundreds of compounds against carbapenem-resistant *K. pneumoniae*. To achieve this, a cell-based assay, mimicking infection in human cells will be validated in a 96-well plate format. The validated assay will be transposed onto a high-density microarray plate comprising of chemically encapsulated compounds for screening. Using an automated fluorescent imaging system, the activity of compounds against fluorescently labeled bacterial strain will be measured and statistically quantified. The anticipated outcome of this study is the development of a highly efficient screen that can simultaneously determine efficacy, cytotoxicity, specificity, and predict clinical response of compounds in biologically relevant cell-lines while enabling the rapid identification of potential drug candidates for carbapenem-resistant *K. pneumoniae*.

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