Drug targets to prevent expression of sulphonamides and trimethoprim resistance in MDR *Escherichia coli.*

Sajid Nisar, University of Copenhagen, Denmark

Abstract

In this project, a brand-new approach to control of antimicrobial resistant (AR) bacteria is suggested. AR-bacteria prevail in the presence of therapeutic antibiotics. Surprisingly, next to nothing is known about the changes they undergo, when they have to prioritize the expression of the resistance mechanism over optimal growth. We hypothesize that they must undergo severe changes in basic metabolism to be able to cope with therapeutic doses of antibiotics, and that this constitutes a window of opportunity for development of future medicines against AR-bacteria.

The project will compare the growth performance of isogenic strain of *Escherichia coli* MG1655 with and without chromosomally encoded sulphonamides (*sul1* and *sul2)* and trimethoprim (*dfrA1)* resistance genes, in the presence of therapeutic concentrations of antibiotics. A transposon library of the bacterium will be constructed according to the sequence based differential transposon technique (TRADIS), and the library will be screened for growth with and without antibiotics to score mutants that can grow without sulphonamides and trimethoprim but not in the presence of these drugs. The mutations will be mapped by sequencing, and mutants where the transposon is not in the resistance genes will be selected. The hypothesize is that the genes identified in this way are essential for expression of the resistant phenotype, and hence they encode proteins which may be new targets that only are available when sulphonamide resistant-bacteria are fully occupied with fighting the drug.

The hypothesis will be tested by construction site specific genetic knock out of the genes in both MG1655 and WT (pathogenic) sulphonamide resistant *E. coli* and characterize these mutants for expression of resistance genes, growth with and without antibiotics and for wild type strains, infection ability in mice with and without concurrent sulphonamide treatment will be investigated.

Publication

Bilal, Shahrukh, Sidra Anam, Tauqeer Mahmood, Rana Muhammad Abdullah, **Sajid Nisar**, Furkhanda Kalsoom, Muhammad Luqman, and Faisal Rasheed Anjum. **"Antimicrobial profiling and molecular characterization of antibiotic resistant genes of Proteus vulgaris isolated from tertiary care hospital, Islamabad, Pakistan."** *Pak. J. Pharm. Sci* 32, no. 6

(2019):2887-2891.(https://www.semanticscholar.org/paper/Antimicrobial-profiling-andmolecular-ofantibiotic-Bilal-Anam/c02b87f3342921a8f170984823675bd38867eb98)

Biography

I am Sajid Nisar, a first Year PhD student in the section of Veterinary Clinical Microbiology, Department of veterinary and Animal Sciences, University of Copenhagen, Denmark. I am veterinarian by profession. I did my Doctor of Veterinary Medicine (DVM) degree from University of Agriculture Faisalabad, Pakistan in 2016. I did my M. Sc (Hons.) in Public Health from the University of Agriculture Faisalabad, Pakistan in 2018. I am a member of American Society for Microbiology (ASM) . I am experienced researcher with excellent analytical skills, having work experience on Interdisciplinary fields including zoonotic diseases, climate change, public health and antibiotic resistance etc. Currently I am investigating the cellular responses to sulphonamides in combination with other antimicrobials in Multi-drug resistant *Escherichia coli.*

Email: zmr695@sund.ku.dk