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## Dissertation

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|------------------------|-----------------------------------------------------------------------------------------------------------|
| <b>Title</b>           | <i>Characterization of carbapenemase producer Enterobacteriaceae isolated in the United Arab Emirates</i> |
| <b>Faculty Advisor</b> | Dr. Agnes Sonnevend-Pál                                                                                   |
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### Abstract

The efficient control of the spread of carbapenemase producer Enterobacteriaceae, a major public health threat world-wide, requires knowledge on the molecular epidemiology and genetic background of the emerging carbapenemase genes. Our aim was to investigate the genetic support of New-Delhi metallo-beta-lactamase and OXA-48-type carbapenemase genes in carbapenem resistant Enterobacteriaceae isolated in the United Arab Emirates. The first seven NDM-producer Enterobacteriaceae, collected during 2009-2011 in the UAE and subsequently five NDM and OXA-48-type carbapenemase co-producer Klebsiella pneumoniae isolated during 2011-2013 in three hospitals of the Emirates, were characterized. Strains' clonality and the transmissibility of carbapenemase genes were assessed. The genetic support of carbapenemases was studied by characterization of plasmids and by sequencing the genes' surrounding. All isolates harbored the blaNDM-1 gene on conjugative plasmids. Furthermore, IncX3 plasmids with almost identical restriction patterns were present in Enterobacter cloacae, Escherichia coli and Citrobacter freundii. The NDM plasmid of one K. pneumoniae, harboring blaOXA-48 also, was almost identical to these IncX3 plasmids. Three of the five double carbapenemase producer ST14 K. pneumoniae possessing blaNDM-1 and blaOXA-232 were clonally related. The fifth, unrelated K. pneumoniae co-produced NDM-1 and OXA-162. These findings proved that IncX3 plasmids play an important role in the inter-species spread of the blaNDM gene, and also that the emergence of NDM- and OXA-48-type carbapenemase co-producer K. pneumoniae is partially a clonal phenomenon in the UAE. Since the carbapenemase producer Enterobacteriaceae are extremely drug resistant, leaving few treatment options, the efficacy of alternative antimicrobials was also assessed by testing the effect of the himenochirin-1B analogue antimicrobial peptide on selected strains and the fosfomycin susceptibility of 45 carbapenem non-susceptible Escherichia coli isolates. The [E6k,D9k]hymenochirin-1B showed high potency against all selected NDM-producer. Furthermore, fosfomycin could be a valuable therapeutic option against carbapenem-resistant E. coli, since the susceptibility of all isolates tested was retained.

## Research Relevance and Potential Impact

Ms. Baloushi's research set the UAE's experience with carbapenem resistant Enterobacteriaceae, into a global context. The molecular investigation of multi-drug resistant organisms highlighted the mode of spreading of these bacteria. Furthermore, she proved that fosfomycin could be a useful option for the treatment of carbapenem resistant Escherichia coli infections.