



MÁSTER EN INVESTIGACIÓN BIOMÉDICA

Research Project Proposal

Academic year 2022-2023

Project Nº 31

Title: *In vitro* studies of the polymyxin E nonapeptide for a new combination therapy against β -lactam resistant bacteria

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Summary

Infections caused by antibiotic resistant bacteria (ARB) are worldwide public health problem. The costs in human lives (1.2 million deaths in the world per year) and economic costs (1,500 million euros/year only in the European Union) make it necessary to solve the problem from a global approach (*One Health*). The challenge is the development of new antibiotics and alternative treatments against the main ARB, such as the extended spectrum β -lactamases (ESBL) producers. Our group has shown that several ARB strains of *P. aeruginosa*, *E. coli*, and *K. pneumoniae* become sensitive to β -lactams in the presence of low concentrations of polymyxin E nonapeptide (PMEN), derived from the antibiotic colistin and much less toxic. In this context, the main objective of the project is to evaluate the *in vitro* efficacy of the PMEN peptide to sensitize ESBL producers to antibiotics.

First, the synthesis of the PMEN will be carried out from colistin by enzymatic hydrolysis and following the method described by Vaara (1983)¹. Then, the minimum inhibitory concentration (MIC) of three β -lactam antibiotics, three β -lactamase inhibitors and the PMEN will be determined against 3 strains (*E. coli*, *K. pneumoniae* and *P. aeruginosa*). According to the results, a triple combination (PMEN-antibiotic-inhibitor) will be selected to study the synergistic effect against these strains by *Checkerboard* assays. Finally, the *in vitro* efficacy of the selected treatment will be evaluated against a selection of 15 ARB isolated from different environments (human, environmental, food and animal), by inhibitory kinetics studies.

¹ Vaara M., Vaara T. Polycations sensitize enteric bacteria to antibiotics. *Antimicrobial Agents and Chemotherapy*. 1983, 24 (1): 107-113

yes	
no	X

Does the project include the possibility of supervised animal manipulation to complete the training for animal manipulator?