6th World Congress and Expo on **Applied Microbiology**
&
8th Edition of International Conference on **Antibiotics, Antimicrobials & Resistance**
&
12th International Conference on **Allergy & Immunology**
October 21-22, 2019 Rome, Italy

Cell-penetrating peptidomimetics derived from cathelicidin LL-37 showed inhibition of Na+/K+ and Cu+ ATPases in mycobacterial plasma membrane and synergy in combination with isoniazid and kanamycin

Sandra Chingate-Lopez[1, 2], **Fanny Guzman**[3] and **Luz Mary Salazar**[1]
[1]Universidad Nacional de Colombia, Colombia
[2]Universidad Manuela Beltrán, Colombia
[3]Pontificia Universidad Católica de Valparaíso, Chile

The ATPase enzymes are membrane proteins have been studied as drug targets, because they are involved in several cellular functions that allow cell viability, so the development of drugs as inhibitors of ATPase activity in pathogens is an interesting strategy. Antimicrobial peptides are molecules generated in the host innate response with effects on mycobacteria. LL-37 is a human cathelicidin involved in the formation of channels in the cell membrane and bacterial lysis. In this study, the antimicrobial activity, as well as the effect on the mycobacterial cell membrane ATPase activity of LL-37 derived peptide with unnatural amino acids was assessed. By bioinformatic methods, the amino acid sequence of LL-37 with the best features of helical structure and antibacterial value was determined, the corresponding peptide had changes for D-Lys and N-methyl-Gly in the sequence, generating the peptides LLAP-D and LLAP-P. *In vitro* assesament of LLAP-D and LLAP-P were tested in strains of Mycobacterium smegmatis mc2155 and Mycobacterium tuberculosis H37Ra, obtaining a minimum inhibitory concentration of 1000-250 µg/mL, hemolytic activity less than 5% and the confocal microscopy shown the interaction with the cell membrane in Mycobacterium smegmatis mc2155. LLAP-D and LLAP-P displayed inhibition Na+/K+, Cu+ and Zn+2 ATPases in mycobacterial plasma membrane and synergy in combination with isoniazid and kanamycin. The results suggest that LLAP-D and LLAP-P could be considered as a potential antimycobacterial agent against target cell membrane ATPases.