PROFILE

The main line of the Research Group at **CIB Margarita Salas** has focused on the pneumococcal "Choline Binding Proteins", or CBPs. Some of these proteins are peptidoglycan hydrolases and play relevant roles in bacterial physiology. In recent years he has studied phage lytic enzymes as novel antimicrobials, also called endolysins or enzybiotics. In particular, those targeted against several bacterial respiratory pathogens, including Gram-positive pneumococcus and Gram-negative Pseudomonas aeruginosa

SPEAKER

Dr Pedro García González is a Research Scientist at Centro de Investigaciones Biológicas Margarita Salas (CIB-CSIC). He is head of the group "Host-parasite interplay in pneumococcal infection" at CIB.

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PRODUCT

Polypeptides with antibacterial activity

MECHANISM OF ACTION

Phage lysins, or enzybiotics, are enzymes that degrade specific bonds of the bacterial peptidoglycan, which leads to the lysis and death of the targeted bacteria. Normally, enzybiotics against Gram-positive bacteria are modular proteins that contain an enzymatically active domain, which determines the bond to be excised, and a cell wall binding domain, which recognizes the cell wall structure to be anchored. Enzybiotics against Gram-negative bacteria are usually monomodular with an enzymatic domain.

Enzybiotics represent an alternative to standard antibiotics, since the target is the bacterial peptidoglycan, a well conserved polymer that acts as a protective barrier against the inner osmotic pressure. When these enzymes are exogenously added, the rapid binding to the susceptible peptidoglycan and breaking of such polymer, leads to the lysis and death of the targeted bacteria

TARGET INDICATIONS

The compounds are conceived against respiratory infectious diseases produced by certain Gram-negative bacteria like Pseudomonas aeruginosa, Acinetobacter baumannii and Moraxella catarrhalis, particularly against those multiresistant strains. The synergistic activity between these polypeptides and some antibiotics is an additional therapeutic advantage

CURRENT STATUS

- We have constructed several polypeptides (wild type enzymes, fusion proteins, and peptides derived from the same enzybiotics) that have an in vitro killing effect against Pseudomonas aeruginosa, Acinetobacter baumannii and Moraxella catarrhalis.

- In addition, preliminary experiments with P. aeruginosa suggest an important synergistic effect between the tested peptides and some antibiotics.
- These data are obtained with only ¼ of the corresponding MICs for the peptides and antibiotics, increasing the rate of mortality by several orders of magnitude.

INNOVATIVE ASPECTS

- These phage-based antimicrobials form part of the so called "phage therapy", and constitute an alternative to standard antibiotics.
- But enzybiotics present several advantages over antibiotics and entire phages (virions), among them: specificity, low chance of resistance, killing effect against multiresistant strains, synergistic effects with some antibiotics or other enzybiotics, easy handling to clone the corresponding genes and the subsequent protein expression and purification, absence of severe side effects.
- Nowadays, the possibility to construct a "tailor made enzybiotic" against any bacterial pathogen is closer.

IPR

This technology is protected by EP20382666 with date of receipt on 24th July 2020 and title "Polypeptides with antibacterial activity". Owned 100% CSIC. The patent protects a group of polypeptides and their use as an antimicrobial agent against certain pathogenic bacteria.

PARTNERING OPPORTUNITIES

As the promising results summarized here still lack several in vitro and in vivo experiments, we would like to collaborate with any pharmaceutical company interested in these remaining assays and in the eventual formulation of the better compounds..