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Chemical derivatives of Cm-p5, a mollusc-derived peptide, enhanced its antifungal properties and improved significantly its antibacterial activity *in vitro*

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Antimicrobial peptides are an essential part of the first line of defence against microbial pathogens in many organisms. Current treatments for fungal infections are limited by drug toxicity and pathogen resistance. Cm-p5 (SRSELIVHQRLF) has a significant fungistatic activity against pathogenic *Candida albicans.* Cm-p5 was characterized by circular dichroism and nuclear magnetic resonance revealed an a-helical structure in membranemimetic conditions and a tendency to random coil folding in aqueous solutions. Additional studies modeling Cm-p5 binding to a phosphatidylserine bilayer *in silico* and isothermal titration calorimetry using lipid monophases demonstrated that Cm-p5 has a high affinity for the phospholipids of fungal membranes (phosphatidylserine and phosphatidylethanolamine), only moderate interactions with a mammalian membrane phospholipid, low interaction with ergosterol, and no interaction with chitin. Adhesion of Cm-p5 to living C.albicans cells was confirmed by fluorescence microscopy with FITC-labeled peptide. In a systemic candidiasis model in mice, intraperitoneal administration of Cm-p5 was unable to control the fungal kidney burden, although its low amphiphaticity could be modified to generate new derivatives with improved fungicidal activity and stability. Chemical and sequential derivatives have been synthetized to enhance the antimicrobial spectrum of Cm-p5. A cycled derivative (cys-cys Cm-p5) improved the minimal inhibitory concentration of the parental peptide from 10 to 5 μg/mL against *Candida albicans.* Cys-Cys CM-p5 was not toxic for human macrophages, the major host cell for the bacterial pathogen *M. tuberculosis.* Antimicrobial activity against extracellular, virulent *M. tuberculosis* reached >80% at 300 μg/ml concentration and was nearly as efficient as the first line antimicrobial drug rifampin.

Biography

Anselmo J Otero-Gonzalez is a presently working as a Microbiologist at the Havana University. He completed his PhD from National Centre for Scientific Research, Havana (1978) and Doctorate in Science from Havana University (1987). In 2008, he began working as a Senior Researcher at the Antimicrobial Peptide Lab, Havana University and sebsequently at (1981) Uppsala Separation School, Biomedical Centre University of Uppsala, Sweden, (1983) Department of Genetics, Pennsylvania University, Philadelphia, USA, (1991) European Collection of Animal Cell Cultures, Porton Down, Salisbury, (1992) Swedish Centre of Disease Control, Stockholm, Sweden, (2000) Harvard School of Public Health, Harvard University, Boston, USA, (2011-12) Harvard Medical School, Boston, USA and (2008) Bioorganic Department, Leibniz Institute for Plant Biochemistry, Halle (Saale), Germany. He has published 90 articles and 145 abstracts.

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