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Mechanism of action of antimicrobial protein $rBPI_{21}$: Biophysical approach

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Antimicrobial peptides/proteins (AMPs) are currently looked as new candidates to overcome the bacterial resistance against therapeutic antibiotics. However, their mechanism of action remains unclear, despite several theories having been proposed. The understanding of the processes that govern AMPs activity is the best way to provide rational design of new antibiotics for further clinical use against bacterial infections. Human AMPs are part of the innate immune system and synthetic versions of these AMPs are good candidates, due to their low toxicity and high antimicrobial activity. rBPI21 is an AMP based on the human neutrophil BPI protein, with potential clinical use for meningitis. By fluorescence spectroscopy and dynamic light scattering approaches $rBPI_{21}$ was shown to interact quantitatively more with negatively charged liposome systems containing phosphatidylglycerol (PG), which mimic bacterial membranes. The preference for the anionic PG membranes is followed by membrane aggregation/fusion and, at higher $rBPI_{21}$ concentration there is a leakage of liposome content. Regarding bacteria interaction atomic force microscopy approach was used. $rBPI_{21}$ was shown to induce membrane perturbations, culminating in bacterial cells content leakage, both on the Gram-negative bacteria *Escherichia coli* and on the Gram-positive *Staphylococcus aureus*. The interaction of $rBPI_{21}$ with bacteria was decreased in the presence of free lipopolysaccharide aggregates, demonstrating the affinity of $rBPI_{21}$ for free LPS, as studied by force spectroscopy. The overall observed results potentiate the use of the $rBPI_{21}$ in clinics against bacterial infections. Also, the development of new synthetic peptides based on $rBPI_{21}$ structure is a valuable route to develop new therapeutic agents with antibacterial properties.

Biography

Marco M. Domingues has completed his Ph.D. at the age of 27 years from Lisbon University. During his Ph.D. he had the opportunity to move to Brazil for 5 months to learn calorimetry, at Federal University of Rio de Janeiro. Also, he went to São Paulo University to learn Small-angle X-ray scattering. He has published 12 papers in international peer-reviewed journals.

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