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Poster abstract submission

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Poster title

Development of the Atrial Natriuretic Peptide as new powerful drug against Pseudomonas aeruginosa and Staphylococcus aureus resistant strain biofilms: its mechanism of action and therapeutic potential

Poster abstract

1B of people suffer globally from a chronic respiratory disease. Pseudomonas aeruginosa (Pa) is an opportunistic pathogen responsible for repeated exacerbations in patients with chronic lung diseases such as bronchiectasis, COPD or CF, maintaining an inflammation vortex, degrading pulmonary function, quality of life and prognosis. During these infectious episodes, bacteria are protecting themselves in a "shield" called a biofilm increasing their adaptability and tolerance against the host's immune defences and antibiotic treatments. Current treatments do not result in complete bacteria eradication leading to recurrence of exacerbations, long duration antibiotic cures majoring risk of resistance.
There is an urgent need to develop disruptive anti-infective strategies. Dispersing biofilm is a promising approach that allows antibiotics to come back into direct contact with bacteria. In the present study, we evaluated the dispersal ability of the natural human hormone Atrial Natriuretic Peptide (ANP) on mature Pa biofilms. We also evaluated ANP's capacity to disperse Gram-positive Staphylococcus aureus mature biofilms often mixed with Pa's during the infectious process.
We both observed that ANP prevents the formation of Pa biofilms and strongly disrupts pre-formed biofilms in a dose-dependent manner. Interestingly, we demonstrated that ANP dispersal activity requires the presence of the Pa AmiC sensor protein, suggesting specific activity on bacterial physiology. As ANP has no antibacterial activity, we validated in vitro that it acts as an adjuvant agent, enhancing the anti-biofilm action of various antibiotics to allow almost complete eradication of biofilms (see graph). Finally, we investigated the effects of ANP alone or in combination with tobramycin on biofilm dispersion in vivo using a chronically infected mouse model. We observed a significant reduction in bacterial load in the lungs of infected mice after three consecutive days of ANP exposure, either alone or in combination with

tobramycin, compared with a single tobramycin exposure. Finally, we found, in vitro, that ANP can strongly disperse mature biofilms formed by various strains of S. aureus, including methicillin-resistant strains. Overall, these data suggest that ANP could be not only a new therapeutic tool for controlling Pa infections and improve chronic respiratory patients' outcomes but more broadly to fight against many other infections caused by various antibiotic-resistant pathogens.

Research topic

Biological therapeutics

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