

Delivery of antimicrobial peptides for the treatment of mycobacteriosis

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Background: MSc. Bioengineering / Faculty of Engineering - University of Porto / Portugal
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BACKGROUND AND OBJECTIVES

Mycobacterium tuberculosis, which resides inside macrophages, has always been recognized as one of the most “successful” pathogens. Standard treatments have already been used for decades and, therefore, resistances to the first-line medicines are increasing. Additionally, poor patient compliance with stringent therapies is often pointed out as a major reason leading to treatment failure.

Antimicrobial peptides (AMPs), a promising new class of broad spectrum antibiotics, are less prone to result in pathogen resistances due to their target (cellular membranes) and rapid action. In our laboratory we search for AMPs with potent activity against mycobacteria and try to develop efficient delivery systems based on self-assembled colloidal nanocarriers. Additionally, these systems are expected to reduce peptide toxicity and enhance selective uptake on infected cells. Finally, the use of encapsulated drugs in mycobacterial therapy may help reducing drug administration schedules which would ultimately improve patient compliance.

WORK PLAN

1. Optimization of therapeutic formulations for AMPs controlled delivery.
2. In vitro and in vivo delivery of AMPs to infected macrophages; Analysis of mechanisms of therapeutic action and potential side effects.
3. Study binding, internalization mechanisms and intracellular fate of the nanocarriers (University of Oxford).
4. In vivo biodistribution of the nanocarrier (University of Groningen).
5. Study the global pharmaco-economic impact of AMPs as new therapeutic agents to fight tuberculosis.

RESULTS

We have used encapsulated AMPs (Fig. 1) to tackle an infection promoted by *M. avium* in mouse macrophages *in vitro*. During 7 days the peptide has killed more than 99% of initial bacterial burden. The bactericidal effect has already been confirmed using infected mice *in vivo*, by applying the therapeutic formulation via the pulmonary route (Fig. 2). Currently, we are moving for more potent mycobacteria, such as *M. tuberculosis*, which shows identical susceptibility to the antimicrobial formulation.

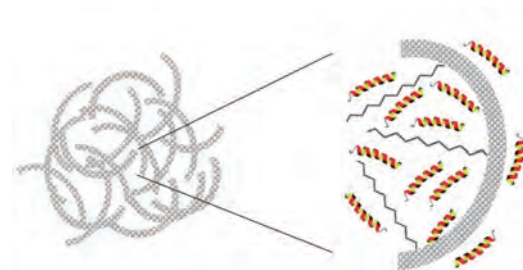


FIGURE 1

Schematic representation of the peptide nanocarrier.



FIGURE 2

Intratracheal drug delivery using a MicroSprayer® aerosolizer in mice.