Nanotherapeutics for antibiotic resistant emerging bacterial pathogens

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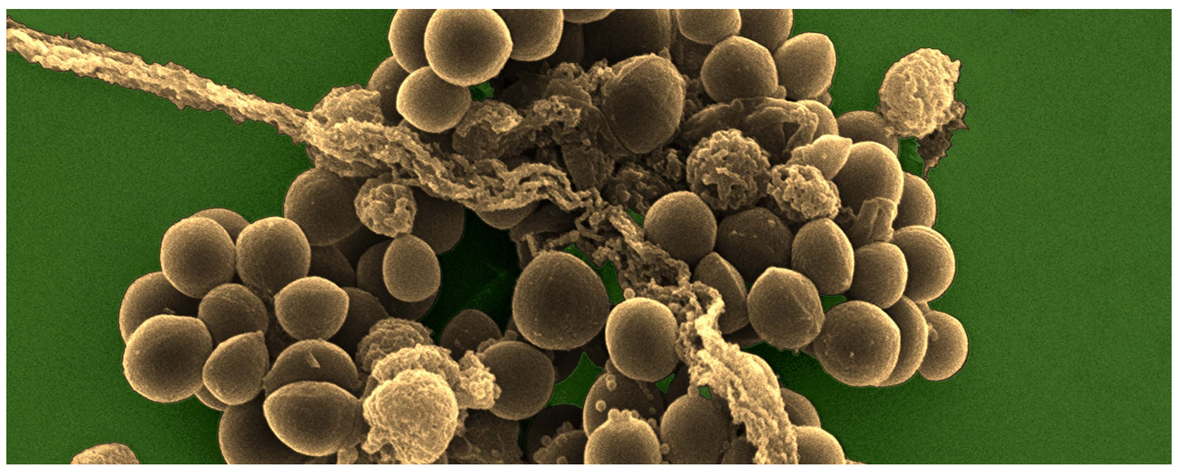
NAREB
Nanotherapeutics for Antibiotic Resistant Emerging Bacterial pathogens

Objectives

The NAREB project aims to propose nanotechnology solutions to the problem of Multi-drug resistant (MDR) Mycobacterium tuberculosis (M. tuberculosis) as well as methicillin resistant Staphylococcus aureus (MRSA), by the design, the preparation and the optimisation of several nanoformulations of current antibiotics and novel antibacterial drugs. The objectives to achieve the main goal are:

- Selecting antibacterial molecules and the design of nanocarriers with strong antibacterial activity
- *In vitro* and *in vivo* testing of the best therapeutic combinations using innovative bioimaging
- Assessing safety, regulatory and production (GLP/GMP) aspects for the most promising nanoformulations
- Establishing the Clinical Development Plan for the preparatory work for the subsequent clinical testing of the selected nanoformulations.

NAREB aims to optimize nanoformulations of antibacterial therapeutics in order to improve the therapy of multi-drug resistant tuberculosis and MRSA infections in European patients.



Strategy

The NAREB strategy id organized around 8 complementary research work packages (WP) focusing on:

- **Screening candidate therapeutic molecules**, to select drugs and drug candidates to be associated with nanoparticles to improve their properties, bioavailability and efficiency
- **Designing smart nanocarriers with antibacterial activity** for improving current therapies and fighting thus against the acquisition of antibiotic resistances
- **Assessing the *in vitro* activity of nanoparticles containing therapeutic molecules and to develop diagnostic tests**
- **Monitoring the *in vivo* efficacy of selected nanotherapeutics and assessing the biodistribution**
- **Assessing the safety of the developed nanosystems** by measuring the indirect effects of nanoparticles on immunological and signalling responses to exposure, using both in vitro and in vivo model
- **Developing the translational regulatory aspects and Clinical Development Plan** by establishing a management pathway for the product development process towards clinical studies
- **Setting up an effective dissemination of the foreground of the project** both inside and outside the consortium, **managing the Intellectual Property rights and exploitation of the foreground of the project**. Furthermore**, training for academics in medical regulatory issues and product development from discovery to clinical trial stages** will also be arranged.
- **Ensuring the general coordination of the activities of the project**

Furthermore, **external advisory boards** composed of experts who are independent of NAREB, will periodically review scientific results and progress of the scientific and clinically oriented activities as well as provide support for any ethical and safety issues that arise.

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Context

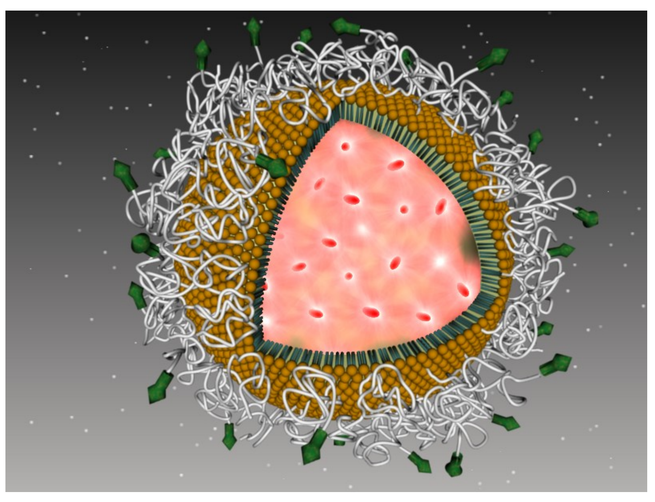
Increases in antibiotic resistances in all genera of bacteria are a raising concern worldwide. The frequency of antimicrobial resistance (AMR) in bacteria has increased in line with increasing usage of antimicrobial compounds. The extensive use of antimicrobials in human medicine over the past 70 years has now led to a major threat to clinical practice due to a relentless rise in the number and types of microorganisms resistant to these medicines.

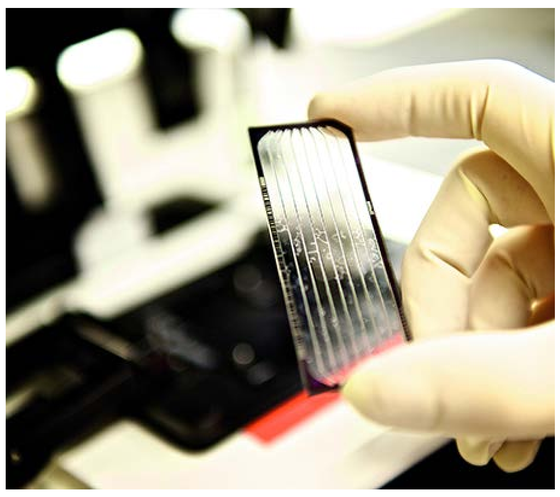
The World Health Organisation (WHO) has recognized **antibiotic resistance as one of the three major threats to global health**, and is predicting a forthcoming 'disaster due to the rapid, unchecked increase in antimicrobial resistance' largely as a consequence of the paucity of new classes of antibacterials in development.

Infections caused by MDR TB and MRSA lead to serious diseases which usually require intensive care treatment with long time of hospitalization. The portfolio of available antibiotics for treating antibiotic resistant bacterial infections is very limited and comprises of molecules inducing severe side effects and/or difficult to administrate like aminoglycosides and vancomycin that require parenteral injection. New drugs or at least new formulations of known drugs that provide better efficacy are urgently needed for a faster, more efficient, and less impairing treatment.

The possibility of **using novel drug delivery systems** for known and new antibiotic drugs opens the way to an innovative management of infections caused by drug resistant bacteria, which are otherwise difficult to treat. The successful use of nanoparticles for delivering and concentrating antimicrobial molecules to the site of infections should allow the use of antibiotics that have proved their efficiency *in vitro* but that show poor *in vivo* bioavailability.

The development of effective and safe nanotherapy approaches is particularly relevant in the antibacterial field, where typically high dose levels of drug are administered.





Expected Outcomes

The success of the utilization of nanoparticles in the improvement of drug targeting in other diseases opens the way for novel applications in nanotechnology-based treatments aimed at controlling MDR-TB and MRSA.

NAREB outcomes will contribute to the improvement of:

- the application of nanotechnology in medicine and the development of new therapy for bacterial infectious diseases, directly benefiting EU citizens
- the competitiveness of the European healthcare sector through novel systems and therapies,
- the cooperation and collaboration between actors from the public and the private sectors, with transfer of knowledge in regulatory issues related to the product development pathway of nanotherapeutics used in humans

With the potential of developing an innovative treatment for tuberculosis and MRSA, the NAREB project will significantly contribute to one of the major health related socio-economic and societal challenge, saving patient's quality of life and to reduce associated healthcare costs.

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