FACULDADE DE CIÊNCIAS E TECNOLOGIA
UNIVERSIDADE NOVA DE LISBOA

MSc in Biotechnology
Dissertation Project – 2nd Cycle

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Scientific area: Structural Biology and Biotecnology
TITLE: Nanoparticles as vehicles for the delivery of CO releasing molecules.

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BACKGROUND

CO releasing molecules (CORMs) are pro-drugs that can effectively release CO in a controlled manner for therapeutic applications. Carbon monoxide has been recognized as an important signalling molecule with noticeable protective effects in inflammation, cell proliferation and apoptosis. In the last decade metal carbonyl compounds have been found to act as CORMs in biological systems capable of carrying and delivering CO to various tissues. These pro-drugs have opened the way to the development of novel pharmaceutical agents appropriate for different therapeutic applications.

Until now, targeting of this class of compounds has not been successful. In the majority of the cases reported in the literature, CORMs are believed to bind to serum proteins and slowly release CO while in circulation.

OBJECTIVES

The aim of this project is to synthetize and characterize gold nanoparticles conjugated with CORMs and compare the efficiency of CO release in human cell lines compared with the free CORM.

Small angle X-ray scattering is going to be used in order to characterize the particles in solution bound to the commercial metal based CORM-3.

Cellular effect will be evaluated (cytotoxicity, pro-inflammatory and anti-inflammatory effects, apoptosis, cellular regeneration, etc) to assess the putative future use of the bioconjugates in therapy.

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PROJECT DESCRIPTION

The work in going to be divided in 5 tasks:

Task 1. Synthesis and functionalization of AuNPs – gold nanoparticles (AuNPs) are going to be prepared using the methods already reported in the literature. Biocompatibility is going to be achieved with small organic molecules as polyethylene glycol, which improves the stability of the particles.

Task 2. Functionalization with proteins (e.g BSA) – characterization of the nanoconjugates.

Task 3. Loading of CORM-3 onto nanoconjugates.

Task 4. SAXS data collection and analysis – the particles prepared in the previous tasks are going to be structurally characterized using small angle X-ray scattering methods. Low resolution data is going to be obtained showing the assemblage of the nanoparticles and the antibodies and CORMs.

Task 5. Evaluation of efficacy and cytotoxicity of the nanoconjugates compared to the free CORM– biological assays (cytotoxicity, pro-inflammatory and anti-inflammatory effects, apoptosis, cellular regeneration, etc) are going to be carried out in order to demonstrate the efficacy of the nanoconjufgates for therapeutic applications.

Based on the success of the proposal, functionalization with specific antibodies may be also used for the targeting of the nanoconjugates to specific cells.

TIMELINE (use fill tool for the cells)

	Month 1	Month 2	Month 3	Month 4	Month 5	Month 6	Month 7	Month 8	Month 9	Month 10
Task 1										
Task 2										
Task 3										
Task 4										
Task 5										
Thesis										