



CiMUS International PhD Programme

1. Project title:

Design and Characterization of siRNA/mRNA-Loaded Nanoparticles for the Treatment of Liver Fibrosis

2. Research Project:

Metabolic dysfunction–associated steatotic liver disease (MASLD) is one of the most prevalent chronic liver diseases worldwide, affecting approximately 30–40% of the global population. MASLD encompasses a broad disease spectrum ranging from simple steatosis to metabolic dysfunction–associated steatohepatitis (MASH), which can progress to liver fibrosis, cirrhosis, and hepatocellular carcinoma. Despite its prevalence and severity, effective and targeted pharmacological treatments for liver fibrosis remain extremely limited.

Liver fibrosis is driven primarily by the activation of hepatic stellate cells (HSCs). Targeting activated HSCs therefore represents a highly attractive therapeutic strategy. Our groups have uncovered a previously unrecognized role for human epidermal growth factor receptor 2 (HER2) in HSC activation and fibrogenesis. We demonstrated that HER2 expression is markedly increased in HSCs from both animal models and patients with liver fibrosis, that HER2 promotes de novo lipogenesis and activation of HSCs *in vitro*, and that genetic silencing of HER2 significantly attenuates fibrotic activation. These findings identify HER2 as a novel and druggable target in liver fibrosis associated with MASLD.

Building on this discovery, the current project aims to translate these mechanistic insights into a therapeutic strategy by developing multifunctional polymeric nanocapsules capable of encapsulating siRNA or mRNA while preserving their stability and bioactivity. These nanocapsules can be functionalized to selectively target liver cells and have demonstrated superior tissue diffusivity compared with conventional nanocarriers. Preliminary *in vivo* data show that our loaded polymeric nanocapsules preferentially accumulate in hepatic stellate cells and significantly reduce liver damage and fibrotic markers in animal models. The objectives of the project are: (i) to optimize and characterize the nanoparticle formulation and (ii) to assess efficacy, safety, pharmacokinetics, and pharmacodynamics in animal models of MASLD-associated fibrosis.



3. Job description:

Key Responsibilities:

The selected candidate will contribute to the design, execution, and interpretation of preclinical studies evaluating siRNA/mRNA-loaded polymeric nanocapsules for MASLD-associated liver fibrosis, including optimization of nanoparticle formulation, dosing, and administration strategies. They will assess how nanoparticle physicochemical properties (such as size, surface charge, and release kinetics) influence biodistribution, hepatic stellate cell targeting, and therapeutic efficacy, and will perform integrated analysis of multi-level datasets encompassing molecular, histological, imaging, and metabolic outcomes.

Candidate Requirements

- Graduate in Biomedical Sciences, Molecular Biology, Pharmacy, Medicine, or a closely related field.
- Background in liver biology, metabolic diseases, and/or nanomedicine.
- High level English at speaking and listening.
- Ability to work effectively in a multidisciplinary and collaborative environment, interacting with both academic and industrial partners.

Desirable:

- Basic knowledge in molecular and cellular biology techniques, i.e protein/RNA measurement, as well as in Pharmaceutical Nanotechnology.

4. Supervisor and Co-Supervisor:

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Research group: Molecular Metabolism

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Name: María José Alonso Fernandez Email: mariaj.alonso@usc.es

Research group: Nanomedicine and Drug Delivery

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