IBEC-VHIR INTERNATIONAL PhD PROGRAMME

Position

1. Project Title/ Job Position title:
   Urease-Powered Nanobots for Targeted Therapeutics in Inflammatory Bowel Disease (IBD)

2. Research project/ Research Group description

Nanotechnology has revolutionized biomedical applications, particularly in targeted drug delivery. Enzymatically powered nanobots have emerged as a groundbreaking tool for navigating complex biological environments. Recent advancements, such as in Serra et al. *ACS Nano,* 2024, demonstrate their potential for crossing mucus layers in ex vivo colon of mice. Similarly, hybrid micromotors in Li et al. *Sci. Robot.* 2024, improved prevention and treatment efficacy in a mouse model of Inflammatory Bowel Disease (IBD), exhibit efficient propulsion in biological fluids, making them ideal for dynamic environments. These studies collectively provide a strong foundation for developing therapeutic delivery systems tailored to diseases like IBD.

IBD poses significant clinical challenges, with current treatments often hampered by poor targeting and efficacy effects as well as systemic side effects due primarily to the high levels of drugs required to reach the region of inflammation in the digestive tract to exhibit the desired effects. The viscous and heterogeneous environment of the gastrointestinal tract complicates therapeutic administration and therefore large quantities of drugs need to be administered. In addition, these anti-inflammatory drugs are currently metabolized in the body, generating high levels of undesired metabolites and reducing the parent compound available to reach the IBD target. All of this underlines the need for innovative approaches. Enzyme-powered nanobots offer a promising solution by combining propulsion mechanisms with drug delivery systems. These nanobots can penetrate mucus barriers and deliver drugs directly to inflamed tissues, enhancing therapeutic efficacy while minimizing off-target effects.

This project will harness urease-powered nanobots for IBD treatment, addressing challenges in drug delivery. The candidate will synthesize and optimize nanobots, develop advanced drug loading and release mechanisms, and validate their performance in vitro and in vivo. This multidisciplinary research will create a transformative platform for precision medicine in gastrointestinal disorders. This smart system will transport anti-inflammatory drugs and tight junctions remodelling drugs to develop an accurate treatment to this increased and prevalent worldwide pathology without effective treatments.

The **Samuel Sánchez group at IBEC** specializes in enzyme-powered nanobots, focusing on design, optimization, and biomedical applications, including propulsion mechanisms and drug delivery. The José **Raul Herance group at VHIR** excels in preclinical research, medical molecular imaging, drug testing, and in vivo models, with expertise in studies focused on gastrointestinal and inflammatory diseases. Together, they offer a synergistic platform for innovative nanomedicine development using IVIS, CT, RM, PET or SPECT.

3. Job position description (max. 2.000 characters)

This PhD project focuses on developing enzyme-powered nanobots for targeted drug delivery in Inflammatory Bowel Disease (IBD). Building on advancements from **Simo, Serra et al. (Nat. Nanotechnol., 2024)** and **Serra et al. (ACS Nano, 2024)**, the research combines nanotechnology, chemistry, biology, and preclinical research to address challenges in delivering therapeutics within the complex gastrointestinal environment.

The project will be conducted at the **Institute for Bioengineering of Catalonia (IBEC)** and the **Vall d'Hebron Institute of Research (VHIR)**. Tasks 1 and 2, focused on nanobot synthesis, optimization, and drug delivery development in vitro, will take place at IBEC. Task 3, involving part of the in vitro and also the in vivo testing, will be conducted at VHIR, leveraging their expertise in preclinical research and humanized patient-derived models.

Objectives and Tasks:

This multidisciplinary project aims to create a transformative platform for precision therapeutics in IBD. By combining the expertise and state-of-the-art facilities at IBEC and VHIR, the candidate will gain a unique skill set in nanotechnology, drug delivery, and translational research, contributing to innovative solutions for gastrointestinal disorders.

The tasks performed by the candidate will be:

1. **Synthesis and Optimization of Nanobots** (IBEC):
   The candidate will fabricate and optimize urease-powered nanobots to enhance propulsion and functionality in gastrointestinal conditions. This includes optimizing surface chemistry and engineering designs for effective navigation through the viscous intestinal mucus layer. Testing the motion in mucus will be characterized by rheology, confocal imaging and other techniques.

2. **Drug Loading and Release** (IBEC):
   Develop strategies for encapsulating therapeutics with high loading efficiency and different release mechanisms to enable site-specific drug delivery to inflamed tissues.

3. **In vitro:** Test nanobots in advanced mucus-penetrating and epithelial barrier models, assessing their efficacy and safety. Model cell lines will be tested in IBEC and VHIR whereas patient derived cells will be studied only in VHIR.

4. **In Vivo Testing** (VHIR): Optimize and evaluate the nanorobots targeting and therapeutic potential in xenograft and patient-humanized models of IBD, focusing on biodistribution, inflammation reduction, and tissue repair.

Group Leader IBEC

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