Title: Transforming Healthcare: Treatment of Inflammatory Bowel Disease with Biocatalytic Nanobots

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Introduction: Inflammatory bowel disease (IBD), including Crohn's disease and ulcerative colitis, affects over seven million individuals globally, presenting significant healthcare and economic challenges (1). The inflamed gut microenvironment is characterized by excessive reactive oxygen species (ROS), which exacerbates mucosal damage (2). To address these limitations, a modular polymeric nanobot (NB) system is under development, with each module offering distinct functionalities. This study focuses on designing the NB core to mitigate oxidative stress and encapsulate bioactive compounds, laying the groundwork for subsequent modules that will enhance stability, navigation, and targeted delivery along the gastrointestinal (GI) tract.

Methods: The NB core was fabricated from chitosan using ionic gelation with sodium tripolyphosphate (TPP) acting as a crosslinking agent (3). To improve structural rigidity and maintain functional stability under physiological conditions, glutaraldehyde was incorporated during the synthesis process. Phenethyl isothiocyanate (PEITC), known for its antioxidant, anti-inflammatory, and anticancer properties (4), was encapsulated. Efficiency (EE) and drug loading (DL) were quantified. To reduce oxidative stress, catalase was conjugated to the NB core, enabling the decomposition of hydrogen peroxide (H_2O_2) into oxygen. Physicochemical characterization was carried out using scanning electron microscopy (SEM), dynamic light scattering (DLS), and Fourier-transform infrared spectroscopy (FT-IR). Enzymatic activity assays and *in vitro* release studies were performed to validate the NB core's functionality.

Results: The NB core exhibited a hydrodynamic diameter of approximately 311 nm and a zeta potential of +44 mV, supporting colloidal stability and efficient mucosal adhesion. High PEITC loading efficiency and sustained release were achieved under colonic conditions. Catalase retained over 90% of its enzymatic activity upon conjugation, effectively decomposing H_2O_2. Preliminary *in vitro* simulations confirmed both enzyme stability and the release of PEITC under conditions mimicking inflamed gut environments.

Conclusions and Impact: This biocatalytic polymeric NB core addresses critical challenges in IBD therapy by simultaneously alleviating oxidative stress and delivering bioactive compounds. As the foundational module of a multifunctional nanobot platform,

it provides a promising strategy for precision-targeted therapies in the GI tract. Ongoing work will incorporate additional modules to enhance stability, guide navigation, and broaden therapeutic functionalities.

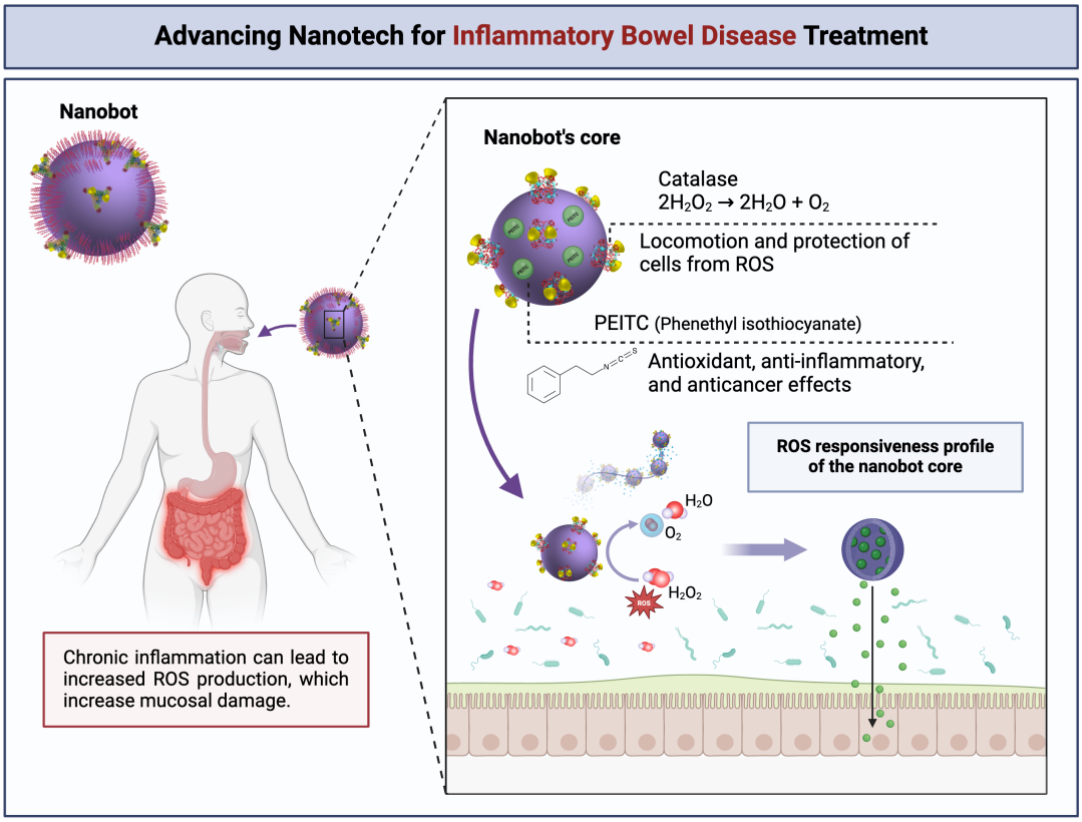

Figure 1. Advancing Nanotechnology for Inflammatory Bowel Disease (IBD) Treatment. The schematic illustrates the proposed mechanism of a nanobot-based therapeutic approach to addressing chronic inflammation in IBD. The nanobot is designed with a core containing catalase, which converts hydrogen peroxide (H_2O_2) into water (H_2O) and oxygen (O_2), reducing reactive oxygen species (ROS)-induced cellular damage. The core also incorporates phenylethyl isothiocyanate (PEITC), a compound known for its potent antioxidant, anti-inflammatory, and anticancer properties.

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Presenter biography: Ana Sofia Sousa holds an MSc in Pharmaceutical Sciences and is a PhD student at CBQF at Universidade Católica Portuguesa and i3S/Ipatimup at the University of Porto, Portugal. Her PhD research focuses on engineering multifunctional micro/nanoparticles to address intestinal inflammation. Additionally, she is involved in the gBiOT project, which aims to develop microrobotic technology for treating disorders of the gastrointestinal tract. Sofia's research interests encompass health sciences, biotechnology, nanotechnology, and bioproducts, reflecting her commitment to addressing global health and sustainability challenges.

Learning Objectives:

Describe the design and function of the biocatalytic polymeric nanobot core for IBD management
Analyze the functionalities of the NB core and the role of catalase activity and PEITC encapsulation in reducing oxidative stress and providing therapeutic benefit agents
Assess the modular approach that underpins next-generation gastrointestinal nanobot systems.