

gBIOT - Nutraceutical biopolymeric-biocatalytic microbot against gut inflammatory disorders



AS Sousa^{1,2,3}, MM Pintado¹, RD Matos^{2,3}, CC Sousa¹, MF Machado¹, M Coelho¹, PM Rodrigues¹, AM Magalhães^{2,3}, ER Coscueta^{1,*}

¹Universidade Católica Portuguesa, CBQF - Centro de Biotecnologia e Química Fina – Laboratório Associado, Escola Superior de Biotecnologia; ²3S – Instituto de Investigação e Inovação em Saúde, Universidade do Porto³; IPATIMUP – Instituto de Patologia e Imunologia Molecular da Universidade do Porto

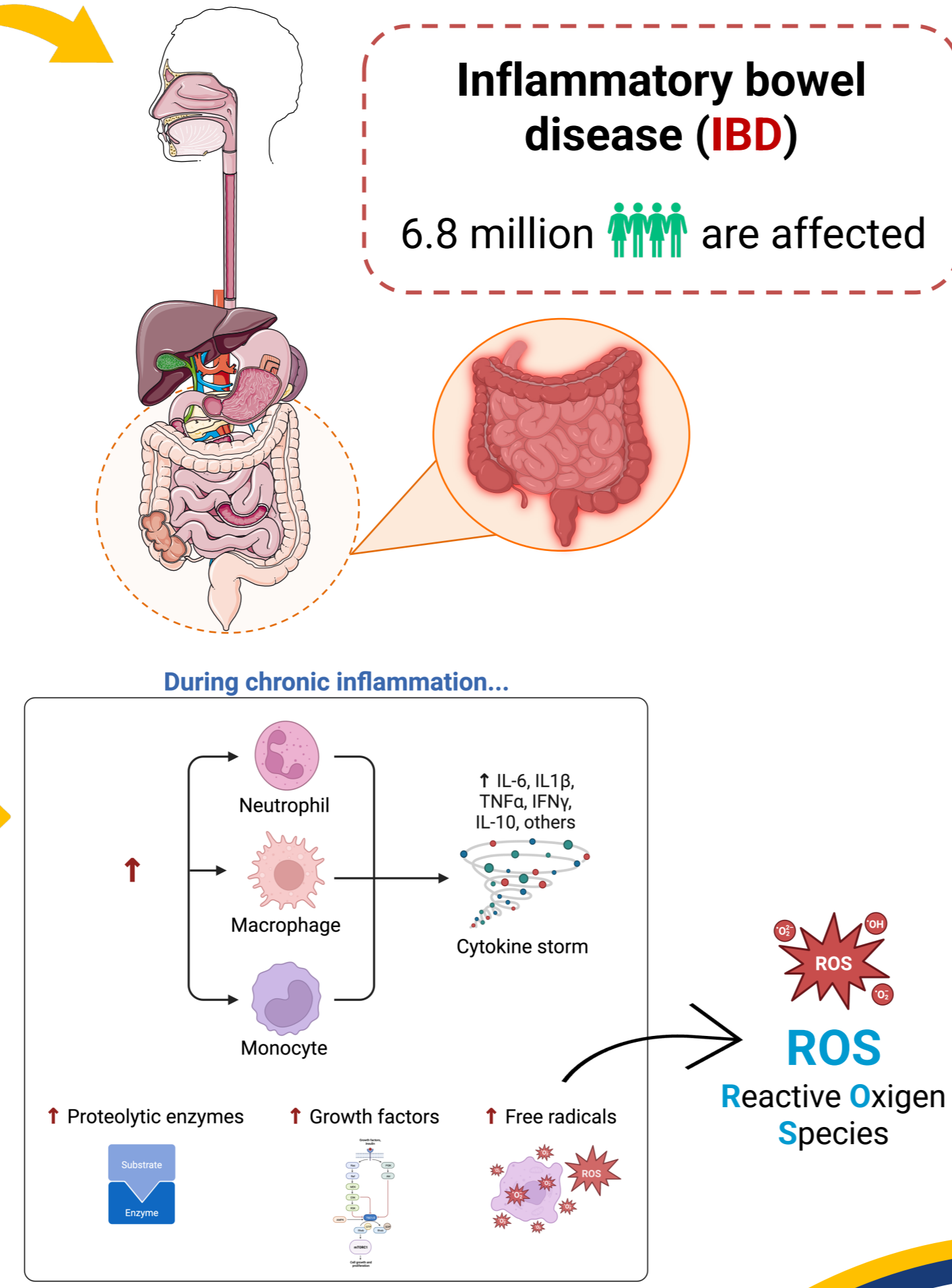
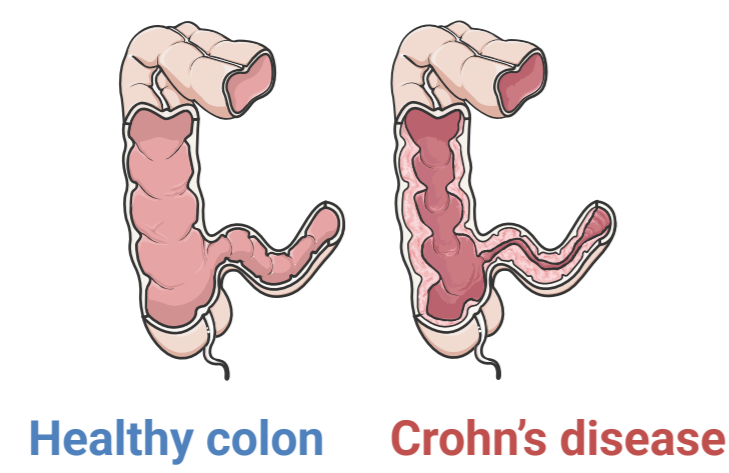
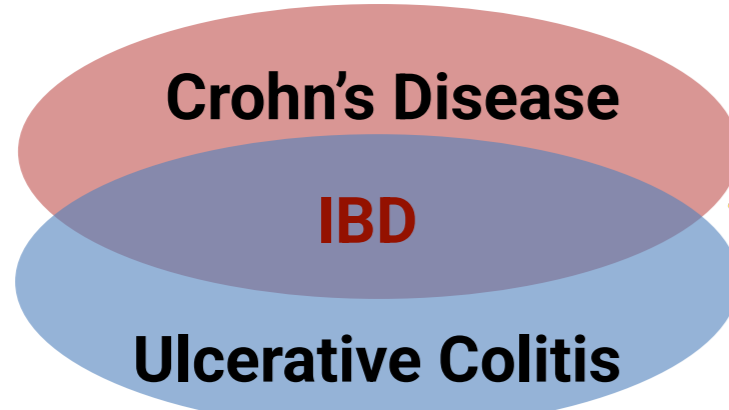
*Contact: ecoscueta@ucp.pt

CONTEXT

Gastrointestinal diseases have increased in incidence and prevalence over the past decade, affecting up to 40% of people worldwide.



IBD is characterised by chronic intestinal inflammation, especially in the colon



METHODS

ENCAPSULATION TECH

Drug delivery strategy

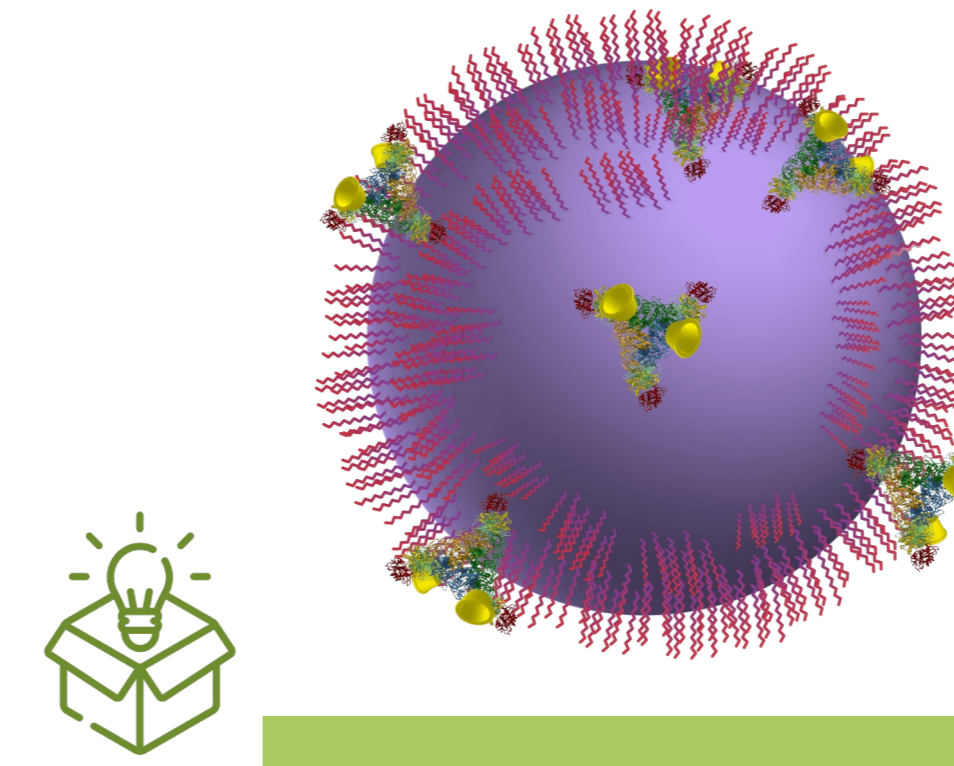


- Controlled release
- Protection of active components from damaging environmental conditions
- Avoiding localized retention
- Reducing the effective dose and toxicity of active components

MICROBOTS

Devices expected to do specific tasks at the atomic, molecular, and cellular levels:

Move, feel/manipulate their environment, and display intelligent behaviour (perceiving the environment, processing such perceptions, and responding to maximize an expected result).



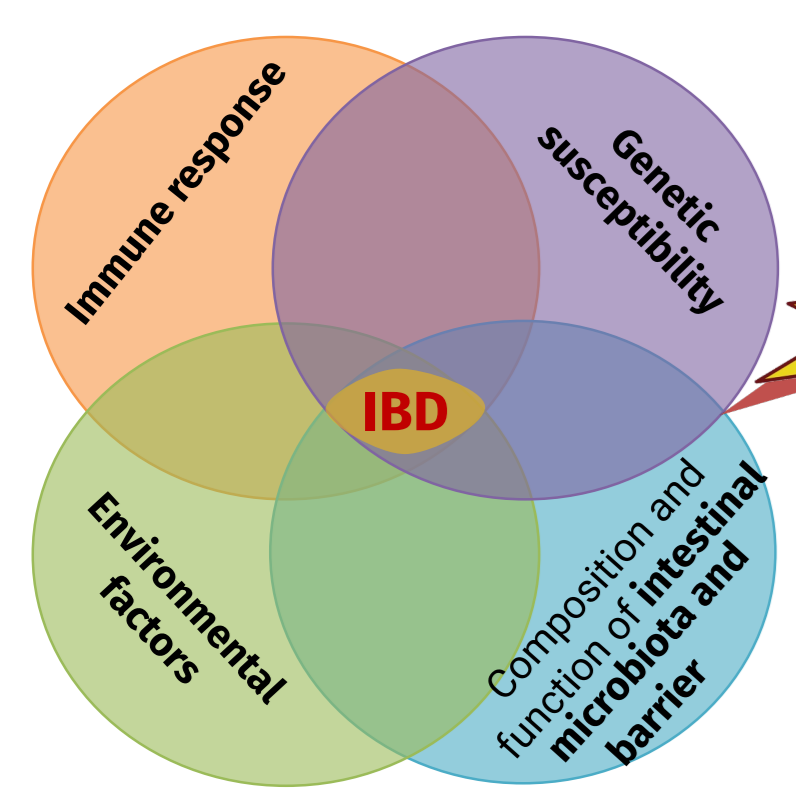
How does the microbot move?

By anchoring enzymes in micro/nanoparticles, biocatalysis can produce a propulsive force that generates self-propelled micro/nanoparticles. In this regard, the enzyme urease is a successful example that allows for enhanced Brownian motion of micro/nanoparticles in the presence of urea as a biofuel.

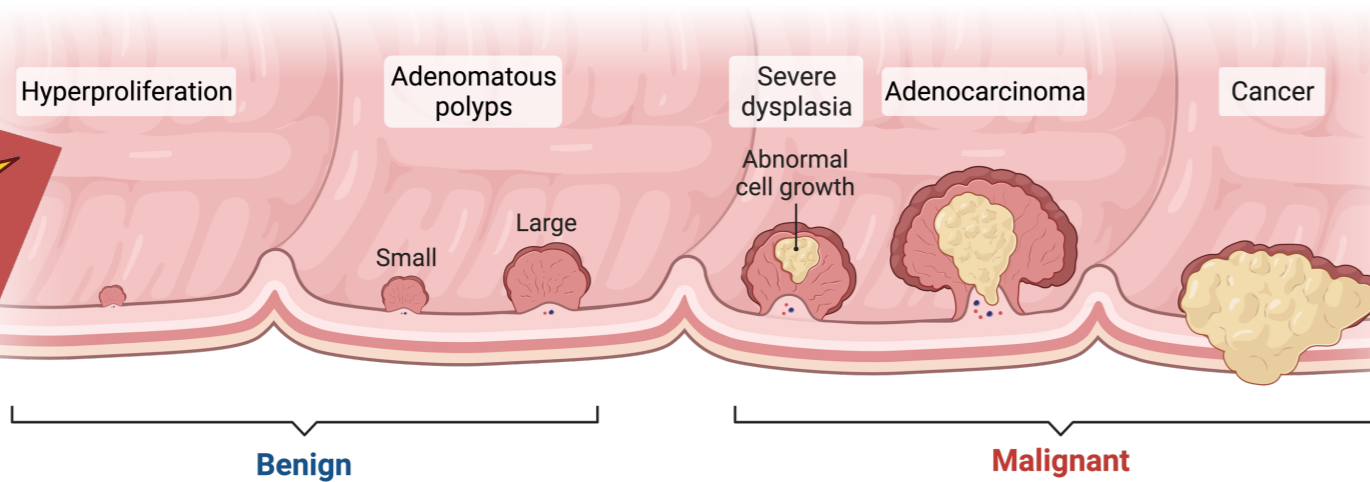
WORKING HYPOTHESIS

"It is technically feasible to develop a biocompatible microbot capable of reaching the colon by propelling itself through the surrounding gut urea, balance ROS levels and release anti-inflammatory compounds selectively in the inflamed mucosa"

What is the aetiology of IBD?



Benign and Malignant Colorectal Cancer (CRC)



How common is CRC?

CRC is the 3rd most common cancer type worldwide & the 2nd most deadly cancer

Data source: Globocan 2020

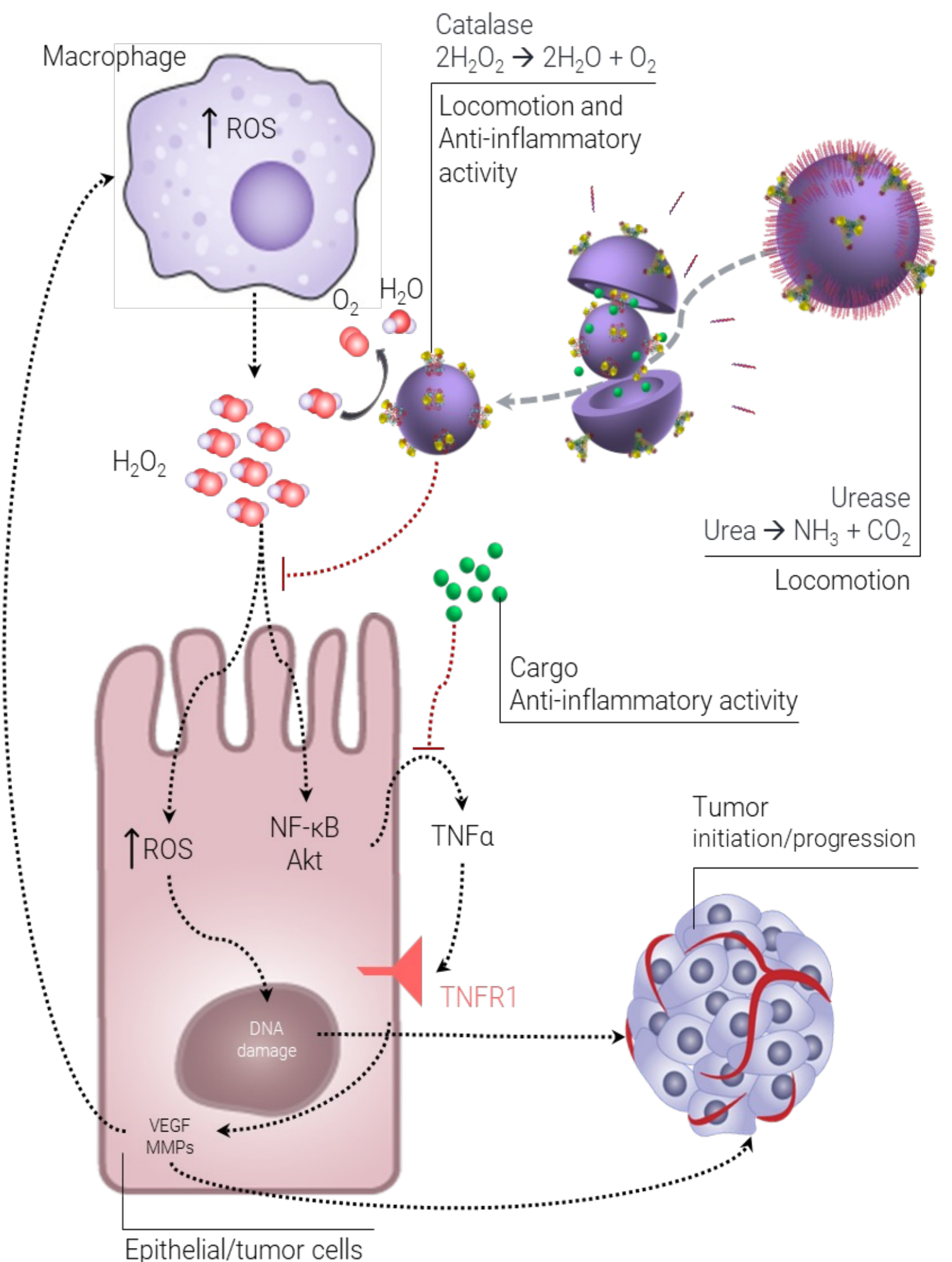


EXPECTED RESULTS

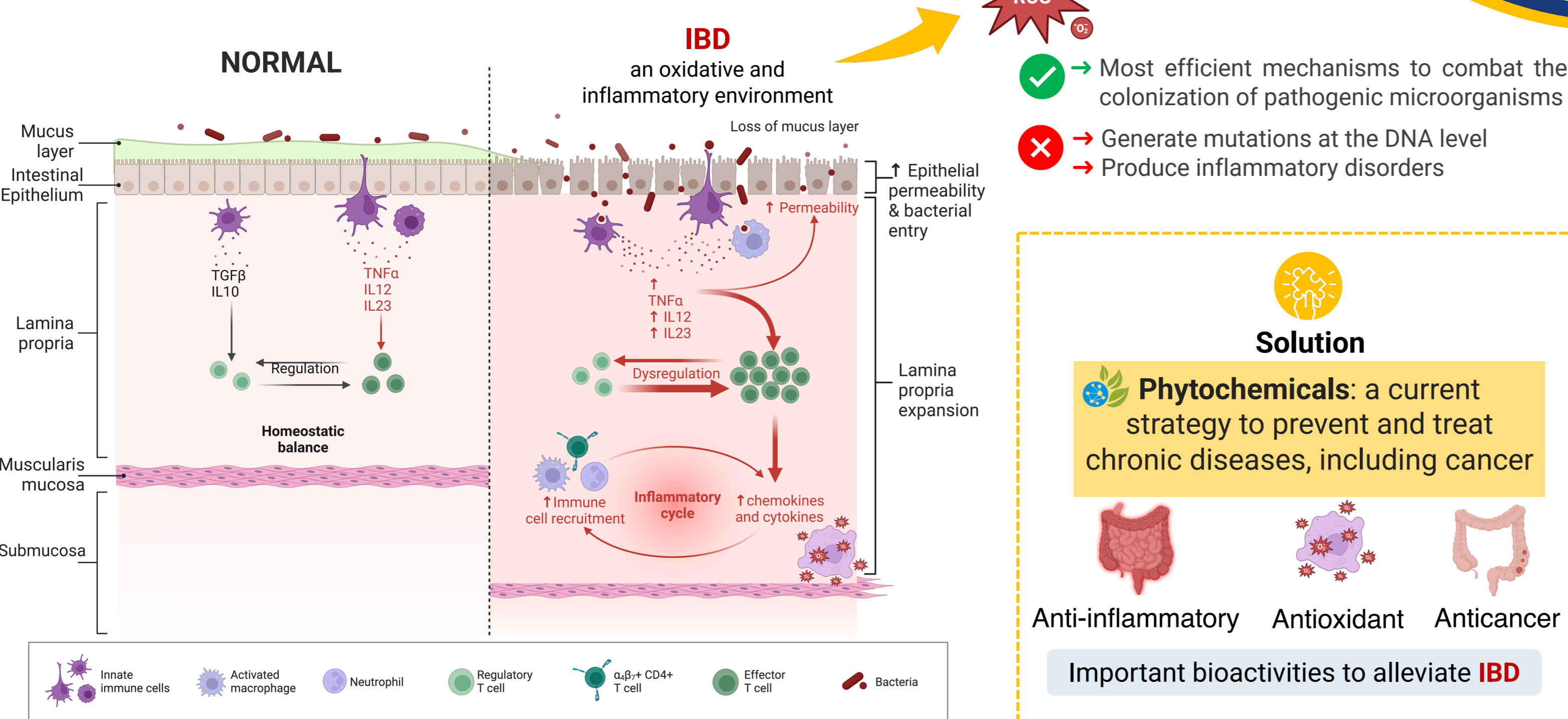
gBiOT will develop a target-efficient biocatalytic and biocompatible polymeric microbot capable of detecting and transforming the environment and delivering bioactive compounds.



- ✓ Develop a "rocket" modular microbot specifically and efficiently oriented to the colon, modifying the inflammatory state chemically and catalytically.
- ✓ Load the microbot with natural bioactive compounds.
- ✓ Validate the prototype *in vitro* and *in vivo* for the target functionalities: bacterial enzyme-activated sensitivity, anti-inflammatory properties, and anticancer activity.
- ✓ Explore the creation of a nutraceutical ingredient: direct encapsulation of natural extracts in the microbot.



Healthy and Inflamed Epithelium



GOAL

Achieve Remission

- Improve symptoms
- Control inflammation
- Prevent carcinogenesis

TREATMENT:

BETTER QUALITY of LIFE

Effective plans focus on OVERALL HEALTH

while minimizing SIDE EFFECTS and DISCOMFORT

gBiOT aims to develop an intelligent system efficiently oriented to the colon, loaded with natural bioactive compounds, and capable of reducing microenvironmental oxidative stress in gastrointestinal diseases.

REFERENCES

Cani, P. D., & Jordan, B. F. (2018). Gut microbiota-mediated inflammation in obesity: a link with gastrointestinal cancer. *Nature Reviews Gastroenterology and Hepatology*, 15(11), 671–682.

Coscueta, E. R., Sousa, A. S., Reis, C. A. & Pintado, M. M. (2022). Phenylethyl Isothiocyanate: A Bioactive Agent for Gastrointestinal Health. *Molecules* 27, 1–12.

Franzin, M., Stefančić, K., Lucafò, M., Decorti, G. & Stocco, G. (2021). Microbiota and drug response in inflammatory bowel disease. *Pathogens* 10, 1–28.

Lee, S. H., Bajracharya, R., Min, J. Y., Han, J. W., Park, B. J., & Han, H. K. (2020). Strategic approaches for colon targeted drug delivery: An overview of recent advancements. *Pharmaceutics*, 12(1).

Llopis-Lorente, A. et al. (2019). Enzyme-powered gated mesoporous silica nanomotors for on-command intracellular payload delivery. *ACS Nano*, 13(10), 12171–12183.

Mathews, S. C. et al. (2022). Prevalence and Financial Burden of Digestive Diseases in a Commercially Insured Population. *Clinical Gastroenterology and Hepatology* 20, 1480-1487.e7.

Morgan, E. et al. (2022). Global burden of colorectal cancer in 2020 and 2040: incidence and mortality estimates from GLOBOCAN. *Gut* *gutjnl-2022-327736*.

Ng, S. C. et al. (2017). Worldwide incidence and prevalence of inflammatory bowel disease in the 21st century: a systematic review of population-based studies. *The Lancet* 390, 2769–2778.

ACKNOWLEDGEMENTS

This work was supported by FCT - Fundação para a Ciência e Tecnologia through grant Ref.º 2022.02926.PTDC "Nutraceutical biopolymeric-biocatalytic microbot against gut inflammatory disorders", project UIDB/50016/2020 and author Ana Sofia Sousa individual PhD grant number 2021.07407.BD.

