

Safety and Efficacy of an Olive Oil-Derived Nutraceutical in Inflammatory Bowel Disease (IBD) Patient-Derived Organoids: A Sustainable Approach to Precision Medicine

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INTRODUCTION & AIM

Inflammatory bowel disease (IBD), encompassing Crohn’s disease and ulcerative colitis, represents a group of chronic, relapsing inflammatory disorders of the gastrointestinal tract. These conditions are driven by dysregulated immune responses that cause persistent intestinal inflammation and tissue damage, leading to significant morbidity. Current pharmacological treatments, although effective in part of the patient population, often show variable efficacy and are associated with adverse effects, highlighting the need for safer and more personalized therapeutic approaches. Patient-derived organoids (PDOs) have recently emerged as a powerful *in vitro* model that faithfully reproduces the histological and molecular features of the original intestinal tissue. PDOs from IBD patients retain individual inflammatory and genetic signatures, providing an ideal platform for studying disease mechanisms and evaluating patient-specific therapeutic responses [1]. In this study, we investigate the potential of IBD-derived organoids as a personalized system to test a natural compound derived from extra virgin olive oil, a functional food known for its anti-inflammatory and antioxidant properties. Our aim is to assess the ability of this Natural compound to modulate inflammatory responses in IBD organoids, and to explore PDO-based platforms as innovative tools for screening nutraceutical compounds [2].

METHODS

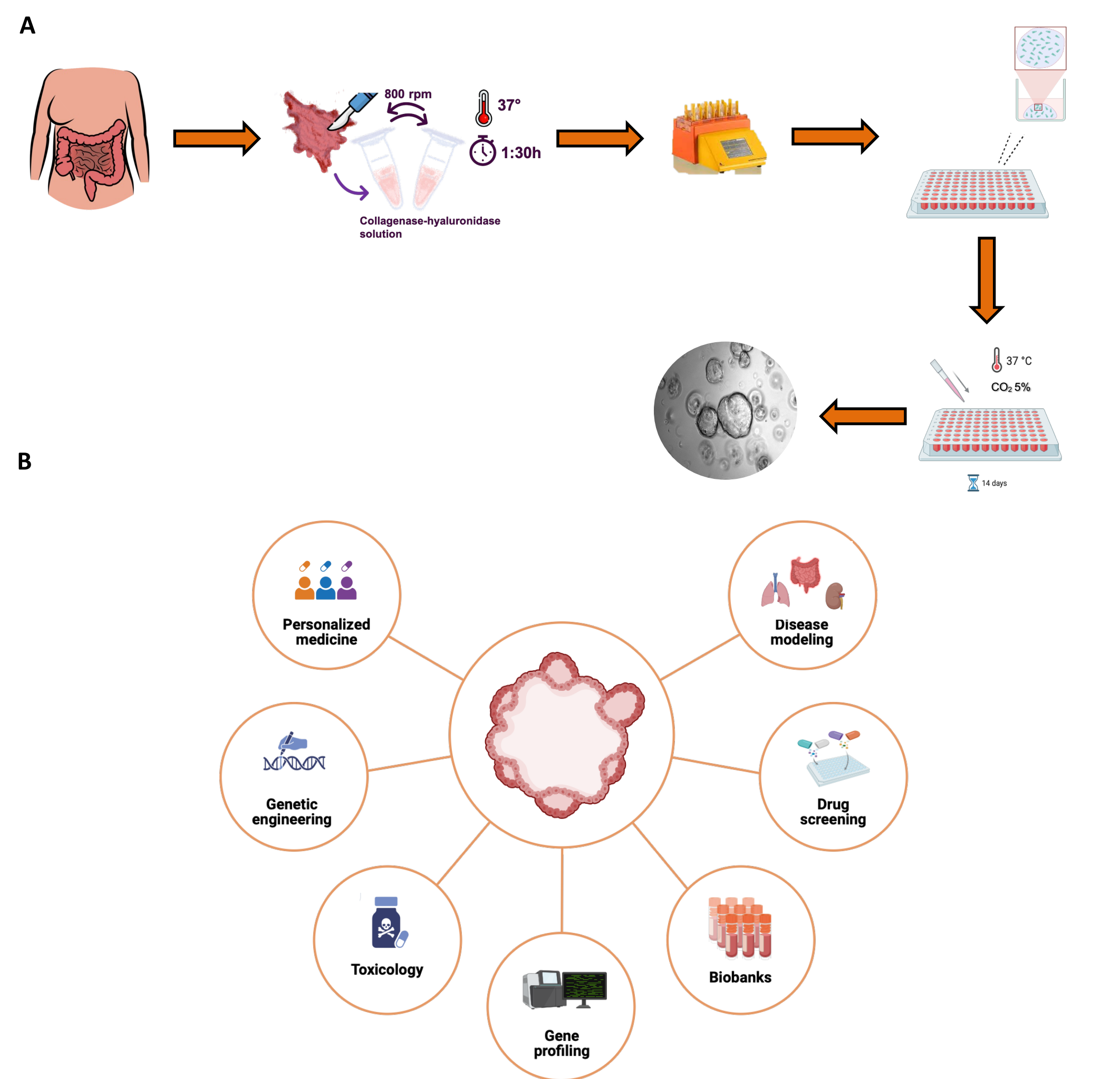


Figure 1A. Steps in human intestinal organoids derived from Healthy patients (hIOs) and Inflammatory Bowel Disease ones (hIBDOs). Image generated with BioRender sotware.
Figure 1B. Overview of organoid applications across biomedical research. Organoids are mainly employed for human disease modeling, assess drug responses, advance personalized and toxicological assessment. Image generated with BioRender sotware.

FUTURE WORK

- **Model optimization and molecular refinement** to enhance reproducibility and biological relevance.
- **Regulatory standardization** through validation and collaboration with EFSA and FDA.
- **Automation and scale-up** to enable high-throughput applications in safety and drug testing.

References:
[1] Lucafò M, Muzzo A, Marcuzzi M, et al. Patient-derived organoids for therapy personalization in inflammatory bowel diseases. *World J Gastroenterol.* 2022;28(24):2636–2653.
[2] Vrdoljak J, Kumric M, Vilovic M, Martinovic D, Tomic IJ, Krnic M, et al. Effects of olive oil and its components on intestinal inflammation and inflammatory bowel disease. *Nutrients.* 2022;14(4):757.

RESULTS & DISCUSSION

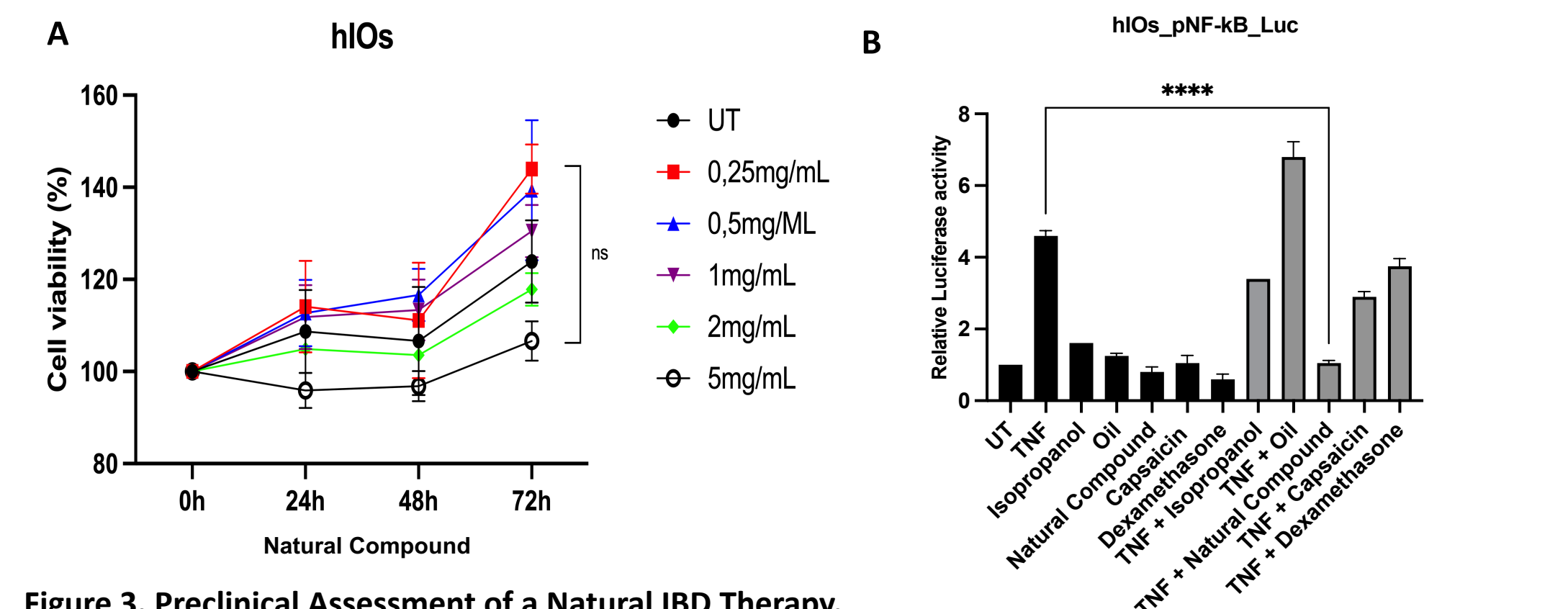
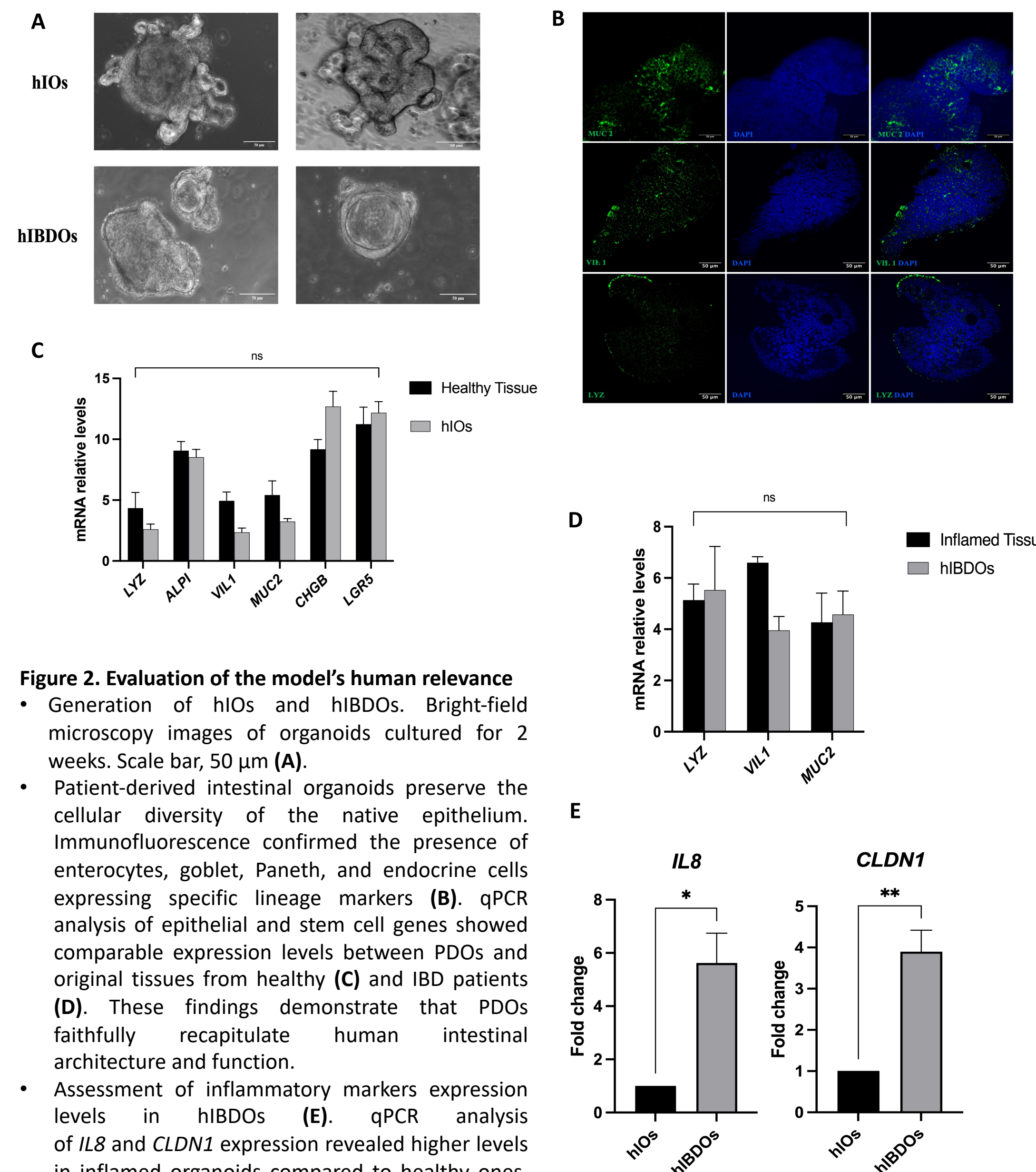


Figure 3. Preclinical Assessment of a Natural IBD Therapy. A natural compound derived from extra virgin olive oil, with putative anti-inflammatory properties and a favorable food safety profile, was evaluated as a potential therapeutic candidate for IBD. Cytotoxicity testing in human intestinal organoids (hIOs) using MTT assays (0.25–5 mg/ml, up to 72 h) showed no significant effects on cell viability, supporting its biocompatibility (A). To assess its anti-inflammatory potential, a 3D luciferase reporter model (hIOs_NF-kB_Luc) was established. Upon TNF α stimulation, the model exhibited a strong induction of luciferase activity, which was significantly reduced following treatment with the natural compound, more effectively than with a standard therapy or an alternative natural molecule, confirming its safety and efficacy as an anti-inflammatory agent (B).

CONCLUSION

Given the variability in patient responses and the limitations of current pharmacological treatments, our findings highlight the potential of PDO-based platforms to screen and validate olive oil-derived natural molecules as innovative, personalized strategies for managing IBD. This approach not only aligns with the growing interest in nutraceuticals and diet-based interventions but also opens new avenues for developing safer and more effective therapies grounded in natural medicine