

**NYU**

Patient-Derived Organotypic Slice Culture (OSC) Prognostic Tool for Improved Inflammatory Bowel Disease Treatment Outcomes

A rapid, individualized, clinically-actionable predictive tool for assessing patient response to inflammatory bowel disease (IBD) immunotherapies.

Technology

The Axelrad Lab at NYU Langone has developed an innovative *ex vivo* patient-derived microenvironment model to predict individual patient responses to IBD immunotherapies with the goal of improved IBD clinical outcomes. This model uses human intestinal organotypic slice cultures (OSC) derived from primary tissue collected from mucosal pinch biopsies commonly taken during routine clinical screenings (e.g. colonoscopies). Collected primary tissue is embedded into agarose blocks, sectioned with a vibratome into 125µm-thick slices, and then independently cultured using specific organoid growth media (hOGM). The tissue slices are ready for drug screening within hours, and resulting cryptoids (organoid-like structures) grow within as little as two days, offering a faster alternative to traditional organoid models that take weeks to generate (Figure 1). Cryptoid growth rate is the readout for assessing therapy efficacy, as growth is severely inhibited by tissue inflammation. Previously, the Lab demonstrated that colon organoids derived from ulcerative colitis (UC) patients could predict responses to anti-TNFα and JAK inhibitor therapies. While traditional organoid models provide insight into disease mechanisms, they are inconvenient to use due to lengthy maturation times and often exclude crucial tissue physiology elements, including the mucosal immune and stromal environments. This OSC model overcomes these challenges by preserving the native colon tissue composition and architecture, including the inflammatory milieu of the colon mucosa, permitting more accurate prediction of an individual's therapeutic responses by measuring changes in cryptoid growth and viability. In all, this OSC model introduces a holistic model of inflammation using intact human tissue and lays the groundwork for a precision medicine platform to predict personalized IBD therapy responses.

Development Status

Completed studies have shown the OSC model to be feasible across a wide range of individuals and intestinal tissue sites. Further, it has been shown that cryptoid growth rate is inversely associated with tissue inflammation. Future studies will use anti-TNFα agents and JAK inhibitors to demonstrate that the cryptoid growth (regeneration) readout in the OSC model is a surrogate marker for patient mucosal healing, the primary treatment goal for patients with IBD. This approach is being extended to determine feasibility in chronic inflammatory diseases of other tissues.

Background

Technology ID

AXE02-01

Category

Life Sciences/Diagnostics

Life Sciences/Platform

Technology

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Life Sciences/Research

tools/Drug Development

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IBD is a chronic relapsing inflammatory condition of the gastrointestinal tract that affects more than 3 million people in the U.S. Despite the availability of advanced biologics like anti-TNF α and novel small molecules such as JAK inhibitors, only about half of patients with IBD achieve the desired therapeutic responses. Traditional evaluation methods, such as relying on clinical indices and biomarkers, often fall short in predictive accuracy due to the heterogeneous nature of UC pathogenesis. Consequently, many patients continue to suffer from suboptimal responses that not only prolong symptom burden and reduce quality of life but also heighten the risk of disease complications. The restriction of therapy response to only a subset of patients indicates distinct epithelial and inflammatory signatures that predict specific drug responsiveness. Therefore, there is a significant unmet need for predictive models that incorporate stromal and immune components to determine individual drug effectiveness early in the treatment process, thereby precisely matching UC patients with therapies that will be efficacious for their specific disease profiles.

Application

- **Predictive tool:** *Ex vivo* patient compatibility testing for IBD therapeutics: clinical-stage and approved treatments.
- **Drug development platform:** Identification and development of new preclinical treatments.
- **Research tool:** To investigate the IBD microenvironment and inflammatory response mechanisms.

Advantages

- **Individualized insight:** Recapitulates patient-specific intestinal tissue structures and components, maximizing predictive accuracy.
- **Convenient sourcing:** Primary colon tissue for the OSC model is collected during already necessitated clinical procedures, not requiring further specialized procedures.
- **Rapid culturing time:** Supports rapid cryptoid generation within just 2 days, shortening clinical readout time.
- **Scalable testing capacity:** Allows testing of over 20 therapies per patient.
- **Enhanced visualization of individual crypts:** Slice culture facilitates clear visualization of and growth from individual colon crypts.
- **Standardized and reproducible:** Consistent capturing of crucial tissue elements and crypt bases across sequential slices.

Intellectual Property

NYU has filed a U.S. provisional patent application covering the methods of (i) generating the OSC model from patient samples, (ii) using the model to screen for new IBD therapies, and (iii) using the model to determine individual patient response to immunotherapies in a clinical setting.

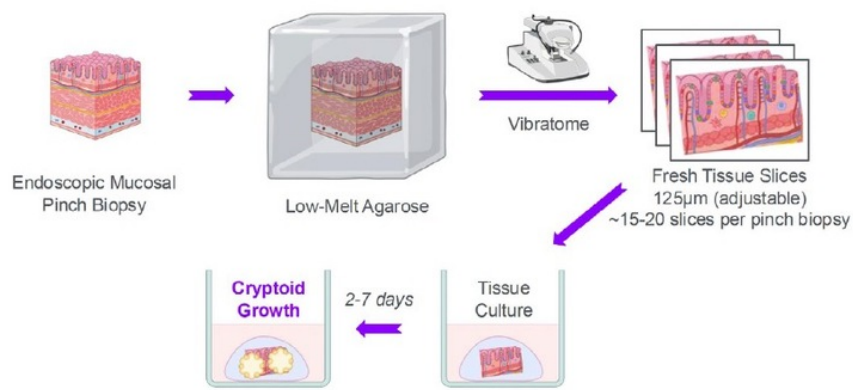


Figure 1: Schematic illustrating the workflow for generating the organotypic slice culture (OSC) model from a patient's intestinal tissue collected from mucosal pinch biopsies. Created with BioRender.com.