Personalized Ex Vivo Platform for Testing Patient Responsiveness to Therapeutics for Inflammatory Disorders

A novel and innovative organoid co-culture system for studying immune-mediated tissue damage and testing patient responses to therapies for inflammatory disorders.

Technology

The Cadwell lab, while at NYU, has developed a method to replicate a patient's inflammatory disease state outside the body, providing an *ex-vivo* platform to assess patient responsiveness to different therapeutic interventions for inflammatory diseases like intestinal graft-versus-host disease (GVHD) or inflammatory bowel disease (IBD). Briefly, small-intestinal or colonic crypt cells are cultured in contact with an extracellular matrix (Matrigel) to form an intestinal organoid, which is combined with a stimulated immune cell suspension. The Cadwell lab has demonstrated the effectiveness of this technology by using it to identify new therapeutic strategies to prevent gastrointestinal (GI) tissue damage in GVHD. As described in *Matsuzawa-Ishimoto et al. Blood 2020*, they discovered that the *Atg16L1* gene increases susceptibility to T-cell mediated killing using organoids from GVHD mouse models in their co-culture system. Furthermore, they used the co-culture system to identify two therapeutic approaches to prevent GI tissue damage by inhibiting necroptosis or interferon signaling. Thus, this innovative and promising organoid platform can be used to test patient responses to therapies, develop new drugs for inflammatory disorders, and support basic research of these diseases.

Background

The current standard of care for treating inflammatory disorders typically involves a 'step-up' strategy, where patients receive progressively more intense and high-risk treatments if they do not improve with less aggressive options. This strategy not only generates a significant burden on the healthcare system but also diminishes patients' quality of life. Thus, there is an unmet need for innovative *ex-vivo* platforms to accurately predict patient responsiveness to therapies with the goal of tailoring more effective personalized treatment plans. Such approaches would effectively address the significant challenge of varying patient responses to therapies for inflammatory disorders.

Development Stage

The technology has demonstrated utility in pre-clinical studies of human disease, for example IBD, and current work is ongoing to refine production protocols and applications.

Applications

Technology ID

CAD01-04

Category

Life Sciences/Therapeutics/Inflammat Disease
Life Sciences/Platform Technology
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Learn more

- **Testing patient compatibility with therapies (both approved and experimental) for multiple inflammatory diseases:** Intestinal graft-versus-host disease (GVHD), inflammatory bowel disease (IBD), autoimmunity associated with cancer immunotherapy, gastrointestinal cancers, and radiation enteritis.
- **Drug discovery and development:** Identification of new, more personalized inflammatory disease therapies.
- **Research tool:** Platform can be leveraged to understand the mechanism of immune-mediated tissue damage in the aforementioned disease states.

Advantages

- **Improved treatment response rate:** Predicts patient response *ex vivo* prior to therapy administration.
- **Personalized medicine:** Enables the creation of customized treatment plans for each patient.
- **Recapitulates immune-mediated tissue damage:** Replicates the interaction between activated immune cells and GI tissue where damage occurs.
- **Rapid and tunable testing platform:** Organoids can be generated within 1-2 weeks of patient-derived sample procurement using different types of primary samples. Robust system: Organoids can be freeze-thawed and are stable for >10 passages.

Intellectual Property

NYU holds a pending U.S. non-provisional application and pending counterpart continuation application covering the composition and methods of preparing an organoid co-culture and treating *Atg16L1*-driven immune-mediated tissue injury with necroptosis or interferon signaling inhibitors.

References

1. Matsuzawa-Ishimoto et al. , https://pubmed.ncbi.nlm.nih.gov/32232483/