

Clinically Relevant Science

Introducing the Human Inflammatory Bowel Disease (IBD) Fresh Tissue Assay from REPROCELL: the most clinically relevant IBD model on the market. Our living tissue model captures the heterogeneous landscape of IBD¹ by combining drug efficacy data with a medical history of each human donor.

Meet clinical needs in IBD research

The incidence of IBD is increasing² and there is a clinical need for safer, more precise IBD treatments^{3,4}. However, failure to predict the safety and efficacy of drugs during preclinical research means that attrition rates are high⁵.

REPROCELL offers the most clinically relevant IBD assay on the market, which uses human tissue donated by real IBD patients.

Why use human tissues instead of traditional animal models?

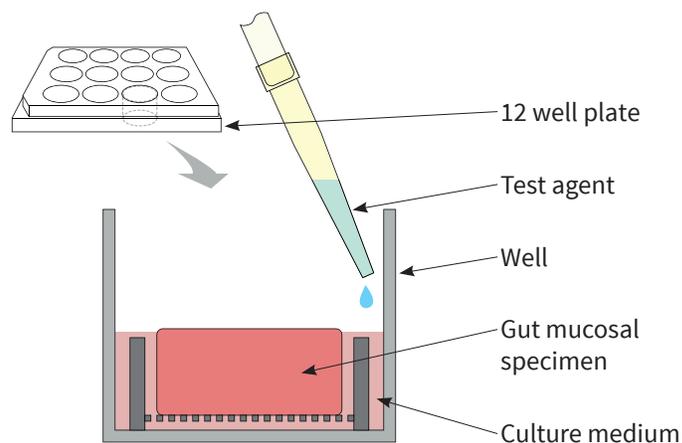
- ✓ **Avoid** species differences
- ✓ **Increase** therapeutic relevance⁶
- ✓ **Improve** understanding of IBD pathology⁷
- ✓ **Proof of concept** in diseased human tissues
- ✓ **Reduce** late-stage failures
- ✓ **Strengthen** IND submissions
- ✓ **Explore** complex cell interactions in whole tissue

Five reasons to choose REPROCELL's Human IBD Fresh Tissue Assay

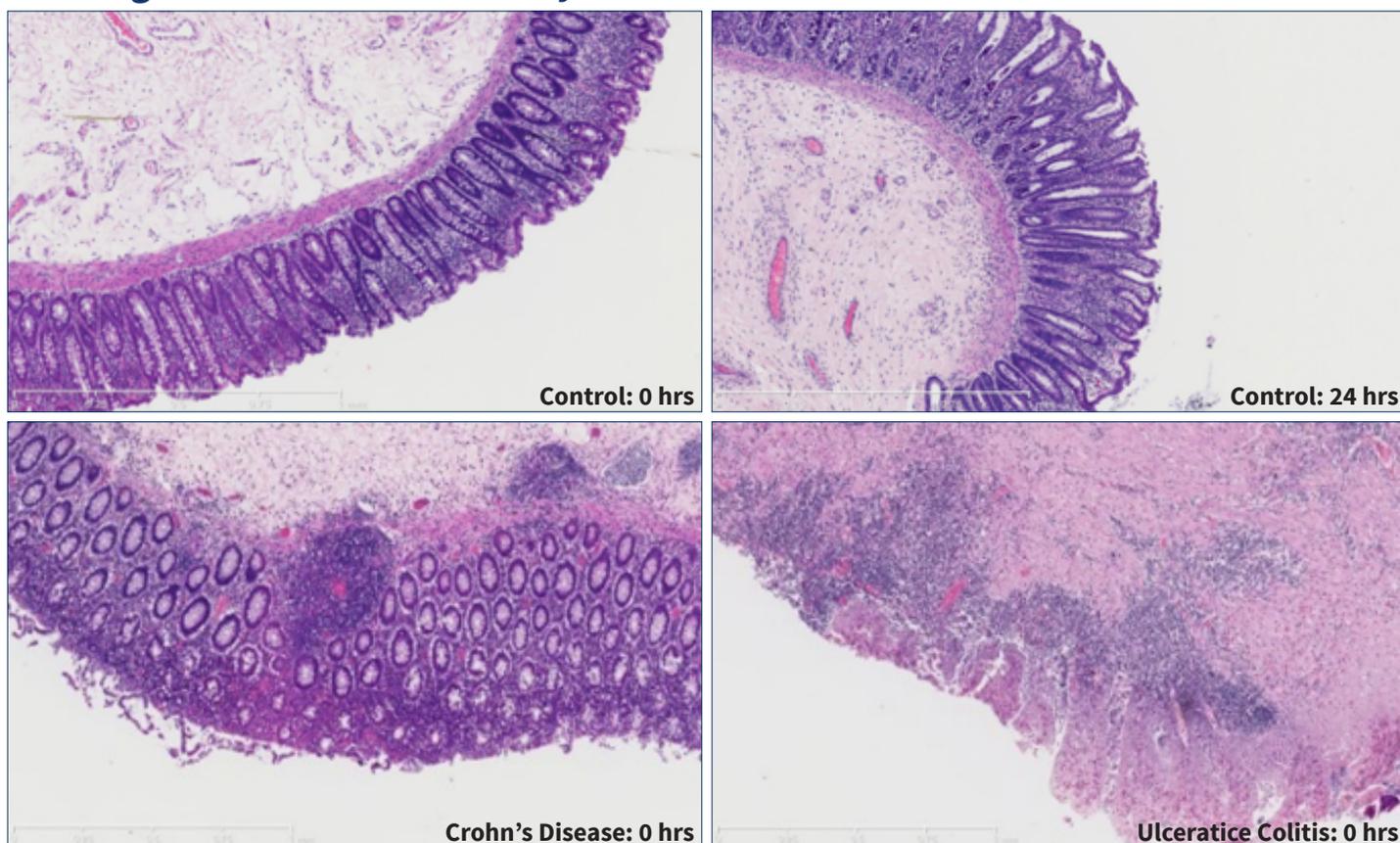
1. Access the only commercially available assay using intact, living human tissues.
2. Add commercial value by demonstrating efficacy in tissues from your target patient group.
3. Identify lead test agents with likelihood of success in patients.
4. Compare your test agents to current standard of care drugs.
5. Combine with REPROCELL's molecular biology services to relate phenotype to genotype.

Breaking Barriers

More scientists would like to use human tissue in their research⁷. However, poor biobanking infrastructure and technical difficulties present significant barriers. Through our global network of biorepositories, we can access a frequent supply of high-quality intestinal tissues from Crohn's and Ulcerative Colitis (UC) patients. They are then maintained for 24-hours in our *ex vivo* culture system, where they can be exposed to a variety of novel and standard-of-care drugs.

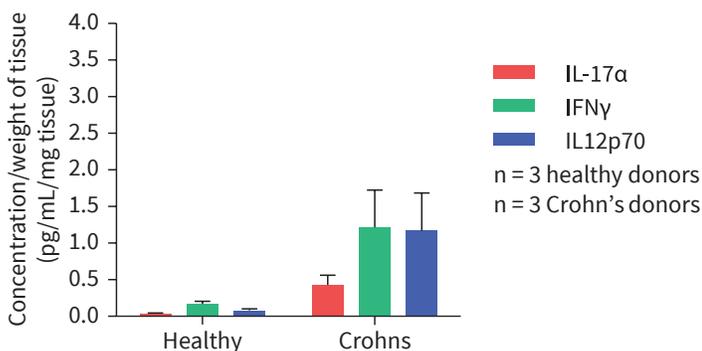


Histological validation of healthy and diseased tissues



At 0 hours, the control tissue shows good crypt morphology, intact lamina propria and muscularis mucosa. **24 hours later**, the crypt morphology and muscularis mucosa are maintained. Although there is slight degradation of epithelial structure, it is generally intact. **At 0 hours**, **Crohn's disease tissue** shows shortened and widespread crypts, increased lamina propria cellularity and granuloma. **Ulcerative Colitis tissue** demonstrates crypt destruction, widespread mucosal erosion and severely thickened muscularis.

Functional validation of healthy and diseased tissues

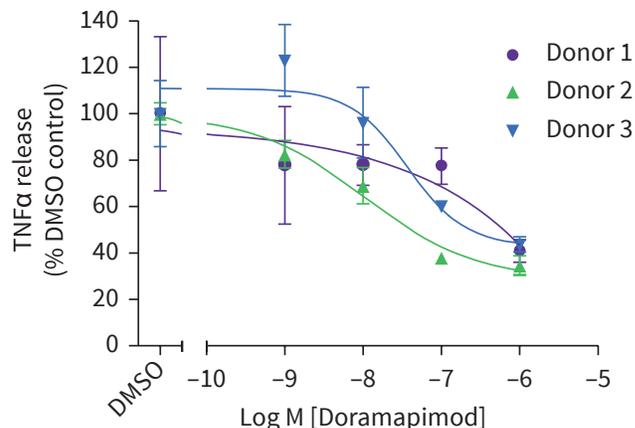


As part of our functional validation, biopsies are screened for inflammatory mediators commonly upregulated in IBD. In this example, over 40 inflammatory mediators were measured to investigate the cytokine release profiles in healthy and diseased tissue. The disease group showed greatly increased levels of a range of key cytokines and chemokines commonly upregulated in IBD, including IL-17α, IFNγ and IL-12p70.

Investigate interpatient variation in drug response at the preclinical stage

Intestinal biopsies were obtained from 3 UC patients. Following an 18-hour culture period, TNF α release was measured across a wide concentration range of the test agent Doramapimod (see graph).

Differences in response were evident across patient samples, suggesting variation in the UC patient population, as is known to occur clinically.



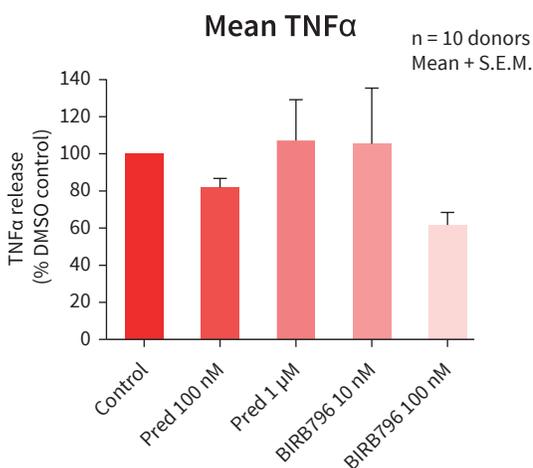
Precision Medicine

Precision medicine aims to deliver the right drug to the right patient at the right dose. However, most presently available drugs fail to work in a high percentage of patients; including treatments for IBD³.

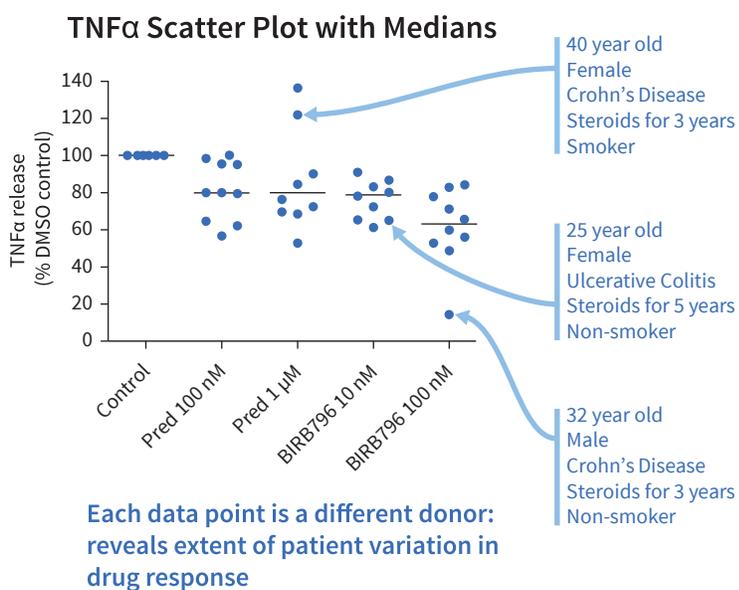
At REPROCELL, we offer early stage characterization of the patient population. By combining measurements of drug efficacy with clinical histories and access to state-of-the-art molecular phenotyping, we can investigate inter-individual variation in drug response at the preclinical stage.



Relate drug response to clinical history



Compare the mean responses of your test agent to standard-of-care compounds



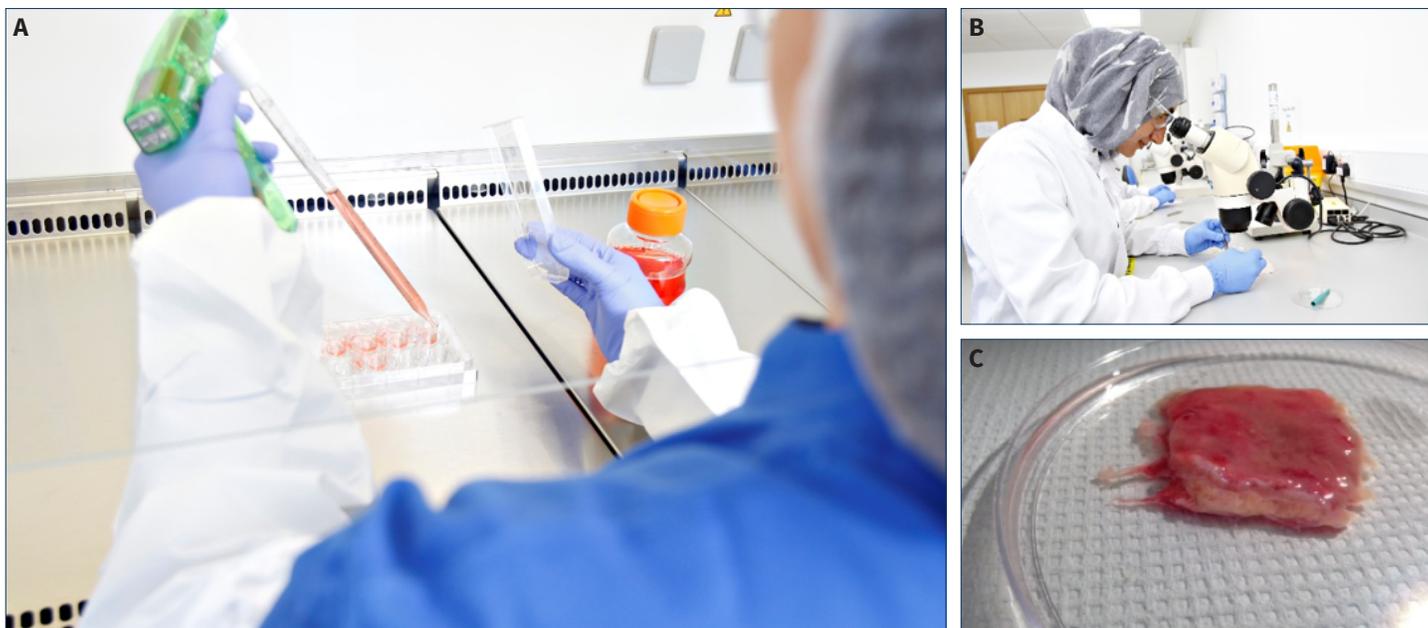
Each data point is a different donor: reveals extent of patient variation in drug response

“Biopta’s human tissue services have played a critical part in our compound selection and have added considerable value to our lead compound”

— President & Head of R&D, Canadian Biotech

What is included in our IBD predictive drug discovery services?

- ✓ A customized project to meet your research goals.
- ✓ An expert Study Director assigned to manage each project as your single point of contact from initiation to report.
- ✓ Rapid access to human healthy and diseased tissues, through our industry-leading human tissue network.
- ✓ GLP projects available.
- ✓ Ownership of all data generated during the project.



REPROCELL's Research and Development team based at our Centre for Predictive Drug Discovery, Glasgow, UK. **A:** REPROCELL Study Director preparing a 12 well plate for experimentation. **B:** Research and Development preparing tissue biopsies. **C:** A sample of fresh, living tissue from an IBD patient.

References

1. Ananthakrishnan. Epidemiology and risk factors for IBD. *Nature reviews Gastroenterology and Hepatology*. 2015, 12:205-17.
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3. Schork. Time for one-person trials. *Nature*. 2015, 520:609-611.
4. Bowes *et al.* Reducing safety-related drug attrition: the use of *in vitro* pharmacological profiling. *Nature Reviews Drug Discovery*. 2012, 11:909-22.
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6. Jackson *et al.* The use of human tissue in safety assessment. *Journal of Pharmacological and Toxicological Methods* (2018).
7. Edwards *et al.* Human tissue models for a human disease: what are the barriers? *Thorax*. 2014, 0:1-3.