

Oxford Transplant Foundation Project Report

Original project title: Normothermic Machine Perfusion to Reduce Ischaemia-Reperfusion Injury after Intestinal Transplantation

Updated project title: Dissecting Common Immunopathological Pathways in IBD and Intestinal Transplantation via Advanced Spatial Omics

Project Evolution

Following the award of this pump-priming grant, and after extensive discussion with my supervisory team, the focus of the project was redirected from normothermic machine perfusion towards the immunological landscape of intestinal transplantation. The change in direction was presented to and approved by the trustees at their meeting on 12th May 2026, at which point it was agreed that the awarded funds could be combined with my current project. The scientific rationale for both projects remains at improving long-term outcomes for intestinal transplant recipients.

Background

The intestine is one of the most immunogenic organs used in transplantation, resulting in rejection rates that remain significantly higher than other solid organ transplants. To manage this, intestinal transplant recipients require more intensive immunosuppression than other transplant patients, which carries a substantial burden of its own, including increased susceptibility to serious infections and a markedly elevated risk of malignancy. Despite these challenges, the clinical immunosuppressive protocols used in intestinal transplantation have changed little since the introduction of calcineurin inhibitors, and there remains a critical unmet need for more targeted therapeutic strategies.

In contrast, inflammatory bowel disease (IBD) which is also characterised by immune dysregulation within the intestinal mucosa has seen considerable therapeutic advances over recent decades. A new generation of highly targeted biologic agents has transformed outcomes for IBD patients, yet these agents have never been systematically evaluated in the context of intestinal transplant rejection. Histological examination of intestinal transplant rejection and IBD flares reveal strikingly similar patterns of mucosal immune activation, raising the possibility that the underlying inflammatory pathways could significantly overlap. If so, the more extensive therapeutic repertoire developed for IBD may represent an available therapeutic resource for transplant recipients.

Project Aims

This project uses Xenium in situ spatial transcriptomics to characterise the immune microenvironment of intestinal transplant tissue across four clinically defined states:

baseline (no rejection), acute steroid-responsive rejection, acute steroid-resistant rejection, and chronic rejection. These transcriptomic profiles will be compared with equivalent spatial data from IBD tissue, generated using the same platform to enable direct comparison. The analysis will focus particularly on the molecular targets of biologic therapies currently approved in IBD, including the IL-23/IL-17 axis, TNF signalling, and leukocyte trafficking pathways to determine whether there is a biological rationale for repurposing these agents to treat or prevent rejection in intestinal transplant recipients.

Progress to Date

Significant groundwork has been completed during the first year of this project. Ethics approval and biobank access have been successfully obtained through the Translational Gastroenterology Unit (TGU) Biobank (ethics reference: 21/YH/0206; project reference: 25-CY-immune pathway_IBD and intestinal transplant). The project has additionally been accepted by the Oxford Centre for Histopathology Research (OCHRe), which will provide access to the archival tissue sections required for analysis. Tissue sections spanning all four clinical rejection states have been identified and requested, these are awaiting preparation and dispatch.

Using the funds awarded through this grant, a Xenium 5K prime panel run has been purchased, secured at a 30% institutional discount and is ready to be deployed as soon as the prepared tissue sections are received.

Next Steps and Timeline

Upon receipt of the tissue sections, the Xenium run will be initiated immediately. Following data acquisition, computational analysis will be performed using established spatial transcriptomics pipelines, including cell segmentation, neighbourhood analysis, and differential pathway activation across rejection states. Transcriptomic signatures will be correlated with Banff histopathological rejection grading and clinical outcome data.