

PERSONALIZED INTESTINAL ORGANOID AND IMMUNE CELL CO-CULTURE MODEL FOR EVALUATION OF BIOLOGICAL THERAPY EFFICACY IN ULCERATIVE COLITIS PATIENTS

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Personalized co-culture models of UC patient-derived colonic epithelial cells and macrophages showed that upadacitinib and ozanimod restored inflammatory cytokine-induced barrier disruption, but with individualized patient-specific responses.

KEY POINTS

- In co-cultures from 12 UC patients and 11 controls, inflammatory cytokine stimulation (TNF- α and IFN- γ) decreased transepithelial electrical resistance, which was restored after treatment with upadacitinib (UC: increased by 226.64 $\Omega \cdot \text{cm}^2$, control: by 116.82 $\Omega \cdot \text{cm}^2$) or ozanimod (UC: by 188.5 $\Omega \cdot \text{cm}^2$, control: by 193.77 $\Omega \cdot \text{cm}^2$).
- Inflammatory cytokines significantly increased CXCL9 gene expression in epithelial cells (UC: fold change 3064.49, padj. = 2.07×10^{-5} ; control: fold change 664.44, padj. = 2.00×10^{-2}) and macrophages (both groups padj. = 0.01).
- Both biological agents modulated inflammatory cytokine secretion in epithelial cells and macrophages, but patient-specific heterogeneity resulted in non-significant summarized changes in CCL5, CXCL9, and TNF- α expression after 48 hours of treatment.
- The study revealed individualized responses of UC patients to upadacitinib and ozanimod, demonstrating varying impacts and effectiveness across subjects in this preclinical personalized co-culture model.

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