

A primary colon organoid epithelial barrier model with crypt architecture to model IBD for drug screening

Alexander Sotra, Boyang Zhang

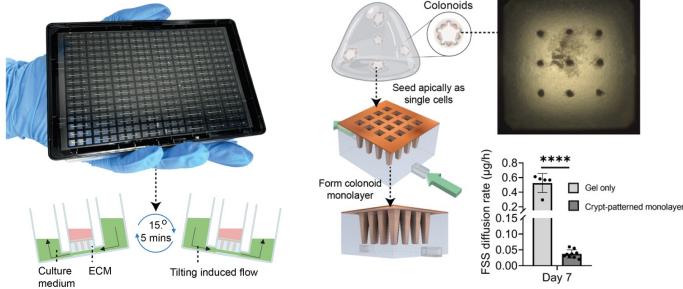
Introduction

Colon models are essential tools for research on drug absorption and inflammatory disease modelling. However, traditional *in vitro* systems often fail to accurately recapitulate the structural and cellular complexity of native colon epithelium. The **AngioPlate384** platform addresses this shortfall by enabling the scalable production of crypt-patterned colon tissues from primary human colon organoids with colonic endothelium support, which help to provide key insights into cellular localization, tissue-drug responses, and pathophysiological processes. This poster outlines the principles behind the AngioPlate384 and its application in colon model development.

AngioPlate™384 for colon modelling

128 colon tissue with crypt-patterning can be cultured in the AngioPlate384. Colon organoids are broken down to single cells and seeded apically over pre-patterned ECM. Culture over 7 days yields confluent tissues with barrier function.

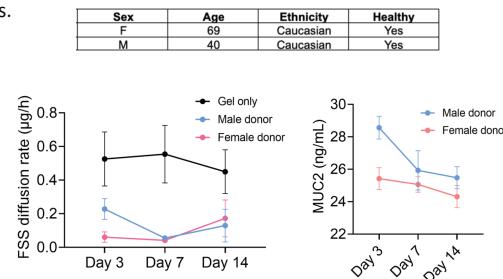
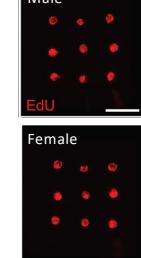
AngioPlate™384



Multiple donors show reproducibility

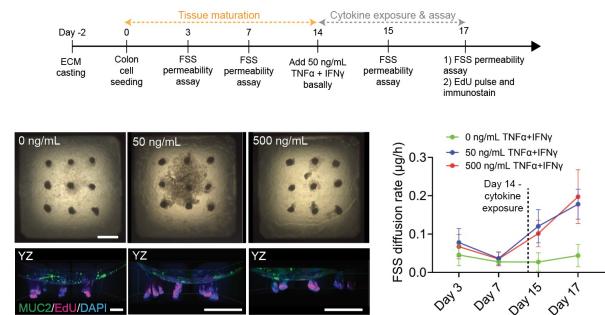
Male and female donors can be cultured on-chip successfully. Both donors demonstrate comparable barrier function over 14 days of culture as well as apical MUC2 expression. Similar tissue readout results are important for reproducibility when expanding drug screening on multiple donors.

Sex	Age	Ethnicity	Healthy
F	69	Caucasian	Yes
M	40	Caucasian	Yes



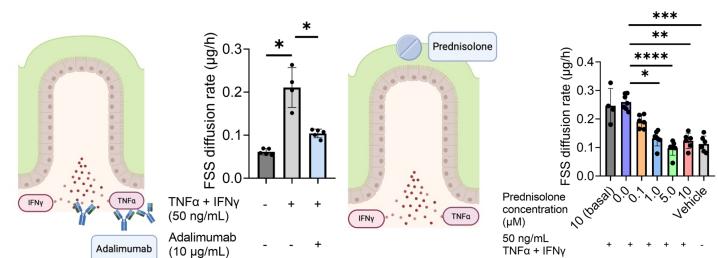
Demonstrating colon inflammation

Traditional cell lines like Caco-2 cells readily used in pharmaceutical drug screening fail to decrease barrier integrity when exposed to pro-inflammatory cytokines TNF α and IFN γ . Herein, primary colon organoid derived tissues decrease barrier function while enabling EdU+ proliferative cell localization in the crypt niche.



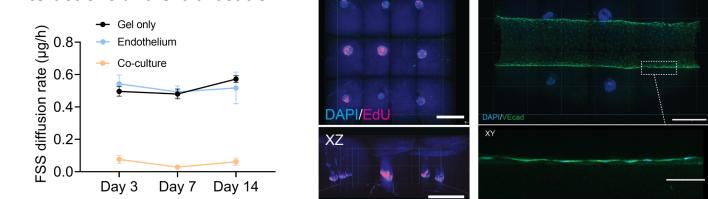
Drug screening to prevent inflammation

Adalimumab is a gold standard IBD treatment. The antibody is delivered intravenously and binds to TNF in the blood stream to reduce inflammation. Additionally, prednisolone is an effective treatment against inflammatory bowel diseases. Taken orally, it decreases inflammation by inhibiting inflammatory cell signalling. Here, we show basal Adalimumab prevent inflammation and a dose response from apical prednisolone (EC50 = ~0.125 µM).



Colon endothelium co-culture

Blood vessels composed of colon endothelial are co-cultured in the basal channel of the AngioPlate384. The model forms barriers with stem cells in the crypt niche while endothelial cells show localized junctions. The co-culture could be used to investigate immune cell interactions and extravasation.



Conclusion

The AngioPlate384 provides robust and scalable production of crypt-patterned colonoid tissues for drug screening, and modeling colon injury and diseases. A co-culture with endothelial cells can further investigate immune cell interactions in inflammatory bowel diseases.

References

1. Sotra, A., Jozani, K. A. & Zhang, B. A vascularized crypt-patterned colon model for high-throughput drug screening and disease modelling. *Lab on a Chip* 23, 3370–3387 (2023).
2. K., & Lutolf, M. P. (2024). Patient-derived mini-colons enable long-term modeling of tumor-microenvironment complexity. *Nature Biotechnology*, 43(5), 727–736. <https://doi.org/10.1038/s41587-024-02301-4>