Quantifying the transport of biologics across intestinal barrier models in real-time by fluorescent imaging

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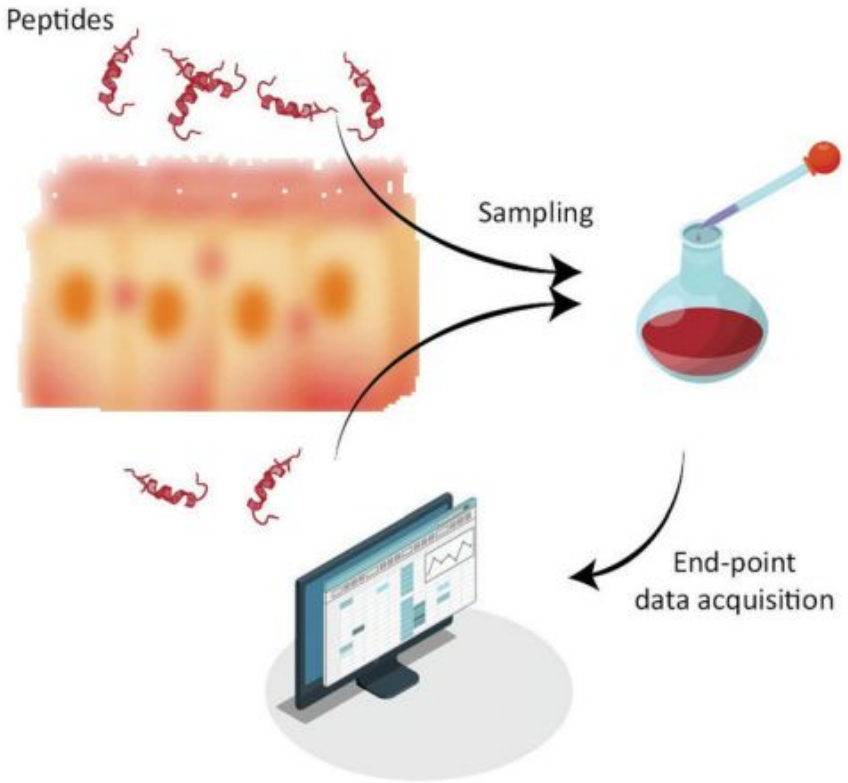
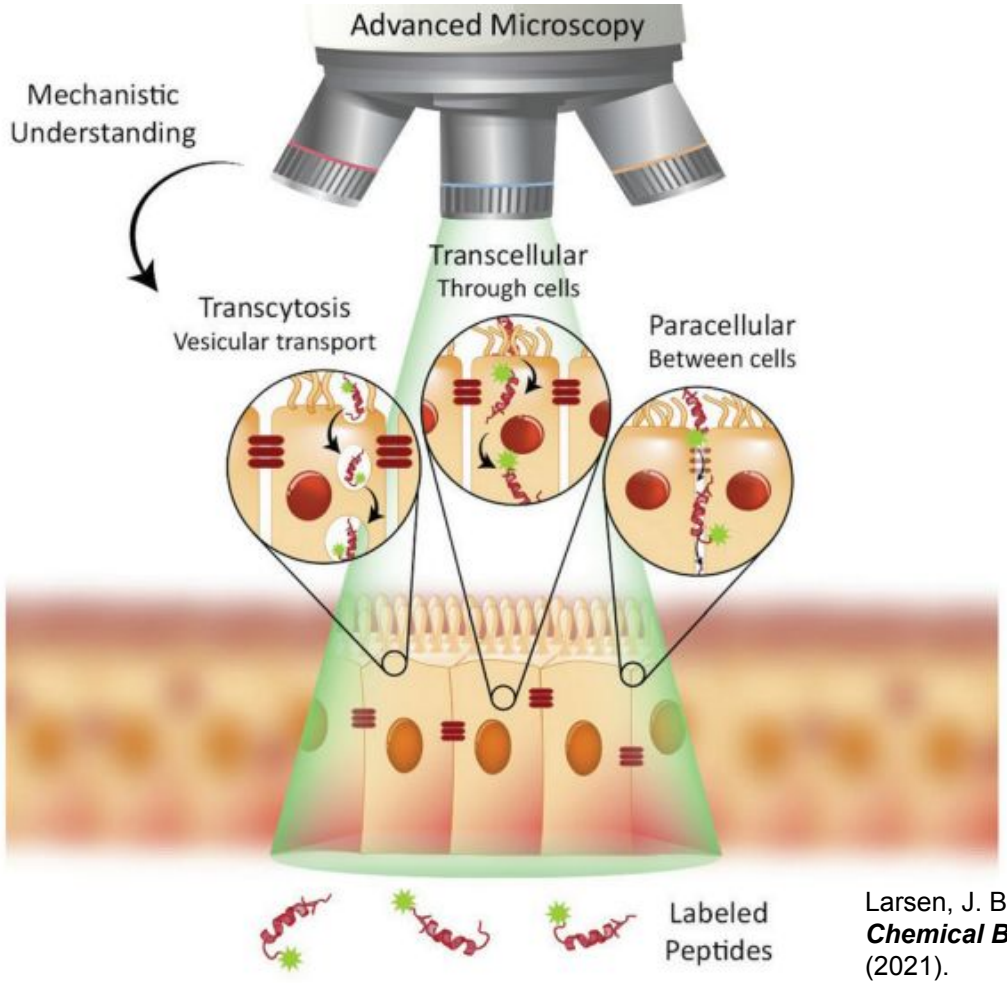
Advanced Delivery Science

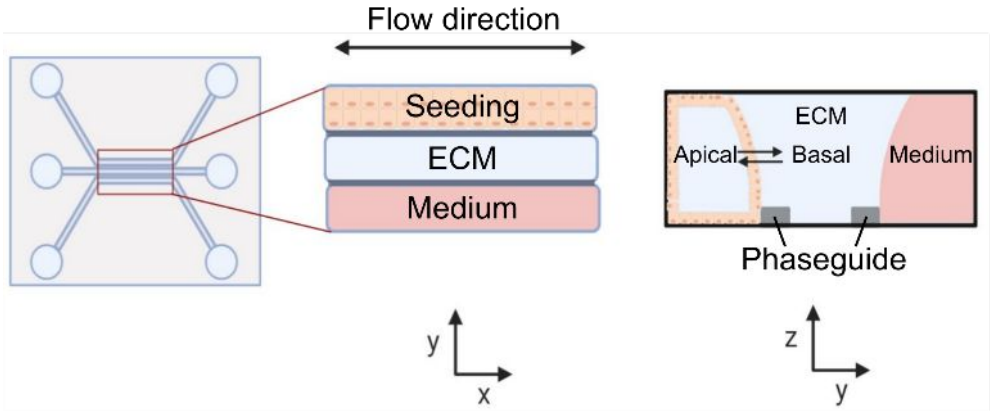
Live cell imaging as a read-out for drug uptake and transport

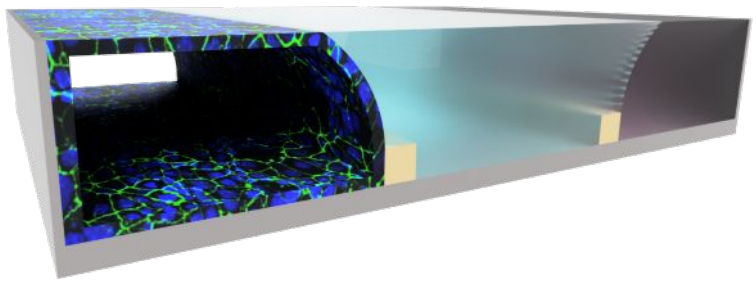


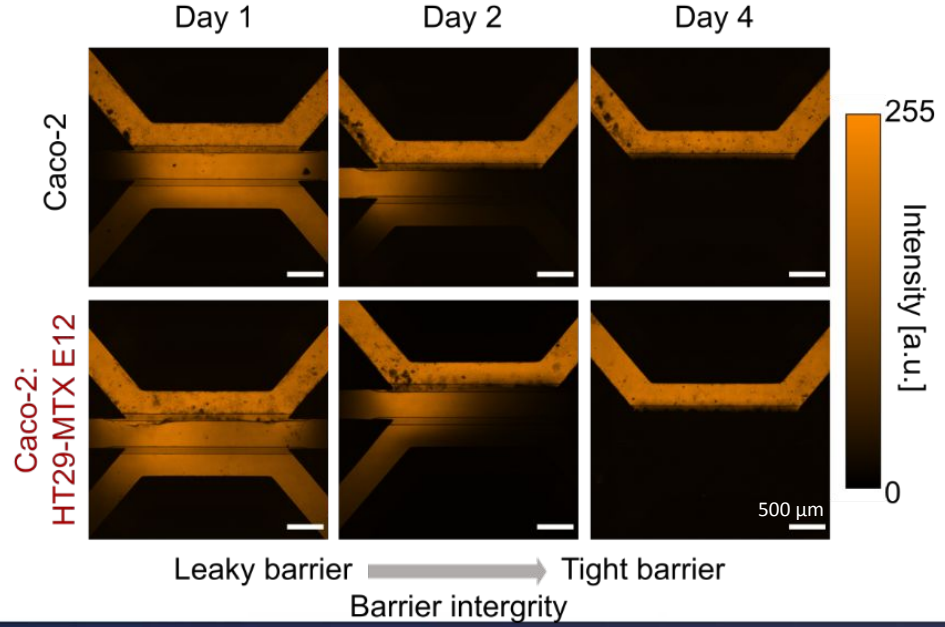


Larsen, J. B.,.. **Weller A.** *et al.* ***RSC Chemical Biology*** **2**, 1115–1143 (2021).

Development and verification of leak-tight small intestinal chip model







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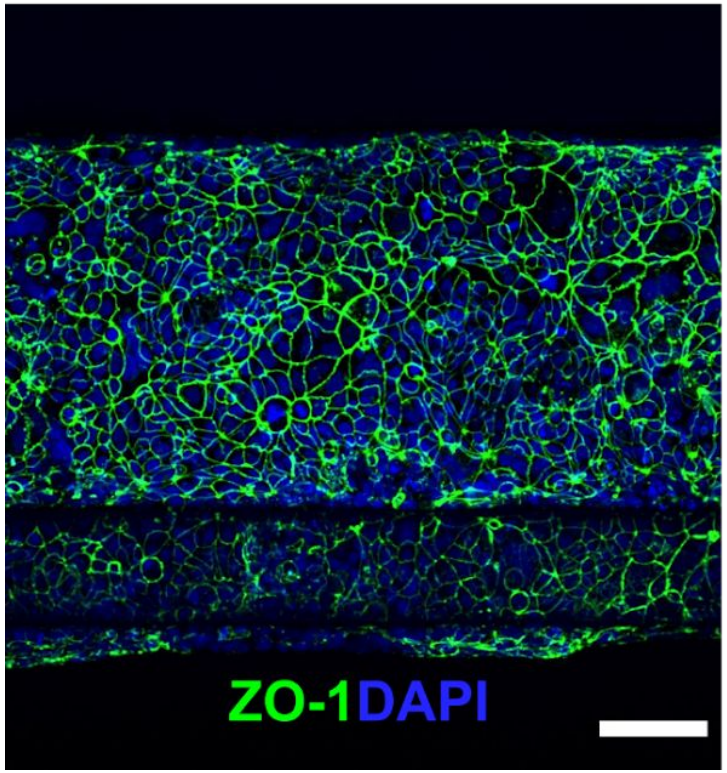
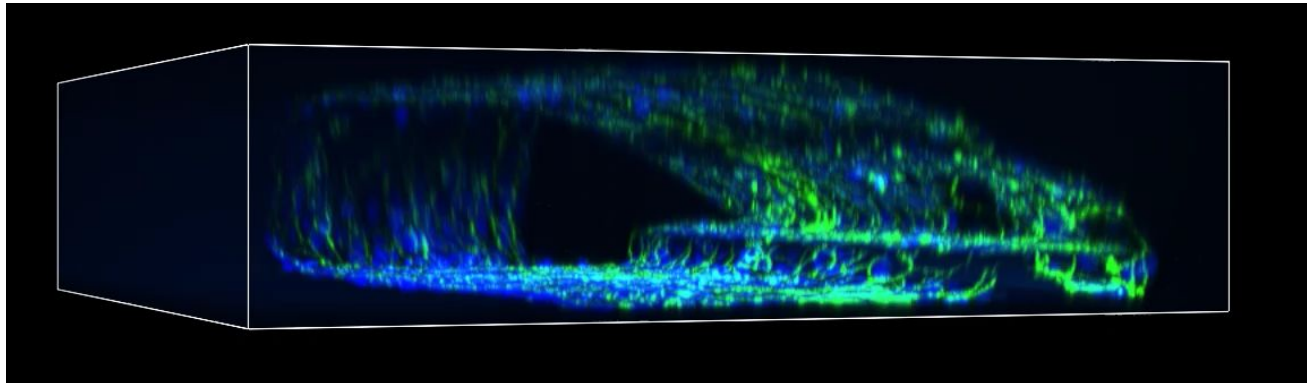
*Scale bar is 500 µm

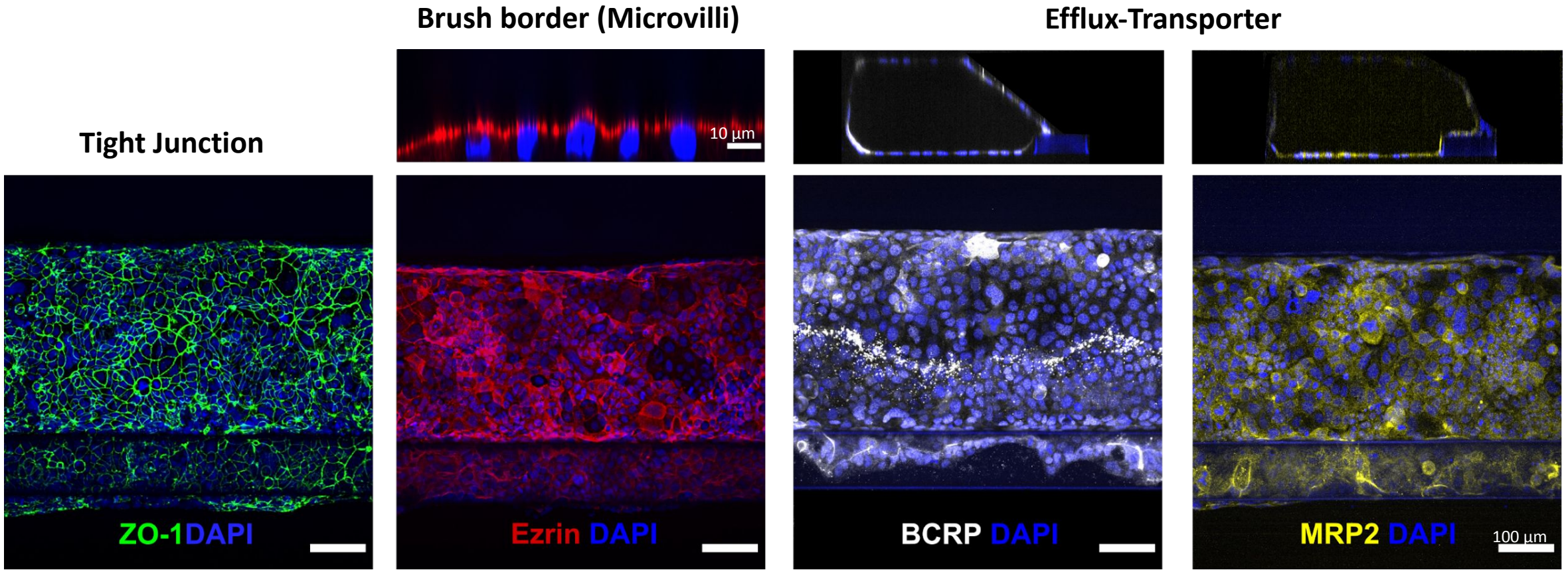
Cell tubules show full phenotypical differentiation into epithelial cells determined by in-chip immunostaining

Tight Junction





Cell tubules show full phenotypical differentiation into epithelial cells determined by in-chip immunostaining



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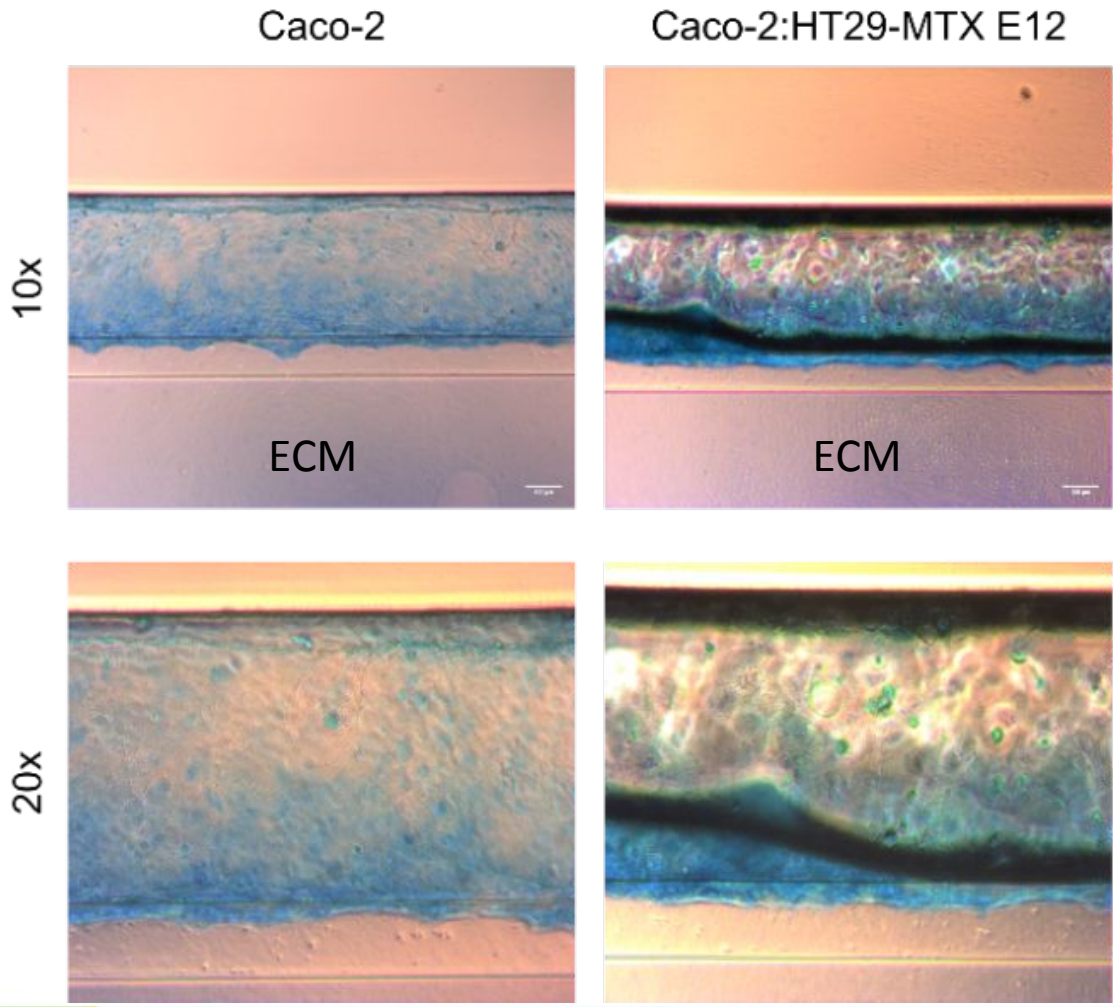
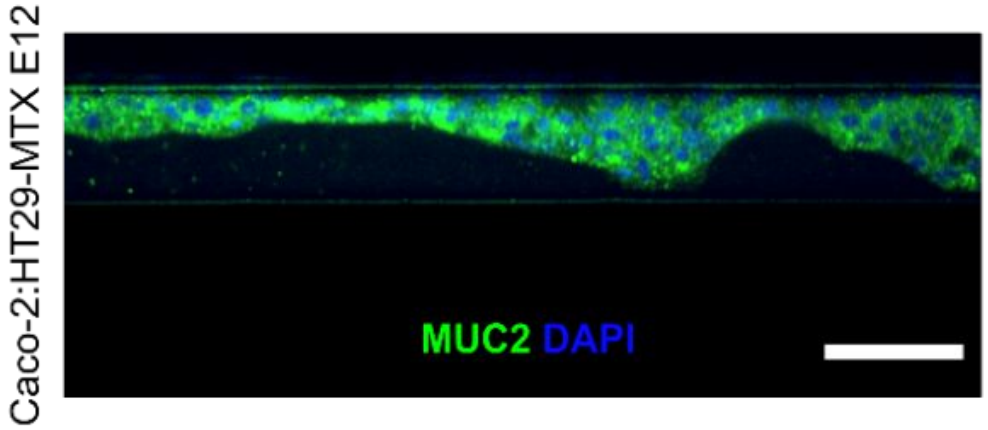
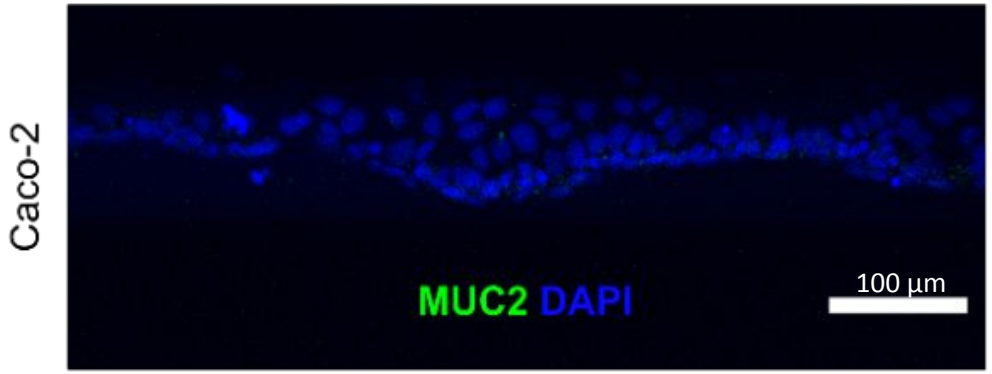
The presence of HT29-MTX E12 leads to mucus expression along the interface in coculture tubules







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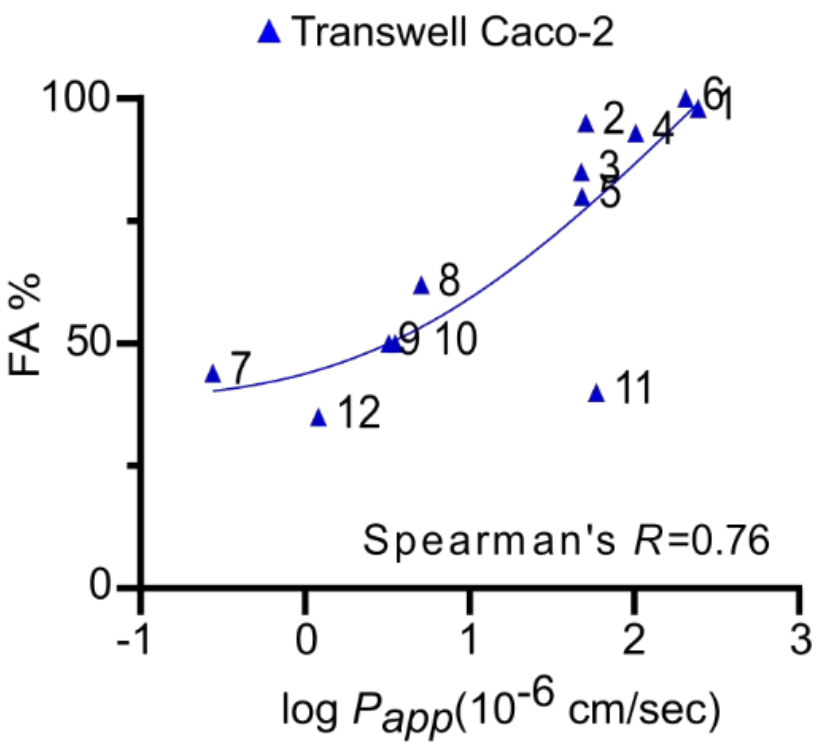
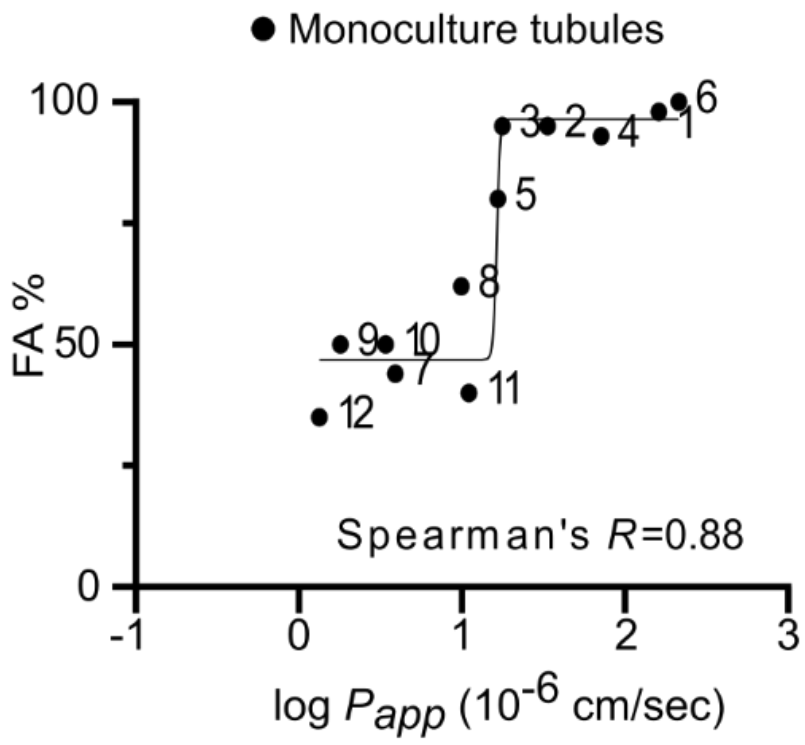
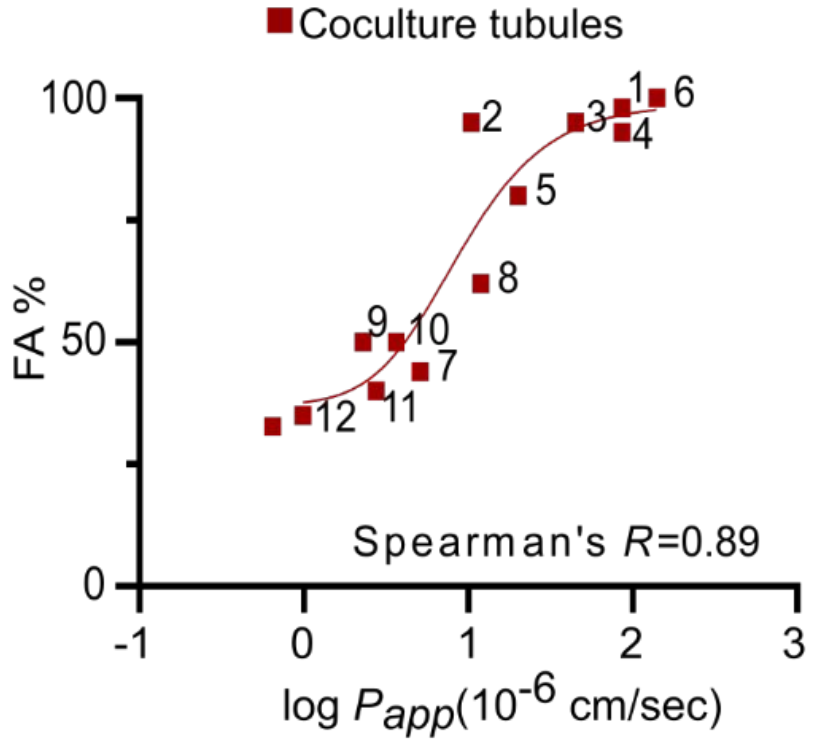
Epithelial tubules display strong *in vivo* drug transport predictability







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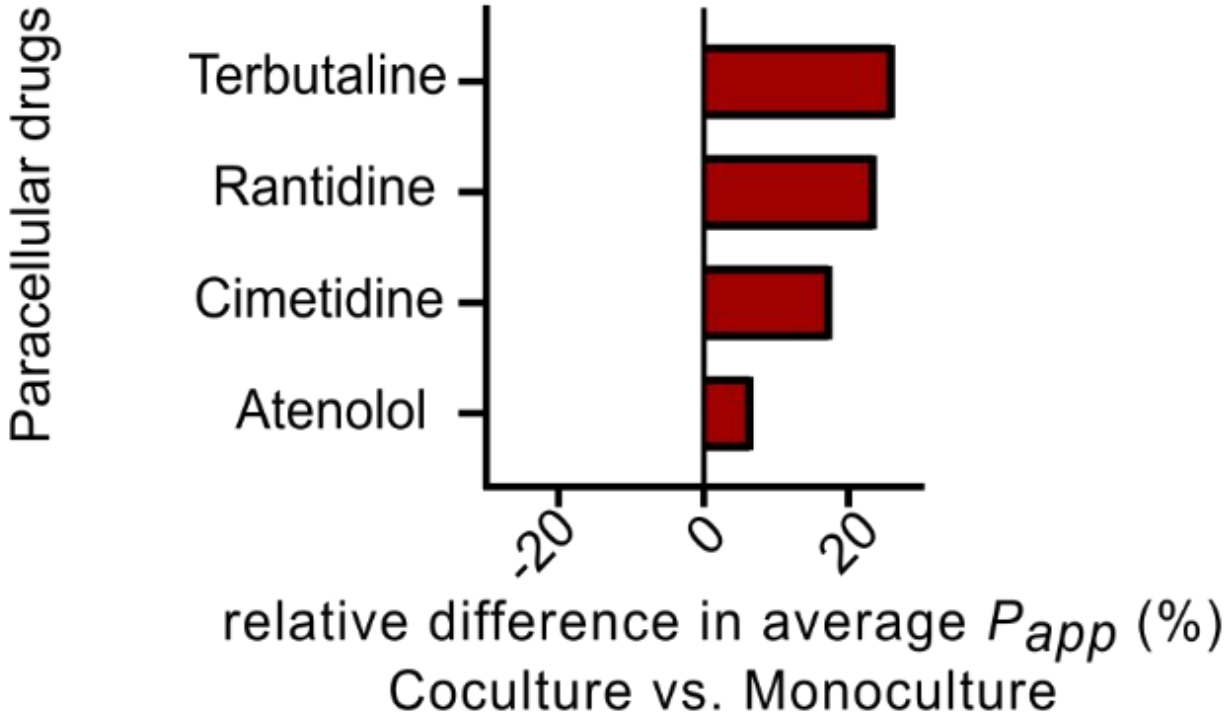
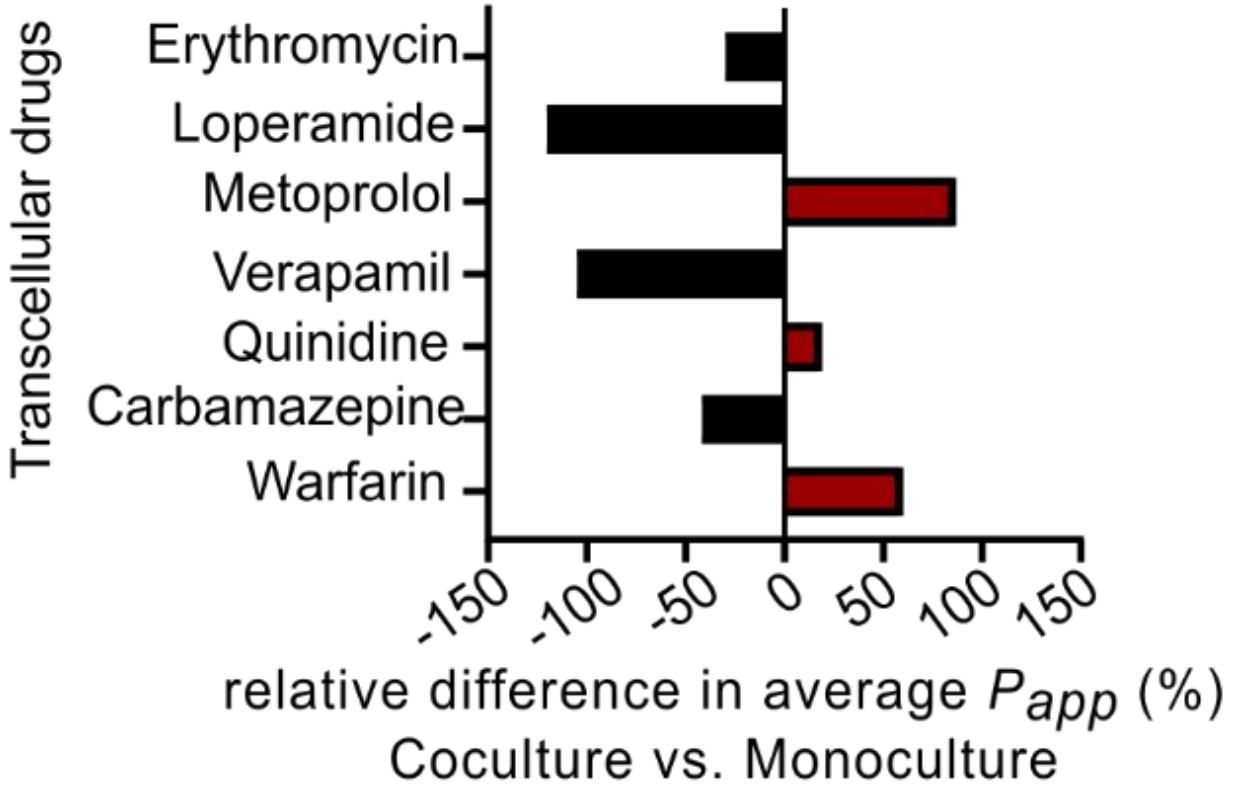
Coculture tubules exhibit increased paracellular transport





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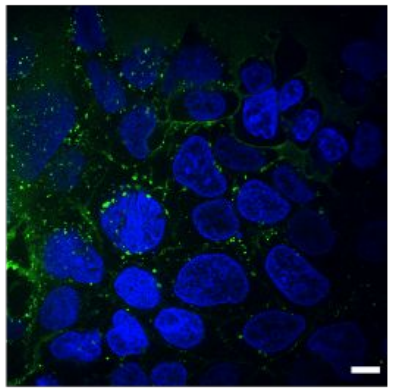
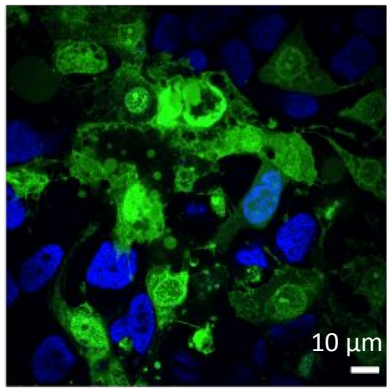
Internalization and image-based quantification of TAT-FITC transport across coculture tubules

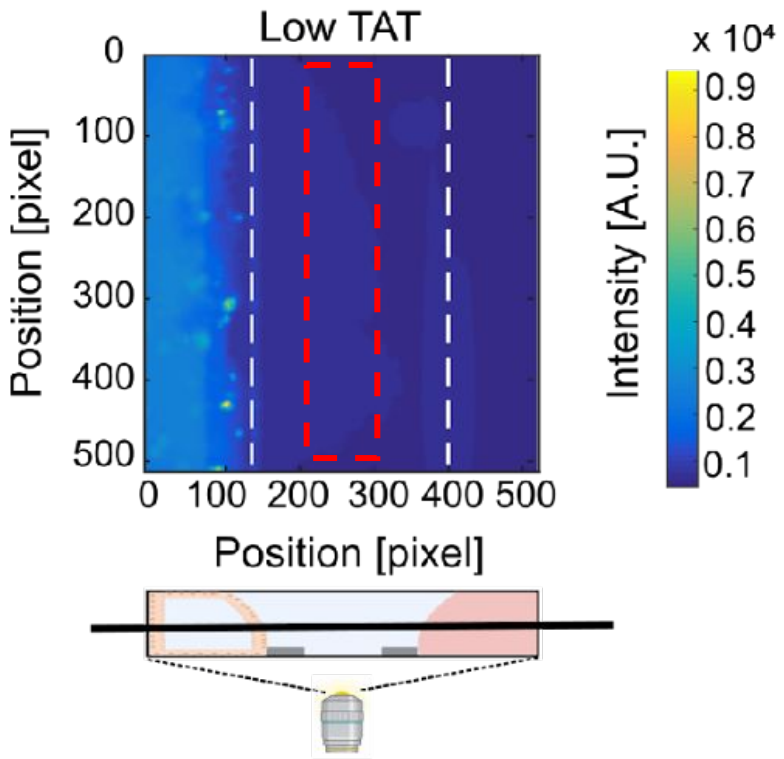
F-Tyr-Gly-Arg-Lys-Lys-Arg-Arg-Gln-Arg-Arg-Arg-NH2

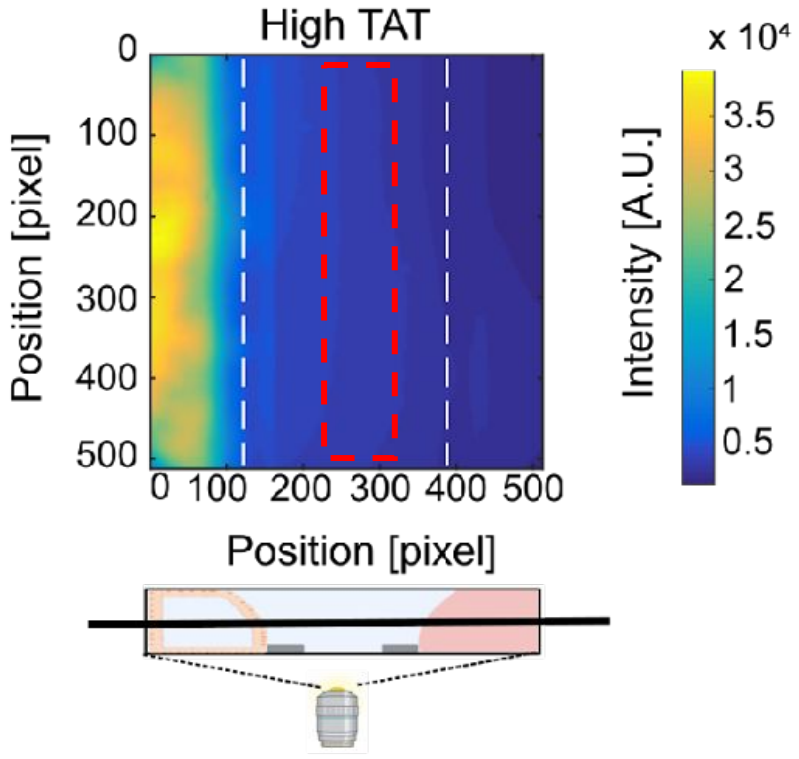
Low TAT-FITC



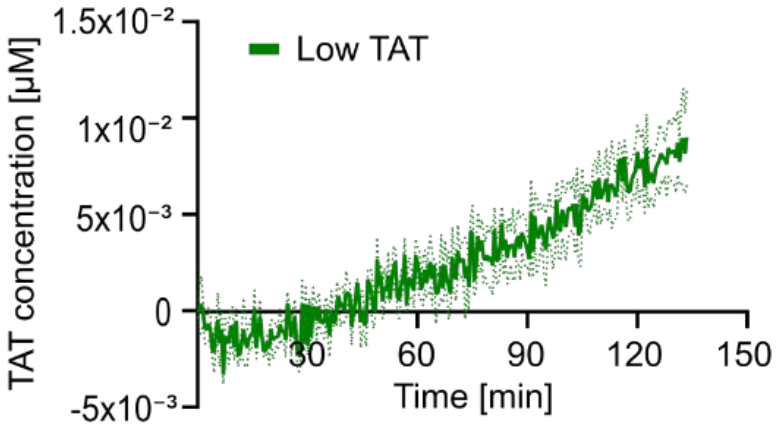
High TAT-FITC

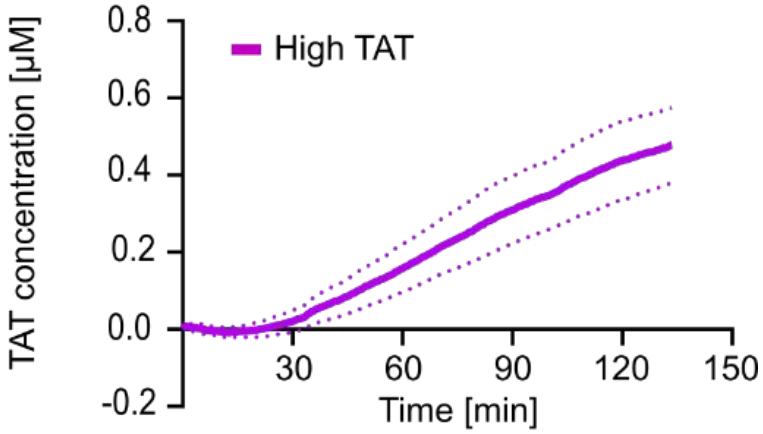


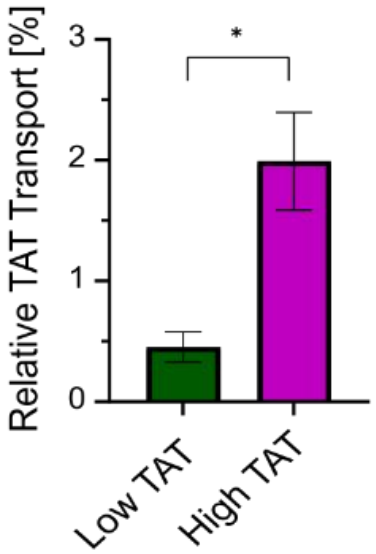


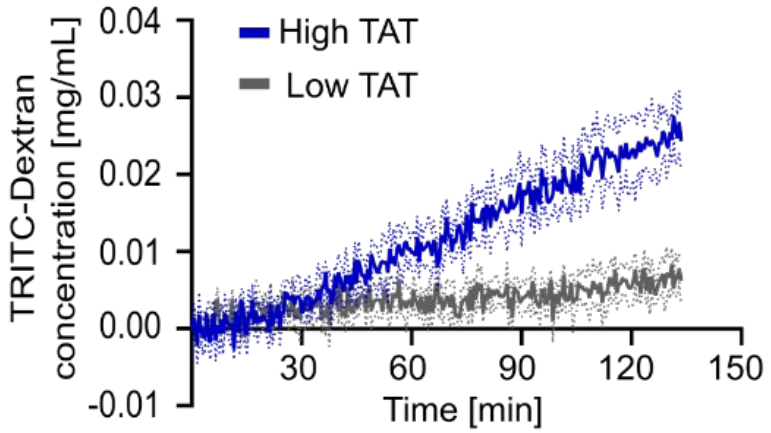


Concentration-dependent transport of TAT-FITC









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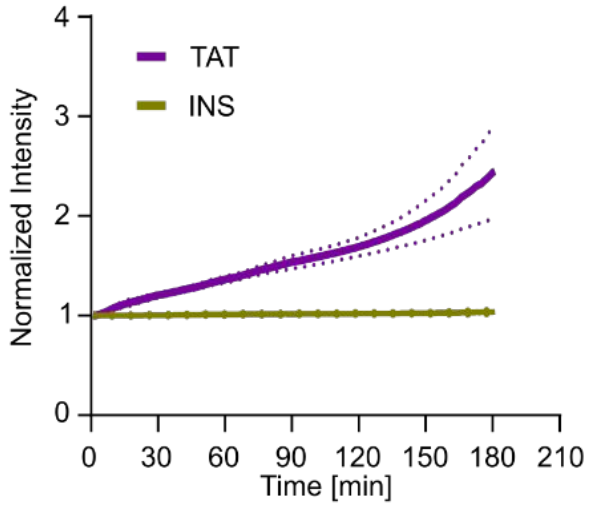
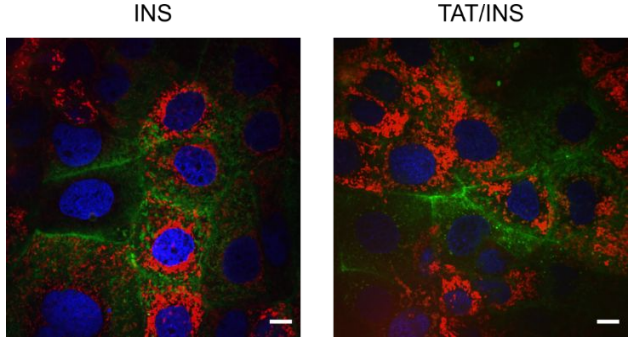
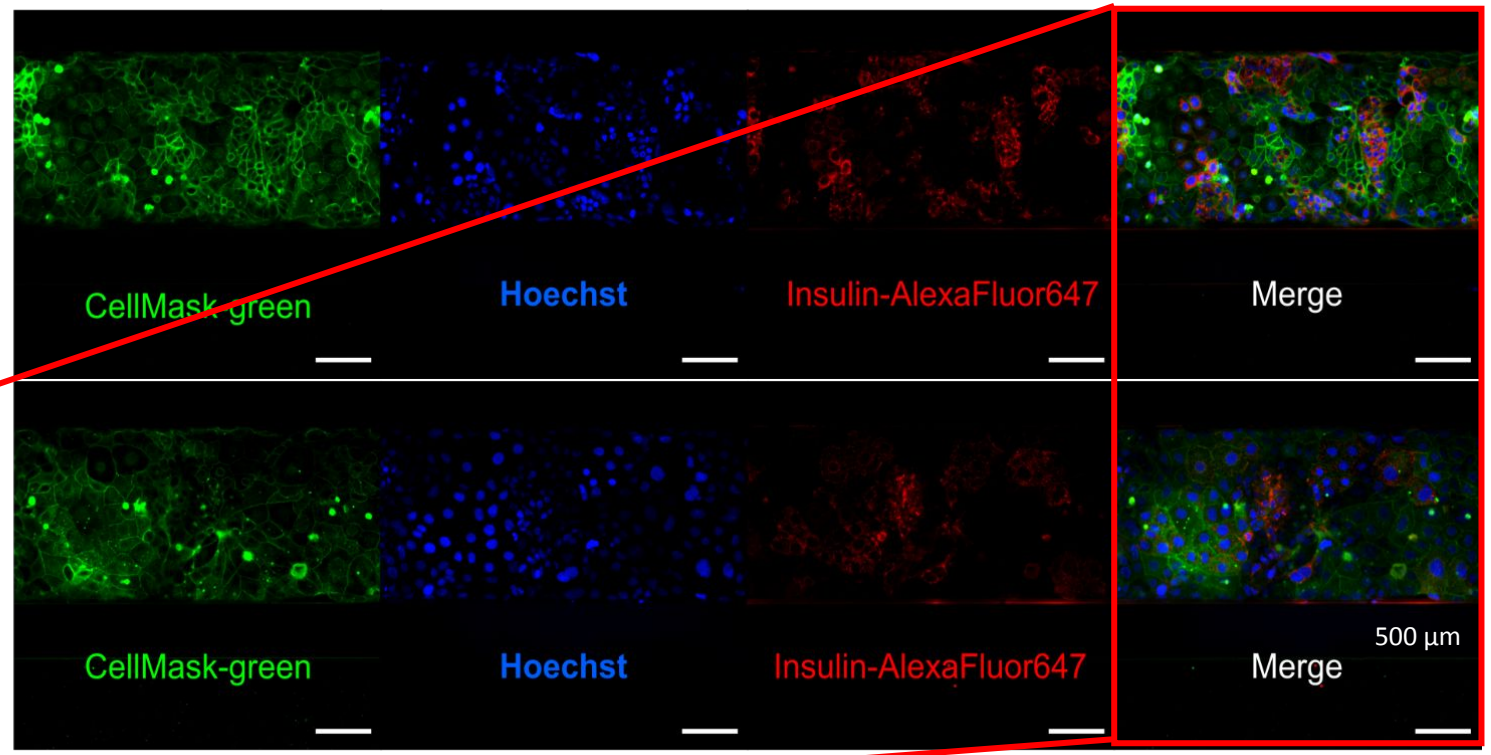
Multiplexing approach enables simultaneous and direct tracking of molecules across the epithelial cell barrier



Intracellular localization of Insulin



Intracellular distribution of Insulin in cell tubules



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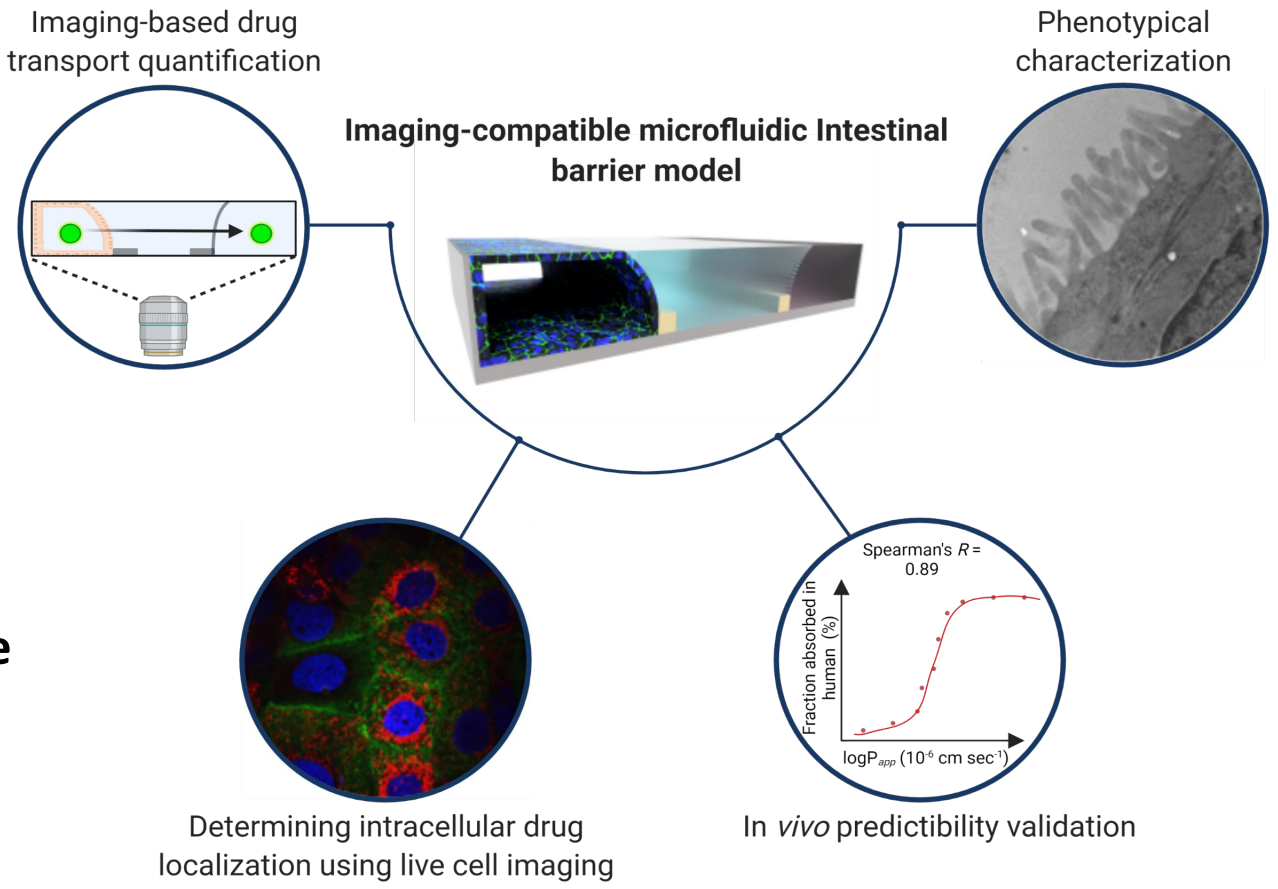
Summary

- Fully **differentiated and polarized** 3D epithelial barrier model
- Validation as platform for drug transport studies
  - **High correlation to human absorption**
- Sensitive **image-based determination of concentration-dependent TAT-FITC transported uptake mechanism**
- **Multiplexing approach** for simultaneous and direct tracking of molecules



Acknowledgment

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Thank you for your attention!