

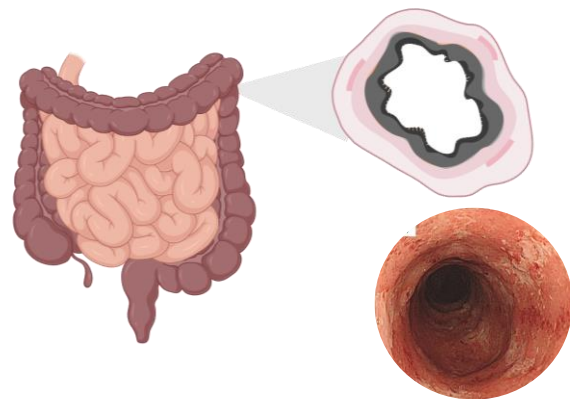
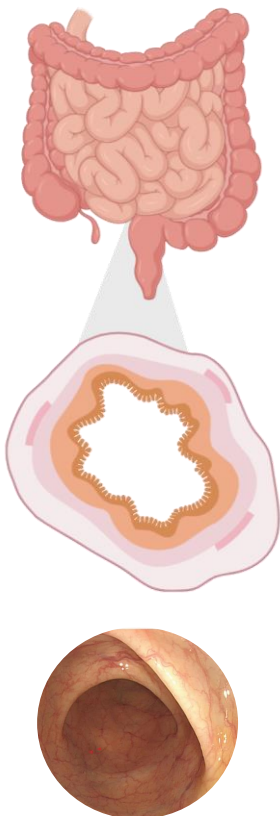
A gas-promoted in situ bioadhesive foam as a platform for antibody fragment (FAb) delivery across the colon to treat inflammatory bowel disease

Wunan Zhang



Inflammatory bowel disease

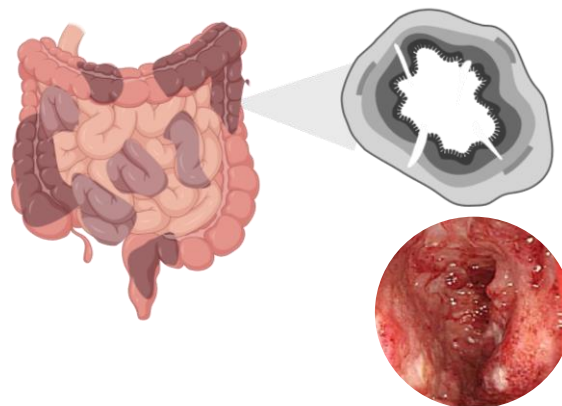
Healthy



**Ulcerative
Colitis**



1.5 million in US
2.2 million in Europe



**Crohn's
Disease**

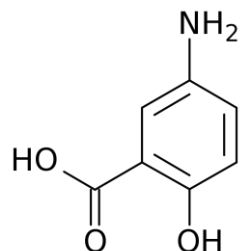


Indeterminant Colitis

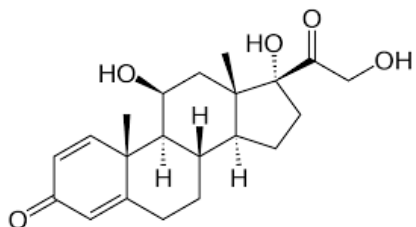
Enigmatic Etiology



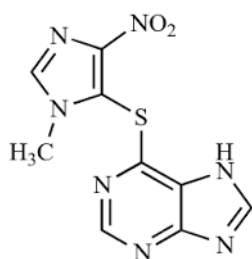
Development of IBD treatment



5-aminosalicylates



Corticosteroids

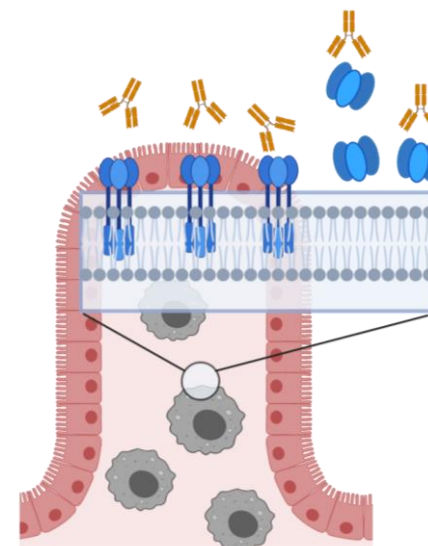


Immunosuppressant

Soothe inflammation
syndrome

1930s

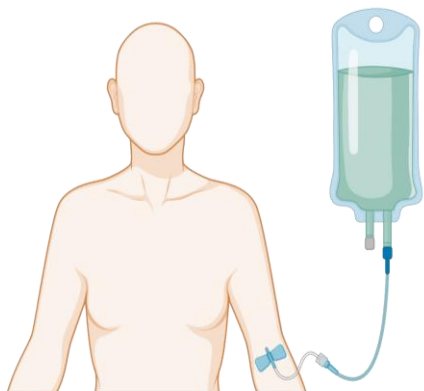
Infliximab (Anti-TNF α
monoclonal antibody)



Block cytokine
pathway

1990s

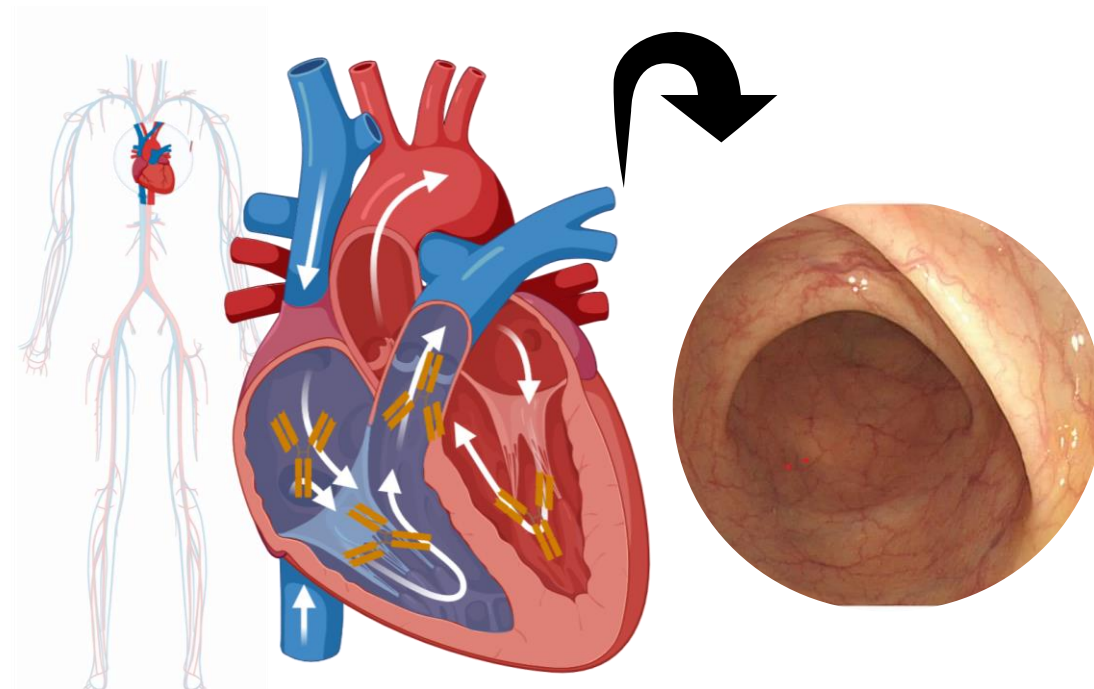
Delivery strategy in IBD



Anti-TNF- α antibody
Anti-Integrin antibody
Anti-IL antibody

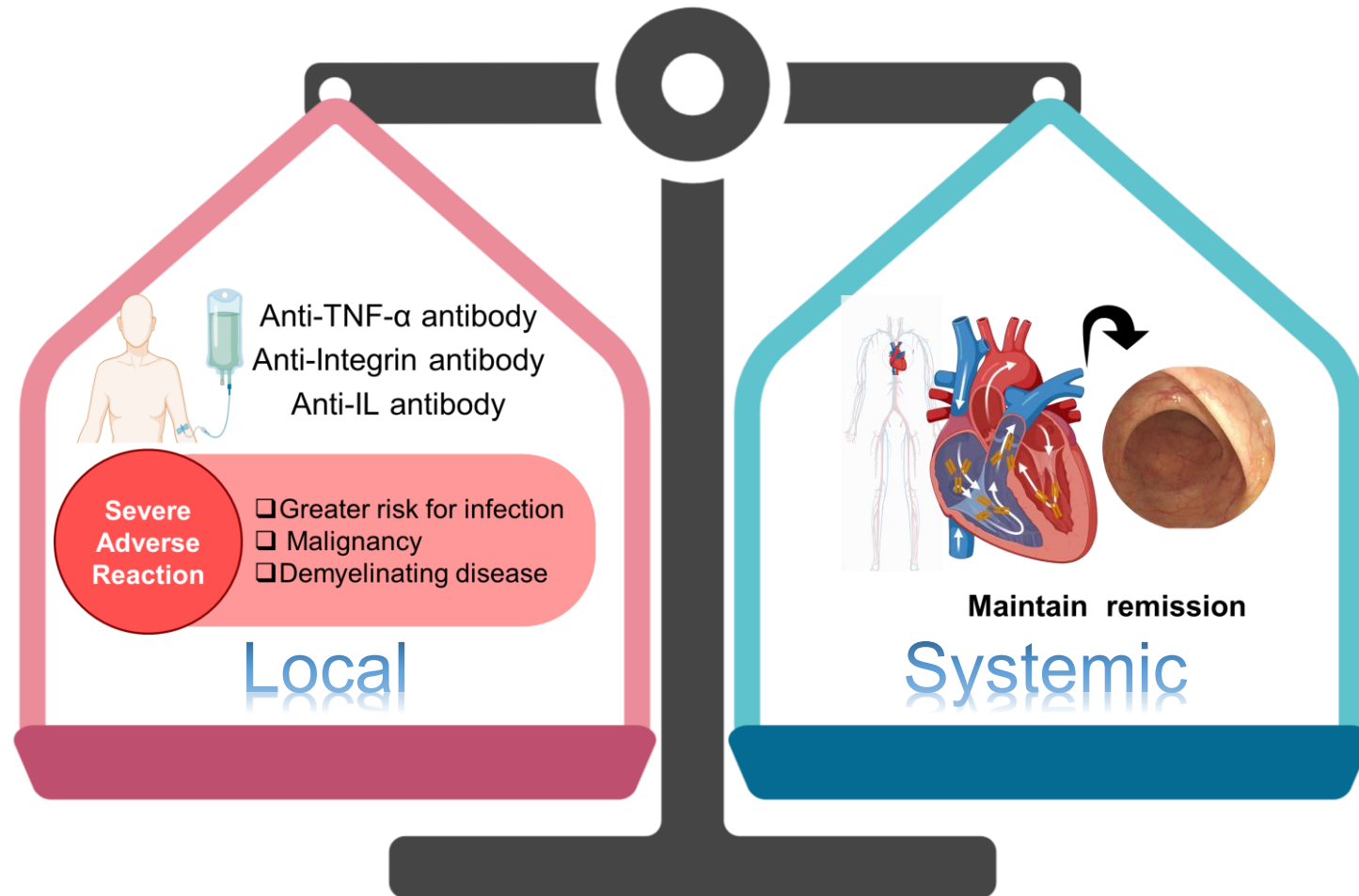
**Severe
Adverse
Reaction**

- ☐ Greater risk for infection
- ☐ Malignancy
- ☐ De-myelinating disease

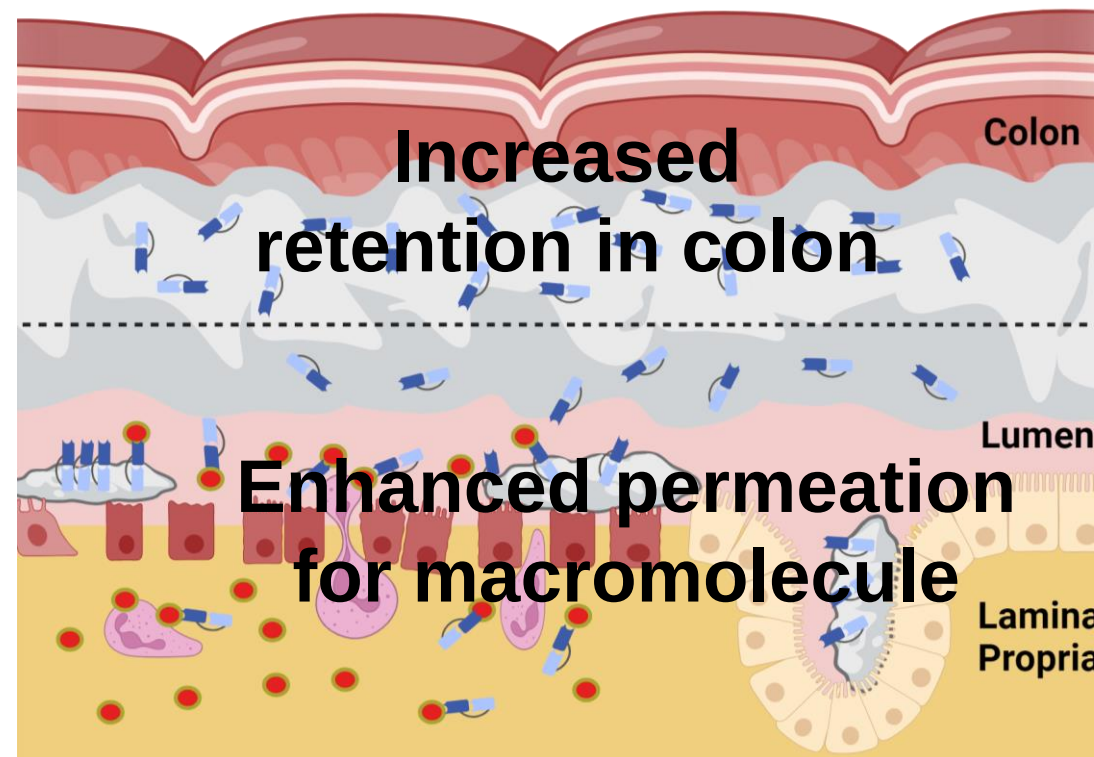


Maintain remission

Delivery strategy in IBD



Foam in IBD



An *in situ* foam

Foam: Dispersion of a large volume of gas into a liquid or a solid phase

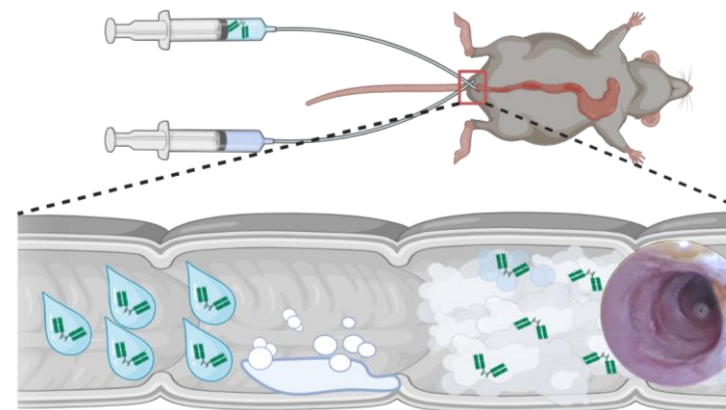
Device



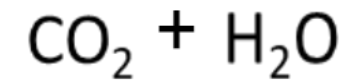
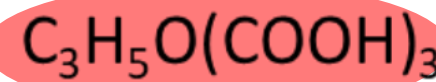
Propellant



In situ foam



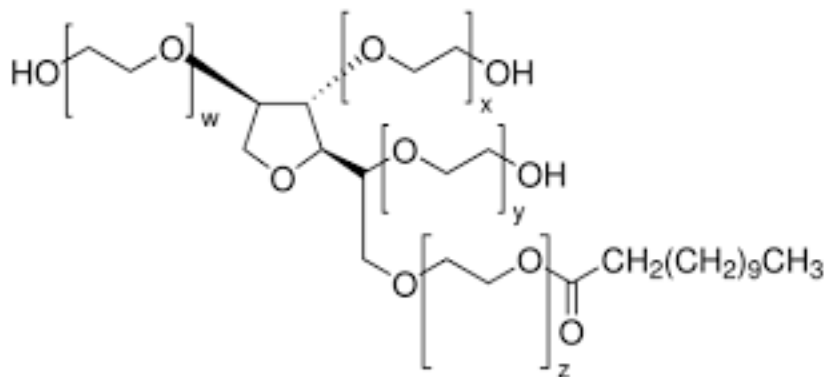
+



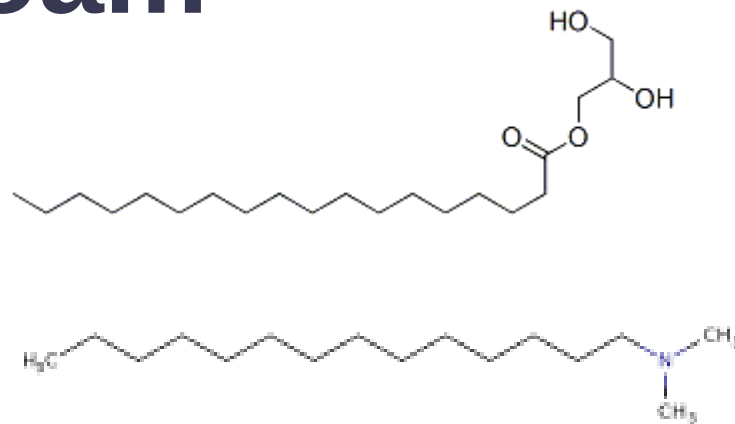
Stock Solution

Foaming Reagent

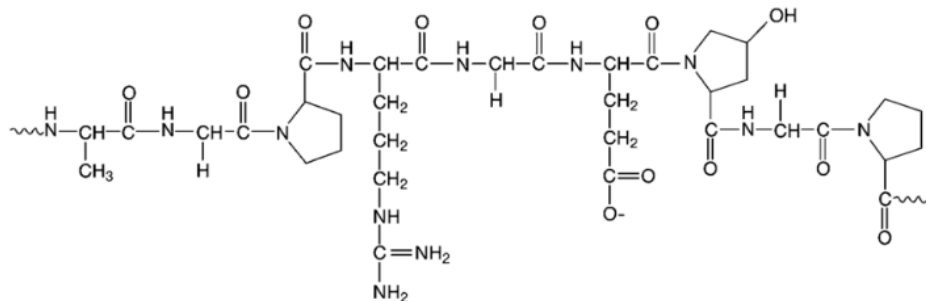
Excipients for foam



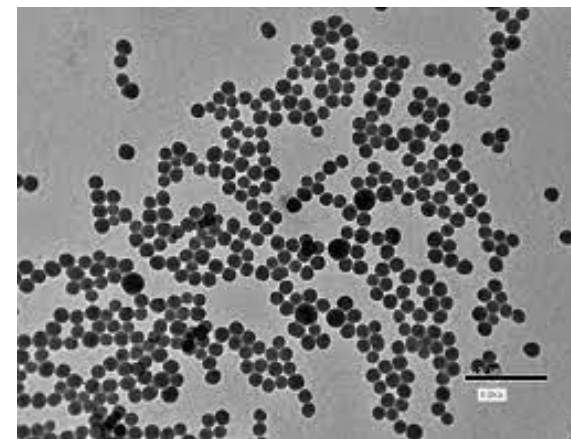
Tween 20



Gelot 64



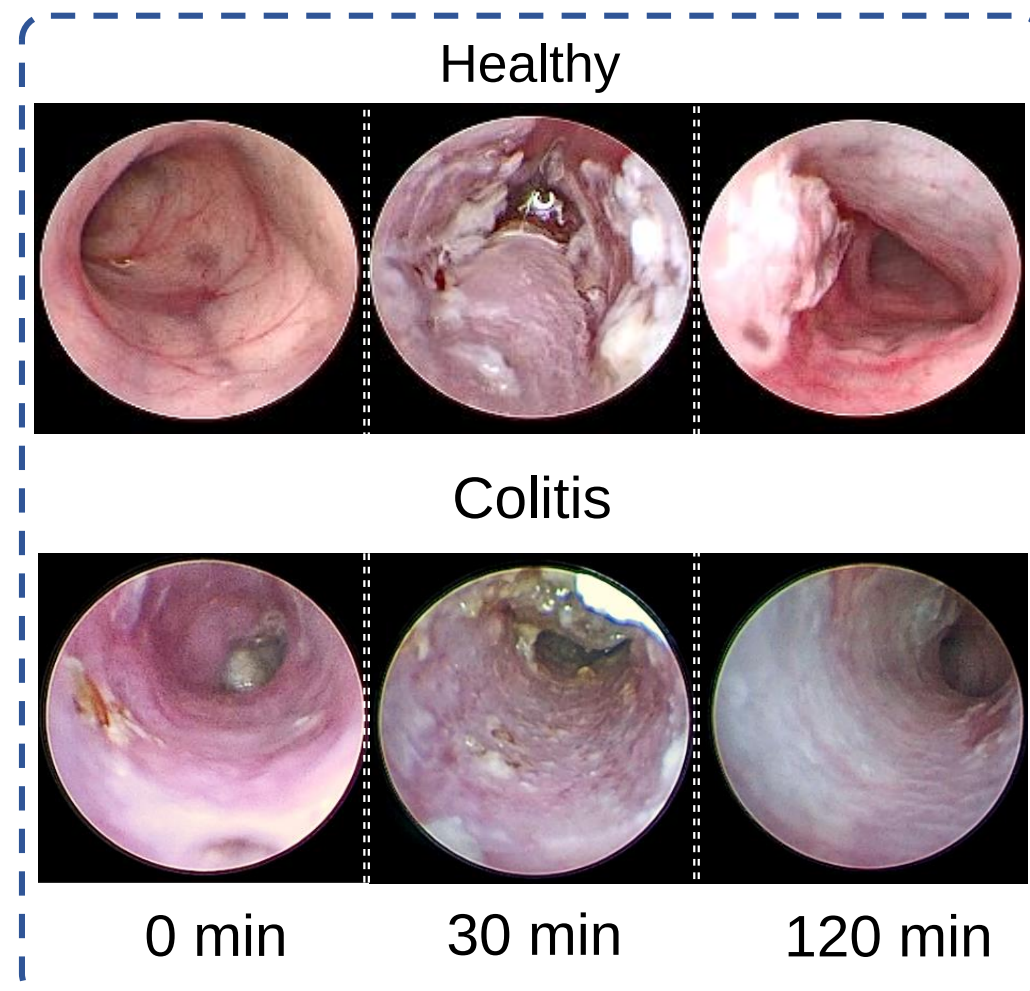
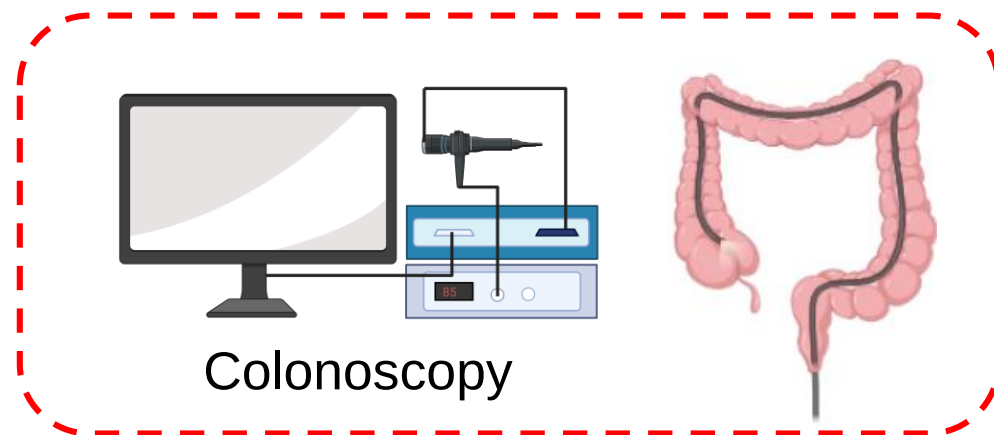
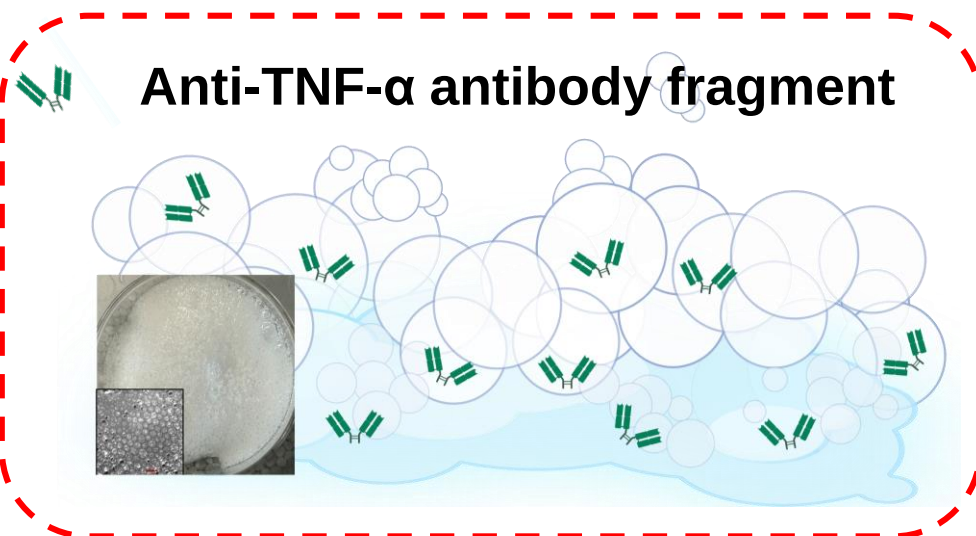
Gelatin



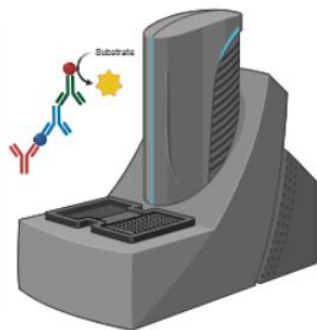
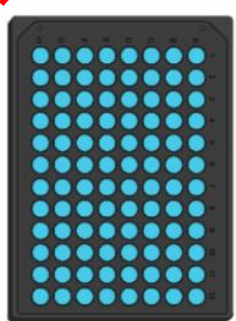
Silica nanoparticles



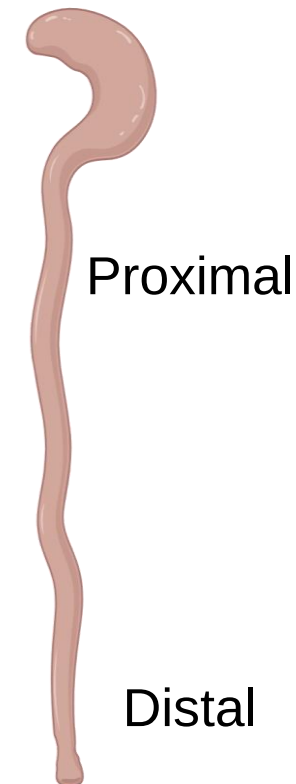
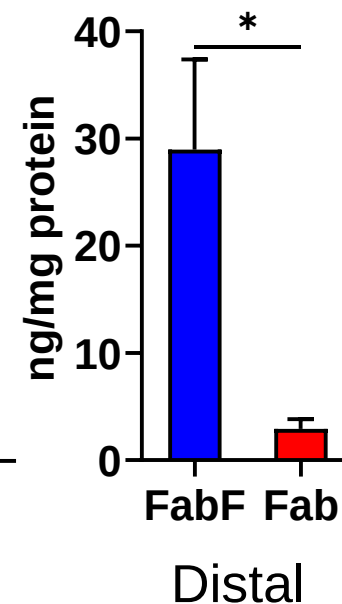
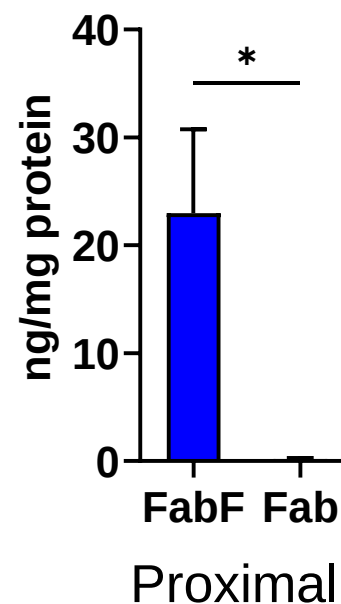
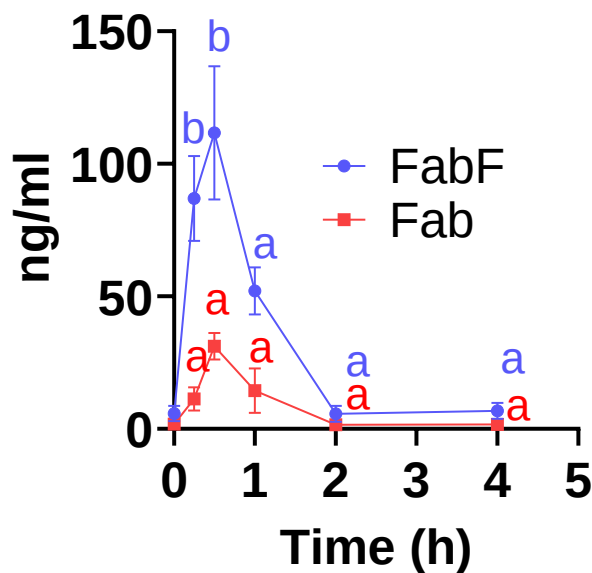
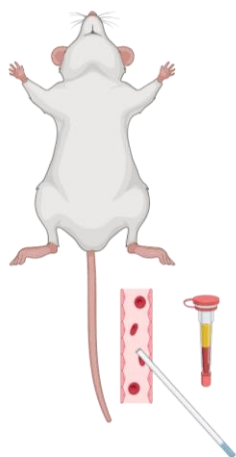
Foam adhesion



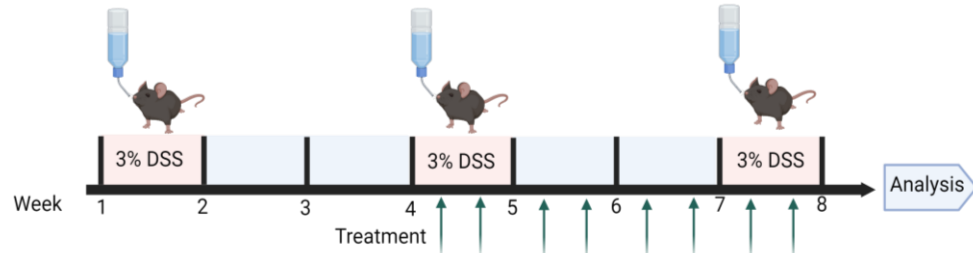
Foam enhanced PK and distribution



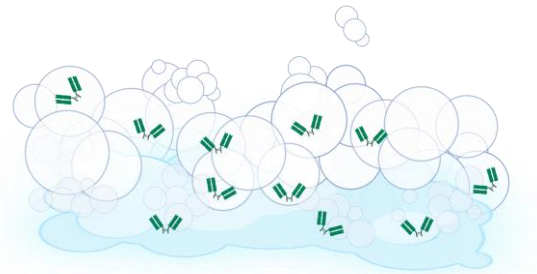
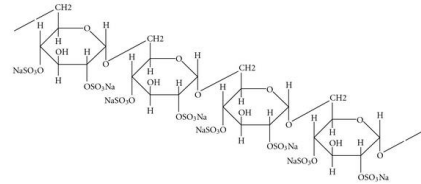
Mesoscale



Foam Efficacy



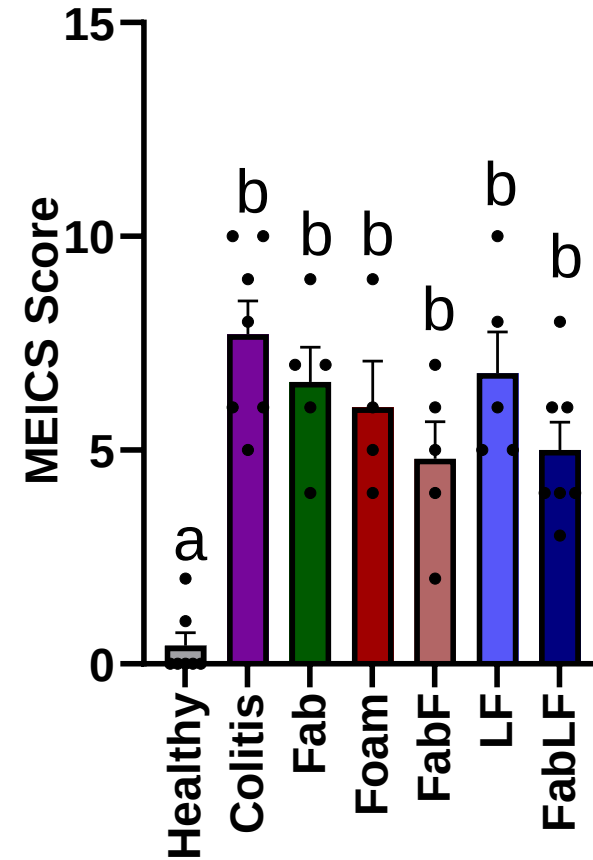
DSS (Dextran Sodium Sulphate) MW :36,000-50,000



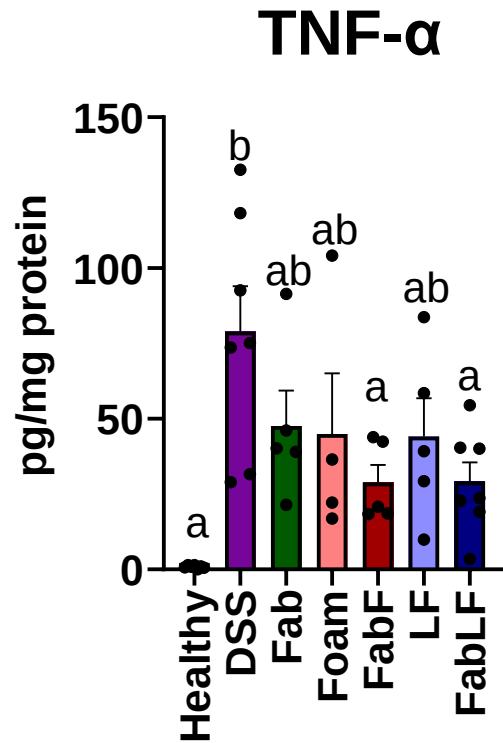
FabF



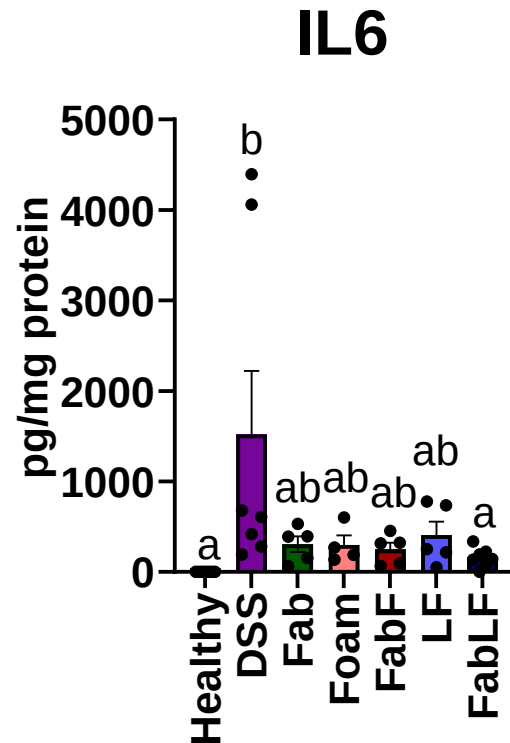
FabLF



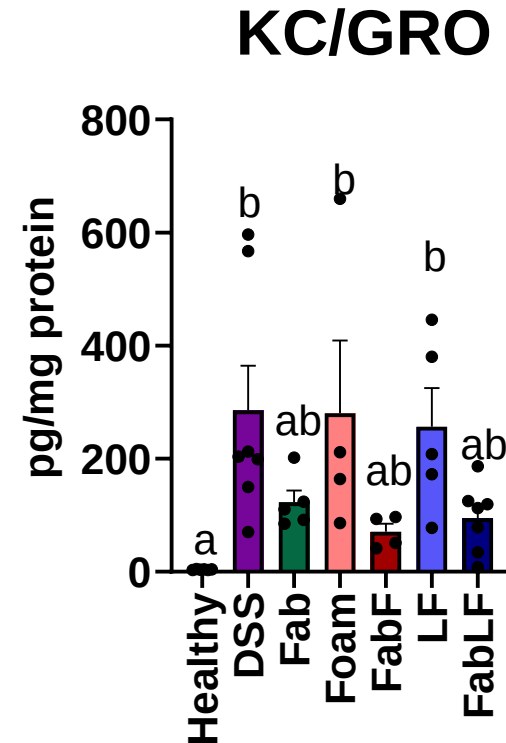
Foam Decreases Cytokines



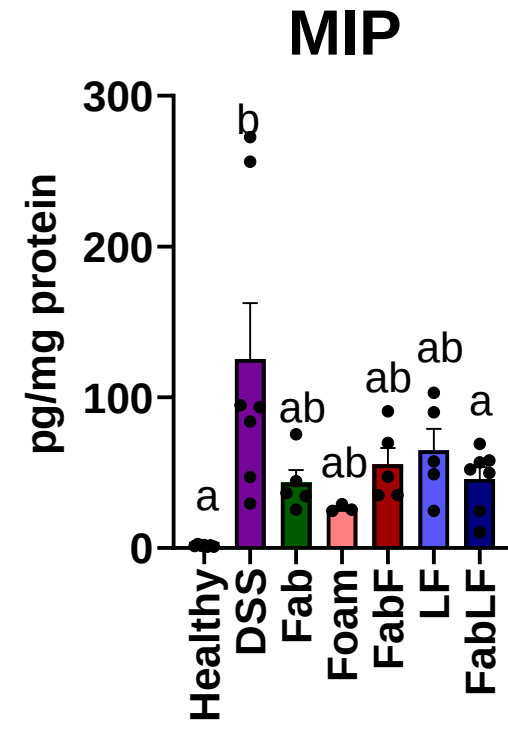
66%



90%

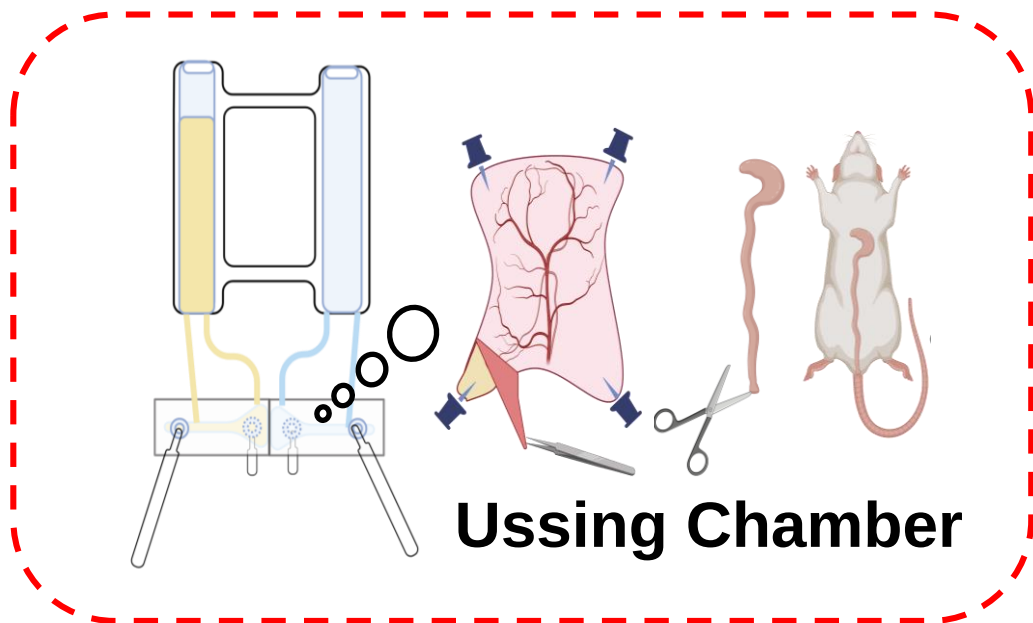


68%

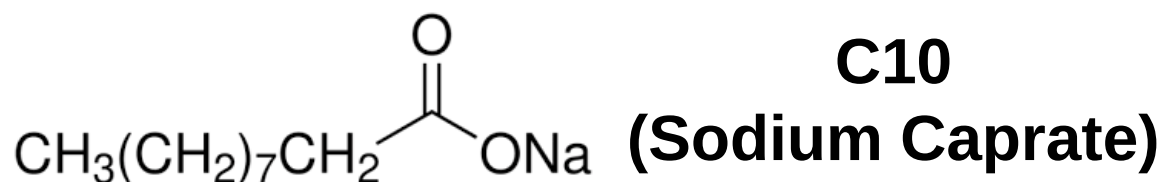


63%

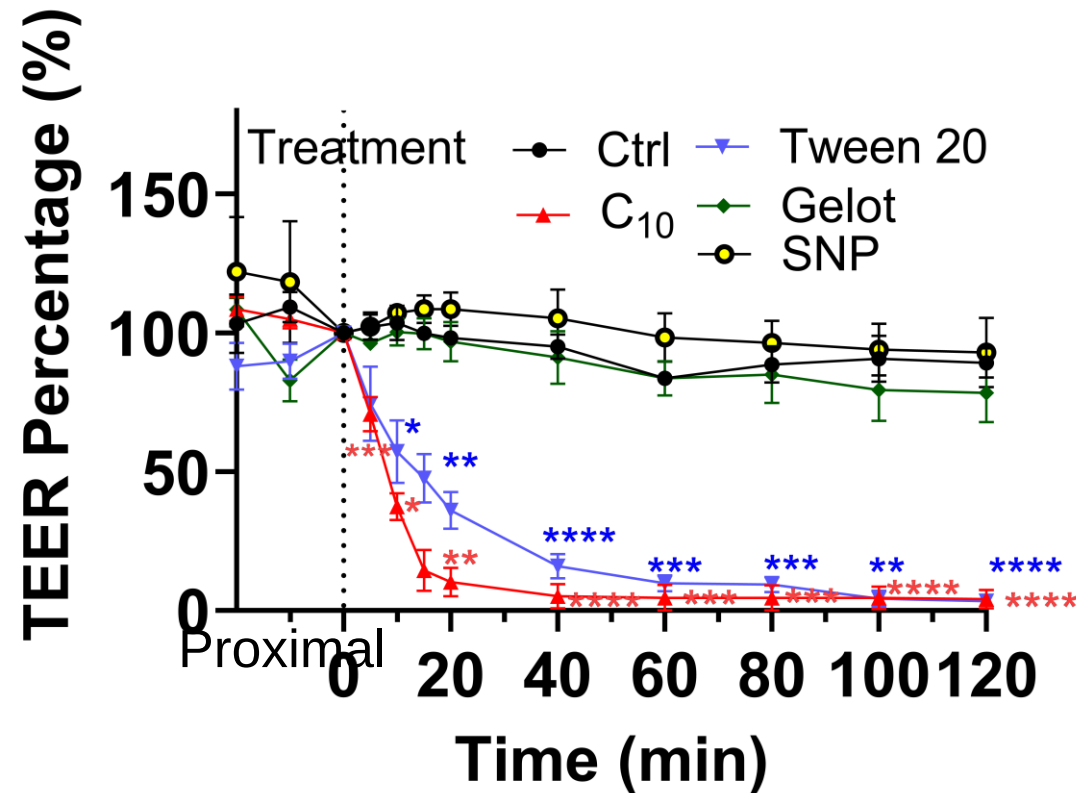
What caused the increased permeation



Ussing Chamber



TEER: transepithelial electrical resistance

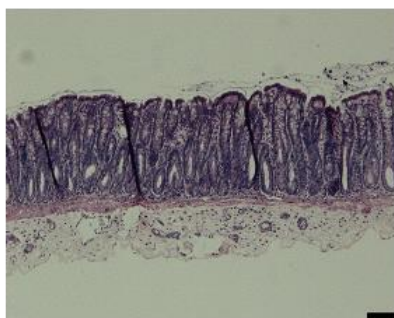
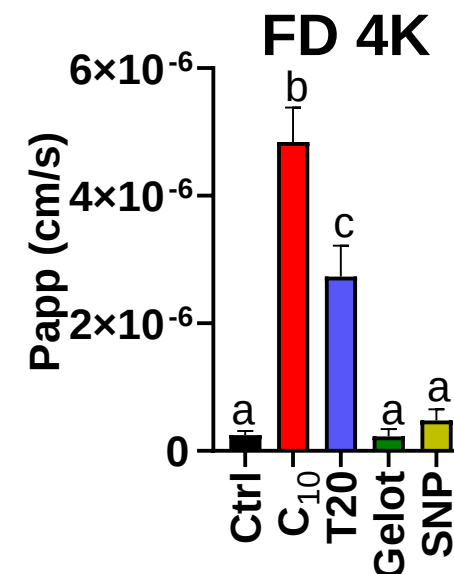
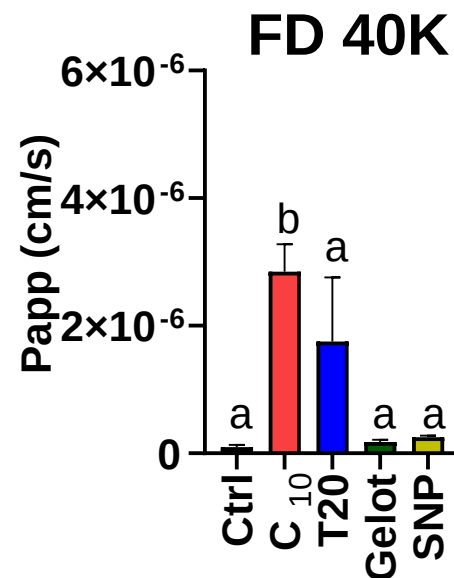
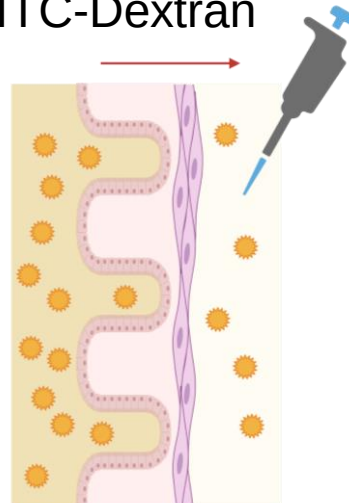


What caused the increased permeation

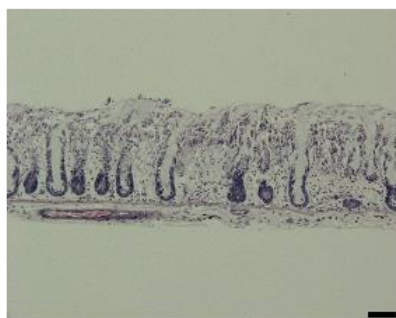
$$P_{app} = \frac{dQ}{dT} * \frac{1}{A * C_0}$$

dQ/dT is the rate of diffusion across the epithelium (mg/s),
A is the monolayer surface area and C_0 was the initial apical concentration (mg/mL)

Transepithelial flux of
FITC-Dextran



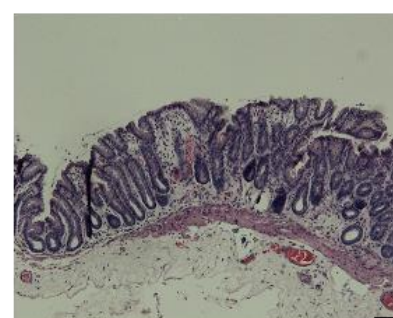
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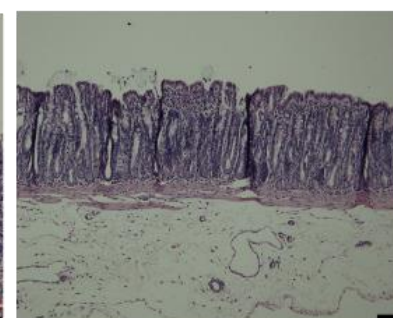
C10



Tween 20

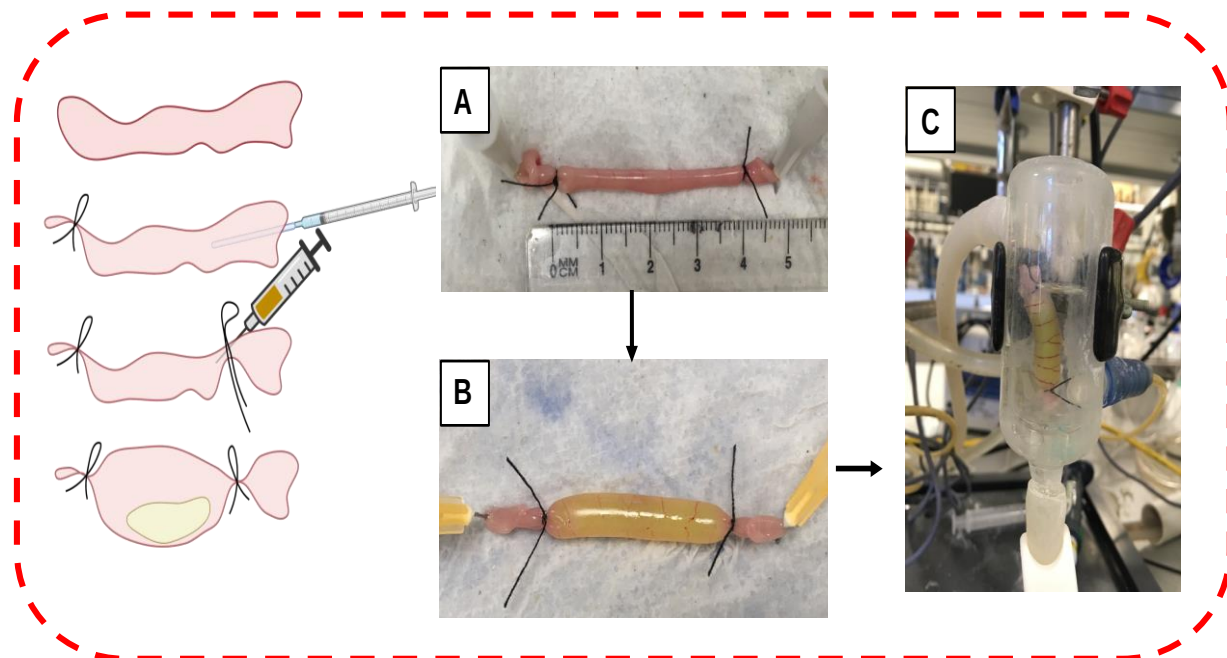


Gelot 64



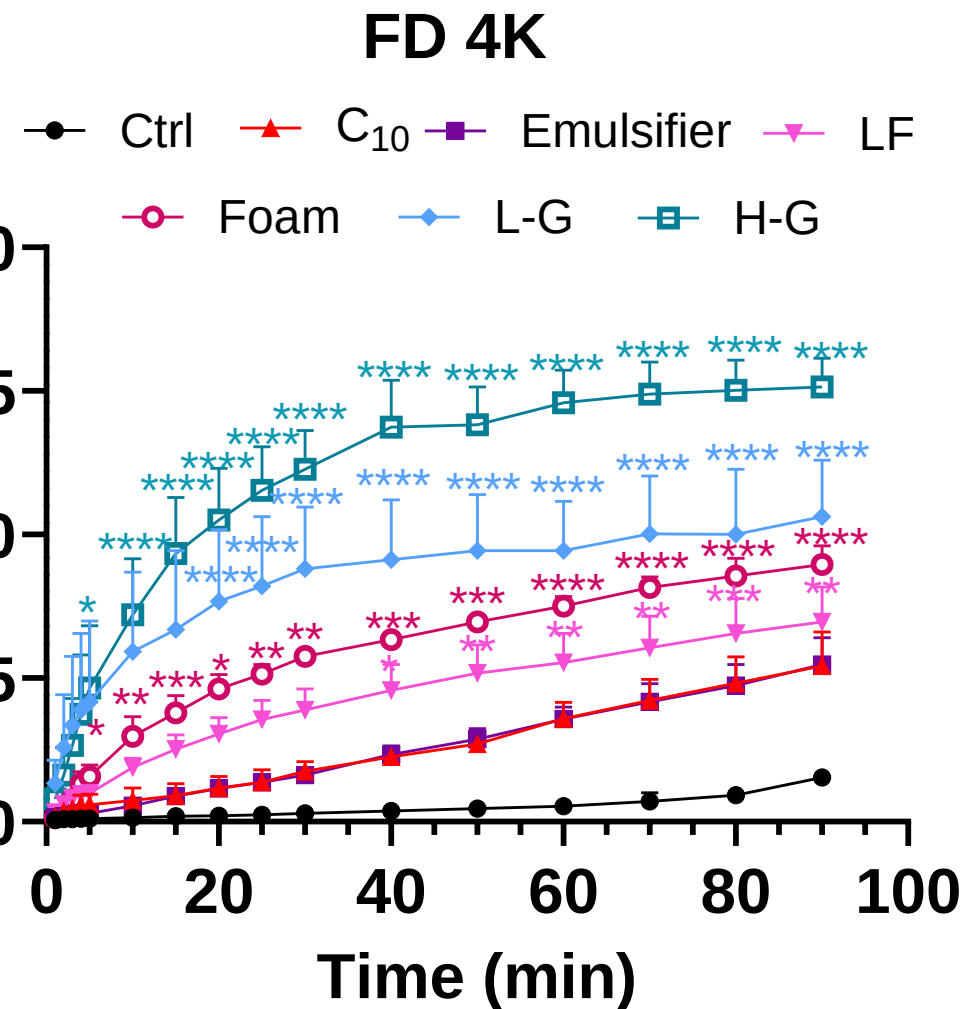
SNP

CO₂ is the key

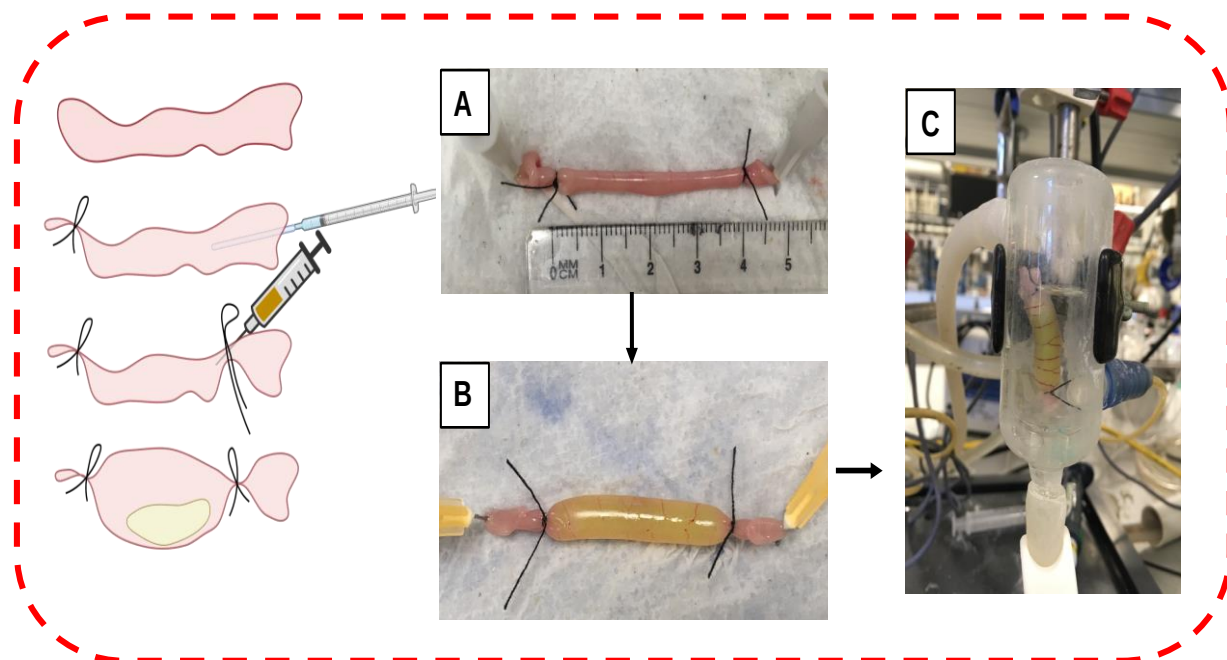


Non-everted gut ex vivo model

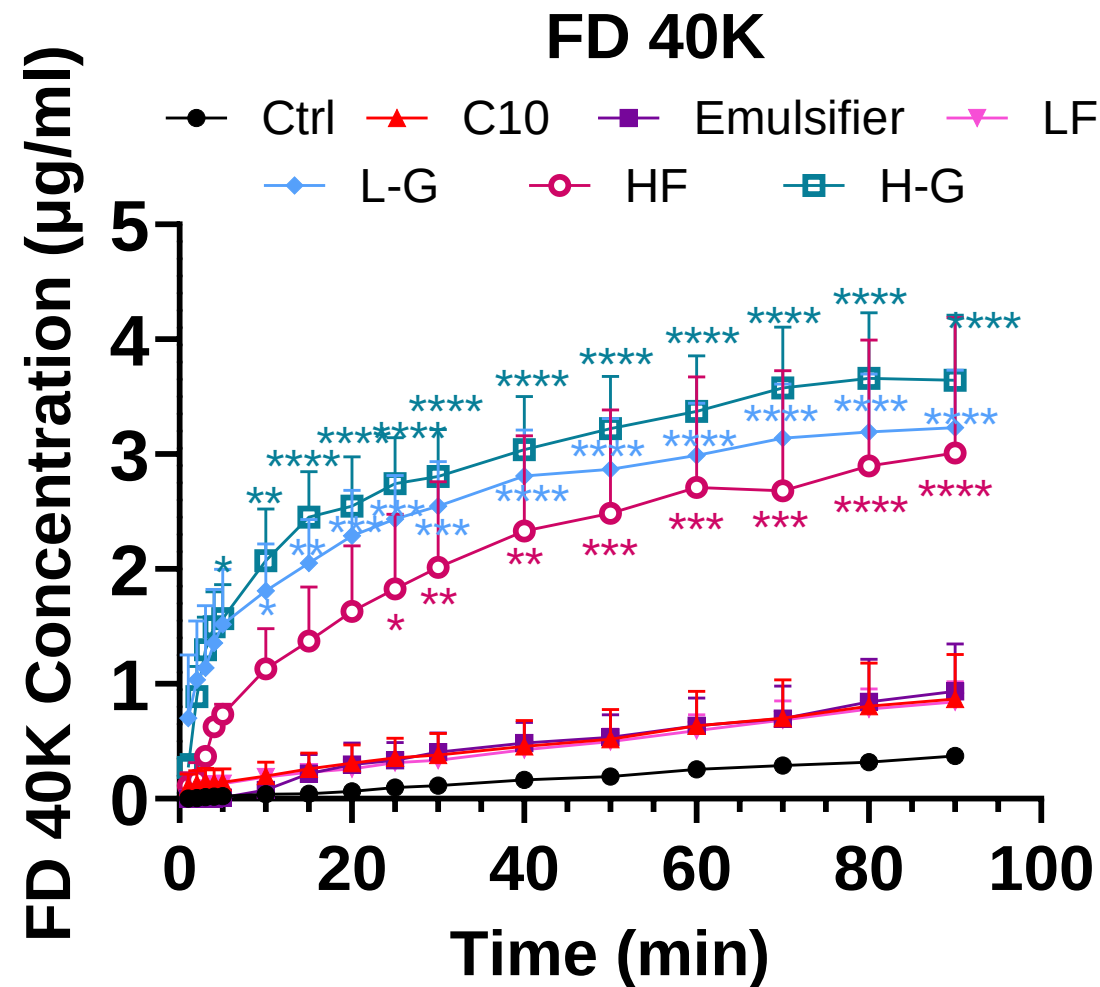
FD4K Concentration (µg/mL)



CO₂ is the key



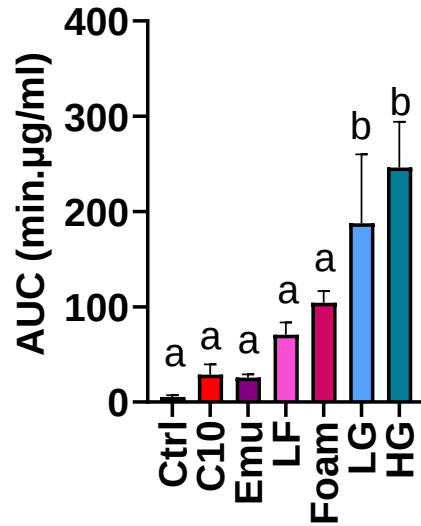
Non-everted gut ex vivo model



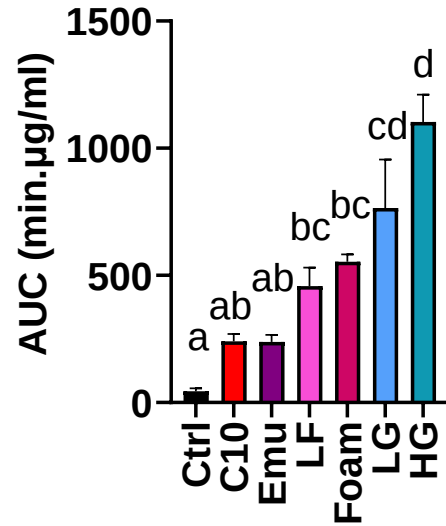
CO₂ Increases the Permeation

FD 4K

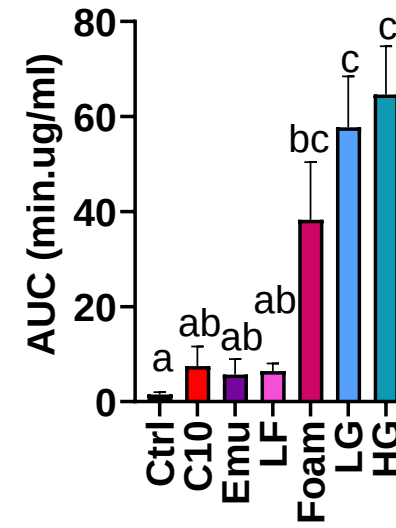
FD 40K



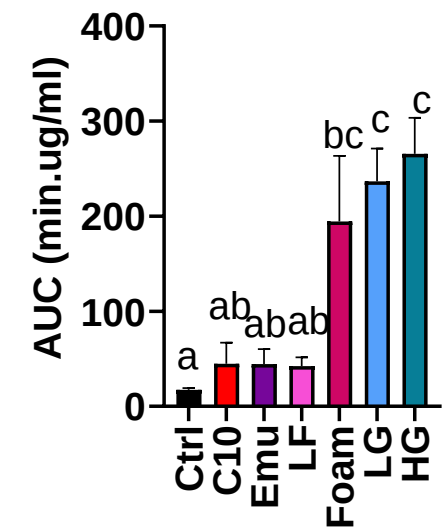
30 min



90 min

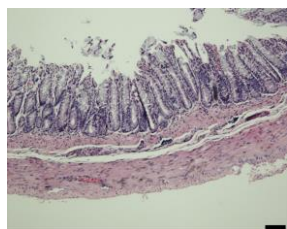


30 min

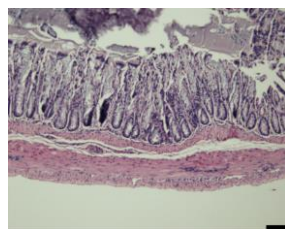


90 min

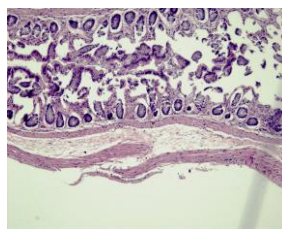
CO₂ as a Permeation Enhancer



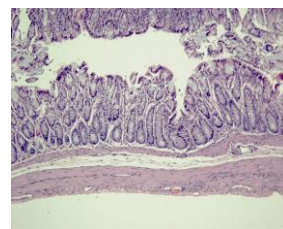
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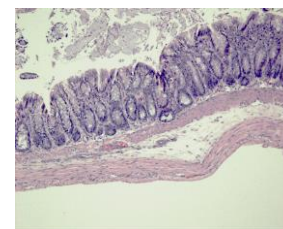
Emulsifier



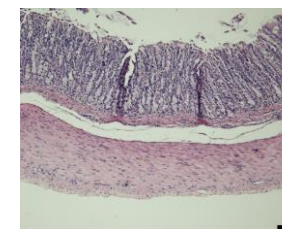
C10



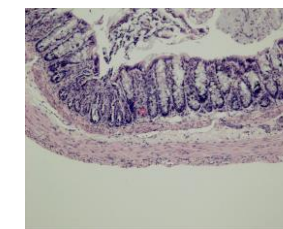
LF



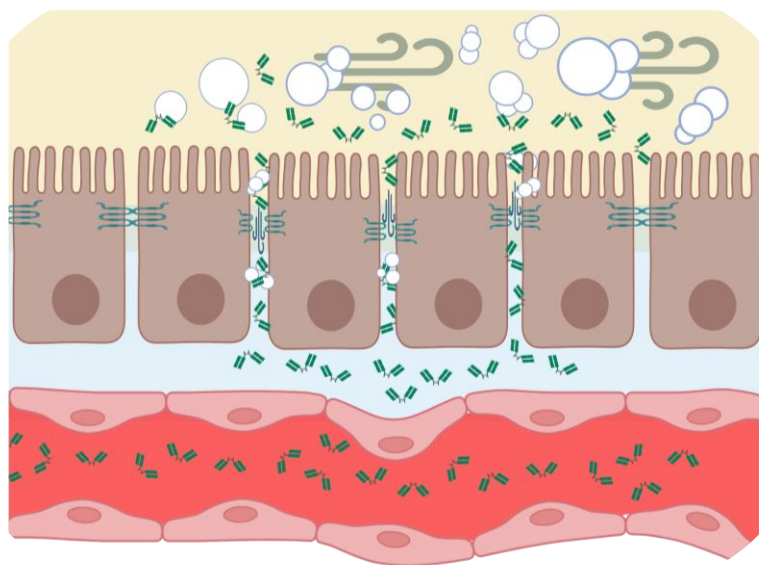
LG



HF



HG



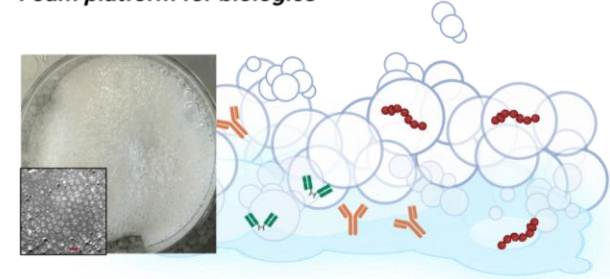
Gas-promoted formulation

Single dose of CO₂ could be efficiently incorporated within foam formulation as a gas permeation enhancer to facilitate the absorption of macro molecules.

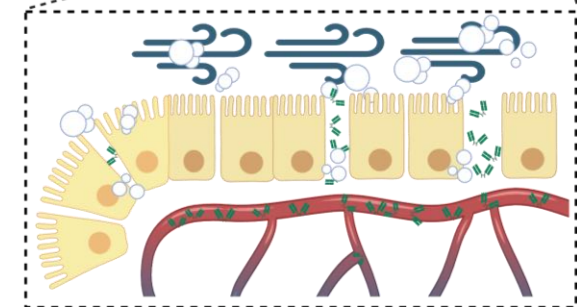
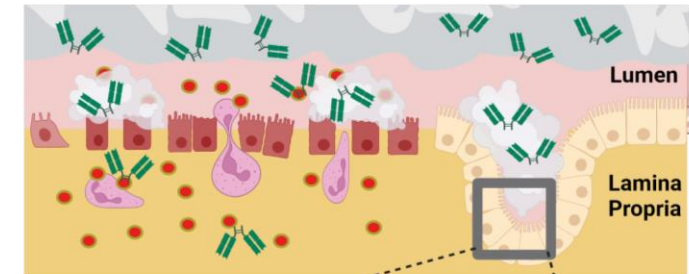
Summary

- We developed and in situ foam formulation for macromolecules via rectal administration
- The foam could improve the distribution and retention of Fab in colon and enhance Fab absorption
- The Foam demonstrated therapeutic effect in the chronic model
- Single dose of CO₂ was efficient to serve as permeation enhancer for colon delivery

Foam platform for biologics



Prolonged colon retention



Gas promoted absorption

Acknowledgement

Prof. Ana Beloqui (UCLouvain)

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Prof. David Brayden and Dr. Fiona McCartney (University College Dublin)

Inês Ladeiro Domingues and Espoir Kambale Kavungere (UCLouvain)



INTEGRATING
Delivery Science
ACROSS DISCIPLINES

