

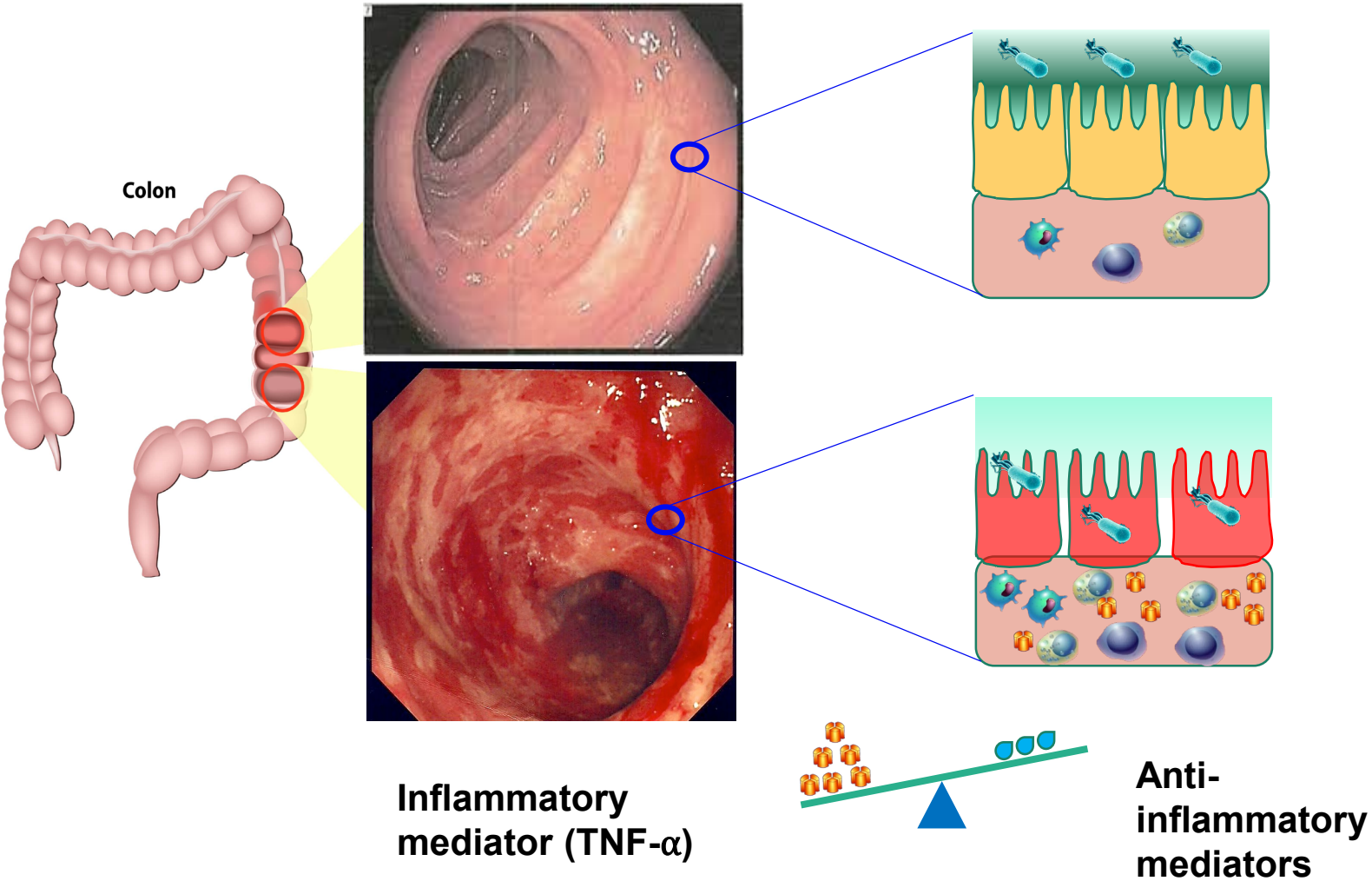
Local colonic application of monoclonal antibodies: does mucus hinder their permeation?

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- Ulcerative colitis
- Why local application of monoclonal antibodies?
- Mucus as a barrier
- Methods
- Results
- Conclusions
- Further work

Ulcerative colitis

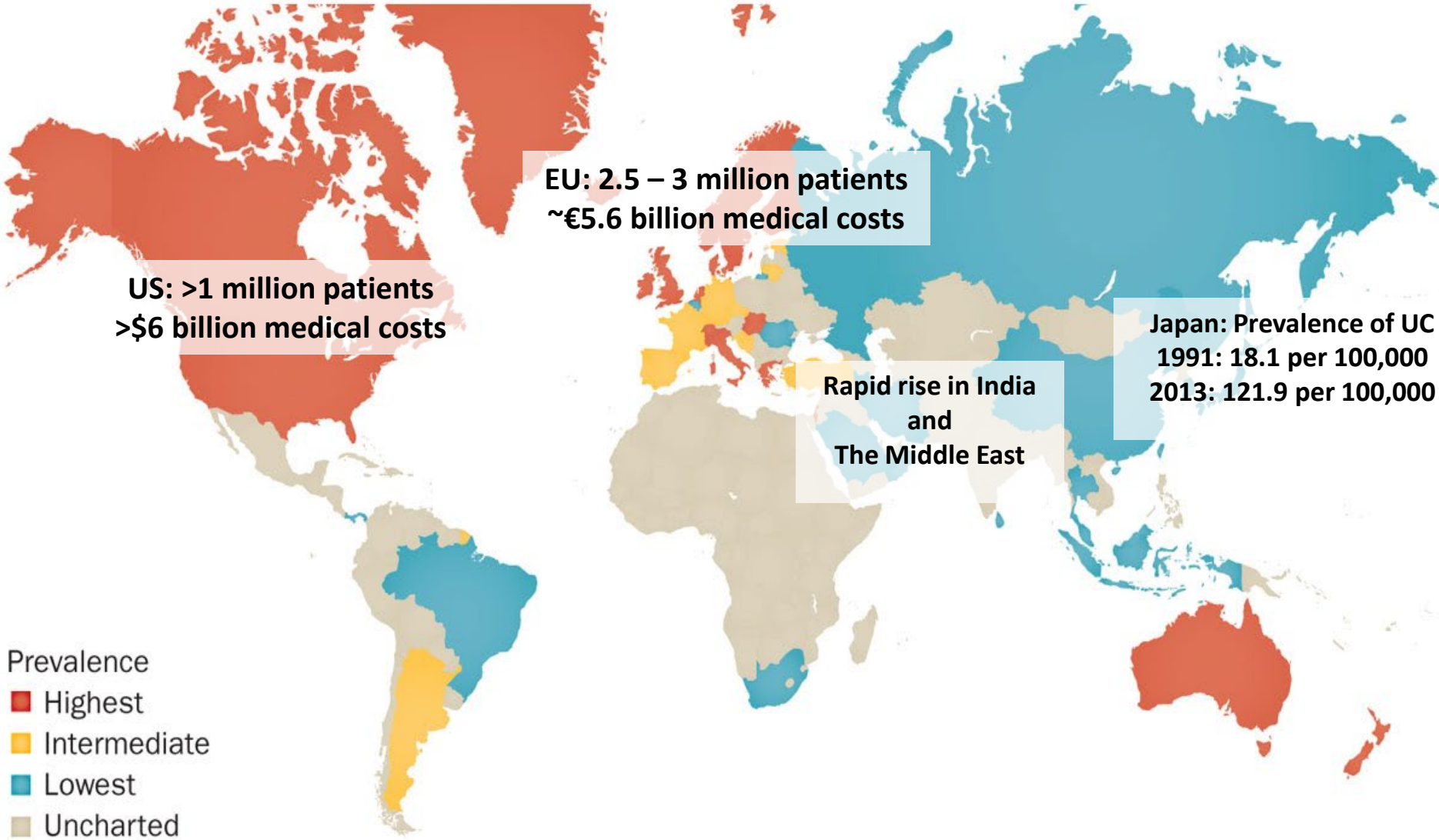


Inflammatory mediator (TNF- α)

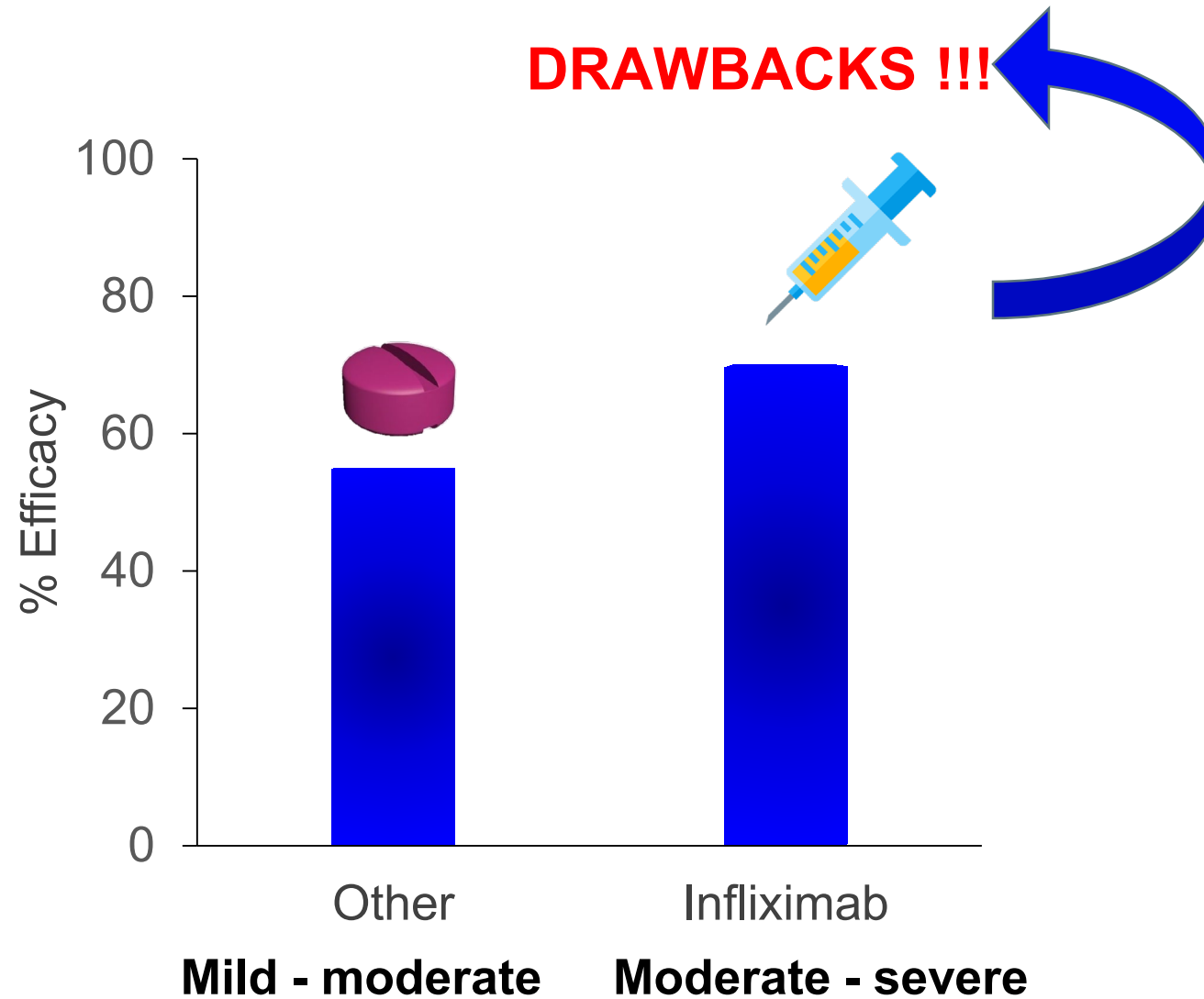
Anti-inflammatory mediators

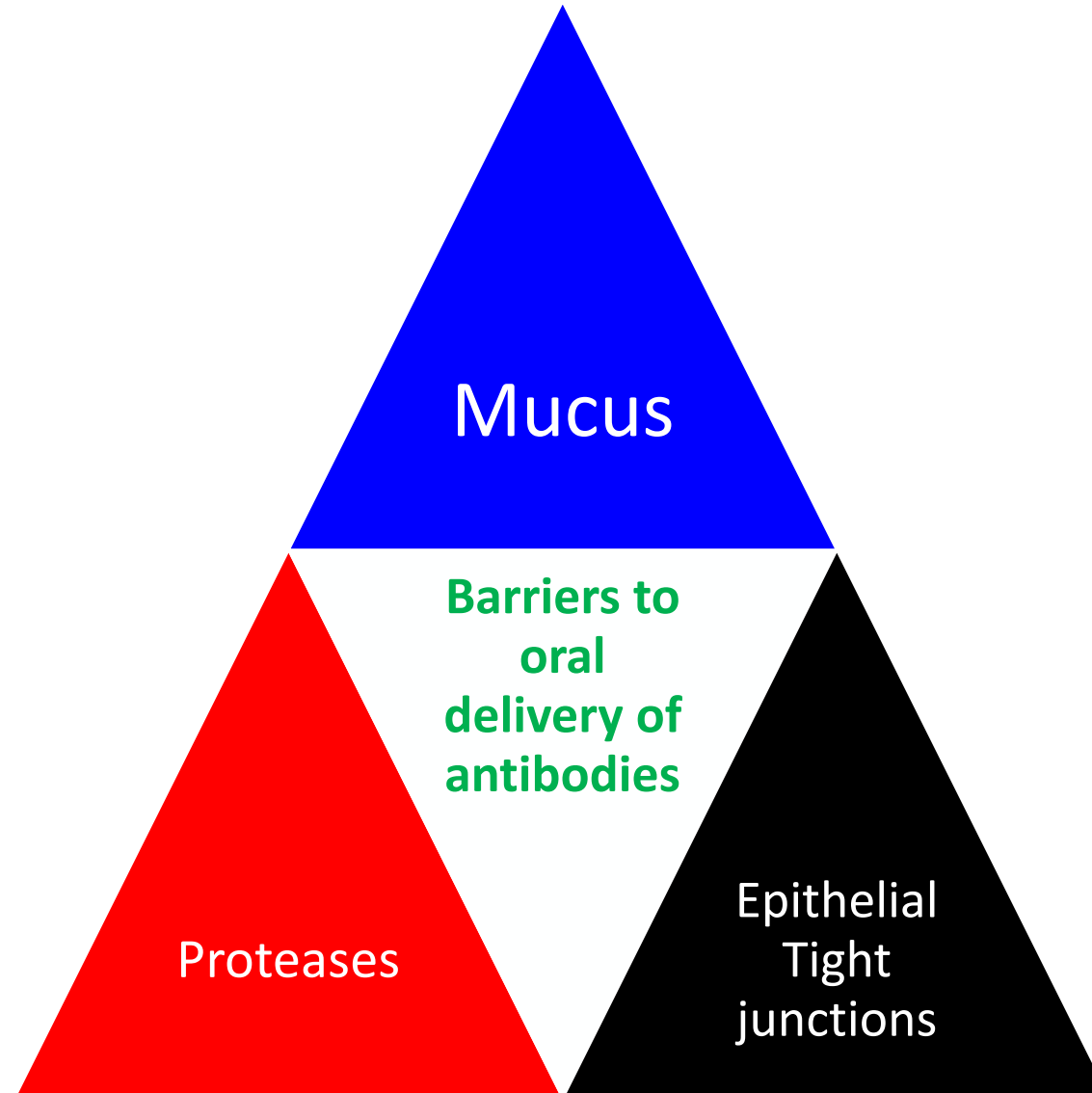


Prevalence of Ulcerative Colitis

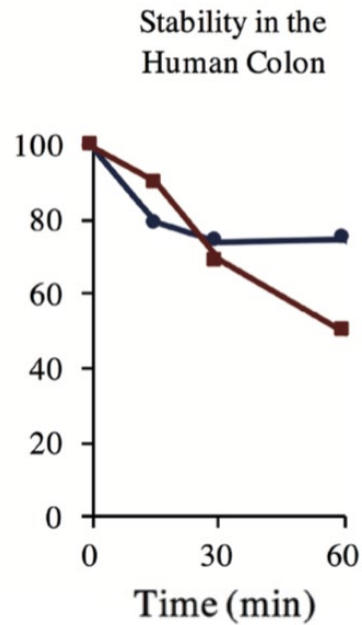


Why deliver monoclonal antibodies orally?

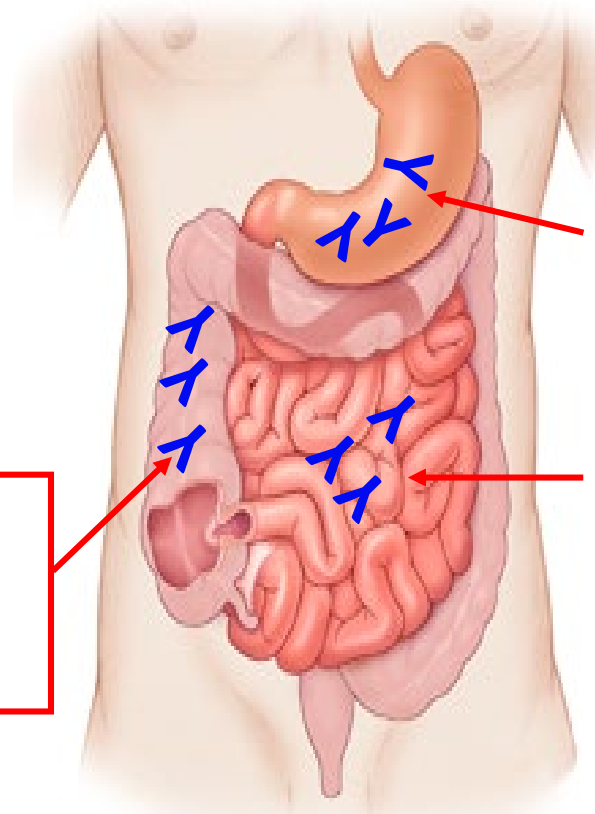




Stability of monoclonal antibodies in the gastrointestinal tract



Colon:
good
stability



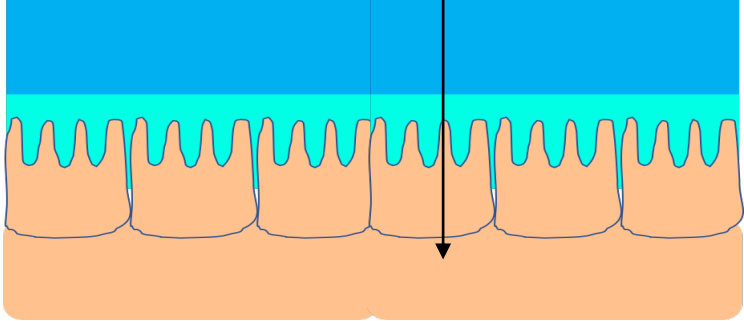
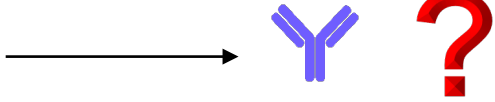
Stomach:
Degrades

Small intestine:
Degrades

Would mucus hinder the permeation of monoclonal antibodies?

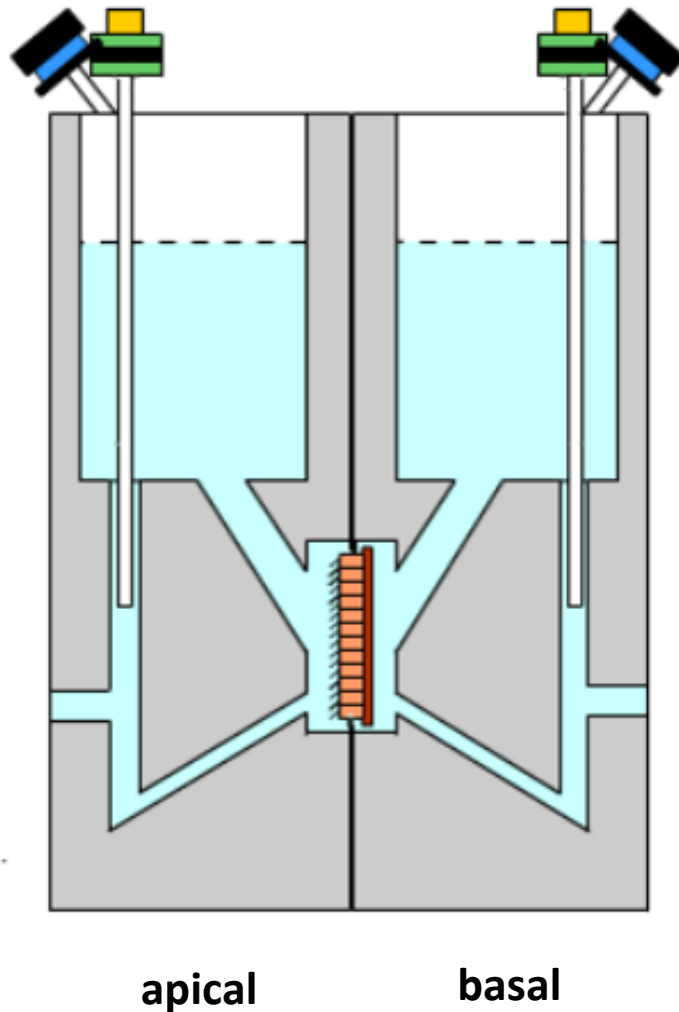


Infliximab
(~150 kDa)



Methods to quantify infliximab in rat mucus & mucosa

Ussing chamber for permeation studies



Mount tissue

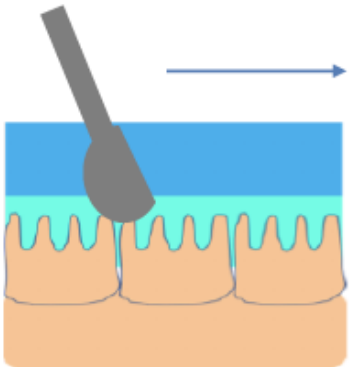


Stabilise with bicarbonate ringer's



Add infliximab 0.2mg/ml apically
to bicarbonate ringer's solution
@ pH 6.0 / 7.4 for 2 hours

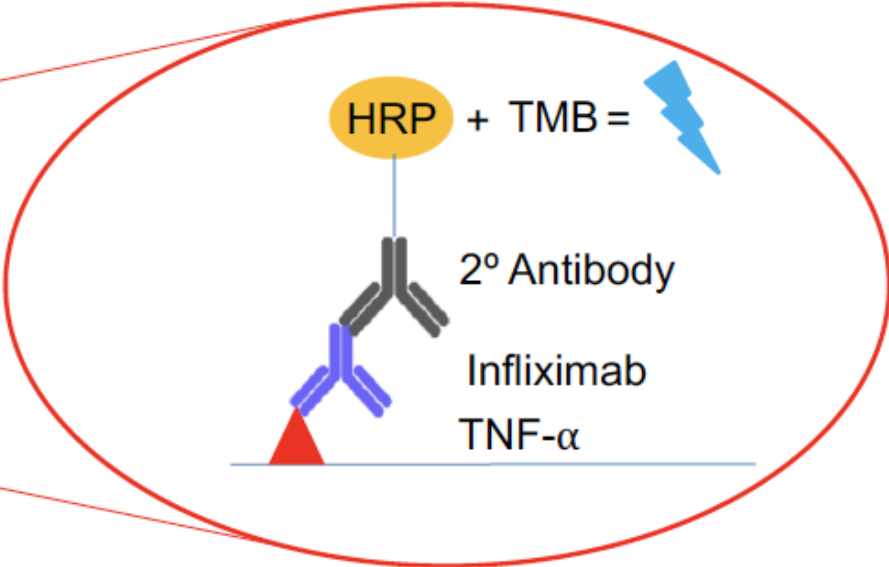
Quantification of infliximab



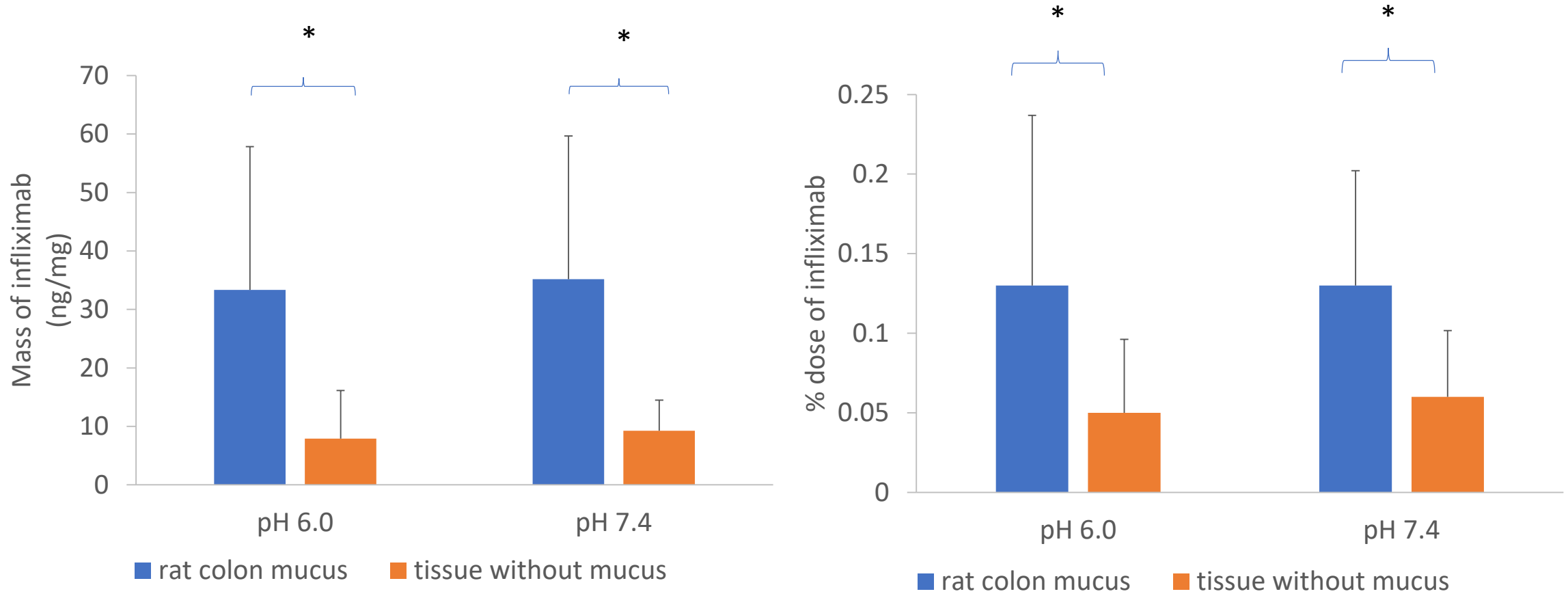
Quantify infliximab in:

Rat colon mucus

Rat colon tissue without mucus

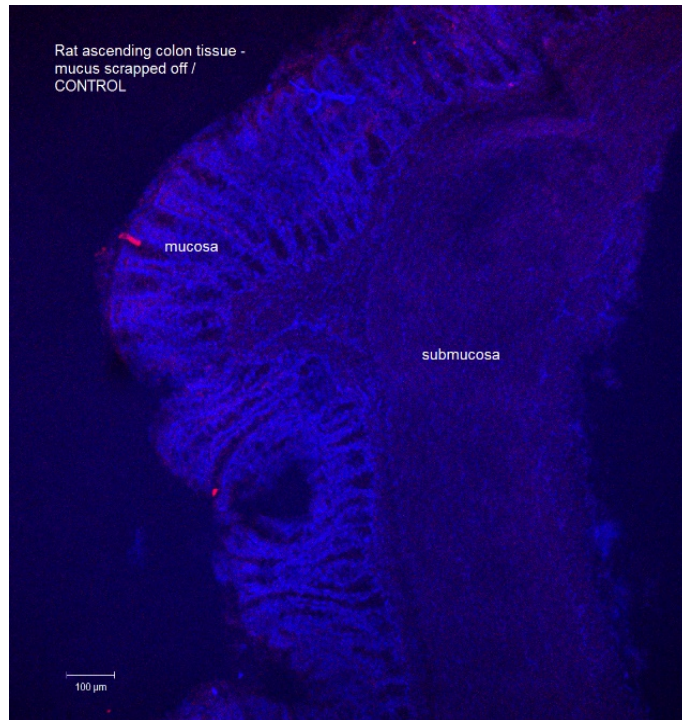


Infliximab accumulation in rat colon tissue and mucus

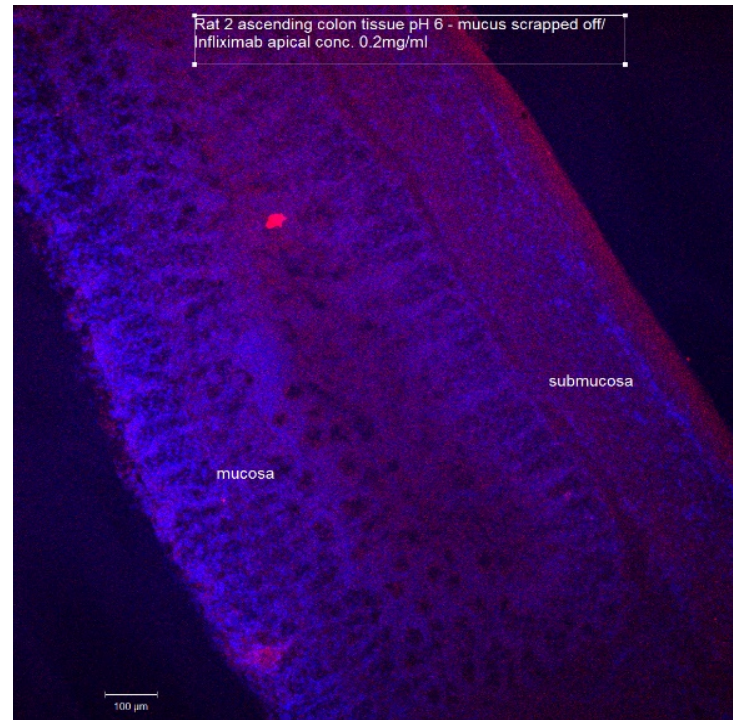


* $p < 0.05$

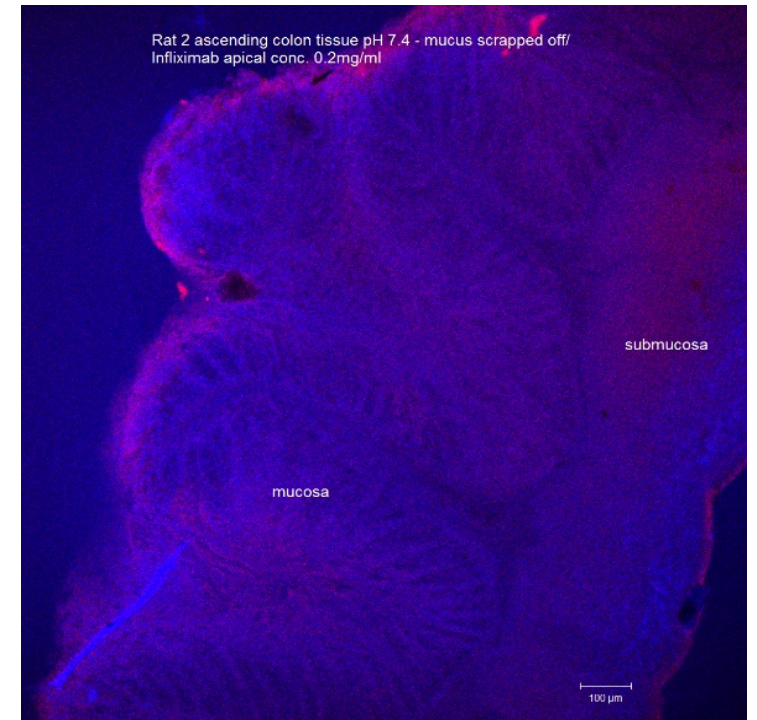
Infliximab localized in rat colon tissue with mucus scrapped off



CONTROL



pH 6.0 apical
mucus scrapped off



pH 7.4 apical
mucus scrapped off

- Mucus is a barrier to the permeation of infliximab.
- Infliximab may be entrapped in mucus owing either to its interaction with Fc gamma binding protein (FCGBP) or via interactions with mucin.
- pH did not have an effect on infliximab accumulation in mucus indicating that electrostatic interactions may not be responsible for their entrapment.

- Try permeation with higher concentrations.
- To determine the effect of mucus on permeation of infliximab from
 - i) rat models of colitis and
 - ii) tissues from human subjects (healthy and ulcerative colitis).

Thank you