Branched PEGylation as a strategy to overcome the mucosal barrier

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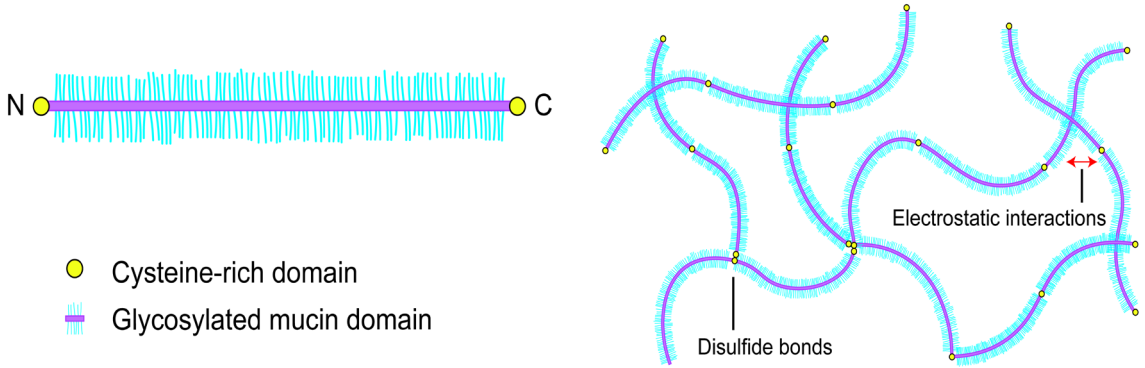
NEXT-GENERATION DELIVERY INNOVATIONS

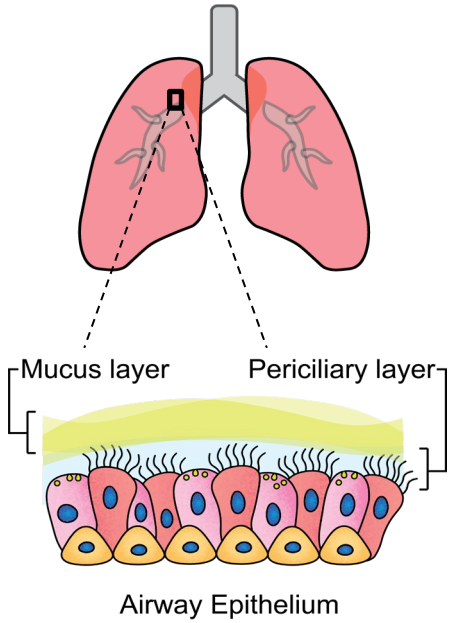
Challenges in respiratory delivery

The mucus barrier



Mucus traps inhaled particles

Epithelial cells and mucociliary clearance



The periciliary layer quickly clears particles before they can enter cells

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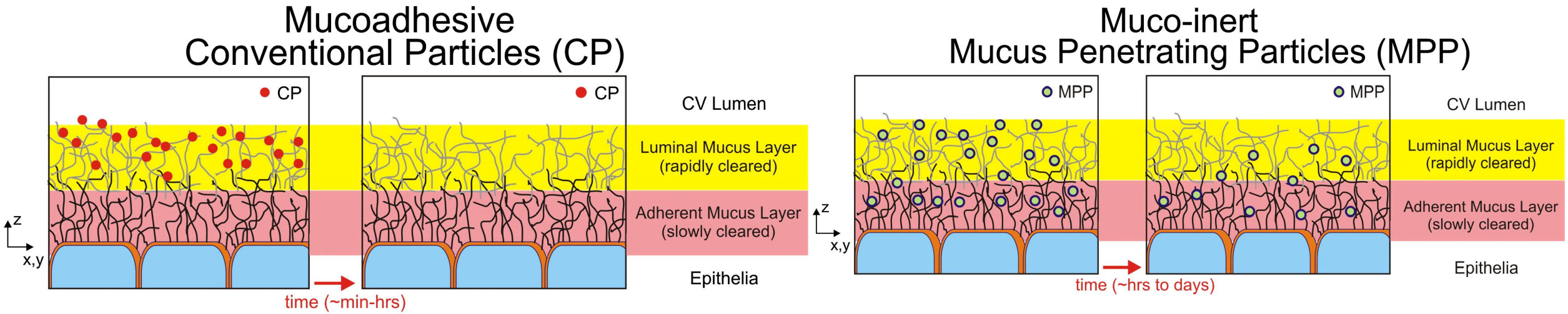
Mucus Penetrating NPs



NP: nanoparticle
Lai et. al, ADDR, 2009

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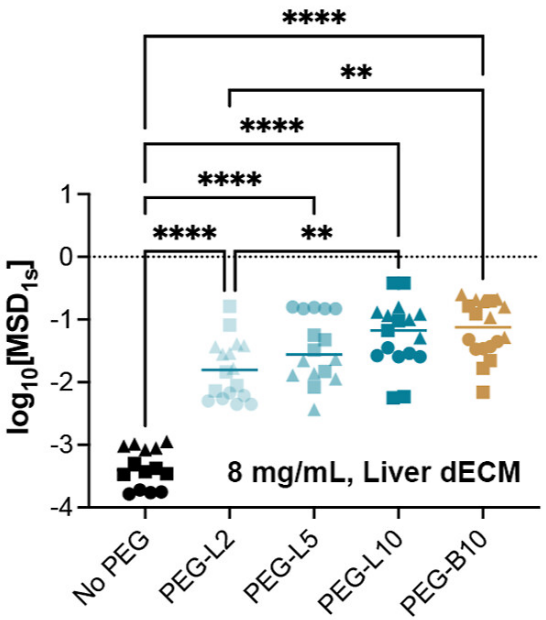
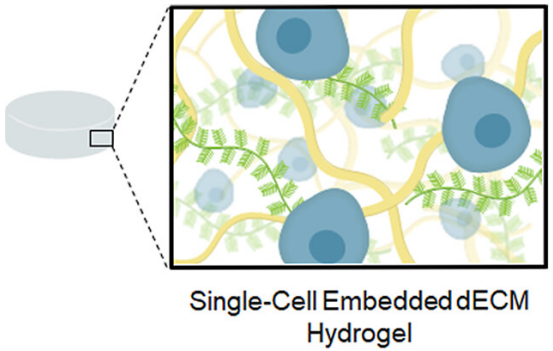
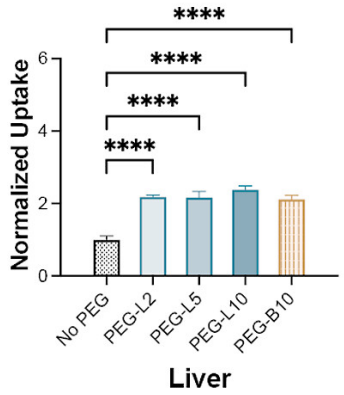
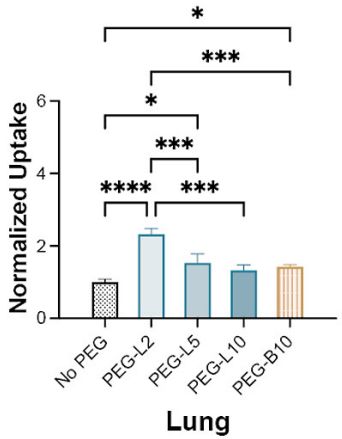
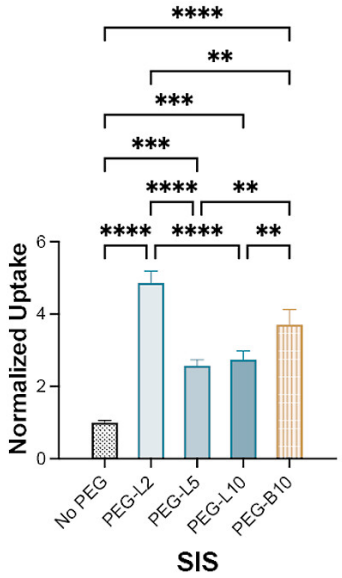
Branched PEG in ECM











PEG: polyethylene glycol
ECM: extracellular matrix
Cahn et. al, ACS Nano, 2024

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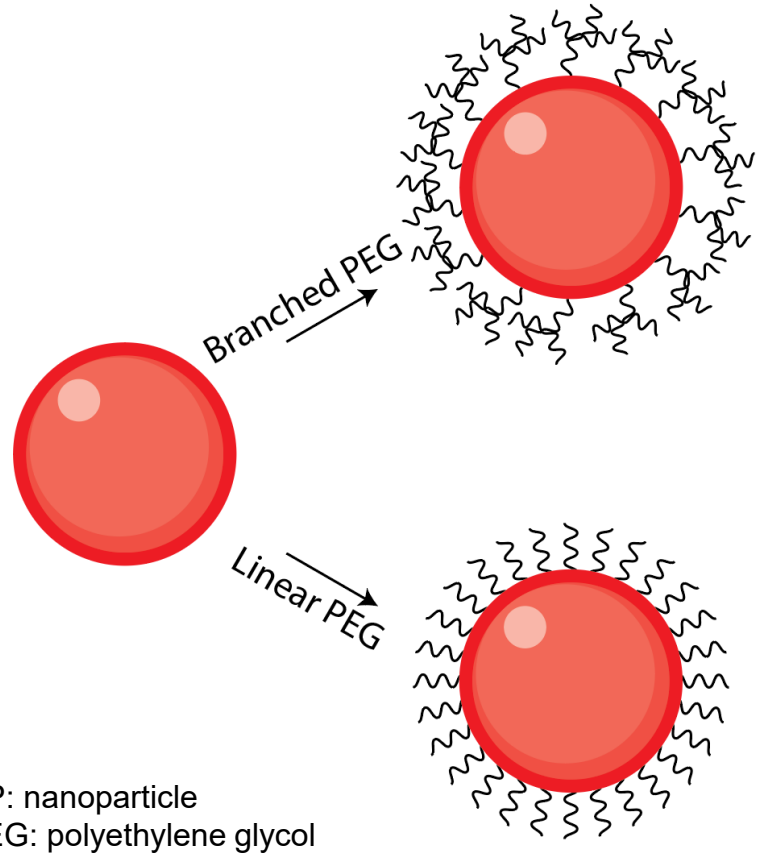
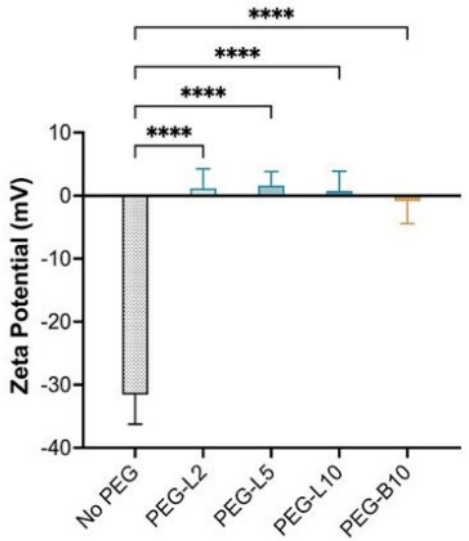
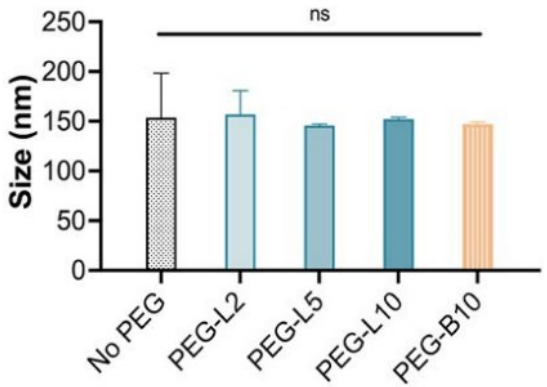
Varying PEG coating on NPs







Does branched PEG lead to better mucus penetration and cell uptake than linear PEG?

NP: nanoparticle
PEG: polyethylene glycol
Cahn et. al, ACS Nano, 2024

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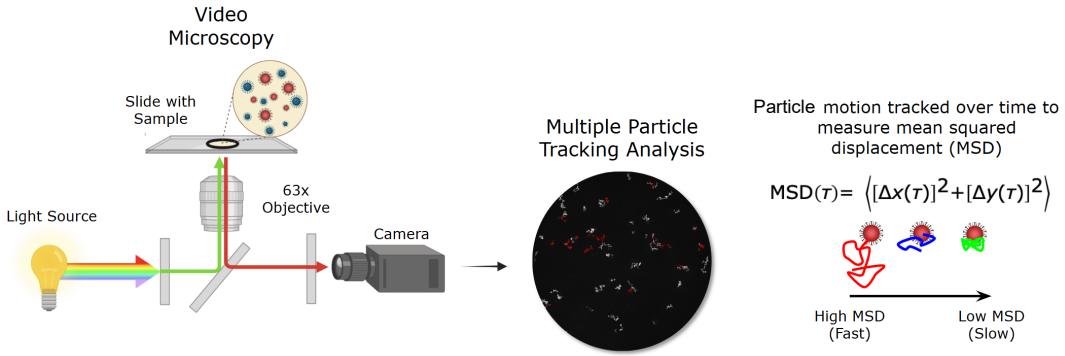
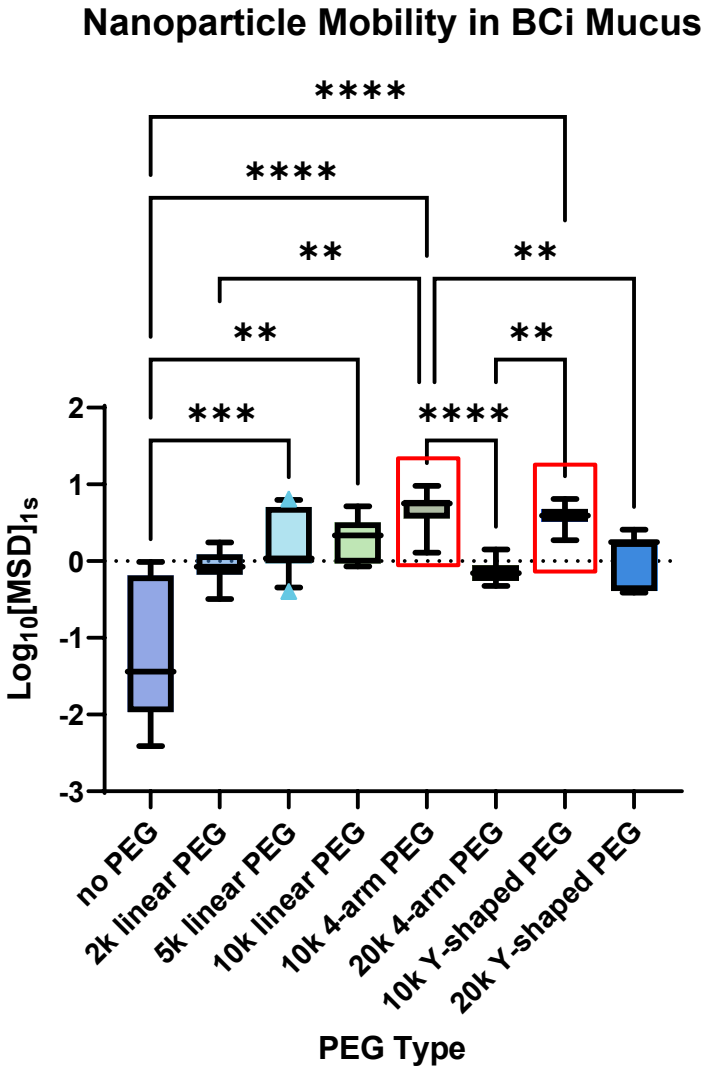
NP diffusion in mucus





Low MW branched PEG confers the best NP mobility in mucus

NP: nanoparticle
PEG: polyethylene glycol
MW: molecular weight

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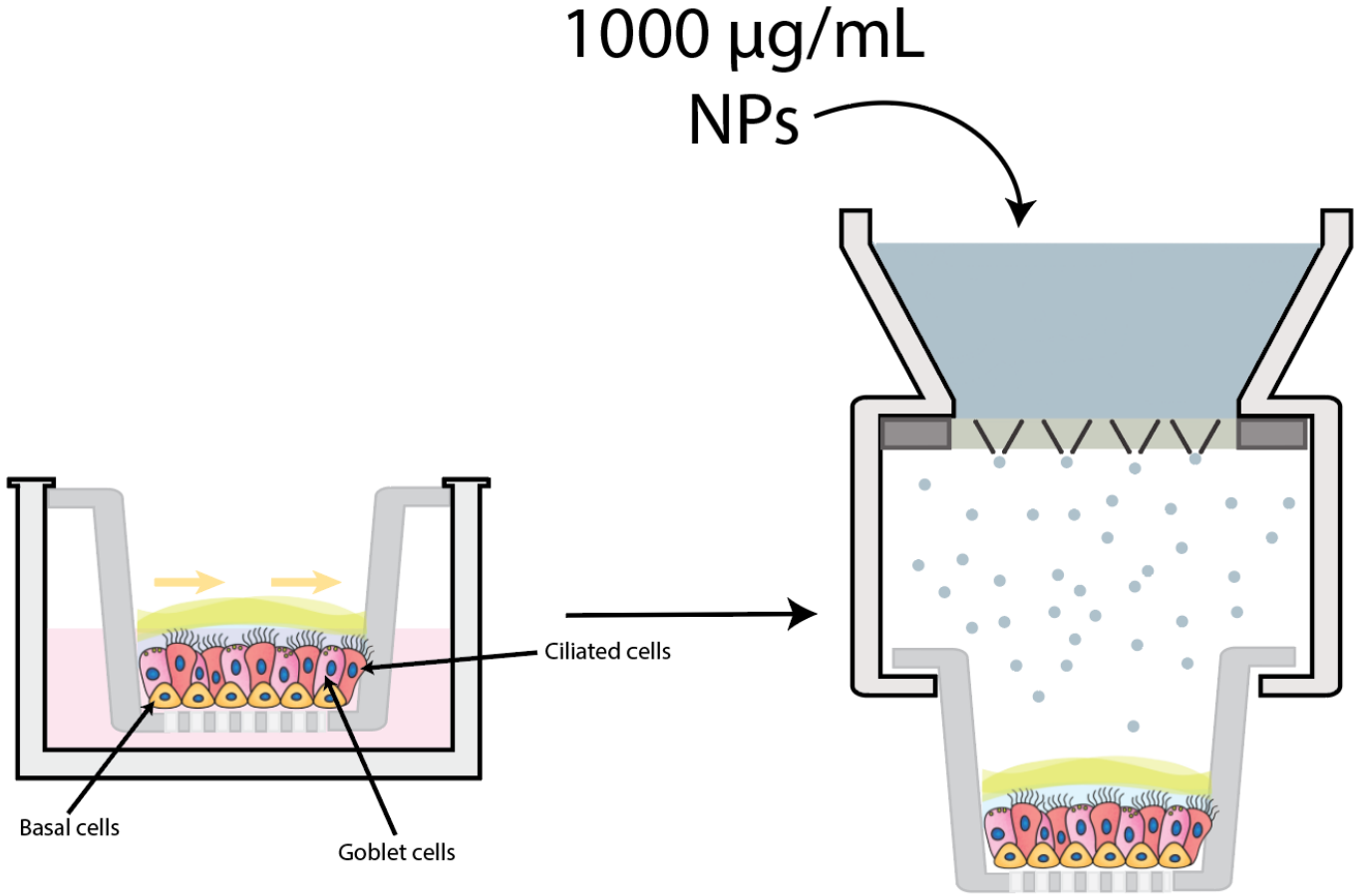
Aerosolized NP Uptake



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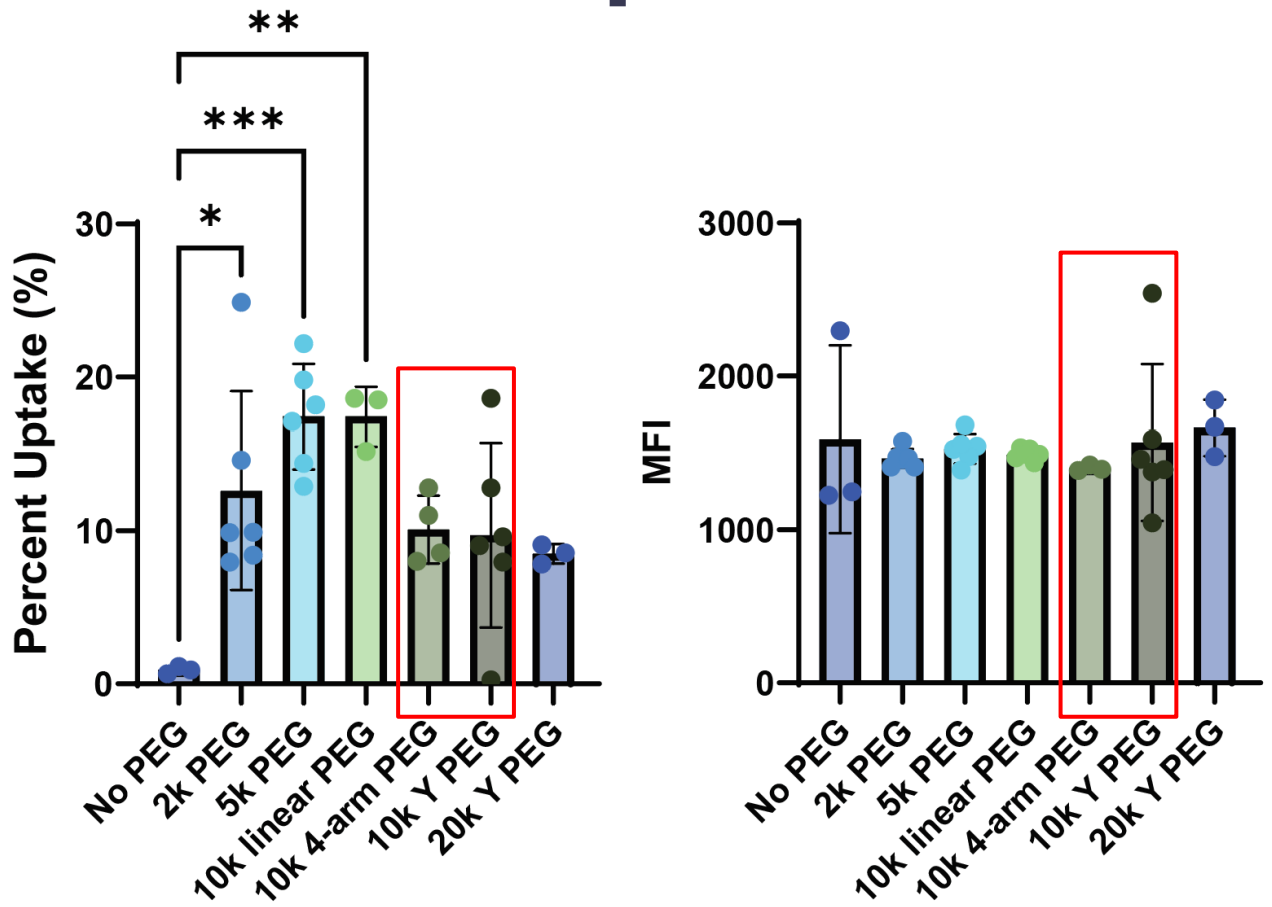

Conclusions & Future Directions

Conclusions

- NPs coated with low MW branched PEG show increased mobility in mucus
- Nebulizing NPs onto airway cultures results in similar uptake for linear and branched PEG

Future Directions

- Investigate NP uptake in specific cell types (i.e. goblet, ciliated cells)
- In vivo study of intranasally administered NPs

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