Tracking Nanoparticle Transport through Mucus

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INTRODUCTION

- Mucus is a polymer-based viscoelastic glycopeptide gel, which presents a critical barrier for nanoscale pulmonary drug delivery systems (Fig.1).
- Size filtering and adhesive interactions between particles and mucus hydrogel play an important role in modulating penetration through mucus (Fig.2).
- Particle movement in mucus has been documented in the literature, but the translocation of particle across mucus has received less attention.
- The aim of this study was to gain a better understanding of particle translocation across a mucus barrier using a novel in vitro model.

METHOD

- Collection and characterization of mucus
  Porcine gastric mucus was prepared as illustrated in Fig.3.

- Manufacture of nanoparticles
  PVA nanoparticles were manufactured using a nanoprecipitation method (Fig.4).

- Nanoparticle translocation assay
  An in vitro transport assay for the evaluation of nanoparticle translocation across mucus was developed using a Transwell diffusion cell (Fig.5).

RESULT

- Nanomaterial analysis
  Two different nanosized fluorescent objects were detected in the receiver chamber of the Transwell. One was identified as mucin fragments and the second as nanoparticles (Fig.6).

- Nanoparticle mucus interaction
  Two fluorescent objects were quantified together using total fluorescence intensity. Changes in fluorescence intensity were interpreted as mucus disruption.
  - Mucus interaction with 200 nm PS particles led to the highest disruption compared to 50 and 700 nm at pH 8.5 (Fig.7a).
  - The mucus gel at pH 2.5 appeared to be a more resistant barrier than at pH 6.5 and pH 8.5 (Fig.7b).
  - Negatively charged particles disrupted the mucus gel more than the neutral particles after 48 h at both pH 6.5 and pH 8.5 (Fig.7c & d).

CONCLUSION

- Nanoparticle translocation through mucus could not be quantified using the developed Transwell system due to the interference of mucin fragments.
- This highlights that tracking particle transport through mucus must be proceeded by a careful analysis of the mucus gel.
- Particle-mucin interactions can be modulated in strength by particle properties including size, surface charge and pH.