POLYMAT

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Redox responsive nanogels for mucosal drug delivery

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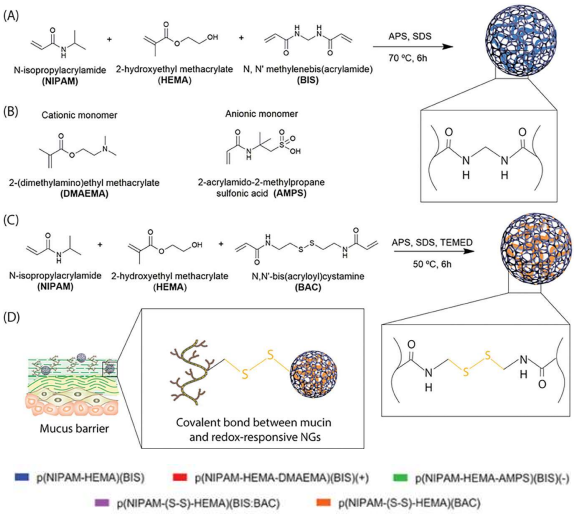
Introduction

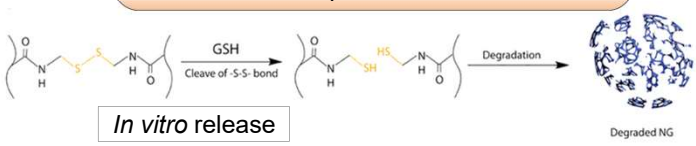
Mucus is a biological hydrogel that coats and protects all non-keratinized wet epithelial surfaces. It presents a major barrier to deliver therapeutic biomacromolecules to lungs and other mucosal tissues. Thiol bearing materials recently gained interest due to their ability to overcome mucosal clearance and thus to deliver drugs to submucosal layers in sufficient concentrations. Herein, polymeric nanogels (NGs) incorporating disulfide groups are developed for transmucosal delivery that coopts the precision and nanoscale spatial resolution inherently afforded by *in situ* polymerization to produce precisely engineered redox-responsive particles. Unprecedented control over NGs design such as size, polarity/lipophilicity, redox response, surface decoration, targeting ability, etc., proves advantageous for transmucosal delivery and release bioactive molecules.

Results and discussion

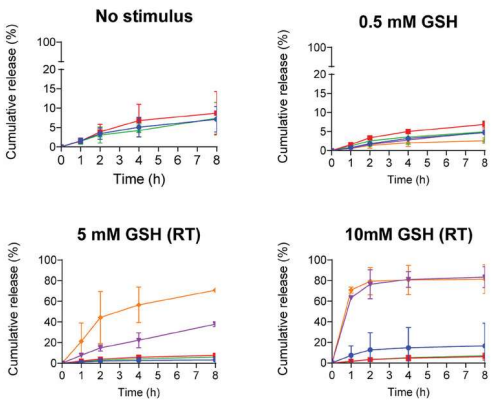
Synthesis of nanogels



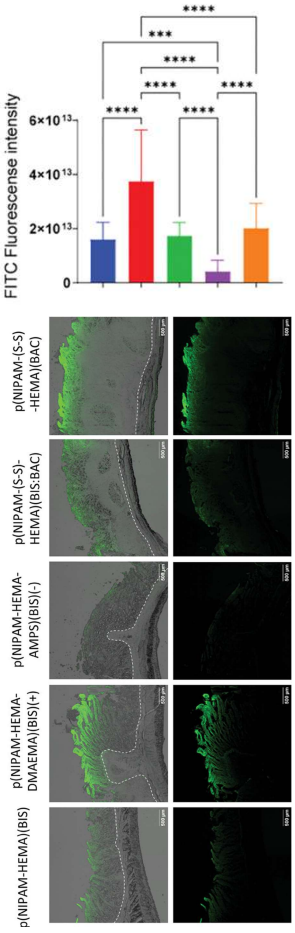
Redox responsive behaviour



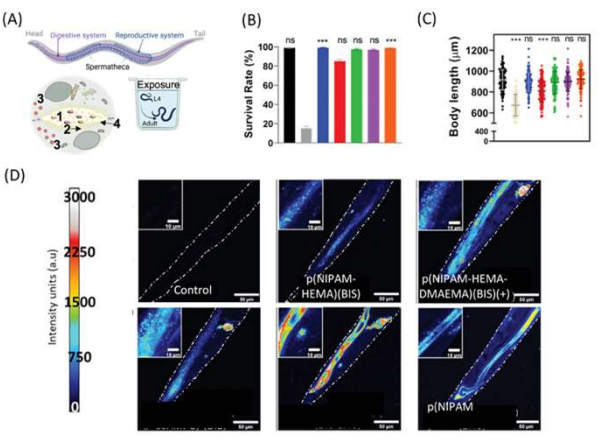
In vitro release



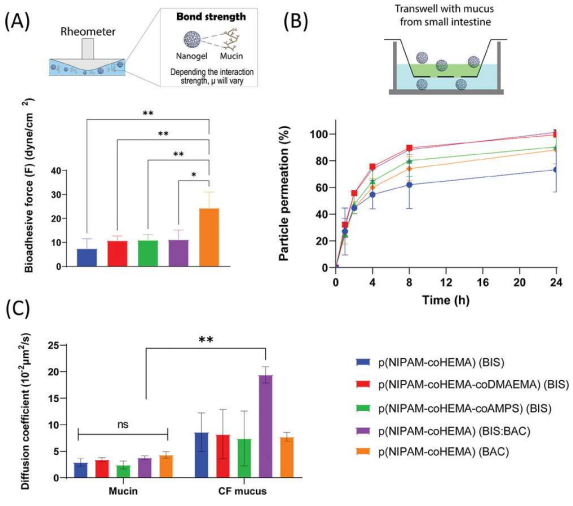
Ex vivo small intestine model



In vivo C. elegans model (nematode worm)



NGs-Mucin/Mucus Interactions



Conclusions

- Stable, biocompatible, spherical mutli-responsive NGs with size ~220 nm were successfully synthesized.
- Presence of disulfide bonds provided degradable points that later enabled the cargo release in reductive conditions.
- We evaluated the NGs' interactions with mucus and their ability to penetrate mucosal barriers by using different models.

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References

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2. Udabe, Jakes, et al. Advanced Functional Materials 34.45 (2024): 2407044.
3. Udabe, Jakes, et al. Biomacromolecules 25.9 (2024): 5968-5978.