UNIVERSITY OF ILLINOIS CHICAGO

Versatile, topical antibiotic delivery with glutathione-conjugated hydrogels

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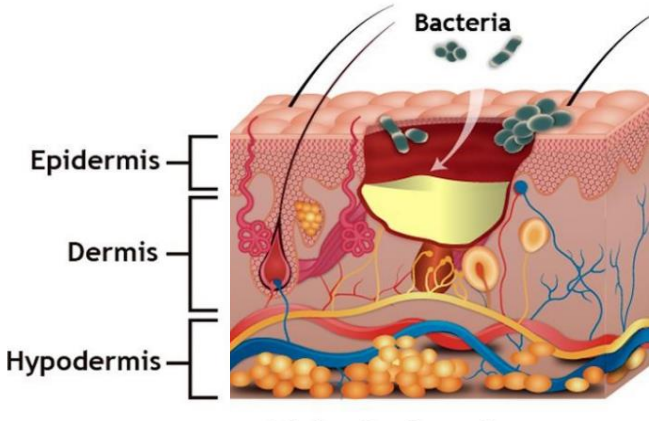
CRS 2022 Annual Meeting & Expo

July 11 – 15, 2022 | Montreal Congress Center, Montreal Canada

Advanced Delivery Science

Substantial morbidity and healthcare burden of skin and soft tissue infections



- > 14 million outpatient visits annually and 2% of hospital admissions
- > $15 billion total cost of SSTIs in the United States

Skin and soft tissue infection (SSTI)

Kaye, Keith S., et al. Clinical Infectious Diseases 68.Supplement_3 (2019): S193-S199.
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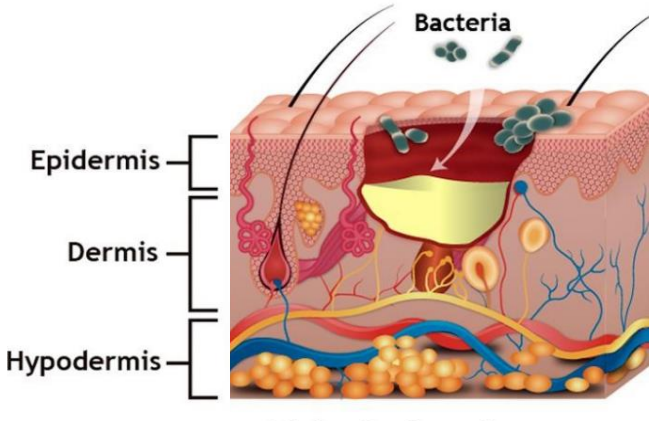

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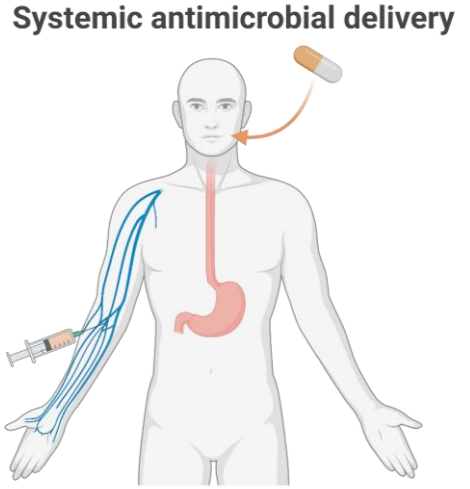
Skin and soft tissue infection (SSTI)

High incidence of treatment failure and SSTI recurrence with conventional delivery

- Poor drug perfusion into diseased tissue→ ↓ efficacy and ↑ antibiotic resistance
- Risk of systemic toxicity
- Burden on healthcare system



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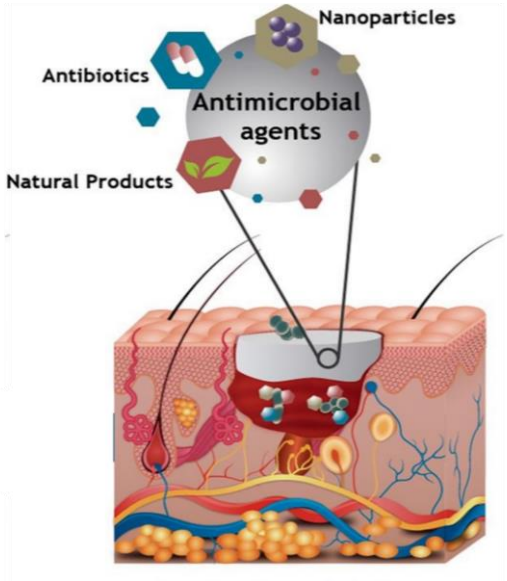
Advanced drug delivery technologies for local treatment of SSTIs



Antimicrobial Dressing

Localized delivery of therapeutics for SSTI and wound therapy

- Spatiotemporal control over the drug dose at the infection site
- Decrease undesired systemic side effects
- Provide beneficial secondary functions

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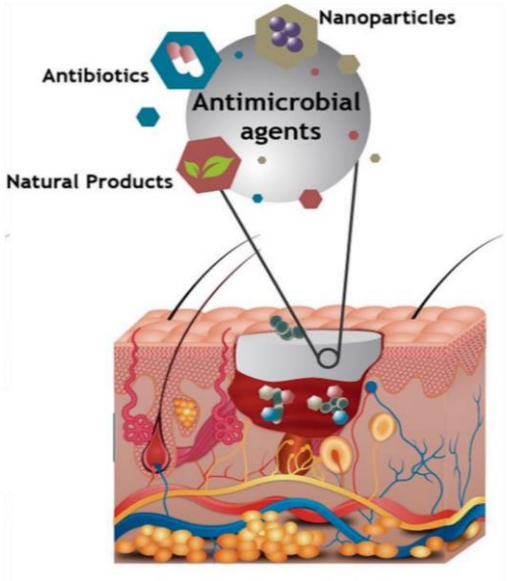

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"One product-fits all" approach

- Fixed/ rigid formulations (e.g. silver dressings)
- Complexity of formulation and drug loading
- Poor control for sustained delivery

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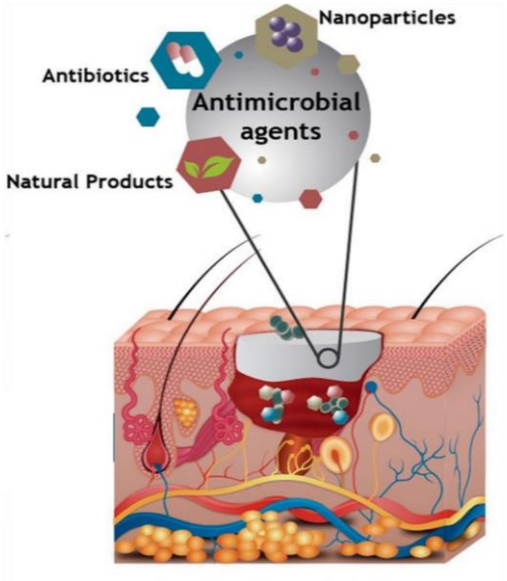

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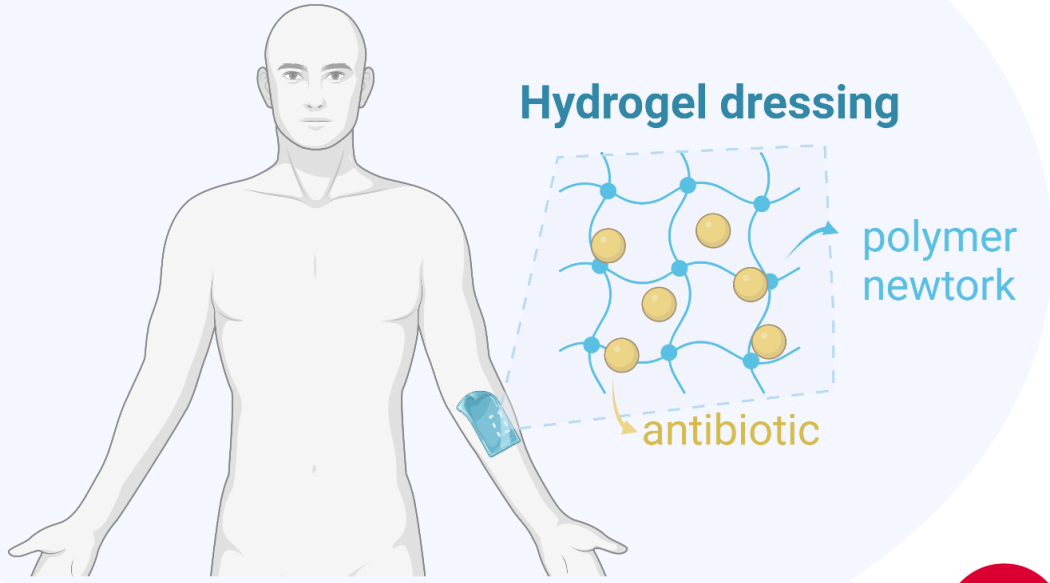
Hydrogels are attractive vehicles for localized delivery of drugs



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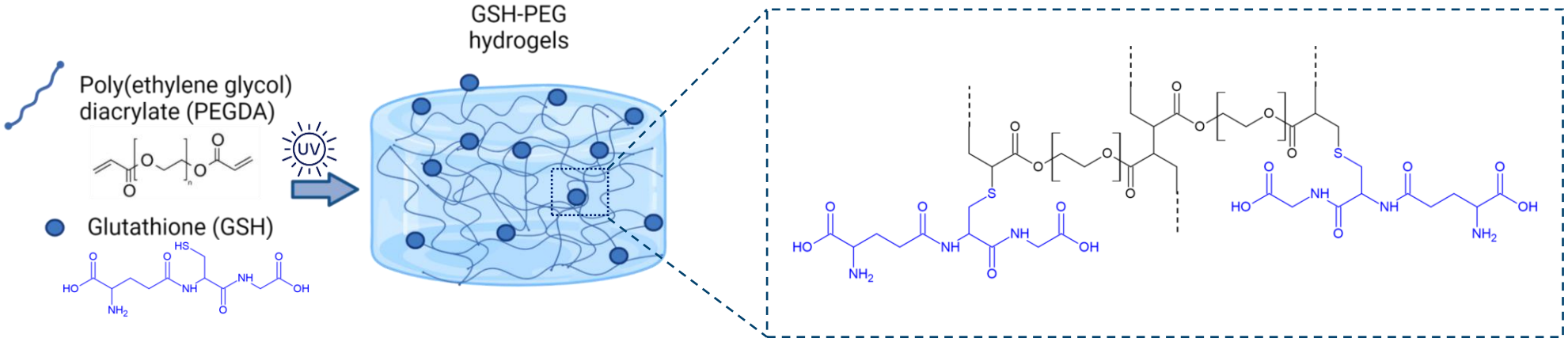
Exploiting glutathione-conjugated hydrogels for drug delivery



Buhrman, Jason S., et al. Journal of Controlled Release 171.3 (2013): 288-295.

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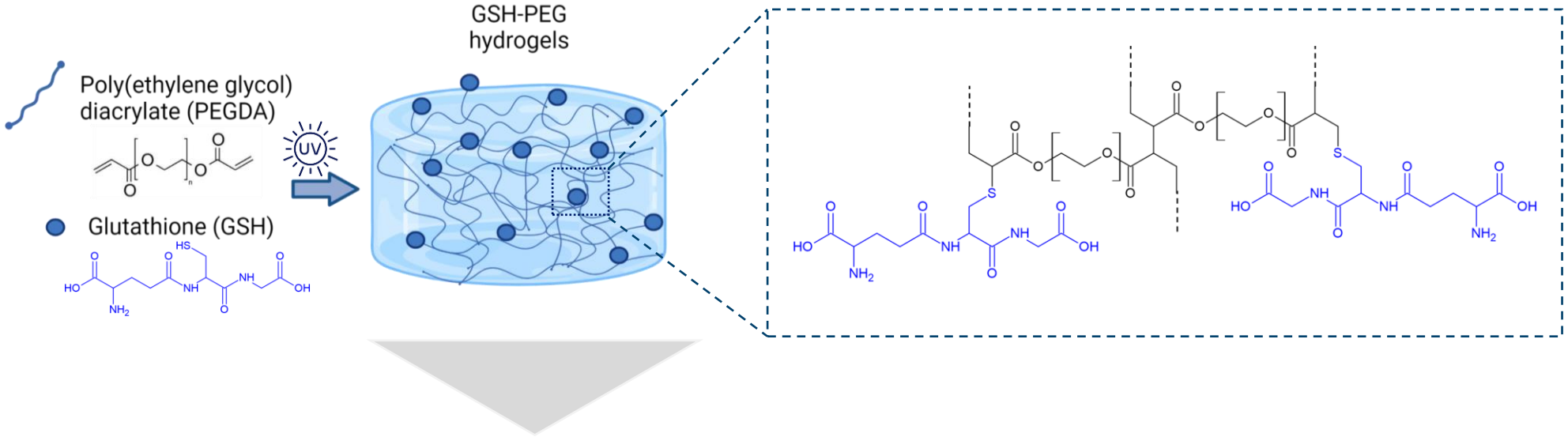
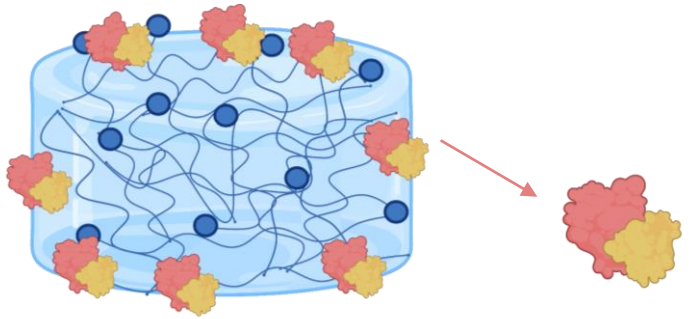


Delivery of active GST-fusion proteins

Enzyme-ligand interaction



GST-mellitin

GST: Glutathione S-transferase

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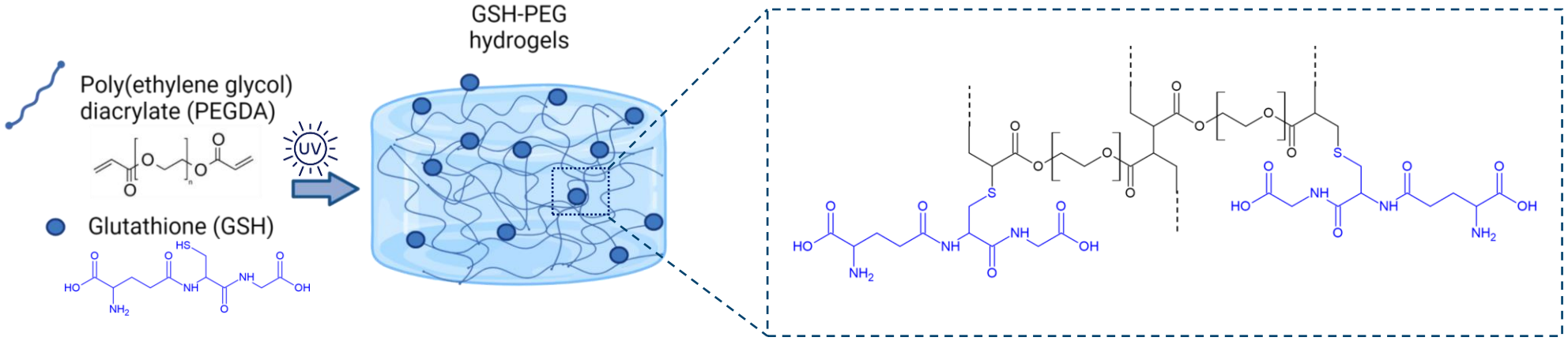
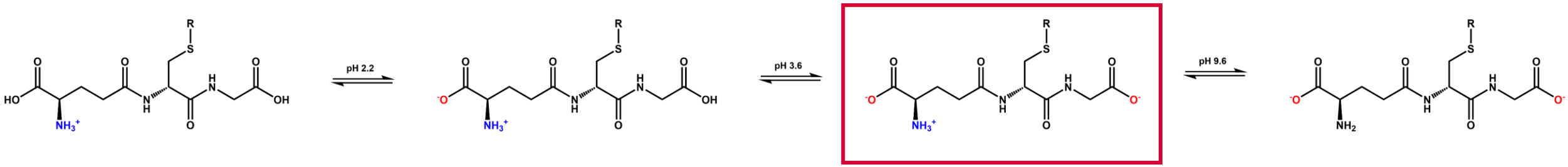
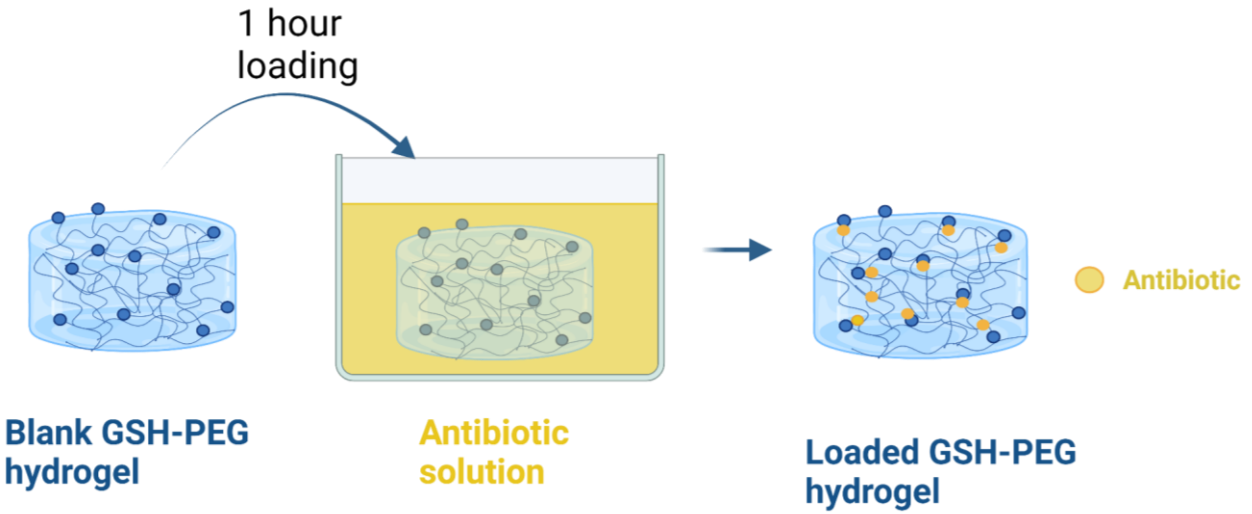




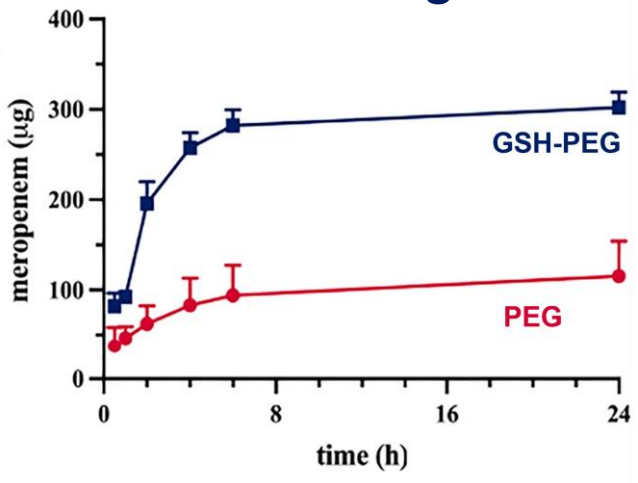
Conjugated GSH at physiologic pH=7.0

Exploiting glutathione-conjugated hydrogels for topical antibiotic delivery



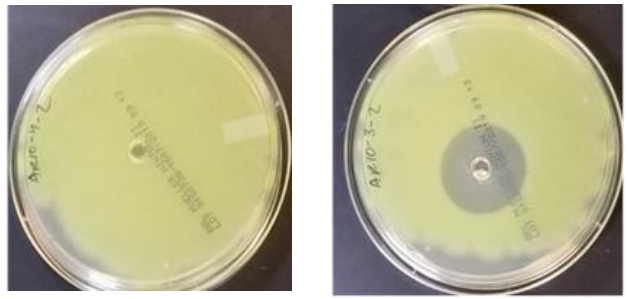
Non-covalent interactions allow for **reversible** association of drug with the GSH-PEG hydrogel

Sustained drug release



Bacteria growth inhibition

Agar diffusion assays

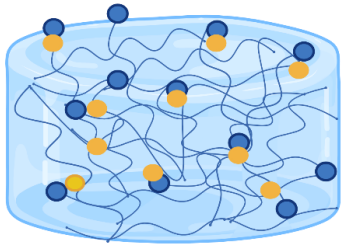


Unloaded

Drug loaded GSH-PEG

Sokolowski, Karol, et al. Pharmaceutical Research 38.7 (2021): 1247-1261.

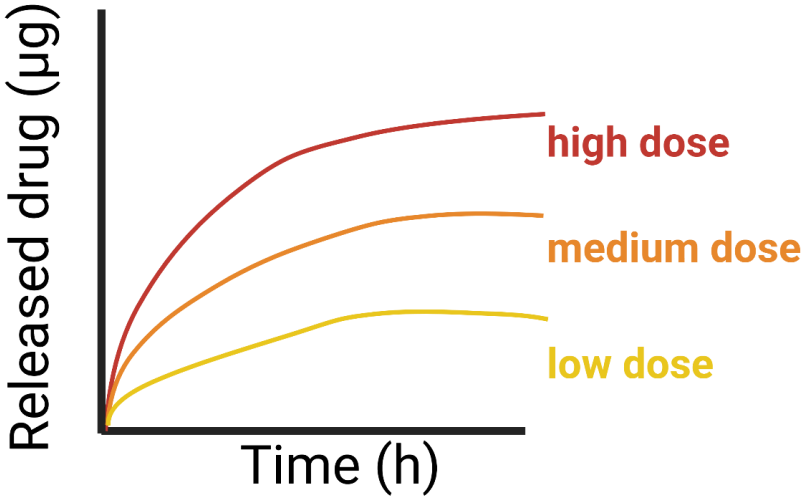
Are GSH-PEG hydrogels efficacious topically?



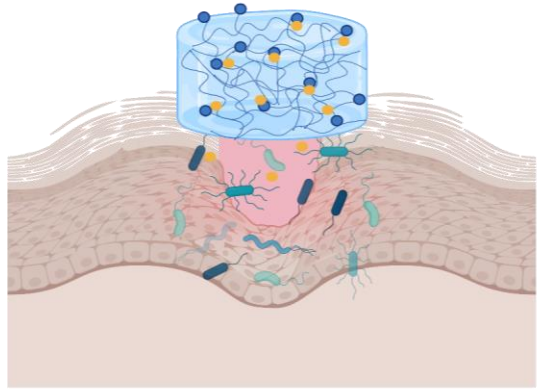
Antibiotic

Loaded GSH-PEG hydrogel

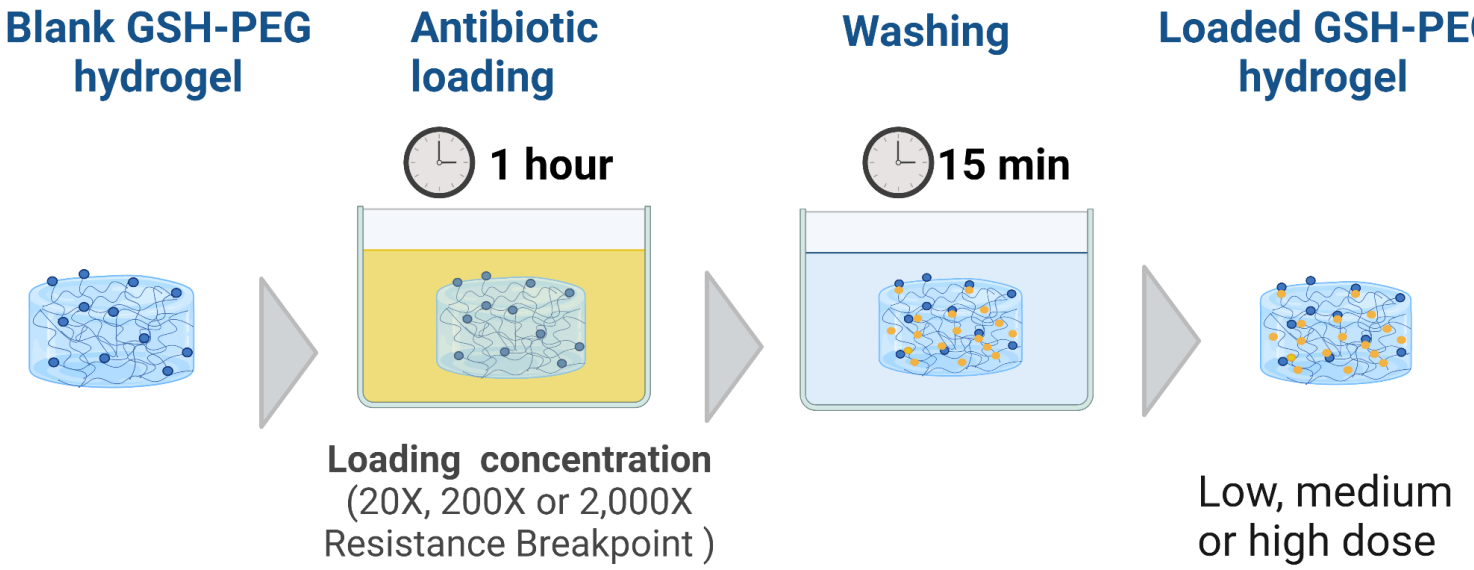
Assess the **dose-dependent controlled release** of antibiotics from hydrogels



Evaluate the **antibacterial activity** of drug loaded hydrogels against bacteria isolates **in *ex vivo* skin infections**



Varying antibiotic loading solution concentration allows for dose selection



Antimicrobial Agent	Organism	Resistance Breakpoint (µg/mL)*
Vancomycin	*Staphylococcus aureus*	16
Meropenem	*Pseudomonas aeruginosa*	8

*Clinical & Laboratory Standards Institute (CLSI) guidelines

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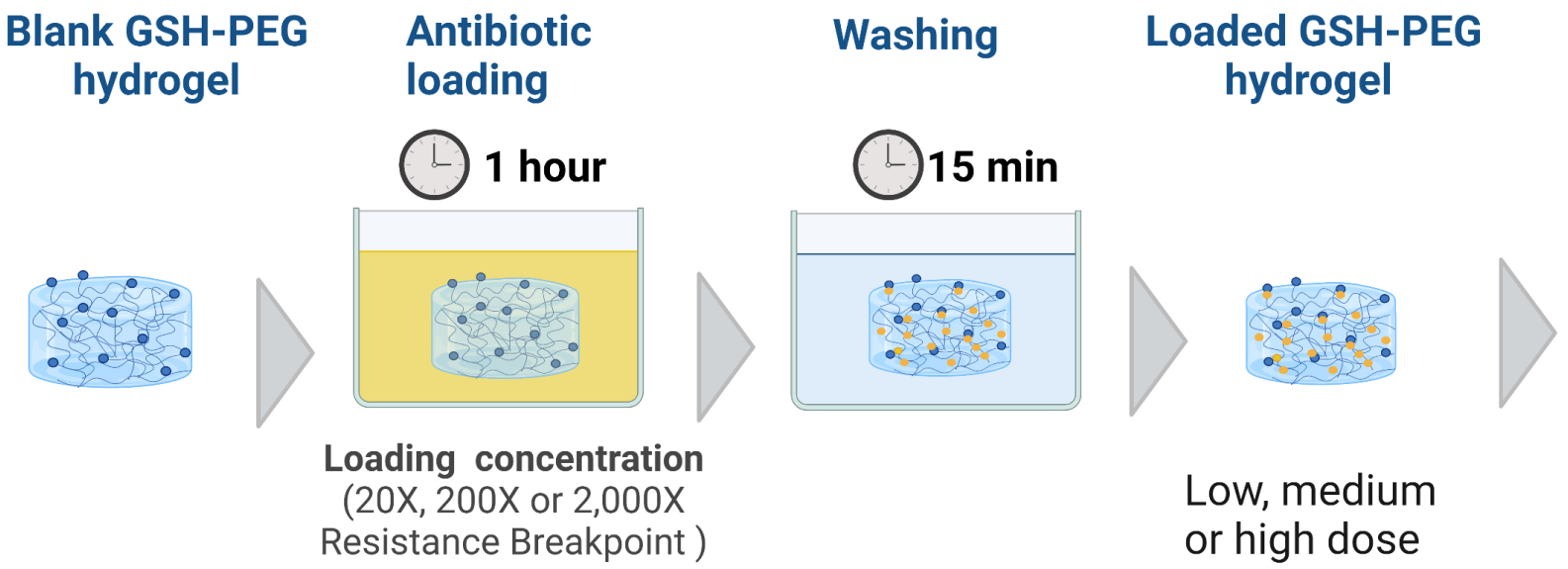

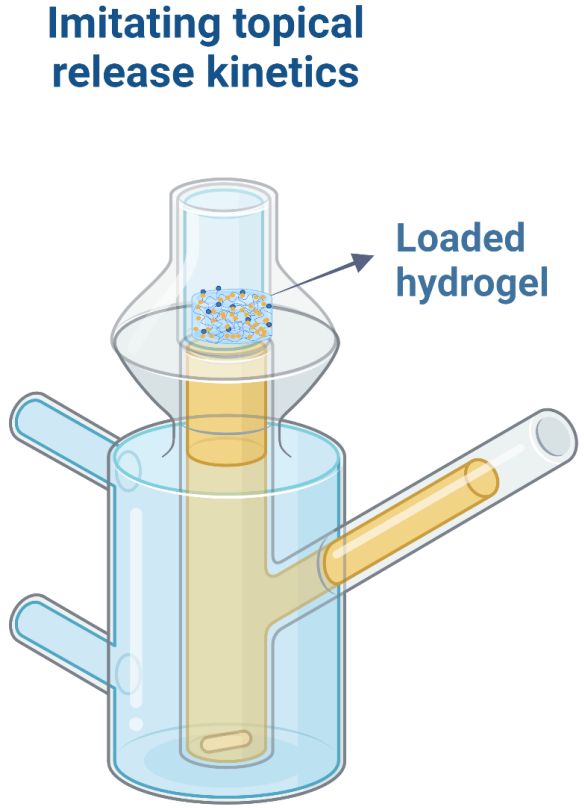

Franz diffusion apparatus

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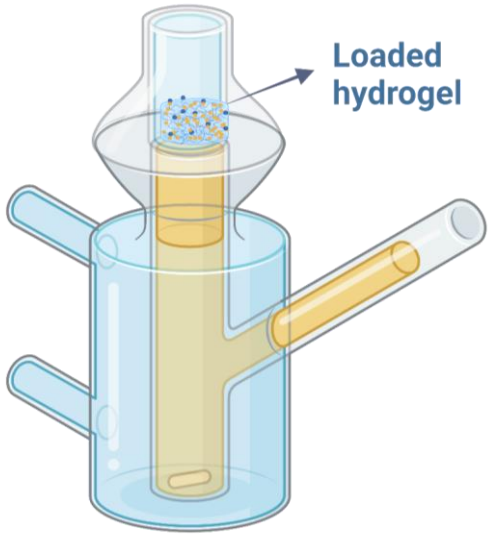
Dose-dependent controlled release of antibiotics from GSH-PEG hydrogels

Imitating topical release kinetics



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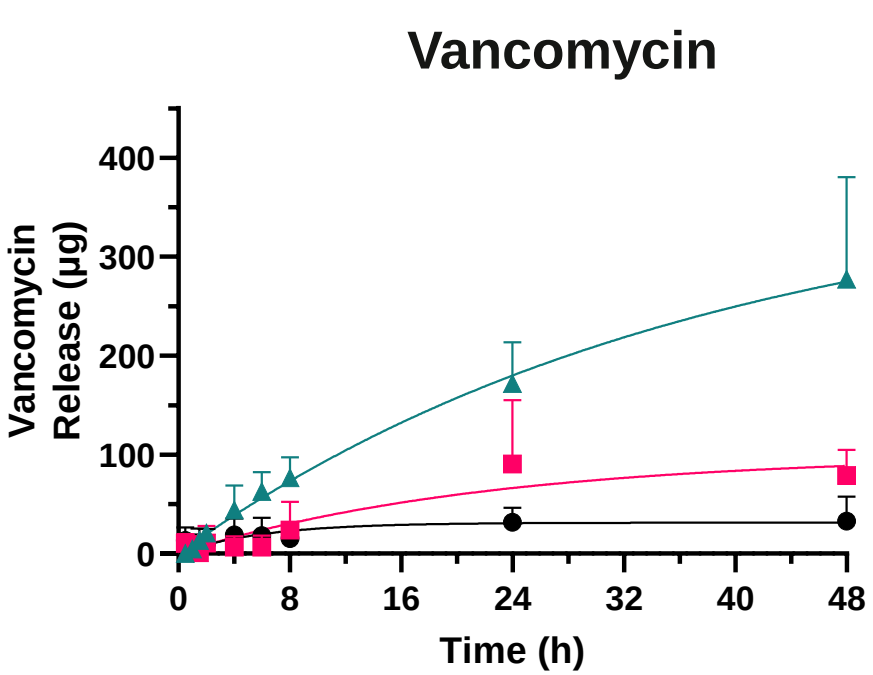

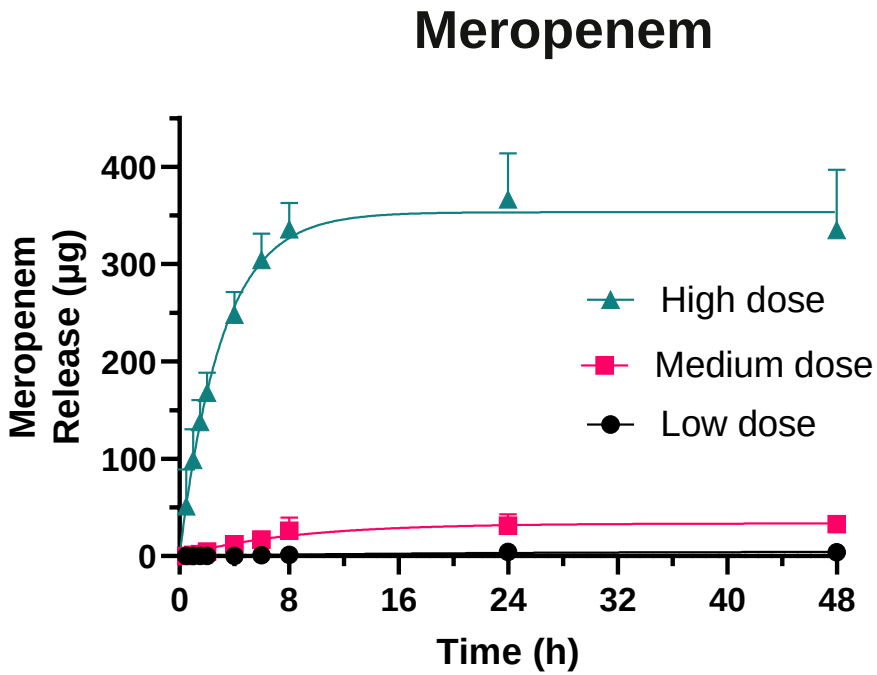

One-phase release of antibiotic from GSH-PEG hydrogel

- Vancomycin $t_{1/2:}$ 22.6 h
- Meropenem $t_{1/2:}$ 2.2 h

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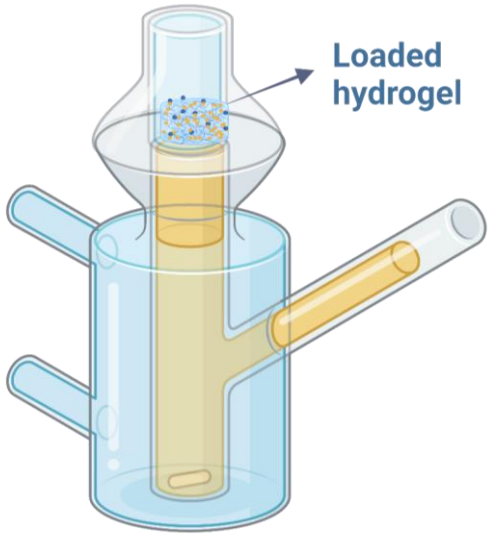

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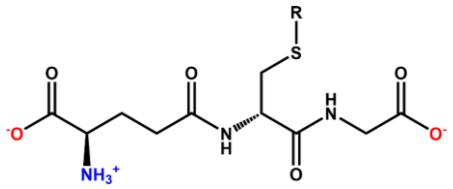

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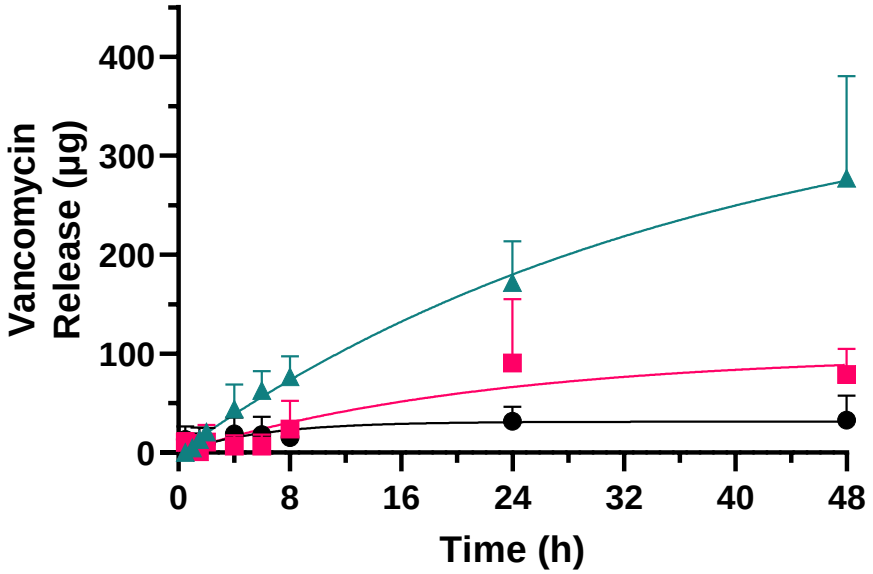

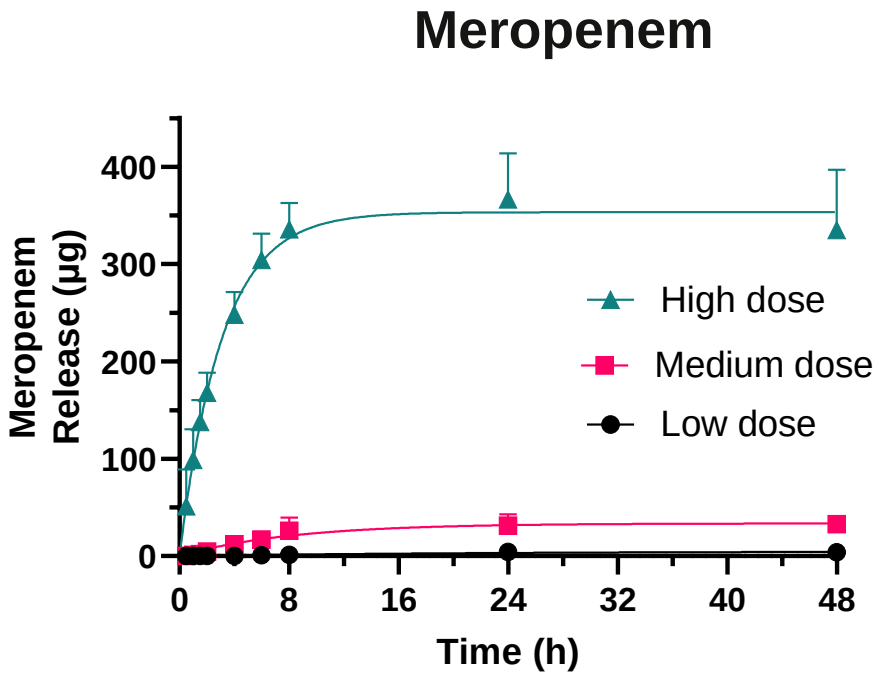

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  Cationic, MW= 1,449.3 g/mol
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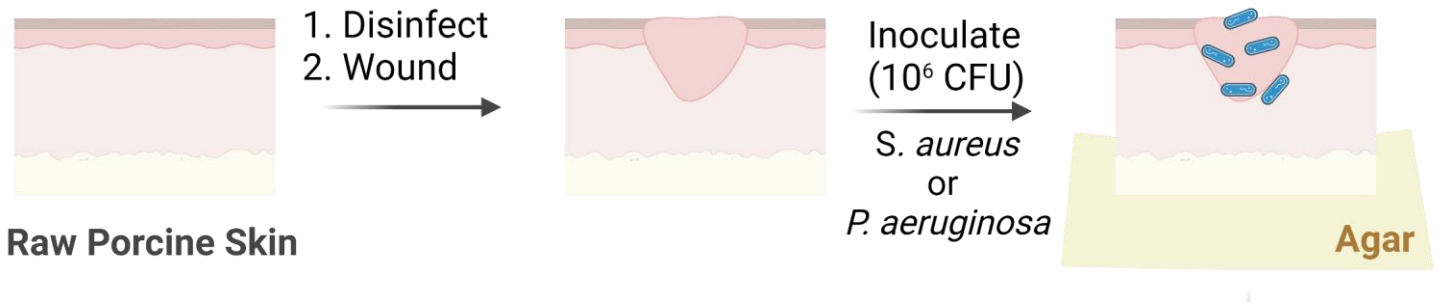
Ex vivo skin application of antibiotic-loaded GSH-PEG hydrogels



CFU: Colony Forming Units

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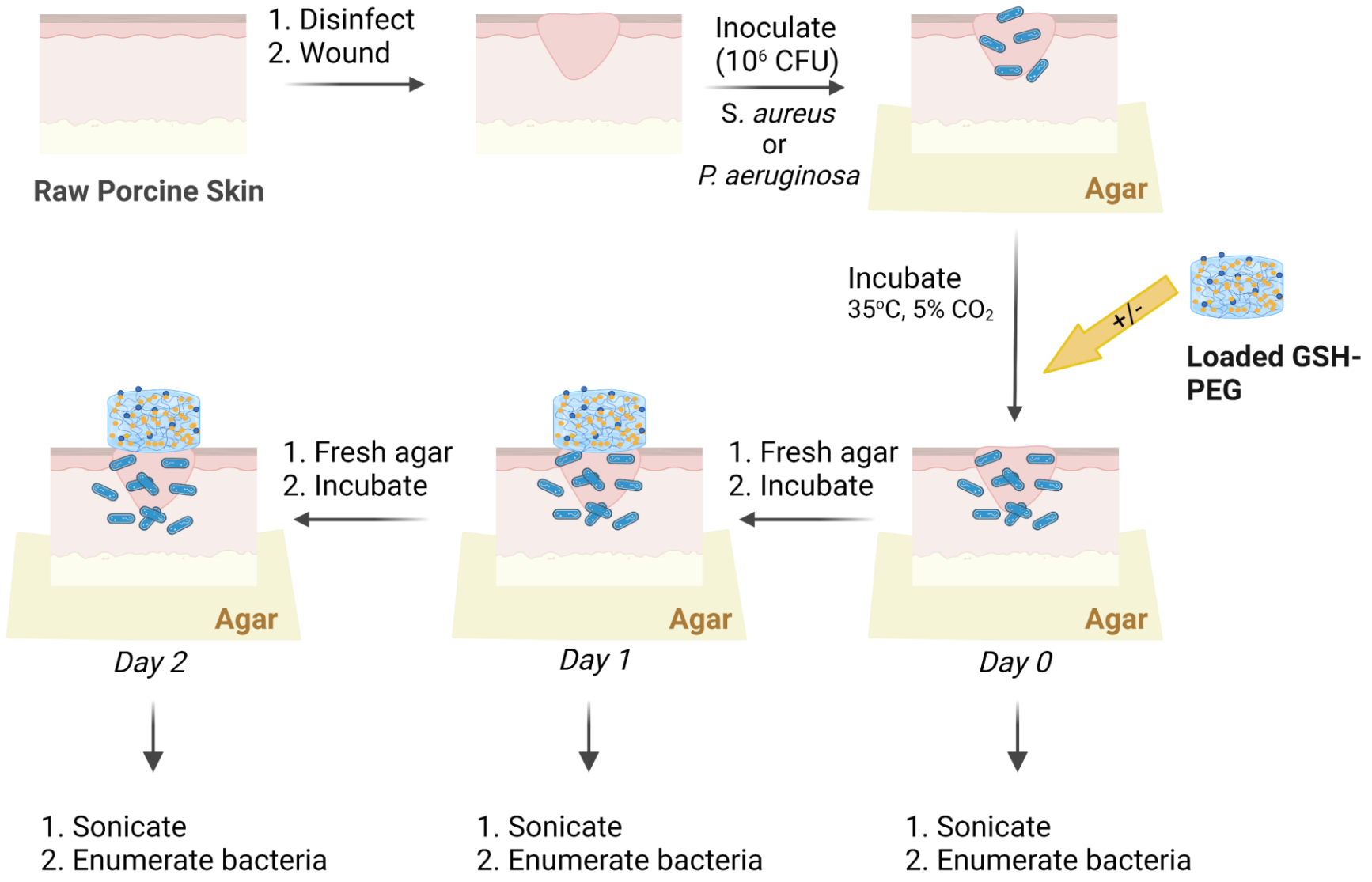

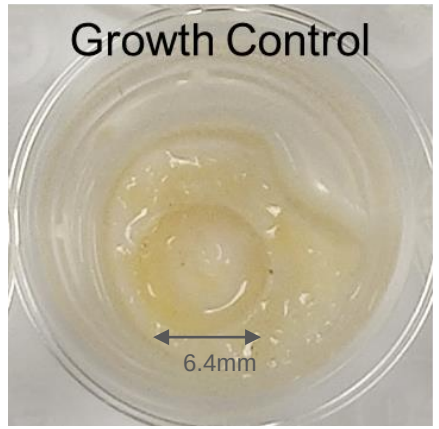

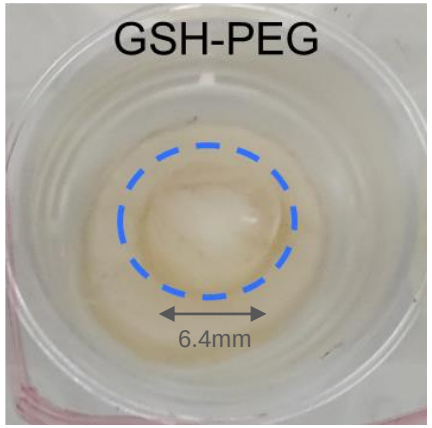

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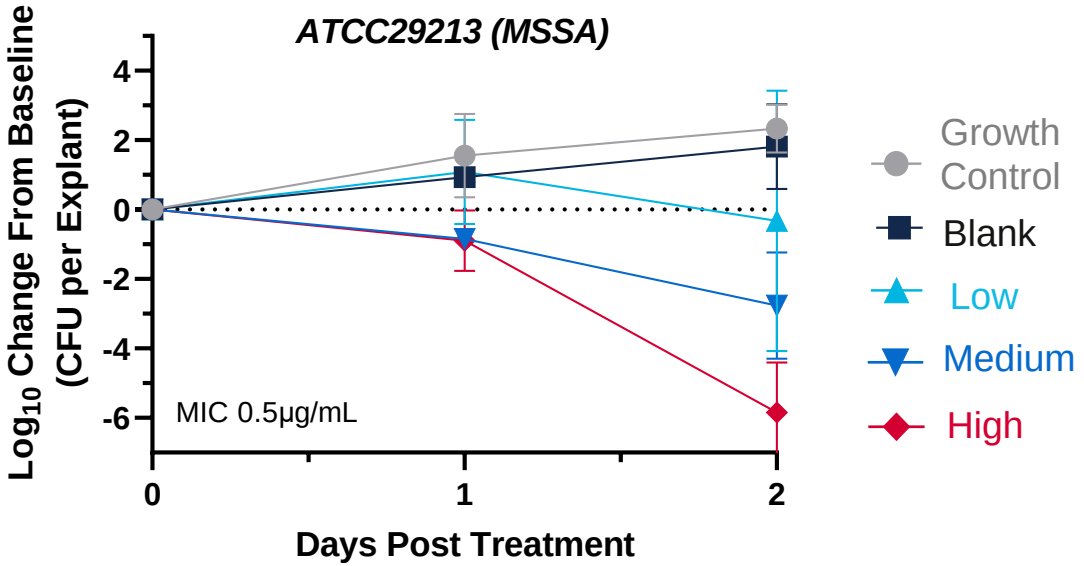
Dose-dependent treatment of *ex vivo skin* infections with GSH-PEG hydrogels

Vancomycin-loaded GSH-PEG hydrogels for *Staphylococcus aureus*



MIC: Minimum Inhibitory Concentration
Effective bacteria killing considered as a ≥3log (≥99.9%) reduction in bacteria burden from starting inoculum

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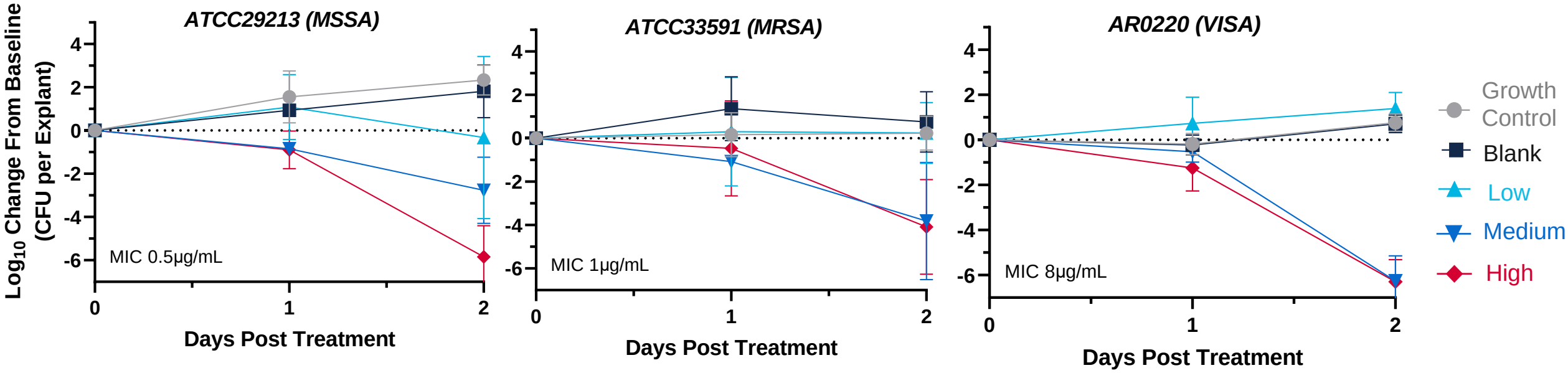

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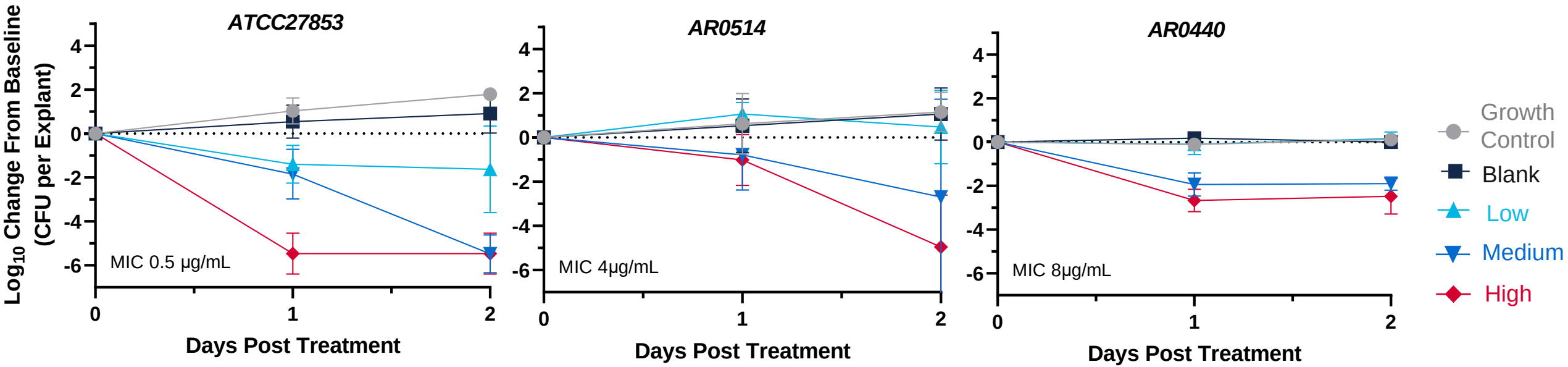
Dose-dependent treatment of *ex vivo skin* infections with GSH-PEG hydrogels

Meropenem-loaded GSH-PEG hydrogels for *Pseudomonas aeruginosa*



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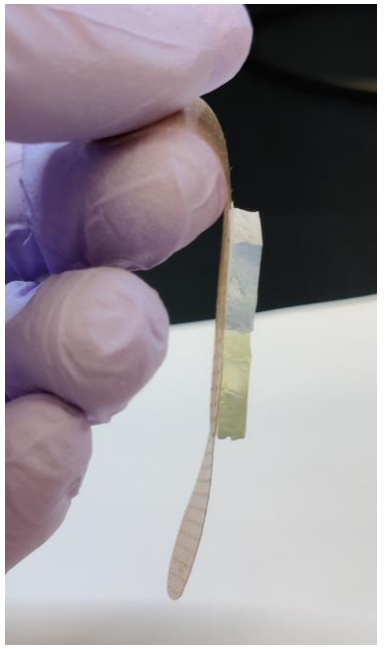
Conclusions and future directions

- **Dose-dependent** controlled **release** of antibiotics from GSH-PEG hydrogels
- Meropenem and vancomycin were successfully **delivered topically** to kill **Gram-negative and -positive bacteria**, respectively



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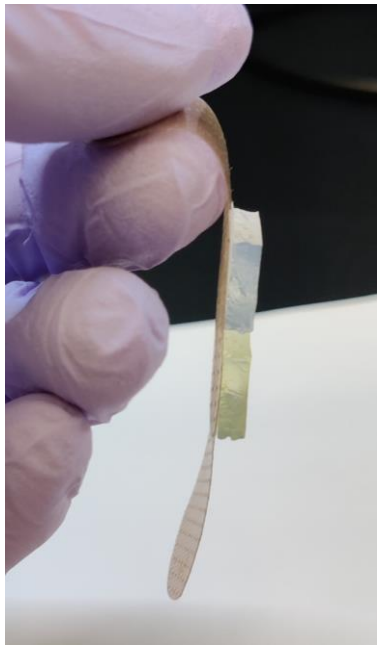

Simple, rapid loading process amendable for clinical use

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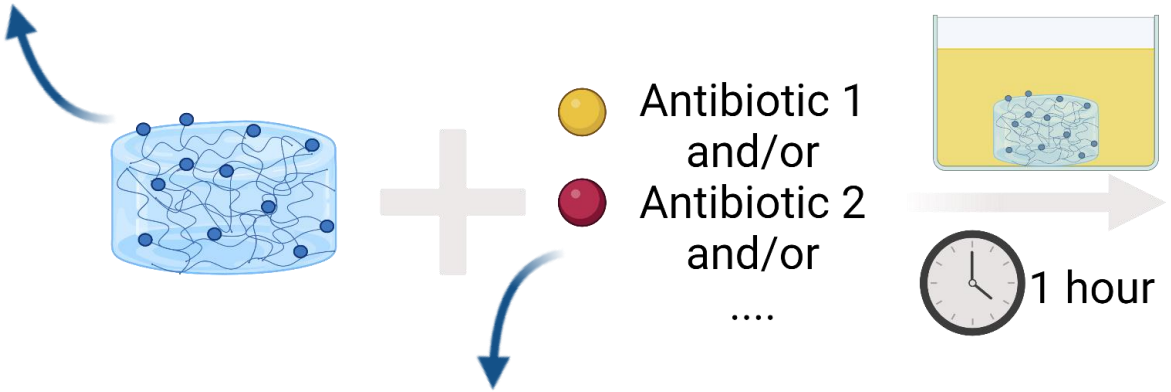
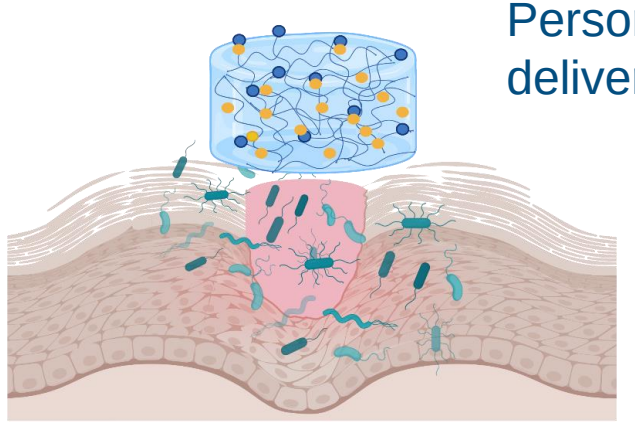


Potential to expand beyond single agent delivery



Personalized topical delivery for SSTI therapy

Thank you!

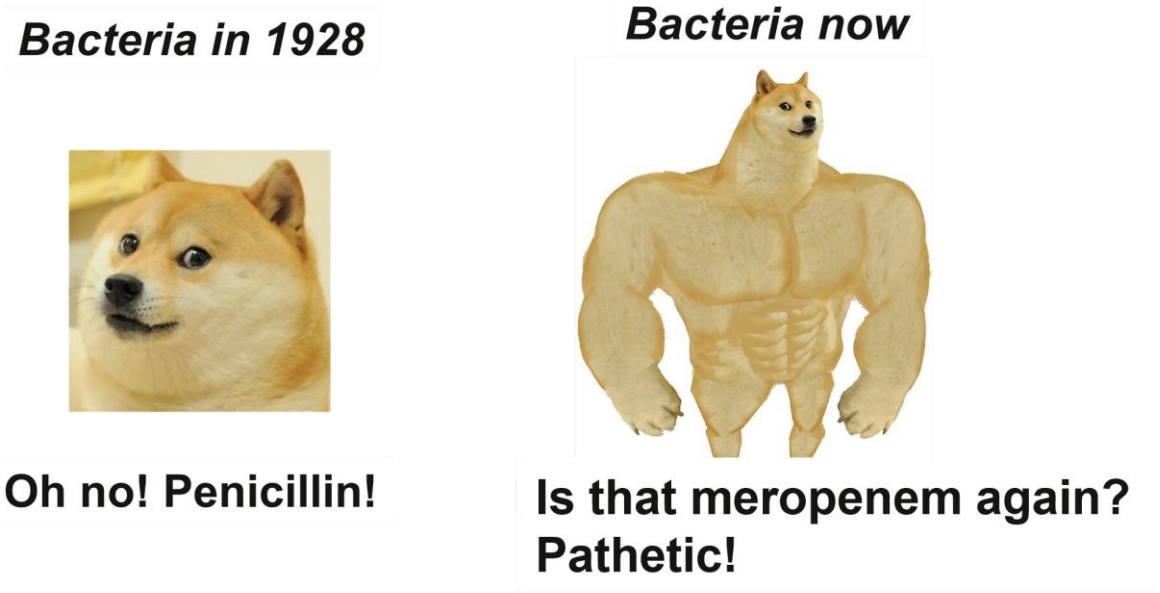
Current and past Gemeinhart Lab members

- Prof. Richard A. Gemeinhart
- Dr. Karol Sokolowski
- Catherine Dial
- Sonia Alavi
- Hai Pham
- Dr. Tim Langridge

Contact: aandri6@uic.edu

Collaborators

- Dr. Eric Wenzler's Lab (UIC)
- Dr. Zackery Bulman's Lab (UIC)



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