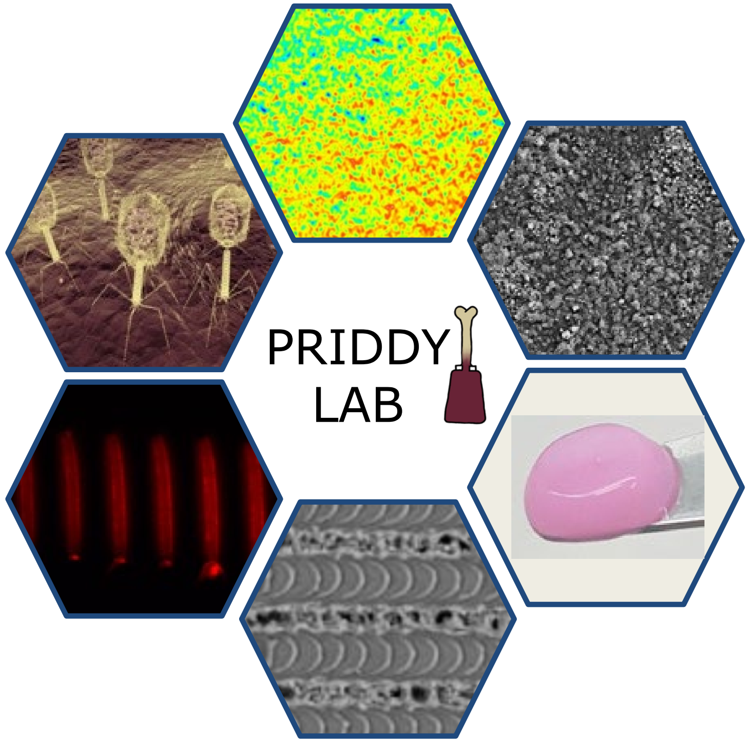
# Designing biomaterials for treating bone injury and infection

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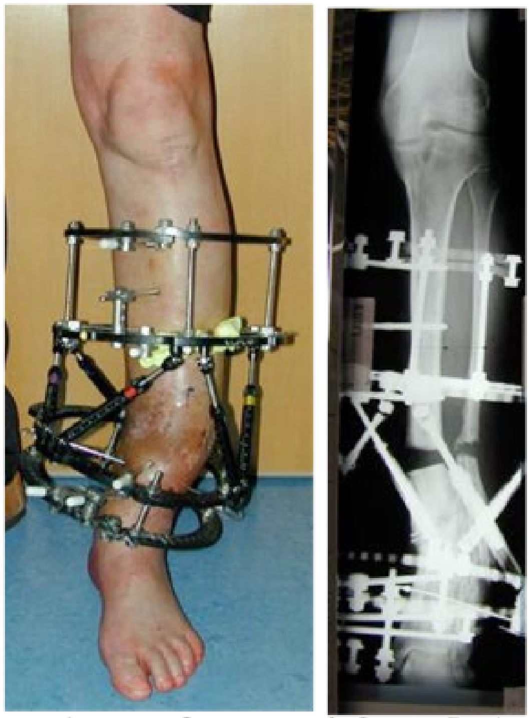
# Clinical motivation: Bone injury and infection



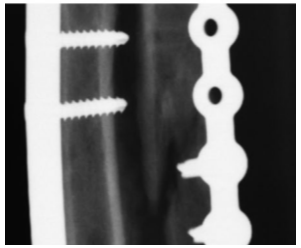
- Large bone defects
  - 1.6 million bone grafting procedures annually[1]
  - Bone is second most commonly transplanted tissue
- Autograft treatment is gold standard
  - Limited graft tissue
  - Donor site morbidity, pain
- Challenges
  - Critically sized defects
  - Unique defect geometries
  - Infection



Images Courtesy of Georg Duda.

| | % Success |
|---|---|
| Arthrodesis | 80-90% |
| Fracture | 95% |
| Cavity | ~100% |
| Allograft Host Junctions | 95% |
| Nonunion | 80-90% |
| Defects (>2 cm) | <50% |

Data courtesy of George Muschler



Roux et al., 2021

1. AAOS, 2008

# Designing better biomaterials and therapeutics

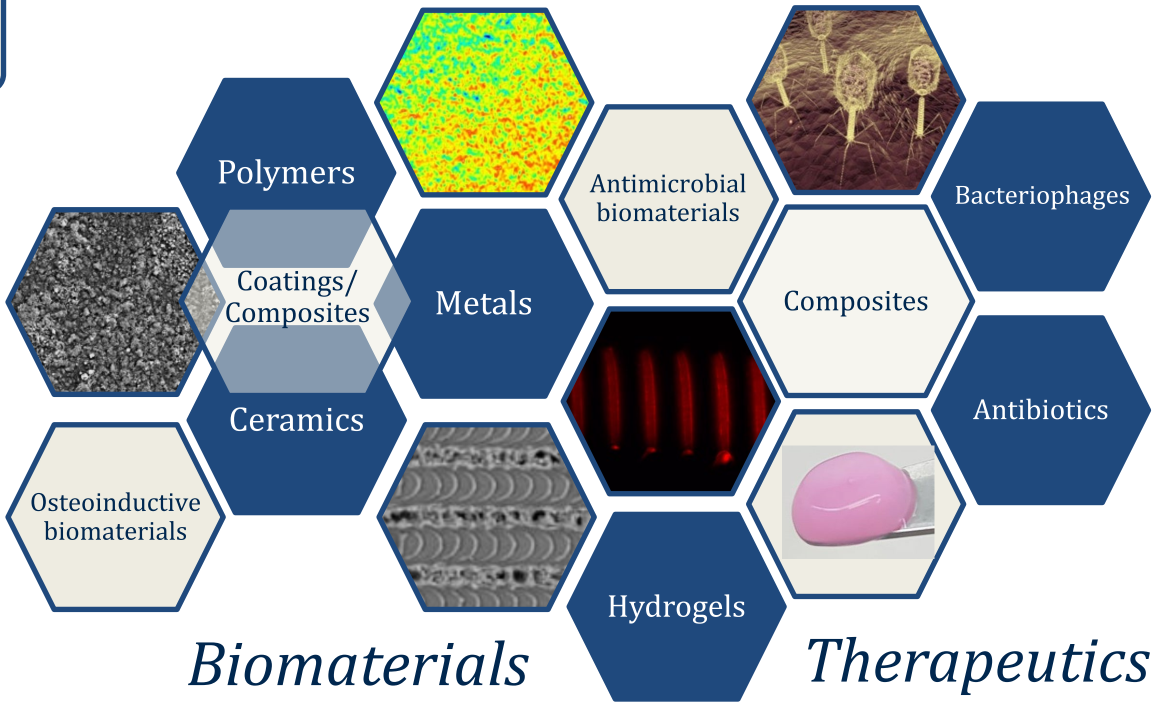


**Bone healing**
- Large bone defects
- Fracture fixation

**Infection mitigation**
- Osteomyelitis
- Composite tissue infection

*Clinical challenges*

*Engineering solutions*




## Selection Criteria

- Potency and duration of activity
- Release kinetics
- Mechanism(s) of action
- Ease of fabrication and administration
- Multifunctional (e.g., hardware, combo therapy)
- Effective volume/dose

Cobb et al., *J Orthop Res* (2020)

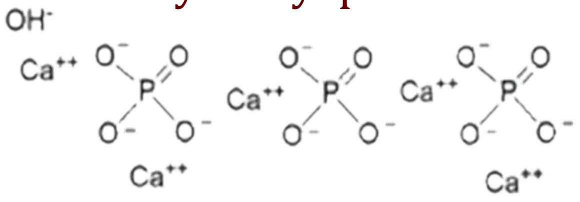
**Objective:** Utilize a ceramic (hydroxyapatite) coating to enhance the surface functionality and degradation kinetics of load-bearing materials



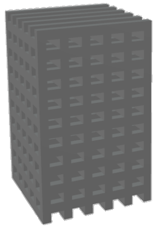
# Hydroxyapatite (HA) coating of:

- **Polymeric materials**
- **Magnesium alloys**

Hydroxyapatite

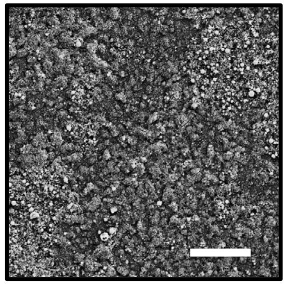



Polymer scaffold



PLA, PLGA

HA-coated polymer scaffold



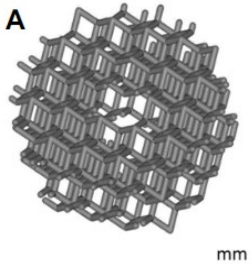
Materials Science & Engineering C 120 (2021) 111686

J Mater Sci
Materials for life sciences

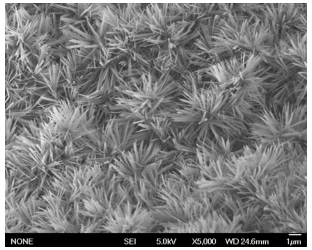
A hybrid coating of polydopamine and nano-hydroxyapatite enhances surface properties of 3D printed poly(lactic-co-glycolic acid) scaffolds

Weitong Chen[1], Luke Nichols[1], Landon Teer[1], Kailey Clinton[1], and Lauren B. Priddy[1,*]

Mg scaffold



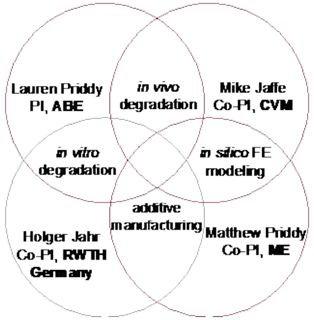

HA-coated Mg scaffold




Journal of MATERIALS RESEARCH
DOI:10.1557/

Hydroxyapatite coating promotes stable physicochemical properties of pure magnesium in a longitudinal degradation study

Anna S. Rourke[1,b)], Mary Catherine Beard[1,b)], Sophie E. Jones[1], Matthew W. Priddy[2], Lauren B. Priddy[1,a)]

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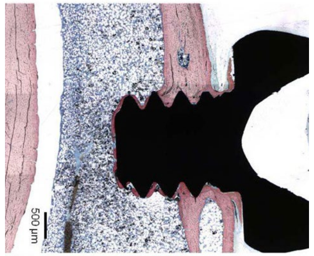
## Motivation

- The emergence of **degradable bone implants** would advance the field of orthopedic implants by:
  - Reducing the need for an implant removal surgery
  - Avoiding pain associated with permanent implants
- Magnesium (Mg) is attractive as a degradable orthopedic implant material
  - Similar mechanical properties to native bone [1]
  - Magnesium ions induce bone growth [2]

Angrisani et al., 2012



Agarwal et al., 2015

## Challenge

- On its own, **Mg degrades relatively fast** compared to the rate of bone healing
- **Coating of Mg** with a biocompatible material such as the ceramic **hydroxyapatite (HA)** may **slow the degradation** of Mg

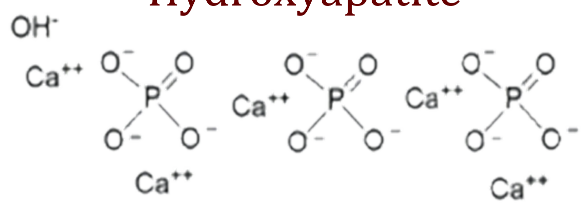
[1] Gartzke, Ann-Kathrin, et al. "A simulation model for the degradation of magnesium-based bone implants." *Journal of the Mechanical Behavior of Biomedical Materials,* 101 (2020): 103411.
[2] Kraus, Tanja, et al. "Magnesium alloys for temporary implants in osteosynthesis: In vivo studies of their degradation and interaction with bone." *Acta Biomaterialia,* 8.3 (2012): 1230-1238.

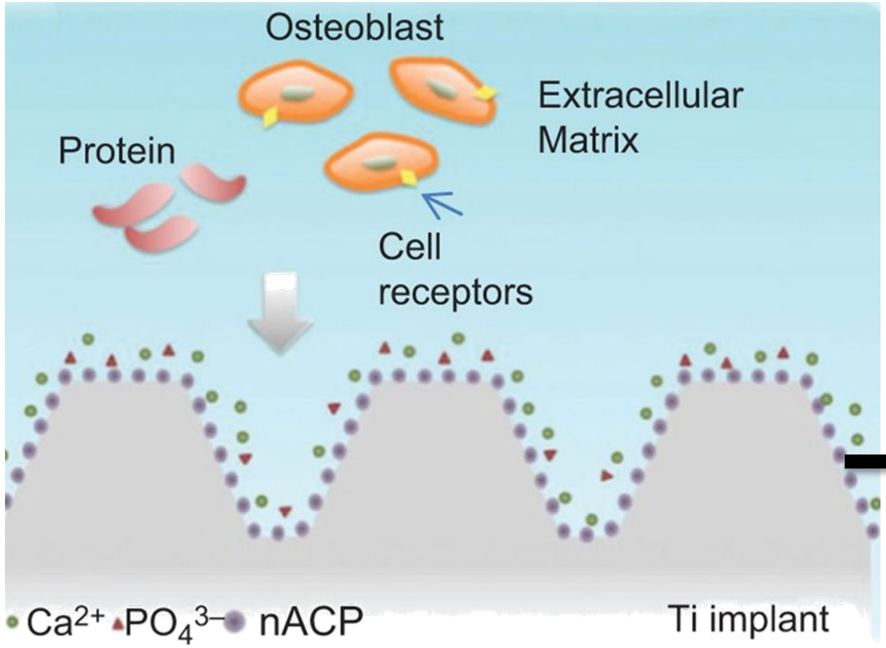
# Why coat with hydroxyapatite (HA)?



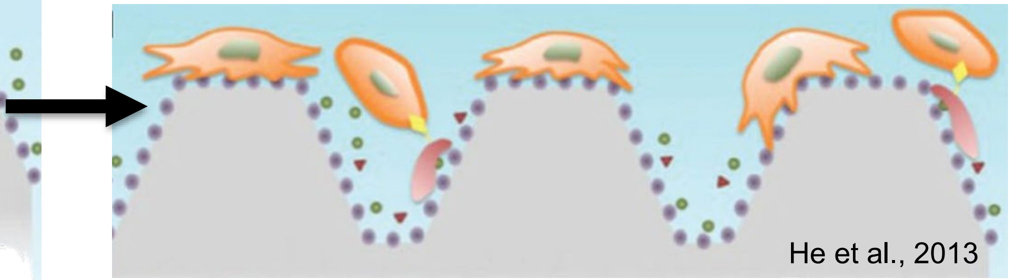
- Similar to the inorganic phase of bone
- Increase surface roughness and hydrophilicity
- Mediate local pH
- Promote cell attachment, proliferation, and differentiation
- **Modulate degradation rate**

Hydroxyapatite




**Favorable environment for cells**

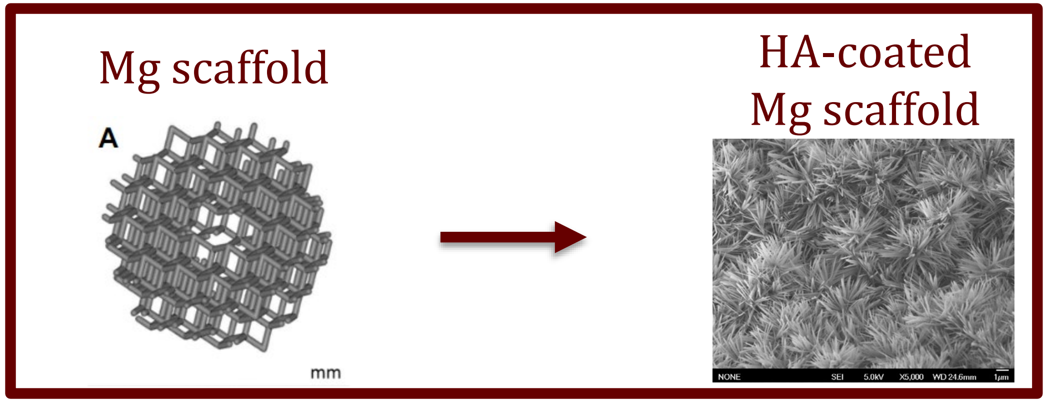


# HA coating to mitigate the degradation of Mg scaffolds



## Objective

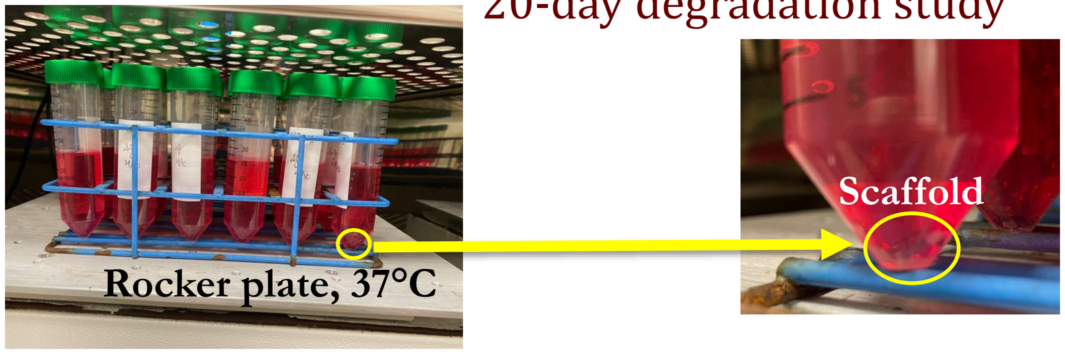
- Evaluate the efficacy of HA coating to slow the degradation of additively manufactured (AM) Mg alloy (WE43) scaffolds using *in vitro* and *in silico* models of degradation




## Hypothesis

- HA coating would hinder the degradation of AM WE43 scaffolds

20-day degradation study



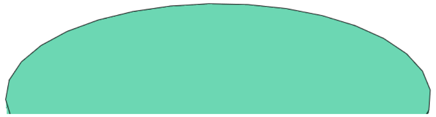

## Findings

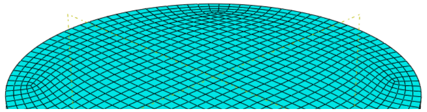
- HA coating method modified from solid disc study → thorough coating of porous scaffolds
- Only non-coated scaffolds had a reduction in mass; no change in mass of HA-coated scaffolds
- Higher surface height values for HA-coated scaffolds than for non-coated scaffolds
- HA coating mitigated degradation of porous AM magnesium scaffolds

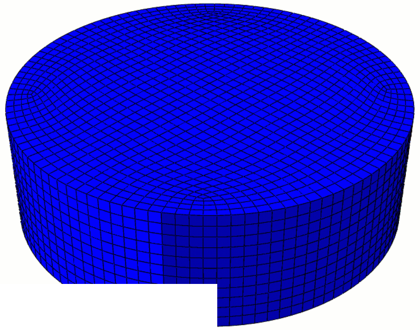
# Finite element modeling of Mg degradation



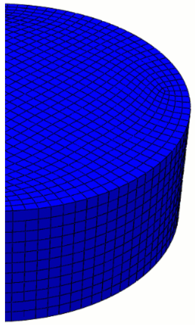
## Experiment 1: Pure Mg and HA-coated Mg



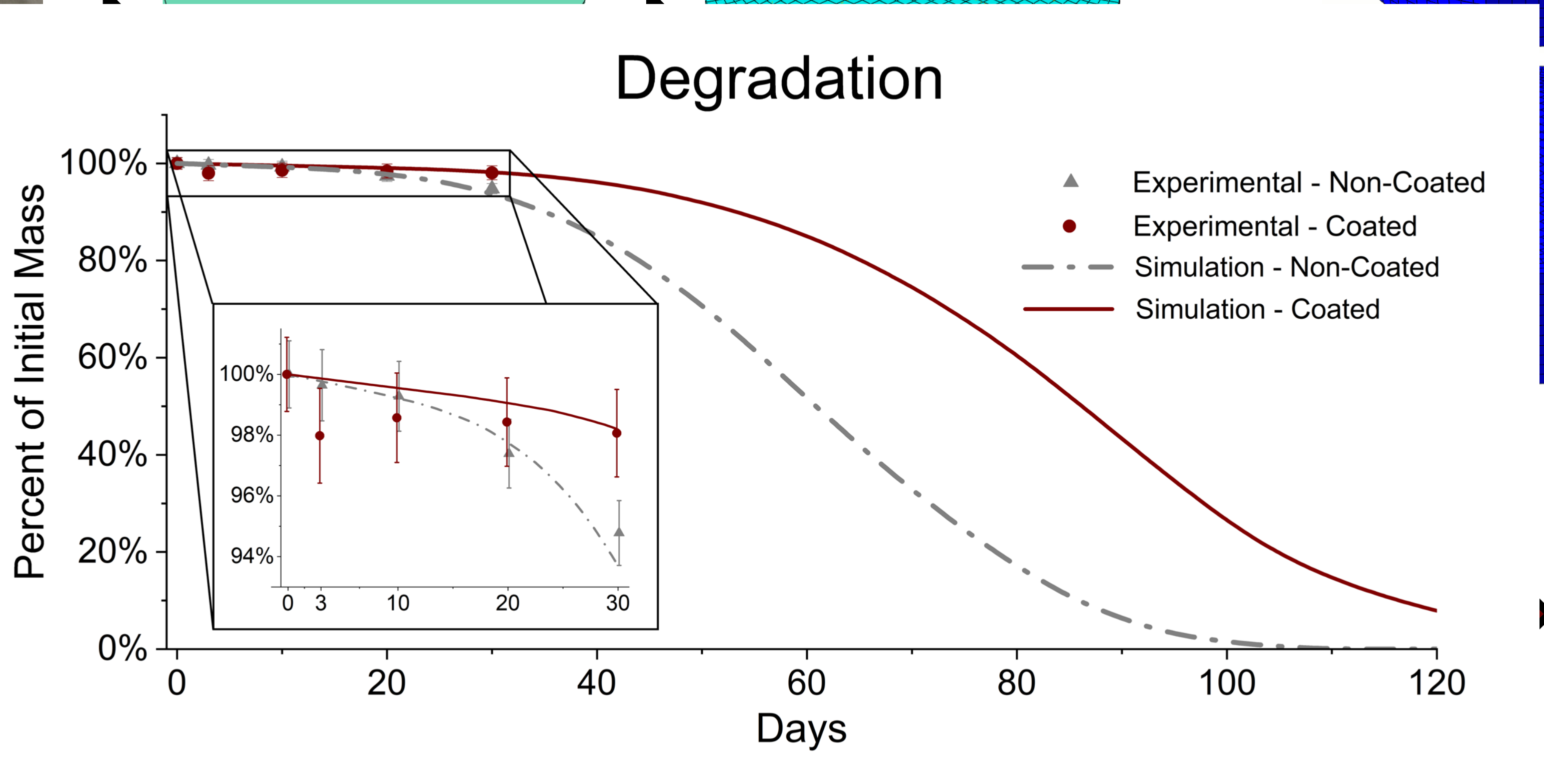




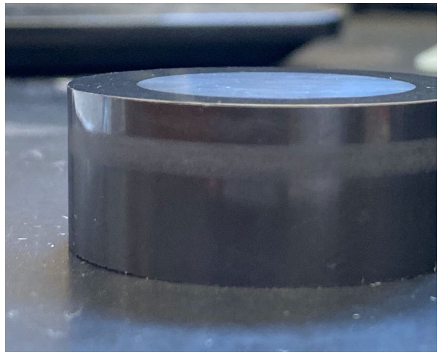
Pure Mg

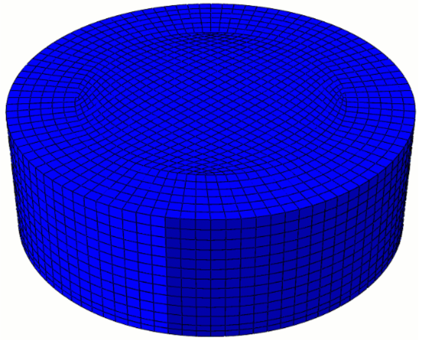


HA-coated pure Mg




## Experiment 2

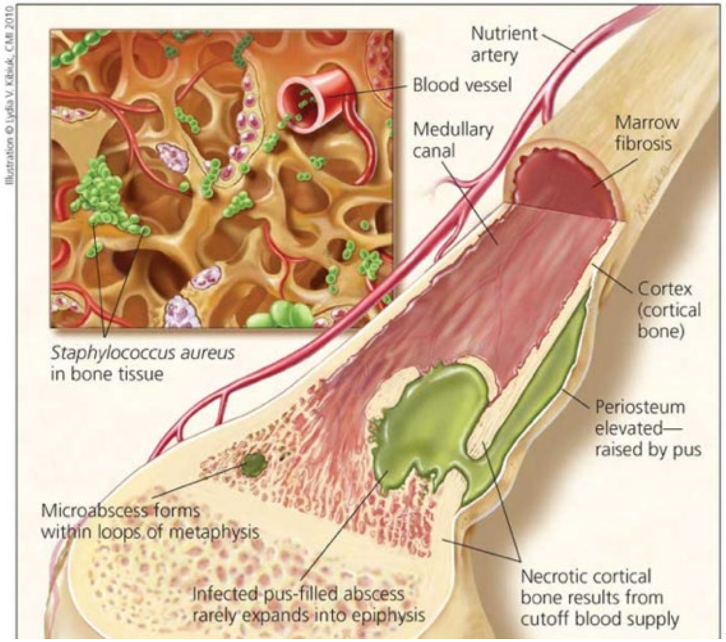




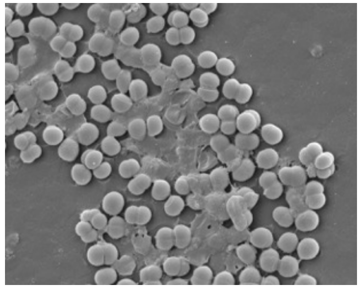
# Bone infection: treatment challenges and outcomes



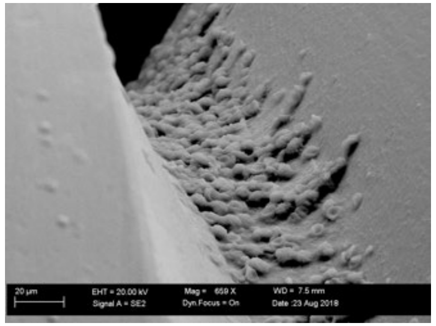
- Most commonly caused by *Staphylococcus aureus*
  - Trauma, orthopedic implants
- Debridement followed by long-term, systemic antibiotic administration
  - Limited capacity to penetrate bone tissue, biofilms
  - Antimicrobial resistant strains
  - Recurrence of infection
  - Increased risk of amputation, especially in diabetic population
- Poly(methyl methacrylate) (PMMA) beads
  - Gold standard for local delivery of antibiotics
  - Nondegradable → revision surgery for removal
  - Limited efficacy against implant-related infections



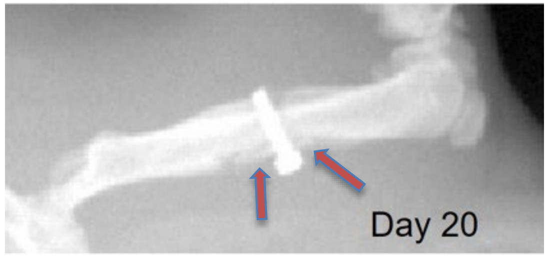

baromedical.ca



Zalavras et al., 2007
Hatzenbueler et al., 2011
Xing et al., 2013



Cobb et al., 2020


Osteolysis evident from chronic osteomyelitis

# Designing better biomaterials and therapeutics

- **Bone healing**
  - Large bone defects
  - Fracture fixation
- **Infection mitigation**
  - Osteomyelitis
  - Composite tissue infection

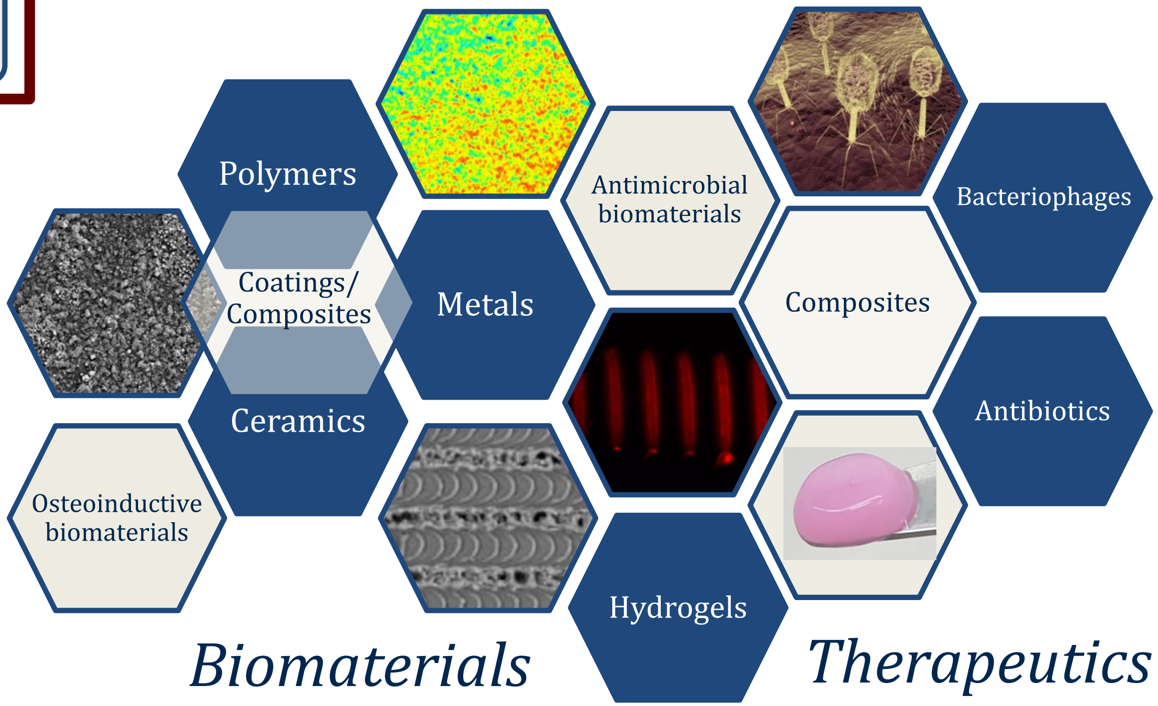
marine drugs

MDPI

inedrugs

*Clinical challenges*

*Engineering solutions*




### Selection Criteria

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- Effective volume/dose

Cobb et al., *J Orthop Res* (2020)

# Chitosan-based biomaterials for treatment of *S. aureus* infection



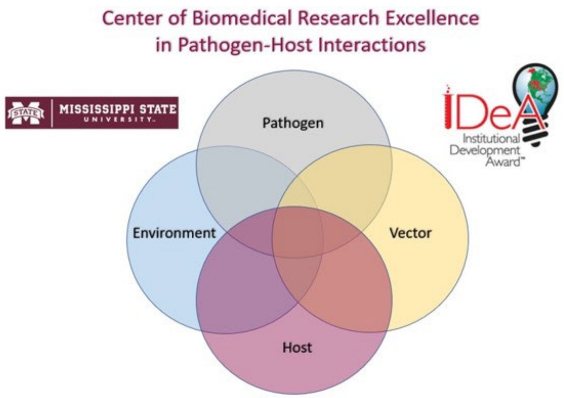
## Objective

- Evaluate the efficacy of chitosan-based materials to treat *S. aureus* infection in chronic and acute models of osteomyelitis and *in vitro*

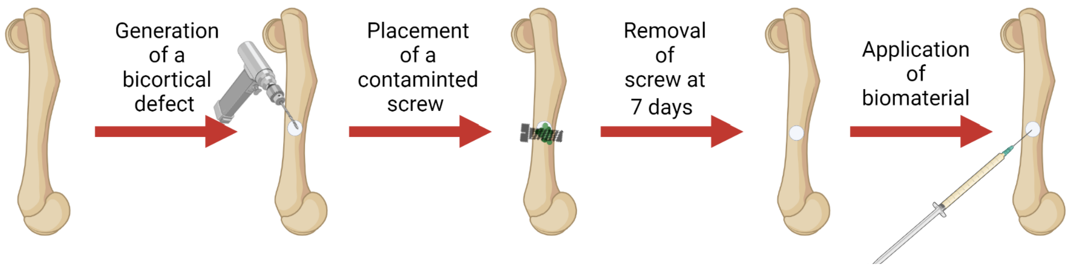
## Hypothesis

- Antimicrobials delivered via chitosan-based biomaterials will effectively combat *S. aureus*

*S. aureus* strain: ATCC 6538-GFP[1]




**Chronic osteomyelitis model**




Orthopedic screw loaded with $5 \times 10^4$ CFU of ATCC 6538-GFP *S. aureus*

## Findings

- Fosfomycin delivered via *both* chitosan hydrogel (CH) and PLA microparticles reduced bacterial load in both bone and soft tissue in a chronic OM model
- Alternative antimicrobials were successful in:
  - Reducing bacterial burden in soft tissue in acute OM model
  - Mitigating bacterial growth *in vitro*

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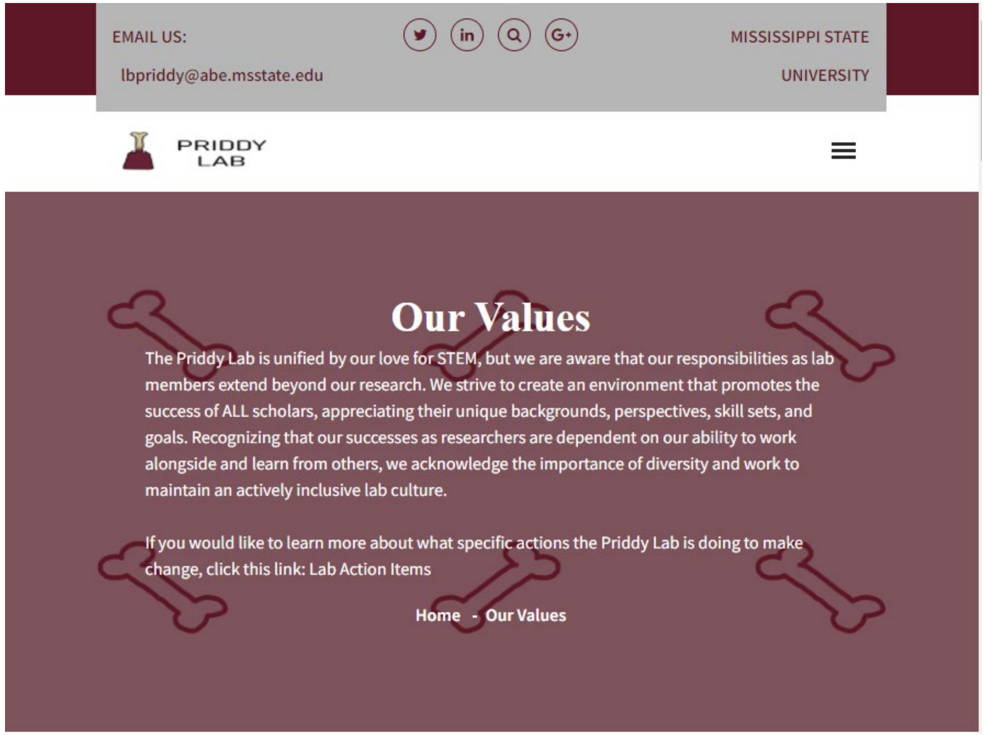
# Equity and inclusion in the Priddy Lab



- Informal discussions – at weekly lab meetings
  - “Minute for diversity, equity, and inclusion”
- Our values – on lab website
  - Inclusion, equity, and access
  - Mental health
  - STEM outreach
- Manuscript on our efforts towards an inclusive lab – accepted March 2024




**Developing Diversity, Equity, and Inclusion Initiatives in a Biomedical Engineering Lab**

Xavier J. Person[1], Luke J. Tucker[1], Malley A. Gautreaux[1], Sophie J. McLay[1], Kamryn B. Clymer[1], Anastasia D. Elder[2,3], Lauren B. Priddy[1]

*Perspectives on Undergraduate Research and Mentoring*

# Thanks to…



Center of Biomedical Research Excellence in Pathogen-Host Interactions

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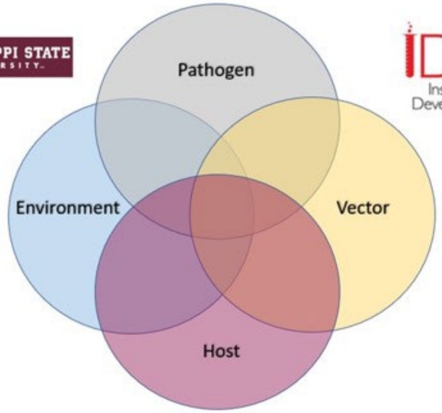


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