

NDnano Summer Undergraduate Research 2025 Project Summary

1. Student name & home university: Shirley Wei, University of Notre Dame

2. ND faculty name & department: Prof. Nallathamby, Aerospace and Mechanical Engineering

3. Summer project title: Phage-mimicking nanoparticles as broad spectrum antibacterials

4. Briefly describe new skills you acquired during your summer research:

I learned and conducted checkerboard assay to explore synergy between nanoparticles and antibacterial. I also learned how to modify metal coupon surfaces with nanoparticles and polymers, doing live/ dead assay. I also gained experience preparing biological samples for SEM imaging and conducting ICP-OES sample preparation.

5. Briefly share a practical application/end use of your research:

This research contributes to the development of broad-spectrum antibacterial coatings for medical devices and surfaces. These coatings could help reduce the risk of infection in clinical settings by providing a passive antimicrobial barrier, independent of traditional antibiotics

6. 50- to 75-word abstract of your project:

To address the rise of antibiotic-resistant infections, we investigated phage-mimicking nanoparticles as potential broad-spectrum antibacterials. Nanoparticles were tested alone and in combination with antibiotics using checkerboard assays against drug-resistant strains. Their interaction with surfaces was studied using metal coupon modifications, SEM imaging, and ICP-OES. This study demonstrates the potential of nanoparticle-based systems as alternative or supplementary tools for preventing bacterial contamination.

7. References for papers, posters, or presentations of your research:

[1] Guevara, A., Armknecht, K., Kudary, C., & Nallathamby, P.D. (2024). *PLGA nanoparticle formulations loaded with antibiotics induce sustained and controlled antibiotics release for prolonged antibacterial action against MRSA and Pseudomonas aeruginosa FRD1*. *Military Medicine*, 189(Suppl_3), 230–238. <https://doi.org/10.1093/milmed/usae079>

[2] Song, Z., Borgwardt, L., Høiby, N., Wu, H., Sørensen, T.S., & Borgwardt, A. (2013). *Prosthesis infections after orthopedic joint replacement: The possible role of bacterial biofilms*. *Orthopedic Reviews*, 5(2), 65–71. <https://doi.org/10.4081/or.2013.e8>

[3] Kurtz, S.M., Lau, E., Schmier, J., Ong, K.L., Zhao, K., & Parvizi, J. (2008). *Infection burden for hip and knee arthroplasty in the United States*. *The Journal of Arthroplasty*, 23(7), 984–991. <https://doi.org/10.1016/j.arth.2007.10.017>

[4] Hopf, J., Waters, M., Kalwajtys, V., Carothers, K.E., Roeder, R.K., Shrout, J.D., Lee, S.W., & Nallathamby, P.D. (2019). *Phage-mimicking antibacterial core-shell nanoparticles*. *Nanoscale Advances*, 1, 4812–4826. <https://doi.org/10.1039/C9NA00431C>

One-page project summary that describes problem, project goal and your activities / results:

Metal-based implants, such as titanium alloys, are widely used in clinical settings for procedures like joint replacements. However, post-surgical infections caused by drug-resistant bacteria pose a persistent threat to patient recovery and implant longevity [1][2]. Approximately 1% of hip and knee replacements in the U.S. fail due to infection, which often involves biofilm-forming pathogens resistant to standard antibiotic therapy [3]. The Nallathamby Lab is developing phage-mimicking nanoparticles (PhaNPs) as a new platform for broad-spectrum antibacterial action [4]. My research this summer focused on three different aspects to support this initiative: synergy evaluation with antibiotics, morphological imaging with SEM, and surface modification of implants to prevent bacterial adhesion.

Firstly, I explored the synergy between nanoparticles and conventional antibiotics could produce synergistic antibacterial effects. I developed a customized checkerboard assay protocol and applied it to assess interactions between nanoparticles and antibiotics against bacterial strains such as *P. aeruginosa*, and *MRSA USA300*. By calculating the fractional inhibitory concentration (FIC) indices, I was able to quantify synergy or indifference for each combination, laying the groundwork for future therapeutic formulation screening.

Second, I focused on morphological changes induced by sub-MIC concentrations of nanoparticles. Using SEM to image seven clinically relevant pathogens: *A. baumannii*, *MRSA USA300*, *K. pneumoniae*, *P. aeruginosa*, *C. striatum*, *E. faecalis*, and *S. pyogenes*. The SEM analysis revealed distinct structural disruptions in treated cells, suggesting potential membrane interactions between the PhaNPs and the bacteria.

Third, I modified titanium metal coupons with phage-mimicking nanoparticles and polymers, then used live/dead assays to evaluate bacterial colonization. After incubation with *E. coli*. The modified surfaces showed no bacterial adhesion. This finding highlights the potential application of these coatings in reducing implant-associated infections.

Collectively, these three studies have shown that the PhaNPs are effective against multi-drug resistant bacteria. Further experiments will be conducted to continue evaluating the effectiveness of PhaNPs in various biomedical contexts.