Student name and home university:

Conor Sheehan, University of Notre Dame

ND faculty name & department:

Dr. Prakash Nallathamby, AME

Summer project title:

Polycationic Polymer Carrying Phage-mimicking Antibacterial Nanoparticles as Infection Preventing Coatings for Metal Alloy Implants

Briefly describe new skills you acquired during your summer research:

I have learned new skills such as eukaryotic cell culture, mlRage, live/dead assays, and fluorescence microscopy.

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

The final goal of the project would be to use the polymer carrying nanoparticles

50- to 75-word abstract of your project:

Due to bacteria developing a resistance to antibiotics, medical implant surgeries have an increased rate of infection. This project focuses on determining if nanoparticles linked with polycationic polymers have an antibacterial effect when placed on implants while also testing the particles for their biocompatibility.

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

[1] Wang J, Wu G, Liu X, Sun G, Li D, Wei H. A decomposable silica-based antibacterial coating for percutaneous titanium implant. Int J Nanomedicine. 2017 Jan 6;12:371-379.

[2] Song Z, Borgwardt L, Høiby N, Wu H, Sørensen TS, Borgwardt A. Prosthesis infections after orthopedic joint replacement: the possible role of bacterial biofilms. Orthop Rev (Pavia). 2013 Jun 14;5(2):65-71.

[3] Kurtz, Steven M., Edmund Lau, Jordana Schmier, Kevin L. Ong, Ke Zhao and Javad Parvizi. 2008. "Infection Burden for Hip and Knee Arthroplasty in the United States." ***The Journal of Arthroplasty*** **23(7):984-991**

[4] Hopf,J., Waters, M., Kalwajtys,V., Carothers K.E., Roeder,R.K., Shrout,J.D., Lee,S.W., and Nallathamby, P.D.
"Phage-mimicking antibacterial core–shell nanoparticles"Nanoscale Advances, 2019, 1, 4812–4826

[5] Khwaja S, Curry A, Chaudhry IH, Green KM. Can keratinocytes cause failure of osseointegration? J Laryngol Otol. 2009 Sep;123(9):1035-8. doi: 10.1017/S002221510800409X. Epub 2008 Dec 9. PMID: 19063771.

Summary:
Metal-alloy based implants are widely and successfully used in medicine for many problems such as knee and hip replacements, however complications can arise in these procedures due to bacterial infection [1][2]. About 1% of both knee and hip replacement surgeries fail as a result of bacterial infection, demonstrating the need for preventative measures [3]. Phage-mimicking antibacterial nanoparticles from the Nallathamby lab, linked with polycationic polymers, are being tested on implant metal coupons from Zimmer Biomet as potential antibacterial coatings [4].

Testing began by gathering the control data and confirming that bacteria can grow on metal implants. Using live/dead assays to confirm, methicillin resistant *Staphylococcus aureus USA300* and biofilm forming *Pseudomonas aeruginosa FRD1* were successfully grown on the metal alloys. The metals were placed face down on agar plates with the bacteria and incubated for 16 hours. The project continued by testing the growth of both bacteria on implants containing the nanoparticles from the Nallathamby lab without the polycationic polymers. Before testing with the bacteria, the optimal concentration of nanoparticles needed to coat the metals was tested by varying the concentrations of particles in solutions when stirring with the metals for 16 hours. SEM and IR-spectroscopy were used to confirm the presence of the particles and it was determined that 1.5% weight per volume with respect to silica is the optimal concentration of nanoparticles in solution. Both *S. aureus USA 300* and *P. aeruginosa FRD1* successfully grew on all the metal alloys containing just the nanoparticles, again confirmed with live/dead assays and SEM. Future experiments will attempt to grow bacteria on the metals covered in nanoparticles carrying the polymers PEI 600 and PEI 1800, and observe the difference in bacteria growth compared to the previous control work to determine if there is an antibacterial effect.

The viability of human keratinocyte cells, a major influencer of osseointegration, was tested by growing HaCaT on the implants [5]. The growth of these cells on the implants were confirmed by live/dead assays and SEM. With the cell's ability to grow on the metal confirmed, future experimentation will examine the growth of the cells on metals containing the polymer carrying nanoparticles. Observing the difference in HaCaT cell growth on the metals with the polymer carrying nanoparticles will determine how biocompatible the treatment of the metal coupons is.

Work will continue on the project in the fall and will focus on obtaining the data of the metals containing the polymer carrying nanoparticles. If this study proves successful, future experiments will focus on how the molecular weight and structure of the polymers used influences antibacterial efficacy.