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Targeted Antibacterial Therpeutics for Multi Drug Resistant Pseudomonas aeruginosa

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Targeted Antibacterial Therapeutics for Multi Drug Resistant *Pseudomonas aeruginosa*

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Project Description

In the US alone, antibiotic-resistant superbugs currently cause 2 million cases of illness and 23,000 deaths a year, according to the Centers for Disease Control. *Pseudomonas aeruginosa,* a gram negative opportunistic pathogen is one of the leading cause of deaths in nosocomial respiratory tract infections.[1] An estimated 51,000 *P. aeruginosa* infections occur in the United States each year. More than 6,000 (13%) of these are multidrug-resistant (MDR), with roughly 400 deaths per year attributed to these infections.[2] The constant rise in the number of MDR species calls for attention to look more into pathogen selective (targeted) anti-infective treatment. One such targeted anti-infective treatment is to have a nanocarrier to carry a payload of antibiotics to be delivered to the cell surface of a select pathogen.[3]

Student Duties, Contributions and Outcomes

I. Synthesis of nanocarrier – Synthesis of hollow mesoporous silica nanoparticles (HMSNPs) (size vary from 20-100 nm) using modified Stober and template method.

II. Surface functionalization of nanocarrier – HMSNPs would be surface functionalized using a antibody that recognizes P. aeruginosa.

III. Loading of antibiotic cargo – Cationic antimicrobial peptides (CAMPs) cargo would be loaded using electrostatic interactions to HMSNPs (CAMP- HMSNPs).

IV. Purification – Synthesized HMSNPs would be purified using repeated high-speed centrifugation and collected particles would be concentrated in a compatible solvent.

V. Characterization – Functionalized HMSNPs would be characterized using Fourier transform –infra red (FT-IR) spectroscopy, fluorescence spectroscopy, dynamic light scattering.

VI. Application – Antibacterial efficacy of CAMP- HMSNPs with *P. aeruginosa*

Manuscript/Poster Preparation – Participating student would be strongly encouraged to write up their research project results in the format of Journal of American Chemical Society (JACS) or least have the results in form of a poster presentation for ACS regional meeting. A successful project would be strongly considered for publication with additional data where the student could be a co-author or combined first author along with a graduate student of the group.

Faculty Requirement and Mentorship

Expected Student Background – Students should have strong background in General Chemistry. Fundamental knowledge of Organic Chemistry is a definite advantage. Student major in Biology, Chemistry, and or Chemical Engineering would be benefited. *Expected results and deliverables* – Participating student would be exposed to state-of-art nanomaterial synthesis and characterization in a real world application. Students would be exposed to simple synthesis of small molecules and bio conjugation chemistry. Students would be encouraged to maintain standard laboratory notebooks and would be exposed to good laboratory practices. They would be expected do a scientific presentation each week and hence be exposed to a peer review setting where their work would be critically analyzed. *Faculty Supervision and Mentoring* – Dr. Jayawardena will supervise all the steps in nanoparticle preparation and application. Including

final manuscript preparation. Group meeting would be held weekly where the student will present his/her progress or problems of the project with the entire group. The student will have access to the instructor at least once a day.

Prior Awardees

RCEU 2018 - Quantification of the Limit of Detection of Pathogenic Bacteria Using a Glyconanomaterial Based Rapid Point-of-Care Diagnostics System – James Johnson

RCEU 2018 - Functionalized Nanomaterial as a Tool for Rapid Point-of-Care Diagnostics – Melinda Mustain

RCEU 2018 - Synthesis of Multivalent Glyco-Magnetic Nanoparticles for Rapid Point-of-Care Diagnostics System – Veer Devarasetty

Student contribution: all students work surmounted to a provisional patent submitted by UAH, data for two SERMACS poster presentations, *manuscript in preparation* Rapid Point-of-Care Diagnostic of Mycobacteria using Multi-Core Shell Magnetic Silica Nanoparticles

References

(1) Klevens, R. M.; Edwards, J. R.; Gaynes, R. P.; National Nosocomial Infections Surveillance, S. The Impact of Antimicrobial-Resistant, Health Care–Associated Infections on Mortality in the United States. *Clinical Infectious Diseases* **2008**, *47*, 927-930.

(2) Bassetti, M.; Vena, A.; Croxatto, A.; Righi, E.; Guery, B. How to manage Pseudomonas aeruginosa infections. *Drugs in Context* **2018**, *7*, 212527.

(3) Nathan, C. Fresh Approaches to Anti-Infective Therapies. *Science Translational Medicine* **2012**, *4*, 140sr142-140sr142.