

## SOAR Proposal- 2018

### The Effects of Multiple Amino Acid Mutations of a Key Quorum Sensing Peptide, CSP-1.

Faculty Mentor: Michael Bertucci, Ph.D., Associate Professor of Chemistry

Student Researcher: Kylie Chichura

Start Date: June 4, 2018

Length of Project: 10 weeks

#### Project Summary

The goal of this project is to synthesize a library of synthetic analogues of CSP-1 to determine key structure-activity relationships of the peptide in binding to its cognate receptor. The research relates to quorum sensing, a cell-density dependent form of bacterial communication used by *S. Pneumoniae*, a species which has been proven to have many detrimental effects on human health. Quorum sensing is controlled by extracellular chemical molecules synthesized by bacteria; the quorum sensing molecule in *S. Pneumoniae* is CSP-1, and the focus of this research project. Multiple mutations of the amino acid sequence will be made to modify the peptide and create an inhibitor. These peptide derivatives, which have never been made before, will elucidate the structure-function relationship between CSP-1 and its chemical structure.

This project will help me develop skills specifically in using Solid Phase Peptide Synthesis (SPPS), a technique of chemical synthesis used to create peptides for scientific research, MALDI-TOF Mass Spectrometry, an analytical technique used to identify chemical samples, and High-Performance Liquid Chromatography (HPLC), a machine/chemical technique used to purify a sample of unwanted side-products. I will learn how to run *S. pneumoniae* bioassays while at the University of Nevada in Reno, Nevada. The project will hone my skills as an independent researcher and prepare me for my graduate studies and career as a scientist. I will be required to think independently, using my knowledge of chemistry and experience in this field of research to make productive decisions to complete my project goals.

#### Roles and Responsibilities

I, Dr. Bertucci, will serve as Kylie's direct mentor for the first 7 weeks of her project, while my collaborator (Dr. Yftah Tal-Gan) at UNR will be her mentor for the final 3 weeks. I will travel to Reno with Kylie for the first week of her trip (Week 8) and then return to Pennsylvania and advise her each day via phone/video call. I will be responsible for monitoring Kylie's progress, working with her one-on-one as she explores academic literature and formulates her experiments, and providing consultation on learning new techniques and interpreting data. In addition, I will gather the supplies and chemicals Kylie needs to carry out her proposed research and arrange travel to and lodging in Nevada and the American Chemical Society Conference in August.

Kylie will be conducting all the research and experiments to forward her project goals. As part of this work, she will be responsible for maintaining a laboratory notebook to document her results and progress. At the end of the summer, Kylie will catalogue all of the peptides that she has synthesized, the

biological data she has acquired, and other relevant documentation in an organized fashion for reference by future students and publication. Kylie will participate in daily research meetings to set a daily research agenda and discuss results from the previous day's work. As summative evaluations of her progress and opportunities for academic and professional development, Kylie will present her work at the Moravian College Student Scholarship and Creative Arts Day, the University of Nevada, Reno, and the National Meeting of the American Chemical Society in Boston, MA.

#### Timetable of Expected Milestones

**WEEK 1 - 2:** Synthesis of doubly-substituted CSP-1 activators

**WEEK 3 - 5:** Purification of CSP-1 activators; Synthesis of doubly-substituted CSP-1 inhibitors

**WEEK 6 - 7:** Purification of CSP-1 inhibitors; Preparation of samples for shipment to University of Nevada, Reno

**WEEK 8 - 10:** Completion of *S.pneumoniae* bioassays at the University of Nevada, Reno

#### Engagement in Discipline-Specific Research

This project directly relates to biochemistry, organic chemistry, and molecular genetics. Kylie is currently majoring in chemistry and has taken organic chemistry during her sophomore year. She will be exposed to these subject areas more deeply through the described research in the context of a significant global health issue. She will be able to employ techniques and strategies she has learned in class and her laboratory courses, which will be beneficial in reinforcing the related chemical concepts. Kylie will become experienced in Solid Phase Peptide Synthesis using a microwave, High-Performance Liquid Chromatography, and MALDI-TOF Mass Spectrometry, all contemporary laboratory techniques that will prepare her for graduate school and her future occupation.

#### Contributions to the Discipline & Community

Kylie's work will contribute to the discipline by gaining new information on specific molecular structures that are involved in quorum sensing in *S. pneumoniae* and how these molecules can be modified through synthetic organic chemistry to prevent cell communication. There is a currently a deficiency in the literature with respect to chemical approaches to address this problem. This project can be expanded upon with future research mentees due to the numerous ways the target peptide signaling molecule can be structurally altered to enhance inhibition of the bacteria's pathogenicity.

Kylie will have the opportunity to present the project at the National Meeting of the American Chemical Society in August in Boston, MA. She will also present her findings to the college community at the Undergraduate Student Scholarship and Creative Arts Day.

## **Student Purpose Statement**

### **The Effects of Multiple Amino Acid Mutations of a Key Quorum Sensing Peptide, CSP-1.**

Student name: Kylie Chichura

Major: Chemistry

Graduation date: May 2019

Faculty Mentor: Dr. Michael Bertucci

On-Campus Housing: Yes

I am grateful for the array of opportunities for undergraduate research offered at Moravian College. Since I am aiming to attend graduate school and obtain a Ph.D. in chemistry, it is vital for me to gain experience in the laboratory. I had an interest in quorum sensing because it involves studying the chemistry of biological systems. As a chemistry major, I had not been required to take any biology courses in my undergraduate career. This project has allowed me to expand my research and recognize my newfound interest in biology. As a result of my research, I will be more prepared to take biochemistry in the fall.

Bacterial resistance to antibiotics is well-known problem in today's society. Quorum sensing, the main focus of this project, aids in the development of an alternative to antibiotics. I am thoroughly interested in this research and application in medicine, especially after listening to educational talks and reading articles. I am eager to learn more about the processes involved in medicinal advancements.

From this project, I hope to gain insight as to what exactly I aim to accomplish after graduation. I will use my experiences and knowledge in the laboratory to make new discoveries and contribute to previous ones. The opportunity to collaborate on an original experiment exceeds what I learn in a standard 3-hour lab period. Immersing myself in a summer long research project will allow me to develop advanced problem solving and communication skills that will help me in my future endeavors.

## The Effects of Multiple Amino Acid Mutations of a Key Quorum Sensing Peptide, CSP-1.

Faculty Mentor: Michael A. Bertucci, Assistant Professor of Chemistry

Student Researcher: Kylie Chichura

### Expense Proposal

Towards the completion of the research and experiences discussed above, we are requesting funding for the following expenses:

Acetonitrile - HPLC Grade (4 x 4L):	\$216.76 + shipping
Fmoc-Lys(Boc)-Wang Resin (25 g):	\$192.00 + shipping
<b>Total:</b>	<b>\$408.76 + shipping</b>

Fmoc-Lys(Boc)-Wang Resin is a necessary starting material for Kylie to make her CSP-1 derivatives, while the acetonitrile is a solvent required for purification of her peptides by HPLC. These reagents will be integral for Kylie's synthesis and purification of her proposed peptides. Currently, we do not have these chemicals present in the chemistry department at Moravian and they will be used exclusively for research purposes.