



February 14, 2023

American Society of Pharmacognosy
Undergraduate Research Award Selection Committee
Northbrook, IL 60062

Dear Committee Members,

We are extremely pleased to offer our enthusiastic support to **Oli Horyn** for an American Society of Pharmacognosy Undergraduate Research Award for her project, titled "Investigating the Mechanism of Action of the Sesquiterpene Lactone Laurenobiolide." Ms. Horyn is undertaking this project as a joint effort between the laboratories of Dr. Matthew Bertin and Dr. Kathryn Ramsey in the Department of Biomedical and Pharmaceutical Sciences at the University of Rhode Island. Dr. Bertin is an ASP member with extensive expertise in natural products chemistry and biosynthesis. Dr. Ramsey is a microbiologist with considerable expertise in molecular genetics in pathogenic bacteria, particularly the pathogens *Francisella tularensis* and *Staphylococcus aureus*.

It is worth noting that Ms. Horyn's project uses two pathogens, both can be safely handled in standard BSL2 conditions. In particular, the Ramsey laboratory exclusively uses the model organism *F. tularensis* subsp. *holarctica* LVS (Live Vaccine Strain), which does not infect or cause disease in humans. Additionally, all of Ms. Horyn's work using *Staphylococcus aureus* is performed using a methicillin-sensitive (non-MRSA) strain.

Ms. Horyn is an academically outstanding upper-level student (third year) and has been a member of the Ramsey laboratory since the spring of 2021. During the summer of 2021, when she held a RI-INBRE Summer Undergraduate Research Fellowship (SURF), she became proficient at using a particular technique (disc diffusion assays), validating the susceptibility of several *F. tularensis* mutant strains to various antibiotics. She then focused on a particular antibiotic, kasugamycin, and Ms. Horyn identified a number of spontaneous kasugamycin-resistant mutants. After isolating these mutants and extracting their DNA, Oli was able to validate that they all had mutations in the *ksgA* gene, which is known to lead to kasugamycin-resistance. While we did not identify any novel mutations, this work provided the ideal training for her current proposed research project.

Over this past summer, Oli was awarded a RI-INBRE Summer Undergraduate Research Fellowship + (SURF+), having already participated in the RI-INBRE SURF program. During this time, she started working collaboratively with the laboratory of Dr. Matthew Bertin to investigate a novel antimicrobial, laurenobiolide. Prior work performed in Dr. Bertin's lab revealed that this compound inhibits growth of methicillin-sensitive *Staphylococcus aureus* (MSSA). Oli's goal was to determine if this antimicrobial activity extended to organisms other than *S. aureus* and additional strains of *S. aureus*. She was able to validate sensitivity of methicillin-sensitive *S. aureus* and *F. tularensis*, but not *E. coli*, to laurenobiolide. In our discussions of her results, this raised an important question: how does laurenobiolide exert its antimicrobial effects at the molecular level? Given her experience, she hypothesized that identifying a resistant mutant would provide insight into how laurenobiolide functions to inhibit bacterial growth. Oli is well suited for this work, and we enthusiastically support the continued development and undertaking of her research project.

Together with the graduate students in the Ramsey and Bertin laboratories, we will supervise all the proposed work in this project to ensure safety, rigor, and reproducibility. We have the facilities and equipment necessary for the success of this project and are excited to have Ms. Horyn continue her exciting work. Determining the mechanism of action of a natural product potential drug lead is always a major objective for natural product chemistry and pharmacognosy work. Oli is well on her way to accomplishing this and she will be the lead author on an impactful journal article.

In summary, Ms. Horyn is an outstanding student with great enthusiasm for laboratory research. Her undergraduate research experience, including the exciting work proposed here, will benefit her as she works towards her goal of working in the pharmaceutical industry. She is extremely well-prepared to carry out the proposed experiments and we support her application for an American Society of Pharmacognosy Undergraduate Research Award without reservation and with enthusiasm.

Sincerely,



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