2021 Presidential Faculty-Student Collaboration Grant Application

Application Deadline - 5 pm, Monday, February 22nd, 2021.

Please direct inquiries about applications to Sarah Wolter (swolter2@gustavus.edu).

Overview

Guidelines

Presidential Faculty-Student Collaboration Grants are available annually to support collaborative endeavors involving faculty and students.

*Grant monies may be used to support faculty summer stipends, summer compensation for students, student housing on campus, equipment, materials, transportation, etc.

*Applications will be accepted for stipends and project costs, and for stipends only.

*One faculty member cannot receive both the Research, Scholarship, and Creativity grant and the Presidential Faculty/Student Collaboration grant in the same year.

*Monies may also be used as matching funds for outside support awarded to the faculty member.

*Student eligibility is limited to full-time returning students.

*Grant recipients conducting research with human subjects must receive IRB approval prior to disbursement of grant funds; grant recipients conducting animal research must receive IACUC approval prior to disbursement of grant funds.

*Applicants whose previous grant reports are past due will not be eligible to apply.

*Awards are made in the spring for the following academic year; project expenses must be incurred and reimbursed during that fiscal year (June 1 - May 31).

Please see https://gustavus.edu/kendallcenter/grant-opportunities/grant-examples.php for examples of previously funded applications.

What does the Faculty Development Committee mean by "collaboration"?

Collaboration is understood to include in-depth faculty-mentored undergraduate scholarly or creative projects in any discipline. For the purposes of this grant, collaboration means the active involvement of the faculty member in the student's project. This might be a full-fledged faculty-student project partnership, a student project that is closely mentored by the faculty member, or a student's active and meaningful participation in an ongoing faculty research project. Successful proposals will demonstrate a mentoring relationship between faculty and student that encourages scholarly/creative work in a collaborative environment.

Criteria for selection

To distinguish among proposals that meet all criteria identified in the application, the committee looks for evidence of exceptional merit, compelling project design, impact on student experience, and feasibility of project. The committee encourages applications from all departments and disciplines, and from faculty at all stages. Priority will be given to quality proposals submitted by candidates who have not been funded through a Presidential Student/Faculty Collaboration grant in the past three years.

I. Personal Data

Faculty First Name *

Scott

Faculty Last Name *

Bur

Faculty Gustavus E-mail *

sbur@gustavus.edu

Faculty Campus Phone Number *

507-933-7038

Rank/Status *

- ○ Visiting Faculty
- ○ Continuing Instructor
- ○ Assistant Professor
- ○ Associate Professor
- ◉ Full Professor

Faculty Department(s) and/or Program(s) *

Chemistry

Administrative Assistant Name *

Judith Helmeke

Student First Name *

Amber

Student Last Name *

Simon

Student Gustavus E-mail *

asimon2@gustavus.edu

Student Major(s) *

Biochemistry and Molecular Biology

Anticipated Graduation Year *

2023

II. Information on Previous Grants & Permission to Share Proposal

To be completed by the faculty member applicant.

Have you previously received a Presidential Faculty/Student Collaboration Grant? *

- (●) Yes
- ( ) No

If you replied "yes" to the previous question, briefly describe your previous Presidential Faculty/Student Collaboration Grant project(s) and outcome(s).

In 2017, Emma Santa and I were awarded a Presidential Faculty/Student Collaboration Grant. Together, we began a new area of research for my lab. With Emma's help, we obtained some critical preliminary data that led to a successful NSF grant application. The project also ignited a spark in Emma, and she is currently pursuing a PhD in chemistry at the University of Wisconsin. This project that Emma helped me start is in an emerging field (chemical biology) the used the tools of chemistry to investigate long-standing questions in biology. Student interest in this area has been surprisingly robust.

Previous to Emma, David Guptill (2008) and Adam Langenfeld (2004) worked with me on projects funded by Presidential Faculty/Student Collaboration grants. While we made good progress, these were "high-risk/high-reward" projects - and I may return to them in the future. Ultimately, David's experience led him to pursue graduate studies in chemistry. He was accepted into one of the top synthetic organic labs in the country (in Tom Hoye's group), largely based upon his experience starting with the Presidential Faculty/Student grant. Adam Langenfeld also fell in love with research, and ended up pursuing an MD/PhD from the University of Illinois in Urbana-Champaign. He is currently working in pediatrics at a twin-cities hospital.

If successful, my proposal can be used as an example to assist future faculty applications. This decision will not in any way influence the evaluation of my application. Click "Yes" to give permission. *

- (●) Yes
- ( ) No

III. Participant Biographies

Please compose your answers offline and copy/paste into the appropriate text boxes. While answers inputted into this form should be available if you close the form and return in the same browser, we cannot guarantee that this function will work.

Brief biography of faculty participant and explanation of how this project fits into their career trajectory. Note: applications from faculty at all career stages are encouraged. *

Most of my research career has been rooted in traditional medicinal chemistry. Although not specifically focused on drug discovery, the methods we developed to make molecules were directly useful for drug discovery efforts. I've worked with over 40 students in independent research, either during the summer or academic year, in my 17-year career at Gustavus.

The pharmaceutical world has changed since my time at Parke-Davis (now part of Pfizer) in the early 90's. The methods used to examine drug candidates have also changed. In light of these changes, I used my most recent sabbatical to reinvent my research. The project outlined here continues that reinvention. I have found that this area of research is both personally fulfilling and still appropriate for an institution like Gustavus. In fact, the student interest has been remarkably high. More than anything else I've pursued, this project represents the merging of my life as a scholar and my life as an educator.

Brief biography of student participant and explanation of how this project fits into their educational trajectory and their qualifications to engage in this project. Note: biography and explanation must be written by the student. *

I am a sophomore planning to major in biochemistry/molecular biology with a physics minor. I'm a very curious person, and I'm very passionate about learning about science, which has motivated me to put lots of effort into my science classes. I plan on pursuing a career in biochemical research, so being able to work with Prof. Bur for a summer would allow me to gain both experience and a better idea of what kind of research I want to pursue. I took Prof. Bur's Organic Synthesis research course over J-term, so I already know a lot about the project and what we're trying to do. Being a part of Prof. Bur's research team over the summer would be an excellent opportunity for me to further my abilities in the field of biochemistry.

IV. Project Information

Please compose your answers offline and copy/paste into the appropriate text boxes. While answers inputted into this form should be available if you close the form and return in the same browser, we cannot guarantee that this function will work.

A. Project description: Briefly describe the proposed project, its relationship to existing scholarship in the field, and the nature of the collaboration between faculty member and student. *

Malaria is a protozoan infection caused mainly by two species: Plasmodium falciparum and P. vivax.(1) In sub-Saharan Africa, over 99% of the disease is caused by P. falciparum, which is transmitted through the bites of infected female Anopheles mosquitoes. While world-wide rates of infection are decreasing, approximately 429,000 deaths were attributed to malarial infections in 2015, and 70% of these deaths were in children under the age of five. In the same year, approximately 212 million new infections were reported. More that 90% of deaths and new infections are reported in Africa, specifically sub-Saharan Africa. Insecticide-treated netting, mosquito population control through insecticide spaying, and artemisinin-based combination therapies are the front-line prevention and treatment methods. As a result of their use, infection rates fell 21% and mortality rates by 29% from 2010 - 2015. Unfortunately, in that same time frame, 60 of the 73 reporting countries reported resistance to at least one insecticide, and 50 reported resistance to two or more insecticide classes. In addition, P. falciparum resistance to artemisinin has been reported in several countries.

A protein called GCN5 is known to play a critical role in human gene expression by mediating interactions that are critical for knowing what part of the DNA to transcribe. P. falciparum has a similar protein called PfGCN5 that has also been shown to be critical for gene expression.(2) Selective disruption of this PfGCN5 protein, therefore, is an attractive new therapeutic approach to malaria. This could, for example, kill the parasite or hinder its ability to infect.(3) In addition, developing molecules that disrupt specific mechanisms in the regulation of gene expression would provide significant tools to study this poorly understood regulation process. There are no literature reports of this approach to disrupt Plasmodium gene expression, though there is precedent with a few human regulatory proteins.

Over the last several years, my research group and I have identified a few small molecules that bind to a specific region of the PfGCN5 protein, called a bromodomain, that is critical for its regulatory function. We have used Protein-Observed 19F (PrOF) NMR to measure how strongly our molecules bind to the protein. One of these molecules binds more tightly than PrOF NMR can measure. Accordingly, we must develop protocols for a new analytical technique.

In addition, there are over 40 different bromodomains in human proteins, and we need to ensure selectivity of our molecules for the PfGCN5 bromodomain relative to the others. Finding small molecules (as opposed to proteins) that are selective for one bromodomain over another has been challenging, with few examples in the literature. Our previous modeling work suggests we may have a molecular architecture that provides this elusive selectivity. We have chosen two human bromodomains (PCAF and CECR2) that are closely related to our GCN5 bromodomain to serve as representative examples to test selectivity. While we have obtained the genetic material needed to express these proteins, we have not yet expressed or isolated them. Finally, understanding how the molecule binds to the protein (e.g. orientation in space relative to the protein) will provide insight into further modifications we should make to improve the binding. We have worked out general condition to grow crystals of our protein with a molecule bound to it, and we can submit these for x-ray diffraction experiments that tell us the three-dimensional structure of the protein-molecule complex. We need to find specific conditions for our best binding molecules.

Collaboration: I am still learning more of the nuances of the protein expression and isolation, and I am very new at protein crystallography and SPR; I am, therefore, as much of a student as Amber. Amber and I will be working together to learn SPR and to troubleshoot problems in our synthesis of the molecules. The goal is for me to be synthesizing molecules along with Amber. We will also be working closely together to optimize the protein expression and isolation, each trying different conditions, and consulting with each other almost constantly about what we should try next. Much like the optimization of protein expression, we will need to work closely and experiment with different conditions to grow the crystals for x-ray analysis.

1. World Malaria Report 2016. Geneva: World Health Organization; 2016.
2. Cui, L.; Miao, J.; Furuya, T.; Li, X.; Su, X.-z; Cui, L. Eukayot Cell 2007, 6, 1219 - 1227.
3. Josling, G. A.; Petter, M.; Oehring, S. C.; Gupta, A. P.; Dietz, O.; Wilson, D. W.; Schubert, T.; Längst, G.; Gilson, P. R.; Crabb, B. S.; Moes, S.; Jenoe, P.; Lim, S. W.; Brown, G. V.; Bozdech, Z.; Voss, T. S.; Duffy, M. F. Cell Host Microbe, 2015, 17, 741-751.

B. Project design: Please describe your project design and activities, including locations, staff, schedule of work, budget rationale, and anticipated project completion date. *

First Priority: We will make more derivatives of our molecules to determine what changes are detrimental to binding. We will work with collaborators at the University of Minnesota to learn an analytical technique called Surface Plasmon Resonance (SPR) that we can use to measure the binding interaction between our molecule and our protein. If conditions allow for travel, we will go to the U of MN, be trained on the SPR system, and collect data for several molecules. If conditions do not allow travel, we will work with our collaborators to have them collect data. This will give Amber experience in organic synthesis and in a new analytical technique. This is also a new technique for me, so Amber and I will be learning this together. For synthesis, Amber and I will be working in NHS 4416, which is equipped with 8 fume hoods and plenty of bench space.

Second Priority: We will develop expression and isolation protocols for the two new bromodomain proteins (PCAF and CECR2). We will test our most promising molecules against both of these proteins to see if we have any selectivity for the PfGCN5 bromodomain. This will give Amber experience with basic techniques in protein expression and isolation. Since these are new proteins, Dr. Bur will be intimately involved with developing the protocols and troubleshooting any problems that arise. For protein expression and isolation, we will use equipment in the Biochemistry and Molecular Biology prep lab and cold room (NHS 4402).

In protein expression and in organic synthesis, there is a lot of "hurry up and wait" - we scramble to get an experiment going, but then we have to wait for the process to finish. This can be up to 20 hours where we can be working on something else. I expect we will be able to engage in both of these priorities simultaneously.

Third Priority: Depending upon the success of priority one activities and the time remaining in the summer, we will grow protein crystals with our molecules bound to the protein. These crystals will be submitted for x-ray diffraction analysis. (These are sent to an outside lab.) Amber will gain experience in growing protein crystals and interpreting x-ray crystallographic data to determine the 3-dimensional shape of our molecules bound to the protein. My experience in this is very limited, so I will also be learning how to do all of these things.

Schedule of work: In general, the work days are structured with a 9 am - 10 am group meeting (discuss results, troubleshoot, and discuss next steps) and a 10 am - 5 pm block of lab time. As protein expression is dependent upon the life cycle of the bacterial cells, timing for the day may be altered. On average, Amber will not work more than 40 hours per week regardless of the schedule required for cell growth. Priority one activities will continue throughout the summer, priority two activities will primarily occur during the first half of the summer, and priority three activities will be primarily in the last half of the summer.

Budget: See budget rationale for explanation of specific requests.

Completion Date: This is a multi-year, multi-student project. As such, there is no anticipated completion date yet.

C. Desired project outcomes: What are the anticipated outcomes for this project? Where do you anticipate publishing, presenting, exhibiting, or otherwise disseminating this project? *

This is, of course, a much bigger project than can be fully accomplished in one summer. Nevertheless, I anticipate enough work can be done to have some concrete outcomes to report:

Scholarly publications and presentations: Ultimately, we expect to publish the results of this project, although this may take longer than the reporting cycle for this grant. In the short term, we will give a preliminary poster presentation at the MCMS undergraduate research symposium in November. Depending upon progress, we may also present at a regional or national American Chemical Society meetings either this fall or next spring.

Competitive proposal for external funding: The progress made will provide compelling data for a renewal of my NSF grant. This may not occur during the reporting period of the Presidential Faculty/Student Collaboration grant, yet the progress Amber makes will be critical to the success of the renewal.

Research experience for Amber Simon: Previous Presidential Faculty/Student Collaboration grants have had tremendous impact on students' vocational discernment. In addition, their experiences under the grant have positioned them for placement in excellent graduate programs. Each of the previous students with whom I've worked under a Presidential Faculty/Student Collaboration grant has increased the reputation of Gustavus as a pipeline of excellent students.

D. (There is no text reply option, only a radio button that says "Option 1.") COVID-19 restrictions may disallow some planned travel, though we have an alternative plan..

D. How will restrictions due to Covid-19 potentially affect your project? [This is not a criteria for selection of the grant.]

V. Budget

Download the Presidential Faculty/Student Collaboration budget form here: https://drive.google.com/file/d/1irwy0HSXSc7tZdiCOcvuDuo87JbgAGeS/view?usp=sharing. Then upload the completed budget form by clicking "Add File" below. *

2021 Presidentia...

Provide a rationale/justification for your budget.

Travel, if allowed, will include driving to the 28th street train station, then taking the train to the U of MN campus. I have an active NSF grant that will cover milage and the cost of training on the SPR instrument. We anticipate approximately $50 in train fare for Amber.

Equipment necessary for the project is already owned by the College or is available at the U of MN (i.e. SPR instrument).

Materials are mostly comprised of chemicals and consumables, such as gloves. It is my experience that each student uses approximately $600 worth of consumables and chemicals each summer (more if starting a brand-new project).

No additional personnel costs are expected with this project. My active NSF grant will cover costs associated with analysis of samples that require additional costs.

VI. Additional Information

Have you applied for funding from another source to support this project but do not yet know the outcome of that application? *

- ○ Yes
- ◉ No

If you replied "yes" to the previous question, please 1) indicate the funding source(s) and amount requested, 2) explain how the Presidential grant funds will be used in addition to the other funding if received, and 3) explain how the Presidential grant project would be impacted if external funding is not received.

Have you received funding from another source to support this project? *

- (●) Yes
- ( ) No

If you replied "yes" to the previous question, please 1) indicate the funding source(s) and amount requested, and 2) explain how the Presidential grant funds will be used in addition to the other funding received.

This is a large, multi-year, multi-student project. To support this work, I currently have an NSF grant that will provide funds for travel and some materials/equipment ($236,068 over 3 years, including Facilities and Administrative costs). Importantly, this active grant allows me to hire 3 additional students for the summer. Two of the students will be working on parts of the project that do not overlap with Amber's contribution. One student will be working on synthesizing derivatives of our molecule for testing, along with Amber and I.

A project like this thrives with students at several experience levels because senior students can help mentor and train students who are earlier in their career. This "pipeline" is difficult to build with current funding structures. The FYRE program and courses such as my research J-term, which Amber completed, offer an introduction to the project. It is common, however, that the student selection process for an NSF grant explicitly favors students with more experience. Promising students like Amber find themselves "stuck in the middle" without a way to support continuing experiences. From this perspective, the current NSF funding and the Presidential Faculty/Student Collaboration grant work synergistically to enhance Amber's experience by providing a larger research community that better supports her while accelerating the pace of the research project. In the process, she will gain the valuable experience needed to be competitive for opportunities such as Research Experiences for Undergraduates (REU) and Summer Undergraduate Research Fellowship (SURF) programs.

If you apply for and receive funding for both the Presidential Faculty-Student Collaboration grant and the Research, Scholarship, and Creativity grant, which will you accept? Grant guidelines specify recipients can only accept funding for one of the grants in a year.

- ( ) Presidential Faculty-Student Collaboration grant
- ( ) Research, Scholarship, and Creativity grant

If there are any additional materials that you think would be helpful to the committee in deciding upon your application, please upload them here.

If there are any additional materials that you think would be helpful to the committee in deciding upon your application (e.g. links to Google Drive files), please include URLs here.

VII. Applicants' Signature

Signature *

Scott Bur