

RESEARCH CORPORATION FOR SCIENCE ADVANCEMENT
Cottrell Scholar Award Application

EDUCATIONAL PROPOSAL

STATEMENT AND SIGNIFICANCE OF THE PROBLEM

There is significant need for an increase in both the quantity and diversity³² of STEM graduates at the undergraduate level. Early research experiences are well-known to be crucial to development of young research scientists, increasing retention, GPA, and pursuit of graduate studies.^{33, 34} Importantly, these opportunities are particularly important for underrepresented groups in science such as women and minority groups.^{35, 36} These experiences both provide a foundation of skills and knowledge as well as improve the confidence of young researchers and assist in acculturating them to the world of scientific research. Notably, earlier research experiences, occurring at the first or second year of college, have been shown to correlate with improved outcomes.³⁷ Unfortunately, it is exceedingly rare that universities and colleges have sufficient resources to offer every Introductory-level student a research assistant position in a faculty member's laboratory. **Thus, it is important to develop transferable, scalable, and economical methods to provide some of the benefits of an early research experience to all students early in their academic career.** Such experiences should both inspire and assist students to pursue further research experiences. Here, we propose to incorporate primary research from the Research proposal into an interdisciplinary introductory science class. In doing so, we hope to

- i.) **Expand student opportunities to experience primary research**
- ii.) **Acculturate students to research through an active community of near-peer scientists**

INSTITUTIONAL EDUCATIONAL PRIORITIES

The Keck Science Department (KSD) of The Claremont Colleges is relatively unique in that it is a joint venture between three top-tier primarily undergraduate institutions (PUIs): Claremont McKenna, Pitzer, and Scripps Colleges. Further, its membership amongst the Claremont Colleges, which include Pomona College and Harvey Mudd College in addition to the three aforementioned colleges, situates KSD in a vibrant, diverse and collaborative environment unlike any other in undergraduate-focused education. As with any top-tier PUI, the Keck Science Department maintains a high emphasis on both innovative research and innovative pedagogy and frequently mixes the two; in the past three years, faculty in the department have received NSF CAREER awards (pedagogy and research), a major collaborative NSF IUSE award (primarily pedagogy), and a number of NSF MRI and NSF RUI awards (primarily research). The department received, along with the other two Claremont Colleges, a \$3.6 million joint award from Howard Hughes Medical Institute to collaboratively develop research and educational programming. The strong pattern of funding in both pedagogical and scientific research demonstrates an active community of scientists dedicated to the teacher-scholar model which is ideal for my development. Notably, Emily Wiley, who is cited as a mentor on the education portion of this grant, has received NSF funding for incorporation of research into her upper-division Molecular Biology course; her mentorship is expected to be an invaluable asset during development of this plan.

Importantly, this unique environment has been correlated with positive student outcomes; over the past three years, an average of 120 science majors have graduated from the department each year. During this time, students receiving Chemistry, Biochemistry, or Molecular Biology degrees (students with whom I work most closely) have gone on to top-tier Ph.D. programs including Harvard (two), Yale, Stanford, Caltech, and UCSF. Notably, **all of these students had an initial research experience at KSD.**

KSD is also relatively unique in that it has a highly multidisciplinary structure; the department operates as a singular department without traditional discipline divisions, housing over 30 full-time faculty members in physics, chemistry, biology, and environmental sciences. The department's unique multidisciplinary structure has enabled a number of innovative pedagogical advances focused around interdisciplinary education. Most notably, the Introduction to Biological Chemistry (IBC) is an interdisciplinary introductory science course developed in the Keck Science Department. IBC combines the first semester of the Introductory Biology and Introductory Chemistry courses, is co-taught by a biologist and a chemist, and services 50-60 students per year in the Fall semester. This course focuses on interweaving the introductory materials to create synergistic learning opportunities that jumpstart students' academic careers and begin to show students the importance of interdisciplinary thinking in modern science. While IBC is only in its fourth year, and, thus, has not been assessed yet, a related program in our department, AISS, has been shown to increase retention in the sciences as well as increase students seeking research opportunities;^{38, 39} anecdotal evidence suggests that many of these successful attributes also apply to IBC.

In Fall 2015, our department will offer IBC for the fourth time; I will teach the chemistry portion of IBC for the first time. While the lecture portion of the curriculum for IBC has been effectively integrated in the first three years of IBC, the IBC laboratory curriculum has remained segregated and is not substantially different than the

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traditional Introductory Biology and Introductory Chemistry curricula. Unfortunately, this creates a disconnect, sending the incorrect message that these two different disciplines do not overlap in the laboratory. This is also an opportunity to innovate and create a more research-like laboratory program in IBC. **Here, I propose to incorporate an active research project into IBC labs; the project will highlight interdisciplinary themes within the class and will improve the alignment of the learning objectives of the lecture portion of the course with the laboratory portion. Through strategic use of student-researchers, we will also highlight the culture of research, building a near-peer network to help socialize students to research science.**

PLAN OF PROCEDURE: AN INTERDISCIPLINARY RESEARCH-FOCUSED LAB COURSE FOR IBC

Overview. A number of collaborative, large-scale research questions that require modular, simple, repeating experiments have been effectively incorporated into laboratory classes.^{40, 41} **Here, we propose to directly incorporate experiments proposed in the Research proposal of this grant into IBC, giving approximately 50-60 students per year the opportunity to participate in a genuine hypothesis-driven research problem while furthering research in the PI's laboratory.** Notably, incorporating a faculty member's research can be beneficial as it may result in increased faculty involvement in overcoming the challenges of incorporating research into a laboratory course.

Scientific Rationale. In our research proposal, we discuss using Statistical Coupling Analysis (SCA) to identify amino acid sectors (*i.e.* groups of evolutionarily covarying amino acid residues that are computationally predicted to share a common biochemical function) in the bioluminescent enzyme luciferase. Previous studies applying SCA to other classes of enzymes have used mutagenesis of amino acid positions to successfully assign biochemical function to amino acid sectors in diverse protein classes such as PDZ domains,⁴² serine proteases,⁴³ and chaperones.²⁴ Each of these analyses required the generation and characterization of a large number of mutant enzymes. Here, we propose to give each student in IBC a specific SCA-identified amino acid residue to mutate to alanine and to characterize. The research outcome of these experiments will be i.) generation of a large number of alanine mutants and ii.) initial biochemical characterization of sectors, which will be further verified and applied in the Leconte lab. The learning outcome of these experiments will be to i.) give students an early opportunity to participate in a genuine research experience and ii.) to familiarize students with how research projects progress.

Plan of action. We have compiled a ranked list of the amino acid positions that contribute most to the four sectors identified in the Research proposal. IBC has two laboratory sections containing 25-30 students in each section. Each section will receive a different sector and pairs of students will be charged with cloning and characterizing one enzyme over approximately ten of the fifteen laboratory periods allotted for the course. Students will be involved at all steps; they will design the primers for cloning (Week 1), perform all of the steps to clone and confirm the sequence of the mutant enzyme (Weeks 2-5) and to express the protein as well as controls (Week 6). Students will perform several characterization assays on lysates to determine which properties, if any, were impacted by the alanine mutation (Week 7-10). At the conclusion, the students will be asked to compare data from within the section and between the sections and, if appropriate, between years of the course. Analysis within the laboratory section will allow students to hypothesize whether assorted alanine mutations within a given sector tend to impact common specific biochemical parameters. Since the two laboratory sections will study different sectors, analysis comparing the sections will allow students to perform statistical hypothesis testing to determine whether one sector impacts particular biochemical properties more than others. At the conclusion of the course, students will write a formal report describing the genesis and characterization of their mutant enzyme as well as discussion of the class's data as a whole. We anticipate that at least four years of students in IBC will be needed to complete the analysis for luciferase.

Precedent. KSD has a strong culture of incorporating research into coursework; this community is expected to be a significant asset for this project. In particular, Emily Wiley will co-teach IBC (she teaches the Biology portion); Prof. Wiley has significant experience incorporating research into upper-division Biology classes and she is expected to be a tremendous asset in the development here (see letter of support). Personally, I have some experience with similar projects at KSD. In Fall 2013, I hosted seven students from the Scripps College Academy Math And Science Scholars program (SCA MASS), which provides opportunities and college preparation for young women with limited resources seeking to become the first generation in their families to attend college. I designed and executed a similar project (equivalent to the first 5 weeks of the proposed research) related to a biochemical question about DNA polymerases from my own research. The following summer, a research student in my group characterized the enzymes cloned by the SCA MASS students; the results of these experiments were included in a submitted publication from my lab. The program was successful

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in enabling the students to directly contribute to and experience contemporary scientific research. Notably, the students also largely benefitted from interactions with my student assistant. I noticed during this time that, in addition to the act of performing research, much of the value of an early research experience comes from mentoring relationships with older students, which inspired me to propose to have deliberate, thoughtful, and pervasive student involvement in the execution of this education proposal (see below).

PLAN OF PROCEDURE: CREATE AN ACTIVE COMMUNITY OF NEAR-PEER SCIENTISTS

Overview and rationale. An important part of an early career research experience is not only the experience of doing research, but also important mentoring experiences with both faculty and near-peer students (*i.e.* students 1-3 years ahead of students on a similar academic track). Interactions with near-peers can be highly impactful as students can more easily relate to these students than faculty. Importantly, these are also valuable experiences for the student mentor; it can be incredibly empowering to be considered an expert and mentor. **Here, we propose to intentionally create several mechanisms to foster networks of interactions between students of varying academic career stages.** We will intentionally create opportunities for the first-year students in IBC to interface with their research-active near-peers.

Plan of action. We will use funds from this grant to facilitate these interactions through several points. The most important area of contact will be through student research and teaching assistants (RTAs). Each year, two students will be chosen from the previous year's class to perform a dual role in continuing the research. Both students will i.) perform research in my lab detailed in the Research proposal over the school year and summer following their semester in IBC and ii.) serve as TAs for the two sections of IBC lab the following year. This will socially enrich the connection between the IBC lab research and the active research in my lab, which will reinforce that the lab is contributing to an active area of research. To further encourage this connection, RTAs will be responsible for presenting the research overview at the start of the semester. To foster connections, RTAs will be required to periodically host mentoring lunches, funded through this grant, for IBC students. In addition, we will seek other opportunities to incorporate student researchers in the department into the course through short format talks in class and lab. We will use small honoraria to have students discuss how they use the lab technique that we are doing that week in their own research, cementing the value of the technique beyond the class. Through these interactions with research active near-peers, students will be exposed to the culture of research and begin to imagine themselves as research scientists. It will also strengthen the perception that their lab training is valuable as a stepping-stone to future research. Further, it is a valuable experience for the student RTAs and presenters as it will give them the opportunity to develop communication skills.

Precedent. These types of mentoring interactions often occur informally on an *ad hoc* basis. Nearly every successful scientist can point to a number of influential near-peers in their early career. The unique aspect here is finding as many opportunities as possible to build these interactions with as many students as possible. With the former, *ad hoc* approach to creating these interactions, a few lucky students will get this type of mentoring. With this deliberate, focused approach to creating these interactions, we hope that **all students receive these types of positive, formative mentoring experiences.** This is particularly important for students from underrepresented groups who can be disproportionately omitted from these types of *ad hoc* mentoring experiences, but will be serviced effectively here.

DISSEMINATION AND IMPACT. The proposed experiments are a novel method to incorporate research into the classroom environment both because of the use of SCA and the intentional and deliberate focus on fostering a student-researcher community. Following assessment, we hope to disseminate our findings as well as our best practices to the broader scientific community through presentations at national meetings such as the American Chemical Society National Meeting and the American Society for Biochemistry and Molecular Biology, and publication in education journals such as the *Journal for Chemical Education* and *Biochemistry and Molecular Biology Education*. **It is essential to ensure that the broader community has the opportunity to benefit from both the scientific and educational research enclosed here; every effort will be made to do so.**

While this project has a finite length limited by the number of mutants needed to characterize the sectors, the project will have lasting impact beyond this initial study. First, the process of using SCA to create testable biochemical hypotheses in IBC is an approach that can be applied to a number of enzymes of high biotechnological value and which, if successful, will be used for enzymes other than luciferase for years to come. Second, the scientific data generated is expected to be of high utility for research into luciferases in my lab and by others. Finally, we are interested in developing the model of near-peer RTAs, which, if successful, may be applicable in many other related situations in our department and beyond.

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ASSESSMENT PLAN. *Define expected outcomes of your educational plan. How will your evaluation design provide information to improve your project as it develops and progresses? How will you determine whether your stated project objectives are being met according to the proposed timeline?*

Our learning objectives for this proposal are focused on both generally improving student attitudes toward science as well as increasing retention in science.

To assess student attitudes, we will use the Classroom Undergraduate Research Experience survey (CURE). This survey, developed collaboratively by faculty from Grinnell College, Hope College, Harvey Mudd College, and Wellesley College and funded by HHMI, quantifies student experiences and attitudes. CURE is particularly attractive because of its widespread use; this enables us to compare our student population to a broader range of students taking the survey, including those performing other types of undergraduate in-class research experiences or inquiry-based learning experiences, which can serve as a good comparison group. CURE is also advantageous in that it tracks demographics and learning styles, which are expected to help us assess and adjust our practices to ensure that we meet the needs of the broadest range of students possible. We will give the CURE survey pre- and post-class. We will compare our student survey results with other students who have taken the CURE survey, both in our department and elsewhere.

To assess retention in science of students enrolled in the course, we will actively monitor i.) college major ii.) the students seeking out research opportunities iii.) career choices of students after graduation. Importantly, this is information that we actively track for all of our students in our department, and the analysis of this will only require culling a departmental database. We will compare our student population to past years of students from IBC who have not had the unique laboratory experience proposed here. We will also compare our student outcomes for those of other students in our department and to publicly available data.

Identify departmental or institutional colleagues who might play a role in this educational endeavor (as mentors, collaborators, etc.) as appropriate and describe the role they will play.

Professor Emily Wiley is a national leader in bringing research into classroom environments. She has received a NSF CAREER award, been a co-PI on a NSF IUSE award, and has published extensively on bringing research into classroom environments. Prof. Wiley will co-teach IBC and will serve as a mentor on this project. I have included a letter of support from Prof. Wiley after the list of recommended reviewers.

Jennifer Hull is a staff member who works full time in assisting preparation and execution of AISS and IBC labs. She will assist in the setup and testing of the laboratory experiments in the education proposal.

LETTER OF SUPPORT. A letter of support from Marion Preest, Interim Dean of the Keck Science Department of Claremont McKenna, Pitzer, and Scripps Colleges is attached.

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LIST OF REFERENCES. Annotate the proposal with a list of references from the primary literature. Include all authors and titles. If more space is required, attach a maximum of one additional page. Use Arial 10 or 11 point font.

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