Rational design of multifunctional enzyme-like catalysts for assembly-line chemical synthesis

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Evaluation of how well the academic objectives of the proposal were met

The main objectives of this proposal was to publish our preliminary findings in peptide catalysis and then submit applications for external funding. Both of these objectives were accomplished during the grant period. In the Fall of 2017, we published our first paper on the development of our new enzyme-like catalysts (ACS Catal. 2017, 7, 7704–7708). This publication should serve as a springboard for additional publications in the area (on which we are currently working) and help ensure external funding for this project. During 2017-2018, we submitted 3 grant applications to the NIH to help support this project. These submissions have resulted on good scores, but that lie just outside the funding range. We currently have a pending grant application that we are optimistic will be funded in the coming year.

The second main objective for this project is to provide research opportunities for undergraduate students to help prepare them for graduate school. During the grant period, 5 undergraduate students have actively participated on this project. I meet personally with each student each week and discuss their project and the progress they are making. We also held a group retreat for 3 days in the summer of 2018 where we discussed projects, made plans for the year, and did other professional development activities.

Evaluation of the mentoring environment

The mentoring environment in my lab and on this project is geared toward helping undergraduate students have a positive and productive experience with research. Each undergraduate student is paired with a graduate student on a project who is principally responsible for training students in laboratory procedures. Each week, I meet with each undergraduate student and undergraduate to discuss their progress and work during the week. This helps ensure that each student is receiving the attention they need to continue to progress. I also hold weekly group meetings where students are expected to present their research progress to the group at least once a semester, and also present on recent literature publications on related topics. We regularly have group activities, including a 3-day group retreat in the summer. This year, we spent 3 days in Capital Reef doing team building activities (hiking), setting goals for the year, and doing other professional development activities (we all read and discussed “The productivity project.”). These activities are geared at helping students prepare for graduate studies in chemistry.

List of students who participated and what academic deliverables they have produced or it is anticipated they will produce

Millicent Campbell: Current Senior in Biochemistry. Millicent participated in all aspects of the proposal, including the synthesis of new peptide catalysts, their characterization, and their application to new catalytic reactions. She has worked on this project since joining my research group in 2016. As a result of her work, Millicent presented a poster at the National American Chemical Society Meeting in New Orleans in March 2018. Millicent also presented her work in an oral presentation at the Spring Research
conference at BYU in 2017 and in 2018. Millicent has recently begun working on a new modeling project with graduate student Jacob Parkman to help model the reactions catalyzed by our peptide catalysts. Millicent is currently preparing applications for graduate school in chemistry. We are currently preparing a manuscript on computational enzyme design on which Millicent will be included as a co-author.

Erika Weir: Erkia Weir is currently a junior biochemistry major in our department and worked on this peptide catalysis project during all of 2017 and for 1.2 of 2018. She participated in catalyst synthesis and catalysis. In 2018, she also attended the National Meeting of the American Chemical society in New Orleans, LA where she presented a poster on her work. Whe also attended the National ACS meeting in San Francisco in march of 2017, but did not present on that occasion. She is currently preparing for graduate school in chemistry.

Nathan Lyons: Nathan is currently a senior undergraduate in chemistry who worked on this project for much of 2017. He helped synthesize various new peptide catalysts and characterize their structure. He also helped test catalytic activity. We are currently preparing a peptide catalyst publication where Nathan will be included as a co-author for his contributions.

Shannon Smith: Shannon is currently a senior PD Bio major who joined this project in May of 2018. She has learned the basics of peptide synthesis and is currently working to synthesize new catalysts.

Jordan Tretbar: Jordan began working on this project in January of 2018. He works closely with Michal Kinghorn to synthesize and test new peptide catalysts.

Ryjul Stokes: Ryjul was a senior undergraduate who worked on this project during his senior year, including winter of 2017. He pursued an independent project where he designed and synthesized a new peptide catalysts and tested its catalytic activity. Ryjul is currently a graduate student at the University of California – San Diego.

Description of the results/findings of the project

During the project dates, we were able to finish and publish our first report in the area of peptide-based enzyme-like catalysts. This work was a proof of principle report that demonstrated that many of our ideas about how to mimic enzymes truly worked when conducted on our simple peptide catalysts. In addition to this first publication, I also had the opportunity to present this work at a Gordon Research Conference in 2017, the highest conference in our field. This work was very well received by colleagues in the field. During Fall 2017 and winter 2018, I also presented this work at 26 different universities and companies all over the United States, including Wisconsin, Michigan, Illinois, Princeton, Columbia, Stanford, Caltech, Scripps La Jolla, UC Irvine and others.

During the grant period, we have also begun to pursue a modeling project where we are learning to utilize the tools of computational enzyme modeling to predict the structure and activity of our catalysts. These efforts are providing valuable information about the optimal peptide structure that will enable the most efficient catalysis with our peptides. This new direction is leading to additional publications in the field and a new a training environment that allows students to gain experience in computational modeling of peptide structures.

We have also developed and submitted new external grant applications based on this work. We currently have a submission pending with the national institutes of health, for which we are optimistic we will obtain funding in the next year. This submission includes our preliminary publication work, the design of new peptide-based catalysts, and the new computational directions we are pursuing in the lab.

Description of how the budget was spent
Graduate Student Salary: The salary of Michael Kinghorn was covered during spring and summer of 2017. Michael was the principle mentor for each of the undergraduate students on the project. I also met with Michael and each student on a weekly basis to direct efforts and review the work accomplished.

Chemicals and Supplies: The cost of supplies and chemicals for this project was also covered by the grant funds.

Travel Funds: Funds were also provided for students to travel to a national chemistry conference to present a research poster on their work, as described above.

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