Example of a Golwater Scholarship application (short answers & essay)
LMU Student: Dillon Rinauro, 2018 Honorable Mention

Mr. Rinauro has granted ONIF permission to share his application materials with prospective LMU applicants, which includes his responses to the short answer questions and his research essay.

Please review [LMU’s Academic Honesty Policy](#), especially the section on plagiarism, before reading Mr. Rinauro's application materials. Do not share these documents without the express permission of ONIF or Dillon Rinauro.

One final note: Please adhere to the most recent Goldwater application instructions, including [formatting requirements for the research essay](#).

Please email fellowships@lmu.edu with any questions.
Career Goals/Professional Aspirations

In one or two sentences, describe your career goals and professional aspirations (see example below). This statement will be used in publications if you are selected as a scholar or honorable mention. I aspire to complete a Ph.D. in biochemistry so that I may conduct research on neurodegenerative diseases which are thought to be linked to various amyloidogenic proteins.

What are your career goals and professional aspirations? Indicate which area(s) of mathematics, science or engineering you are considering pursuing in your research career and specify how your current academic program and your overall educational plans will assist you in achieving your career goals and professional aspirations. I intend to obtain a Ph.D. in biochemistry, focusing on neurodegenerative diseases pathways such as Alzheimer's disease, Parkinson’s disease, and Huntington’s disease. I also hope to conduct research that critically analyzes protein aggregation in type II diabetes. Some doctoral research groups
that I hope to work with are the Miranker lab at Yale or the Ramamoorthy lab at the University of Michigan. Both labs study general models of amyloid formation in the aforementioned diseases using NMR, X-ray crystallography, and mass spectrometry. These labs will prove to be critical in my understanding of the mechanism behind such diseases so that I may begin to selectively investigate potential therapeutics.

To accomplish this goal, I have been conducting research for over two years on amyloidogenicity of islet amyloid polypeptide (IAPP) in type II diabetes. I have also investigated several compounds that would serve as potential inhibitors of the aggregation of IAPP and AB42. I have familiarized myself with the research of p53, a protein involved in cell-cycle regulation, which is suspected to similarly aggregate in cells. In January 2017, I began working on a collaboration project with Dr. Jeremy McCallum, who has developed over forty organic compounds that may have the potential to inhibit the aggregation of IAPP. I am also investigating the potential inhibitive properties of IAPP-variants on hIAPP. My current coursework will also assist me in achieving my career goals and professional aspirations by solidifying my background in amyloidogenic diseases, a field which is heavily rooted in biochemistry. Further, my experiences as a research student will be able to prepare me for graduate and professional work by allowing me to familiarize myself with the techniques and equipment necessary to develop a cure for these neurodegenerative diseases.
Upon completion of my Ph.D. in biochemistry, I plan to research methods of inhibiting the aggregation of AB42 in Alzheimer’s Disease, alpha-synuclein in Parkinson’s Disease, and polyglutamine in Huntington’s Disease. The purpose of inhibiting the aggregation of these proteins, rather than eliminate them entirely from the human body, is because their current monomeric function is unknown. Currently, no long-term treatment options exist for these diseases that directly target the underlying causes, only short-term drugs that merely mitigate the effects. With an aging population and increasing numbers of new cases, the importance of a drug that can treat this disease has never been more urgent.

Describe an activity or experience that has been important in helping shape or reinforce your desire to pursue a research career in science, mathematics or engineering.: My passion for the brain and the nervous system began when I started working at a retirement home during my sophomore year in high school. I worked in close proximity to the residents of The Willows Retirement Home, many of which suffered from Alzheimer’s and other neurodegenerative diseases. Having the opportunity to spend time with these residents, as well as with my own loved ones who have battled the disease, initially inspired me to work towards becoming a neurologist. However, it became evident to me later on that this was not the best way to aid those living with these detrimental conditions. My plan ultimately changed when I first met Dr. Moffet as I set foot on LMU’s campus for the very first time in April 2015. It was then that I was captivated by his
work using tea extracts as potential therapeutics for neurodegenerative disease. My plan was later solidified when I was offered a position in his lab, which was shortly followed by my acceptance into LMU’s Summer Undergraduate Research Program (SURP 2016). While Dr. Moffet ultimately made the decision to transition to research on type II diabetes, my experiences in his lab have been pivotal, as they have allowed me to better understand how amyloidogenic diseases occur. This is because I soon realized that the research being conducted and the knowledge learned from this experience, because of the similarities in amyloidogenic diseases, could be very easily applied to amyloidogenic diseases of the brain.

Goldwater Scholars will be representative of the diverse economic, ethnic and occupational backgrounds of families in the United States. Describe any social and/or economic impacts you have encountered that influenced your education - either positively or negatively - and how you have dealt with them. I am a working class, multiracial, gay male raised in a predominantly white, Christian community. I attended a high school where over half of the student population was economically disadvantaged and a third of the student population was an ethnic minority. While I was classified as one of these students, the vast majority of my friends were white and privileged. Like me, many of my friends were enrolled in several advanced placement courses; however, I nearly always found myself to be the only individual applying for financial
aid to offset the cost of AP exams.

In the classroom, I was (and still am) constantly faced with the model minority complex. As an Asian-American, I remember often being asked by my peers in my science and math classes, “why did you get that problem wrong? You’re Asian! You’re supposed to be the smart one.” These statements, while I admit were an attempt to acknowledge my abilities, deeply affected me. At first, I was discouraged and I became increasingly self-deprecating. After years of low self-esteem, I began using these pejoratives and feelings of economic disenfranchisement to my advantage by striving for near-perfection. What turned out to be a seemingly negative experience transformed into a positive drive that greatly improved my work ethic and my problem-solving skills. If not for this drive, which is still evermore present in my life, I strongly believe that I would not be pursuing a career as a medical scientist.

Research Activities

Research Activity #1: Investigation of Metal Cations

Starting Month: 01
Starting Year: 2016
Ongoing: No
Ending Month: 06
Ending Year: 2016
Average Hours/Week (Academic Year): 3
Average Hours/Week (Summer): N/A

Name of Project Mentor: David A. Moffet
Title of Project Mentor: Professor

Description of research. Include a discussion of your role in and contributions to the research and the skills you acquired by working on the project.: The purpose of this research project was to determine if transitions metals could inhibit the aggregation of IAPP. I first created 10 mM solutions of various metal cations such as iron, lead, tin, zinc, and nickel by dissolving 0.15 mmol of chloride salts in 15 mL of DI water. The aforementioned cation solutions were then mixed with a concentrated solution of hIAPP of 70 micromolar and would incubate the solution at 37 degrees C at 200 rpm. I measured fractions of the solution at 5-minute increments and recorded the maximum absorbance height. Ultimately, the project found that zinc, nickel (II) and copper (II) metal cations were strong inhibitors of IAPP. Prior research suggested these compounds inhibit the aggregation of human IAPP, thus no new cations were discovered. It is also noteworthy mentioning that the concentration needed to successfully inhibit the aggregation of IAPP was significantly higher than biological levels, and would thus be toxic to humans.

Do you or will you have Papers/Publications associated with this research project?: No

Do you or will you have Presentations associated with this research project?: 
Yes

If yes, how many presentations are associated with this work?: 1

Citation: Rinauro D, Hoying C, Palato L, Pilcher S, Burke M. Investigation of Metal Cations as Potential Inhibitors of IAPP Aggregation. Poster session presented at: 8th Annual Undergraduate Research Symposium, Loyola Marymount University; 2016 April; Los Angeles, CA.

Local, National or International: Local

Presentation type: Poster

Additional Research Activities

Research Activity #2: Construction of p53-mutant library

Starting Month: 05
Starting Year: 2016
Ongoing: No
Ending Month: 07
Ending Year: 2017

Average Hours/Week (Academic Year): N/A
Average Hours/Week (Summer): 20

Name of Project Mentor: David A. Moffet
Title of Project Mentor: Professor
Name of Project Mentor: Luisa Nogaj
Title of Project Mentor: Professor

Description of research. Include a discussion of your role in and contributions to the research and the skills you acquired by working on the project.: p53 is a well-known protein involved in preventing cancer; thus, it is often called “the guardian of the cell” because it is a central enzyme in cell-cycle regulation. If a malfunction occurs during mitosis, p53 starts a cascade that ultimately kills off that cell. Cancer biologists estimate that over 50% of all cancers have either an inactivated p53 or circumvented p53 in some way. p53 mutants may aggregate in the cell in some fashion. In this project, I connected the central domain of p53 to EGFP and inserted the most common cancer-causing p53 mutations via PCR. This was used as a screening system in order to establish a method to screen for aggregation propensity of p53 mutants found in naturally occurring cancers. The p53 mutants that aggregate will likely fluoresce green, whereas mutants that allow p53 to function normally will not fluoresce. This system can be used in the future to screen for drug candidates.

Do you or will you have Papers/Publications associated with this research project?: No

Do you or will you have Presentations associated with this research project?: No

Additional Research Activities
Research Activity #3: Synthesis of PGG Analogs

Starting Month: 01
Starting Year: 2017
Ongoing: Yes
Average Hours/Week (Academic Year): 2
Average Hours/Week (Summer): 20
Name of Project Mentor: David A. Moffet
Title of Project Mentor: Professor

Description of research. Include a discussion of your role in and contributions to the research and the skills you acquired by working on the project.

Do you or will you have Papers/Publications associated with this research project?: Yes
If yes, how many publications are associated with this work?: 1

Citation: Moffet D, Rinauro D, Palato L, Njoo E, Pilcher S, Menefee K, Tun A, Shapiro S, Jauregui B. 2018. Synthesis of PGG Analogs to Inhibit the Aggregation of IAPP.

Status: In Preparation

Do you or will you have Presentations associated with this research project?: No
If yes, how many presentations are associated with this work?: 1

Citation: Moffet D, Rinauro D, Palato L, Njoo E, Pilcher S, Menefee K, Tun A,
Shapiro S, Nossiff O, Jauregui B. 2018. Synthesis of PGG Analogs to Inhibit the Aggregation of IAPP. Poster session presented at: the American Society for Biochemistry and Molecular Biology; 2018 April 21-25; San Diego, CA.

Local, National or International: National

Presentation type: Poster

Additional Research Activities

Research Activity #4: Inhibitive Properties IAPP-variants

Starting Month: 10
Starting Year: 2017
Ongoing: Yes
Average Hours/Week (Academic Year): 5
Average Hours/Week (Summer): N/A
Name of Project Mentor: David A. Moffet
Title of Project Mentor: Professor

Description of research. Include a discussion of your role in and contributions to the research and the skills you acquired by working on the project.: With the research exploring the amyloidogenicity of islet amyloid polypeptide in animal species coming to an end, I have begun directing my attention towards the investigation of potential inhibitive compounds and molecules as a strong correlation between the aggregation of IAPP and the contraction of type II diabetes
appears to exist. This project, in particular, focuses on the effects of animal IAPP-variants in the presence of hIAPP. It is my and my professor’s belief that when IAPP-variants, or partial sequences thereof, are simultaneously present with hIAPP that some will only dimerize instead of forming toxic oligomeric cylindrin folds by interacting in a particular manner. The dimers theoretically will be non-toxic to beta cells and can more than likely be used as a therapeutic. In this research, I will conduct Thioflavin-T assays, atomic force microscopy assays, and MTT assays on hIAPP in the presence of animal IAPP-variants.

Do you or will you have Papers/Publications associated with this research project?: Yes

If yes, how many publications are associated with this work?: 1

Citation: Moffet D, Rinauro D, Palato L, Pilcher S, Menefee K, Tun A, Shapiro S, Nossiff O, Jauregui B. 2018. Inhibitive Properties of IAPP-variants on hIAPP. Status: In Preparation

Do you or will you have Presentations associated with this research project?: Yes

If yes, how many presentations are associated with this work?: 1

Citation: Moffet D, Rinauro D, Palato L, Pilcher S, Menefee K, Tun A, Shapiro S, Nossiff O, Jauregui B. 2018. Synthesis of PGG Analogs to Inhibit the Aggregation of IAPP. Poster session presented at: the American Society for Biochemistry and Molecular Biology; 2018 April 21-25; San Diego, CA.
Local, National or International: National
Presentation type: Oral

Absence of Research Experience

Other Activities

Organization: Chemistry Society
Organization Type: College/University
Role/Involvement: executive board member
Leadership Position: Executive VP 2016-2017, VP of Service 2017-Present
Length of Involvement: More than one academic year

Additional Other Activities

Organization: Ignatians Service Organization
Organization Type: College/University
Role/Involvement: Executive board member
Leadership Position: VP of Spirituality 2018
Length of Involvement: More than one academic year

Additional Other Activities

Organization: Curis Educatione Iluventutis
Organization Type: College/University
Role/Involvement: Executive Board Member
Leadership Position: Treasurer 2016-2017
Length of Involvement: More than one academic year

Additional Other Activities
Organization: Lions for Venice Family Clinic
Organization Type: College/University
Role/Involvement: Executive Board Member
Leadership Position: Reflections Chair 2018
Length of Involvement: Academic Year

Additional Other Activities
Organization: Associated Students of LMU
Organization Type: College/University
Role/Involvement: Executive Branch
Leadership Position: Director of Environmental Responsibility 2017-2018
Length of Involvement: Academic Year

Recognitions
Recognition: CRC Most Outstanding Freshman
**Type:** College/University

**Award Description:** Awarded to the most outstanding first year student out of approximately 300 students of Seaver College of Science & Engineering.

**Award Year:** 2016

### Additional Recognitions

**Recognition:** R. Michael Ziegler Award

**Type:** College/University

**Award Description:** A selective award that is given to one student each year majoring in either physics, chemistry/biochemistry, or the natural sciences. Selections are made by the dean of the Seaver College of Science & Engineering.

**Award Year:** 2016

### Additional Recognitions

**Recognition:** Arrupe Scholar

**Type:** College/University

**Award Description:** An award up to full-tuition given to the top 4 percent of students at LMU. Named for Fr. Arrupe, the long-time Superior General of the Society of Jesus whose vision of educating men and women for others has become the hallmark of Jesuit education.

**Award Year:** 2015
Additional Recognitions

Recognition: Student of the Year
Type: College/University
Award Description: Given to students within Whatcom County with the highest GPA and most rigorous coursework. Selections made by the Rotary Club of Bellingham, Washington.
Award Year: 2015

Additional Recognitions

Recognition: Ignatian New Member of the Year
Type: Community
Award Description: Awarded to a single new member out of 180 individuals who has demonstrated outstanding service to his or her organization and service sites.
Award Year: 2017

Accomplishments and Skills

Accomplishment/Skill (non-research): Alpha Sigma Nu Induction
Description: Alpha Sigma Nu is the only Jesuit Society that recognizes students who excel in scholarship and service. Students inducted must be the top 4% of their class.
Determining Amyloidogenicity of Islet Amyloid Polypeptide (IAPP) in Type II Diabetes for Animal Species

Introduction
It is estimated that 25.8 million children and adults in the United States have diabetes, with nearly 2 million new cases each year.\(^1\) While the cause of type 2 diabetes remains unknown, research has found that as the disease progresses, patients lose pancreatic β cells (the cells that produce insulin) with up to 45% loss of pancreas mass in severe cases of the disease.\(^2\) Researchers have also observed that in 95% of patients afflicted with type II diabetes, islet amyloid polypeptide (IAPP) is found as extracellular deposits of amyloid and fibers.\(^3\) For unknown reasons, IAPP accumulates in the pancreas, where it aggregates (collects) into a variety of oligomers and has been shown to be a toxic agent to β cells in vitro.\(^4\) Evidence thus suggests that IAPP aggregation may correlate with the ability of a species to develop type 2 diabetes. Extensive research has been conducted on the IAPP of mice and rats, and they are not known to aggregate; these two species do not develop type II diabetes. The IAPP of monkeys, humans, and cats has also been extensively researched and found to aggregate; these species do develop type-II diabetes. A list of animals that do and do not develop diabetes has been compiled (see Figure 1). In this research project, funded by the National Institute of Health, I am testing the hypothesis that such a correlation exists between the ability to contract diabetes and the propensity of IAPP to aggregate. I first did so by conducting an in silico study using TANGO software that predicts the likelihood of the IAPP-variant aggregating. I then conducted in vitro analysis by performing atomic force microscopy assays. Finally, as a future study, I will conduct in vivo assays on pancreatic β cells that measure cytotoxicity and mitochondria viability.

TANGO Software Analysis
To establish whether a correlation exists between amyloidogenicity (the culpability and extent to which the peptide aggregates) of IAPP and the propensity for an individual to develop type-II diabetes, I used TANGO software (amyloid aggregation propensity predicting algorithm; see Figure 2) to evaluate each animal IAPP-variant sequence. This software projected the propensity to aggregate based on the residues present. These predictions, while not perfect (for example, chicken/duck was shown to aggregate in Figure 5, but was assigned a lower score than dog, which did not aggregate) provided a quantitative estimate as to whether or not the organismal peptide will
aggregate. The computational predictions made through TANGO are largely consistent with in vitro results as well as prior research on the tendency of certain animal species to develop type II diabetes. This research suggests that the FLV (15-17 amino acids) region\(^5\) and the SNNFGAILSS (20-29 amino acids) region\(^6\) of the hIAPP (human islet amyloid polypeptide) peptide sequence are aggregate-prone. When the TANGO analysis was conducted, the same two distinct amyloidogenic residue sequences were computationally identified; however, it should be noted that the culpability of these to develop into amyloid aggregates differs across the various species of interest. These computational predictions from TANGO software, thus support prior research and are highly indicative that mutations throughout these regions can significantly reduce the propensity for IAPP to aggregate.

**Atomic Force Microscopy (AFM) assays**

Peptides for each IAPP-variant listed in Figure 1 were ordered from Watson Bio and allowed to incubate in a Tris buffer solution for one week. Peptides were suspended in Tris buffer at a final concentration of 70 \(\mu\)M and were allowed to incubate at room temperature for 7 days. Fiber formation was measured at day 5 and day 7 using an atomic force microscope. Three trials were conducted, which were consistent with each other and literature suggestions. Fibers were present on polar bear, cat, horse (Figure 4), and chicken/duck samples (Figure 5) by day 5. These organisms are also known to contract type II diabetes, which is consistent with the theory of amyloidogenicity. No fibers were present by day 7 for degu, cow, seal, sheep, or rat (Figure 6). These organisms are not known to contract type II diabetes which is also consistent with the theory of amyloidogenicity. Dolphin IAPP (Figure 7) was also shown to not aggregate. This figure is of particular interest because dolphins have been observed to have the ability to turn diabetic symptoms on and off, thus this finding may contribute to the mechanism behind how said species is able to do so.

**Future Studies**

Members of the Moffet lab and I have given oral presentations at the annual Southern California Conference for Undergraduate Research in 2016 and 2017, as well as the American Chemical Society’s National Exposition in April 2017. Moving forward, DNA collected from two elephant species, two camel species, and black rhino at the San Diego Zoo will be sequenced by Dr. David Moffet, Dr. Luisa Nogaj and myself. This stage is critical to the project because the sequence of the IAPP gene is unknown for these five species. IAPP variants for each species will be ordered, my peers and I will test the propensity for each IAPP-variant to aggregate while in the presence of Thioflavin T, a molecule that fluoresces in the presence of amyloid fibers. I will also conduct atomic force microscopy assays using the same protocol aforementioned. Finally, I will compare aggregation data produced in this experiment to literary research of subject species’ ability to contract type II diabetes. Once this research is collected and a correlation is
determined, future projects investigating the inhibitive properties of IAPP variants and organic compounds on hIAPP will be conducted. For example, compounds such as PGG are known to be strong IAPP-aggregation inhibitors. Thus other small, analogs of this compound may prove to be even better inhibitors of aggregation. The implications of the research discussed above may also suggest that other IAPP-variant peptides can be used to halt aggregation at dimers. If a compound or IAPP-variant is found to inhibit the aggregation of IAPP, while simultaneously increasing cellular viability, this data can be used to create a potential therapeutic for approximately 25.8 million individuals suffering from type II diabetes.

References: