



FALL UNDERGRADUATE RESEARCH FAIR

Information Booklet

Thursday, October 25, 2018
Jordan Hall of Science
University of Notre Dame



UNIVERSITY OF
NOTRE DAME

SCIENCE

College of Science – Fall Undergraduate Research Fair 2018

Welcome!

The purpose of this event is to provide science students with an opportunity to get many of their questions answered about undergraduate research. Not only about how to get more involved in research, but also how to get more out of the research experience itself.

Throughout and beyond the College of Science there are many different ways in which students can get involved in research. Often it's just a question of looking in the right places and being persistent in the hunt for the right opportunity. However, getting the right opportunity is also about getting as much information as possible from a diversity of sources. This could be as simple as a fellow student but there are many organizations, institutes, and centers on campus that are also more than willing to help a student find and support their research endeavors. Furthermore, there are many ways for students to get even more out of their research experience, through publishing and presenting their research to their peers.

Through a combination of listening to speakers, poster presenters, and representatives from various institutions, students should be able to get some ideas about how best to get started looking for research opportunities. Also, students should be able to see how they can add value to their research experience by participating in other related activities. The sooner a student begins the search, the sooner they will be able to start participating in undergraduate research and getting the most from that experience!

Thursday, Oct 25th, 2018

Jordan Hall of Science

Schedule and Table of Contents

		Page
6 - 7 pm	Undergraduate Research Opportunities in Chemistry – Jordan 101	
7 - 8 pm	Information Tables - Jordan Galleria	2-7
	Research Poster Presentations - Jordan Galleria	8-62
	Refreshments	
8 - 9 pm	Undergraduate Research Internship Information Night – Jordan 101	63-64

Information Tables

Advanced Diagnostics and Therapeutics (advanceddiagnostics.nd.edu)

[Advanced Diagnostics & Therapeutics](#) is a community of affiliated researchers who tackle a wide range of biomedical and environmental health through innovation, invention, and real-world applications. Each year, AD&T awards two undergraduate [Feinstein Institute for Medical Research](#) (FIMR) - [Precision Medicine](#) Research Fellowships. These fellowships are competitive awards given to highly qualified undergraduate and graduate students from Notre Dame that enable them to spend eight weeks in summer residence conducting laboratory and clinical research at the Feinstein Institute in Manhasset, New York. The fellowships are concurrent with FIMR's existing visiting scholars program, which takes place from approximately June 1 to July 31 each year. Each student receives a stipend to cover daily living expenses. The cost of transportation to and from FIMR and their home or campus is covered (within reason and subject to approval). The Feinstein Institute provides apartment housing on the institute's campus, which is a 30-minute train ride from New York City, at no cost to the fellows. These fellowships afford Notre Dame students an opportunity to experience hands-on research in a world-class setting. The summer 2019 application will open November 1st with an information session on Tuesday, November 13th at 6 pm in 141 McCourtney Hall.

Contact: Corrine Hornbeck (chornbec@nd.edu), Administrative Assistant

Center for Career Development (undergradcareers.nd.edu)

The Center for Career Development provides undergraduate students with career counseling and career development services, self-assessments, workshops, presentations for academic departments, career fairs, and mock interviews, in addition to other services. We encourage students to take ownership of their career direction, and be willing to devote the time and energy necessary to conduct a successful search for jobs, internships, fellowships, and/or the identification of graduate school programs. Students have the opportunity to utilize our online databases, including Go IRISH, to pursue postgraduate opportunities, sign up for interviews, and conduct career-related research.

Contact: Robyn Centilli (Robyn.O.Centilli.1@nd.edu)

Center for Nano Science and Technology (nano.nd.edu)

Notre Dame's Center for Nano Science and Technology (NDnano) promotes collaborative research in science and engineering. The Center's 70+ affiliated [faculty members](#) work to address unsolved scientific and technical questions with an aim to promote the greater good.

Each year, NDnano awards several paid fellowships to undergraduate students who will spend 10 weeks of their summer engaged in a research project mentored by one of the Center's faculty. To date, [more than 200 students](#) from Notre Dame and several other universities in the U.S. and abroad have participated in the program, gaining valuable research skills and experience. The application process for summer 2019 fellowships will open the first day of classes in January at nano.nd.edu.

Contact: Heidi Deethardt (deethardt.1@nd.edu), Administrative Assistant.

Flatley Center for Undergraduate Scholarly Engagement (CUSE, cuse.nd.edu)

CUSE has a mission to promote the intellectual engagement of Notre Dame students through (1) creating opportunities for undergraduate research, scholarship, and creative endeavors in all colleges by connecting students to resources such as faculty mentors, projects, funding, and venues for presenting and publishing their work undergraduate research and (2) encouraging and facilitating applications for national fellowships like the Rhodes Scholarship, National Science Foundation Graduate Research Fellowship, Truman Scholarship, and Goldwater Scholarship.

Contacts: Yvonne Mikuljan (urnd@nd.edu), Assistant Director of Undergraduate Research

Harper Cancer Research Institute (HarperCancer.nd.edu)

Investigators in the Harper Cancer Research Institute (HCRI) are dedicated to conducting innovative and integrative basic cancer research that confronts the complex challenges of cancer. HCRI utilizes an interdisciplinary approach to cancer research. Students in our labs work across scientific fields on project collaborations. Over sixty HCRI faculty members bridge the College of Science, College of Engineering, College of Arts and Letters, and the Indiana University School of Medicine-South Bend. Some of the research projects currently taking place on campus involve using nanotechnology to better target chemotherapeutics, searching for new cancer markers and targets, reducing side effects of chemotherapy, and developing less expensive and more accurate diagnostics. Research cures cancer.

Contact: Angela Cavalieri (cavalieri.2@nd.edu), External Relations and Special Events Program Coordinator.

Undergraduate Research Opportunity Program (urop.nd.edu)

The Undergraduate Research Opportunity Program (UROP) provides grants to students who wish to pursue independent research or creative projects. Together with the College of Science, UROP also offers the DaVinci Multidisciplinary Summer Grants for those students who wish to engage in research or creative projects that cross the traditional boundaries between the sciences and the liberal arts.

Contact: Karla Cruise (kcruise@nd.edu), Director of Student Programs.

Kellogg Institute for International Studies

The Kellogg Institute for International Studies engages an interdisciplinary community of scholars in research and education on the critical challenges of democracy and human development around the globe. Kellogg Institute student programs allow exceptional undergraduates to focus and develop their international interests and scholarly abilities. Research grants, fellowships and internships complement the Kellogg International Scholars Program, which matches students with faculty in a unique research perspective. Internships and fellowships provide undergraduates with hands on experiences in the developing world that can be transformative. Such encounters prepare students for the International Development Studies minor and for independent field research. Students can present their research at the annual Human Development Conference in the spring. More information about the Institute can be found at kellogg.nd.edu

Contact: Holly Rivers (hrivers@nd.edu), Associate Director, or Rachel Thiel (rthiel@nd.edu), Program Coordinator.

Minor in Sustainability

The Minor in Sustainability is open to Notre Dame students in all majors and include courses drawn from all five undergraduate colleges and the Law School. Through a multidisciplinary approach, the minor prepares students to serve as leaders in their communities - local, national, and international - by making constructive contributions to the development of more sustainable practices in their own personal and professional lives, the lives of others, and the lives of future generations. Through the Sustainability & Stewardship Alumni Network, we connect students with Notre Dame alumni in a wide variety of sustainability careers and assist students in identifying internships, study abroad programs, and graduate schools that match their interests. The minor also supports undergraduates, graduate students, and faculty who are interested in conducting research in sustainability by connecting them with relevant community partners, government agencies, and national and international research programs.

Contact: Rachel Novick (rnovick@nd.edu), Director.

Museum of Biodiversity (biodiversity.nd.edu)

The Museum of Biodiversity, located near the northern end of Jordan Hall, showcases the Department of Biological Sciences' extensive collection of fossils, amphibians, fishes, birds, mammals, and insects that have been collected over the last 150 years. As part of the museum, the herbarium preserves the scientifically important collection of dried and pressed plants of the Greene-Nieuwland Herbarium. There are many opportunities for undergraduate research projects including identification and organization of specimens contained in museum collections, development of databases of plants and animals and their distributions, identification of rare, endangered, or invasive species, and development of thematic displays. Projects can be supported by the Robert E. Gordon Museum of Biodiversity Undergraduate Research Support Fund.

Contacts: Barbara Hellenthal (bhellent@nd.edu), Curator, and Ron Hellenthal (Ronald.A.Hellenthal.1@nd.edu), Director and Emeritus Professor.

Nanovic Institute for European Studies (nanovic.nd.edu)

The Nanovic Institute for European Studies is committed to enriching the intellectual culture of Notre Dame by creating an integrated, interdisciplinary home for students and faculty to explore the evolving ideas, cultures, beliefs, and institutions that shape Europe today. We help students from the College of Science plan and conduct focused, original scientific research in Europe. We support your high-quality European internships in laboratories and other scientific settings and make it possible for you to immerse yourself in local languages, to live among Europeans, and to see the world from a different perspective. Our students return to Notre Dame transformed with a new sense of confidence, awareness, and maturity that helps them to succeed. For more information on the Nanovic Institute and our undergraduate grant programs, please go to nanovic.nd.edu, or contact Chris Stump.

Contact: Chris Stump (cstump@nd.edu), Student Coordinator.

ND Energy (Center for Sustainable Energy at Notre Dame, energy.nd.edu)

ND Energy is a University Research Center whose mission is to build a better world by creating new energy technologies and systems and educating individuals to help solve the most critical energy challenges facing our world today. ND Energy engages undergraduate students in energy-related research and educational opportunities through programs such as the Slatt Endowment for Undergraduate Research in Energy Systems and Processes, the Energy Studies Minor, and the Student Energy Board. These programs help prepare students to become successful leaders who will understand the complexities of society's energy challenges and make a difference in the global energy economy. Learn more at energy.nd.edu.

Contact: Anne Berges Pillai (apillai@nd.edu), Education and Outreach Associate Program Director, or Barbara Villarosa (bvillaro@nd.edu), Business and Communications Program Director.

Scientia (scientia.nd.edu)

Scientia, ND's own student-run Undergraduate Journal of Scientific Research, is looking for student reviewers and news writers for this year's publication. Reviewers should have some research experience and be interested in reading, critiquing, and commenting on student research writing. News writers can be from any discipline and must simply want to write about some of the important and interesting things happening in the College of Science.

Contacts: Ruby Hollinger (ruby.c.hollinger.2@nd.edu) and Eric Sah (eric.sah.2@nd.edu)

University of Notre Dame Environmental Research Center (UNDERC, underc.nd.edu)

Celebrating forty years of environmental education and research, UNDERC provides students with a unique opportunity to not only take part in hands-on field courses in environmental biology, but also the chance to gain invaluable experience in field research. UNDERC consists of two 9½ week, 3 credit summer programs. The first, UNDERC-East, is located on over 8000 acres of university-owned forest in northern Wisconsin and the Upper Peninsula of Michigan. The second summer of the program, UNDERC-West, takes place on the grasslands and montane forests of the Flathead Reservation in western Montana. Each course is composed of a set of modules (East: insect, forest, aquatic, and vertebrate ecology; West: environmental history tour, grassland/wildlife, montane, and Native American ecology) as well as an independent research project for each student mentored by a faculty member or graduate student. Admission to East is open to sophomores and above, while West requires previous participation in East. Apply by early November on the UNDERC webpage and decisions are announced in early December to enroll in the preparatory course (1 credit, Spring semester).

Contacts: Michael Cramer (mramer@nd.edu), Assistant Director-East, David Flagel (dflagel@nd.edu), Assistant Director-West, and Gary Belovsky (belovsky.1@nd.edu), Director.

Wireless Institute (wireless.nd.edu)

The Wireless Institute (WI) advances understanding and innovation of wireless technologies, applications, and policies to benefit a mobile connected society through industry collaborations. The WI engages faculty from the Departments of Electrical Engineering, Computer Science and Engineering, Sociology, Law and Finance. This is the second year of the Advanced Wireless Research Experience (AWaRE) REU program. AWaRE provides opportunities for undergraduate EE and CSE majors to experience hands-on innovative research alongside faculty and graduate students during the 10-week summer program.

Examples of last summer's projects can be found at <https://wireless.nd.edu/REU>

This year's deadline for application is February 2019.

Contact: Tiffanie Sammons (tsammon1@nd.edu), Administrative Assistant for more information.

Poster Abstracts

Progress Towards C5 Pleuromutilin Analogs

Alexandra Bodnar
Major: Biochemistry
Mentors: Sarah Reisman and Sean Feng

Antibiotic resistance is a continuously growing global threat. As a result, the development of new antibiotics is of the utmost importance. Isolated from *Clitopilus passeckerianus*, pleuromutilin is a secondary metabolite that exhibits impressive antibiotic activity both in vitro and in vivo against Gram-positive pathogens and mycoplasmas (minimum inhibitory concentration (MIC) against methicillin-resistant *Staphylococcus aureus* (MRSA) = 0.5 $\mu\text{g/mL}$, MIC against *Mycoplasma hominis* = 0.3 $\mu\text{g/mL}$). Reisman and co-workers recently completed the synthesis of pleuromutilin in 18 steps, enabling the flexibility and efficiency necessary to construct structural analogs of this natural product as potential antibiotics. The C10, C12, and C15 methyl groups reside in a hydrophobic pocket of the binding site, and variations at these positions may lead to tighter binding and therefore increased biological activity. Our group has focused on varying substituents at C5 position and we have implemented conformational analysis to determine which groups to vary at this position.

What inspired you to participate in undergraduate research?

I took organic chemistry as a freshman and was hooked. I love being able to work closely with graduate students and faculty who share the same research interests as I do.

How did you get your research position, and what preparation did you undertake for it?

I applied to the Amgen Scholars program in February of 2018. I reached out to my mentor in November of 2017 and gained her support for my application. I then worked with a graduate student in the Caltech lab to write a research proposal that I submitted when I applied to the Amgen Scholars Program. My two years of research experience at Notre Dame helped prepare me for this experience.

Where was your research experience located?

California Institute of Technology

What did you get out of your research experience?

My research experience solidified my desire to pursue a PhD in chemistry and introduced me to a different subfield of organic chemistry. I was also introduced to the world of biotechnology when our program visited the Amgen headquarters, where we toured several labs and listened to researchers talk about their work in industry.

The Effects of Single-Prolonged Stress on Nociception and Opioid Self-administration in Rats.

Kathy Casillas

Major: Neuroscience and Behavior

Advisor: Gregory Collins PhD, Department of Pharmacology, UT Health Science Center San Antonio

Posttraumatic stress disorder (PTSD) affects approximately 36 million individuals in the United States. The disorder is characterized by persistent mental and emotional stress occurring as a result of injury or severe psychological shock, and has been shown to be highly comorbid with chronic pain and drug abuse. The mechanisms that underlie these relationships are unknown. There are a variety of animal models that have been used to study aspects of PTSD but few of them have explicitly conditioned stimuli to the traumatic stress. The current study will use a single-prolonged stress (SPS) model of PTSD in conjunction with a 4kHz tone and a clove scent to investigate the effects of traumatic stress and stress-paired stimuli on pain sensitivity and sensitivity to the reinforcing effects of fentanyl in rats. The SPS procedure consists of a two-hour restraint period, 20 minute forced group swim, anesthetization by ether, followed by 7 days of isolation. One group of 16 rats (housed in pairs) will be used to compare mechanical (Von Frey) and thermal (Plantar test) nociceptive sensitivity before and after stress and control procedures. Another group of 16 rats (housed in pairs) will be trained to self-administer fentanyl prior to undergoing SPS or control procedures in order to evaluate the effect of stress and stress-paired stimuli on fentanyl's reinforcing effects. Post-SPS nociceptive sensitivity and fentanyl self-administration will be evaluated at the conclusion of the isolation period and again in the presence of the stress-paired stimuli, once the measures return to baseline, to determine if the effects of SPS are exacerbated by stress-paired stimuli of past traumatic stress. We expect that the rats who undergo the SPS protocol will exhibit increased pain sensitivity in addition to increased sensitivity to opioids in self-administration compared to control rats. These changes in sensitivity to pain and the reinforcing effects of opioids could account for the comorbidity of chronic pain and opioid abuse in individuals with PTSD.

What inspired you to participate in undergraduate research?

I enjoy asking questions that haven't been asked before and designing the experiments that will lead me toward the answers. Undergraduate research also provides me the experience needed to better discern what I wasn't in a postgraduate career.

How did you get your research position, and what preparation did you undertake for it?

I worked in a Family Studies lab throughout my sophomore year and enjoyed the translational research. I hoped to gain experience in a basic science research lab so I sought out summer opportunities to gain experience in new methodologies. I applied for an undergraduate research fellowship through an online application. After submitting an essay, letters of recommendation, and my CV, I was offered the position.

Where was your research experience located?

My research experience was located in the Department of Pharmacology at the UT Health Science Center at San Antonio.

What did you get out of your research experience?

I learned that research is a slow climb toward answering big questions and that discovery is more likely to come from "Huh, that's weird" moments than "Eureka!" moments.

Validation of a Platform for Immuno-profiling of Mouse Tissue Specimens using Image Analysis-Based Immunohistochemistry and Multiplex Immunofluorescence

Andre Catao

Major: Science-Business

Advisor: Edwin Roger Parra, Department of Translational Molecular Pathology, University of Texas MD Anderson, Houston, TX

Coauthors: Luisa Solis, Barbara Mino, Mei Jiang, Auriole Tamegnon, Lakshmi Kakarala, Tong Li, Jianling Zhou, Ignacio Ivan Wistuba,

Cell immune-profiling in mouse models is becoming an important tool to identify not only predictive markers for human response to immunotherapy, but also to characterize the tumor microenvironment and understand its importance in greater detail. Using the MHC Class I and II, T-cell lymphocytes are able to target pathogenic or cancerous cells. Seven antibodies were selected to create a panel: CD3 ϵ , CD4, CD8 α , CD44, FoxP3, Granzyme B and CK19, that are able to characterize the immune system in the tumor microenvironment. By validating these antibodies in immunohistochemistry(IHC) and immunofluorescence(IF) it was possible to obtain their optimal conditions. The goal was to build “mouse immune panels” with the use of multiplex immunofluorescence (mIF) in mouse paraffin tissues to generate an imaging data analysis system. With this system, we will be able to characterize and study the interactions between these immune cells and malignant cells in mouse models.

What inspired you to participate in undergraduate research?

I got my first start in research using automated RT-PCR for pathology purposes and thought it would be natural to continue in pathology and creating diagnostic tools.

How did you get your research position, and what preparation did you undertake for it?

I was accepted to the Interdisciplinary Translational Education and Research Training (ITERT) program at MD Anderson. I initially prepared by reading literature regarding topics the lab was conducting research on.

Where was your research experience located?

University of Texas MD Anderson, Houston, TX

What did you get out of your research experience?

I got to experience what it is like to work in a major cancer center and as well as make new friends who both go to Notre Dame as well as many other institutions across the country.

Forecasting Zika incidence using dengue surveillance data from Colombia

Henri Chung

Major: Biological Sciences

Advisor: Dr. Perkins, Department of Biological Sciences. University of Notre Dame

Coauthors: none

Effective public health response to infectious disease outbreaks stands to benefit from accurate forecasts. The recurring seasonal nature of vector-borne disease incidence in countries where diseases such as dengue are endemic has resulted in the use of time series to inform models for forecasting future disease incidence. However, time series analyses are limited in their ability to make accurate predictions when there is little or no prior data available, such as during the recent 2015-2016 Zika epidemic in Colombia. In this increasingly common context of a disease emergence event, data from diseases with similar ecology and epidemiology could be used to form a basis of prior understanding for forecasting the emerging disease of interest. Similar to Zika virus, dengue virus is transmitted primarily by the *Aedes aegypti* mosquito and has epidemiological characteristics, such as incubation period and duration of immunity, similar to Zika. Here, we fitted time series models to weekly dengue incidence data from 2007-2015 at the departmental level in Colombia to predict peak time, peak height, and cumulative incidence of the Zika epidemic during the 2016 season. Individual models and predictions were made for each department, accounting for geographic differences in transmission. We compared our predictions to Zika incidence data and categorized our results based on the strengths of seasonality in the data. Our results suggest that model performance was heavily dependent on the strength of seasonality in departmental incidence. Models fitted to data from departments with stronger seasonality performed better at forecasting peak height and cumulative incidence than those fitted to data from departments with more irregular seasonal patterns of dengue incidence. However, the models we used were unable to accurately predict peak week, irrespective of seasonality in a region. Our results show some promise for formalizing the use of data from historically endemic diseases in forecasting emerging diseases, but at the same time they highlight limitations about the contexts in which doing so may or may not be successful.

What inspired you to participate in undergraduate research?

“I wanted opportunities to apply material learned in class in interesting ways. I also liked the computational opportunities involved with research that weren’t available in my classes”

How did you get your research position, and what preparation did you undertake for it?

“I joined Perkins Lab in the fall of 2017. I had heard about some of his research from other students and was interested in participating. I was part of another computational biology lab concurrent with me joining Perkins lab and was interested in exercising research in the subject further. The previous lab had prepared me with some introductory skills required for this lab.”

Where was your research experience located?

“University of Notre Dame”

What did you get out of your research experience?

“I was able to learn from graduate students and post-docs in the lab about many different aspects of public health and computational biology. In total the lab boasts a tremendous amount of work between them which makes up a wide variety of research topics and I was able to learn a lot from all of them.”

The Effects of Molecularly Targeted Drugs on PD-L1 Expression in Breast Cancer Cell Lines

Elizabeth Cinquegrani

Major: Science Preprofessional

Advisor: Powel H. Brown M.D., Ph.D., MD Anderson Cancer Center, Department of Clinical Cancer Prevention, Houston, Texas

Coauthors: Jing Qian, Yanxia Ma

Triple negative breast cancer (TNBC), which lacks estrogen, progesterone, and Her2 receptors, presents a significant challenge for effective treatment due to the relative lack of targeted therapies. Immune checkpoints have recently surfaced as a promising realm of treatment. Tumor cells have been shown to express certain immune checkpoint molecules, whose role in regulating the immune system affects the immune response to those tumors. The specific immune checkpoint protein investigated in this project is programmed death ligand 1 (PD-L1), an immune checkpoint molecule that is expressed on some TNBC tumor cells and acts to decrease the immune system's anti-tumor properties upon binding to its T-cell receptor. Increasing PD-L1 expression acts to drive the inflammatory response to tumors through the recruitment of cytotoxic T-cells to the tumor site⁵. However, many tumors do not sufficiently express PD-L1, rendering them unresponsive to immunotherapy. The goal of this project is to identify drugs that can alter the expression of PD-L1 in TNBC tumor cells, allowing for targeted therapy against the PD-L1/PD-1 pathway. In this project, breast cancer cell lines were subjected to treatment with several drugs known to increase PD-L1 expression in order to establish a basis for future *in vivo* experimentation, as well as to prepare for the continuation of the wider drug screen.

What inspired you to participate in undergraduate research?

I have always been drawn to research because of the endless potential for discovery that exists when creativity and science come together. Breast cancer research specifically is a field with so much potential for advancement in treatment, and lab research serves as the driving force behind the birth of that progress.

How did you get your research position, and what preparation did you undertake for it?

I applied to the MD Anderson Summer Undergraduate Research Program after a representative from MD Anderson came to Notre Dame to talk about summer research opportunities. Thanks to the partnership between Notre Dame and MD Anderson, I, along with other students from Notre Dame, was selected to take part in the program. My time in Dr. Prospero's breast cancer research lab at Notre Dame, as well as the background knowledge gained from previous science courses, prepared me well for this experience.

Where was your research experience located?

MD Anderson Cancer Center

What did you get out of your research experience?

My summer research experience has truly been formative, not only to my knowledge of the research process, but also to my overall development into an individual prepared for success in my future career. I have developed a greater ability to think independently and critically, as well as to solve problems in the face of difficulty, skills that are invaluable to success in the medical field. Because of this experience, I now feel more confident as I face the challenges lining the road ahead, and I look forward to pursuing a future in medicine equipped with the knowledge and skills this summer research experience has instilled in me.

An epigenetic approach to understanding malignant peripheral nerve sheath tumors (MPNSTs)

Christina Del Greco

Major: Biological Sciences

Advisor: Jack Shern, Pediatric Oncology Branch, Center for Cancer Research, National Institutes of Health

Coauthors: Xiyuan Zhang

Malignant peripheral nerve sheath tumors (MPNSTs) are soft tissue sarcomas that present malfunction in the *NF1* gene. More than half of all MPNSTs present a loss of histone H3 lysine 27 trimethylation (H3K27me3) due to nonfunctional polycomb repressive complex 2 (PRC2), often due to a loss of the *SUZ12* and/or *EED* components. EZH2, an essential component of PRC2 that methylates lysine 27 on histone H3, is upregulated in MPNSTs from patients and cell lines regardless of the status of *SUZ12* and *EED*. Furthermore, MPNST cells that lack *SUZ12* exhibit fewer binding sites on the genome than their counterpart with wildtype *SUZ12*. This indicates that EZH2 could potentially have an additional function independent of PRC2. As a result, this study investigates the PRC2-independent function of EZH2 by localizing EZH2 within MPNST cells. Additionally, because this study emphasizes the epigenetics of MPNSTs, a number of drugs that target either an epigenetic regulator or a downstream target of H3K27me3 loss are screened in MPNST cells with or without the intact PRC2.

What inspired you to participate in undergraduate research?

“I was fairly certain that I wanted to go to graduate school, and figured that the best way to be sure was to get lab experience. I was specifically inspired to work at the NIH because while I want to get a PhD, I don’t want to work as a professor or in industry, so this was a great opportunity to experience what working in a government lab setting would be like.”

How did you get your research position, and what preparation did you undertake for it?

“I applied to the National Institutes of Health’s Summer Internship Program as soon as the application opened, as I was told it was a rolling application and that applying early would increase my chances, and received an interview and an offer from my research mentor in January. For preparation, I mostly read up on what the lab had published recently.”

Where was your research experience located?

“The National Institutes of Health in Bethesda, Maryland”

What did you get out of your research experience?

“I got the chance to work on a fascinating cancer research project in a laboratory setting with incredible funding and resources, which made me more excited about going to graduate school and getting to dive into a project for a longer period of time. On top of that, this experience really helped me determine that I want to narrow my scientific focus on cancer genetics!”

Synthesis and Characterization of a Platinum (II) Carbene Complex and Platinum (II) Carbene Radical Complex

Anthony P. Deziel

Major: Chemistry

Advisor: Vlad M. Iluc,

Dept. of Chemistry and Biochemistry, University of Notre Dame

A square planar platinum(II) carbene complex [$\{PC(sp^2)P\}^H PtPMe_3$] ($[PC(sp^2)H_2P]^H =$ bis[2-(di-*iso*-propylphosphino)phenyl]methylene) was synthesized through the dehydrohalogenation of [$\{PC(sp^3)HP\}^H PtCl$] in a microwave reactor. The *tert*-butyl substituted analogue, [$\{PC(sp^2)P\}^{tBu} Pt(PMe_3)$] ($[PC(sp^2)P]^{tBu} =$ bis[2-(di-*iso*-propylphosphino)-4-*tert*-butylphenyl]methylene) was synthesized via an analogous route. The nucleophilic nature of the carbene carbon was confirmed through DFT calculations and reactivity with HCl. Additionally, [$\{PC(sp^2)P\}^H Pt(PMe_3)$] was treated with one half of an equivalent of I_2 to generate a paramagnetic product, [$\{PC(sp^2)P\}^H PtI$]. The Evans method and EPR spectroscopy revealed that a one electron oxidation occurred at the carbene carbon, thus generating a persistent radical carbene.

What inspired you to participate in undergraduate research?

“I wanted to become more active in the chemistry community at Notre Dame, to get a taste of what graduate school would be like, and to get a unique experience of lab research that you cannot get from a lab course.”

How did you get your research position, and what preparation did you undertake for it?

“I became a member of the Iluc Group in the spring of 2017. I chose the Iluc Group after reviewing recent publications and finding that the chemistry done by the group was interesting and exciting. I sent an e-mail to Dr. Iluc and we discussed whether the group would be the right fit for me, and if I was the right fit for the group.”

Where was your research experience located?

“University of Notre Dame”

What did you get out of your research experience?

I got a much deeper understanding of chemistry, and also made some new friends! I learned more about the process of research, how to write scientifically, and what graduate school would be like.”

Investigating Patterns of the Gut Microbiome in Long-Tailed Macaques

Bailee Egan

Major: Biological Sciences

Advisor: Hope Hollocher, Dept. of Biological Sciences, University of Notre Dame

Widespread variation among gut prokaryotic microbiomes has led to the question of whether general patterns exist across these bacterial communities and whether these patterns are biologically meaningful. This study investigates two trends in gut microbiome research: the Firmicutes-Bacteroidetes ratio (F/B ratio) and the identification of enterotypes. The F/B ratio reflects a commonly observed inverse relationship between Firmicutes and Bacteroidetes, two predominant phyla linked to obesity and diet. Enterotype characterization has been proposed to classify gut compositions into three types, based on the bacterial genera *Prevotella*, *Bacteroidetes*, and *Ruminococcus*. The F/B ratio and use enterotypes have not been studied extensively beyond humans and captive animals, and current literature suggests that these results may not be representative of wild systems. Therefore, we characterize the gut microbiomes of wild long-tailed macaques (*Macaca fascicularis*) from Singapore using *16S* sequencing to examine the F/B ratio and enterotypes. We test whether changes in the F/B ratio are associated with distinct changes in community structure and diversity and identify taxa that strongly correlate to the F/B ratio. Enterotypes are generally assessed by clustering the samples and identifying taxa most strongly correlated each cluster. We test for the presence of the standard enterotypes within our macaques and also examine if alternative enterotypes exist to compare with other findings in humans and captive animals as well as in other wild systems.

What inspired you to participate in undergraduate research?

Because I am interested in computational biology, research in the Hollocher lab has helped me learn the tools and skills for entering this field. While some of skills are taught in upper-level courses, working on an independent research project is a much better way to acquire a skillset than performing a class project.

How did you get your research position, and what preparation did you undertake for it?

I have worked in the Hollocher lab since the fall of my sophomore year after applying for the position as a freshman. I applied to the COS-SURF for funding to be able to continue my work from the academic year.

Where was your research experience located?

University of Notre Dame

What did you get out of your research experience?

Not only have I learned numerous bioinformatics tools, I also have improved in my scientific writing, thinking, and presenting. Being engaged in research full-time during the summer has also allowed me to learn what a career in research would be like.

Molecular Cloning of a Fluorescence-Based Reporter Plasmid for Cell-Free Protein Synthesis

Mariana Ferre

Major: Neuroscience and Behavior

Advisor: Jose A. Rodriguez-Martinez, Dept. of Biology, University of Puerto Rico, Rio Piedras

Coauthors: None

Cell-free protein expression, also known as in vitro protein synthesis is a convenient and fast method for making proteins because it bypasses the need to culture living cells, which can be time and resource consuming. Among multiple cell-free protein expression systems available, the wheat germ extract system has become a popular choice for producing eukaryote proteins due to high yields and commercial availability. The goal of my work was to generate a fluorescence-based reporter plasmid to be used in a wheat germ based cell-free protein expression system. Because of its unique optical properties, the Green Fluorescent Protein (GFP) can be used as a positive control for the high-throughput synthesis of proteins by a cell-free system. To construct the reporter plasmid, I used a Gibson Assembly strategy to clone a GFP gene in a wheat germ extract compatible plasmid. The GFP gene was successfully cloned in two plasmids, bearing an hexahistidine tag on either the N-, or C-terminus of the GFP. Sanger sequencing was performed to validate our cloning strategy. After validation, we will use the reporter plasmid as a positive during the high-throughput production of eukaryotic transcription factors by wheat germ cell free protein synthesis.

What inspired you to participate in undergraduate research?

Throughout high school I had always been interested in research and was able to shadow researchers in the Clinical Research of PR, Inc., but it wasn't until this summer that I got the chance to do research of my own.

How did you get your research position, and what preparation did you undertake for it?

As I was researching different opportunities for summer, I came across Prof. Rodriguez-Martinez's lab with the help of another Notre Dame student. I was immediately interested by his subject of research (molecular recognition of nucleic acids) and emailed him about my interest, courses I had taken in college, including lab, and an attached resume. He replied and, once I got to Puerto Rico after my finals, I started working in the lab until August.

Where was your research experience located?

JARM Lab (University of Puerto Rico-Rio Piedras, San Juan, Puerto Rico)

What did you get out of your research experience?

When I began my research in JARM lab, I thought I would like research, but figured I would only work in the lab for a month. Nevertheless, working in this lab exceeded my expectations. After just a few short weeks, I had already learned about all the equipment and solutions in the lab and was introduced to my project, which I worked on for the remained of the semester. Throughout my work, my TA did not just tell me what to do; instead, he challenged me and gave me different readings and "assignments" related to my subject of research. This way, I learned about both the experimental procedures and the theory behind my research. Additionally, I learned about many the procedures used in lab, how to analyze data, and how to adjust certain protocols and research methods when I am lacking successful results. I quickly found a drive and passion for my work and was always eager to arrive to lab in the morning and continue working on the "puzzle" that was my research. In short, this past summer was one of academic and personal growth and I enjoyed my experience in research so much I ended up working for ten weeks instead of four.

THE EFFECTS OF SOCIAL INTEGRATION ON COGNITIVE FUNCTIONING AMONG OLDER ADULTS

Morgan Foley¹, Christopher Nguyen Ph.D.², Deborah Lowe, Ph.D.², John Linck, Ph.D.², and Jim Scott, Ph.D.² Major: Neuroscience and Behavior

Advisor: Dr. Deborah Lowe and Dr. Christopher Nguyen

¹Department of Neuroscience and Behavior, University of Notre Dame, Notre Dame, IN

²Department of Psychiatry and Behavioral Sciences, University of Oklahoma Health Sciences Center, Oklahoma City, OK

Introduction: The concept of cognitive reserve suggests that certain aspects of life experience like educational or occupational attainments, lifestyle factors, or participation in cognitively stimulating activities, may supply reserve that allows some people to cope with progressing neurodegenerative disease pathology better than others. Furthermore, perceived social support has also been linked to a positive relationship with cognitive functioning among older adults. This study explored whether perceived social support and/or social integration contribute to neuropsychological outcomes, beyond the effects of other established cognitive reserve factors.

Methods. A sample of 151 elderly patients completed a questionnaire exploring cognitive reserve factors as part of a comprehensive test battery at an outpatient neuropsychology clinic ($M_{age} = 71.4 \pm 7.4$; $M_{education} = 13.7 \pm 3.6$; 58% female). Perceived Social Support is defined as the belief that others would be responsive to one's needs through caring, validation, and/or providing information, assistance, or tangible resources. Social Integration is defined as the presence or absence of membership in groups, such as churches, clubs, and voluntary organizations.

Results: A hierarchical regression model revealed that after accounting for demographic factors (age, gender, education), mood, cognitive reserve (Bilingualism, Musical Abilities, Exercise) and social resources variables (Social Integration, Perceived Social Support, Satisfaction of Support, Number of Close Friends), only Social Integration significantly predicted neurocognitive functioning (Repeatable Battery for the Assessment of Neuropsychological Status Total scores; $\beta = .381, p = .008$).

Conclusion: Results confirm prior findings of a relationship between social integration and preserved neurocognitive functioning in aging. Implications are discussed.

What inspired you to participate in undergraduate research?

I am interested in research because I have been able to first-hand see what scientific research can do. My godmother's life was saved from a newly developed drug many years ago, and I now want to extend my knowledge to help others as well.

How did you get your research position, and what preparation did you undertake for it?

My mother worked for the Oklahoma City Veterans Affairs Hospital, so I received contact information of a chief neuropsychologist from her. I emailed him and inquired about any potential research volunteer opportunities. In order to prepare, I had to go through HIPAA training as well as IRB training, and I worked on my own excel skills.

Where was your research experience located?

My research was located at the University of Oklahoma Health Sciences Center Outpatient Neuropsychology Clinic.

What did you get out of your research experience?

My research experience was within the context of an outpatient hospital, so many skills I gained were very unique to my experience. I gained professionalism by working in a real-world work environment, and I gained exposure to the clinical setting. Each week, I sat in on a "hot-seat" type lecture with neurology residents, where I was able to see what my future might hold if I continued on the pre-med track. Finally, I gained two mentors who were personally invested in my future in research at Notre Dame and are willing to help me if I were to need anything.

The Effects of Lysophosphatidic Acid and Fatostatin in Regulating SREBP1 Expression/Activation in Ovarian Cancer Cells

Emily Franz

Major: Biochemistry

Advisor: M. Sharon Stack, Harper Cancer Research Institute, Department of Chemistry and Biochemistry

Coauthors: Jing Yang

In ovarian cancer (OvCa), the leading cause of death from gynecological malignancy, a unique mechanism of intra-abdominal metastasis is observed in 80% of women at the time of diagnosis. Obesity and excess accumulation of adipose tissue are known risk factors for several types of cancer progression, including high grade serous ovarian cancer (HGSOC). A link between increased body mass index and enhanced ovarian cancer risk is supported by meta-analyses. Our recent study of tumors grown in mice on control diet relative to western diet (40% fat) showed a striking increase in nuclear-localized sterol regulatory element binding protein 1 (SREBP1) and increased intracellular lipid content. As a master transcriptional regulator of *de novo* lipogenesis, SREBP1 can induce metabolic reprogramming of tumor cells. SREBP1 is synthesized in the ER and transported to the Golgi via SREBP cleavage-activating protein (SCAP), where it undergoes proteolysis. Mature SREBP1 is released from the Golgi, translocates to the nucleus, and binds sterol regulatory elements to activate expression of target genes. Lysophosphatidic acid (LPA), a lipid mediator involved in proliferation, migration and invasion of cancer cells, is highly expressed in ascites of ovarian cancer patients. LPA treatment of ovarian cancer cells enhances lipid accumulation, induces translocation of SREBP1 into the nucleus, and regulates SREBP1-responsive genes, which suggest that LPA plays a role in regulating tumor *de novo* lipogenesis through activation of SREBP1-regulated transcriptional pathways in ovarian cancer cells. We further examine the effect of interference with SREBP1 processing by small molecule inhibitor—Fatostatin. Fatostatin binds to SCAP, inhibits the ER-Golgi translocation of SREBP1 and prevents the processing and maturation of SREBP1. Fatostatin also inhibits ovarian cancer cell growth. Our investigation would provide critical insight into the obesity risk factor associated with OvCa metastasis through the role of SREBP1, and provide a novel target for clinical cancer treatment strategies.

What inspired you to participate in undergraduate research?

“I love the problem-solving nature of research and its ability to provide answers that further scientific knowledge and provide insight into the treatment of diseases such as cancer.”

How did you get your research position, and what preparation did you undertake for it?

“I joined Stack lab in 2017 after being mentored by one of their graduate students. Through the support of the HCRI Summer Undergraduate Research Fellowship and the Center of Ethics and Culture Sorin Fellows Summer Grant, I was able to continue this research over the summer.”

Where was your research experience located?

“The Harper Cancer Research Institute at the University of Notre Dame”

What did you get out of your research experience?

“I gained both intensive lab experience and a strong appreciation for the hard work, methodology, and impact of scientific research. This and the Stack lab community further stimulated my aspirations of attending graduate school after graduation.”

Mucus Production and Regulation in Idiopathic Pulmonary Fibrosis

Samantha Garcia

Major: Neuroscience and Behavior

Advisor: Dr. David Schwartz, Chair of the Department of Medicine, University of Colorado Anschutz Medical Campus

Coauthors: Evgenia Dobrinskikh, Ivana Yang, David Schwartz

Idiopathic Pulmonary Fibrosis is the most common and severe interstitial lung disease characterized by progressive fibrosis of the pulmonary interstitium that affects 5 million people globally. While its pathogenesis is not completely understood, primary risk factors were found to include smoking and the common gain of function promoter variant MUC5B rs35705950, playing a role in proliferating fibroblasts in which it is morphologically classified as a usual interstitial pneumonia. IPF patients are more likely to have cough-related symptoms with the MUC5B promoter variant, and express 14.1-fold more MUC5B than unaffected control. MUC5B overexpression results in chronic mucus hypersecretion and accumulation in the peripheral airspace, which in turn impairs mucociliary transport, results in mucus adhesion in the bronchoalveolar region, and consequently induces and potentiates chronic inflammation and injury. NEDD4-2 is an E3 ubiquitin protein ligase that ultimately regulates Na⁺ absorption through Epithelial Sodium Channels and Cystic Fibrosis Transmembrane Regulators. SPDEF is a transcription factor that regulates mucin-production (including MUC5B) and that proteins involved in regulating mucins. Immunohistochemistry staining for NEDD4-2 and SPDEF expression and distribution was detected on formalin-fixed, paraffin-embedded tissue sections from control lungs and IPF patient lungs, within each with or without the MUC5B promoter variant. Less NEDD4-2 signal was observed in IPF patients with MUC5B promoter variant rs35705950. NEDD4-2 is downregulated in the airway epithelial cells in the lungs from IPF patients. More staining of SPDEF was detected in airway epithelial cells and in the cystic walls in the lung tissues from IPF patients compared to airway epithelial cells in control patients. More SPDEF signal was observed in IPF patients with MUC5B promoter variant rs35705950. SPDEF is upregulated in the airway and hyperplastic epithelial cells lining the cystic walls in the lungs from IPF patients. Future directions include Immunofluorescent (IF) staining for NEDD4-2 and SPDEF co-stained with different epithelial cell type markers (SPC – type II cells, CCSP – Club cells, Ac-Tubulin – ciliated cells, etc.) on tissues from the same patients will provide a quantitative way to analyze their expression and distribution in control and IPF lungs.

What inspired you to participate in undergraduate research?

I love the process of creating a story from collecting data in research. It is so satisfying when even though your results are not as expected or hoped for, they overall contribute to developing a story about the big picture in question.

How did you get your research position, and what preparation did you undertake for it?

I got my research position by applying to the Colorado Undergraduate Summer Program (CUSP) at CU Anschutz Medical Campus. Out of 120 applicants, I was one of 15 accepted into this program. I prepared by doing some independent background research on pulmonary disease before I arrived in Colorado.

Where was your research experience located?

University Of Colorado Anschutz Medical Campus

What did you get out of your research experience?

An exciting summer in Colorado, new friends, and learning new research techniques. I also learned the dynamics of a collaborative lab environment, and got to attend a plethora of medical lectures that were part of program.

Implications of Biodiversity Loss: 3D Modeling Techniques to Determine the Rugosity of Coral Reefs

Madeleine Girgis

Major: Biological Sciences

Minor: Sustainability

Advisor: Dr. Laura Kloepper, Dept. of Biology, Saint Mary's College

Coauthors: none

Biodiversity is threatened in every biome on the planet in today's increasing climate, and marine environments are highly at risk. Coral reefs are especially sensitive, and are severely harmed by ocean acidification, pollution, and warmer water temperatures. Determining the rate of these reef ecosystems' decline is crucial in deciding how best to implement necessary changes. One way to determine the biodiversity and health of a coral reef is by measuring rugosity. Rugosity is a measure of surface roughness, and is used by marine biologists to determine a coral reef's biodiversity. As the rugosity of a reef increases, the potential for number of species able to live in that reef also increases. Therefore, higher rugosity translates to a higher biodiversity. In this study, three-dimensional (3D) modeling techniques were used in five regions of Banco Capiro Reef in Tela Bay, Honduras to study the changes in rugosity of the reef over a period of two summers. To generate a 3D model of a reef, a two by two meter PVC quadrat was laid over a section of reef. A GoPro video was taken over the quadrat and analyzed using PhotoScan and Rhinoceros software. The data was analyzed to determine the change in rugosity of the five regions of Banco Capiro over two years. A paired t-test was used to compare the differences in average rugosity between two years. There was no significant difference in rugosities calculated between the two years ($t = 0.2717$, $p > 0.05$). It is predictable that the rugosity of the reef would not change over the course of one year, as corals have very slow growth rates. Should the rugosity of Banco Capiro decrease in coming years, the implications would threaten a weaker reef environment to host biodiversity.

What inspired you to participate in undergraduate research?

"I know that I want to go to graduate school for marine biology, so research experience in the field is invaluable. Additionally, I love SCUBA diving and I couldn't pass up the chance to participate in an ongoing marine conservation study."

How did you get your research position, and what preparation did you undertake for it?

"I was a summer volunteer research assistant to PhD candidates during this data collection, and therefore had access to the data that I helped collect. I found the program online, and I conducted my own analysis using this data."

Where was your research experience located?

"Tela Bay, Honduras."

What did you get out of your research experience?

"I gained experience researching in the field that I want to pursue, confidence working alongside researchers, and practice analyzing and presenting data."

The New St. Andre Ion Beam Analysis Facility for Applied Physics at Notre Dame

Alec Gonzalez
Major: Physics

Advisor: Graham F. Peaslee, Dept. of Physics, University of Notre Dame
Coauthors: Emi Eastman, Briana Linton, Mallory McCarthy, John Wilkinson, Sean McGuinness, Asha Majumdar

The St. Andre 3MV pelletron accelerator became operational in March 2018. Summer 2018 was the first time the accelerator was run almost daily to achieve its mission to perform applied physics research. Currently, the main focus of this accelerator is to perform Particle Induced Gamma-ray Emission (PIGE) spectroscopy on a variety of targets to measure total organic fluorine. In this technique, an accelerated proton probes light target nuclei and the release of characteristic gamma rays from the target can be used to quantify the number of atoms present in the target. Because the beam current and tune varies daily, a set of fluorine standards were created in order to normalize results from day-to-day operation. Initially, standards were created by mixing cellulose and fluorine in specific mass ratios and compressing the mixtures into pellets. These standards were irradiated for three minutes apiece multiple times at multiple energies ranging from 2.2 MeV to 6.0 MeV. The raw data is analyzed by summing the background-subtracted counts of the 109-keV and the 197-keV gamma rays (characteristic of Fluorine-19) and dividing it by the total beam current (measured in microcoulombs) on target. The counts per microcoulomb of each standard are plotted against proton energy to deduce the detection sensitivity and to identify the optimal bombarding energy to run PIGE *ex vacuo*. Preliminary results will be presented together with initial beam energy calibrations, and the entire methodology developed in this project will next be applied to every other light element that can be measured by PIGE to provide publishable minimum detection limits for a wide variety of elements. Some examples of where total fluorine measurements of consumer products were measured will be presented as well.

What inspired you to participate in undergraduate research?

I am fascinated with accelerators, and I couldn't pass up the opportunity to learn how to operate one. I was also really interested in Dr. Peaslee's research because of its real-world applications.

How did you get your research position, and what preparation did you undertake for it?

In January 2018, I first spoke with Dr. Peaslee about joining his research group and possible research projects. A couple months later, he asked me to work for him in the summer, so I submitted a research proposal and the Notre Dame College of Science Summer Undergraduate Research Fellowship provided funding for my research.

Where was your research experience located?

University of Notre Dame

What did you get out of your research experience?

I learned how to operate and troubleshoot a particle accelerator. I also learned how experimental physics research works and how to work together as part of a lab group. Dr. Peaslee and the grad students in my group gave me great advice on graduate school and my future in physics.

Dragonfly Naiad Preference for Color and Luster in the Presence of a Predator

Amelia Grose

Major: Environmental Sciences

Advisor: Todd A. Crowl, Dept. of Biological Sciences, Florida International University

Coauthors: none

Horizontally polarized light attracts aquatic insects. Consequently, aquatic insects, including odonate (dragonfly) naiads, are drawn to water and shiny surfaces, which both polarize light. Aquatic insects' main predators—insectivorous fish—are also drawn to horizontally polarized light. Generally, movement and behavior of insects depends on predator presence. I investigated the effect of the presence of predators on odonate naiad behavior by placing insects in tanks with colored shiny and matte tiles. I recorded naiad position with and without insectivorous fish present. I hypothesized that the insects would move toward the shiny tiles without a predator present because of increased light reflection and toward the matte tiles with a predator present to offer more camouflage, and that they would generally prefer darker colors due to increased light reflection and camouflage. During the trials, I observed no preference in colors within the different odonate size classes, although there was a significant preference when comparing all of the naiads together. Overall, the greatest number of odonates moved to the green and black tiles. In tanks including fish, odonates showed no significant color preferences, although green and black were again most popular. The odonates also showed no preference for a particular luster—shiny or matte. The insects placed themselves in three areas of the tank—on the tiles, on the edges of the tiles, or above the tiles on the walls of the tank—instead of remaining on the tiles. Further study is needed to determine the effect size (instar level) has on changes in naiad behavior toward color and to elucidate more precisely the effect predators have on naiad movement.

What inspired you to participate in undergraduate research?

I have always been excited about discovering and learning, and my classes at Notre Dame (especially Aquatic Entomology and Ecology Lab) have encouraged me to pursue research.

How did you get your research position and what preparation did you undertake for it?

I applied to the UNDERC program before winter break my sophomore year, and I met with my assigned mentor to develop my project and prepare for the summer of research.

Where was your research experience located?

University of Notre Dame Environmental Research Center (UNDERC)

What did you get out of your research experience?

I learned how to develop my own research project from start to finish, including how to deal with setbacks in field research and how to write my own scientific paper. I also had an exciting summer learning about different aspects of ecosystems in an incredible environment with people who became my close friends over 10 weeks.

Advances in Micromegas design for use in the ND Cube, an Active-Target Time Projection Chamber

William P. Jackson

Major: Physics, Economics

Advisor: Dr. Tan Ahn, Department of Physics, University of Notre Dame

The Active-Target Time Projection Chamber (TPC) is a versatile tool for studying nuclear interactions and nuclear structure with the advantage of providing a thick target for low-intensity beams and good energy resolution from imaging charged-particle tracks. At Notre Dame, we are developing an Active-Target TPC called the ND-Cube. My research focused on the design of the Micromegas, the electrode array for this detector, an important piece of the ND-Cube. In this design process, I looked into different configurations of tiles to be used on the target, and designed the PCB using a Autodesk EAGLE, a dedicated PCB design program. The result of this design process was an electrode structure composed of hexagonal tiles, optimized for use in the imaging of charged-particle tracks. We will have this board fabricated, and a micromesh will be applied by CEA to complete the Micromegas. In the future, we will look into improving our current design to better fit the needs of future experiments, as well as other design variants I developed in this project for use in other important imaging situations.

What inspired you to participate in undergraduate research?

I was inspired to do research by the presentations we saw in a sophomore level seminar class, where I saw Dr. Ahn and many other present on their research. It seemed too good to be true that I could participate in such research as an undergraduate, and I became interested in the many different research groups in the department.

How did you get your research position, and what preparation did you undertake for it?

I got my research position by approaching Dr. Ahn after his presentation to our class and we talked about possible aspects of the ND-Cube I could work on. I then started to work in EAGLE, the main design program I would be using. I spent time in the semester leading up to my summer of research becoming familiar with both this program, as well as the different aspects of the project that would influence my design, such as components that were already fabricated.

Where was your research experience located?

I did my research at the University of Notre Dame in the Department of Physics.

What did you get out of your research experience?

I gained a lot from my summer spent at Notre Dame. I learned how to work independently toward a larger final product, as well as how to work within a team to solve problems as they arise in the research process. I gained priceless experience working in experimental physics, which I hope I can translate into other aspects of my time here at Notre Dame and beyond.

Hematopoietic Stem Cell Differentiation controlled by microRNA/E3 Ubiquitin Ligase Networks

Seok Hee (Jenny) Jang

Major: Science Business

Advisor: Richard Dahl, Department of Biological Sciences, University of Notre Dame

MiRNAs are small non-coding RNA molecules that function in post-transcriptional regulation of gene expression. MiRNAs are essential for the normal hematopoietic differentiation and function. The Dahl laboratory has identified the miRNAs of the *mirn23a* and *mirn23b* genes as essential for the maintenance and differentiation of hematopoietic stem and progenitor cells (HSPCs). Unfortunately, the exact mechanism of how these miRNAs direct hematopoietic differentiation of HSPCs is known. Analyzing RNA-seq data analysis of myeloid progenitors, natural killer cells, and macrophages derived from wildtype (Wt) and *mirn23a*^{-/-} mice, we identified putative targets. To verify targets western blots were performed with cell lysates obtained from Wt, *mirn23a*^{-/-}, and *mirn23a* overexpressing cells. This candidate approach identified several E3 ubiquitin ligases as potential targets, however we only observed TNFAIP3 (A20) being negatively affected by *mirn23a*. Additionally we also observed that *mirn23a* could decrease expression of the transcription factor *Ezh2* and cell surface protein *Sirpa*. Future experiments will examine how these miRNA targets effect HSPC differentiation and macrophage function.

What inspired you to participate in undergraduate research?

I wanted to acquire and be proficient in various laboratory skills that will be difficult to develop over the school year. Leukemia has been my primary interest in the field of research, so I was extremely delighted to study the mechanism of hematopoietic stem cell differentiation. In fact, I am glad that I am now able to be more efficient in the laboratory over the semester with the very skills that I have learned during the summer.

How did you get your research position, and what preparation did you undertake for it?

I have been a member of the Dahl Lab since the May of 2017. However, I began preparing for the summer research since the fall of 2017 by familiarizing myself with the most recent publications and how they relate to the current focus of the research. After learning the fundamental skills for tissue culture, western blot, RNA extraction, and qPCR, I was guided by Professor Dahl to write a proposal that focused on a specific skill to analyze various targets on the *mirn23a* miRNA cluster. The research funding over the summer was graciously provided by the Center for Stem Cells and Regenerative Medicine Summer Undergraduate Research Fellowship (SCReM-SURF).

Where was your research experience located?

Harper Cancer Research Institute at the Indiana University School of Medicine in South Bend, Indiana.

What did you get out of your research experience?

An exciting summer at South Bend, effective time management skills, and interdisciplinary skills. I have also learned how to conduct interdisciplinary research, write grants, and analyze various data from both western blots and qPCR. The summer research has not only opened up more opportunities for me to pursue after graduation, but also a solid foundation for my possible graduate studies.

Potential use of antimicrobial peptides conjugated to antimicrobial nanoparticles for orthopedic implants and other medical devices

Veronica Kalwajtys

Major: Biochemistry

Advisor: Shaun Lee, Dept. of Biology, University of Notre Dame

Coauthors: Margo Waters, Juliane Hopf, Prakash Nallathamby, Francisco Fields

This project investigated antimicrobial peptides (AMPs) conjugated to antimicrobial nanoparticles (ANPs) as a possible alternative antibiotic that could be used as a coating for orthopedic implants and other medical devices. The nanoparticles used in this project were made by the Nallathamby Lab. They consisted of silica, gold, and silver. Four different AMPs have been conjugated to the ANPs to assess whether these antimicrobial compounds would be effective when combined. Three of the AMPs used in this study are from a library of synthetic peptides that were designed by the Lee Lab and that were based on a synthetic bacteriocin called syn-safencin. The fourth peptide conjugated to the ANPs was designed by Weibing Dong et al., and it is a synthetic variation of chensinin-1, an AMP produced by the Chinese brown frog *Rana chensinensis*. The antimicrobial peptide-nanoparticle compounds (AMP@ANPs) were tested for antimicrobial activity and cytotoxicity to human cells to assess their potential to be used clinically. *S. aureus* USA300, *P. aeruginosa* FRD1, *C. striatum*, and *E. faecalis* were all tested in antimicrobial activity assays with the AMP@ANPs. All four bacterial strains tended to exhibit reduced growth when treated with the AMP@ANPs, especially the AMP@ANPs of the highest silver concentrations. Many of the AMP@ANPs also exhibit low cytotoxicity to HaCaT cells. The AMP@ANPs' effectiveness in inhibiting bacterial growth and their relative biocompatibility with human cells suggest that they could be used for many medical purposes. These compounds have potential to be used to prevent infections of orthopedic implants, dental implants, and wounds, just to name a few applications.

What inspired you to participate in undergraduate research?

"I am interested in the problem of antibiotic resistance, and I wanted to learn about the research process outside of a classroom setting."

How did you get your research position, and what preparation did you undertake for it?

"I have been a part of the Lee Lab since September 2017, and this past summer I worked with the Nallathamby Lab on the nanoparticle-peptide project that was a collaboration between the two labs. My summer research was funded by the Notre Dame College of Science Summer Undergraduate Research Fellowship."

Where was your research experience located?

"University of Notre Dame"

What did you get out of your research experience?

"I learned about the work that goes into making scientific discoveries, developed lab skills that will be useful to me in the future, and got to spend a great summer at Notre Dame."

Spontaneous mutations associated with Japanese encephalitis virus pathogenesis

David Kim¹, Joseph L. Goldhardt², Sang-Im Yun², Byung-Hak Song², Young-Min Lee²

Major: Science PreProfessional

Advisor: Susan Gursky

College of Science, University of Notre Dame, South Bend, IN

²*Department of Animal, Dairy, and Veterinary Sciences, Utah State University, Logan, UT*

Japanese encephalitis virus (JEV) is a member of the genus *Flavivirus* in the family *Flaviviridae*. JEV causes encephalitis in children and young adults and is prevalent in the Asia-Pacific region with new introductions recently detected in Europe. The viral genome encodes three structural and seven nonstructural proteins. There is no specific antiviral drug available for JEV, but several killed and live vaccines are commercially available in endemic areas, with the live vaccine SA₁₄-14-2 being the most commonly used vaccine. The highly attenuated SA₁₄-14-2 strain is derived from its wild-type parental strain SA₁₄. To better understand JEV pathogenesis, we created a series of mutants by swapping various genomic regions between SA₁₄ and SA₁₄-14-2 and examined the virulence of these mutants in mice. One of these gene-swapped mutants, whose genome contains the SA₁₄E gene in the genetic background of SA₁₄-14-2, had a level of neuroinvasiveness lower than that of SA₁₄. The goal of this study was to sequence the genomic RNA of this particular mutant. After isolating the RNA from the homogenized mutant-infected mouse brains, we were able to generate three overlapping cDNA fragments that span the entire viral genome. By sequencing these cDNAs and comparing its assembled full-length sequence with the parent, we noted three silent point mutations. Currently, we are sequencing more mutants to continue our analysis of this particular mutant's genomic RNA. Altogether, this data offers new information that helps us further understand how JEV causes disease.

What inspired you to participate in undergraduate research?

My primary motivation for participating in undergraduate research was that I wanted to start applying my education and skillset towards actual problems that exist in today's society (in this case, disease caused by viruses).

How did you get your research position, and what preparation did you undertake for it?

In order to receive this research position, I had to contact Dr. Young-Min Lee whom I had been briefly introduced to before and establish a position for the duration of the summer.

After confirming the position, I had to spend many hours completing both online safety modules as well as protocol training in the lab itself. In addition, I also had to familiarize myself with the lab's research topic by reading many of their scientific articles and papers.

Where was your research experience located?

This research experience took place at USTAR Building 650, Logan, Utah.

What did you get out of your research experience?

This research experience not only taught me how to perform various modern molecular cloning techniques but also how to work cooperatively with team members, be meticulous and precise in the lab, and how to think critically about problems.

Uncovering competitive mechanisms of tree competition with data assimilation

Marissa Kivi

Major: Applied & Computational Mathematics & Statistics

Advisor: Dr. Jason McLachlan, Dept. of Biological Sciences, University of Notre Dame

Coauthors: Ann Raiho, Dr. Jody Peters

Understanding competitive interactions between tree species is critical to accurately predicting how forest communities will adapt to future shifts in climate and land use. However, the complexity and extended time scale associated with these interactions limit our understanding of them. Using data-informed models, we worked to better understand the oak-maple dynamic at Harvard Forest in Massachusetts, where this interaction has been most well-studied in northeastern United States, yet is still poorly understood. In 1984, Dr. Craig G. Lorimer analyzed four decades of permanent plot records for nine locations at Harvard Forest and hypothesized that Harvard Forest would transition over time to become a red-maple forest. He attributed the transition to the success of a dense red-maple understory which would fill the small overstory gaps left by fallen oaks. Building upon Lorimer's approach, we assimilated statistically-estimated tree-ring forest biomass data into the LINKAGES model from 1962 to 1984 and then, in Lorimer-fashion, we forecasted forest composition at Harvard Forest from 1984 to 2009 and quantified the accuracy of his 1984 hypotheses. Using analyses of correlation coefficients, we determined the species parameters most significant to the resulting compositional differences found among 200 ensemble members. We found parameters affecting red oak canopy size and maximum age of red maple were most influential in determining if a forest would become dominated by red oak or red maple. From there, we examined differences in stand age, canopy structure, and climatic data among the different members to better understand those trade-offs happening between red oak and red maple in the different forest types. Our analysis of ensemble members dominated by red oak trees indicates that the majority of red oak's biomass in the model is supplied by large overstory trees that are not easily overcome by competitors, and that red oak trees are largely absent in the model's understory due to the species' limited regenerative processes. Therefore, our results illustrate the importance of canopy structure in oak-maple forests and reaffirm Lorimer's hypothesis that Harvard Forest will be dominated by red maple over time, as older red oaks in the forest reach their natural end.

What inspired you to participate in undergraduate research?

"I want to contribute to the scientific community's efforts to understand and combat the great environmental changes our planet is experiencing. Ecological research is the best way for me to apply my studies to my passions."

How did you get your research position, and what preparation did you undertake for it?

"I have been working in the McLachlan Lab on the PalEon Project since the fall of my freshman year at Notre Dame. Over the past three years, I have worked on a variety of different projects. However, for my senior year, I had really wanted to have an individual project in which I could combine all my favorite things: math, computer science, conservation, and ecology. I spoke with my advisor, and now, here I am!"

Where was your research experience located?

"McLachlan Lab at the University of Notre Dame"

What did you get out of your research experience?

"This research experience held many lessons for me that I had not expected. I learned the importance of goal-setting, the value of collaboration, the steps to writing an abstract, and how to present results. I found myself many times (happily) down the rabbit hole of scientific literature, and developed a passion for a forest I have never seen."

Fluoroquinolone Resistant E. coli for Protein Folding Assay

Matt Klauer

Major: Biochemistry

Advisor: Dr. Patricia Clark, Dept. of Chemistry and Biochemistry, University of Notre Dame

Coauthors: none

Ciprofloxacin, an antibiotic of the fluoroquinolone class, is one of the most commonly prescribed antibiotics in the world. However, its widespread use has led to rapidly developing bacterial resistance. QnrB1 is a newly discovered protein that confers quinolone antibiotic resistance to *E. coli* cells. For laboratory research, the protein was transformed into a tetracycline promoted plasmid, which allows for fine-tuned expression of the gene. The protein was isolated and characterized, and studied for its influence on cell growth. *E. coli* that expressed the gene for QnrB1 showed no difference in growth without the addition of a fluoroquinolone. However, under 200 ng/mL ciprofloxacin, cells producing QnrB1 were 95% resistant while cells without showed only 3% of original growth. The findings suggest that QnrB1 confers significant resistance to up to 500 ng/ml ciprofloxacin. The fluoroquinolone-resistant *E. coli* are now being used in assays to study the folding of QnrB1 protein. Future directions of this project are investigating the activity of a synonymous codon mutant of QnrB1. This mutant will form a QnrB1 protein with the same amino acid sequence as wild-type, but the synonymous codons cause a different rate of translation off the ribosome.

What inspired you to participate in undergraduate research?

My goal is to participate in pharmacology research and drug discovery. Undergraduate research was a great first step to learn about the research process.

How did you get your research position, and what preparation did you undertake for it?

I reached out to Dr. Clark at the end of my freshman year because I was interested in the idea of solving problems of how proteins fold. We discussed possible roles that I could fill in the laboratory, and she had an opportunity for me to shadow one of the graduate students. This summer, I took on my own project under the full-time COS-SURF grant.

Where was your research experience located?

University of Notre Dame

What did you get out of your research experience?

I got a lot of experience working full time in lab with my own project. It was a great taste of what graduate school research will be like for me next year. I learned how to juggle multiple projects at the same time.

Estimation of a predictive function for MMR vaccination behavior as a function of year and age

Sojung Koh

Major: ACMS

Advisor: Alex Perkins, Dept. of Biology, University of Notre Dame

Coauthors: none

Measles is a highly contagious viral disease that can potentially cause pneumonia, encephalitis, and even death. Measles transmission is currently on the rise globally and is recently facing situations of lower rates of vaccination. If such low rates persist, the increasing number of unvaccinated individuals will lead to worsening outbreaks and could possibly even lead to the re-establishment of endemic measles if vaccine coverage deteriorates to a large enough extent. We developed a model designed to predict the probability an individual has received at least one dose of MMR vaccine as a function to their age, the current year, and their demographic characteristics. We formulated this model as a bivariate B-spline hazard function in two continuous dimensions: year and age. Refinements of this model that depend on demographic characteristics were explored, with particular demographic features used in the model being chosen on the basis of model selection with the Akaike information criterion. The model was fitted to three datasets published by the Centers for Disease Control and Prevention that reflect surveys carried out in a subset of the population for infants, toddlers, and teenagers, mostly at the state level, and stratified as a function of demographic characteristics. The model's geographical detail provided insight about which parts of the country might be more susceptible to outbreaks and in need of higher vaccination coverage. The model we developed has implications for estimation of vaccination coverage for measles and helps extract nuanced information about vaccination behavior from publicly available data sources.

What inspired you to participate in undergraduate research?

"I have always been looking for a branch between the quantitative and qualitative aspects of medicine. I was interested in exploring this relationship through undergraduate research."

How did you get your research position, and what preparation did you undertake for it?

"I submitted a research proposal based on an extension of my academic-year research, and the Notre Dame College of Science Summer Undergraduate Research Fellowship provided funding for my research."

Where was your research experience located?

"University of Notre Dame"

What did you get out of your research experience?

"I learned much about the nature of researching and how it is possible to combine mathematics in order to make scientific inquiries. I was able to ask a lot of questions and cooperate with my lab members in order to obtain the greatest learning experience I could ask for."

Effects of the Fibrinolytic System in a Murine Model of Renal Fibrosis

Mackenzie Kraker

Major: Biochemistry, Theology (supplemental)

Advisor: Victoria A. Ploplis, Ph.D., W.M. Keck Center for Transgene Research,
Associate Director, Professor of Chemistry and Biochemistry, University of Notre Dame

According to the National Kidney Foundation, chronic kidney disease affects 30 million American adults, and millions of others are at increased risk. Acute renal tubular necrosis is a symptom of chronic kidney disease and, in this study, was induced by a high dosage of folic acid in a mouse model. In this study, the renal damage was initiated in three distinct genotypic mice with deficiencies in the fibrinolytic system: urokinase-type plasminogen activator deficient ($uPA^{-/-}$), plasminogen activator inhibitor-1 deficient ($PAI-1^{-/-}$), and wildtype (WT). The effects on the kidneys of each genotype were assessed, locally, through histochemical and immunohistochemical analyses. Initial quantification of fibrino(ogen) and collagen deposition demonstrated that, compared to $PAI-1^{-/-}$ mice, $uPA^{-/-}$ mice have increased levels of fibrin and collagen deposits which suggest a more compromised fibrinolytic system and kidney diseased susceptibility in $uPA^{-/-}$ mice. Initial analysis of renal tubule morphology via a semiquantitative scoring method determined that the $uPA^{-/-}$ and WT kidneys undergo more damage relative to $PAI-1^{-/-}$ mice, as demonstrated by a more severe vacuolization status. Additional morphological and gene expression analyses are ongoing to further elucidate the role of the fibrinolytic system in regulating renal damage.

What inspired you to participate in undergraduate research?

I wanted to apply the concepts and techniques which I have learned in my science classes in a hands-on way and hopefully make a medical impact with my research.

How did you get your research position, and what preparation did you undertake for it?

I have been a member of the W.M. Keck Center for Transgene Research since September 2017. I shadowed an upperclassman undergraduate researcher for my first semester in the lab since my project was similar to her research. I received a College of Science Summer Undergraduate Fellowship (COS-SURF) to fund my research this past summer and continue to work in the lab this school year.

Where was your research experience located?

W.M. Keck Center for Transgene Research at the University of Notre Dame

What did you get out of your research experience?

During the school year I am only able to come into the lab for a few hours a couple days a week, so I was able to make much more progress in my research working in the lab all day five days a week during the summer! I learned many valuable skills such as how to write proposals and research summaries, trouble shoot experiments, analyze and present data, and develop and execute a research plan. I am also grateful for the friendships formed with other undergraduate researchers working at the Keck Center this summer.

Development of a ¹³C labeling strategy to monitor lipid upgrading by the zooplankton *Oxyrrhis marina*

Krystyna Kula

Major: Biology

Advisor: Dr. Christopher Reid, Department of Science and Technology, Bryant University

Coauthors: Keyana Roohani¹, Amanda Montalbano², Tatiana Rynearson², Susanne Menden-Deuer²

1. Department of Science and Technology, Bryant University

2. University of Rhode Island Graduate School of Oceanography

Lipid molecules are fundamental to many biological systems, including marine ecosystems. These high yield energy sources can be used as biomarkers in assessments of marine food webs. Previous studies on changes in neutral lipid composition in the zooplankton *Oxyrrhis marina* during satiated and starvation conditions showed an accumulation of wax associated fatty alcohols as energy stores, which are mobilized for energy during periods of starvation. This project focused on the determination of a stable isotope labeling strategy for monitoring *O. marina* lipid metabolism. The baker's yeast *Saccharomyces cerevisiae* was used successfully as an alternative prey for the dinoflagellate. *S. cerevisiae* was labeled using carbon-13 sodium acetate as a carbon source. *S. cerevisiae* was grown to an optical density of 1.0 at 600 nm, corresponding to 10⁹ colony forming units, and lyophilized. *O. marina* was fed yeast dissolved in sterile filter seawater and monitored for three days to ensure feeding. The heavy carbon was used to track lipid progression through the organisms. Gas chromatography and FAME analysis were used to determine lipid carbon-13 incorporation by comparing samples grown in the presence and absence of the carbon-13 labeled acetate. Carbon-13 was successfully incorporated into the *S. cerevisiae* cells with a 53% (C18:1) to 95% (C15:0) rate of incorporation, and initial *O. marina* feedings showed carbon-13 incorporation in lipids. Continuation of the characterization of lipid metabolism in marine ecosystems can lead to a better understanding of trophic upgrading and better establish the method of using lipids as biomarkers in microbial predators.

What inspired you to participate in undergraduate research?

Going into the summer, I both knew that I liked biology but also that I did not want to become a doctor. I wanted to give research a try – I liked the idea being organized and performing an experiment that was a little different than anything anyone else had done before.

How did you get your research position, and what preparation did you undertake for it?

I applied to the summer program through the National Science Foundation! Once I found out what research I would be partaking in, I made sure I had at least a surface level of the topics and laboratory skills needed to be successful.

Where was your research experience located?

Bryant University in Smithfield, Rhode Island.

What did you get out of your summer research experience?

New knowledge about how real research is conducted and a more realistic view of what a job as a researcher would look like. Getting up and performing research for seven or eight hours a day is very different than going to biology or organic chemistry lab for a few hours each week!

Optimization of Temporal Imaging of Regulation of Mitotic Spindle Orientation by Matrix Metalloproteinase 3 (MMP3)

Mary Clare Lipa

Major: Biochemistry

Advisor: Laurie Littlepage, Department of Chemistry and Biochemistry, University of Notre Dame

Coauthors: none

Matrix Metalloproteinases (MMPs), a family of zinc-dependent endopeptidases that regulate the tumor microenvironment, are known to be crucial mediators in sculpting tissue architecture and MMP3, a specific member of the MMP family is often overexpressed in breast cancer. We previously found that MMP3 contributes to genomic instability in the mammary epithelium. To visualize the mechanism by which MMP3 alters cues from the microenvironment to cause these changes in mammary epithelial cells, we began to optimize the microscopy conditions used for temporal imaging of organoids in 2-D and 3-D with visualization of both DNA, the mitotic spindle, and the spindle's orientation. Primary mammary epithelial cell organoids from MMP3 HET/KO mice were isolated, transfected with CellLight™ Histone 2B-GFP, BacMam 2.0 to visualize the chromosomes and identify dividing cells, and red PKH26 to visualize cell membranes and to distinguish organoids from the extracellular matrix. Organoids and the epithelial cells derived from them were plated in Matrigel and imaged using time-lapse microscopy for 1-3 days. Optimal conditions for imaging of organoids used a 24-well glass bottom plate, adding 13.5 μ L/well of Histone 2B-GFP, and imaging every 15 minutes for 24 hours. Using 2-D time-lapse microscopy, the percent of mitotic cells was not statistically significant between epithelial cells isolated from MMP3 HET and KO mice. These optimized conditions next will be used in 3-D organoid cultures for time-lapse microscopy to elucidate the mechanism behind the genomic instability induced by MMP3 in vivo.

What inspired you to participate in undergraduate research?

I wanted to be able to apply the concepts I was learning in the classroom to a real project where I could potentially make a difference in someone's life.

How did you get your research position, and what preparation did you undertake for it?

I have been a member of the Littlepage Lab since January of 2017. The summer before freshman year, I volunteered at Loyola University's Cancer Clinical Trials Office and that exposed me to cancer research for the first time. This summer, I received the College of Science Summer Undergraduate Research Fellowship from the University of Notre Dame to fund my own research for the first time.

Where was your research experience located?

University of Notre Dame

What did you get out of your research experience?

This summer I truly got to experience how a lab works on a full time basis. Instead of just coming in for a few hours at a time and helping out a graduate student, I was in charge of planning my own schedule and accomplishing necessary tasks for my project, giving me a lot more confidence in my abilities as a scientist.

Merkel Cell Carcinoma (MCC) Cells Possess Features That Allow Evasion From Natural Killer Cell (NK) Cytotoxicity

Yanting “Raven” Luo

Major: Biological Sciences

Advisors: Dr. Derin, B. Keskin, Dr. Catherine Wu, and Phuong Le, Department of Medical Oncology, Dana-Farber Cancer Institute

Coauthors: none

Cancerous cells that express HLA Class I presenting tumor antigens may be targeted by Cytotoxic T-lymphocyte (CTL) for destruction. By downregulating Class I HLAs, cancer cells may become invisible to CTLs. However, the absence of Class I HLA alerts NK cells. The lack of Class I HLA-NK binding induces the activation of NKs, which drive cancerous cells into apoptosis through granzyme and perforin action. In the special case of Merkel cell carcinoma (MCC), a rare but lethal cancer of the sensory merkel cells of the skin, it is unknown how the cancer cells manage to avoid both CTL and NK cytotoxicity. We hypothesized that MCC may be avoiding immune response by producing inhibitory cytokines. In our discoveries, we confirmed that MCC is relatively resistant to NK despite downregulation of the expression of HLA Class I. However, we found that secreted inhibitory cytokines were not sufficient to induce this NK resistance. Future research aims to predict epitopes to study MCC interaction with CTL and find the reason behind the capacity of MCC to evasion.

What inspired you to participate in undergraduate research?

“I love building a system of knowledge and then conducting rigorous investigations to expand that knowledge system. Research is such a process. Biological research in particular allows me to explore the mechanisms of disease and the intricacies of living organisms.”

How did you get your research position, and what preparation did you undertake for it?

“I applied and got accepted into the Harvard Immunology Undergraduate Summer Program, which is a Harvard Medical School summer program for undergraduate students interested in research and immunology. They placed me in Dr. Wu’s lab as I had mentioned in my personal statement. I had a brief, casual Skype interview with Dr. Wu and received directions from the postdoc Dr. Derin Keskin to do some pre-reading for my project at the lab. In addition, the summer program organized immunology overview lectures and guest lectures, which helped guide me into the field, since I had not taken an immunology class before.”

Where was your research experience located?

“Dana-Farber Cancer Institute, Boston, MA”

What did you get out of your research experience?

“I worked on an exciting cancer immunology research project in an established lab with a patient mentor in a small group; I met people of the robust life sciences community in Boston that came from all over the world, each of whom are incredible and offered me many words of advice and encouragement; I had the perfect introduction to immunology and grew further towards my goal of becoming an independent scientist.”

Aggressive Tibial Pseudarthrosis as Primary Symptom in Infant with Neurofibromatosis Type 1

Lucie Ly

Major: SSCP, Theology (supp.)

Advisor: Kasturi Haldar PhD, Barbara Calhoun, RN, MSN, PNP, The Boler-Parseghian Center for Rare & Neglected Diseases, University of Notre Dame

Coauthors: Madeline Zupan, Alec Biscopink

Neurofibromatosis Type 1 (NF1) is a rare autosomal dominant disorder characterized by multiple nerve and skin tumors termed neurofibromas. The disease is caused by an abnormality in the NF1 gene which regulates the protein neurofibromin, a tumor suppressor. Successful diagnosis of NF1 is hampered by the wide clinical heterogeneity of the symptomatology. Pseudarthrosis (PA) or false-joint is a particularly rare yet debilitating symptom of NF1. Tibial bowing and subsequent fracture in young children creates a section of bone loss with the appearance of a joint. Invariably to date, pseudarthrosis has been reported as secondary to NF1. In this study, we describe a manifestation of NF1 in a 4-month old female infant (case SS) in which PA was seen as the primary symptom, and in absence of an NF1 first-degree relative. Café-au-lait spots developed at 6 months subsequent to PA, but with number and size well below the National Institutes of Health criteria for NF1 diagnosis. To assess the SS case in the context of the local population as well as other population studies, a meta-analysis was conducted. To evaluate the continued uniqueness of pseudarthrosis as a primary symptom of NF1, a literature search was conducted, but no definitive cases were found. However, a recent case of a 4-month-old NF1 infant in Lithuania diagnosed with pre-fracture pseudarthrosis as the presenting symptom was discovered and is currently being further explored. The comorbidity of NF1 and pseudarthrosis was then examined as well as the pathology, prevention, diagnosis, prognosis, and treatment. Suggestions were made to revise the NIH criteria for NF1 either through additional diagnostic criteria or by a distinct NF1 diagnostic criteria for children. Future studies could further examine the success of combinatorial treatments and new diagnostic techniques such as quantitative ultrasound (QUS) as well as preventative therapies for pseudarthrosis.

What inspired you to participate in undergraduate research?

“I had never participated in anything like this before, and love broadening my horizons by learning new things in different ways. The experience intrigued me academically, but I was also drawn by the fact that my work would have real-life implications.”

How did you get your research position, and what preparation did you undertake for it?

“I was made aware of an opening in the Haldar lab that interested me, and was advised to take Dr. Haldar’s Rare and Neglected Diseases course which exposed me to many of the diseases I deal with in my work and taught me many of the skills I had to use in my research position.”

Where was your research experience located?

“University of Notre Dame”

What did you get out of your research experience?

“I was challenged to become a more independent scientist and to use my creativity and analytical skills to forward my project. This research experience and the knowledge I have obtained will certainly remain relevant as I pursue medicine in the future.”

Multi-resolution approximation and Wavelets in the analysis of economic and financial data

Yihong Ma

Major: Finance

Advisor: Daniele Schiavazzi, Department of ACMS, University of Notre Dame

Coauthors: none

Many phenomena in economics and finance are characterized by lack of smoothness and present jumps, discontinuities or sharp gradients. For example, in economics, regression discontinuity design (RDD) is often used to characterize the effects of introducing a certain policy, while jump process modeling of financial data is widely employed. On the other hand, multi-resolution analysis (MRA) and wavelets have received significant attention in pure mathematics from the late 80s. My research focuses on applications of multiresolution analysis to economic and financial data. I'm currently reviewing the math behind simple wavelets and the wavelet transform, and plan to apply MRA to practical problems, such as a study (Kristian L. Holden, 2016) on how textbook funding affects student test performance in schools.

What inspired you to participate in undergraduate research?

I have a great passion for computer science and statistics, and I'm particularly interested in their application to practical problems in economics and finance. I was inspired by this research, which combines theoretical aspects in function approximation to concrete applications in the fields where I would like to pursue my future career.

How did you get your research position, and what preparation did you undertake for it?

I am taking professor Schiavazzi's ACMS 40760 class on "Introduction to stochastic modeling" this semester. As soon as I found out that professor Schiavazzi had undergraduate research positions available, I talked with him and showed my interest.

Where was your research experience located?

University of Notre Dame

What did you get out of your research experience?

Even though I'm just at the beginning of my research path, I am learning to have a scientific approach to problems, I am improving my Python skills, I am acquiring new knowledge in parallel computing and experience using high performance computing resources through the Center for Research Computing. The research experience with professor Schiavazzi is providing a solid basis for my future career in graduate school.
a solid basis for my future career development.

Quantitative Analysis of The Effect of Inhibiting Drugs Targeting The REST/coREST Complex on Medulloblastoma Cell Line Survival

Kyle McGeehan

Major: Neuroscience and Behavior

Advisor: Dr. Vidya Gopalakrishnan, Dept. of Pediatrics, MD Anderson Cancer Center

Coauthors: none

Medulloblastoma tumors can arise due to the suppression of cell differentiation by a transcription factor (REST/coREST complex) allowing for uncontrolled cell growth and tumor formation.

Enzymes that are a part of the REST/coREST complex modify the histone tails to promote their compaction and prevent transcription from occurring. The question remains whether certain therapeutics can specifically target these enzymes in the REST/coREST complex preventing its function and promoting transcription killing the tumor cells. In order to analyze the therapeutic effects of two different drugs (Salarius 13 and MS-275), MTT assays were performed to measure the relative metabolic activity of various cell lines. Administration of Salarius 13 and MS-275 resulted in cell death from the tumor cells. The analysis of these therapeutics suggests that the REST/coREST complex can be targeted to prevent further tumor formation and actually promote tumor cell death. With further experimentation and increasing data, these therapeutics can be analyzed in pre-clinical trials to investigate their effects in an animal model (mice). Ultimately, the goal is to bring these therapeutics to clinic and help cause tumor recession in patients.

What inspired you to participate in undergraduate research?

I am very passionate toward science in general, but especially cancer research. My family and many other families have been impacted by cancer and I wanted to help develop the current understanding and possible treatments to alleviate the suffering.

How did you get your research position, and what preparation did you undertake for it?

I had applied for the summer undergraduate research program at MD Anderson Cancer Center, specifying my strong interest in brain cancer. To prepare for my position, I had read numerous background papers in the topics that I was going to be researching.

Where was your research experience located?

MD Anderson Cancer Center (Houston, Texas)

What did you get out of your research experience?

I got out a solid foundation on how to conduct research in a laboratory, knowing how to run experiments and utilize controls. In addition, I learned many different techniques used in research which helped me transition to my current research position at the University of Notre Dame.

Dietary Iron and Synaptic Development: An investigation of dietary iron manipulation on the formation of glutamatergic synapses at the neuromuscular junction in *Drosophila melanogaster*

Brooke McGill

Major: Neuroscience and Behavior

Advisor: Charles R. Tessier, Dept. of Medical and Molecular Genetics, Indiana University School of Medicine-South Bend

Coauthors: none

Iron is an essential co-factor for proteins involved in a wide array of biological processes including oxygen transportation, cellular respiration, DNA synthesis, and other metabolic functions. Iron is particularly critical in the brain. Abnormal iron levels are correlated with disorders ranging from Parkinson's and Alzheimer's to broad cognitive and motor development diseases. Iron deficiency is correlated with the reduction of glutamatergic synapses in the hippocampus of rodents, but studies disagree on whether there is increased or decreased branching of the neuron under conditions of iron deficiency. An invertebrate model provides a convenient and cost-effective way to study the effect of dietary iron on glutamatergic synapse formation. Invertebrates are well suited for genetic and cytological manipulation since many of the genes involved in iron metabolism are conserved and glutamatergic synapses are readily accessible at the neuromuscular junction (NMJ). The relationship between dietary iron and glutamatergic synapse formation was examined using dissections of the *Drosophila* neuromuscular junction, immunocytochemical staining, and fluorescence microscopy. Preliminary data shows an increase in the number of glutamatergic synapses formed at the NMJ in *D. melanogaster* under conditions of dietary iron deficiency, but no difference in axonal branching between iron-deficient and non-iron-deficient *Drosophila*. Data collection and analysis of synapse formation under altered dietary iron conditions at the *Drosophila* NMJ is ongoing to improve our understanding of the importance of iron in synapse formation.

What inspired you to participate in undergraduate research?

“I was very interested in developmental disorders because of volunteering with people with disabilities and learning about developmental disorders in my classes, and I wanted the opportunity to learn more about developmental disorders through asking and answering my own research questions.”

How did you get your research position, and what preparation did you undertake for it?

“My advisor sent out a flyer about Dr. Tessier's lab and when I saw that his lab studied fragile X syndrome, a developmental disorder associated with autism, I immediately emailed Dr. Tessier to inquire about working in his lab.”

Where was your research experience located?

My lab that I work in is located in the Mike and Josie Harper Cancer Research Institute in South Bend.

What did you get out of your research experience?

I have learned how to plan and organize a study in order to carry out an experiment that will yield publishable results. I have also learned what goes into writing a good grant and research article.

Genetic Testing in Hospitalized Children with ASD: Prevalence and Influences

Margaret Meserve

Major: Neuroscience and Behavior

Advisor: Dr. Matthew Siegel, Maine Medical Research Institute

Coauthors: Briana Taylor PhD, Christine Peura

Although the etiology of autism is still widely disputed and unknown, scientists and doctors have begun to include genetic testing as part of the recommended treatment for all diagnosed individuals. The purpose of this study was to examine the prevalence of genetic testing within a population of children with Autism Spectrum Disorder (ASD) who were hospitalized in specialized inpatient units across the country. The rate of genetic testing and the diagnostic yield from these tests were collected using parent reported data compiled through the Autism Inpatient Collective (AIC) and the Autism and Developmental Disorders Inpatient Research Collaborative (ADDIRC). Additional information was utilized to look for potential factors within demographics, medical history, family history and behavior that could influence access, referral and reporting of genetic testing. The results demonstrated that children seeking care in an inpatient psychiatric facility received genetic testing at a higher rate than the general ASD community (<40%), although the diagnostic yield for these tests matched the national standards (10-40%). The results also suggest that family medical history, child behavior, and demographic characteristics predict likelihood of genetic testing. Patients who were female, non- or minimally verbal, had a history of seizures, demonstrate high levels of stereotyped behaviors or had a family history of bipolar disorder were all significantly more likely ($p=0.00-0.018$) to have received genetic testing than their counterparts. Further research is needed to understand the exact pathways by which some families are referred and receive genetic testing while others do not.

What inspired you to participate in undergraduate research?

I have a lot of questions and like the chance to produce new knowledge. Also, I wanted to try my hand at independently studying a topic that I have great interest in.

How did you get your research position, and what preparation did you undertake for it?

I applied for the position after speaking with my mentor and arranging a time for me to come ask questions. The face to face interaction definitely helped make me a strong candidate. I prepared by reading the papers written by the AIC and ADDIRC in the past.

Where was your research experience located?

Maine Medical Research Institute and Spring Harbor Hospital

What did you get out of your research experience?

A poster that I'm very excited about and a project that I'm proud of. I also had the opportunity to shadow several different professionals in a field that I hope to make part of my career.

Decreased ovarian function is associated with chronic oxidative stress.

Jasmine Moawad

Major: Science-Business

Advisor: Animesh Barua, PhD, Dept. of Cell and Molecular Medicine, Rush University

Premature ovarian failure is a significant public health problem and is considered one of the factors of infertility in women. Failure of follicular growth and ovulation contributes to infertility. Although ovarian functions are controlled primarily by pituitary and gonadal hormones, epigenetic and individual lifestyle also contribute to abnormalities. Chronic inflammation and oxidative stress in the ovary are hallmarks of many diseases including cancers. We used laying hens as an animal model to determine if decreased follicular growth and/or reduced ovulation rates are associated with chronic oxidative stress and if so, whether dietary supplementation with antioxidants improves ovarian functions. Two experiments were conducted in this study. In the *exploratory* study, laying hens with normal ovarian function and decreased ovarian function were analyzed for follicle count, estrogen and progesterone receptor expression, and superoxide dismutase (SOD2) expression, a marker of cellular oxidative stress. In the *prospective* study, hens with decreased ovulation rates were supplemented with 2% ASH root powder in their diet. ASH (*Ashwagandha* or winter cherry, *Withania somnifera*) is an *over-the-counter* herbal supplement recommended for use as antioxidant. Compared with normal hens, hens with decreased ovulation rates showed fewer number of preovulatory follicles in their ovaries and more atretic/dead follicles were observed in their stroma. Western blotting indicated a higher intensity of SOD2 expression in hens with decreased ovulation rates, and gene expression assays showed weak expression for estrogen and progesterone receptors in hens with decreased ovulation rates. Hens with dietary ASH supplementation showed decreased SOD2 expression and improved egg laying rates. Results of this study showed decreased rates of ovulation is associated with increased oxidative stress in the ovary and dietary supplementation of antioxidants may improve ovarian functions including ovulation rates.

What inspired you to participate in undergraduate research?

“I wanted to have a more hands-on approach to learning. It was great to learn about the research process and see what goes into every big discovery.”

How did you get your research position, and what preparation did you undertake for it?

“I contacted a surgeon I knew at Rush University and asked him about research opportunities for over the summer. He was kind enough to put me in touch with his colleagues conducting research, and Dr. Barua told me he had an opening in his lab. I then met with Dr. Barua, and he gave me some reading materials in preparation.”

Where was your research experience located?

“Rush University”

What did you get out of your research experience?

“I learned to think more inquisitively. It’s not enough to know that something works, but it’s important to also ask why it works. I also gained a stronger interest to continue my research.

A time frequency analysis on pre-stimulus subsequent memory effects: healthy young vs. older adults

Kim Nguyen

Major: Neuroscience and Behavior

Advisor: Dr. Joshua Koen, Dept. of Psychology, University of Notre Dame

Coauthors: none

The efficacy of encoding processes is an important determinant for whether information can be subsequently recollected. Aging, in particular, is associated with a reduced ability to recollect prior events, and there is substantial evidence that these deficits in recollection result from reduced efficacy of encoding. Many studies have indicated neural differences at encoding states between young and older age groups. This has been demonstrated by the presence of age differences in subsequent memory effects (SMEs) – differences in neural activity during encoding associated with successful compared to unsuccessful recollection. There is also growing interest in whether age differences in successful encoding depend on neural activity before stimulus onset - pre-stimulus subsequent memory effects (preSMEs). A recent event-related potentials (ERPs) study (Koen et al., 2018, *Journal of Cognitive Neuroscience*) investigated age differences in preSMEs. During the study, 24 healthy young and older adults were presented with a task cue 2000 ms before each word, which signaled a semantic judgment (i.e. shoebox or manmade). After a 1500 ms delay, a word stimulus was briefly presented and participants were required to make the cued semantic judgment. During the test phase, participants made remember/know and source memory judgments to identify trials associated with successful versus unsuccessful recollection. The test responses were used to create ERP bins at study, associated with successful and unsuccessful recollection. ERPs elicited by the task cues were predictive of subsequent recollection (i.e., a preSME) in young but not older adults. However, ERPs are limited in that they are only sensitive to time- and phase-locked EEG activity. The purpose of the current study is to re-analyze the EEG data reported by Koen et al. using time-frequency analysis. Specifically, we will examine whether specific frequency bands (e.g. alpha, theta, beta) show preSMEs, and whether these effects differ between young and older adults. Power in the theta (4-7 Hz), alpha (8-15 Hz), and beta (16-30 Hz) will be estimated with Morlet wavelets for each participant, and group analyses will be conducted using permutation based statistics. We make three predictions: 1) young adults will score higher in the recollection test, 2) power increases in theta (4-7 Hz) frequency preSME bands will be seen in successful recollection performance in young adults, and 3) theta waves will not be modulated by memory performance in older adults in either conditions.

What inspired you to participate in undergraduate research?

I've always loved tinkering with new ideas and the lab portions of classes. I also knew that I wanted to go into neurology post-graduation, and so being involved in research has allowed me to learn more about the field of neurology!

How did you get your research position, and what preparation did you undertake for it?

I was previously in a different lab. Unfortunately, because the project was a longitudinal study, there would not be enough data for me to write a senior thesis for my honors program. My past research mentor and graduate students all recommended I contact Dr. Koen since his work included memory studies and ERP waves, something that I was familiar with in my past summer research internship, for my senior thesis. I emailed Dr. Koen during the summer and read his past papers to prepare for the research position.

Where was your research experience located?

University of Notre Dame.

What did you get out of your research experience?

I learned how to analyze EEG waves, detect artifacts, and have had a great time developing my senior thesis under the mentorship of Dr. Joshua Koen. I have also made new friends with the other lab members! My research experience has helped me apply my neuroscience and behavior knowledge and contribute to the field.

Utilizing a Bayesian Point Process Statistical Model to Determine Forest Fires from Charcoal Data

Luke Onken

Major: Biological Sciences and Theology

Advisor: Luke Onken, Dept. of Biological Sciences, University of Notre Dame

Coauthors: Aidan Draper, Elon University

Forest fires bring devastation to many people throughout the United States and the world. Better education of what causes these forest fires and different policies enacted by lawmakers provide for potentially less forest fires and better prevention. The model we are using is a Bayesian Point Process model created by Malcom Iitter, a post-doctorate researcher at Michigan State University. This model predicts changing fire return intervals over thousands of years using charcoal particles found in sediment cores of lakes. The model is run for each lake individually (univariate model) and for all of the lakes in the region collectively (multivariate model). The multivariate model provides cross-lake information on background intensity, but the univariate model alone allows us to calculate the changing probability of foreground and background fire and as well as the mean fire return interval. After validating that we could run and understand the model fit to an Alaskan data set, we applied and tweaked this model for a group of lakes in Minnesota collectively known as the Big Woods lakes, specifically Crystal Lake. The model for Crystal lake estimated high amounts of background charcoal, which could either correctly indicate high input of regional charcoal or the model could be attributing charcoal from frequent local fires to regional sources. We expect that running the multivariate model across the entire Big Woods dataset will provide better estimates of regional background charcoal of the region, and better constrain the foreground intensity of Crystal Lake.

What inspired you to participate in undergraduate research?

“Undergraduate research, especially in this field, can have an impact around the world. I want to be a part of that.”

How did you get your research position, and what preparation did you undertake for it?

“I have been a member of the McLachlan lab since August of 2017, and conducting research in this summer was a natural next step for me. After submitting a research proposal, the Notre Dame College of Science Summer Undergraduate Research Fellowship provided funding for my research.”

Where was your research experience located?

“University of Notre Dame”

What did you get out of your research experience?

“Research here at Notre Dame over the summer allowed to better understand what life as a graduate student might be like. Also, I truly felt like I contributed to the scientific com**Dural**

Insufficiency Presenting Intraoperatively in Adolescent Patient with Shprintzen-Goldberg Syndrome, A Case Report

Gabrielle O'Dougherty

Major: Neuroscience and Behavior, Music with Concentration in Violin Performance

Advisor: Dr. Kasturi Haldar, Dept. of Biology, University of Notre Dame

Coauthors: none

Shprintzen-Goldberg Syndrome (SGS) is an extremely rare connective tissue disorder characterized by craniofacial, skeletal, and cardiovascular deformities. Patients present with premature fusion of cranial bones in infancy (craniosynostosis), distinctive facial features, elongated fingers and limbs, umbilical and abdominal hernias, developmental delays, intellectual disability, and cardiac problems. In addition, individuals with SGS may have brain anomalies including fluid build-up in the brain (hydrocephalus); dilation of the lateral ventricles; and Chiari 1 malformation, a condition caused by the skull at the nape pushing brain tissue into the spinal column. Only 50-60 cases of SGS have been recorded in literature worldwide but the symptoms closely resemble those found in Loeys Dietz and Marfan syndrome making accurate diagnosis difficult without genetic testing.

My research explored a unique and complex manifestation displayed by a nine year old female with SGS discovered during a combination LeFort III and Monobloc osteotomy surgery for underdevelopment of the midface (midface hypoplasia). This surgery was complicated by a blood loss of 750 mL due to the patient's grossly insufficient dura. This was not detected preoperatively because the dura cannot be seen on CT scans. We examined alternative measures that can reveal dural issues preoperatively in patients with collagen disorders. Additional study is needed to assess the prevalence of this symptom in SGS and related collagen disorders.

What inspired you to participate in undergraduate research?

I wanted undergraduate research to be a part of my undergrad experience because I wanted to see how research questions get answered in the lab setting and I wanted to determine if I would enjoy a career in research. I am passionate about rare disease research because I have heard from patient families who have gone to great lengths to help their children suffering from rare diseases. It is a beautiful opportunity to participate in helping these families.

How did you get your research position, and what preparation did you undertake for it?

I got my research position by taking the class "Clinical Research in Rare and Neglected Diseases" with Barbara Calhoun and Dr. Kasturi Haldar. This class got me interested in working with rare diseases and I asked for a position doing research in the Boler-Parseghian Center for Rare and Neglected Diseases that summer.

Where was your research experience located?

"University of Notre Dame"

What did you get out of your research experience?

My experience has allowed me to become a skilled clinical researcher. I have learned how to assess and summarize medical reports, write case studies, and present my work. My research has also given me the opportunity to collaborate with patient families and their doctors.

1-Antitrypsin (Prolastin-C) reduces pain in a mouse model of sickle cell disease by decreasing neutrophil elastase activity

Sophia Pantano

Major: Biology

Advisor: Kalpna Gupta, PhD, Dept. of Hematology, Oncology, and Transplantation,
University of Minnesota

Sickle cell disease (SCD) is an inherited recessive disorder caused by a point mutation in hemoglobin leading to sickle shaped red blood cells (RBC) under low oxygen. The vasoocclusion resulting from the accumulation of these sickle RBCs in the blood vessels leads to acute pain which may be superimposed on chronic pain and inflammation in SCD. SCD is associated with increased neutrophil elastase activity. α 1-Antitrypsin (A1AT) is a serine proteinase inhibitor, or Serpin, that has an inhibitory effect on elastase. We found that A1AT reduces pain in sickle mice, and hypothesized that the underlying mechanism involves decreasing neutrophil elastase activity. We treated sickle (HbSS-BERK) and non-sickle (HbAA-BERK) mice with 80 mg/kg A1AT (Prolastin-C, Grifols Therapeutics Inc. NC, USA), an FDA-approved drug, through intraperitoneal injection daily for 3 days and examined the neutrophil elastase activity and central nociceptive mechanisms. We found elastase was upregulated in vehicle-treated HbSS mice compared to HbAA in plasma ($p < 0.002$), and lung ($p < 0.05$). Prolastin-C treatment of HbSS significantly reduced elastase activity in the dorsal root ganglia ($p < 0.03$), plasma ($p < 0.002$), and lung ($p < 0.001$). Our results demonstrate a novel role for A1AT as a therapeutic target for treating pain in SCD.

What inspired you to participate in undergraduate research?

I had no prior research experience before my participation in the Life Science Summer Undergraduate Research Program (LSSURP), but have always been curious about unanswered questions in the biological sciences.

How did you get your research position, and what preparation did you undertake for it?

I heard about the LSSURP at the FURF last fall. I submitted my personal statement and application for the program in the winter and was notified of my acceptance in late spring.

Where was your research experience located?

University of Minnesota- Twin Cities

What did you get out of your research experience?

I gained detailed knowledge about the specific topic I was researching as well as skills and experience regarding the research process in general. I learned how to conduct research and present my findings in a professional setting- skills critical to my future as a researcher. I also attended many seminars through my program involving career-development and professional networking.

Comparing hydraulic resistance to drought of tree species in the Northern temperate deciduous forest

Angela Pantell

Major: Environmental Science

Advisor: Ben Castro, Pontificia Universidad Católica de Chile

Coauthors: None

This study aimed to compare the hydraulic drought resistance capabilities of different tree species in the Northern temperate deciduous forest. Species differ in the ability of their xylem to resist embolism and hydraulic failure caused by the dramatic decreases in water potential during droughts. Climate change is predicted to increase the frequency of droughts in these areas of the Northern hemisphere, so having an understanding of the ability of individual species to resist drought is essential for anticipating how these forest communities could change in the future. We sampled three gymnosperm species and three angiosperm species using a vacuum apparatus to measure embolism and a pressure chamber to measure water potential. These measurements were used to construct xylem vulnerability curves to compare the water potential at which 50% of hydraulic conductivity was lost (Ψ_{50}) as well as the range between 50% and 88% loss of conductivity (hydraulic safety margins) of these species. We found that, contrary to our original hypotheses, the angiosperms had more negative Ψ_{50} points and larger hydraulic safety margins than the gymnosperms. This suggests that the gymnosperms could be at higher risk to drought-induced mortality caused by climate change than the angiosperms. This information can be used to ensure that the Northern temperate deciduous forest is managed in a way that protects threatened species and preserves the unique communities of these forests.

What inspired you to participate in undergraduate research?

I have always loved being involved in research and being able to ask and answer meaningful questions. I was very excited to perform this research to learn how a unique forest type is at risk due to climate change.

How did you get your research position, and what preparation did you undertake for it?

I applied to UNDERC through the standard application released every fall. We had a one-credit class in the spring semester to prepare for our summer research.

Where was your research experience located?

University of Notre Dame Environmental Research Center – East

What did you get out of your research experience?

I learned a lot about plant physiology and how this knowledge can be applied to understand human impacts on unique ecosystems. I got better at scientific writing and research as well.

Optimization of an artificial genetic switch mediated by DNA loop formation using TALE dimeric proteins

Will Phillips

Major: Biochemistry Minor: Theology

Advisor: Jim Maher, Dept. of Biochemistry and Molecular Biology, Mayo Clinic College of Medicine and Science

Coauthors: Nicole A. Becker, Tanya L. Schwab, and Karl J. Clark

The understanding and exploitation of gene regulation are relevant to studies of gene function and control of pathogenic genetic variants. The *lac* operon in *E. coli* has long been a model system for understanding gene control due to its accessibility and ease of manipulation. The tetrameric *lac* repressor protein (LacI) can bind at least 3 DNA operator sequences *in vivo*, one that overlaps the *lac* promoter region (O₁) and two auxiliary sequences at distal positions (O₂ and O₃). Repression mediated by O₁ binding alone can be significantly enhanced by the simultaneous binding of O₁ and one of the auxiliary operators to form a tightly-bent DNA loop. Evidence suggests that DNA looping enhances repression by increasing the local concentration of LacI at O₁ and by constraining the promoter inside the small DNA loop. In a previous study, Becker *et al.* devised a looping system for gene control where the LacI looping anchor is substituted with an engineered protein fusion containing a sequence-specific Transcription Activator-Like Effector region fused with a FKBP Dimerization domain (TALED). TALEDs were targeted to *lac* and engineered operator sequences. The dimerization domains, which control looping and gene repression, are under small molecule control. The present study aims to improve this system by systematically varying the relative orientation of TALED binding and the length of the intervening DNA sequence in the repression loop. Results indicate that the ideal spacing is near 171 base pairs and that O₂/O₂ constructs are superior for the operators spacings studied. Future directions include experiments varying operator spacing by 1 to 2 base pairs and implementation of the inducible looping system in yeast and mammals.

What inspired you to participate in undergraduate research?

Undergraduate research has been a great opportunity to build my critical thinking skills, to develop laboratory techniques, and to enjoy the process of discovery.

How did you get your research position, and what preparation did you undertake for it?

I applied to Mayo Clinic's summer undergraduate research fellowship online. My undergraduate research experience at Notre Dame with Dr. Paul Huber prepared me for the work I did over the summer.

Where was your research experience located?

Mayo Clinic Graduate School of Biomedical Sciences in Rochester, Minnesota

What did you get out of your research experience?

I learned many new techniques and had an opportunity to work very independently on a project. I also met many of the faculty and students at the graduate school and had the opportunity to hear many of them present their research. The experience reaffirmed my interest in a research-oriented career.

Vortex frames for velocity field denoising in 4D flow MRI

Sean Pietrowicz

Major: ACMS

Advisor: Daniele E. Schiavazzi, Ph.D., Dept. of Applied and Computational Mathematics and Statistics, University of Notre Dame

In recent years, the ability to measure time resolved, three-dimensional velocity fields in-vivo in patients has become a reality due to advances in MRI scanner technology. However, these three-dimensional velocity fields include noise and distortions that limit their diagnostic power. In an effort to minimize the effects of this “noise”, one must filter the data using algorithms that, for example, eliminate divergence and enforce conservation of mass. Finding and refining this algorithm is the focus of this research. I will start by reviewing existing methods proposed in the literature, I will compare their performance and propose a new approach based on a finite frame analysis of incompressible flow. This method will be applied to velocity fields acquired through Magnetic Resonance Velocimetry and Particle Image Velocimetry.

What inspired you to participate in undergraduate research?

I have enjoyed the theoretical aspects of my studies in the past, but I was looking for a way to take these concepts outside of lecture and apply them to real-world problems.

How did you get your research position, and what preparation did you undertake for it?

My research advisor, Professor Schiavazzi, reached out to students in ACMS 40760 to assist in his ongoing research of filtering three-dimensional velocity data. My preparation entailed reading my advisor’s previous research and gaining familiarity with the software necessary to model our data and perform further tests.

Where was your research experience located?

The ACMS department at University of Notre Dame

What did you get out of your research experience?

Although my research is still ongoing, I have already gained knowledge of *Visualization Toolkit* software and explored ACMS concepts in cutting edge physics-based applications.

Attenuation of Inflammation Results in Seizure Reduction and Neuroprotection in TNFR1 Knockout and Low Inoculum TMEV Model

Melissa Pirko

Major: Chemistry

Advisor: Charles L. Howe, Translational Neuroimmunology Lab, Mayo Clinic

Coauthors: Melissa T. Pirko¹, Hunter L. Olson¹, Erin Triplet, B. S.², Reghann LaFrance-Corey, M.S.², Charles L. Howe, PhD.²

Viral infections are one of the various key triggers to the innate immune response that can occur within the brain. Neuroinflammation, including activation of local microglia as well as recruitment of peripheral immune cells, is important in the progression of multiple neurological disorders. Epilepsy is a disorder characterized by recurrent, unprovoked seizures--abnormal neuronal firing in the brain--and also involves a substantial immune response, including recruitment of peripheral monocytes and local release of inflammatory cytokines. Over 50 million people worldwide are affected with the condition and suffer symptoms ranging from short-term memory loss to tonic-clonic seizures. Theiler's murine encephalomyelitis virus (TMEV) has been used as a mouse model for studying epilepsy with infected mice developing symptoms within three to seven days of infection (Stewart *et al.* 2010). TMEV is a single stranded RNA Picornavirus that is used as a very powerful model of encephalomyelitis within mice and can simulate the development of febrile infection related epilepsy syndrome and other seizure disorders. TMEV infection is followed by rapid recruitment and activation of monocytes and intrahippocampal release of TNF α . We have previously established that abrogation of the monocyte recruitment reduces seizure burden. The goals of the present study were to investigate whether TNF α leads to neuronal death and behavioral dysfunction and how the overall level of viral pathogen during an acute infection impacts the induced immune response and subsequent neuronal pathology. Mice were infected by i.c. injection with the standard dose of Daniel's strain (DA) TMEV or a low viral dose. We compared the subsequent neuronal loss and functional outcomes to a TNFR1 knockout line, in which the signaling from TNF α is prevented. Seizure burden was measured using the Racine scale of behavioral seizures. Hippocampal function was assayed using the Barnes maze task of spatial navigation. We quantified viral clearance in the low inoculum model with plaque assay, and measured inflammatory reaction through bead array.

What inspired you to participate in undergraduate research?

"I love asking questions and answering them in the lab. Also, I could not turn down the opportunity to synthesize small-molecules that kill tumors." "Ever since I was a child, I have always known I wanted to pursue a career in science, so I knew I would gain a lot from working in a research lab, especially at Mayo. I have also been interested in neurology as my dad was a neurologist who conducted MS research and had a similar focus as my PI, Dr. Howe."

How did you get your research position, and what preparation did you undertake for it?

"I was able to obtain my position through networking with Mayo Clinic researchers. I prepared for my position by filling out tons of paperwork and refining skills obtained in my lab classes and my undergraduate lab at Notre Dame."

Where was your research experience located?

"Mayo Clinic in Rochester, MN"

What did you get out of your research experience?

"I can't even begin to describe how much I've gotten out of my research experience! I've gotten a behind-the-scenes view of Mayo Clinic, how graduate students conduct research, and various lab techniques that I've been able to apply at the lab I work at in Notre Dame. My research experience reconfirmed my interest in research."

Modeling measles importation by passenger air travel

Marya Poterek

Major: Science-Computing

Advisor: Dr. Alex Perkins, Dept. of Biological Sciences, University of Notre Dame

Coauthors: Dr. Alex Perkins

Despite the elimination of endemic measles in the United States in the 1990s, the number of measles cases and outbreaks in the United States has begun to rise in recent years, as measles-mumps-rubella (MMR) vaccination rates in the US are declining and transmission internationally is on the rise. Measles is a highly infectious illness that can cause serious symptoms and even death in susceptible individuals, and cases imported to the US often result in large outbreaks that can be devastating to vulnerable populations. The majority of these imported cases reach the US via international passenger air travel through major metropolitan hubs. As a result, a significant proportion of US measles outbreak behavior can be modeled by connecting air travel data with location-specific measles transmission and prevalence statistics. This study sought to develop quantitative parameters for measles outbreak development in large US cities that are significant transit hubs, as influenced by case importation through plane travel. Assessing the probability of an individual's contact with and subsequent contraction of measles required data input from World Health Organization and Centers for Disease Control and Prevention (CDC) case and disease incidence reports in conjunction with open access global air network projections, which facilitated the establishment of country-specific importation probabilities using maximum likelihood estimation methods. Parameters were verified by comparison of model output, given a 90% data input, to existing CDC outbreak statistics, and revised accordingly. The resulting calibrated model has sufficient predictive abilities to assess the likelihood of a measles importation event and a resulting outbreak given situational and environmental data.

What inspired you to participate in undergraduate research?

I love the process of identifying questions of interest and finding answers to them. I also am really interested in infectious disease ecology and the applications of mathematical modeling to current outbreaks.

How did you get your research position, and what preparation did you undertake for it?

I have been a member of Dr. Perkins' lab since my sophomore year, and began working on this project this past spring. I submitted an application for the COS SURF, which funded my research this summer.

Where was your research experience located?

University of Notre Dame

What did you get out of your research experience?

I gained a better understanding of what it means to conduct research full time, and am now confident that I want to pursue graduate studies. I hope to conduct similar research and continue learning about mathematical modeling.

A Series of Autologous Bone Marrow Concentrate Injections Effectively Reduces Pain in Patients with Symptomatic Knee Osteoarthritis: A Case Series

Patrick Quinn

Major: Neuroscience & Behavior

Advisor: Kaitie Whitney; The Steadman Clinic; Vail, CO

Co-authors: Laurel Winsor, Michael Mullen, Rachel Van Sloun, Kaitie Whitney, Thos A. Evans

Current research provides short-term follow up evidence regarding outcomes of a single intra-articular injection of autologous bone marrow aspirate concentrates (BMAC) in patients presenting early stage knee OA. However, investigation of a series of BMC injections could provide evidence of prolonged functional improvements and pain reduction for patients with moderate to severe OA. Three clinical cases of three symptomatic moderate to severe knee Degenerative Joint Disease (DJD) patients that underwent a series of autologous BMC injections using a superolateral patella approach were investigated to determine the effect of such BMC injections. The first patient, a 74-year old man suffering from bilateral knee DJD and extensive posterior knee pain, underwent two bilateral knee BMC injections of 11mL and 9 mL approximately 11 months apart. Patient 2, a 70-year old female presenting chronic right knee pain and right knee DJD, underwent two right knee BMC injections of 7mL each, approximately 4 months apart. The final patient, a 71-year old female with a history of bilateral knee DJD, underwent three BMC procedures. The respective BMC volumes for the right knee, 6.5 mL and 6 mL, and the left knee 6mL and 7.5 mL were injected into the intraarticular section of the knees. After the BMC injections, the first patient reported 100% resolution of his left knee pain and approximately 80% in his right knee. Patient 2 reported a 90% pain relief of the right knee for up to 7 weeks after her first BMC injection and an improved average right knee pain scale of 2 out of 10 eight weeks after her BMC injections from 4 out of 10 reported at initial evaluation. Finally, Patient 3 reported greater than 50% relief with mild joint tenderness of the right knee and significant pain relief of the left knee 8 weeks post initial BMC injections, and 90% relief of right knee pain at 20 weeks post initial right knee BMC injection. Despite inconsistent results in past studies, these outcomes suggest that a series of BMC injections effectively reduces pain in patients with symptomatic, late-stage knee OA. These results suggest that with optimized procedure timelines, serial BMC injection could be a promising treatment to treat osteoarthritis and degenerative joint disease given that current treatments focus on symptomatic relief opposed to environmental change of the joint.

What inspired you to participate in undergraduate research?

“I have always been extremely curious about the human body. With so much cutting-edge research occurring at Notre Dame and at The Steadman Clinic, I was drawn towards research because of the opportunity to make a real difference in medicine. Through research, I have aimed to positively contribute to the health of future patients.”

How did you get your research position, and what preparation did you undertake for it?

“I was fortunate to undergo bilateral hip surgery as a patient at The Steadman Clinic three years ago, an experience that changed my life and led me to the wonderful individuals at the Clinic. By staying in touch and eventually returning to the Clinic afterwards to shadow the doctors, I was offered an opportunity to intern this past summer. In preparation for the internship experience, I studied up on the topic of novel Platelet Rich Plasma techniques and tried to learn as much as I could about the aspects of medicine that I would be investigating.”

Where was your research experience located?

“The Steadman Clinic in Vail, Colorado”

What did you get out of your research experience?

“Interning at The Steadman Clinic was one of the most influential and formative experiences of my life. I received the invaluable experience of not only working with world-renowned doctors and researchers, but also directly viewing the sacredness and tranquil beauty of the human body. The experience instilled in me the importance of living my life with an attitude of service and how a life of integrity can ultimately change the world for the better.”

Examining Native and Invasive Flower Preferences in Wild Bee Populations

Eileen Reeves

Major: Environmental Sciences

Advisor: Dr. Rose-Marie Muzika, Professor Emerita at University of Missouri

Co-Author: None

This experiment set out to determine if introduced and invasive flowers are less appealing to native pollinators, potentially contributing to the effects of habitat loss on these vulnerable insect populations. Invasive plants pose threats to native ecosystems by crowding out native plants and displacing native species. Wild bee populations face threats from habitat loss and fragmentation. To determine non-native flowers' effects on wild bees, I observed plots of either native or introduced wildflowers and counted the number of visits made by different genera of bees. I found no significant preference for native or introduced flowers in five of the six genera observed. One genus, *Lasioglossum sp.* showed a significant preference for introduced flowers.

What inspired you to pursue undergraduate research?

I am very passionate about ecology and the potential research has to solve some of the biggest threats facing our planet now. This program allowed me to hone research skills and get involved in a topic about which I am deeply passionate.

How did you get your research positions, and how did you prepare for this research?

I applied to the UNDERC program, and was eventually accepted to conduct research as part of the practicum in field biology over the summer. I prepared for the research by considering and researching potential research topics I could investigate while at the field station.

Where was your research experience located?

The University of Notre Dame Environmental Research Station on the Michigan/Wisconsin border.

What did you get out of it?

This experience taught me how to formulate a research question, gather the data, and analyze said data. My project was conducted mostly on my own, with input from a mentor. I gained valuable research skills such as writing a procedure, modifying said procedure to work with the environment, and working with other researchers. Also, I got a fantastic summer spent in a beautiful part of the country, and new friends!

Total Synthesis of Aurachin C 1-10

Nicolas Robalin

Major: Chemistry and Theology

Advisor: Dr. Paul Helquist

With the rise of antibiotic resistance in bacteria, the development of inhibitory compounds has grown in importance. The creation of compounds to limit antibiotic resistance is a promising field of chemical biology. The formation of biofilms is a key way in which bacteria resist antibiotics. Aurachin C 1-10 (Aurachin C Analogue, N-Hydroxy-2-*n*-decyl-3-methyl-4-quinolone) has been shown to be a potent inhibitor against the formation of biofilms in *E. Coli*. Aurachin C 1-10 inhibits two enzymes, cytochrome *bo* and cytochrome *bd*, which are vital oxidases in the aerobic respiratory chains of *E. Coli*. Unfortunately, Aurachin C is a scarce compound in nature. My project was able to find a more efficient pathway for synthesis of Aurachin C 1-10. A 6-step synthesis starting with aniline to reach Aurachin C 1-10 was achieved with more efficiency than previous attempts. The synthesis of the compound will further help study the inhibitory effects of quinolone derivatives on the formation of biofilms.

What inspired you to participate in undergraduate research?

I wanted to look into a career in research. Organic chemistry was interesting so I joined a lab that specializes in organic synthesis.

How did you get your research position, and what preparation did you undertake for it?

The research presented was done at Vanderbilt in a Research Experience for Undergraduates. I applied to participate in the program during my Sophomore year for the summer following. I prepared for the position by gaining experience in Dr. Helquist's lab.

Where was your research experience located?

Nashville, Tennessee at Vanderbilt University

What did you get out of your research experience?

I gained valuable experience. I became a better chemist. I saw how graduate school is.

Minimalist TAVR without in-room full surgical backup in a Montanacommunity hospital

Kellen Round

Major: Science Business

Advisor: Michael C. Reed, MD, International Heart Institute of Montana

Coauthors: Michael C. Reed, MD

Transcatheter aortic valve replacement (TAVR) has revolutionized the treatment of aortic stenosis in thousands of people worldwide. Accompanying the rise of TAVR has been the simultaneous effort to minimize the cost and resource-utilization of the procedure. As it stands, TAVR is more expensive than surgical aortic valve replacement. Minimalist TAVR with conscious sedation has been proven to dramatically lower cost. In addition, while procedural safety is critical, given the infrequent need for conversion from TAVR to open surgery, the routine use of in-room full surgical staff and equipment including perfusion, surgical trays, and scrub staff may be excessive once centers have gained sufficient experience. We sought to examine the safety of minimalist TAVR without in-room full surgical back-up. We looked at 200 consecutive patients from January 2017 to July 2018 who received TAVR at our hospital. Patients 1-100 (January 2017 – November 2017) had full in-room surgical back-up. Patients 101-200 (November 2017-August 2018) had a cardiovascular surgeon scrubbed in the case but no other surgical equipment and staff was in the room. Full surgical back-up equipment and staff were in-house and available for emergency conversion. For statistical analysis, a significance level of 0.05 was used to interpret the resulting p-values, and values greater than this threshold indicated that the difference among procedural outcomes before and after minimalist approach was not statistically significant. There was no significant difference in the baseline characteristics of the two subject groups, nor was there a significant difference in major clinical outcomes between the two groups. Thus, at an experienced community hospital program, minimalist TAVR without routine in-room surgical backup is feasible and safe. Major complications are not increased with a shift to a fully minimalist approach, and procedural costs and resource-utilization are likely reduced.

What inspired you to participate in undergraduate research?

While my research was mainly independent, the over-arching reminder that I was contributing to a broader community of physicians, patients, hospitals, and other individuals in the industry excited me. I think my inspiration developed as I reminded myself that although one person cannot single-handedly find the answer to treating disease, an assortment of contributors can work together to provide the best product for a patient.

How did you get your research position, and what preparation did you undertake for it?

I was offered the position unexpectedly as I shadowed Dr. Reed during winter break. To prepare for my project, I spent several days in the catheterization lab to gain comfort with the procedure itself, the language used in the field, and a general background knowledge that allowed me to communicate my findings.

Where was your research experience located?

International Heart Institute of Montana at Providence St. Patrick's Hospital in Missoula, MT.

What did you get out of your research experience?

For the first time, I learned the scientific process with a hands-on approach. This was not a previously-designed lab experiment, but rather arose from a question Dr. Reed had with the intention of finding an answer. I now recognize the importance of collaboration in research, even though small details can be frustrating at times. Most importantly, I found a new passion for cardiology and the treatment of heart disease.

Exact Formulas for Invariants of Hilbert Schemes

Matthew Schoenbauer

Major: Mathematics

Advisors: Ken Ono, Dept. of Mathematics and Computer Science, Emory University

John Duncan, Dept. of Mathematics and Computer Science, Emory University

Larry Rolen, Dept. of Mathematics, Vanderbilt University

Coauthors: Nate Gillman, Dept. of Mathematics & Computer Science, Wesleyan University

Xavier Gonzalez, Mathematical Institute, University of Oxford

A theorem of Göttsche establishes a connection between cohomological invariants of a complex projective surface S and corresponding invariants of the Hilbert scheme of n points on S . This relationship is encoded in certain infinite product q -series which are essentially modular forms. Here we make use of the circle method to arrive at exact formulas for certain specializations of these q -series, yielding convergent series for the signature and Euler characteristic of these Hilbert schemes. We also analyze the asymptotic and distributional properties of the q -series' coefficients.

What inspired you to participate in undergraduate research?

“I had done mathematical research in the past, and this summer I wanted to explore analytic number theory through this intense research program at Emory University.”

How did you get your research position, and what preparation did you undertake for it?

“I applied to the program via MathPrograms.org, a commonly used site for applying to research programs. I was high on the waiting list to get into the program, but I had to have the Glynn Family Honors Program and the Department of Mathematics at Notre Dame provide the stipend.”

Where was your research experience located?

“Emory University”

What did you get out of your research experience?

“The summer was extremely intense. I learned a lot about the mathematical research process, efficient working methods, as well as a great amount of math. I also learned how to use mathematical software that was useful for the research.”

Copper (I) & Copper (II) Binding to the Ectodomain of Human Copper Transporter 1

Erica Slogar

Major: Chemistry and Chemical Engineering

Advisor: Kathryn L. Haas, Dept. of Chemistry and Physics, Saint Mary's College

Coauthors: none

Copper requires transmembrane proteins to enter cells. Transmembrane proteins transport copper and also protect copper from producing reactive oxidative species. Reactive oxidative species can cause oxidative stress, which can cause disease and result in cell death. Human copper transporter 1 (hCtr1) is a transmembrane protein that binds copper. hCtr1 maintains cell vitality by safely transporting copper (Cu) across cell membranes, thus preventing reactive oxidative species production. Model peptides of the hCtr1 ectodomain interact with both Cu(I) and Cu(II); however, the stoichiometry of Cu ions to extended regions of the ectodomain have not been probed until now. Through spectroscopic methods, including UV-Vis and synchrotron radiation, stoichiometries of Cu(I) and Cu(II) binding to Ctr1-14 and Ctr1-45 model peptides were investigated. These preliminary experiments reveal that multiple Cu ions in both the Cu(I) and Cu(II) oxidation states can bind to the hCtr1 ectodomain.

What inspired you to participate in undergraduate research?

“I wanted to make a difference in healthcare, and research became the first step towards my goal. I also wanted to be a part of a team so that I could help progress discoveries.”

How did you get your research position, and what preparation did you undertake for it?

“I have been a member of the Haas Group since May of 2017. I met Dr. Haas at a faculty research presentation, and after talking with her about her research, I decided to join her group for the summer of 2017. Previous lab courses had prepared me mentally for research, but most of what I learned came directly from Dr. Haas. My research has been supported by”

Where was your research experience located?

“Saint Mary's College”

What did you get out of your research experience?

“I gained experience both inside and outside of the lab that I could not have gotten elsewhere. Dr. Haas showed me how key collaboration is in research, because no one can accomplish goals by themselves.”

Synthesis of Saturated Indole Derivatives with a Highly Diastereoselective Palladium-Catalyzed Decarboxylative [4+1]-Formal Cycloaddition of Vinyl Benzoxazinones and N-Tosylhydrazones

Andrew Smith

Major: Chemistry

Advisor: Dr. Brandon Ashfeld, Dept. of Chemistry and Biochemistry, University of Notre Dame

Coauthors: Zachary Tucker

Natural products provide important structural and biological inspiration for developing drugs that treat a variety of diseases and disorders. Indole alkaloids are a large class of molecules synthesized in the metabolism of many plants, and are highly effective as neurological or antitumor agents, such as serotonin and vinblastine. Indole alkaloids applied in treatments today are principally acquired by extraction, a costly and inefficient method to producing the drugs; however, variable enantioselective synthetic strategies have been designed yielding the structures or their precursors in higher yields. This work demonstrates a highly diastereoselective method to synthesize saturated indole derivatives, via a palladium-catalyzed decarboxylative formal [4+1]-cycloaddition of vinyl benzoxazinones and N-tosylhydrazones. The strategic disconnect demonstrates the synthetic versatility of carbenes as C-1 synthons, generated *in-situ* from N-tosylhydrazones via a Bamford-Stevens type mechanism. While poor enantioselectivities have been observed employing traditional chiral ligands, excellent diastereoselectivity and good-to-excellent yields have been achieved without the need of complex ligands. Current efforts are focused on extending the substrate scope of this method beyond the initial vinyl benzoxazinone structure to synthesizing complex, highly functionalized dihydroindole derivatives in an enantioselective fashion.

What inspired you to participate in undergraduate research?

“Ever since I started taking classes in organic chemistry, I had always wanted to have opportunities to truly synthesize new products, especially those with potential to combat diseases like cancer.”

How did you get your research position, and what preparation did you undertake for it?

“I had been working in the Ashfeld lab in the spring of 2017 and he had mentioned that I should consider applying for a grant to work during the summer. I submitted a research proposal based on work developed by my graduate mentor, Zachary Tucker, and with the ND Ignite Fellowship as well as the College of Science Summer Undergraduate Research Fellowship I was able to help him complete work over the summer.”

Where was your research experience located?

“The University of Notre Dame.”

What did you get out of your research experience?“

The summer provided me the opportunity to truly commit myself to the lab experience, including collaborating with other graduate students, reporting results, perfect laboratory techniques, and approach issues in the lab analytically.”

Effect of Dengvaxia campaigns in neighborhoods of differing transmission intensity as the result of socioeconomic status variation

Magdalene Walters

Major: Biological Sciences

Advisor: Dr. Alex Perkins, Dept. of Biology, University of Notre Dame

Coauthors: none

The recent confirmation by Sanofi Pasteur of variation in its dengue vaccine's, Dengvaxia, effectiveness in those who have not experienced natural infection, has shed light on the importance of small-scale variation in communities experiencing dengue. Mosquito-borne diseases have been shown to vary in transmission intensity between areas of different socioeconomic status. To date, no other studies have examined the implications of small-scale spatial variation (i.e. neighborhood-level) of dengue transmission between areas of varying socioeconomic status on Dengvaxia campaigns. This study utilizes a modified SIR framework to examine the implications of differing vaccination campaigns between two areas of varying transmission intensities which experience travel between each area. It was hypothesized that targeted vaccination campaigns in one neighborhood with high transmission intensity would benefit an unvaccinated nearby area with low transmission intensity. The effectiveness of vaccination campaigns was evaluated using a metric that identified the percentage of nine year olds who had not experienced a natural infection in their lifetime (termed SP9). Results show that when one neighborhood with a higher transmission intensity than an adjacent neighborhood is vaccinated, both communities show a reduction in SP9 as long as the higher transmission intensity is above a certain threshold. This work has implications for vaccination campaigns in communities that experience spatial heterogeneity in transmission, including that due to socioeconomic status.

What inspired you to participate in undergraduate research?

I have always been interested in the health of populations, and found epidemiological work to be a great outlet for this interest. While I wasn't initially interested in vector-borne diseases, I have found research with the subject to be a great intersection with my work in poverty studies.

How did you get your research position, and what preparation did you undertake for it?

I joined the Perkins group in the fall of 2016 as a sophomore. Prior to that, I completed a course with Dr. Arthur Lim which exposed me to theoretical models utilized in biology. While that class used Matlab, I have since taken several other graduate level courses in quantitative biology which have developed my skills with modeling and R.

Where was your research experience located?

University of Notre Dame

What did you get out of your research experience?

Most notably, my research has played a big role in my decision to not go to medical school. I discovered that I am more interested in the systematic bettering of health by examining health infrastructure than in medicine.

Control of CAR-T Cell Immunotherapy by Bispecific Adaptor Molecule: In-vitro Cytotoxicity and Cytokine Production Studies

Emilia Z. Wang,

Major: Neuroscience and Behavior, University of Notre Dame

Advisor: Dr. Yingjuan Lu, Director of Translational Research, Endocyte Inc.

Chimeric antigen receptor (CAR) T-cell therapy utilizes gene-modified T cells to improve anti-tumor activity. CAR proteins expressed on CAR T-cell surfaces allow T cells to specifically recognize an antigen on targeted tumor cells. This personalized immunotherapy has shown high remission rates and durable responses and gained FDA approval in treating CD19+ hematologic malignancies. Continuing efforts are being made to manage related side effects including severe cytokine release syndrome, neural toxicity, and tumor lysis syndrome. These side effects are associated with uncontrolled CAR T-cell activation and proliferation *in vivo*. A novel approach is under development at Endocyte to make CAR T-cells more controllable. Different from conventional CAR T-cells, which are designed to bind directly with cancer cells, Endocyte technology uses a bispecific small-molecule ligand, EC17 (folate-FITC), to redirect FITC-specific CAR T-cells against folate receptor (FR)-positive tumors. In-vitro cytotoxicity and cytokine production studies showed that the functions of CAR-T can be finely controlled by the bispecific adaptor

What inspired you to participate in undergraduate research?

“I am also curious about real-world applications of things I learn about in class and so I often like reading and learning about current ongoing research. In high school, I had the opportunity to do some research in a lab and I wanted to continue in college.”

How did you get your research position, and what preparation did you undertake for it?

“I interned at Endocyte briefly during high school and this internship is a spinoff from that experience.”

Where was your research experience located?

“West Lafayette, Indiana”

What did you get out of your research experience?

“I learned how to write up proposals, design and conduct experiments, and analyze data independently. I learned how to communicate and coordinate with coworkers to carry out experiments that involved collaboration from more than one department. I also had the opportunity to present my work at the monthly R&D meeting, which allowed me to fine-tune my public speaking skills

Roles and Effects of Human MALAT1 Mutations on MALAT1-miRNA Interactions

Matthew C. Wang¹, Phillip J. McCown¹, Luc Jaeger², Jessica A. Brown¹¹

Major: Biochemistry

Department of Chemistry and Biochemistry, University of Notre Dame, Notre Dame, IN 46556, USA;

²Department of Chemistry and Biochemistry, Biomolecular Science and Engineering Program, University of California at Santa Barbara, Santa Barbara, CA 93106, USA
Major: Biochemistry
Advisor: Dr. Jessica Brown, Department of Chemistry and Biochemistry, University of Notre Dame

MicroRNAs (miRNAs) are small, noncoding RNA molecules that are used to regulate gene expression by targeting messenger RNA (mRNA) for degradation via Watson-Crick base pairing. It has been proposed that long noncoding RNAs (lncRNAs) sequester miRNAs from their mRNA targets via a sponging mechanism. Thus, mutations in lncRNAs may disrupt miRNA-lncRNA interactions, causing unexpected and potentially detrimental changes in gene regulation and expression. One such human lncRNA, metastasis-associated lung adenocarcinoma transcript 1 (MALAT1), is predicted to contain at least 155 miRNA interaction sites, and 655 mutations have been identified in cancer patients. Here, we describe the effects of select MALAT1 mutations on miRNA binding and discuss their potential ramifications on cell development, with a focus on cancer-related effects. Mapping and analysis of known MALAT1 mutations reveals 13 mutations that, either individually or in conjunction with one another, disrupt the binding of seven miRNAs to MALAT1. Three of these miRNAs (miR-23abc-3p, miR-9, and miR-17-5p) are verified interactors, while four (miR-106-5p, miR-20ab-5p, miR-519d-3p, and miR-93-5p) are predicted interactors. Most of these mutations, corresponding to binding sites for the tumor-suppressing miR-106-5p, miR-17-5p, and miR-519d-3p, as well as the tumor-enhancing miRNAs miR-20ab-5p and miR-93-5p, affected regions of MALAT1 we predict to be unstructured. Several mutations affecting binding sites for the oncogenic miR-23abc-3p and miR-9 are predicted to destabilize the secondary structure of MALAT1, as the mutations for these miRNAs occur in regions of MALAT1 we predict to be structured. Overall, mutations in MALAT1 affected miRNAs in a variety of cancer-related roles, suggesting a greater role for MALAT1, and other lncRNAs, in gene expression and cancer regulation.

What inspired you to participate in undergraduate research?

I was excited by the idea of being able to develop my own experiments and pursue my own interest, as opposed to doing traditional, prepared experiments in my laboratory courses. I was also motivated by my aspirations of pursuing a Ph. D. in biochemistry.

How did you get your research position, and what preparation did you undertake for it?

I both interviewed with Dr. Brown and filled out an application. To prepare, I read primary literature recommended by Dr. Brown and participated in online and in-lab training.

Where was your research experience located?

I conducted research in the Stepan Chemistry Building at the University of Notre Dame.

What did you get out of your research experience?

I gained valuable experience in laboratory techniques, scientific writing, and problem-solving in a situation where, unlike laboratory courses, known answers are not available.

Simulation of the ND Cube Active-Target Time Projection Chamber

Lihao Yan

Majors: Physics and Philosophy

Advisor: Prof. Tan Ahn, Dept. of Physics, University of Notre Dame

Studies of detectors are precursors for major nuclear physics developments and are needed to advance the field. In particular, detectors with high efficiency are needed to study reactions with radioactive beams. These radioactive beams are needed to study nuclei that are difficult to access, but these beams have low intensities. One way to address this problem is to use an Active-Target Time-Projection Chamber (TPC). Active-Target TPC's are one of the next generation detectors that improve efficiency by using a thick gas target with track imaging. At the University of Notre Dame, we are developing an Active-Target Time Projection Chamber called the ND Cube. Upon the completion, the ND Cube will be able to track reaction trajectories and provide good resolution for reactions even with a thick target. It is necessary to understand its behavior through simulation to optimize the efficiency of the ND Cube. I simulated the electric field and the behavior of electron drift lines inside the ND Cube using the finite element analysis software COMSOL and CERN's Garfield++ toolkit. Based on the simulation, the resolution and the expected transport of the electrons in the detector can be determined. We found a standard deviation of $\sigma = 0.85\text{cm}$ for each electron drifting in 55cm of air at 1 atm, which determines the resolution of our imaged tracks. In the future, after the ND Cube is built, the simulation result will be used to compare and analyze the experimental data. The simulation may also be used to resolve possible systematic errors due to non-uniform electric fields.

What inspired you to participate in undergraduate research?

"I am so excited to participate in the cutting-edge physics research that could make an impact to our world. It is also a great way to challenge myself and realize my potentials"

How did you get your research position, and what preparation did you undertake for it?

"I directly walked into Prof. Tan Ahn's office when I was a freshman, and I was fortunate enough to be accepted into his research group. I have done physics research using finite element simulation software in high school before which is probably the reason why Prof. Ahn accepted me into his group.

Where was your research experience located?

"University of Notre Dame's Nuclear Science Laboratory"

What did you get out of your research experience?

"After learning and practicing the software ANSYS, I have obtained the skill of using the finite element analysis method to solve problems. This skill can be applied to various physics and engineering problems in many areas including the analysis of tension, temperature, and vibration. Learning this physics analysis method will accelerate my mastery of the other physics methods that I will learn in future courses.

As a physics major, this summer physics research experience enabled me to have a head start in the nuclear physics field. I cultivated the mindset of doing research and working alongside a professional physics researcher. The long-term experience of research motivated me to cultivate a habit of being a physicist. I have learned how to make plans, divide huge tasks into small parts, and manage my time efficiently.

This valuable experience not only contribute to the reliability of the ND Cube project but also have enduring effects for my future physics career path. I intend to use this summer as a precious opportunity to experience the life of being a physics researcher. I will decide whether I want to pursue that kind of life in the graduate school. This is also a chance for me to decide whether I want to specialize in the nuclear physics area. In addition, since I am conducting simulation and experiment at the same time, I have explored whether I am more into the theoretical aspect or the experimental aspect of physics. This experience also provides me a greater chance of participating in research labs in the future. I firmly believe that this experience during the summer will be the very start of my career path in physics."

Cost-effectiveness of Dengvaxia vaccination of people with prior dengue virus exposure in ten Latin American and Asian countries

Yutong Yao,
Major: Science Preprofessional and Economics
Advisor: Guido España Ph.D, Alex Perkins Ph.D

As of March 2018, the Dengvaxia vaccine for dengue from Sanofi Pasteur has been registered in 20 countries in Latin America and Asia. In light of recently announced safety concerns for people with no prior dengue virus exposure, the World Health Organization revised its position on this vaccine to recommend that it only be used in people with prior dengue virus exposure. To date, no studies have estimated the public health impact and cost-effectiveness of Dengvaxia when applied only to people with prior dengue exposure. To provide such an assessment, we used a computational model of dengue virus transmission to simulate the impact of routine vaccination programs under various ranges of transmission intensity and with screening tests of varied sensitivity and specificity. We also simulated different combinations of routine vaccination at different ages and catch-up campaigns with different age ranges and coverages. This study analyzed and compared the cost-effectiveness of screening-based vaccination targeted at nine-year-old children and of an intervention with various catch-up cohorts based in ten countries across Asia and Latin America. We applied the simulated infections derived from the model to the cost-effectiveness analysis framework provided by WHO. The work also relied on literature for local vaccine cost and cost per DALY. An intervention would be evaluated as cost-effective if the threshold cost of the intervention was predicted positive. Overall, our results suggest that screening-based vaccination could be cost-effective in five countries: Colombia, Brazil, Mexico, Thailand, and the Philippines, which have a GDP per capita ranging from \$5,742 to \$29,360. We have also found that screening-based vaccination would be cost-effective with a threshold cost ranging from \$5 to \$50 in the first five countries when the transmission intensity is high ($SP_9 > 0.5$) with a highly sensitive and specific diagnostic; for Puerto Rico, the intervention could be cost-effective even when the transmission intensity is low ($SP_9 \leq 0.3$) and the threshold cost could reach \$100 under stronger transmission.

What inspired you to participate in undergraduate research?

“I started with looking for opportunities to learn beyond the curriculum. It is a great opportunity to explore something you have been interested in but never done before by applying what you have known. It is also an attractive opportunity to explore my interest in infectious disease control and get to know professors at ND before taking their classes.”

How did you get your research position, and what preparation did you undertake for it?

“Interested in disease forecasting, I found Dr. Perkins and emailed him about research opportunities for undergraduates in his lab. I was in the lab for one year learning some basics of modeling and finishing a historical project before I started the first research project. Other than that, research is more like a long-term learning that one cannot really prepare for it all before start. I was also recommended to apply for the summer research program at MD Anderson last year, which has an outreach program with ND. I read a couple of papers before started the program, but the learning really took place after the research started and continued as everything moved forward.”

Where was your research experience located?

“I have been in Dr. Perkins’ lab for two years at Notre Dame and I was in MD Anderson Cancer Research Center in Houston, Texas.”

What did you get out of your research experience?

“The skills to analyze data and design experiments efficiently. Research always start from nothing and end up with novel discoveries despite frequent failure in between. I enjoy cooperating with peers and researchers from a wide range of background.”

The Role of Wnt5a Signaling Pathway in Ovarian Cancer Progression

Allison Young

Major: Science-Business

Advisor: M. Sharon Stack, Department of Chemistry and Biochemistry, Integrated Biomedical Sciences Program, Harper Cancer Research Institute

Coauthors: Marwa Asem^{1,2,3}, Carlysa Oyama³, Rebecca Burkhalter³, Steven Buechler⁴, Daniel L. Miller⁵, and M. Sharon Stack^{1,2,3}

¹Department of Chemistry and Biochemistry, ² Integrated Biomedical Sciences Program, ³Harper Cancer Research Institute, ⁴Department of Applied and Computational Mathematics and Statistics, University of Notre Dame, Notre Dame, IN, ⁵Department of Pathology, The Johns Hopkins University School of Medicine, Baltimore, MD

Ovarian Cancer (OvCa) is the most fatal gynecologic malignancy and the fifth leading cause of overall cancer death among American women with a low (27%) 5-year survival rate, as 75% of women are diagnosed with disseminated intra-peritoneal (IP) metastasis. The process of OvCa metastasis differs from most other cancers in that cells detach from the primary tumor and shed into the peritoneal cavity, adhere to the peritoneal mesothelial cell (MC) monolayer, intercalate within this layer, and invade into the submesothelial matrix, where they proliferate and form secondary lesions. Wnt5a is a noncanonical Wnt ligand that binds to several cell membrane receptors and activates downstream signaling pathways that are fundamental for normal developmental processes during embryogenesis. In the past decade, the aberrant activation or inhibition of Wnt5a signaling is emerging as an important event in cancer progression, exerting both oncogenic and tumor suppressive effects. In OvCa, Wnt5a is prevalent in OvCa ascites, suggesting a role for Wnt5a in promoting disease progression. Data obtained from TCGA (n=583) show high expression of Wnt5a in human OvCa tumors. Our data show for the first time that primary peritoneal mesothelial cells (MC) and visceral adipose tissues, which are primary metastatic sites for OvCa, express strikingly high levels of Wnt5a. In turn, Wnt5a enhances OvCa cell adhesion to peritoneum, migration and invasion in a panel of organotypic and ex vivo functional assays. Furthermore we observed striking morphological changes characteristic of an invasive phenotype in OvCa cells treated with recombinant Wnt5a and formation of tunneling nanotubes (TNT) between OvCa cells and MC both in vitro and with ex vivo explants. These data support our hypothesis that Wnt5a promotes ovarian cancer progression. Future studies will confirm these findings and assess the contribution of host-Wnt5a to OvCa progression by generating inducible Wnt5a knockout (KO) mice for use in allograft tumor studies. This is complemented by experiments using Wnt5a-knockout MC (both human LP9 peritoneal MC and primary murine MC) and a panel of in vitro and ex vivo assays.

What inspired you to participate in undergraduate research?

“Undergraduate research presents the opportunity to deeply engage with topics outside of the laboratory. I have seen how cancer affects people with the disease, and I have enjoyed learning the scientific background behind it.”

How did you get your research position, and what preparation did you undertake for it?

“I learned about the opportunity to participate in undergraduate research from upperclassmen, and sought their advice. I reached out to Dr. Stack at the Harper Cancer Research Institute and met with her to discuss the opportunity to participate in her lab. The summer before I began at Harper, I held a research internship at the Glick Eye Institute in Indianapolis.”

Where was your research experience located?

“Harper Cancer Research Institute”

What did you get out of your research experience?”

I learned about the scientific process, as well as the exciting field of cancer research. I had the opportunity to present at a poster session; at this session, I met a woman who runs a support group for people undergoing cancer treatment. She told me that she goes to research fairs to gather information, and shares it with them to show that people are pushing for a cure. It was really inspiring to see the role research plays outside of the immediate scientific community.”

Undergraduate Research Internship Information Night

Helen Streff, hstreff@nd.edu, Plenary speaker (Will talk about internship strategy: searching, applying, etc. as well as her internship experiences)

BIO:

- Junior biology major with current plans to attend graduate school and enter the pharmaceutical or biotech industry.
- Internship after first year was part of the University of Minnesota's Life Sciences Summer Undergraduate Research Program (LSSURP). Specifically, I was part of the CREATE program (Cancer Research Education and Training Program) and worked in Dr. Scott Dehm's prostate cancer lab in the Masonic Cancer Center. Summer of 2018, I conducted CRISPR research at Amicus Therapeutics in Cranbury, New Jersey. The program had ~15 undergraduates participating in diverse areas from research to patient advocacy to medical affairs.
- I chose the LSSURP internship based on the proximity to my hometown and the cancer emphasis of the CREATE program. I then decided on the Amicus internship because I wanted to try industry and experience a new area of the country.
- LSSURP is a fantastic program, and I am so glad I participated in it. It was very organized, rewarding, and provided me with a great sense of what graduate studies in biology would be like. Amicus Therapeutics was a wonderful way to try research at a company. It helped confirm that I want to attend graduate school and enter the biotech industry. Additionally, the experience refined my interest from cancer research in general to cancer genetics research.

Meridith Balbach, Balbach.1@nd.edu (Will talk about her internship experiences, focusing on the University of Louisville's Brown Cancer Center's R25 Cancer Education Program)

BIO:

- Senior, biology major and anthropology minor, currently applying to medical school.
- Internship following my first year (summer 2016) was at Indiana University School of Medicine through Indiana CTSI, working in a translational research lab studying acute kidney injury using a rat model. I learned microscopy, tissue scoring, basic surgical techniques, but probably most valuable was how to read scientific literature, hear of new discoveries during weekly seminars, design experiments to test research questions and to communicate with my mentors.
- I conducted another internship at the University of Louisville's Brown Cancer Center through their R25 Cancer Education Program. I worked with a radiation oncologist on a clinical trial that investigated the potential of a radioprotective drug to eliminate toxicities associated with re-irradiation of lung tissue. Opportunities included reading radiology reports to assess tumor response and physician's notes to score toxicity, attendance at weekly cancer research seminars, professional development workshops and extensive shadowing in radiation oncology.

Katheryn Barnhart, kbarnha1@nd.edu (Will talk about her internship experiences at the University of Notre Dame's Environmental Research Center and with the United States Bureau of Reclamation)

BIO:

- Senior Environmental Sciences major with plans to take a gap year working in industry or conducting field research and then enter graduate school to focus on human interactions with climate change.
- Internship at UNDERC (University of Notre Dame Environmental Research Center), was conducted summer 2017 exploring the impact of climate on release calling in gray tree frogs (*Hyla versicolor*).
- Internship with the Bureau of Reclamation, Socorro, New Mexico summer 2018, involved conducting presence/absence surveys of endangered and threatened bird species as part of a larger governmental project.
- My UNDERC internship was obtained through the University of Notre Dame and the governmental internship via application at usa.gov.