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SUMMARY OF MY EXPERIENCES AS AN UNDERGRADUATE RESEARCHER IN THE U.S. AND AS A FULBRIGHT STUDENT RESEARCHER AT THE INSTITUTE OF IMMUNOLOGY AND EXPERIMENTAL THERAPY IN POLAND

Podsumowanie moich doświadczeń w prowadzeniu badań naukowych w Stanach Zjednoczonych oraz w Polsce w Instytucie Immunologii i Terapii Doświadczalnej w ramach stypendium Fulbrighta

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A – przygotowanie projektu badania | study design, **B –** zbieranie danych | data collection, **C –** analiza statystyczna | statistical analysis, **D –** interpretacja danych | data interpretation, **E –** przygotowanie maszynopisu | manuscript preparation, **F –** opracowanie piśmiennictwa | literature search, **G –** pozyskanie funduszy | funds collection

SUMMARY

Over the course of my undergraduate studies in Molecular and Cellular Biology and the experiences following my graduation, I became increasingly interested in research that can directly improve patient care. My research experiences in the U.S. include studying cytochrome P450 enzymes in Nanodiscs at the University of Illinois Urbana-Champaign and examining immune evasion by acute lymphoblastic leukemia cells at the University of Colorado Cancer Center. Beyond work in the laboratory, I also participated in a year-long project to implement a water delivery system in Honduras, leading to my interest in infectious disease research. My interest in this field grew after learning about phage therapy, a way of treating antibiotic-resistant infections, during an honors virology seminar. Only a few research groups are dedicated to studying phage therapy, which includes the Institute of Immunology and Experimental Therapy (IIET) in Poland. I was fortunate enough to receive a U.S. Fulbright research grant to study the immune response to phage therapy under the mentorship of Prof. hab. n. med. Andrzej Górski at the IIET. In this article, I will discuss my involvement at U.S. and European institutions, the insights I have gained, and how other students can similarly get involved in research.

Keywords: U.S. Fulbright Student, undergraduate, research opportunities, international exchange

STRESZCZENIE

Studia magisterskie z zakresu biologii molekularnej i komórkowej oraz późniejsze doświadczenia zawodowe sprawiły, że zaczęłam coraz bardziej interesować się badaniami mogącymi bezpośrednio poprawić poziom opieki nad pacjentem. W USA w Nanodiscs na Uniwersytecie Illinois w Urbana-Champaign prowadziłam badania nad cytochromem P450, a w Cancer Center na Uniwersytecie Kolorado pracowałam nad mechanizmami unikania odpowiedzi immunologicznej stosowanymi przez komórki rakowe ostrej białaczki limfoblastycznej. Oprócz pracy w laboratorium, brałam także udział w jednorocznym projekcie dotyczącym wdrażania systemów dystrybucji wody użytkowej w Hondurasie, który przekierował moje zainteresowania naukowe w stronę chorób zakaźnych. Dodatkowych inspiracji dostarczyło seminarium wirusologiczne, na którym dowiedziałam się o terapii fagowej, nowoczesnej metodzie leczenia infekcji wywołanych bakteriami opornymi na antybiotyki. Zaledwie kilka grup badawczych na świecie zajmuje się terapią fagową, wśród nich znajduje się polski Instytut Immunologii i Terapii Doświadczalnej (IIET). Miałam niezwykły zaszczyt otrzymać grant naukowy Polsko-Amerykańskiej Fundacji Fulbrighta, który pozwolił mi studiować zagadnienia z zakresu immunologii i jej wpływ na terapię fagową, pod kierunkiem prof. dr. hab. n. med. Andrzeja Górskiego z IIET. W poniższym artykule pragnę przedstawić swoje doświadczenia i spostrzeżenia dotyczące kontaktów z amerykańskimi i europejskimi instytucjami, udziału w międzynarodowych projektach badawczych, a także opiszę, w jaki sposób inni studenci mogą zaangażować się w podobne przedsięwzięcia.

Słowa kluczowe: stypendysta Fulbrighta, doktorant, wymiana międzynarodowa, możliwości naukowe

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Research experiences at U.S. institutions

Over the course of my undergraduate studies, I became increasingly interested in basic science research that can directly improve healthcare. My involvement in projects both in and out of the laboratory has shown me how scientific expertise can be harnessed for the practical benefit of people in the real-world.

In 2015, I graduated from the University of Illinois Urbana-Champaign *Magna Cum Laude* with a B.S. degree in Molecular and Cellular Biology with Honors and minor in Chemistry. In my second year, I began working as an undergraduate student researcher in the laboratory of Dr. Aditi Das, PhD, studying human cytochrome P450 (CYP) enzymes using Nanodiscs as lipid bilayer models. CYPs are responsible for the metabolism of numerous both xenobiotic and endogenous substrates. My independent project focused mainly on two specific CYP enzymes, CYP5A1 and CYP2C8. CYP5A1 produces the clotting agent thromboxane in platelets [1]. I worked to establish the role of an active site residue that influences thromboxane production, leading to the publication of a research article that I co-first-authored [2]. I also presented this work at the 2014 Midwest Enzyme Chemistry Conference and won best undergraduate poster presentation [3]. The other part of my project focused on CYP2C8, which metabolizes the chemotherapeutic drug paclitaxel (Taxol), as well as dietary polyunsaturated fatty acids to produce eicosanoid signaling molecules [4]. I examined how polymorphic variants of CYP2C8 alter the electron flow between CYP2C8 and its redox partner enzyme cytochrome P450 reductase.

Over the course of working in the lab of Dr. Das, I also published two first-author review articles pertaining to recombinant CYP expression techniques [5] and the involvement of CYPs in producing a specific class of eicosanoids called endocannabinoids [6]. In 2013, I was also awarded two fellowships to support my research, namely the University of Illinois Molecular and Cell Biology Research Fellowship and an American Heart Association Research Fellowship. In my final semester of study, I submitted a departmental senior research thesis that was awarded highest distinction. Overall, the experience of performing this research taught me how to pose scientific inquiries, design experiments, and how to overcome various challenges, both scientific and administrative. Most importantly, I realized for the first time that understanding the underlying science behind physiological phenomena has the potential to improve lives and was inspired to incorporate research into my future career.

In exploring a career as a medical researcher, I also completed an intensive 10-week fellowship at the University of Colorado Cancer Center under the guidance of Dr. Christopher Porter, MD. Here, I studied the cellular pathway BCR-ABL in driving immune system evasion by acute lymphoblastic leukemia cells. This project helped to greatly expand my skills to include cell- and animal-based studies. I presented my work at a final poster symposium [7] and was included as a co-author on an upcoming poster presentation at the American Society of Pediatric Hematology/Oncology annual meeting.

Involvement in international development

Beyond my work in the laboratory during my undergraduate years, I also participated in a year-long project devoted to engineering and implementing a clean water delivery system in rural Honduras. This project was unique in that it took into account not just technical concerns, but also the sociocultural and political dynamics of the community being served by the water system. Similar projects had previously failed, not due to technical inadequacies, but rather because of a lack of genuine understanding for local cultural practices and failure to engage the project beneficiaries in decision-making. Therefore, we engaged the community throughout the process of construction, governing water use, and by educating community members about infectious waterborne diseases. My role was to design and carry out health education in the local community that ensured people understood, for instance, why chlorination of their water would be important in combating gastrointestinal illness. What I took away from the project was an appreciation for the use of technical expertise in a way that considered the unique needs of the community. In addition, this experience opened my eyes to global health concerns,

especially that of inadequate antibiotic stewardship in developing regions, inspiring me to pursue infectious disease research.

Experience as a U.S. Fulbright researcher in Europe

My interest in infectious disease research grew after learning about phage therapy, a way of treating antibiotic-resistant infections, during an honors virology seminar. This motivated me to apply for a U.S. Fulbright research grant to conduct research at the Ludwik Hirszfeld Institute of Immunology and Experimental Therapy (IIET) PAS in Wrocław, Poland under the guidance of Prof. dr hab. n. med. Andrzej Górski. I was fortunate enough to receive this grant and currently my research at the IIET aims to characterize the human immune system response following phage delivery. Novel antibiotic drugs are increasingly difficult to design and resistance to existing drugs is a growing concern worldwide. Bacteriophages (or simply "phages") are viruses that target and eliminate bacteria, and may therefore prove essential to combating complex bacterial infections. Interestingly, the successful therapeutic potential of phages was first demonstrated by French microbiologist Dr. Felix d'Herelle in 1919. However, with the advent of antibiotic drugs only a handful of laboratories in Eastern Europe continued research on therapeutic phages throughout the 20th century [8]. Of particular note is the IIET in Poland that is one of two phage therapy centers worldwide. The IIET has been instrumental in developing phages to treat a variety of bacterial infections, including the methicillin-resistant Staphylococcus aureus "superbug" that now plagues hospitals worldwide [9–10]. Positive clinical results in treating patients using phage therapy have been obtained at the IIET for decades. Nevertheless, a more complete and rigorous understanding of phage-mediated bacterial elimination is needed for this treatment to gain wide-spread clinical use. In particular, the antibody response of the human immune system during phage therapy is not fully understood and may be a limiting factor for phage therapy [11]. Therefore, a main goal of my project has been to better characterize the immune system responses using in vitro phage characterizations and in vivo animal models.

Outside of working in the lab during my Fulbright grant, it was also interesting to examine the similarities and differences of conducting research and providing medical care in Europe versus the United States. Conversations with researchers at the IIET were very enlightening, as was the meeting with Dr. Daniel de Vos and Dr. Jérôme Gabard who are leading an EU--funded Phase I/II clinical phage therapy trial to treat burn victims [12–13]. In February 2016, I also participated in an EU-NATO Fulbright Seminar in Belgium. During the conference, we met with leaders at NATO headquarters, the European Court of Justice, and the European Commission, and the U.S. Missions to the EU and NATO. Each of these presented chances to learn about the current issues facing the EU/U.S. and how EU institutions influence regulations, including those pertaining to research funding and healthcare. To learn more specifically about Polish healthcare system, I have spoken with Prof. Górski who is a practicing MD/PhD about his experiences. More personal conversations with co-workers and friends about their understandings of the Polish medical system have also been informative. I hope that by increasing my awareness about these issues, I can serve as a more informed medical researcher and care provider.

In all, my experiences thus far have inspired me to pursue a career as a physician-scientist, as this will allow me to utilize research for the good of future patients in both developed and developing nations. In particular, the field of infectious diseases is of great interest to me and I hope to integrate basic science research with clinical practice in an international setting.

Hints and tips

- Maintain contact with anyone and everyone whose work you find interesting, regardless if they are directly in your field. Be curious and keep an open mind to learning about different topics.
- Express consistent interest in research by devoting time to working in a laboratory for extended periods of time, ideally on a specific project.
- Study and do well in fundamental science coursework, but remember that having a perfect grade record does not always correlate with success in conducting research. Research also requires one to think creatively, solve problems and remain resilient to overcome challenges.
- Take writing intensive coursework, read research papers, and practice language skills because science careers require one to communicate with others both orally and in writing. Learning how to use clear, convincing language in publications, grants, fellowship applications, poster presentations, and conference talks is essential.

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The conflict of interests

The author does not report any conflicts of interests.

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