**Basic Information**  
Full Name: Megan Dunlevy

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College: Arts and Sciences

Major: Biological Sciences- Biomedical Studies

Title of Project: Biomedical Research Mentoring Program

Thematic Area (choose only one): Research

Expected Project Start Date: 01/06/14

Expected Project End Date: 04/18/14

**Project Information**

1. Provide a detailed abstract of your proposed honors experiential learning project.

The Biomedical Research Mentoring Program is run though honors and pairs first and second year students with mentors at UC College of Medicine or Cincinnati Children`s . The purpose of the program is to give first and second year students lab experience and give the mentors a chance to teach an undergraduate. I have chosen to take a position in the Pan lab at the Cincinnati Children`s Hospital. I will be directly working under Dr. Salim El-Amouri. I will be working 11 hours a week in the lab for 15 weeks.

With Salim I will be exploring the effects of over expressing the enzyme Alpha-L- iduronidase (IDUA) in a mouse model of MPS 1. MPS 1 is a lysosomal storage that is caused by a defective IDUA gene. In patients with MPS or any lysosomal storage disorder experience a buildup of lysosomes which can cause damage to the nervous system and to other peripheral organs such as the liver, spleen, and heart. Some form of mental retardation is also common in patients with MPS or any of the lysosomal storage diseases. In MPS 1 IDUA is not produced in high enough quantities so the lysosomes brake down the proteins and sugars they ingest. Inserting the IDUA gene into mice with MPS 1 and over expressing that gene has been shown to correct some of the damage to the peripheral organs and the central nervous system. The goal of my project is to examine the use of over expressing IDUA as a possible treatment option for patients with MPS 1.

Currently I plan on entering Medical School after graduating and earning my medical degree. My work in this lab could help if decide if I would like to specialize in hematology, oncology or in another field of medicine. I don’t plan on research being a part if my career now but if I like research I may enter a combined MD/ PhD program. These programs focus on research along with clinical medicine and the graduates of these programs are involved with research and clinical medicine. By completing this experience I hope to figure out if research is something I would like to make part of my career.

**Clearly and thoroughly address how each of the following elements will be exhibited in your work:**

1. Connection to Learning Outcomes within the Honors Thematic Area (identified above)

As this will be my first experience in a research lab the first learning outcome that I want to address is "Ability to identify and apply appropriate methodologies". I want to learn basic lab techniques such as pipeting, cloning , virus packaging, cell culture, and polymerase chain reaction . These lab techniques are used by every research lab as well as in some clinical labs. I want to be able to be effective in a research lab after this experience in case I choose to make research apart of my career or in case I wish to pursue a different research position. But beyond just knowing how to perform the various techniques, I also want to understand why certain techniques are preformed in certain circumstances. In the lab classes I have taken so far the question of why is rarely answered. We are told to perform the experiment a certain way because it will give the results we want but we are never told why certain techniques are used and others are not. I want to understand why the technique is used so I can apply it to other projects. I will achieve this by keeping a detailed lab notebook with step by step instructions for each technique along with notes explaining the use of the chemicals being added and why the steps are preformed.

I also want to address the "Disseminate the research results and knowledge gained" learning outcome. I feel that if you can`t discuss your research with others, you really don’t understand your research. I also want to improve my presenting skills. I will present my findings at the Undergraduate Research Conference in the spring to improve my presenting skills. Presenting will also give me an opportunity to discuss my research with people in and out of the scientific community. Beyond explaining my research to another scientist, I also want to be able to explain it to people without much of a scientific background. I believe that if you can explain something to a person with little or no background in the field you can a clear understanding of the topic. A good test of how well I know something I know a topic is how well I can explain the topic to someone with a very limited background in the field that I am disusing. Presenting my research will show me just what exactly I got out of my research experience.

I will address the "Possess a well-developed awareness of literature in the field" learning outcome as well. I will address this learning outcome by reading several articles that my mentor sent to me to prepare myself for research. At the end of this experience I hope to be able to read a scholarly article and understand what the article is about. I will outline the article in my own words to further my understanding of the article. I will also be reading the protocols of experiments as I do the experiment. I plan on saving the protocols in my lab notebook so I can go back and look at them as my experience in the lab grows.

1. Connection to Goals and Academic Theories (include reference list, as appropriate)

I have known that I wanted to be a doctor for a long time now. I am less sure though on what I should specialize in. By doing this project I hope to decide whether I want to purse I career in hematology, oncology or a completely different specialty. This project has a hematological focus however the floor that my lab is located on is a hematology/ oncology floor and there is a lot of sharing both materials and information between all of the labs . I had never given much thought to a career in research until I heard a speaker talk about a combined MD/PhD program and I was very intrigued by the possibility doing research and practicing clinical medicine. I hope to determine by doing this project if research is something that I would like to remain involved in throughout college and into my professional career. I also want to determine what upper-level classes I would like to take once that time comes. If I enjoy this research I may choose to take classes that relate to the research that I did. To prepare myself for research I will read papers previously by the lab I will be working in to gain a sense of what they have already done. Prior to starting research the PI or principal investigator of the lab Dr. Pan sent me several articles. The first article *Reprogramming erythriod cells for lysosomal production leads to visceral and CNS cross-correction in mice with Hurler syndrome* by Daren Wang, Wei Zhang, Theodosia A. Kalfa, Gregory Grabowski, Stella Davies, Punam Malik, and Dao Pan provides information on how the IDUA gene is introduced into a red blood cell and over expressed. The article discuses how the IDUA gene is implanted into a hematopoietic stem cell and after the cell differentiates into a red blood cell the IDUA gene is expressed. The article also touches on how the IDUA expressing red blood cells have lead into correction of organ an central nervous damage due to MPS. My research is very similar to the research described in this paper. I am working with transforming macrophage cells with a gene similar in function to IDUA as a possible treatment for another lysosomal storage disease, Gaucher`s disease. Two of the articles I was sent to read discus the challenges to getting IDUA across the blood-brain barrier. The blood-brain barrier is a highly selective membrane that isn't permeable to many substances besides oxygen, carbon dioxide, hormones, and glucose. The difficulties in treating MPS 1 is getting the treatment into the brain to correct the damage within the brain. *Engineering a lysosomal enzyme with a derivative of receptor-binding domain of apoE enables delivery across the blood–brain barrier* by Daren Wang, Salim S. El-Amouri, Mei Dai, Chia-Yi Kuan, David Y. Hui, Roscoe O. Brady, and Dao Pan and *Cell and gene-based therapeutic approaches for neurological deficits in Mucopolysaccharides*  by Dao Pan both discuss ways to cross the blood-brain barrier with IDUA. The last article *Secreted Luciferase for In Vivo Evaluation of Systemic Protein Delivery in Mice* by Salim El-Amouri, Phuong Cao, Carol Miao, and Dao Pan discusses the mechanism to deliver IDUA within an organism. In my research I also think about the way that my gene of interest is delivered thought out the organism. The gene the inserted in the DNA of a cell in the organism in hopes that the cell will produce the protein that the gene codes for. This method will spread the gene of interest to the body cell however this method will not reach the brain. In order to reach the brain we must think of alternative methods. One of such methods is to alter the structure of the receptors on the blood-brain barrier to allow large molecules to pass.

1. Initiative, Independence, and/or Creativity

In order to receive this position I showed initiative by writing four letters of interest and interviewing with each of the labs that I applied to. My initiative in writing the letters and interviewing is what got me this position with Salim. I will be fairly dependent on Salim until I have learned all of the basic lab techniques but after I have learned the techniques I will become more independent. As I learn more I will be more confident and more likely to take on and ask for independent parts of the overall project. As my knowledge grows my creative input will also grow. By the end of the semester, I hope to have input in to designing new experiments and projects.

1. Reflection

I plan on reflecting on my experiences in the lab in two ways. First I will be keeping a lab journal filled with instructions on how to do the various lab techniques I learn. These instructions will be detailed and step by step so I can look back at them one day and be able to perform the technique easily. After I have completed this experience I will scan a few of the pages from my lab journal and post them on my learning portfolio. I also plan on doing a weekly video blog to address more of my personal feelings about what I am thinking as I spend more time in the lab. The blog would also be posted in my learning portfolio. The blog away of informing my family and friends of what I am doing. The blog will also allow me to reflect on my more personal feelings of my research and how the research is going. Doing a weekly blog will also give me practice in explaining what I am doing to people without a heavy science background. My blog will follow a set pattern each week. I will open with what I did that week and my general feelings on the lab that week. Then I move into any progress with my lab training and how it's going. Next I will give a progress check on my learning outcomes for this project. I will check in and see how my bank of lab skills is growing and if my understanding of the literature has increased any. Finally I will end my blog with any tie ins between the lab and my classes, my plan in the lab for next week and finally I will post any results that I have from that week.

1. Dissemination

As I mentioned earlier one of the learning outcomes I want to accomplish with this project is to "Disseminate on the research results and knowledge gained". I plan on disseminating my research by presenting at the Undergraduate Research Conference on April 11th 2014 held by UC`s office of Undergraduate Research, Scholarly Endeavors, and Creative Practice. I would present my research in a poster presentation. The audience at the conference will be a mixture of the population of campus. There will be other undergraduates and faculty in attendance. My presentation at the conference will be most interesting to members of the scientific community but people outside the scientific community can still learn something from my presentation. Members of the scientific community will learn the methodology behind what I did and the applications of my research. People outside the scientific community will learn about a genetic condition they have probably never heard of, the symptoms of that disease, and what can be done to treat it. Everyone who sees my presentation can learn how to get involved in research and learn what research is really about.

1. Project Advisor (list the person’s name, title, and contact information)

Salim El-Amouri

Postdoctoral fellow

Gene Therapy/Cancer and Blood Disease Institute, CCHMC

Building S, CCHMC

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1. Budget (if applicable)

I would be working 11 hours a week for 15 weeks. This will total165 hours spent in the lab with additional hours spent reviewing and reflecting on what I did in the lab.

9. Citations

El-Amouri, Salim, et al. "Secreted Luciferase for In Vivo Evaluation of Systemic Protein Delivery in mice."Molecular Biotechnology (2013): 53:63-73.

Pan, Dao. "Cell and gene-based therapeutic approaches for neurological deficits in Mucopolysaccharides ."Current Pharmaceutical Biotechnology (2011): 884-896.

Wang, Daren, et al. "Engineering a lysosomal enzyme with a derivative of receptor-binding domain of apoE enables delivery across the blood–brain barrier."Proceedings of the National Academy of Sciences of the United States of America (2013): 2999-3004.

"Reprogramming erythroid cells for lysosomal enzyme production leads to visceral and CNS cross-correction in mice with Hurler syndrome."Proceedings of the National Academy of Sciences of the United States of America (2009): 19958–19963.