1. List past and present research activities associated with your interests in mathematics, science, or engineering in which you regularly participate. Explain the duration, degree, and significance of your involvement, including what responsibilities you had in the project. In the absence of formal research experience, describe briefly any other skills or accomplishments, i.e., posters, presentations, publications, etc., significant and relevant to this application.

My experience in academic research began in September of 2011, my freshman year of college. I began work in the lab of Dr. Erik M. Jorgensen, a biologist at the University of Utah. In Dr. Jorgensen's lab, I worked under the guidance of Dr. Christian Frøkjær-Jensen, a postdoctoral fellow. With Christian, I worked to expand a technique that he had previously developed, in which modified transposons can be utilized to make transgene insertion sites within the genome of the nematode Caenorhabditis elegans. Over the course of my first year in the lab, I was able to create three putative insertion sites within the genome of the worm which can be utilized in future experiments examining the effects of genetic position on expression levels.

Over the summer of my freshman year, I had the opportunity to continue my research in the lab of Dr. Leonid Kruglyak at Princeton University. In Dr. Kruglyak's lab, I worked under the guidance of Dr. Erik Andersen, a postdoctoral fellow. I continued to work with C. elegans, though this time the project was to assess the genetic factors that confer a greater resistance to the herbicide paraquat, with respect to body and brood size. I was responsible for the creation of the transgenic and near-isogenic lines to be used in high-throughput assays and partially for the analysis of the resulting data. As a result of this project, we were able to identify putative genetic effects on brood and body size for animals grown in paraquat.

Upon my return to the University of Utah in the fall of 2012, I returned to my work in Dr. Jorgensen's lab, but began work with another postdoctoral fellow, Dr. Rob Hobson. This year, I am investigating the effects of the protein family stonin on the proper functioning of the C. elegans nervous system. Though Dr. Hobson has designed this project, I will be responsible for carrying out many of the genetic screens and analysis necessary to complete it. As a result of this project, we hope to characterize the protein stonin through both structure/function analyses and genetic screens to refine our understanding of the function of stonin at the cellular and organismal levels.

In addition to conducting research in a laboratory setting, my work thus far has also allowed me several opportunities to explore other aspects of the scientific process such as grant writing and presentation. For my second semester of research in Dr. Jorgensen's lab, I applied for and received a grant from the Undergraduate Research Opportunities Program at the University of Utah to help fund my work. At the end of this semester, I presented my work at both the Bioscience Symposium for Undergraduate Researchers and the Undergraduate Research Symposium. Additionally, I was able to publish an abstract of my work in the university's Undergraduate Research Abstracts Journal. My work from Dr. Kruglyak's lab will be presented at the Utah Conference on Undergraduate Research and the National Conference on Undergraduate Research, both taking place in the spring of 2013. Additionally, in the spring of 2013, I will apply to present my current work in Dr. Jorgensen's lab at the Undergraduate Research Symposium and Bioscience Symposium for Undergraduate Researchers and will also

submit an abstract of this work for publication in the 2013 volume of the Undergraduate Research Abstracts Journal.

2. List activities in which you have participated at your school, such as clubs, publications, debating, dramatics, music, art, and student government. List in order of importance to you. Note: We suggest you use a columnar format with the following labels: College Activity, Dates Participated, Offices Held

College Activity, Dates Participated, Position Held:
Undergraduate Research Opportunities Program, 8/2012-Present, Undergraduate Research Ambassador
Undergraduate Research Opportunities Program, 1/2012-5/2012, Undergraduate Research Assistant
Intramural Football, 8/2012-10/2012, Team Captain
Intramural Football, 8/2011-10/2011, Player

3. What are your professional aspirations? Indicate which area(s) of mathematics, science, or engineering you are considering making your career and specify how your current academic program and your overall educational plans will assist you in achieving this goal.

I intend to conduct academic research and teach at the university level. Specifically, I would like to investigate the problems associated with our understanding of gene expression and regulation. Despite being only a sophomore, I am already taking classes in genetics and genetic engineering at the senior level. I plan to continue challenging myself, not only for my own personal gain in terms of knowledge, but also to make sure that I have the tools necessary to take on some of the biggest problems in biological research. As my work this past summer taught me, it is not only biology classes that I must take in order to be successful. Instead, I learned that the most successful researchers are often those that are well versed in a variety of fields. Knowing this, I am planning to adjust my plan of study to include more courses in the fields of mathematics and computer science, two disciplines that I believe will be invaluable to the field of biology in the coming years.

4. Describe an activity or experience that has been important in clarifying or strengthening your motivation for a career in science, mathematics, or engineering.

At the age of twelve, I was diagnosed with Ulcerative Colitis, an inflammatory bowel disease that is thought to have a genetic basis and an environmental trigger. Through my teenage years, I had planned to join the Air Force through the ROTC program and spend my career in the military. Unfortunately, I learned that Ulcerative Colitis is a disqualifying condition and I would not be allowed to enlist. At this point in time, I was taking an Honors Biology class in high

school and became deeply intrigued with the workings of the genome and its varied effects on phenotype. As I progressed through my biology courses, my interest broadened and I fell in love with the idea of discovering, through research, the unknown workings of the genetic system. I now plan to attend graduate school and conduct research in the fields of gene expression and regulation. I am hopeful that the research I conduct in the future may have an impact on the issues pertinent to diseases like Ulcerative Colitis.

5. Goldwater Scholars will be representative of the diverse economic, ethnic, and occupational backgrounds of families in the United States. Describe any characteristics or other personal information about yourself or your family that you wish to share with the selection committee.

Since both my parents are teachers, a great importance was placed on education from an early age. As a result, I have always been passionate about the acquisition of knowledge. In addition, I have found that sharing information with others can be just as rewarding as learning. I find teaching to be a very valuable and gratifying experience. It not only allows others to gain from my personal knowledge, but also allows me to frequently challenge and solidify my understanding of a particular topic. I credit my parents with being the main inspiration for my decision to pursue a career in academia.

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C. elegans as a Model for the Effects of Genetic Variation on Susceptibilities to Environmental Stresses

In 1974, Dr. Sydney Brenner established the nematode *Caenorhabditis elegans* as a genetic model organism [1]. Since that time, *C. elegans* has played a critical role in discoveries important to human health, including the identification and characterization of the genes involved in three key pathways mutated in human cancer [2], the sequencing of the first genome from a multicellular animal [3], and the first development of tools for gene knockdown (RNA interference) and tracking proteins *in vivo* [4]. In fact, much of the early work on *C. elegans* led to three Nobel Prizes. Although *C. elegans* is a powerful genetic model in studies of medical relevance, it has yet to be harnessed to investigate gene-environment interactions in terms of populations and their inherent genetic variation.

Our genes control roughly half of the differences among individuals; the environment controls the other half. In addition, genetic variation exists between any two individuals within a species. It accounts for many of the differences between individuals including not only obvious traits, such as hair and eye color, but also not so obvious traits such as predisposition to many illnesses, including Crohn's disease [5] and Alzheimer's disease [6]. On a personal level, research into gene-environment interactions and genetic variation appeals to me because of the implications it has on the diagnosis and treatment of diseases like Ulcerative Colitis and Primary Sclerosing Colangitis, two diseases with which I have been diagnosed. Genetic variation has already been shown to play an important role in the diagnosis of these diseases [7], and it is suspected that there may be an environmental condition that can trigger the associated physiological symptoms. However, the research necessary to uncover the genetic-environmental effects associated with these diseases, if carried out in humans, would be costly, both in money and time, and difficult due to our limited ability to manipulate the human genome. Further research into genetic variation and gene-environment effects using the nematode *C. elegans* has the potential to uncover genetic susceptibilities at a much faster rate and for a much lesser cost.

C. elegans has been utilized to assess the toxicity of many chemicals using high-throughput screening, a process that allows for relatively quick data collection and analysis [8]. This work has led to the characterization of several gene-environment interactions. However, this work, and most of the other work like it, has focused on only one strain of *C. elegans* and has not begun to examine how the effects of the toxins are suppressed or enhanced by genetic variation within the species. Because approximately 38 percent of *C. elegans* protein-coding genes are conserved to some extent in humans [9], there is reason to believe that by determining how variation in these genes affects stress responses in worms immediate advances can be made in human medicine. For these reasons, I would like to propose a research project that will help to expand our knowledge of gene-environment effects, determine the role of genetic variation in disease, and suggest diagnostic tools and treatments for human diseases. This project will build heavily upon research I have already conducted.

The basis for this project comes from research I conducted during the summer of 2012 in Dr. Leonid Kruglyak's laboratory at Princeton University. I worked with Dr. Erik Andersen to determine the genetic basis for higher tolerance to the herbicide paraquat with relation to body and brood size in *C. elegans*. Over the course of this project I was introduced to many of the methods I intend to use in the proposed project. These methods include quantitative genetic analysis and the statistical tools necessary to understand these data. Over the course of this project, I was able to detect the genetic effects of paraquat on worm growth. The results of this project, which I will present at several upcoming symposia, lend credibility to the idea that *C. elegans* can effectively model gene-environment effects.

Previous to my work in Dr. Kruglyak's lab, I worked in Dr. Erik Jorgensen's laboratory at the University of Utah with Dr. Christian Frøkjær-Jensen to expand a technique that Dr. Frøkjær-Jensen had developed to create transposon-based transgene insertion sites within the genome of *C. elegans*. This work was particularly helpful because it gave me the necessary skills to carry out experiments involving molecular genetics, a critical skill necessary to determine connections between genes and environmental effects. My current research project in Dr. Jorgensen's lab, with Dr. Rob Hobson, will give me the tools to analyze the gene-environment effects at the mechanistic level. This project focuses on determining the exact role of proteins of the stonin family on the proper functioning of the *C. elegans* nervous system. I

will conduct several screens to identify the effects of changes to the stonin protein structure on the phenotypes of affected worms. This research has implications in later segments of the proposed project, as it can be used to identify how variants confer a greater or lesser susceptibility to environmental stressors at the molecular level.

The proposed research will begin with the collection and acquisition of as many genetically unique *C. elegans* isolates as possible. These isolates will harbor genetic variation that can influence sensitivity to different compounds or environmental conditions. Then, using quantitative genetic methods such as those that I learned from my experience in Dr. Kruglyak's lab, I will determine regions of the genome that control susceptibility to the compound or environmental condition in question. Next, through a series of backcrosses, the identified region of the genome will be isolated into a control genetic background so that any changes in phenotype from the control strain can be attributed directly to the identified region. This process will be repeated, with each successive region being smaller than the previous, eventually identifying the specific gene responsible for the difference in the observed stress response. In order to quickly and easily track the presence of the genetic interval, I will make use of the transposon-based gene insertion method that I learned in my first year in Dr. Jorgensen's lab. Once the gene(s) responsible for controlling the stress response are known, work can begin to try to determine the exact role of the pathway or process in which the genes act and to assess conservation to humans. This portion of the project will draw upon techniques I use in my current work in Dr. Jorgensen's lab, and will consist of several screens to determine where and how the gene works to cope with the environmental stress. Based on the information attained from this project, suggestions can be made toward the development of human diagnostic tools and treatments.

My roles in the aforementioned research projects have just begun to touch upon the impact I would like to have on the field of genetics. There are projects, like the one I proposed above, that will have a profound effect on our understanding not only of biology, but also of human health and medicine. I am excited to be conducting research that may one day lead to diagnostic tools to detect and treatments to reduce or eliminate the physiological symptoms of diseases like those that I have. Biology has the potential to alleviate the greatest of human sufferings and expand our knowledge of ourselves far beyond the current state. I am excited to assume my role in the future of the biological sciences.

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