Please describe your significant research experiences. In your statement, please specify your researcher supervisor's name and affiliation, the duration of the experience, the nature of the problem studied, and your contributions to the project. (10,000 character limit)

While my experiences as an undergraduate have been diverse, research has unquestionably been the most important and rewarding component of my undergraduate education. Committing myself to the world of scientific research has instilled an investigative mindset and a passion for the scientific process and an appreciation for the results of medical research. Research has proven to be a fantastic supplement to my undergraduate coursework, allowing me to strengthen my conceptual understanding of the material taught in my science classes and leading to an improvement in my academic performance as I became more involved in research outside of the classroom. Participating in research and the consequent interactions with my peers and advisors continues to provide me with a toolbox of hard and soft skills that has paid dividends in my coursework and professional relationships.

I first began my research as a freshman in the lab of Dr. Richard Gardner in the University of Washington Department of Pharmacology, investigating the mechanism of the ubiquitin pathway in yeast cells. Research in the Gardner lab focuses upon ubiquitin, a covalent protein modifier found naturally in nearly all eukaryotic cells that plays an important role in cell cycle regulation. Ubiquitin modifies substrate proteins in a three-step cascade, with its specificity defined by a protein known as the E3 ubiquitin-protein ligase, which is the subject of ongoing research in the Gardner lab. For my first year in the Gardner lab, I primarily assisted with research projects of graduate students and with various tasks throughout the laboratory investigating the biochemical interactions of San1, a known yeast ubiquitin-protein ligase, with its substrate proteins. While I desired more independence in the lab, this period allowed me to master essential research techniques, including yeast and bacterial transformation, PCR, gel electrophoresis, western blotting, and oligonucleotide design. Having time to learn these techniques while being closely mentored in the lab provided a valuable opportunity to increase my efficiency in the lab and also gain confidence in my work at the lab bench. Taking additional time to gain a detailed understanding of the scientific background, purpose, and significance of my new lab skills also helped immensely in my related scientific coursework, as I found myself with a stronger understanding of the topics presented in class due to my experience practicing these related techniques in lab.

In the fall of 2011, I was awarded a Mary Gates Research Scholarship for my proposal to develop an in vivo survival-based split protein assay to detect the reconstitution of the ubiquitin pathway in E. coli. The proposal and award enabled me to transition from a closely mentored member of the lab to an independent researcher with my own project. Recent work has shown that the ubiquitin protein modification pathway, which naturally occurs only in eukaryotic cells, can be synthetically expressed in E. coli, a prokaryotic organism, when the ubiquitin machinery is transplanted into the cell using protein co-expression plasmids. For this project, I designed a survival-based screen in order to detect an interaction between the eukaryotic protein ubiquitin and its substrate in E. coli, outside of its natural eukaryotic environment. Successful completion of this problem provides a high-throughput method of finding substrate cohorts for ubiquitin-

protein ligases, solving a large problem within the ubiquitin field and holding the potential to lead to promising new forms of drug delivery for the treatment of diseases related to aggregation of aberrant proteins, such as Huntington's disease. In the spring of 2012, I also wrote a detailed scientific proposal to use my screen to discover human homologs for San1 and other yeast ubiquitin-protein ligases, with the eventual goal of using DNA mutagenesis to stimulate and inhibit the ubiquitin pathway, leading to methods to target human diseases related to protein aggregation. I expect research on this project to continue through the 2012-2013 school year in pursuit of these goals. The direct applicability of my project to clinical treatments has been a strong motivator to pursue a career as a clinician scientist. My work on this project was presented to my peers, advisors, and other experts in the field at the 2012 University of Washington Undergraduate Research Symposium. Having experience presenting my work to a scientific audience greatly improved my ability to communicate my ideas in research and exchange innovative thoughts and concepts with my peers.

Although I found the research in the Gardner lab stimulating, I sought research that more closely related to patients. Because of my interest in ophthalmology and my background in bioengineering, I approached Dr. Mark Pennesi at Casey Eye Institute at Oregon Health & Science University (OHSU) prior to the summer of 2010, who offered me a summer-long volunteer position as an undergraduate researcher in his laboratory. Since joining the Pennesi lab, my research has focused on two parallel projects, both involving the advancement of retinal imaging technologies. During my first summer at OHSU, I learned how to operate the Bioptigen optical coherence tomography (OCT) apparatus on mice, taking cross-sectional images of the mouse retina at many timepoints in order to characterize and monitor retinal degeneration in mouse models of retinitis pigmentosa. In addition, I developed Matlab algorithms that were used to calculate retinal layer thickness in order to diagnosis and monitor the progression of degenerative retinal diseases in humans. Working with Dr. Pennesi, who is a clinician scientist with a background in bioengineering himself, allowed me an opportunity to view how scientists can directly apply research to the clinic. Because of my work on this project, I was awarded a Fight for Sight Summer Student Fellowship to continue my work in the Pennesi lab during the summer of 2011. In addition, the results of this project were presented at the annual conference of the Association for Research in Vision and Ophthalmology (ARVO) in May 2011 and recently accepted for publication in the peer-reviewed journal Investigative Ophthalmology & Visual Science.

My second project in the Pennesi lab has been the investigation of adaptive optics imaging technology to measure changes in cone photoreceptor density. My main contribution to this project has been the development of Matlab algorithms to automatically count the number of cone photoreceptor cells and calculate the cone density in the retina using a montage of images acquired from a flood-illuminated adaptive optics camera. My work in the Pennesi lab provides an opportunity to directly apply the knowledge learned in my undergraduate bioengineering courses to medical research, as I have the opportunity to work on computational research work. As a result, the adaptive optics and OCT projects contribute several additional skills to my growing toolbox of research skills, including proficiency in computer programming for engineering applications, practice of basic small animal handling, and surgical techniques, including intravitreal injection, on small animals. In addition, I have played a role in the organization of clinical trials to test the efficacy of adaptive optics imaging systems in a clinical

setting, which has given me experience interacting with patients in a research environment. Seeing our research progress from animal subjects to patients in a hospital has served as a strong motivator to pursue a combined MD/PhD program and work as a clinician scientist, as the ability to see my research having a direct impact on the treatment of patients with degenerative retinal diseases has been incredibly rewarding. My work on this project has resulted in several abstracts and presentations at international conferences during the spring and summer of 2012. I also recently received an NSF fellowship to attend the 11th Summer School on Biocomplexity in Istanbul, Turkey, where I presented the results of my research in the Pennesi lab and attended several lectures from prominent bioengineering faculty members around the world discussing the applicability of bioengineering technology to research in developing countries with point-of-care diagnostics.

As I have continued my research as an undergraduate, I have been fortunate to gain more independence in my research work. When working under a mentor, I often found that my mentor predetermined the research goals and aims, with my role simply being carrying out the desired research. With more experience, I was given the opportunity to collaboratively participate in the experimental design process. In both the Pennesi and Gardner labs, I have had the opportunity to work with my mentors to draft and submit scientific research proposals for competitive research awards, which has provided valuable practice expressing my ideas to peers and faculty members in order to gain support for my work. As a result of writing these proposals, I have received appreciated experience in working collaboratively with my mentors in the experimental design process. Furthermore, during the 2011-2012 school year, I also remotely worked part-time for Dr. Pennesi, contributing to ongoing research by writing computer algorithms to complete tasks required for the progression of research trials with the adaptive optics project. Working for both labs while taking a full course schedule for the entire year helped me manage my time management skills as well as my communication skills, as I was required to constantly communicate with members of both labs and prioritize tasks based on their relative importance.