Personal Statement Before Starting Science For Life Award

I plan to integrate my HHMI research with my classes. I will take genetics, cell structure and function, and multiple neuroscience courses in order to gain a better understanding of the research that I am doing. Beyond undergraduate studies, my HHMI activities will help me develop more sophisticated research skills and to learn to think like a scientist. I will acquire how to plan, organize, and be precise and meticulous in my thoughts and movements. These are essential skills for careers in research and/or medicine. I plan to complete a PhD program in grad school and do scientific research as part of my future career. I met my research mentors, Jada Lewis and Simon D’Alton, as a result of an HHMI Science for Life interview. They were clearly superbly intelligent and passionate about their work, which they were able to explain to me very well. This showed me what fantastic teachers Jada and Simon could be and how much I could learn from them. This was important to me because it modeled how the research could clearly reflect my medical interests and that I could learn to contribute meaningful ideas that would inspire successful projects.

I chose this particular research project for a number of reasons. Protein TDP-43 is implicated in several neurodegenerative diseases (FTD, ALS, AD) which renders it quite noteworthy thus permitting many opportunities for research and projects. Neuroscience research is exciting and is an area of huge growth. This TDP-43 research combined the practical aspect of the many valuable skills I would develop with my deep interest in medical neuroscience.

I plan to work in this lab until I graduate moving on to further projects upon completion of the research above, continuing work under Jada Lewis and Simon D’Alton.

These activities will benefit my long term career goals since I plan to complete a dual medical-PhD program. My prospective career is to be a neurosurgeon and take part in research.

To be a co-author on a peer-reviewed scientific publication I would need to contribute an equal amount of work: complete a significant amount of the experimental work, contribute to writing the paper, and provide some input into experimental design and theory. Potential activities if I make enough valuable contributions and run projects myself include the opportunity to go to a conference and present a poster on my work, attend national conferences, and compete for other awards such as the Science for Life extramural research opportunity or the University Scholars Program.

Abstract

Developmental Expression of Human TDP-43 Renders Neurons Susceptible to Neurodegeneration

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There is a proposed link between Transactivation response DNA-binding protein 43 (TDP-43) and neurodegenerative diseases, primarily in Frontotemporal Dementia (FTD) and Amyotrophic Lateral Sclerosis (ALS). TDP-43 has also been found to be implicated in Alzheimer’s disease (AD). The goal of this research is to contribute to the understanding of TDP-43 function and contribution to disease. Specifically, we are focusing on novel isoforms of TDP-43 and their potential role in neurodegenerative disease, and additionally the study of TDP-43 function through animal models. We have discovered novel isoforms of TDP-43 that appear to reside in the cytoplasm. As cytoplasmic aggregation of TDP-43 is a phenomenon seen in FTD, ALS and AD patients, these isoforms may be pertinent to TDP-43 pathology, thus facilitating disease projection in patients. We hope to understand the formation of abnormal TDP-43 and its contribution and effect to cellular pathways.

TDP-43 represents the common pathologic substrate linking the neurodegenerative disorders of FTD, ALS, and AD [1]. TDP-43 function is involved in the regulation of gene expression and splicing. Normally, TDP-43 is found predominantly in the nucleus with very low levels in the cytoplasm. In contrast, TDP-43 in neurodegenerative disease patients undergoes modifications, including phosphorylation, ubiquitination and redistribution from the nucleus to the cytoplasm. Mutations in TARDBP, the gene encoding TDP-43 protein, are associated with sporadic and familial ALS. A small portion of ALS patients have familial ALS while the vast majority of patients are sporadic. That majority has the same abnormal TDP-43 modification, altered cytoplasmic distribution and accumulations, as the familial ALS patients which suggests that TDP-43 abnormalities are involved in sporadic disease also. It has been noted that TDP-43 is continuously shuttling between the nucleus and the cytoplasm suggesting that the level of TDP-43 in the cytoplasm may play a role in normal conditions. However, what is typical of diseased cells is the almost complete absence of TDP-43 in the nucleus. In these cases, the TDP-43 is observed predominantly in the cytoplasm. This leads many to believe there is a direct positive correlation, or perhaps causation, between levels of TDP-43 in the cytoplasm and the onset or progression of the neurodegenerative diseases above.

Personal Statement After Starting Science For Life Award

When I began my research in the laboratory I was inexperienced and intimidated. Working in a lab has exposed me to different people and places; it has been a positive experience. After approximately a year of work, I have learned much in terms of science knowledge and theory. I have experienced the inner working of a lab setting. I have acquired several new techniques that I can apply to further my project and that facilitate a more scientific way of thinking. I have learned to work in a professional environment and how to incorporate college life with working. I have developed good presentation skills and a concise writing style. My interpersonal skills have advanced by collaborating with my supervisor. I think that now I am more open and conversational. Working in the lab has made me think about other parts of my life differently. I am better able to assess teaching style and I now know what style works for me. I am more organized and more precise in my diction to convey clearer thoughts.

I spent my last week of summer aiding an ophthalmologist perform cataract surgery in Oaxaca, Mexico. I attribute my ability to having quickly attained sterile technique and assistant methodology to my laboratory work. My experience in the lab sparked a deeper interest in neurology and biochemistry; I plan to apply for the interdisciplinary neuroscience major and I am considering a double major in biochemistry. Long term, being in the lab fulltime has strengthened my plans of pursuing an MD PhD.