On My College Experience...

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On my college experience...

Since I was a little boy I have always been interested in how things work. Much to my parents’ dismay, I constantly had clocks, TV remotes, and pretty much anything I could get my hands on taken apart, because I wanted to see what was inside. This innate curiosity that I possessed stayed with me into high school where I became increasingly interested in the natural sciences. I loved every biology class that I took and I soon decided that a career in science, whether it be a professor, researcher, or doctor, was right for me.

During the fall semester of my freshman year of college, I became involved in the University of Kentucky Undergraduate Research Program (UKURP) headed by Dr. Robert Tannenbaum. I began my research in the lab of Dr. Phillip Bonner in the Department of Biology working on sensory neuron axon branching and elongation in response to various treatment drugs (mainly botulinum toxin). I have to say that the experience I had in this lab is what ultimately led me to continue in research. I loved the hands-on training that I was getting and the ability to apply my knowledge to a problem to find an answer.

The summer following my freshman year, I participated in the NSF-funded Research Experiences for Undergraduates (REU) program here at UK. This is when I began my work with Dr. Diane Snow in the Department of Anatomy and Neurobiology on spinal cord injury and axon guidance. This has been my area of research for the past three years now and resulted in several poster presentations at local and national meetings and also a talk at the annual Beckman Conference this past July.

One of the most beneficial parts of my experiences in research is the amount of guidance that I have received from my mentor. Aside from the volumes I’ve learned about spinal cord injury and lab techniques, my mentor has also provided me with valuable life lessons that I will undoubtedly take with me for many years to come. Being a young college student in the field of scientific research can be quite overwhelming. In the beginning I remember being timid and unsure about even entering into the program, because I had no idea what to expect. But, after meeting with my mentor, many of those anxieties seemed to disappear. I think it’s knowing that there’s someone there who has been in the exact same place that you have and can relate to how you feel. The Beckman Scholarship Program is an amazing program that provides undergraduates with the tools they need to pursue a career in research, but none of it would be possible without the enthusiasm and dedication of the mentors.

As for my future plans and goals, everything is still kind of up in the air. Right now I am in the process of applying to medical school. Whether or not I’m going I don’t really know. If I do decide to go I will probably do an MD/PhD degree, because I know that I love to do research and would like to continue in this field. I am also kind of interested in business and was considering an MBA sometime in my future. Yeah, I know it sounds pretty crazy but what can I say, I’m a glutton for punishment. What I do know for sure is that my experiences as an undergraduate researcher and a Beckman scholar have undoubtedly prepared me for whatever my future holds.

On the Beckman Program...

Enough good things cannot be said about the Beckman Program itself. I feel extremely privileged to have had the chance to participate in such a remarkable opportunity. I remember hearing about the program when I was a freshman and thinking how cool it would be to have that honor. And, much to my surprise, I was selected the following year for the scholarship. Aside from the prestige that goes with carrying the title of a Beckman Scholar, recipients have opportunities to which most undergraduates don’t have access.

I would say that the most beneficial part of the Beckman Program is the ability to travel virtually anywhere and present your research. The experiences I gained at conferences were priceless. It is quite scary the first time you step on an airplane for a destination that you know nothing about. But, once you arrive at the conference and start interacting with other people, it becomes very exciting. Networking and learning new ideas and techniques from other people is a fundamental part of the research community, and the best places to acquire these skills are at conferences.

To me, the Beckman Program has been the most beneficial part of my undergraduate career. The knowledge and skills I have learned over the past couple of years cannot be taught in a classroom. Only the type of hands-on work facilitated by a program such as the Beckman Scholarship could have allowed me to be where I am today. Once again, I am immensely thankful for the opportunity that I have received and would like to thank everyone involved in allowing the Beckman Foundation to continue to function.
On my research projects ...

Following an insult to the spinal cord, astrocytes at the site of the injury undergo a phenomenon known as astrogliosis, which creates a large mass known as the glial scar (Silver and Miller 2004). The glial scar is inhibitory to nerve regeneration, not simply acting as a physical barrier that neurons cannot cross, but by expressing extracellular matrix proteins that trigger an inhibitory growth response in neurons. One such extracellular matrix molecule family is the chondroitin sulfate proteoglycans (CSPGs), which are found in relatively high concentrations in the glial scar following injury.

Previous assays in vitro and in vivo have demonstrated the inhibitory potential of isolated and purified CSPGs (Asher, Morgenstern et al. 2001). However, in order to transfer this knowledge base to clinical applications, CSPGs as they are produced and released from astrocytes in vivo must be understood, i.e., we need to develop and analyze a physiologically-relevant model.

The hypothesis for the study is: CNS injury induces the upregulation of astrocyte produced CSPGs that subsequently inhibits neural regeneration. The goals of this study were to 1) develop a physiologically relevant in vitro model using adenovirus technology; 2) determine the precise outgrowth behaviors in vitro of sensory neurons contacting astrocytes that over-express inhibitory CSPGs, such as brevican, neurocan, NG2, and phosphocan; and 3) determine the factors that regulate astrocyte upregulation of CSPGs in vitro.

Using an adenovirus vector that encoded for the desired CSPG (i.e., brevican) astrocytes were transfected in alternating lanes of brevican + cells and brevican (-) cells. This novel model closely mimics previous stripe-assay paradigms, while creating a more physiologically relevant model in which to examine neurite behavior. Chick (E9-10) dorsal root ganglion (DRG) neurons were added to this cell paradigm and inhibition was quantified using a simple crossing vs. turning standard. A "crossing" neurite breached the surface of a brevican + cell and a "turning" neurite exhibited some type of avoidance behavior in the presence of a brevican + cell. There was a significant (p < 0.0001) increase in inhibition in the brevican + cells compared to controls.

This technique provides a useful and simple way to express a molecule of interest from a localized area within a dish of confluent cells. Applications of these methods include the ability to create an astrocytic scar in which high levels of CSPGs are expressed, such as that expressed by glial scars in vivo. This model represents a useful tool for assaying neuronal behavior in response to CSPGs in their innate cell surface conformation. Furthermore, localized expression of molecules of interest in culture is useful for axon guidance assays, but may also be extended to the study of synapses or any interaction between two cell types in which one is induced to express a modulatory factor. Presently, studies are being conducted to examine the morphological behavior of growth cones coming into contact with CSPG + astrocytes using microinjection/micromanipulation techniques and time-lapse microscopy. These studies should help elucidate some of the underlying behavioral mechanisms behind the inhibition that has been seen up until this point.

Subsequent studies will add more complex pieces to the story. In vivo, it is known that certain growth factors, present in the glial scar, can up-regulate a variety of molecules. We will use our model to characterize the up-regulation of astrocytic PGs by transforming growth factor (TGF-β1) and epidermal growth factor (EGF). Further, once we identify the mechanisms using our model in vitro, we will be able to test these mechanisms in vivo. Thus, a future series of experiments will determine if CSPG over-expressing astrocytes in vivo have the same inhibitory properties as they do in vitro and what factors, in vivo, regulate inhibition.

Ultimately, the long-term goal of this project is to better understand the physiological role that CSPGs play in response to injury. Such an understanding will allow researchers and clinicians to manipulate the molecules that regulate the expression of CSPGs (e.g., antagonist or antibodies), to restore connectivity following spinal cord injury or traumatic brain injury, to improve motor and sensory function.

References
