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The Role of Integrin Activation in Increased Gliogenesis of Human Neural Stem Cell Cultures

There is currently no effective treatment known for neurodegenerative disorders. A few years ago, one of my aunts was diagnosed with Parkinson's disease at a relatively young age and has been struggling with the debilitating illness since. For this reason, I have a vested interest in neural research. In Dr. Steven Stice's lab, I conduct research on human neural stem cells (hNSCs), which are considered a possible source for replacing degenerated brain cells. Dr. Stice's lab has developed a novel adherent culture system of hNSCs derived from human embryonic stem cells. My research is on signaling cascades involved in neural development and on cellular changes that occur as a result of activating transmembrane proteins.

I have not taken any classes about neuroscience or neural development, so I had to do a lot of research on my topic before I could understand the work I was doing in the lab. I decided to focus on articles published in stem cell journals and neuroscience journals. Using ejournals provided by the library, I was able to search through many popular journals that publish recent articles in the stem cell field. I already knew which journals were best for my topic, so it only became a matter of the library having access to these journals. I was excited to find that the three journals that are best known for their articles in the stem cell and neuroscience fields were all available through the ejournals online. ScienceDirect gave me access to the journals Stem Cells and Development, Neuroscience, and Cell.

My work has focused on the role of integrins, which are integral membrane proteins that have an important function in neural cell adhesion and development; therefore, I have been

studying integrin activity because it may cause neural cells to implant in the human brain. Using the ejournals I mentioned, I was able to find out which articles have been published about integrin activity in stem cells and in neural cells specifically. Through these articles, I noticed that manganese was often mentioned as a tool for making integrins activate and making the cells more adherent. I wanted to study the effects of manganese on integrin activity in our cells, but first I needed to find out if there was any manganese in the media we were already putting on our neural stem cells. Using Google Scholar and PubMed, I searched the names of the media that we use in our lab and was able to find a few articles that listed the components of our media. Manganese was never mentioned in these articles and is not in any of the media we use, so I knew that adding it to the media would change the way our cells grew.

I found one enticing article by Olivier Dormond where he listed antibodies that were used for specific integrin subunits. We do not have any of these antibodies in our lab, but I found out that if other labs sponsored by the National Institutes of Health (NIH) had these antibodies, then we could ask them to send them to us. Dormond cited each reference he used for the six different antibodies he had, so I was able easily find the authors and papers myself by using Web Of Science through GALILEO. I searched for Dormond's paper first, and then used the references list from that to search the articles that he had gotten the antibodies from. Once I found the articles, I had to determine if they were American and sponsored by the NIH, because we would not be able to get the antibodies otherwise. Only two of them fit these parameters, so I also had to find out how long ago the papers were published to see if they were likely to still have the antibodies. Only one of the articles was published recently and fit all of my criteria, and I was able to ask for the antibody that we needed from the authors.

Keeping up to date on the newest discoveries has also proved to be very simple through searching Science Daily and reading newspapers, mainly The New York Times. Stem cells have proven to be so controversial because they can do great things, but they also have moral stigmas against them. They have great potential to help people with degenerative diseases, their most highlighted usage in the articles I have found, but they also serve many functions that do not relate to disease. They provide many new opportunities for everyone to remove pain and hardship from their lives. It is also easy to study neuroscience through Science Daily because they have a section about the "Mind and Brain" and have new articles daily. I have been able to discover the controversy behind my own mentor's research through resources available to me right on campus. The University of Georgia Research Magazine has published many articles on Dr. Stice's research and political activism. The Athens Banner Herald has also supported Dr. Stice's efforts in the Senate. They published an article, which is still available through their website, on the necessity of writing to Congressman and supporting those that want to further stem cell research.

Using many resources I learned about through the library, I significantly increased my knowledge and understanding of stem cell research and neural development. I also have found ways to obtain necessary tools for my research through articles I found on Google Scholar and could actually read for free because they was available at the UGA library. Using Science Direct, I was able to find many journals that contain research papers that discussed the general science of neural stem cell differentiation and my research on manganese quite indepthly. I now also have the tools to keep up with the latest information and discoveries in my area through ejournals and databases.

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The Role of Integrin Activation in Increased Gliogenesis of Human Neural Stem Cell Cultures

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Human Neural Stem cells (hNSCs) have the potential to replace brain cells in patients with neurodegenerative disorders and are derived from human embryonic stem cells. Neural cell adhesion and development depend on integrins, which are integral membrane proteins that act as bidirectional signaling molecules. Using integrin activation, hNSCs can adhere to a substrate or implant in the brain to replace degenerated cells. Through activation of integrins, it is hypothesized that Manganese will direct cells to a glial fate more rapidly than random differentiation. This study's objective is to obtain an increased rate of gliogenesis due to perturbation of integrin activation, which will result in a more purified glial cell population. To increase the rate of gliogenesis, 0.3 mM $MnCl_2$ differentiation media will be added, and hNSCs will be differentiated for 0, 14, and 28 days on polyornithine and laminin coated plates. mRNA will be isolated from each treatment using the Qiagen RNeasy kit and cDNA will be synthesized. RT-PCR will determine glial cell gene expression of the following seven genes: Glial fibullary actin protein (GFAP), GLAST, IL6, CD44, CNTFR, Aqp4, and VIM. Immunocytochemistry will be performed by fixing cells in 4% paraformaldehyde and staining using standard immunofluoresence protocols. Antibodies against representative glial proteins will be used. Protocols for differentiating purified populations for future use in cell therapy can be obtained. Ultimately, if the quantity of glial cells in a purified population is known, then patient-specific cells can be generated for the replacement of brain cells in patients with neurodegenerative diseases.