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Summer 2015

This summer I had the opportunity to begin research in the lab of Dr. Alyssa Summers in Sewanee, investigating the role of Histone Deacetylase Inhibitors (HDACi) in the progression of breast cancer. This research has been conducted by multiple Sewanee students before me, and it has been an awesome opportunity to continue their work on this subject. My responsibilities included researching my topic to learn as much background information as possible, care of two different cell lines for experiments, care of the lab mice on a daily basis, as well as running various experiments on my topic as well as other general experiments. These experiments mainly consisted of Western Blot Analyses. I also assisted my lab partner with experiments pertaining to his project regarding GIMAP proteins.

I began by investigating the role of HDACi in relation to Human Epidermal Growth Factor Receptor 2 (HER2), a client protein of Heat Shock Protein 90 (Hsp90), as well as the TGF-beta signaling pathway, in the progression, or metastasis, of breast cancer. HDACi work by inactivating HDACs, leaving acetylated proteins acetylated. A proposed pathway from research performed previously in the Summers' lab suggests that HDACi could inhibit the HDAC that typically deacteylates Hsp90. Acetylated Hsp90 would therefore not allow for proper signaling to HER2. This lack of signaling would lead to improper folding, and therefore degradation, of HER2. This degradation thus leading to a lack of regulation of the TGF-beta pathway. The lack of regulation of this pathway often leads to greater tumorigenesis through the downstream regulation and expression of SMAD proteins. Western blot analyses with varied concentrations of various HDACi were to be utilized to determine their effect on the expression of HER2, histone 3 (H3), acetylated histone 3 (AcH3), SMAD2, and phosphorylated SMAD2. These

HDACi include Belinostat, a pan-HDACi, and 966-7 a histone 3 specific HDACi. Another added factor was the addition of exogenous TGF-beta to half of the treatments. The two cell lines utilized were MDA-MB-361, a HER2-type adenocarcinoma with HER2+ amplified, and ZR-75-1, a luminal type A ductal carcinoma that is estrogen receptor positive (ER+), progesterone receptor positive (PR+), and HER2–.

Throughout this summer I have learned many necessary research skills both from Dr. Summers and my lab partner, Jacob Zalewski, that will allow me to continue research and be successful in my experiments. I have also learned time management in the lab and the planning that comes along with this time management. Many of the experiments performed are time sensitive, and so, planning the overlapping of multiple experiments is a vital tool in the lab. I have also learned how much effort goes into performing this research and that results are not always attained on the first attempt. Persistence in my efforts has been key this summer and will continue to be a valuable component of my continued efforts in this research. I have also attained better problem solving skills throughout the summer as I have been challenged to come up with different ways of performing different tasks if something doesn't necessarily work. I think the biggest lesson I learned from this summer, however, is that science is science. Things always have the potential to go wrong. Research is not about obtaining results every single time you try something new with your experiment. Research is getting what you thought you would once after multiple tries and many frustrations. Research is all about persistence and dedication. It can be frustrating and heartbreaking, but it is this failure that drives the desire further.

This summer has taught me what I am capable of as I continue work in this research. It has given me confidence going into my junior year here at Sewanee that I will be able to attain my goals of attending medical school as long as I continue to work with persistence and perseverance. Things are not always going to go my way, but eventually I will achieve success. For example, the first experiment I ran for the summer did not turn out how I had hoped it would. Actually, it did not turn out at all and I was left with no results; however, this failure only increased my desire to obtain results. I was successful in my second attempt and attained results. Another example was losing all of my cells in the last week of summer research, something I had been trying to grow all summer for experiments. While I lost everything I had worked for all summer, I have the opportunity to come back in a few short weeks and try again. This setback has only increased my desire to succeed.

This research opportunity has greatly heightened my desire to attend medical school and become a physician. While I have possessed this desire for a few years now, and truly feel it is what I am meant to do with my life, this summer has only increased this desire and drive. It has given me the added push that I needed as I go into my junior year and begin to think more about medical school. I am excited to continue this research throughout my next two years at Sewanee, and this summer has been such an integral component of that opportunity. This summer has given me the needed training I would not have been capable of attaining during the school year with classes and a varsity sport. I am so thankful that I have been able to research in Sewanee this summer. I have learned so much and cannot wait to continue learning more as I continue this

research. Even though it was a time of some setbacks, those setbacks have left me ready to get back in the lab.