RAD(51D) SCIENCE

by Claire Chabot
Photo by Stephen Cupschalk

I came into USC thinking I wanted to do one thing with my life but soon switched to something completely different, in part because of the research I began in Spring 2016. If you are looking to get into research, my advice is to join a major-specific club as a way to meet a potential research mentor. During meetings for the Carolina Association of Pre-Pharmacy Students (CAPPS), presenters would come to discuss the various job opportunities in the field of pharmacy. It was in January of 2016 that Dr. Doug Pittman was scheduled to present on his research in pharmacogenomics. Although I had been interested in this topic for some time, I was still fascinated when he talked about his research linking chromosome integrity and potential chemotherapy targets in ovarian cancer genes. The future of personalized medicine drew me in. Once the meeting was over, I went right up to Dr. Pittman and asked if I could swing by sometime to see his lab. A week later, he gave me a tour of the lab, where I also met Dr. Nicole Reilly (then graduate student and one of my future mentors). I asked if it might be possible for me to come and work on a research project as an undergraduate. After discussing how many hours I would commit a week and other specifics, my training started! I've never considered myself to be an especially direct individual but I am truly glad that I took the risk in asking Dr. Pittman for an undergraduate research position. After all, I had nothing to lose; the worst-case scenario would have led to me continuing my search for a research position in other labs.

I soon found out that research requires patience, a lot of it. When I began in the lab I didn't believe it when Dr. Pittman told me that research was "99% troubleshooting." I thought he was joking until the entirety of the spring semester was spent trying to figure out why nothing was working despite my careful execution of established protocols. In the beginning, most of my time was spent shadowing Dr. Reilly to learn new techniques and having weekly conversations with Dr. Pittman about the theoretical background behind his research. It was difficult not being able to dive right into a project but I understood why once I became somewhat independent with my own project. Now I finally feel confident laying out my weekly plan, presenting my own data, and fully understanding the other projects in the lab. Looking back it is satisfying to realize how much I have grown.

The main focus of the Pittman lab's research is an ovarian cancer susceptibility gene: Rad51D. My specific project mainly involves cloning a Green Fluorescent Protein (GFP) to different Rad51D constructs. I enjoy this project not only because cloning is fun, but also because it serves an important purpose. For starters, one in seventy-three women will develop ovarian cancer and many of their tumors will have mutations in known DNA repair genes such as BRCA1, BRCA2, or RAD51D. The RAD51D gene is essential for cell division, repairing DNA damage, and maintaining genome integrity. These changes increase sensitivity to DNA damage, which previous studies have shown may correlate to RAD51D-deficient patient sensitivity to chemotherapy. I have hypothesized that these RAD51D mutations disrupt RAD51D nuclear localization since improper localization of RAD51D generally causes an increase in DNA damage and subsequent cell death. One long-term goal of this project is to provide insight into how the RAD51D mutations may benefit the fifty percent of ovarian cancer RAD51D-proficient patients by increasing their sensitivity to chemotherapy. If the mutated regions on the RAD51D protein are required for nuclear localization, they can provide a potential target site to block RAD51D function and sensitize cells to chemotherapeutic agents.

I can easily pinpoint some of my favorite moments from the two years I have worked in the Pittman lab. During the process of testing my hypothesis, I generated the fusion between RAD51D and GFP that allows the detection of RAD51D localization. When I finally saw my cells fluorescing under a microscope after about a year of work it was such a thrilling experience, especially after all the pesky troubleshooting it took to get those results. In fact, I was so proud of the work I did that I transformed it into an art project for the Honors College Artists in Residence program that will be on display throughout 2018. Some of my other favourite moments have been earning the Magellan and SURF grants after trading drafts between Dr. Pittman and Dr. Reilly for what seemed like an interminable amount of time.

My experience in the Pittman lab has given me so much confidence, not only in my own potential as a scientist, but also in more practical abilities such as presenting at conferences such as Discovery Day and the National Conference for Undergraduate Research (NCUR). The impact of the Pittman lab has been powerful enough to inspire me to switch my major to biochemistry with a pre-med focus. Throughout your time in college you never know who you are going to meet or how it will shape what you will become, but sometimes it just helps to put yourself out there and try.