

Sean Liu essay

GNBCC Students & Scientists Program, Summer 2012

Dr. Yong Zhu's Laboratory of Epidemiology and Public Health

On June 27th, I sat quietly in a room in the back of Dr. Yong Zhu's lab in Yale's Laboratory of Epidemiology and Public Health. Rick, my partner, sat across from me as we both nervously waited for our supervisors to step in and speak to us about the work that they do. I wasn't quite sure what to expect; I was nervous, anxious, and amateurish in my knowledge of epigenetics and breast cancer. It wasn't my first time in a lab, yet I couldn't shake off the "new guy at work" feeling.

The silence in the room was interrupted by our lab manager, Dr. Zhu, who proceeded to formally welcome us to the lab. Much to my surprise, he asked me and Rick if our dorms were nice, if we had explored New Haven yet, and just talked to us about the school and area without judging us as just high school students.

After having a normal, everyday conversation, Dr. Zhu invited a few of the researchers to join us and explain their field of study. Epigenetics, the study of heritable changes in genetic expression that is not caused by changes in the DNA sequence. It was my first time hearing terms like "DNA methylation" and "CpG islands", but the researchers made all of the terms and concepts clear and assured us that we'd eventually be brought up to speed. It was very comforting to speak with such helpful and sensible people, and every day I was reminded of their amicable attitudes by their helpfulness and frankness. They showed us around the lab, answered all of our questions, suggested restaurants in town, ate lunch with us, joked with us and made us feel at home. While they made sure we enjoyed our stay at Yale, everyone at the lab also made sure that Rick and I learned all we could about how epigenetics could be affected, and how these changes could impact diseases such as breast cancer.

I was given the task of reading papers on epigenetics, microRNA, circadian shifts, and epigenetics roles in cancer development. Rapidly, I developed a firm grasp on how methyl groups could be added onto certain parts of genetic sequences, effectively altering gene expression and leading to abnormalities in cells. I realized that as the lab's prior research suggested, long term disturbances in the circadian rhythm, such as working at night and exposing people to light at night, could alter DNA methylation at CpG sites which could then lead to the development of cancer. Genes that caused cells to grow could become hypomethylated, increasing their expression and drive cells to rapidly multiply as cancer. Conversely, cancer-suppressing genes could be hypermethylated, lowering their expression and inhibiting their function of preventing the development of tumors. Confident that I had understood the basics, Daniel,

our supervisor, gave me a list of 100 instances of significantly hypomethylated CpG sites that occurred in women who had worked the night shift for at least 10 years. For each case, I used resources including UCSC Genome Browser and Oncomine to establish whether the target CpG site was located in CpG islands (clusters of CpG sites), a potential promoter region, and if previous studies also suggested that the related genes were overexpressed in cancers. Through this process, I learned how to take each characteristic into consideration and how to narrow down a studies focus until I had found the most promising gene to study. As Dr. Zhu insisted, we spent much of our time in this preliminary stage. He put emphasis on this stage of thinking, researching, and creating a solid base because he believed that this, not the actual lab work, was the hardest and most essential stage of scientific research. After all, "anyone can go online and read the manual for lab instructions." This experience reminded me that good research comes from good planning, something that I, along with many budding researchers, tend to forget.

After narrowing down my focus to the PIWIL1 gene, I went forward and learned to extract DNA that I needed and prepare solutions for PCR processes. After mixing in minute amounts of DNA, primers, and other materials, our results from the PCR were as expected: PIWIL1 was significantly overexpressed in the breast cancer cell line MCF7.

Despite our internship coming to an end, I was so thrilled with our work that I returned on my own for two more weeks. The lab gladly allowed me to stay and research PIWIL1 more. They advised me on how to find and understand articles related to the scarcely researched PIWIL1. They taught me how to culture cancer cells and how to transfect them with siRNA, forms of microRNA, to lower the expression of PIWIL1 and block its effects. While in the lab, I got to experience many procedures, even those outside of my project. I got a lot of practice in extracting and isolating DNA from samples for another project and shadowed one of the researchers as he conducted his own experiments on PIWI genes.

My internship at Dr. Zhu's lab was a truly amazing and satisfying experience. This opportunity that was generously given to me by the Great Neck Breast Cancer Coalition allowed me to get a glimpse at the scientific world outside of the confinements of a high school. To study the relatively new field of epigenetics and the causes of breast cancer is a truly unique opportunity. In fact, the researchers at our lab were astounded that high school students like me and Rick were already delving into such advanced research. Working on cutting edge research reminds us just how complicated humans are, how puzzling cancer is, and how we must struggle to understand new things that we discover. Yet it also reminds us just how far science has advanced and how much we can already do.

I believe that a vital part of our progress comes from the endeavors of groups like the Great Neck Breast Cancer Coalition, who strive to ameliorate the lives of those affected by breast cancer and guide the next

wave of researchers who will further medicine's progress, and I sincerely could not be happier to have been a part of this program.