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Great Neck Breast Cancer Coalition - Sewanhaka High School  
Dr. Yong Zhu's Laboratory, Yale School of Public Health, Summer '12.

The summer of 2012 came with a once in a lifetime opportunity for me. Due to the extensive efforts of the Great Neck Breast Cancer Coalition and their 'Students and Scientists' Program, two students including myself were sent to Yale University to find and further study genes and their epigenetic impact on Breast Cancer.

Going to New Haven from New York was an experience in itself. After an introduction to the laboratory members, our mentor and supervisor, I was pretty much in awe. No doubt that going in, even after all the reassuring, there was enough nervousness to let a sigh of relief to get through each day. However, after several lunch breaks which included indulging in the age old tradition of obtaining food from the street carts and five weeks of intensive research, we left the lab with several group pictures and newfound friends.

When I discovered that I was about to conduct research using an international database and studying something in its infancy stage in the science world – I needed to sit down and take a deep breath. The excitement of studying something as new as epigenetics was a privilege. Epigenetics is broken down as 'epi' translating to 'around' in Greek which ultimately leads to mean – around genes. What that means is, there is no need for a change in the sequence of DNA for a phenotypic change to occur. Epigenetics deals with phenomena like methylation where methyl groups attach to the cytosine nucleoside and cause 'silencing'. When the cytosine is right before a guanine in the DNA sequence, and there are islands or repeated sequences of these formed, it is known as a CpG Island, the 'p' depicting the phosphate involved in the bonding process of the 2 nucleosides. When a CpG Island is methylated, it may cause the entire gene to be silenced thereby reducing its expression. Say a tumor suppressor gene were hyper methylated, the tumor suppressing function would be lost. Or perhaps an oncogene were hypo methylated, cancer could be looming in the distance.

Once it was discovered that an environmental condition such as exposure to light at night, especially to shift workers, could cause increased levels of methylation in critical circadian genes

and thereby disrupting melatonin levels, a potential for identifying cancerous conditions was present.

With our mentor Dr. Yong Zhu we conducted research in his laboratory at Yale School of Public Health. Before a project was assigned, the Ph.D. candidate who directly supervised us, Daniel Jacobs, gave us multiple publications to read and catch up on the work going on at the laboratory.

Bombarded by what looked like hieroglyphics with intricate diagrams, our mentor and supervisor were extremely helpful in aiding us in our effort to thoroughly understand the novel concepts. Once we were on the same track, we were assigned to a project with the aim of analyzing CpG sites that were found to be the top methylated hits from a list put together by Illumina Human Methylation data taken from night shift workers. The reason night shift workers were the subjects was – as a previous paper published by our mentor explains – a significant change in the hormone melatonin which in turn would disrupt estrogen levels, estrogen being closely linked with breast cancer.

The top 100 hits for hyper methylated and hypo methylated sites were chosen and using the genome browser created by University of California, Santa Cruz and specific tracks in build 36, the sites were analyzed. The goal was to look for sites that were on/near promoters, on/near CpG islands and were upstream of the start of the first exon. The data was recorded in spreadsheets and presented to all laboratory members on July 16th, 2012. After discussing the findings, two genes were chosen for further research and we were assigned to collect information and further analyze genes that had little or no information collected on them (open reading frame). From these, two more genes were selected. After analysis and no significant findings, more information was collected from the Illumina CpG site list to narrow down to the genes that were related to post transcriptional regulation and export/transport of RNA. Twenty five genes were found and after discussions, the NBR2 gene was selected due to its location at the 5' end of the BRCA1 gene.

To finally put our research to the test and conduct the necessary laboratory procedures, not only were the researchers helpful, they made sure we left the laboratory with a newly acquired skill. Procedures like Polymerase Chain Reaction (PCR) and designing primers were explained and we conducted these with aid from our fellow researchers and mentor.

After primer design and preparing a working solution, PCR was conducted to check expression levels and the gene was found to be under expressed significantly in cervical cancer but not as much in breast cancer. More data was collected to determine whether the NBR2 gene shared a promoter with the BRCA1 gene even though it was transcribed in the opposite direction and the publications found were compiled into a single document. The file was handed over to other researchers for further analysis.

While it might seem like a myriad of scientific jargon and complicated procedures, an important task was to break it down to the masses. Spread the word, to be precise. If someone does not understand what Polymerase Chain Reactions are, it was our task to break it down and explain that it was essentially a photocopy machine, simply used for genes and not paper!

If after all the research is done and we cannot share concepts like the exposure to light at night may in fact affect melatonin and consequently estrogen levels to cause a higher risk of breast cancer, then the world cannot gain from our hard work. The Great Neck Breast Cancer Coalition gave us a golden opportunity for just that by organizing a meeting with a television representative, the other students in the program, their parents, other members of the community interested as well as our New York State Senator, Jack Martins.

The support received was tremendous and we knew that five weeks in a single summer had changed a lot. Those five weeks of the summer were truly a golden opportunity that I had jumped at when it was first presented. I am grateful to the Coalition for accepting me into the program and my mentors for their excellent guidance through the experience. It relieves me to know that such organizations and coalitions exist because through such programs and further research, there's no doubt that a cure and prevention of breast cancer will be found in the future.