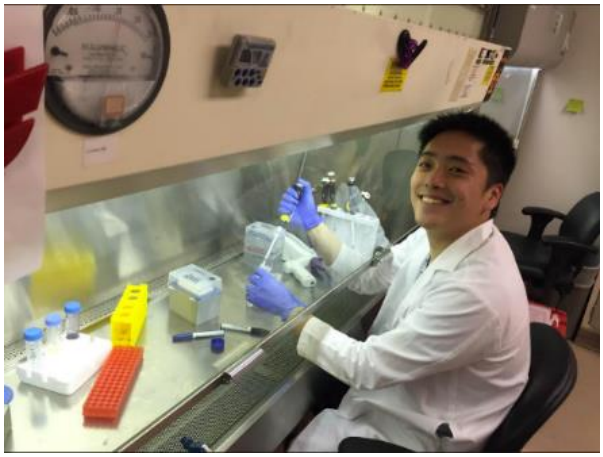

The Role of PD-L1 in the Development of Cisplatin Resistance in Head and Neck Squamous Cell Carcinoma
Kevin Zhang (COL 2017)
Advisor: Daqing Li

I spent the summer of 2016 working under the direction of Dr. Daqing Li in the Department of Otorhinolaryngology of the University of Pennsylvania School of Medicine. The major goals of our project were to explore the role of the Programmed Death-Ligand 1 (PD-L1) protein in the development of a cisplatin resistant phenotype in head and neck squamous cell carcinoma (HNSCC), as well as to demonstrate that targeted disruption of PD-L1 expression in certain cisplatin resistant HNSCC cell lines could constitute a viable approach in re-sensitizing them to chemotherapeutic drugs.

PD-L1 is a membrane-bound glycoprotein responsible for modulating the immunological response through binding of Programmed Cell Death Receptor 1 (PD-1) found on T-cells. Cisplatin is a platinum-based chemotherapy agent commonly used as first-line treatment in many common human cancers including head and neck squamous cell carcinoma. The MRN complex is a protein complex composed of Mre11, Rad50, and Nbs1 that is involved in the repair response to double-stranded DNA breaks. Increased MRN activity in tumor cells has been correlated to their increased resistance to chemotherapy reagents by reversing the DNA damage done by such drugs, effectively preventing neoplastic cell apoptosis and compromising the efficacy of chemotherapy regimens. Recently, elevated PD-L1 levels have also been correlated with chemoresistant phenotypes in certain types of cancers. We have been working to establish a relationship between PD-L1 and the MRN complex in order to show that PD-L1 plays a role in chemoresistance. Our focus was on the manipulation of PD-L1 expression levels in previously established cisplatin resistant HNSCC cell lines via methods including siRNA and plasmid cDNA transfections and observing the effects these changes have on the expression levels of MRN proteins. We also used these experiments to probe for phenotypic changes by using MTT cell viability assays.

While this project will certainly take a lot more time to complete, I have learned many important lessons while working on it this summer. After I experienced numerous technical setbacks, the need for patience and problem solving in order to maintain clear thinking and continued progression became an obvious lesson to keep in mind for the future. Furthermore, I have realized

that research maintains the foundation of applied medicine. In order to continue improving and innovating ways to treat diseases and improve healthcare, emphasis must be placed on the research and development that underlies it all. I look forward to continuing my contribution to this collective effort.