SWURP Reflection

Over the course of the SWURP internship at Scott and White I have had the privilege to work on both a clinical project at the Vasicek Cancer Center of Scott and White Memorial Hospital, under the supervision of Sarah Allenson, and bench research project at the Cancer Research Institute under the supervision of Dr. Jung-He Woo. Though I worked on many clinical projects, the project I devoted the majority of my time to was the STEAM Study. The bench research project I worked on at the CRI was the cAF334- MMAE Efficacy Study. Each project provided me with a meaningful way to learn about and contribute to medical research and additionally helped me to solidify my goals for my future career.

STEAM stands for A Study of Sequential and Concurrent FOLFOXIRI/Avastin vs. FOLFOX/Avastin in First-Line in Patients with Metastatic Colorectal Cancer. The STEAM Study is a randomized, controlled, open-label, multisite study designed and organized by Genentech. The goal of the STEAM Study is to compare treatment arms in which currently approved drugs for the treatment of late stage colorectal cancer are given in different sequences in order to determine if one treatment sequence is more effective than the other as well as to determine the efficacy of bevacizumab in second line therapy. In order to assess the efficacy of different treatment sequences patients have a baseline CT scan and are randomized onto one of three different study arms (Arm A, Arm B, or Arm C). On Arm A the patients receive FOLFOXIRI (5-FU, leucovorin, oxaliplatin, and irinotecan) with bevacizumab for twelve cycles.
On Arm B patients alternate their treatment every two cycles receiving FOLFOX with bevacizumab for two cycles and FOLFIRI with bevacizumab for two cycles, this continues for 12 cycles. On Arm C, the control arm, the patients receive standard of care, FOLFOX with bevacizumab, for 12 cycles. Throughout the study patients on each arm of the study have CT scans every eight weeks in order to measure their tumor and determine their response to treatment. The measurements from the CT scans are the primary data used to compare the efficacy of the three different treatment arms. My primary role on this project was data entry and weekly patient screening using inclusion/exclusion criteria. I screened patients for several other studies at the Vasicek Cancer Center, assisted with the collection of data on a phase I pharmaceutical study, and created medical histories for a phase IV urology study.

At the CRI I have been working with Dr. Jung-He Woo on a cAF334-MMAE Efficacy Study. cAF334 is a chimeric antibody with a mouse epitope and a human IgG 1 Fc region that binds specifically to mouse and human tumor endothelial marker 8, TEM8 (Frankel, Carter, Woo, Mauldin, & Liu, 2011). TEM8 is a highly conserved glycoprotein that is upregulated? Not sure if this is a spelling error or word I don’t know in the tumor vasculature of various types of tumors in both mice and humans (Chaudhary, et al., 2012). Research has suggested that TEM8 is necessary for tumor angiogenesis and plays an important role in the extracellular matrix and growth of certain tumor types (Cullen, et al., 2009). Not only is TEM8 potentially necessary for tumor angiogenesis in certain types of tumors and expressed on a variety of tumor types, it also has limited expression in in normal human tissues, making it a promising target for cancer therapies (Frankel, Carter, Woo, Mauldin, & Liu, 2011). Previous cytotoxicity studies at the CRI revealed that cAF334-MMAE has is greatest efficacy in vitro on IMR32 cells. IMR32 is a type of neuroblastoma that typically presents in young children. At the CRI, cAF334-MMAE
(cAF334 conjugated with an MMAE toxin) is under development as a vascular disrupting agent, an agent that damages the established tumor vasculature, and the current target for the drug treatment is IMR32 tumors. My primary role at the CRI this summer has been the conduction of immunohistochemistry trials. Immunohistochemistry involves the use of antibodies to detect a specific antigen on the cell surface of a tissue sample. The immunohistochemistry project that I have been working on utilizes cAF334 as the primary antibody along with DAB staining to bind to and detect TEM8 on the cell surface of IMR32 tumor cells as well as other normal tissue cells. Additionally, I have assisted with the conduction of the mouse trial that is currently in progress at the CRI. In this trial the test subjects are 50 NIH III nude mice. These mice are knockout mice that are immuno-compromised. Prior to injecting the cancer cells the mice were injected with Anti-Asialo GM1 to kill the natural killer T-cells to insure that the cancer cells would not be rejected by the mouse. The tumor volume of each mouse is measured three times a week. When the mice’s tumors reach a certain size the mice will be randomized onto treatment and control arms and cycles of cAF334-MMAE will be administered to the treatment arm while cycles of PBS is administered to the control arm. Each mouse will receive four treatments and the efficacy of the drug will be assessed by the tumor volume measurements.

Scott and White’s mission is to serve the community by providing health care in a Christian ministry through education and research. The STEAM Study and the cAF334-MMAE Efficacy Study contribute to Scott and White’s mission by advancing the field of medicine through research and also have the potential to contribute to medicine in a significant way. The STEAM Study offers the potential to increase the efficiency of currently approved treatments for late stage colorectal cancer by demonstrating efficacy of the combination of oxaliplatin and irenotican as well as by demonstrating the efficacy of giving FOLFOX and FOLFIRI.
sequentially. Additionally, as a result of the study bevacizumab could be approved for use in second line therapy, thus increasing the treatment options available for those individuals that have already progressed through first line therapy. The experiments I conducted and assisted with on the cAF334-MMAE Efficacy Study will all contribute to the determination of the efficacy and specificity of cAF334-MMAE. If significant efficacy is demonstrated it is possible that cAF334-MMAE will proceed to clinical trials and potentially become and effective and specific vascular disrupting agent approved for use in cancer treatment. If approved for use as a vascular disrupting agent cAF334-MMAE will likely have less side effects than current antiangiogenic factors, such as bevacizumab, due to its specificity to tumor cells. Thus, cAF334-MMAE has the potential to increase efficacy of treatment as well as quality of life for the patients that may one-day benefit from its use.

The research I have participated in over the course of this summer has not only contributed to the advancement of medical knowledge, but has also contributed to my education and my preparation to enter into medical school. At the Cancer Center I was able to shadow a research nurse and an oncologist during many of their appointments, which enabled me to interact with several patients and learn about their different cancers and treatment regimens. Through discussions with Sarah Allenson, the clinical research coordinator that supervised me, and shadowing appointments I learned a great deal about colorectal cancer, pancreatic cancer, a variety of chemotherapy agents, and clinical research. Shadowing at the cancer center this summer also exposed me to many of the difficulties I will no doubt face in my later career as an oncologist, such as breaking bad news to patients and having difficult conversations concerning the patient’s palliative care and treatment. These difficult experiences with the patients I had
come to know were challenging both mentally and emotionally, as they made me contemplate both the ethical and scientific obligations of a research oncologist.

Working at the CRI also greatly contributed to my education and my preparation to enter the field of research in my future career. I was able to learn from and work with one of the leaders in the field of GMP drug development, Dr. Jung-Hee Woo. Under his instruction I learned a great deal of eye-opening information about the GMP development of targeted protein drugs. The experiments I conducted and observed taught me many valuable lab techniques such as cell culture, immunohistochemistry, cytotoxicity assays, and a great deal about column purification techniques. These experiments were based in biochemistry and immunology, as a result I learned a significant amount concerning each of these fields that will help prepare me for my biochemistry and immunology classes that I am scheduled to take in the fall. I also gained a first hand understanding of the long, arduous work that goes into developing drugs for market while gaining experience in a professional laboratory setting.

Not only did I learn a great deal at the Cancer Research Institute this summer, I was also able to work with and befriend several individuals in the lab that I hope to keep in contact with. In addition through working at the CRI I was able to establish connections at UT Southwestern that may result in a research internship position for me next summer.

Overall my internship at the Cancer Center and the Cancer Research Institute at Scott and White has served to allow me to do valuable research in a field that I am interested in as well as help me solidify my future career goals. Before entering into the SWURP internship I was debating upon applying to MD. PhD. programs, but after completing the internship I am certain that the acquisition of an MD. PhD. is the correct career choice for me. This internship has shown me that I vastly enjoy both the clinical and the research aspect of medicine and thus
convinced me that a future career as a research physician in the field of oncology would be a rewarding and stimulating profession to pursue. Through all that I have learned and all the experience I have gained this summer I have not only advanced myself in my preparation for my future career, but also solidified my goals and increased my motivation to continue upon the long road to earning an MD. PhD. and hopefully contributing to the field of oncology research in my future career.
Works Cited

