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2011 Undergraduate Libraries Research Award

Isolation and Characterization of Polyomavirus Middle T Mammary Cancer Stem/Progenitor Cells

“The important thing is not to stop questioning. Curiosity has its own reason for existing.”-- Albert Einstein. Research is an intricate process which formalizes the act of inquiry into the unknown. Often the most rewarding research is also the most complex, and while answers are occasionally reached, more often than not, one question serves as a scaffold for subsequent questions. Although I nonchalantly encountered the opportunity to preform biomedical research, the experience has ignited something inside me that drives me to ravenously dig deeper, ask more questions, and seek further truth. After volunteering for a summer in a lab and also completing a research internship at the USDA, I directed my research focus to the study of cancer biomarkers and glycoproteins. Upon enrolling in CURO in the fall of 2010, I joined the laboratory of Dr. Michael Pierce, and embarked on my research journey which continues today. Shortly after joining the Pierce lab, I was given my own project investigating the role of biomarkers and glycoproteins in breast cancer induction and progression. The project I was given zeroed in on breast cancer stem cells which are believed to generate the majority of tumor growth and malignancy. The challenge to study these cells was irresistible. Effective identification and characterization of such breast cancer stem cells can provide valuable diagnostic tools and subsequent treatment methods for breast cancer.

My unproblematic bliss was short lived as reality quickly set in, and all of the sudden I was a undergraduate challenged to discover something which was itself unknown. In order for me to achieve my research goals I would need to utilize resources designed to assist researchers. I first needed to become educated in areas such as: breast cancer, cell signaling, stem cells,

biomarkers, and other relevant topics. Secondly, I needed to assemble a database of reference materials that I could utilize when confused, and as a source of new ideas. At first, I relied on my research mentors to provide me with publications, but I quickly realized that these sources were often filled with complicated scientific jargon I could not interpret.

--Enter the UGA Library resources.

I cannot emphasize enough the impact that the UGA library resources had to enhance my personal knowledge and subsequently my research project. Using the UGA libraries, my first priority was to educate myself on the basic scientific and physiological principals of cancer; specifically breast cancer. To accomplish this, I used the GIL catalog to locate textbooks and reference materials. The advantage of using GIL was the ability to request books, using GIL Express, directly from other libraries within Georgia. Therefore, if UGA did not currently contain the book or journal article I needed, the integrated library system that GIL provides made it possible to locate and read the full text article from other libraries in Georgia. Using GIL, one of the most useful sources I found was Gene Therapy of Cancer: Translational Approaches from Preclinical Studies to Clinical Implementation because it not only discussed the study of cancer gene therapy before its use in clinical practice, but also the clinical implementation of such studies. Such information helped me foreshadow some of the uses of my research as well as predict how such advances could be used in clinical practice.

Having built a strong fundamental understanding of the physiology and potential uses of cancer stem cells, I narrowed my search to more specific areas relating to breast cancer stem cell research. For example, the mouse model of human breast cancer that I study uses mice transgenic for Polyomavirus Middle T (PyVT) antigen, and I want to better understand why we used this model for breast cancer stem cell research. To do so, I used Web of Science to locate

specific articles pertaining to my research. In Web of Science, I used the advanced search option where I implemented: 2-character tags, Boolean operators, truncation techniques, wildcard techniques, phrase searches, and negative filtration to narrow my search to the exact oncogene I was studying. Citation mapping also proved to be a valuable tool. I could backtrack to an original source, or consolidate divergences from a publication using reverse and forward citation mapping respectively. Relevant articles were added to my marked list which was organized and ranked according to relevancy or number of citations. This method helped me prioritize articles that were significant in my particular field as well as locate articles deemed valuable by the rest of the scientific community. I began to notice a couple of authors that appeared frequently in my selected articles, and used author filtration to target more of their research.

After accumulating a collection of reference materials, I used PubMed to evaluate certain articles' relevance to medicine. PubMed quickly became one of my favorite tools because it not only allowed me to search specific articles and journal databases, but it also allowed me to search according to clinical study category. I was able to search a topic such as breast cancer and then further specify a category such as therapy, diagnosis, or etiology. Furthermore, I was able to define the scope of my search by either selecting the narrow and specific option or the broad and sensitive option. Because of its advanced search tools and its specificity to medical research, I also began to use PubMed as a starting point for my searches as well.

I have spent an entire semester practicing techniques in the lab as well as ardently expanding my knowledge base through the UGA Libraries. However, research rarely unfolds as desired, and I am currently at a brick wall in my research. While I understand the reasons why we use Polyomavirus Middle T transgenic mice as well as the antigen's role in breast cancer, I need to be able to collect the tumor tissue, isolate the stem cells, and culture the cells in lab

before I can explore possible biomarkers. The challenge is that I do not have any previously published protocols to follow. Determined, I have sought the aid of UGA library's resources to locate and combine portions of protocols containing pertinent information for my protocol. By integrating techniques from other cell culture protocols that have been successful, I hope to generate a protocol that will successfully isolate and culture the breast cancer stem cells I am studying. Throughout this process, I have found GoogleScholar to be an irreplaceable tool in my arsenal. The reason GoogleScholar has been so effective is because it allows me to search articles with highly tailored phrase searches, as well as articles written by a particular author, published in a certain journal, and/or published within a set time frame. Through GoogleScholar, E-Journals, GALILEO, and JSTOR databases, I have located articles in journals such as Cell, Cancer Research, Oncogene, and Journal of the National Cancer Institute which provide essential insight into portions of a possible protocol for me to use.

Clearly research is a convoluted path laden with pot holes, divergences, blind spots, and obstacles. While the voyage down such a path may seem treacherous, the potential reward for one's efforts far outweighs the cost. Breast cancer research is a challenging, ever changing, and complex field in which so much more remains to be discovered. The UGA Library resources help me navigate this field and continue to ask questions. Through their extensive databases and sophisticated search tools, I can begin to tackle challenges as I methodically transverse my way down the path that may, someday, lead to a cure.

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CURO 2011 Symposium Abstract

Isolation and Characterization of Polyomavirus Middle T (PyVT) Mammary Cancer Stem/Progenitor Cells

Transgenic mice carrying Polyomavirus middle T (PyVT) antigen are commonly used models to study mammary tumorigenesis and metastasis, and are valuable tools to analyze the molecular and cellular mechanisms of breast cancer induction and progression. The biomarkers expressed in PyVT-induced tumors exhibit similar morphologic and histologic properties to that of human breast cancers, and are associated with a poor prognosis. Recent studies also indicate that mammary tumorigenesis may arise from the mammary stem-like cells which are found in higher concentrations in PyVT-induced mammary tumors. Effective identification and characterization of such mammary stem cells in PyVT-induced tumors can provide valuable diagnostic tools and subsequent treatment methods for human breast cancer. The focus of my research is to obtain, culture, and characterize key biomarkers present on mammary cancer stem cells using tumors obtained from PyVT transgenic mice. My experiments involved setting up appropriate mating and genotyping of the mice using DNA extraction, Polymerase Chain Reaction (PCR), and gel electrophoresis to identify mice carrying the PyVT antigen. After obtaining PyVT mice, I isolated tumor cells and collected mammary cancer stem cells from tumor tissues by flow cytometry using stem cell marker antigen. By understanding more about mammary cancer stem cells, researchers can begin to characterize important molecular biomarkers, proteins, and signaling pathways which can lead to aggressive diagnostic and treatment strategies for human breast cancer.

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