



## **Hyundai Hope on Wheels Hyundai Scholar Research**

**Dr. Tanya C. Watt**

Aflac Cancer Center and Blood Disorders Services of  
Children's Healthcare of Atlanta

Fifteen out of every 100,000 children in the United States are diagnosed with cancer each year, and of these diagnoses, acute leukemia is the most common. Therefore, I have chosen to focus my research endeavors on chemotherapy for acute leukemia. While we have made enormous strides in our cure rates for acute leukemia over the past 40 years, patients who relapse still have a very poor prognosis. It is imperative that we develop new chemotherapeutic agents or novel combinations of chemotherapy in order to provide relapsed leukemia patients with better outcomes.

As a result, I am working on multiple research projects in the hopes of creating more options for physicians and families in the event of a relapse of leukemia. The first involves combining two agents, asparaginase and sirolimus. Asparaginase is widely used for treatment of leukemia. Sirolimus is an immunosuppressive agent initially created to decrease rates of solid organ transplant rejection. Recently, it and other similar drugs are being studied as chemotherapeutic agents due to their ability to affect cell signaling and protein synthesis. To better study this combination of agents, I have created a clinical trial for use in patients with multiply relapsed leukemias.

As a correlate to the clinical trial, I am developing a method of studying signaling pathways within leukemia cells. This method, phospho-flow, is being used in different institutions around the country in order to better understand the signaling pathways that occur within different types of cancer cells. Initially, I would like to use this technique to test the patient's leukemia cells treated with the combination of sirolimus and asparaginase. By testing their cells before and after treatment, I will be able to determine how this combination of drugs actually leads to a decrease in protein synthesis and eventually cell death. Ultimately, as this technique becomes better developed, I foresee being able to test the cells of newly diagnosed leukemia patients against different types of chemotherapy. If we are able to determine which chemotherapy agents will lead to cell death in each patient, we will be able to target each patient's therapy to increase the rates of cell death while minimizing toxicity by not using drugs that will not be effective.

Using the Masters of Clinical Research that I have obtained during my fellowship, I am also in the process of creating other clinical trials for use in patients with relapsed leukemia. A novel form of asparaginase has been developed by members of the Aflac Cancer Center. Preclinical studies suggest that this asparaginase, *Wolinella*, will be equally efficacious but less toxic than currently available asparaginases. I am working on developing a protocol, again for relapsed leukemia patients, to determine if this drug has similar results in patients. This agent was the subject of a poster presentation at the annual American Society of Hematology meeting in December 2007, and will be the subject of a manuscript to be submitted in the upcoming months. As part of the Innovative Therapy team here at the Aflac Cancer Center and Blood Disorders Service, I plan to continue to develop clinical trials focusing on patients who have experienced relapses of their initial disease. By continuing to use what is being learned in the laboratory setting and applying this information to clinical trials, it is my hope that eventually we will have improved cure rates for all types of childhood cancers, and that fewer families will go through the heartbreak of losing a child to cancer.

Finally, as we improve the cure rate, there are many more childhood cancer survivors. For my Masters program, I became interested in the very high rates of basal cell carcinoma that affect children who received radiation therapy as part of their initial treatment for cancer. Basal cell carcinoma is a skin cancer that typically affects patients in their 70s, but in the childhood cancer survivor population, it appears that the rates of skin cancer for survivors in their 30s and 40s is equivalent to that of the rest of the population in their 70s. To better educate families and patients about their risk of basal cell carcinoma, with help from radiation physicists at MD Anderson, we are analyzing the doses of radiation patients received to their skin. The aim of this study is to determine what dose of radiation puts patients at a high risk of later developing skin cancer. Ultimately, we will create guidelines for physicians and families in order to help prevent and treat this high rate of skin cancers.

Through the generous grant from the Hyundai Hope on Wheels program, I hope to develop new ways of treating relapsed leukemia, create methods to better understand how chemotherapeutic agents affect cancer cells, and improve the quality of life of childhood cancer survivors. The combination of these goals will improve our ability to treat all children diagnosed with cancer, and continue to improve the survival rate of childhood cancer.