



Hyundai Hope on Wheels Hyundai Scholar Research

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Understanding Mechanisms of Mer Receptor Tyrosine Activation in Pediatric Leukemia

Cancer is the leading cause of disease-related deaths among children 1 to 14 years of age, and acute lymphoblastic leukemia (ALL) is the most common malignancy in children. Although cure rates for pediatric standard risk ALL have dramatically increased in recent years, it is unlikely that additional minor changes using the available drugs will provide any significant further improvement in survival. The development of new drugs which more selectively kill cancer cells may provide an opportunity to continue to increase survival rates in children with leukemia.

Additionally, subsets of patients respond unfavorably to current treatment protocols. Pediatric patients with early relapse also have very low survival rates. In fact, only 10-30% of patients with early bone marrow relapse on therapy maintain are able to maintain a second remission. Thus, there continues to be a significant need for new treatment strategies to offer ALL patients who relapse or have high risk cancer.

Finally, pediatric cancer survivors have a significant risk of both short-term and long-term toxicities associated with currently used chemotherapy agents. Approximately two of every three pediatric cancer survivors will have at least one adverse late effect (growth delay, infertility, organ dysfunction, cognitive function) and one in four will experience a late effect that is severe. Hence, new therapies that are less toxic are needed to replace some of the standard chemotherapeutic agents or provide increased effectiveness when used with currently used drugs.

My laboratory has discovered a cancer associated protein, Mer, that is abnormally expressed in pediatric leukemia. The abnormal expression of Mer provides the leukemia cell with a survival advantage and helps contribute to the development and progression of leukemia. In addition, the abnormal expression of Mer contributes to leukemia cell being resistant to chemotherapy. My lab is attempting to understand why the Mer protein is abnormally activated in leukemia. With the assistance of the Hyundai Scholars Grant, my laboratory will sequence pediatric patient samples for evidence of Mer mutations. This information will provide us a better understanding of the cause of leukemia in some pediatric cancer patients and enable us to develop more appropriate therapies.

A second aim of the Hyundai Scholars Grant will be to make large quantities of Mer tyrosine kinase inhibitors (currently being developed in my lab) for use in our preclinical studies. We have very promising preliminary data that these inhibitors can make chemotherapy agents more effective in killing cancer cells. The Mer inhibitors, studied with the assistance of these grant funds, hold the potential of providing better treatment outcomes for children with leukemia while decreasing the unwanted side effects associated with currently used chemotherapy drugs.