MLL Project Research Update

Acute lymphocytic leukemia (ALL) is a blood cancer characterized by unchecked rapid growth of undifferentiated abnormal white blood cells. ALL represents the most common pediatric cancer and comprises 20% of acute leukemia in adults. A particularly challenging group of ALL patients are those whose disease is associated with abnormalities in the MLL (mixed lineage leukemia) gene. MLL-associated leukemias are typically resistant to standard chemotherapy and carry a poor prognosis. Modern genomic technologies have revolutionized biomedical investigation. For example, next-generation sequencing and microarray technologies can simultaneously measure millions of DNA structural variants (single-nucleotide polymorphisms) and thousands of genes in cells. We used genomic techniques to analyze patient samples with different types of MLL-associated acute leukemia: acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), and therapy-related acute myeloid leukemia (t-AML) which arise as a direct consequence of chemotherapy and/or radiation therapy. Using a unique analysis method, we identified a cohort of 46 genes which consistently classified t-AML from the other leukemia types. While the genes in this classifier should be considered as a group, some of the individual genes potentially identify novel mutations and pathways representing future therapeutic targets.

Krista Pundt is a second-year graduate student pursuing her PhD in the Department of Pharmacology and Therapeutics, Roswell Park Cancer Institute. Her research into new treatments for acute leukemia is being funded in part by the Jacquie Hirsch Leukemia Research Fund. From a young age, Krista loved to read books on different diseases and always knew she wanted to be a scientific researcher. Krista graduated from D'Youville College in 2011 with Bachelor of Science degree with high honors in Biology and Mathematics and a minor in Chemistry and Natural Sciences. In addition, she was captain of the D'Youville women's crew team and Female Student Athlete of the Year. She also taught fellow science students in the D'Youville Tutoring Center, helped fund-raise for the Scleroderma Foundation, and performed clinical research involving patients at the University of Buffalo Research Center. Currently Krista is investigating the ability of a novel therapeutic agent (PIM-1/2 kinase inhibitor) to inhibit leukemia growth. To date, her preliminary data has shown that this agent can selectively kill ALL cells in culture at very low concentrations. Funding by the Foundation will allow her to continue these promising research efforts. She states: "I hope that my research will someday allow for the successful treatment of leukemia patients like Jacquie Hirsch."