Leukemia and Lymphoma
Research Update 2017

Cincinnati Children's Hospital - Division of Oncology - 3333 Burnet Avenue, MLC 7015 - Cincinnati, OH 45229
cancer@cchmc.org - www.cincinnatichildrens.org/cancer

National Leadership

The Cancer and Blood Diseases Institute at Cincinnati Children's is developing leukemia and lymphoma treatments to save lives in ways that were not possible just a few years ago.

Leukemias are the most common childhood cancer and a frequently occurring cancer in the aging population. Leukemia is a major focus of basic science and drug-development research at Cincinnati Children's. While current treatments cure a majority of children and adolescents with leukemia, the treatment can be harsh and therapies for some high-risk or relapsed patients can be challenging. Cincinnati Children's researchers are leading the way to a cure for all leukemia patients.

Our researchers are probing the causes of leukemia and working with our doctors to develop the next generation of innovative therapies, including improved bone marrow transplantations and new targeted drugs that kill cancer cells without the serious side effects of traditional chemotherapy. Using sophisticated technology, our researchers are finding the "Achilles' heel" of leukemia cells to identify potential targets for new drugs.

Advancing Novel Treatments

Cincinnati Children's researchers are currently testing several new drugs for high-risk and relapsed leukemia. There is a focus on novel, or new and innovative, therapies. Researchers are optimizing drug therapies while introducing new ways of approaching the disease.

At Cincinnati Children's, there is an emphasis on personalized medicine. Our teams have the ability to sequence a patient's genomic makeup, allowing the care team to tailor their treatment plan to the patient in a personal and unique way.

Creating Models of Leukemia for New Treatments through Biology and Modeling

Cincinnati Children's researchers are leading the fight against very aggressive forms of childhood leukemia. Basic science happening right here is allowing new treatments to emerge while uncovering new mutations. Leukemias with mutations in a gene called MLL tend to be resistant to contemporary chemotherapy approaches and very difficult to treat. Researchers have developed a new model in mice for AML using human blood stem cells altered to carry the MLL gene. In fact, the Mulloy Lab was among the first in the country to successfully transform a human blood stem cell into a leukemia cell in this way. This mouse model can be used to safely test potential new drugs.

Research and Clinical Themes

Many researchers at Cincinnati Children's examine how normal blood cells are transformed into leukemia cells and why the body's defenses against DNA damage and cancer don't always work.

Michael Absalon, MD, PhD is focusing on developing new therapies and combinations of therapies for pediatric leukemias and lymphomas. He is currently investigating the therapeutic potential of combining the new targeted drug sorafenib with conventional chemotherapy for relapsed AML.

Mohammad Azam, PhD is researching the structure and function analysis of tyrosine kinases involved in the pathogenesis of leukemia. His research focuses on understanding the mechanisms of tyrosine kinase regulation, oncogene addiction and the development of cancer stem cells.

Jose Cancelas, MD, PhD is studying how the body produces new blood cells inside the bone marrow and how mutations in a gene called BCR-ABL cause a type of ALL that resists most current treatments. He focuses on the study of blood-forming cells during the process of adult hematopoiesis.

H. Leighton Grimes, PhD is currently researching transcriptional control of normal and malignant hematopoiesis, including marrow failure syndromes. The Grimes lab found T cell acute lymphoblastic leukemia are highly dependent on the expression of a single transcription factor. Inhibiting this factor's expression cured the leukemias in animal models in the lap without therapy- limiting side effects.

Gang Huang, PhD is focusing on the genetic changes that turn normal blood cells into leukemia. His research interest includes the genomic, epigenomic, and metabolomic approaches to studying myelodysplastic syndromes, erythrocytosis and myelofibrosis.

Ashish Kumar, MD, PhD is studying a gene called MEIS1 that is over-active in leukemia. Work from Dr. Kumar's lab shows that blocking MEIS1 could be an effective way to fight cancers which are resistant to current therapies.

Lynn Lee, MD is studying the biology of MAP kinase activation and additional gene mutations found in Langerhans Cell Histiocytosis (LCH). He is also investigating novel gene mutations involved in the pathogenesis of severe congenital neutropenia.

Ben Mizukawa, MD is leading the mouse "avatar" project. Each mouse is carefully engrafted with the cancer cells from children whose leukemia cells have been sequenced. These mice serve as living test platforms, allowing scientists to add a new level of precision for determining which treatments are most likely to work against cancers carrying particular genetic mutations.

Maureen O'Brien, MD is currently interested in researching relapsed and high-risk leukemia. Her work focuses on novel targeted agents for relapsed leukemias and lymphomas, immunotherapy for leukemias and lymphomas and leukemia associated with Down syndrome.

Qishen Pang, PhD, studies the role of the cell- signaling protein TNF-alpha in bone marrow failure, a condition that can lead to leukemia. His work has led to a Cincinnati Children's study of etanercept, a drug that blocks TNF-alpha, in children with early bone marrow dysfunction to prevent bone marrow failure and leukemia.

John Perentesis, MD, Director, Division of Oncology, studies the causes of leukemia in children with Down syndrome, who have a significantly higher risk of developing the disease, as well as ways to improve treatment. His Childhood Cancer Drug Discovery Laboratory is working in integrated efforts with the University of Cincinnati's Drug Discovery Center to screen a pharma-grade library of 340,000+ drug-like compounds for activity in a large panel of pediatric and young adult cancers and leukemias.

Christine Phillips, MD has a clinical and translational research focus on the development of novel therapies for pediatric leukemia and in leukemia pharmacogenetics.

Daniel Starczynowski, PhD, studies myelodysplastic syndromes (MDS), conditions that result in defective white blood cell production and an increased risk of leukemia. The long-term objective of the Starczynowski lab is to identify altered genes and signaling pathways, and understand the contribution of these alterations to the pathogenesis of MDS and AML.

Yi Zheng, PhD, Director, Division of Experimental Hematology and Cancer Biology, leads a search for small molecule inhibitors that can disrupt the function of cancer stem cells. His lab has already discovered several such lead small molecules. The molecule "CASIN" can push leukemia-initiating cells into the bloodstream, where they become much more vulnerable to chemotherapy and may make stem cell transplants much more effective.