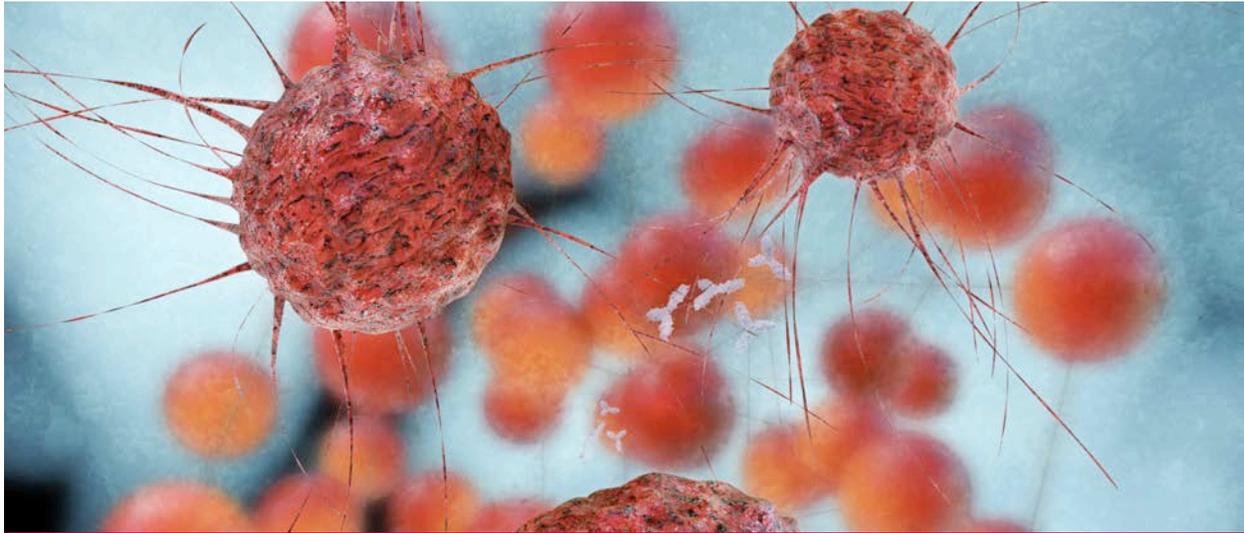


# The Impact of the Ted Mullin Fund

*at the University of Chicago Medicine*

February 2015



THE UNIVERSITY OF  
**CHICAGO**  
MEDICINE

Comer Children's Hospital

Thanks to the dedication of the Ted Mullin Fund supporters over the past eight years, University of Chicago Medicine (UCM) researchers and students are advancing vital research and making great strides in understanding, treating, and preventing pediatric and young adult sarcoma. We are pleased to provide updates on the impact of the Ted Mullin Fund at UCM.

On behalf of the faculty whose work you supported and the patients whose lives you touch, thank you for your ongoing commitment and generosity.

## **Funding Research to Help GREAT Kids**

With support from the Ted Mullin Fund, **Dr. Navin Pinto** and his colleagues are developing a new clinical treatment called the Genomics of Risk Evaluation and Treatment in Children with Cancer (GREAT Kids). Applying our university's strengths in genomics (the study of an organism's entire hereditary information), pharmacogenomics (the tailoring of drug dosages and combinations to each patient's unique genetic profile), and phase I (pilot) chemotherapy trial design, this approach is integrating genetic data from drug-resistant pediatric tumors with drug response data derived from over one hundred chemotherapeutic drugs. All children with cancer, including those with sarcoma, seen at the University of Chicago Medicine are eligible for this trial, where the genetic code of both normal and malignant cells will be obtained in order to better understand the underlying causes of the cancer, and to identify unique genetic changes within the tumor genome that may be amenable to more targeted—and less toxic—treatments.

For patients with relapsed, refractory or incurable malignancies, the genetic information is analyzed against a library of drug sensitivity information from hundreds of tumor samples, including sarcoma samples, in order to design a personalized treatment regimen that may incorporate previously unused therapies for pediatric cancer.



*The University of Chicago Medical Campus.*

## Ted Mullin Fund Scholars

UCM hosted four Ted Mullin Fund Scholars in 2014, each of whom spent their summers working alongside faculty in their laboratories. The Ted Mullin Fund Scholars worked on unique projects, all of which generated new knowledge that will have an impact across pediatric and adult cancers, including sarcoma.

**Katie Bennett**, a student at Williams College, worked in Dr. Eric Beyer's lab with Joanna Gemel, PhD, Assistant Professor of Hematology/Oncology to stain sections of human heart tissue and quantify expression of connexins (a family of proteins that are important for intercellular communication), as well as developing a protocol for quantification of qualitative data—or, more simply, in her words: “how to get numbers from pictures.” Katie also helped Dr. Gemel start a new project that delves into the ways connexins go wrong. Her research will help identify ways that cancer cells communicate with other cells.

*“Beyond the bench skills of tissue culture, Western blotting, immunofluorescence, and bacterial transformation, I learned about the culture of a lab. The people with whom I spent my summer were doctors, physician-scientists, researchers, medical students, and regular undergraduates like myself.*

*Thanks to the Ted Mullin Fund, I witnessed the remarkable passion and intelligence they used to attack problems and ask questions. There are a million ways for a scientific mind to find its niche, and I have confidence that I will find the one that best suits me.”*

*Katie Bennett, Ted Mullin Scholar*

**Rachael Loek**, a student at Case Western Reserve University, worked with Jill de Jong, MD, PhD, on many projects involving zebrafish, which have proven to be an excellent model for studying human disease, particularly blood diseases, since these highly-evolved fish make similar types of blood cells as humans and other mammals. Since many thousands of these specimens can be kept in a relatively small space, zebrafish are an economical model to use for large-scale research projects, which may otherwise be prohibitively expensive using mice. Such projects are a powerful discovery mechanism for identifying new genes that regulate biologic processes.

*“The Ted Mullin Scholarship helped me gain experience that is so vital for the rest of my years in college. Trouble shooting and working through my challenges showed me how to really think about the problem. I cannot express how important this scholarship has already been for my education and I’m excited for what the next few years bring me.”*

*Rachael Loek, Ted Mullin Scholar*

Rachael helped Dr. de Jong conduct experiments for an array of projects, including studying blood stem cells to understand the genes that can cause leukemia. Dr. de Jong ultimately aims to develop novel strategies to discover new regulatory mechanisms that drive normal hematopoietic stem cells, and to understand how those mechanisms can lead to leukemia when they function abnormally.



*The founders of the Ted Mullin Fund, Rick Mullin and Mary Henry, with Dr. John Cunningham and the 2014 Ted Mullin Fund Scholars.*

**Edan Zitelny**, a student at Brandeis University, worked with Kenan Onel, MD, PhD, to conduct research on cancer evolution and the progression of Acute Myeloid Leukemia (AML) and Extramedullary AML. By conceiving of cancer cells as analogous to any other population of organisms in facing selective pressures (competition between cells and the attacks of the body's natural defense mechanisms, for example) that shape their evolution, they hope to identify the genes that drive cancer development with greater precision.

*“This scholarship allowed me the opportunity to work in a world-class lab environment and engage in medical research. It motivated me to remain determined through tough failures and continue to strive for success. I was thrilled to take part in an on-going pursuit to make a difference in the lives of pediatric cancer patients.”*

*Edan Zitelny, Ted Mullin Scholar*

**Joyce Kim**, a student at Carleton College, worked with Susan Cohn, MD, to conduct research on neuroblastoma, a solid, cancerous tumor that begins in the sympathetic nervous system and is found in the abdomen, neck, head, or pelvis. It is the most common cancer in babies and toddlers. Dr. Cohn's lab focuses on investigating the biology of neuroblastoma and other pediatric cancers, and uses this information to develop more effective, targeted therapy.

*“This experience developed my practical skills on bench work and gave me insights on the recent progress of cancer research. I observed the doctors’ perspectives of giving the utmost care to patients, which shaped what kind of a doctor I want to become. Exploring different forms of patient care affirmed my aspiration to become a pediatric oncologist and reinforced my confidence to pursue my dream.”*

*Joyce Kim, Ted Mullin Scholar*

## Scholars Past: Where Are They Now?

This year marked the third year of the Ted Mullin Fund Scholars program. The following are updates from Scholars in years past, who continue to draw on and build upon the experiences they had at UCM.

**Erik Klontz** began formal classwork for an MD/PhD medicine program at the University of Maryland in August 2014.

**Ashley Paquin** is completing her second year as a post-baccalaureate cancer researcher training at the National Cancer Institute.

**Aleks Penev** is currently an MD/PhD candidate at New York University Lagone Medical Center.

**Tony Restaino** is completing his final year at the University of Chicago, majoring in biology with a specialization in Cellular and Molecular Biology

**Maryellen Campbell** is a junior studying economics at Georgetown University.

**Lauren Kasoff** is enrolled in the National Institutes of Health's Postbaccalaureate Intramural Research Training Award program.

**Connor Sholtis** is a senior studying Biology at Amherst College and is currently applying for a Fulbright Fellowship.

**Anna Zimmer** spent this past summer working in a MD Anderson Cancer Center lab doing translational triple-negative breast cancer research.

## Publications

The Ted Mullin Fund was acknowledged in a paper published in the Journal of Molecular and Cellular Cardiology in September 2014. Former Ted Mullin Scholar **Katie Bennett** and UChicago faculty members **Dr. Eric Beyer** and **Dr. Joanna Gemel** were listed as authors of the paper.

## Updates from the Section of Pediatric Hematology/Oncology

Support from the Ted Mullin Fund enriches the entire Section of Pediatric Hematology/Oncology, not only because it supports scholars who staff labs and help researchers, but because it fosters a culture of learning, training, and innovation. We are pleased to share the following Section updates from researchers who are making inquiries into the causes, diagnoses, treatments, and cures for pediatric cancers.

### Staging Disease to Improve Outcomes for Neuroblastoma Patients

**Dr. Susan Cohn** and her team have developed an International Neuroblastoma Research Group (INRG) database for investigators around the world to advance research with sizable populations. To date, clinical and genetic information has been collected from over 11,000 children diagnosed with neuroblastoma from around the world. Numerous studies have been published that would not have been possible without these unique data. Dr. Cohn and the INRG are now poised to link the genomic data that have been generated in laboratories around the world to the clinical data, providing an unparalleled resource for neuroblastoma researchers.

One such project to arise from that rich dataset, is Dr. Cohn's investigation into the genetic factors that contribute to racial disparities in outcome in children with neuroblastoma. She has previously shown that African Americans with neuroblastoma have worse outcomes than



*Dr. Susan Cohn with a young patient.*

Caucasian children. More recently, she and her collaborators have identified genetic variants that contribute to the increased prevalence of high-risk neuroblastoma in the African American population. They are now using INRG data to conduct experiments to determine how these genetic variants contribute to the development of chemotherapy-resistant neuroblastoma, one of the largest threats to a child's ability to respond to therapy in order to be cured.

### New Genetic Understanding That Could Prevent Fatal Secondary Cancers

With his findings published in *Nature Medicine*, one of the most influential journals in medicine, **Dr. Kenan Onel** identified two tiny genetic variations that can predict which patients with Hodgkin's lymphoma and sarcoma are most likely to develop radiation-induced second cancers years after treatment. Knowing in advance who is at risk could help physicians tailor treatment to reduce the risks for patients who are most susceptible to long-term damage. Hodgkin's lymphoma is one of the most treatable cancers, with more than 90 percent of patients surviving after a combination of radiation and chemotherapy. But nearly 20 percent of

patients treated as children develop a second cancer within 30 years. The younger the patients are when treated and the higher the radiation dose, the greater the risk. This late side effect of treatment is the second leading cause of death for long-term Hodgkin's survivors.

This finding means we can better identify children who are most susceptible to radiation-induced cancers before treatment begins and modify their care to prevent this serious long-term complication. In this study, which focused on the interaction between genes and a very specific environmental factor—cancer long after radiation therapy—a small number of genetic differences produced a very big impact. Previous studies have found that this gene, PRDM1, is involved in a variety of fundamental cellular processes, making it important for understanding the causes of second cancers in survivors of pediatric Hodgkin's lymphoma as well as in other cancer patients treated with radiation therapy.

## Personalizing Treatment Through Genetic Knowledge

**Dr. Jill de Jong** and **Dr. Onel** are working on a project in which they inject human cancer cells into zebrafish during an early stage in their development, when their immune system is not fully developed and their bodies are able to accept the cells as their own. The cells express a gene that turns the cancer a fluorescent green, allowing the researchers to visualize cancer within the fish. In real-time, Drs. de Jong and Onel are able to study human cancer and drug resistance, noting how cells change, grow and respond.

Because zebrafish are an excellent model system for studying the molecular underpinnings of cancer and recognizing the uniqueness of each individual patient's cancer, this work is informing the development of new targeted therapies for specific cancers, helping us achieve our vision of personalizing cancer therapy to each individual patient. This system has not yet been tested in sarcoma cell lines, but researchers report potential for future applications in sarcoma.

## Thank you

We are thrilled that you continue to honor Ted's legacy by supporting the next generation of physicians and scientists. Thank you for your partnership—we are grateful to have your support in improving outcomes for pediatric and adolescent/young adults with sarcoma and other cancers. We simply could not do our work without you.

*“Philanthropy allows people space to do the very best in thinking about how we ought to treat patients, and that, in turn, leads to better experiences for our patients.”*

John Cunningham, MD  
*Professor of Pediatrics, Physiology, and Stem Cell Research  
Vice Chair, Department of Pediatrics  
Chief, Section of Pediatric Hematology/ Oncology  
Director, Hematopoietic Stem Cell Transplantation*