**Research Units**

Pathobiology Unit

Patient Oriented Research Unit

Developmental Biology and Genetics Unit

March 26, 2013

Hi Paul and everyone who supports the Eli Seth Matthews Leukemia Foundation,

 I hope everyone is doing well and incredibly excited for “Eli’s Celebration” on May 18th, 2013. Thanks in part to the generosity and support of the Eli Seth Matthews Leukemia Foundation, my lab continues to use new technological advances to explore the complex genetics involved in children’s cancer, and we have some exciting new findings in infant and pediatric leukemia that I would like to share.

Years of research have taught us that children’s cancer is not simply adult cancer in a small body. Most pediatric cancers are distinct diseases that arise differently and require different therapies than adult cancers. The classic cause of cancer is multiple damaging DNA mutations that are acquired due to some external force – suntanning, smoking, toxic chemical exposure. This is why most cancers arise in older adults, because it takes decades to acquire all of this genetic damage. Recent advances in DNA sequencing technology have shown that children’s cancers are not solely due to genetic mutations that are acquired after birth. If not this source of DNA change, then how do such young children get these cancers? We are investigating the possibility that these children may be predisposed to cancer because of a unique personal combination of damaging genetic changes inherited from their parents or alterations in the way in which these important genes are controlled by the cell regardless of whether they have genetic changes or not. These differences might create a genetic environment that does not require years of additional damaging genetic mutations for a cancer to arise. These combinations of variation would also be different in each person, but cause similar dysfunction in important genes for distinct cell functions.

 In December 2012, our lab published a report in the journal *BMC Genomics* describing new DNA sequencing and data analysis methods that we are using to identify the inherited genetics of infants and children with leukemia. The research tools that we have created have been used by multiple labs here at Washington University to explore the genetics behind a variety of pediatric and adult diseases. Our work to date has shown that infants who develop leukemia are born with an exceptionally high allotment of damaging genetic changes in leukemia-associated genes. These aren’t “mutations” acquired after birth, but inherited changes that are present in every cell in the child’s body. We expect that about half of these inherited changes come from each parent, which seem true for infants with ALL, but infants with AML seem to have most of their genetic changes that occur during pregnancy or are inherited from fathers. We are also exploring inherited genetic changes in genes important for proper chemotherapy metabolism in a subset of pediatric high-risk leukemia patients. These results raise the possibility that there is nothing more deadly about these childrens’ leukemia, but that they are born with defects in their ability to handle chemotherapy. We are hopeful that by providing a better understanding of how children develop cancer in the first place, caregivers can ultimately provide better genetic counseling, diagnostics, custom therapeutics and long term monitoring to children and families of children with cancer.

Once again, thank you to everyone at Eli Seth Matthews Leukemia Foundation for your generous support in the fight against children’s cancer. Please, continue to bELIeve!!

Warmest regards,

Todd E. Druley, MD, PhD

Assistant Professor of Pediatrics and Genetics

Division of Pediatric Hematology and Oncology

Center for Genome Sciences and Systems Biology

Washington University School of Medicine