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Alex's Lemonade Stand Foundation & Cure4Cam Team Up to Fund Childhood Cancer Research

Lyndell, PA (May 1, 2018) – Alex's Lemonade Stand Foundation (ALSF) and Cure4Cam Childhood Cancer Foundation have continued their partnership to fund five childhood cancer research projects across the country. ALSF and Cure4Cam share a commitment to funding research to find better treatments and cures for all kids with cancer. Cure4Cam has contributed $200,000 to ALSF to co-fund a Bio-Therapeutics Grant, an Innovation Grant and two Young Investigator Grants.

Cure4Cam's contribution will help fund **Drs. Andras Heczey, MD and Leonid Metelitsa, MD/PhD** of Baylor College of Medicine (Bio-Therapeutics Impact Grant), **Drs. Linda Resar, MD and Andrei Thomas-Tikhonenko, PhD** of The Johns Hopkins University School of Medicine and Children's Hospital of Philadelphia (Innovation Grant), **Dr. Anastasia Tikhonova, PhD** of New York University School of Medicine (Young Investigator Grant) and **Dr. Andrea Flynn, MD** of Children's Hospital of Philadelphia (Young Investigator Grant). Summaries of the research projects are included below.

Young Investigator Grants are designed to fill the critical need for startup funds for less experienced researchers to pursue promising research ideas. The Innovation Grants provide critical and significant seed funding for more established researchers with novel and promising approaches to finding the causes and cures for childhood cancers. The Bio-Therapeutics Impact Grants accelerate the development of clinical trials for promising biologic approaches to treating childhood cancer.

Partnering with charity co-funders, like Cure4Cam, enables ALSF to work together to fund a larger number of the best research projects in pediatric oncology, moving closer to cures for childhood cancer.

"As a proud partner with ALSF, Cure4Cam funds research for new, less toxic and targeted therapies," says Regina Evans, Co-Founder of Cure4Cam. "We believe in a future where cancer treatments for children will be gentler and more effective, and no child or parent will fear the diagnosis of cancer."

For more information about Alex's Lemonade Stand Foundation's charity partnerships, visit AlexsLemonade.org/grants/charity-partners.

RESEARCH SUMMARIES

Andras Heczey, MD & Leonid Metelitsa, MD/PhD of Baylor College of Medicine
Bio-Therapeutics Impact Grant
Natural Killer T cells with an IL-15-armored GD2-specific CAR for Children with Neuroblastoma

Background
The overall goal of this proposal is to develop and clinically test a conceptually new form of cancer immunotherapy for children with neuroblastoma (NB) using native and engineered properties of Natural Killer T cells (NKTs). We found that NKTs target tumor-associated macrophages (TAMs) inside neuroblastoma tumors, thereby removing an essential support for tumor cells. To render NKTs directly cytotoxic against NB cells, we engineered them to express a chimeric antigen receptor (CAR) specific for the GD2 ganglioside (CAR.GD2), which has been targeted with T cells in NB patients in clinical trials that produced promising results. To ensure that CAR NKTs can last longer in patients, we added interleukin-15, a molecule that can help NKT cells expand and survive.

Project Goal
We hypothesize that CAR.GD2 NKTs will be safe and have antitumor efficacy in NB via targeting of neuroblast-supportive TAMs and neuroblasts themselves. The following specific aims will test our hypothesis: 1) we'll evaluate the safety of ex vivo expanded CAR.GD2 NKTs in patients with resistant/recurrent NB; and, 2) monitor the in vivo persistence, functional activity and anti-tumor efficacy of CAR.GD2 NKTs. We will generate patient-specific CAR.GD2 NKTs and treat NB patients at four dose levels. Toxicities will be monitored according to NCI guidelines. We will also evaluate the antitumor and immunological activities of NKT-cell therapy. The results of this study will inform clinical development of NKT-cell based immunotherapy of NB and have a broad applicability for other types of cancer.

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Linda Resar, MD & Andrei Thomas-Tikhonenko, PhD of The Johns Hopkins University School of Medicine
Innovation Grant
Novel Approaches for Epigenetic Therapy for Relapsed Acute Lymphoblastic Leukemia

Background
Acute lymphoblastic leukemia (ALL) is the most common form of childhood leukemia and the leading cause of death in children with cancer. While therapy is often curative, ~15% of children will relapse with recurrent disease and abysmal outcomes. Why some children develop resistant disease remains unclear.

Project Goal
To address this question, we are studying genetic pathways that cause relapse with the goal of designing therapies to treat children with relapsed disease. Our focus is on the HMGA1 gene, which is up-regulated in childhood ALL with the highest levels at relapse. HMGA1 transforms normal blood cells into

leukemia cells and causes aggressive leukemia in mice, recapitulating salient features of childhood ALL. This gene encodes a protein that acts as a "molecular switch" that "opens" DNA to turn on genes that are required by stem cells for rapid cell growth and development. Based on these exciting findings, we hypothesize that: 1) HMGA1 drives relapse in ALL by "flipping on" stem cell genes, and 2) targeting these pathways will put a "brake" on abnormal growth and destroy stem-like leukemic blasts at relapse where HMGA1 expression is highest. To test this, we propose specific aims to: 1) define the stem cell pathways up-regulated by HMGA1 at relapse and 2) screen for novel therapies that disrupt the aberrant pathways induced by HMGA1. This work will elucidate the abnormal DNA landscape imposed by HMGA1 in relapsed ALL and begin to identify new therapies for children with relapsed ALL.

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Anastasia Tikhonova, PhD of New York University School of Medicine
Young Investigator Grant
Identification and Targeting of Microenvironmental Factors Controlling Pediatric Leukemia

Background

T cell acute lymphoblastic leukemia (T-ALL) is a devastating pediatric blood cancer. Despite progress in treating T-ALL, one quarter of childhood patients relapse within five years and receive a bleak prognosis. The general toxicity associated with recent therapeutic efforts to treat T-ALL stresses the urgent need for novel innovative therapies. While much is known about the genetics of leukemic cells, little is understood about how they behave within their native milieu, the bone marrow. Several lines of evidence indicate the leukemia cells require a specialized microenvironment to survive, and that disrupting this microenvironment may be a novel, promising therapeutic strategy. Our recent work identified CXCL12, which produces the vascular endothelial cells that constitute the blood vessel network, as a necessary component of a leukemic niche in the bone marrow. Given that leukemic cells cannot produce CXCL12, they rely on blood vessels for their supply of CXCL12. We found that interrupting this supply after disease onset dramatically reduced leukemic burden, suggesting a potential new therapeutic paradigm to treat this devastating disease.

Project Goal:

Our proposed studies will: 1) examine which other molecular factors produced by the microenvironment are important for leukemia development, and 2) test the therapeutic potential of CXCL12 blockade. This will be one of the first examples of therapeutic targeting of the cancer microenvironment in leukemia. Understanding the role of the microenvironment in the development and maintenance of this blood cancer will suggest novel and effective therapeutic strategies to treat this devastating disease.

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Andrea Flynn, MD of Children's Hospital of Philadelphia
Young Investigator Grant
Targeting Protein Translation to Antagonize MYC-driven Neuroblastoma

Background

Each year in the US over 700 children are diagnosed with neuroblastoma, a tumor responsible for 15% of all childhood cancer deaths. Neuroblastoma arises from the developing nervous tissue (outside the brain), and usually behaves aggressively. Treatment currently includes intensive therapy, yet only about 50% of children with high-risk disease survive long term. Difluoromethylornithine (DFMO) is a drug that is FDA-approved to treat an infection called "Trypanosomiasis." DFMO blocks an enzyme (ODC) needed to make chemicals called polyamines, which have been found to be necessary for human cells to grow quickly, especially cancer cells. Tumors in which a cancer gene called MYC has been turned on are particularly dependent on polyamines.

Project Goal:

We and others have shown that DFMO has strong activity against neuroblastoma (which often has its MYC gene turned on), so we aim to "re-purpose" DFMO as a novel neuroblastoma drug. Here, we will explore which types of genetic changes make neuroblastoma cells vulnerable to DFMO. We found that some neuroblastomas have turned on their ODC1 gene (which makes the enzyme that DFMO targets) in addition to their MYC gene. We can test tumors to see which ones DFMO works best against. We also need to understand what exactly DFMO does besides depleting the tumor of polyamines. Our work so far shows that DFMO treatment poisons the ability of these cells to make proteins, and we will characterize further. With this knowledge, we will be better able to predict which children with neuroblastoma may respond best to DFMO.

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About Alex's Lemonade Stand Foundation

Alex's Lemonade Stand Foundation (ALSF) emerged from the front yard lemonade stand of cancer patient Alexandra "Alex" Scott (1996-2004). In 2000, 4-year-old Alex announced that she wanted to hold a lemonade stand to raise money to help find a cure for all children with cancer. Since Alex held that first stand, the Foundation bearing her name has evolved into a national fundraising movement, complete with thousands of supporters across the country carrying on her legacy of hope. To date, Alex's Lemonade Stand Foundation, a registered 501(c)3 charity, has raised more than $150 million toward fulfilling Alex's dream of finding a cure, funding over 800 pediatric cancer research projects nationally. In addition, ALSF provides support to families affected by childhood cancer through programs such as Travel For Care and SuperSibs. For more information on Alex's Lemonade Stand Foundation, visit AlexsLemonade.org.

About Cure4Cam

The Cure4Cam Childhood Cancer Foundation, inspired by the life of young leukemia patient, Cameron Evans (1998-2012), was started by family and friends to raise community awareness about childhood cancer and funds to support the development of new and more humane therapies for children challenged by these diseases. At the age of 13, Cameron lived by his philosophy that, "The best kind of inspiration is the kind that makes you want to save a life." Since its inception in late 2012, the Cure4Cam Childhood Cancer Foundation, a 501(c)(3) nonprofit organization, has granted over 1 million dollars to childhood cancer researchers all over the U.S. For further information about Cure4Cam, see cure4cam.org.

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