cookies™
for kids' cancer

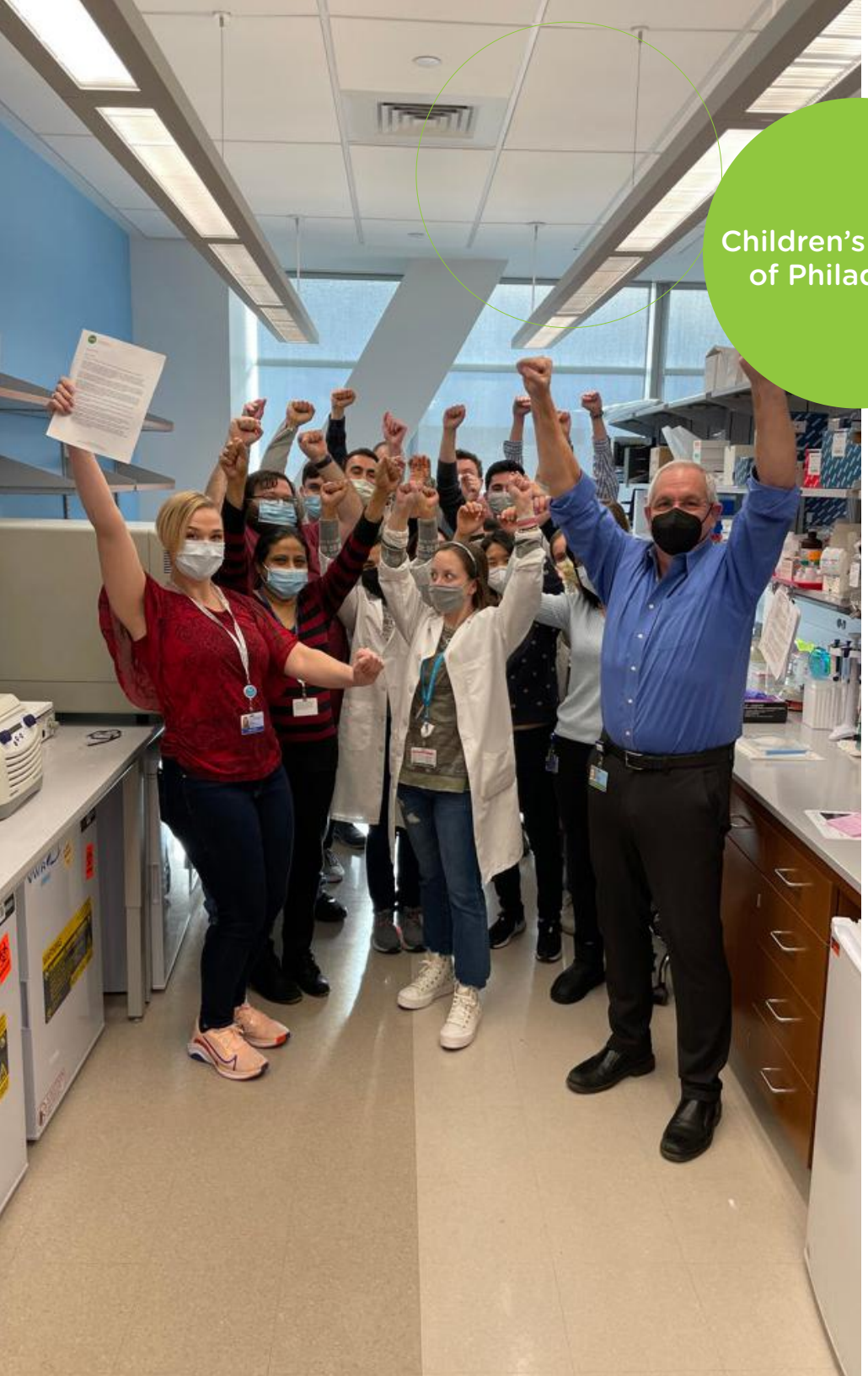
2022 GRANT REPORT

Liam Witt

ABOUT COOKIES FOR KIDS' CANCER

When 2-year-old Liam Witt was diagnosed with childhood cancer in 2007, his parents Gretchen & Larry were shocked to learn about the lack of effective treatments for pediatric cancers due to insufficient funding. They were even more shocked to learn that cancer is the #1 disease killer of children in the U.S. and that 2/3 of kids who go through cancer treatments have long-term debilitating side effects. Those statistics just weren't acceptable. They pledged to support the funding of research for new, improved and most importantly less toxic treatments for kids battling all types of pediatric cancers. With the help of 250 volunteers, Liam's parents undertook a massive bake-a-thon where they baked and sold 96,000 cookies to raise money for research.

That project raised more than $420,000 and — equally important — raised awareness with people asking how they could help. What the Witts thought was a one-time project became the genesis of Cookies for Kids' Cancer which inspires people to Be Good Cookies and get involved by raising money for research for cancers specific to children. Today there have been 16,000 grassroots fundraising events in all 50 states and nearly $20 million granted to the leading pediatric cancer research centers across the country



Children's Hospital of Philadelphia

Grant Amount

$150,000

Recipient:

Dr. John Maris, Children's Hospital of Philadelphia

Project:

Developing a Warehouse of Peptide-Centric CARs for Neuroblastoma

With the funding from Cookies for Kids' Cancer, we aim to develop a warehouse of targeted cell therapies for neuroblastoma, which is the most common cancer diagnosis in infants. We approach this by first identifying highly specific non-mutated proteins found in neuroblastoma cancer cells that are processed and presented on the cell surface by other resident proteins. We then construct genetically engineered immune cells to target these cancer-specific complexes. The intended impact of this research is to expand an emerging therapeutic modality to encompass as many children as possible suffering from refractory or relapsed neuroblastoma. This is a completely new class of immunotherapies specific to childhood cancers. By focusing first on neuroblastoma, we have a strategy to personalize immunotherapies specific to individual patients, and thus we're building a warehouse of "chimeric antigen receptors" (CARs) to engineer into patients' immune cells to eradicate their cancers. This additional funding will help generate the second such CAR, and a third and fourth will be built and tested as well.

Memorial Sloan-Kettering Cancer Center

Grant Amount

$150,000

Recipient:

Dr. Christopher Klebanoff, Memorial Sloan-Kettering Cancer Center

Project:

Therapeutic Targeting of a Recurrent Fusion-Derived "Public" Neoantigen Expressed by Pediatric Desmoplastic Small Round Cell Tumors Using T-Cell Receptor (TCR) Gene Therapy

A subset of cancer mutations, termed neoantigens, activate a class of white blood cells called killer T cells. When used as a form of cancer immunotherapy, neoantigen-specific killer T cells can induce sustained tumor regression without injuring healthy tissues. Many pediatric cancers are caused by a unique kind of mutation, termed driver fusions, which occur when one chromosome becomes fused to another to create an entirely new molecule. We hypothesized that driver fusions might give rise to a particularly immune-stimulating subset of neoantigens because they create chimeric, or "monster", proteins that appear foreign to a patient's immune system. Desmoplastic small round cell tumor (DSRCT) is a rare and highly fatal pediatric sarcoma caused by a fusion involving the EWSR1 and WT1 genes. Current treatments for DSRCT are intensive, result in significant side effects, and ultimately do not cure the disease. We hypothesized that the EWSR1-WT1 fusion protein could create a shared, or "public", neoantigen that might be targeted using an off-the-shelf T cell immunotherapy. In support of our hypothesis, my lab discovered in year 1 of our Cookies for Kid's Cancer grant that the EWSR1-WT1 protein drives a spontaneous immune cell response in patients who have two common tissue types (termed HLA-A*03 and HLA-A*11). However, we also found that killer T cells from patients with specificity for the fusion NeoAg are immunologically exhausted and incapable of growing efficiently. We therefore used non-exhausted T cells from healthy donors to "outsource" the generation of fusion-NeoAg specific T cells. From these cells, we retrieved the unique genetic sequences that encode the instructions for immune receptors which recognize the fusion protein. In proof of concept studies, we discovered that expression of these immune receptors in T cells using genetic engineering reprogrammed their function, enabling the immune cells to selectively eliminate cancer cells while leaving normal cells unharmed. Building directly on this success, in year 2 of the Cookies for Kid's Cancer grant, my lab seeks to extend our findings as an immediate prelude to clinical translation. In Aim 1, we will seek to expand the number of patients who might benefit from a fusion NeoAg immune receptor therapy by functionally validating additional immune receptors compatible with other common tissue types. In Aim 2, we will measure the cross-reactivity profile of our immune receptors and test their pre-clinical antitumor activity using a unique panel of DSRCT tumor cell lines developed at MSKCC. At the conclusion of the funding period, we seek to nominate a lead immune receptor candidate for clinical development in a first-in-child clinical trial. Success of this research will result in an innovative new cellular immunotherapy for patients with DSRCT. Further, it will establish a generalizable research strategy to identify and therapeutically target other fusion-derived proteins expressed by childhood cancers.

Grant Amount

$59,367.34

Recipient:

Dr. Brian Kushner, Memorial Sloan-Kettering Cancer Center

Project:

Phase II Study of Humanized 3F8 Anti-GD2 Monoclonal Antibody and GM-CSF in Patients with Refractory or Relapsed High-Risk Neuroblastoma

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Meaningless mock-up, mock turtle soup spilled on a mock turtle neck. Mach I Convertible copy. To kill a mockingbird, you need only force it to read this copy. This is Meaningless filler.

St. Jude Children's Research Hospital

Grant Amount

$150,000

Recipient:

Dr. Stephen Gottschalk

Project:

CD70-directed CAR T-cell Therapy for the Treatment of Relapsed/Refractory Pediatric AML

AML is a type of leukemia cancer that impacts children. It can occur at any age, but most cases happen in children younger than 2 years and in teenagers. We have developed an immunotherapy for AML that uses AML-specific immune cells. We now wish to evaluate our approach in a clinical study. With the support of Cookies for Kids' Cancer we will implement and start our proposed clinical study that evaluates the safety and anti-tumor activity of our immune cells in pediatric patients with AML.

Grant Amount:

$150,000

Recipient:

Dr. Stephen Mack

Project:

The Activity of Combined Epigenetic and Immune Checkpoint Inhibition in H3K27me3 Deficient Brain Tumors

St. Jude Children's Research Hospital

Pediatric brain tumors are the leading cause of cancer related death in children. Aggressive forms of the disease are defined by loss of the epigenetic modification demarcated by H3K27me3 observed in diffuse midline glioma and ependymoma. While immunotherapies, such as checkpoint inhibitors have been effective for many adult malignancies, they remain largely ineffective against most pediatric gliomas. Our project seeks to systematically define the tumor immune microenvironment of H3K27me3 depleted gliomas, including ependymoma. This characterization initiative that extends from our previous proposal will provide important insight on how the tumor-immune microenvironment modifies tumor progression and response to immunotherapy. These insights may be relevant to defining combination immunotherapies that are effective against H3K27me3 depleted brain tumors.

Grant Amount:
$150,000

Recipient:
Dr. Robin Parihar

Project:
Development of a Human Natural Killer Cell Immunotherapy Against Pediatric Sarcomas

Treatments using the immune system to fight childhood bone and muscle tumors (sarcomas) have shown promise in the lab. However, their ability to cure patients has been limited by a powerful tumor environment that turns off the immune system and does damage to normal cells. We have developed a cancer therapy that uses natural killer (NK) cells, a type of white blood cell with excellent tumor killing capacity and a unique ability to distinguish normal tissues in the body. The NK cells safely target both the tumor environment and sarcoma-associated proteins in a special way that allows them to destroy cancer but leave normal tissues alone. We will test the ability of these NK cells to kill tumors safely in laboratory models, and then make preparations to test safety and effectiveness in kids with sarcoma. My lab and I are incredibly thankful to the generous support of CFKC donors. Your tireless devotion to kids with cancer, and to supporting researchers who want to bring new, less toxic therapies to them, is inspirational and incredibly appreciated. We truly would not be able to do this without you! Despite attempts to improve treatment over the last few decades, children with advanced pediatric sarcoma of muscle or bone continue to die from their disease. New treatments are sorely needed. Treatments that utilize the immune system to fight cancer have shown promise in the lab. Their ability to cure patients, however, has been limited by a powerful tumor environment that turns off the immune system. In addition, because there are very few target proteins specific to sarcoma tumors (i.e., those expressed on the tumor, but not on normal tissues), it is difficult to spare normal cells from damage during immune treatment. Thus, there is a critical need to develop treatments that safely target both the tumor microenvironment (TME) and sarcoma associated proteins so that immune treatments can destroy cancer but leave normal tissue alone. To overcome these challenges, we have developed a treatment that utilizes natural killer (NK) cells, a type of immune cell with excellent tumor killing capacity and a unique ability to distinguish normal tissues in the body. To further enhance their activity, we have modified NK cells to target both sarcoma tumor cells and the TME. We are now testing the ability of these NK cells to kill tumors safely in lab models and making regulatory preparations to test safety and effectiveness in children with advanced soft-tissue sarcoma within the context of a clinical trial. 14 2020 Annual Report Texas Children's Cancer Center Grant: $100,000 (2nd half of a $200,000 grant initiated in 2019) Project: Development of a human natural killer cell immunotherapy against pediatric sarcomas Recipient: Dr. Robin Parihar The burden of pediatric cancer, both physical and emotional, for patients and their families is immense. My lab aims to help discover more specific, less toxic treatments to decrease that burden. We expect our research to lead directly to a cell therapy clinical trial at Texas Children's Hospital for children with soft-tissue and bone sarcomas. We are incredibly thankful to the generous support of CFKC donors that is helping move this research into the clinic.

Children with bone and muscle tumors (sarcomas) that do not respond to initial therapy, or come back after therapy, have very low survival rates. Unfortunately, no treatments tested over the last 30 years have improved this low survival. Recently, new treatments using the immune system have shown promise in the lab. However, their ability to cure patients has been limited by a powerful tumor environment that turns off the immune system. We have developed a cancer therapy that uses natural killer (NK) cells, a type of immune cell with excellent tumor killing capacity and a unique ability to distinguish normal body tissues, to safely target both the tumor environment and sarcoma while leaving normal tissues alone. We have confirmed the ability of these NK cells to kill tumors safely in laboratory models and are now making preparations to test safety and effectiveness in kids with sarcoma.

Texas Children's Cancer Center

USCF Benioff Children's Hospital

Grant Amount:
$150,000

Recipient:
Dr. Elliot Stieglitz

Project:
CLL-1 CAR-T Cells for the Treatment of JMML

JMML is a blood cancer that affects infants and toddlers. Unfortunately, treating JMML with chemotherapy is only effective in half of all patients. With this funding from Cookies for Kids, we are developing a new type of treatment that uses a patient's own immune system to fight the cancer cells instead of chemotherapy.

UCSF Benioff Children's Hospital

Grant Amount:
$150,000

Recipient:
Dr. E. Alejandro Sweet-Coredero

Project:
Targeting the DNA Damage Response Pathway to Treat Metastatic Osteosarcoma

Osteosarcoma is a an aggressive bone cancer that occurs in children, adolescents and even young adults. It can impact any bones but usually is found in the long bones of the legs. Metastatic osteosarcoma is extremely difficult to treat with a survival of less than 20%. The current treatment regimen has remained unchanged for approximately 40 years and includes highly toxic chemotherapy which has significant long-term side effects that can even lead to secondary cancers and death. There is an urgent need for new therapeutic approaches. Unfortunately, the disease has seen no improvements in therapy for over 40 years. Our goal with this grant is to find new combination therapies that can be translated to the clinic to impact survival for this disease. To do this we tested over 50 new combination therapies in 10 cell lines. These cell lines are mostly new cell lines derived from patient samples that were made in our laboratory. Using this strategy, we have identified several new combination therapies that we are now further testing in animal models to see how well they work against metastatic disease. It is important to study these drugs in the context of metastasis because metastasis the biggest clinical problem we need to address. We will evaluate these new combination therapies with the goal of designing a new clinical trial in the next one to two years.

Children's Oncology Group

Grant Amount:
$206,500

Recipient:
Dr. Brenda J. Weigel, PEP-CTN Chair

Project:
Project Pediatric Early Phase Clinical Trial Network (PEP-CTN)

Since 2012, Cookies for Kids' Cancer has been uniquely positioned as the key philanthropic stakeholder in the advancement of the Phase 1 & Pilot Consortium's and now the PEP-CTN's mission. The amount contributed by Cookies for Kids' Cancer (more than $3 million to date) has had a truly remarkable impact, allowing the PEP-CTN to maintain its own operations infrastructure and censure the rapid development, implementation, and reporting of specialized and complex early phase clinical trials, while also leveraging the resources of the COG. Specific accomplishments during this time include: With the support of Cookies for Kids' Cancer, the COG early phase clinical trials network has completed over 30 studies in 10 years, treating nearly 900 children.

The Pediatric Early Phase-Clinical Trial Network (PEP-CTN) is comprised of 21 premier Children Oncology Group (COG) pediatric core member sites in the U.S. and 21 non-core member sites in the U.S., Canada and Australia that were selected through a peer review process. The PEP-CTN builds on the strengths and accomplishments of the COG Phase 1/Pilot Consortium to effectively and efficiently conduct state-of-the-art early phase trials. The PEP-CTN will leverage collaborative interaction with COG disease committees, COG leadership, NCI leadership, and the pharmaceutical industry to prioritize and streamline the development of new, targeted therapies for children with cancer. Innovative trial design and endpoints, genomic biomarkers and other correlative studies will augment the impact of PEP-CTN trials on individual patients and drug development for childhood cancer.

The PEP-CTN successfully leverages the database infrastructure and resources of the parent COG while maintaining its own administrative and operational infrastructure to ensure rapid development, implementation and reporting of specialized and complex early phase clinical trials. The PEP-CTN has expert resources for the conduct of translational biology, pharmacokinetic, and pharmacogenetics studies, and has developed a state-of-the art infrastructure to facilitate image transfer of specialized correlative imaging studies for central review and analyses.

Institutions receiving funding from Cookies for Kids' Cancer this year in conjunction with PEP-CTN include:

- Ann and Robert H Lurie Children's Hospital of Chicago
- Baylor College of Medicine/Dan L Duncan Comprehensive Cancer Center
- C. S. Mott Children's Hospital
- Centre Hospitalier Universitaire Sainte-Justine
- Children's Healthcare of Atlanta - Egleston
- Children's Hospital of Colorado
- Children's Hospital of Los Angeles
- Children's Hospital of Alabama
- Children's Hospital of Philadelphia
- Children's Hospital of Pittsburgh of UPMC
- Children's Hospital of Wisconsin
- Children's Mercy Hospitals and Clinics
- Children's National Medical Center
- Children's Hospital of Orange Country
- Cincinnati Children's Hospital Medical Center
- Cook Children's Medical Center
- Dana-Farber/Harvard Cancer Center
- Duke University Medical Center
- Fred Hutchinson Cancer Research Center
- Hospital for Sick Children
- Johns Hopkins All Children's Hospital
- Johns Hopkins University/Sidney Kimmel Cancer Center
- Lucile Packard Children's Hospital Stanford University
- Memorial Sloan Kettering Cancer Center
- National Institutes of Health Clinical Center
- Nationwide Children's Hospital
- New York Medical College
- NYP/Columbia University Medical Center/Herbert Irving Cancer Center
- Oregon Health and Science University
- Phoenix Children's Hospital
- Primary Children's Hospital
- Queensland Children's Hospital
- Riley Hospital for Children
- Royal Children's Hospital
- St. Jude Children's Research Hospital
- Seattle Children's Hospital
- Sydney Children's Hospital
- Texas Children's Hospital
- University of California San Franciso
- University of Chicago Comprehensive Cancer Center
- University of Minnesota/Masonic Cancer Center
- UT Southwestern/Simmons Cancer Center - Dallas
- Vanderbilt University/Ingram Cancer Center
- Washington University School of Medicine

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