Alex's Lemonade Stand Foundation

Rhabdomyosarcoma Impact Report

Alex's Lemonade Stand Foundation for Childhood Cancer™

AlexsLemonade.org

Alex’s Lemonade Stand Foundation (ALSF) emerged from the front yard lemonade stand of 4-year-old Alexandra “Alex” Scott, who was fighting cancer and wanted to raise money to find cures for all children with cancer. Her spirit and determination inspired others to support her cause, and when she passed away at the age of 8, she had raised $1 million. Since then, the Foundation bearing her name has evolved into a national fundraising movement and is one of the leading funders of pediatric cancer research in the U.S. and Canada.

With Gratitude

Dear Friend,

All of us here at Alex's Lemonade Stand Foundation (ALSF) would like to sincerely thank you for your support of Alex's mission to find new treatments and cures for childhood cancers like rhabdomyosarcoma.

Your support is helping researchers to develop preliminary data, publish their findings, and push forward innovative treatment options. Thanks to you, we are closer to a day where no child will have to suffer from rhabdomyosarcoma.

We are truly honored to fight childhood cancer by your side. Thank you for being the driving force behind life-saving cures! Please don't hesitate to reach out if you need anything from us here at ALSF.

Until there's a cure,

Liz & Jay Scott
Alex's Parents & Co-Executive Directors
Alex's Lemonade Stand Foundation

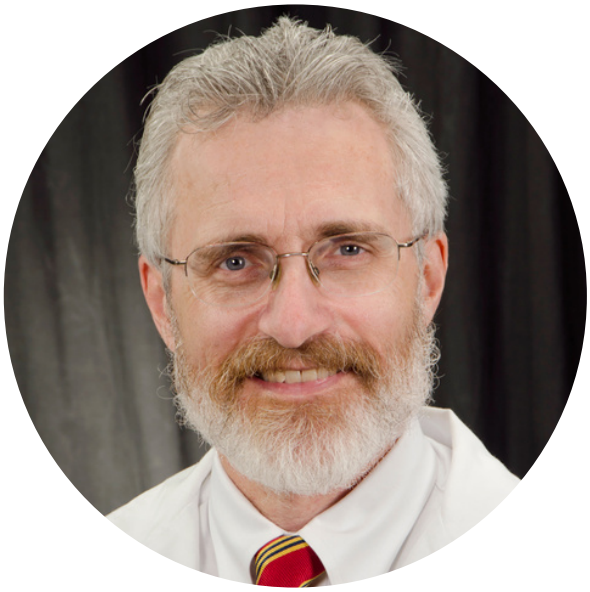
ALSF

Thanks to Supporters Like You

43 **Rhabdomyosarcoma projects (and counting) have been funded**

"The ALSF support is 'keeping the lights on' in the lab and making us competitive for future NIH funding."

— Dr. Craig Mullen,
University of Rochester



"Understanding fundamental processes is critical to developing new targeted therapies. We greatly appreciate ALSF's investment in myself, my research, and my vision."

— Dr. Genevieve Kendall,
Nationwide Children's Hospital

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Meet a **Rhabdomyosarcoma Hero**

Name: **Olivia**
Age: **7**
Loves: **School, art, reading, swimming, riding her bike and playing with her sisters**

While on a beach vacation with her family, Olivia's dad noticed she had a swollen lymph node. For a few days, they thought it might just be a sinus infection and Olivia took antibiotics. But a few days later, there was a large sore inside her mouth.

The next morning, Olivia visited the ER where a CT scan revealed a large mass in her sinus cavity. Her family rushed back to their home in Iowa. That following Friday morning, Olivia was sent for a biopsy, and was diagnosed with rhabdomyosarcoma that afternoon.

Olivia completed 20 days of radiation, 42 weeks of weekly IV chemotherapy, and 24 weeks of oral chemotherapy. In December 2022, Olivia had her final dose of oral chemotherapy and end of treatment scans. Her treatment was successful and today she has no evidence of remaining disease! Olivia will have regular follow up scans and labs every three months for the next five years to monitor the high risk of recurrence for rhabdomyosarcoma.

To Olivia's family, ALSF shows there is a clear effort of awareness and activism for pediatric cancer taking place. Her hope is that through the practices ALSF follows, new, safer protocols can be developed for kids, and families can be met with more hope and confidence.

Research Spotlight: New Projects in Rhabdomyosarcoma

CDK8 as a New Therapeutic Target in Alveolar Rhabdomyosarcoma

Susu Zhang, PhD, Dana-Farber Cancer Institute

Alveolar Rhabdomyosarcoma (aRMS) is one of the most difficult-to-treat childhood cancers with poor overall survival and little change in treatment over the past two decades. To improve the outcome of children with this aggressive cancer, new targeted therapies must be identified, validated in preclinical models, and ultimately translated to clinical trial. Dr. Susu Zhang's recently awarded Young Investigator Grant is focused on fusion-positive aRMS, typically driven by abnormal genes called PAX3-FOXO1 or PAX7-FOXO1. While direct targeting of this kind of genes is quite challenging, an alternative approach would be to target their interaction partners. In the case of aRMS, Dr. Zhang identified a selective dependency on CDK8, a kinase involved in transcription and recruited by PAX3-FOXO1, through the analysis of genome-scale CRISPR-Cas9 screening data. She will perform assays to examine the effects of CDK8 inhibition on aRMS cell phenotypes (e.g., growth, cell cycle, and cell death) using both genetic and chemical approaches.

Synthetic Gene Expression Regulatory Switches (SynGERS) for Improved CAR T Cell Function in Pediatric Solid Tumors

Leidy Diana Caraballo Galva, PhD, Baylor College of Medicine

Immunotherapy using genetically engineered special white blood cells has revolutionized the treatment of children with blood cancers. The strategy has great potential to cure children with solid cancers; however, these tumors use mechanisms to inhibit the engineered white blood cells. When engineered cells lose their functionality in solid tumors, their program changes in response to the cancer cells. In her studies, Dr. Caraballo Galva will introduce mini programs into tumor-redirected white blood cells with the goal of overcoming solid tumors. To achieve this objective, her team has designed "Synthetic Gene Expression Regulatory Switches" which will be turned on only when needed and help the white blood cells grow, last long and eliminate tumors. Importantly, they have designed a library containing these mini programs and will select the best one for further development in the clinical setting to help children with solid tumors.

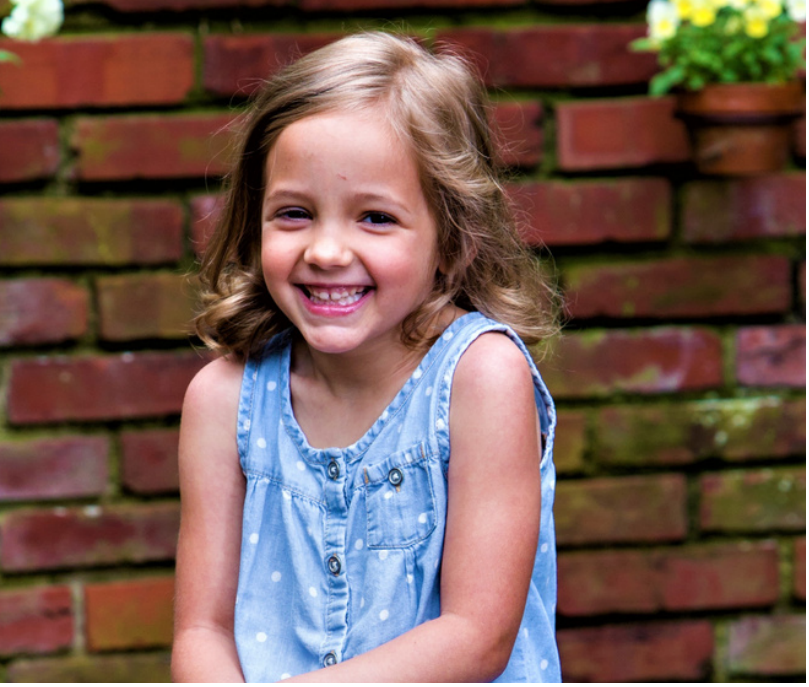
Where Are They Now?

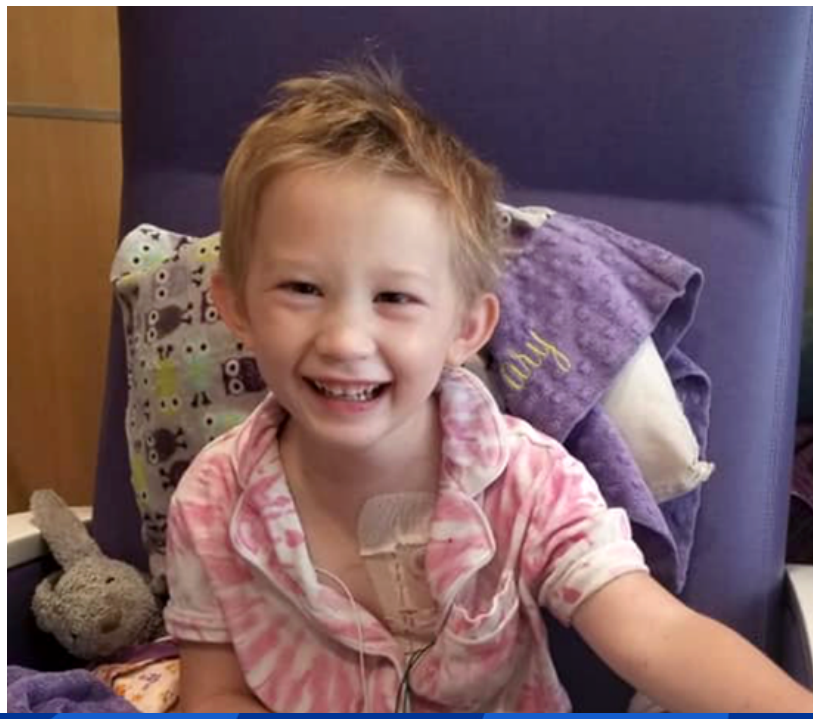
Genevieve Kendall, PhD, 2018 'A' Award Grantee

Past ALSF awardee Dr. Genevieve Kendall of Nationwide Children's Hospital recently co-authored an original research article published in the scientific journal "Developmental Biology" in April. It is currently available to read on their online site. Dr. Kendall et al. detail their generations of zebrafish her3 CRISPR/Cas9 knockouts with loss-of-function mutations. Zebrafish are an excellent model for studying human cancer genes and their underlying biology given that they share over 70% of their genes with humans, and approximately 84% of known human disease genes have a zebrafish counterpart. Through studying zebrafish, researchers like Dr. Kendall are learning more about what drives tumor development and developing potential therapeutic applications.

Dr. Kendall acknowledges that her work was supported by an ALSF 'A' Award. She also received support from a (highly esteemed) NIH/NCI R01 grant. This was due in part to preliminary data gathered from ALSF funding. Dr. Kendall anticipates that the model she's developed will help further elucidate how Her3/HES3 is acting in both development and cancer, which are intrinsically linked. Her research may lead to the discovery of functional genomes and ultimately personalized medications.

Dr. Kendall also acknowledges her ALSF 'A' Award in a co-authored original research article which was published in "Cell Reports" in January of this year. She describes the way in which fusion of transcriptional co-activators, VGLL2-NCOA2, is transforming in transgenic zebrafish and mouse allograft models. She has found that tumors studied over the course of her research resemble immature skeletal muscle and express developmental genes.





Thank You

for all you do to help kids with cancer!