



Alex's Lemonade Stand Foundation

Rhabdomyosarcoma Impact Report



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,

Thanks to your thoughtful support, we have been able to find new discoveries for childhood cancer treatment. ALSF-funded researchers continue to develop breakthrough treatments, lead new clinical trials, and publish their findings in peer-reviewed journals. Thanks to you, we were able to make this progress, which has positively impacted the lives of children with cancers like rhabdomyosarcoma.

Our daughter, Alexandra "Alex" Scott, believed that if we all worked together, we could cure childhood cancer. That idea of collaboration is what inspired others to help her reach her \$1 million fundraising goal. Her idea is the reason we are able to do what we do now. We are always amazed at what can be accomplished when you bring people together. ALSF, scientists and you — we're all coming together for one common goal: to cure childhood cancer. Thank you for all you do in the fight against childhood cancer.

Until there are cures for all kids,



Liz & Jay Scott

Alex's Parents & Co-Executive Directors

Alex's Lemonade Stand Foundation



Thanks

to Supporters Like You

1,000+

Childhood Cancer Research Projects Have Been Funded Since Our Founding

“The ‘high-risk, high-reward’ studies that ALSF supported are some of the very studies that best represent me, our science and serve as the platform for the work we have ongoing and propose for the future. It doesn’t escape me that the support from ALSF has been instrumental, and I extend my deep appreciation to ALSF for supporting our science from the very beginning.”

— Dr. Cigall Kadoch, Dana-Farber Cancer
Institute



“ALSF helped launch my research program 10 years ago and has supported my lab at every step along the way. Their investment in childhood cancer research has transformed the field and nurtured the development of a generation of childhood cancer researchers.” — Dr. Michelle Monje, Stanford University School of Medicine

Research **Spotlight**



Dr. Robin Parihar of Baylor College of Medicine is using his recent 'A' Award Grant to better understand how the tumor environment of pediatric solid tumors like rhabdomyosarcoma decreases natural killer (NK) cell immune activity.

These findings could be broadly applied to enhance NK cell immunotherapies in general. To address the inability of NK

cells to survive, multiply and stay activated to fight tumors, Dr. Parihar and his team have modified NK cells by genetic engineering technology in two unique ways in order to keep NK cells 'on' within the harsh tumor environment. They added an activating signal and deleted an inhibitory signal specifically within NK cells that should safely and durably maintain their activity. They hypothesize that these uniquely co-modified NK cells armed with a tumor-targeting protein called a chimeric antigen receptor (CAR) will multiply, survive and kill cancer cells in the tumor environments of otherwise resistant childhood solid tumors. They will test the ability of these NK cells to kill tumors in laboratory models of the tumor environment developed in their lab, and ultimately in children with advanced solid tumors. Dr. Parihar expects their findings would have the potential to increase response rates in future clinical trials of CAR-NK cells.

Targeting MDM2 for Rhabdomyosarcoma Therapy



Dr. Dawn Chandler of Nationwide Children's Hospital recently submitted her final report summarizing her findings from her 2019 Innovation Grant. In the past two years, Dr. Chandler and her team have been able to make great strides to target genes that will reactivate tumor suppressor pathways that have been turned off in cancers. Tumor suppressor pathways suppress cell growth to prevent cancer and can be targeted for therapy both directly and indirectly. The team has been

working on activating a key tumor suppressor gene, p53, which is regulated by another gene called MDM2. In the first year of this grant, they were able to interfere with alternative splicing of the MDM2 gene so that the important region is included to generate the native MDM2 isoform to increase the tumor suppressor activity of p53. The ability of p53 activation to slow cell growth in cancer cells was achieved by the splicing changes. In the second year, Dr. Chandler and her team tested the ability for the SSOs to be delivered to the tumors to activate p53 and apoptosis for therapeutic benefits. They were unable to see any effects through systemic delivery of the SSOs and are now pursuing alternative methodologies to introduce the SSO sequences to the cancer cells in vivo. Sly, they were able to make great strides and gather the preliminary data to be able to continue these studies with the support of an NIH-R01 award.

ALSF-Funded Projects in Rhabdomyosarcoma

Thanks to you, we have been able to fund outstanding research, leading towards breakthroughs and cures. Read through some of our recently funded research projects in rhabdomyosarcoma below.

PROJECT TITLE	INSTITUTION / PRINCIPAL INVESTIGATOR(S)	GRANT TYPE
Turning Killers into THINKers: TME Hostility-Impervious NK Cells for Treating Neuroblastoma and Sarcoma	Baylor College of Medicine / Robin Parihar, MD/PhD	'A' Award Grants
Using Splice Switching Oligonucleotides (SSOs) to target MDM2 for rhabdomyosarcoma therapy	Research Institute at Nationwide Children's Hospital / Dawn Chandler, PhD	Innovation Grants
Role of the macro lncRNA KCNQ1OT1 in embryonal rhabdomyosarcoma tumorigenesis	Duke University / Corinne Linardic, MD/PhD	Innovation Grants
Identifying targeted treatments for DICER1-associated sarcomas	Research Institute of the McGill University Health Centre / William Foulkes, MD/PhD & Sidong Huang, PhD	Innovation Grants
Investigation of Pediatric Rhabdomyosarcoma Recurrence through Single-Cell Sequencing	St. Jude Children's Research Hospital / Anand Patel, MD/PhD	Young Investigator Grants
Targeting Fusion-driven Sarcomas	National Institutes of Health / Javed Khan, MD	Crazy 8 Pilots
A comprehensive public resource for fusion-negative sarcoma sequencing data	University of California San Francisco / Alejandro Sweet-Cordero, MD & Richard Gorlick, MD	Crazy 8 Pilots
Mechanisms of PAX3-FOXO1 and HES3 Cooperation in Rhabdomyosarcoma	Nationwide Children's Hospital / Genevieve Kendall, PhD	'A' Award Grants
Modeling and Therapeutic Targeting of p21-Activated Kinase Members in High-Risk Rhabdomyosarcoma	Baylor College of Medicine / Jason Yustein, MD/PhD	Innovation Grants
Nuclear Receptor Tyrosine Kinases Mediating Chromatin Remodeling & Checkpoint Adaption	Children's Cancer Therapy Development Institute / Charles Keller, MD	Innovation Grants

[Click here to see a complete list of ALSF-funded projects in Rhabdomyosarcoma](#)

Meet **Childhood Cancer Heroes**

Andrew had been taking antibiotics for an ear infection, but while his ear was getting better, his left eye suddenly grew worse. First diagnosed as pink eye, Andrew's eye became very swollen and began to "stick out." A pediatrician ordered a CT scan, which revealed a mass that was pushing his optical socket and pituitary gland. Andrew underwent an MRI and eventually a biopsy to determine the specific type of cancer. The tumor was deemed inoperable, and Andrew was diagnosed with rhabdomyosarcoma. A secondary tumor was also located in his right leg.



Andrew was then scheduled for 54 weeks of chemotherapy, as well as 24 sessions of proton beam radiation. Throughout treatment, Andrew remained perseverant, encouraging and loving. Today, Andrew is celebrating five years off treatment and thriving.



Ellie was only 4 months old when doctors found a mass on her right shoulder. At first, they thought it was just a cyst. However, three months later while in surgery to remove the cyst, doctors discovered cancerous cells. Ellie was diagnosed with rhabdomyosarcoma. She went through ten months of chemotherapy, finishing when she was just 18 months old.

Sadly, another lump on her neck was discovered six weeks later. "I also noticed that her scar from tumor removal surgery was very 'lumpy' and was thought to be scar tissue," said Ellie's mom, Tara. Ellie was scheduled for surgery the first week of December to remove the lymph node and scar tissue for a biopsy. Doctors discovered that Ellie's lymph node was swollen, but the scar tissue was cancer. Ellie, then 22 months old, began a relapse treatment involving 28 sessions of proton radiation. It was a lot for a little girl just under two, but she fought bravely through it all. Ellie finished chemotherapy while also completing her first year of pre-school. She is now cancer-free.



Thank You

for all you do to help kids with cancer!

