2024

Alex's Lemonade Stand Foundation

Leukemia 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. By the time Alex passed away at the age of 8, she had raised $1 million. Since then, the Foundation bearing her name has evolved into a worldwide fundraising movement and the largest independent childhood cancer charity in the U.S. ALSF is a leader in funding pediatric cancer research projects across the globe and providing programs to families affected by childhood cancer. For more information, visit AlexsLemonade.org.

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 leukemia.

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 leukemia.

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

ALSF is the largest independent childhood cancer charity in the U.S., focused on funding critical research and supporting childhood cancer families.

More than $300M raised since 2005

Funded over 1,500 medical research grants at nearly 150 institutions

Supported nearly 30,000 families through key programs like Travel For Care

ALSF is the only childhood cancer research organization that has been given the NCI Peer-Reviewed Funder Designation for rigorous selection of research and grants.

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Meet a **Leukemia Hero**

VIVIANA

Viviana was experiencing lingering respiratory virus symptoms, on-and-off fevers, and bruises on her legs that her parents assumed were from the playground. She then began to look pale and lost some of her appetite and signature energy. After noticing petechia on her body and broken blood vessels in her eyes, her parents took her to the ER. There, an initial blood test showed strong evidence of blood cancer. Viviana was then transferred to University Hospital's Rainbow Babies, where she was officially diagnosed with B-Cell acute lymphoblastic leukemia (ALL).

After she reached remission, Viviana's family moved to Arizona. She is now being treated at Phoenix Children's and has about two years left of chemotherapy to prevent any relapses and keep her in a remission state. The frontline part of her treatment has been a challenging road, but Viviana has faced it with bravery and resilience.

Viviana is a hero to her parents because she is so strong and never gives up. Her parents want other families to remember something Viviana practices every day: positivity is key. They were inspired by the positivity they found in the mission of Alex's Lemonade Stand Foundation (ALSF) and decided to help raise funds for childhood cancer research by hosting a lemonade stand in Viviana's honor. They served "Sparkling Purple Unicorn Lemonade" in celebration of their hero. The event raised more than $12,000 for ALSF with support from all over America!

Viviana is excited to keep pushing forward and doing what she does best: making others smile.

"We are so happy to be able to give back through ALSF and fund research so that every child has the chance to beat cancer!"
-Alissa, Mom of Childhood Cancer Hero, Viviana

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ALSF-Funded Leukemia Research

Thanks to you, we have been able to continue funding breakthrough research for more cures. Read through some of our recently funded leukemia research projects below:

In vivo transdermal generation of CD33 CAR T-cells towards acute myeloid leukemia

Ruby Sims, PhD
University of California, Los Angeles
Young Investigator Grants, Awarded 2024

Expanding roles of DNA repair protein RAD51 in transcription

Emily Alchaer
Children's Hospital of Philadelphia
POST Program Grants, Awarded 2024

Cardiovascular comorbidities and cardiotoxicity as mechanisms for disparities in treatment outcomes for pediatric Acute Myeloid Leukemia

Emma Gombos
University of Pennsylvania
POST Program Grants, Awarded 2024

DYRK1A inhibition sensitizes SMARCA4 mutated ALL cells to chemotherapy drugs

Ashley Paik
Loma Linda University
POST Program Grants, Awarded 2024

Acute myeloid leukemia; bloodstream infections and supportive care

Caleb Unterlack
Children's Hospital of Philadelphia
POST Program Grants, Awarded 2024

A complete list of ALSF-funded leukemia projects can be found at:
AlexsLemonade.org/childhood-cancer/type/leukemia/grants

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Research **Spotlight**

In Vivo Transdermal Generation of CD33 CAR T-cells Towards Acute Myeloid Leukemia

Ruby Sims, PhD
University of California, Los Angeles

Alex's Lemonade Stand Foundation has always believed that attracting and retaining the best and brightest early career scientists is critical to the future of childhood cancer research. Ruby Sims, PhD is one such scientist. She was awarded a 2024 Young Investigator Grant, designed to fill the critical need for startup funds for less experienced researchers to pursue promising research ideas.

Cellular therapies that engineer a patient's own immune cells to target cancer have revolutionized the treatment of some leukemias and lymphomas. Though currently manufactured externally, next generation therapies focus on engineering immune cells within a patient's body. Dr. Sims' idea: targeting pediatric acute myeloid leukemia (AML) using similar therapies to improve clinical outcomes for patients.

To design the tools required to facilitate these therapies, Dr. Sims' research will focus on three key components. Inspired by the latest COVID19 vaccines, Dr. Sims and her team will optimize a nanoparticle delivery vehicle to carry their immune cell engineering cargo, maintaining high delivery efficiency and the protection of cargo from degradation. To ensure their nanoparticles are delivered to immune cells while sparing other cells, they will add targeting capabilities to the surface of their nanoparticles and compare their specificity against other cell types. Lastly, they will take a unique approach to accessing a patient's immune cells and delivering their nanoparticles. The team will design and optimize a microneedle patch, similar to a pimple patch, loaded with nanoparticles to access immune cells present in the skin. Dr. Sims' and her team will test their ability to access and engineer these immune cells and evaluate their effectiveness in eliminating AML cells. As microneedle patches do not reach pain receptors in the skin, they will provide virtually pain-free nanoparticle delivery, establishing a safe, effective way of engineering immune cells in the body.

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DYRK1A Inhibition Sensitizes SMARCA4 Mutated ALL Cells to Chemotherapy Drugs

Ashley Paik

Loma Linda University

Alex's Lemonade Stand Foundation invests in the future – whether that means helping kids get the treatment they need, or funding researchers to keep expanding the field of pediatric cancer research. The Pediatric Oncology Student Training (POST) Program was designed for undergraduate, graduate, and medical students to participate in the field firsthand under the guidance of an experienced research mentor.

Ashley Paik is 1 of 47 students who were awarded POST grants in 2024. Under the mentorship of Christian Hurtz, a 2018 ALSF Young Investigator Grant recipient, Ashley will be investigating the importance of inactivating SMARCA4 gene mutations for a successful DYRK1A inhibitor-based therapy.

Their lab recently demonstrated that Dual Specific Tyrosine Regulated Kinase 1A (DYRK1A) is required for KMT2A-R ALL cell proliferation and survival. The overall survival rate of children with acute lymphoblastic leukemia has significantly improved over the last decade, but children who are diagnosed with the KMT2A-rearranged (KMT2A-R) gene or CRLF2-R ALL (Ph-like ALL) gene are still experiencing poor clinical outcomes. Not every ALL cell line or patient derived xenograft (PDX) sample is sensitive to DYRK1A, and it is not understood why.

To clarify whether specific mutations render ALL cells dependent on DYRK1A, Ashley and her team performed DNA-single cell experiments using pediatric PDX cases that they either treated with a vehicle control or the novel DYRK1A inhibitor, GNF2133. Strikingly, the sequencing results demonstrated that DYRK1A inhibition specifically reduced ALL clones with inactivating mutations in SMARCA4. Reports indicate that loss of SMARCA4 function renders cancer cells resistant to chemotherapy-induced apoptosis (programmed cell death). Based on these results, the team hypothesizes that DYRK1A inhibition selectively kills ALL cells with inactivating SMARCA4 mutations and consequently renders surviving ALL clones expressing functional SMARCA4 sensitive to chemotherapy drugs.

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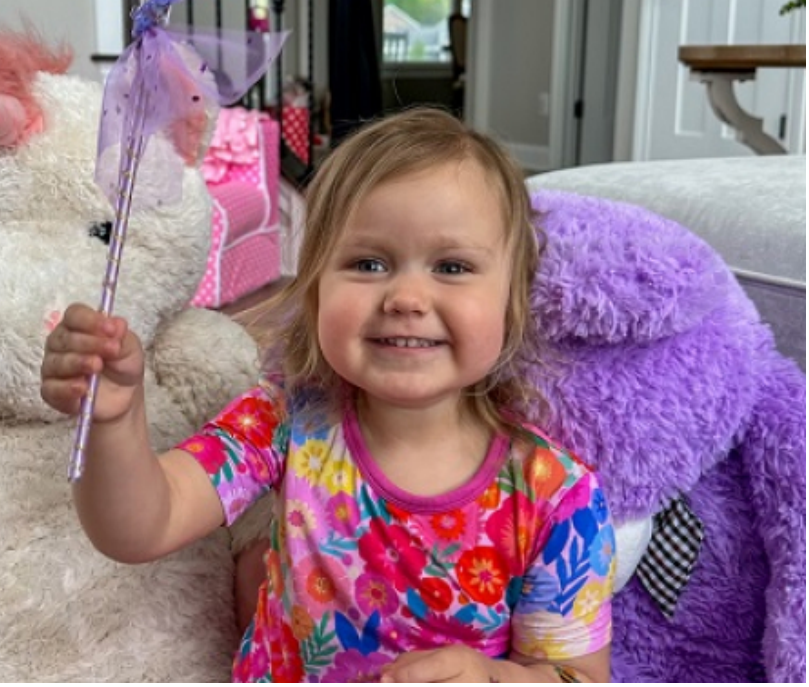

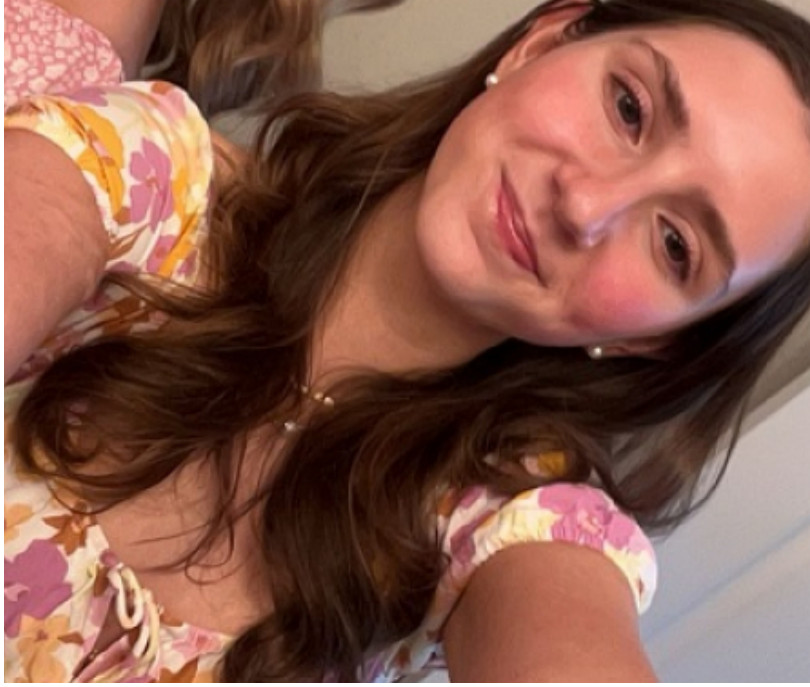

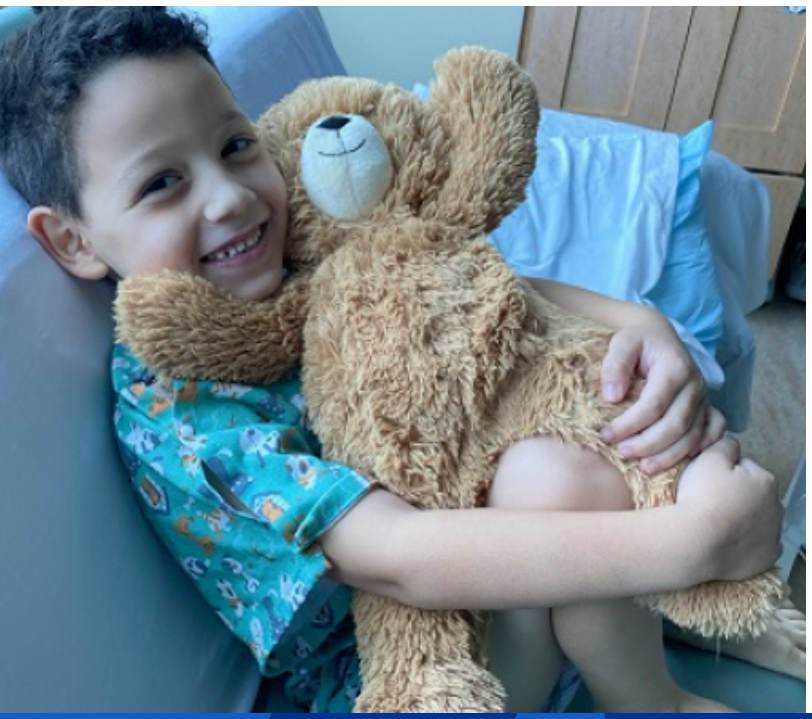

Thank You

for all you do to help kids with cancer!