

It's All About the **Heroes**

All kids with cancer are heroes. Their bravery, strength and love of life inspire those who know them every day. In the face of adversity, they never give up.

Everything Alex's Lemonade Stand Foundation (ALSF) supporters do, from donating to volunteering to spreading awareness, comes back to helping these kids. When Alex set up her first lemonade stand, she didn't just believe in cures for some kids, she believed in cures for all kids. Your dedication fuels the progress toward finding these cures, supporting families and creating safer treatments for all children.



You're helping kids like Nora, a shy but fierce little girl, who recently relapsed from neuroblastoma. After undergoing chemotherapy, a stem cell transplant, radiation, immunotherapy, and multiple surgeries and scans, 4-year-old Nora must face cancer once again. Nora is still in need of her cure.

You're aiding families in need like 5-year-old Matilda's, who was fighting stage II Wilms tumor when the pandemic started. She underwent more than 13 weeks of treatment, which took an extra toll financially on her family. Thanks to your contributions to ALSF's COVID-19 emergency fund, they received gift cards for grocery costs. Today, Matilda is enjoying life in remission.



You've not only helped Jack, but inspired his family to give back. Two-year-old Jack is now cancer-free after a tough battle with acute myeloid leukemia. Jack's family believes you "can't sit back and wait for a cure." The help they received inspired their own virtual bake sale in Jack's honor, donating proceeds to ALSF to support meaningful research.

Kids like Leevi need that research. Leevi is a survivor of anaplastic ependymoma, but faces numerous side effects. As a result of neurosurgery to remove the mass that had wrapped around his brain stem, 2-year-old Leevi struggled with basic functions, like feeding himself. Though he reached remission with a clinical trial, the chemotherapy caused him to lose a lot of weight and develop infections, hearing loss, the inability to walk long distances and more. At 5 years old, Leevi is living proof that safer treatments are needed.

Every cup sold at a lemonade stand, every contribution to an event or in-store campaign brings us closer to better treatments and cures for all kids. **You change the lives of kids with cancer. Thank you for continuing to fight for our heroes.**



ALSF Founder Alex with her cat Herbert.

Freshly Squeezed News

Spring/Summer 2021

Inside:
Curing the Incurable
The Crazy 8 projects searching for cures for all kids.



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Curing the **Incurable**

4 Projects **15 Institutions**

\$18.5 Million in grant funding

One Goal: Cures for all children with cancer



The Crazy 8 Initiative began as a plan to bring together the globe's leading childhood cancer researchers to create the roadmaps to cures for hard-to-treat cancers. Awarded in Spring 2021, these projects are taking on the most deadly childhood cancers including high-risk leukemias, neuroblastoma, medulloblastoma, and bone tumors such as Ewing sarcoma and osteosarcoma. Meet the Crazy 8 researchers who are leading the way to cures.

Yael Mossé

The Goal: Targeted drugs for MYCN, a currently “undruggable” driver of pediatric cancer.

In her clinic, Dr. Yael Mossé sees firsthand the toll that neuroblastoma and its treatments take on the lives of children.

In her lab, Dr. Mossé sees the hope that targeted treatment could bring to children.

Many of the children in Dr. Mossé's care have high-risk neuroblastoma driven by a protein called MYCN. MYCN can also drive other pediatric cancers, including some types of medulloblastoma, rhabdoid tumors and retinoblastoma. Having too much of this protein fuels tumor growth, but in its absence, the cancer won't grow.



So far, no one has figured out how to drug MYCN because it comes from a family of transcription factors that are essential for normal cell processes. “To date, virtually all of the strategies targeting MYCN haven't really led to any responses in kids because all have been indirect,” said Dr. Mossé.

Dr. Mossé brought together a team of complementary researchers, each with unique expertise to attack MYCN with innovative new technologies.

“We are now poised to deliver on the Holy Grail of pediatric cancer and that is to develop a drug that will allow for MYCN to degrade in a cancer cell.” -Dr. Mossé

Fact #1: MYCN The onco-protein MYCN drives a variety of pediatric cancers including some types of high-risk neuroblastoma, medulloblastoma, rhabdoid tumors and retinoblastoma.

Heinrich Kovar

The Goal: Discover the origins of bone sarcomas and develop tumor models that can be used to test targeted drugs to treat this deadly pediatric cancer.

Dr. Heinrich Kovar began his research career studying Ewing sarcoma, a pursuit driven by his love of science. Then, in a twist of fate, his younger brother was diagnosed with Ewing sarcoma. Doctors told his brother that researchers were working to find better treatments. But, for Dr. Kovar's brother, those treatments did not come in time. His brother died, and Dr. Kovar was left with a mission: find cures for Ewing sarcoma.

While there have been some improvements in disease understanding and treatments for Ewing sarcoma over the past 30 years, little is known about why frontline treatment works well for some children and others are left facing a poor prognosis.

Dr. Kovar and his team are driven to change that. With the Crazy 8 Award, his team will study the origins of Ewing sarcoma — developing an understanding of the moment a cell becomes Ewing sarcoma. Then, they will use this knowledge to develop pre-clinical models that can be used to test therapeutics, eventually leading to safe treatments and cures for the children most at risk of dying from Ewing sarcoma.

“I have to do something about it.” -Dr. Kovar



Fact #2: Toxic treatments Childhood cancer survivors are twice as likely to suffer from chronic health conditions as the result of treatment toxicities.

Leonard Zon

The Goal: To barcode pediatric leukemia, trace its development and match targeted therapies to children with uncured cancers.



While there have been significant advances in the treatment of childhood leukemia, two fundamental problems remain: the treatments that work are toxic and sadly, not all children are cured. Dr. Leonard Zon's Crazy 8 team, co-led by Dr. Ross Levine, aims to turn the tide by tracing leukemia back to its roots — to its cell of origin and find targeted therapies that can cure children who are currently incurable.

The team hypothesizes that pediatric leukemias develop from the blood stem cells that arise during fetal life. These stem cells exist beyond these very early stages of development and into early adolescence. Using an understanding of normal blood cells, the team will use cellular barcoding techniques to map and track these leukemia cells.

The cellular barcodes will allow the team to follow blood cells as they develop, to see where in the developmental process leukemia arises. Importantly, this barcoding technology can eventually be extended to learn more about the development of all childhood cancers, making an even larger impact.



“The patients are the motivation. We need to do better.” -Dr. Zon

Fact #3: Cellular barcodes Cellular barcodes work like the barcodes you see at the grocery store; but instead of being a barcode that tells you the item and the price, these barcodes are created by DNA and allow doctors to track cancer cells.

Charles Mullighan

The Goal: Expand and utilize a library of molecular glues to treat several of the deadliest forms of childhood cancer.

Glue sounds like an unlikely tool for a pediatric oncology researcher. But for Dr. Charles Mullighan and his Crazy 8 team, molecular glue offers the promise for effective treatments and cures for children with brain tumors and leukemia.

Molecular glues are a recent concept in drug discovery, and their application to childhood cancer hasn't yet been fully explored. The molecular glue is designed to bind to a specific transcription factor that drives tumor growth, and then directs the cancer cell to break it down. Since transcription factors are master regulators of cell growth and commonly mutated in leukemia and brain tumors, by degrading mutant transcription factors, the cancer cell dies.



The result: a targeted therapeutic that can attack cancer with potentially fewer side effects to the patient. For medulloblastoma and leukemias, which combined make up the deadliest types of childhood cancers, molecular glues hold the promise for more effective and safer treatments and cures.

His team, with a diverse range of expertise, will work to expand a library of these glues that can be used to treat specific targets that are known to drive childhood cancer.

“Collaboration is absolutely essential. We need expertise in chemistry, structural biology, genetics, tumor biology and therapy.” -Dr. Mullighan

To learn more and support these projects, go to Crazy8Projects.org.

Fact #4: Molecular glue Molecular glue is designed to bind to a specific transcription factor that drives tumor growth, and then directs the cancer cell to break it down.





Creative Supporters *from All Over!*



When the annual Great Chefs Events were put on hold, Chef Chris Bianco's family sold homemade lemon cookies and lemonade at their social-distant lemonade stand to keep childhood cancer research moving forward!



Larry, who is fighting cancer himself, believes that children battling cancer are the true heroes. That's why he selflessly chose to donate the sales from his daughter's t-shirt fundraiser to kids and the research that will help them.



In December, the Revolution School's students set a goal to walk 400 miles combined (the distance from Philadelphia to Pittsburgh). Gre, the student who walked the second most miles, donated their portion of the money raised to support ALSF!

Partner Spotlight



Through the past three years, ALDI has been a dedicated supporter in the fight against childhood cancer. In 2020 they donated \$1 million to the cause, and are excited to continue their work this June with the return of their lemon-themed items sold in stores across the country.



Since 2006, Five Below has raised more than \$7 million to change the future for kids with childhood cancer. They were honored as Crystal Cup recipients at this year's virtual Lemon Ball, and are hosting their annual fundraiser in stores throughout May.



Over the past nine years, Northwestern Mutual has funded many new ALSF initiatives to help meet the needs of childhood cancer families. In April 2021, they continued that partnership with a commitment of \$60,000 to fund 12 new Pediatric Oncology Student Training (POST) grants to diverse candidates.

Giving \$5 or more a month can support kids fighting cancer today, tomorrow and every year to come.

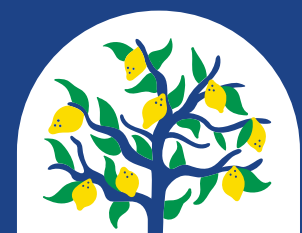


Sustain critical childhood cancer programs with your monthly gift by going to AlexsLemonade.org/One-Cup-Newsletter.



Lemonade Days returns in June!

Join this annual, week-long tradition that unites supporters from across the country in one common goal: to honor Alex's dream of curing childhood cancer. However you choose to host your lemonade stand or event, every cup counts toward cures. **Pick any day(s) between June 5-13 and visit LemonadeDays.org to register your stand.**



ALEXANDRA SCOTT
Legacy Society

You, too, can have a legacy like Alex. The Alexandra Scott Legacy Society honors those who commit to make ending childhood cancer part of their life's mission. Learn more about including ALSF in your will, trust or other estate plans at AlexsLemonade.org/Legacy-Gifts.