OVERCOMING RESISTANCE: ALSF YOUNG INVESTIGATOR MAKES STRIDES IN THE TREATMENT OF BRAIN TUMORS

In order to survive, the cells of the body are constantly recycling within themselves, taking proteins inside the cell, scooping them up, breaking proteins down and releasing the energy back into the cell as new building blocks. All cells in the body—even cancer cells—perform this process known as autophagy.

Jean Mulcahy Levy, MD, an ALSF Young Investigator Grant recipient from the University of Colorado Denver, is studying how stopping this process can be an effective treatment for some types of brain tumors.

Brain tumor cells are constantly performing autophagy. Forced to live in a particularly harsh environment without a lot of oxygen and a limited blood supply, brain tumor cells use autophagy not only to survive, but to grow and multiply.

Dr. Levy’s research discovered that in brain tumors with a certain genetic mutation, inhibiting autophagy can stop the tumors from becoming treatment resistant, allowing the chemotherapy to eliminate disease.

Dr. Levy used chloroquine—a medicine originally created to treat malaria in the 1950s—to inhibit autophagy in lab tests and in three children battling brain tumors. Chloroquine works by stopping autophagy and since the drug is already approved for patient use, it is safe and readily available.

Her work showed that chloroquine is effective in conjunction with chemotherapy. The three children treated by Dr. Levy had positive clinical outcomes. The next step for Dr. Levy’s research is a clinical trial to expand the number of patients treated and continue to prove the safety and efficacy of chloroquine.

“Identifying new treatments, like autophagy inhibition, allows us to treat patients who have exhausted (other) treatment options,” says Dr. Levy.

Dr. Levy’s work, “Autophagy Inhibition Overcomes Multiple Mechanisms of Resistance to BRAF Inhibition in Brain Tumors,” was published in the January 17, 2017 issue of eLife.

Read more about Dr. Levy’s work at AlexsLemonade.org/autophagy
GRETA’S STORY: A PINT-SIZED HERO WHO IS WISE BEYOND HER YEARS

Greta is a sweet girl who loves to be goofy and make jokes so others will laugh. She loves animals, but penguins and elephants are the ones she loves best. She recently took a ballet class and enjoyed it a lot. She’s very curious and inquisitive. Over the summer, she found a praying mantis and was the only child who wanted to hold it! At age 4, she has quite a vocabulary and speaks very clearly. Pint-sized and wise beyond her years, she usually shocks people when she talks.

Greta was diagnosed as an infant at the tender age of 3½-months-old. She had fevers of unknown origin and was unable to keep food down. Finally after a week or so of confusing symptoms, her mother felt she looked rather pale so they made an urgent appointment to see the pediatrician. Greta’s pediatrician noticed an enlarged spleen, took a fingerprick and ran a quick hemoglobin test. Because of an abnormally low result, Greta was rushed to Doernbecher Children’s Hospital, where she was diagnosed with leukemia just a few hours later.

After several rounds of chemotherapy, Greta had a bone marrow treatment using the marrow of her then 2-year-old big sister. Sadly, despite the best doctors and care imaginable, Greta fared poorly through the transplant and spent many weeks in intensive care and on dialysis due to liver and kidney failure. She pulled through and had 6 happy months at home before relapsing.

Outcomes at this point are usually dismal and families will opt for hospice care, but the family felt fortunate when Greta qualified for a new trial that Dr. Rebecca Gardner had just opened at Seattle Children’s Hospital. They packed up their home, shipped their pets to live with family and relocated to Seattle from Portland, Oregon so Greta could have a chance at life via an immunotherapy CAR T trial.

ENTER DR. REBECCA GARDNER

Dr. Rebecca Gardner (ALSF Young Investigator 2011) was the physician at Seattle Children’s Hospital who treated Greta on the immunotherapy trial, funded in part by an infrastructure grant from ALSF. Dr. Gardner took Greta’s T cells and genetically modified them to allow her T cells to recognize the leukemia and eliminate the disease (See the CAR T sidebar on this page to read how this treatment works). Soon after the family arrived in Seattle, Greta became the youngest patient enrolled in the trial.

During the trial, the genetically modified T cells began to seek out and attack a protein called CD19, which is expressed in patients who are diagnosed with Pre-B acute lymphoblastic leukemia (ALL)—the most common type of leukemia seen in children. Greta was treated in August of 2014 with her newly improved CAR T cells and within a week and a half, she was in remission.

In the Phase I portion of this trial, 93% of patients reached remission. The Phase II portion started in June and is currently enrolling and treating patients. Dr. Gardner says the other unique thing about T cell therapy is that drugs and chemotherapy are metabolized by the body and tend to go away. The idea behind T cell therapy is that it’s a “living therapy.” Patients are given a dose of T cells which grow and divide and multiply thus arming the patient with persistent cells which prevent relapse. Two and a half years after being treated, Greta still has those CAR T cells in her body.

Greta’s mother, Maggie says, “We find ourselves thankful literally every day for the hopes and dreams we are seeing Greta realize!” Her family hopes Greta feels empowered to do anything in life that makes her happy and keeps her healthy.

WHAT IS CAR T CELL IMMUNOTHERAPY?

T-cells are a type of white blood cell that work with the body’s immune system to help identify and destroy foreign invaders—like viruses and bacteria. Like other immunotherapy protocols, CAR T cell immunotherapy works to harness the body’s immune system to fight cancer cells. This therapy uses genetically engineered T cells to attack cancer cells that the T cells typically cannot see.

Making a T cell “see” cancer cells begins with collecting a patient’s T cells. Then, those T cells are genetically modified with the addition of the chimeric antigen receptor (that’s the CAR part). The chimeric antigen receptor takes the blindfold off T cells, allowing them to see the cancer.

Once the child receives the newly modified T cells, the immune system goes to work. The T cells multiply, attacking the cancer until it is gone. CAR T cells have shown remarkable success in the treatment of relapsed leukemia and have the potential to be a tool in the fight against other childhood cancers such as brain tumors and neuroblastoma.

Read more about CAR T Cell Immunotherapy at AlexsLemonade.org/blog

YOUR SUPPORT
makes a difference!
Please give at AlexsLemonade.org
ALSF NURSE RESEARCHER WORKS TO END CENTRAL LINE INFECTION RATES

Most children battling cancer have a central venous catheter (CVC) or “central line” surgically placed for the delivery of frequent treatments. The CVC is an alternative to an IV line and cuts down on the number of needle pokes for children in therapy. Hospital staff use the CVC to deliver medication (like chemotherapy and sedation) and also for blood tests. While the CVC remains in place and can be used multiple times (compared to a traditional IV which is removed after one treatment), it also presents a risk for bloodstream infections for children who already have weakened immune systems. These bloodstream infections can be deadly.

“Our goal is to cure patients with cancer,” says ALSF-funded nurse researcher Rita Secola, PhD, RN, CPON, FAAN at the Children’s Hospital Los Angeles (CHLA). “The last thing we want to do is lose them due to an infection.”

Tapping into her nearly 20 years of clinical experience with young patients and families, Secola has been researching what protocols reduce bloodstream infections and what factors make infection more likely in children with a CVC. During her research, Secola and her team discovered that ongoing nurse education and compliance were most critical to reducing infection rates.

Her team worked to develop education modules, checklists and guidelines for the nursing staff. As a result, the CVC infection rates at her hospital remain below the national rate and in recent months have been reduced to zero. Secola will continue to work on further developing guidelines and bringing them to other treatment centers.

School Spirit + Teamwork + Fun = A Successful Event For Childhood Cancer Research

The “Potter Cup” started out as an event between two schools from different districts, with the goal of increasing school spirit and an interest in winter sports. The two school athletic directors came up with the story about a trophy (The Potter Cup) that had been lost for years, but was found in the back of an old storage closet. They said that this trophy was given to the school that won the most events during the winter sports season. They planned on playing two basketball games and holding a wrestling match, but realized they needed some entertainment for the other students in attendance too. An activities schedule was added to the event, complete with food and carnival games.

The first “Potter Cup” was attended by 400 students and raised about $3,000, which went into the schools activities fund. After the inaugural event, they realized its potential and wanted to connect it to a charity.

They chose to support ALSF when a parent mentioned seeing a news story about a little girl who had cancer and was raising money to cure childhood cancer by selling lemonade. Although Alex had passed away, the charity formed by her parents to continue her work was a perfect fit for this event. It is because of the affiliation with ALSF that event attendance grew quickly to more than 1,800 students, plus parents and staff. Over the past 8 years, they have raised more than $246,000 to support Alex’s mission of curing childhood cancer.

ALSF CLASS NOTES:

Here is some great news about current ALSF-funded research projects:

- **Kieuhoa Vo, MD, MAS** (Centers of Excellence Scholar, University of California San Francisco) has been named Director of the COG Phase 1 consortium trials in UCSF’s Early Phase Clinical Trials program.
- **Jen Foster, MD, MPH** (Centers of Excellence Scholar, Texas Children’s Cancer Center/ Baylor College of Medicine) was certified in Pediatric Hematology Oncology and Clinical Pharmacology. She is one of only a few investigators to be double boarded in these specialties.
- **Rameen Beroukhim, MD, PhD** (Innovation Grantee 2015) recently had a breakthrough in pediatric brain tumor research demonstrating that testing pediatric brain tumor tissue for genetic abnormalities is clinically feasible to guide a patient’s treatment (published in Neuro-Oncology January 2017).
- **Lauri Linder, PhD, APRN, CPON** (Nurse Researcher Grantee 2010) was able to identify sources of discomfort in hospitalization of children and adolescents with cancer. This study identified a foundation for actionable change to improve the hospital environment for children receiving cancer treatment (published in Journal of Pediatric Oncology Nursing January/February 2017).
- **Kris Sarosiek, PhD** (Young Investigator Grantee 2014) was recently named Assistant Professor at Harvard School of Public Health. He is using funds raised through Alex’s Million Mile to start his new lab at Harvard. Sarosiek’s recent study shows potential pathways to prevent treatment-associated toxicities (published in Cancer Cell January 2017).
- **Research led by Markus Müschen, MD, PhD** (Innovation Grantee 2011) found a connection between drug-resistance in acute lymphoblastic leukemia (ALL) and increased sugar uptake in the ALL cells (published in Nature February 2017).
- **Kyle Walsh, PhD** (‘A’ Award Grantee 2014) and his team recently concluded that there is an association between higher birthweights and more aggressive osteosarcoma found in unusual sites, which suggests the growth pathways active during gestation play a role in the tumor growth (published in Pediatric Blood and Cancer October 2016).
**Volvo Cars USA**, a Founding Partner of ALSF, has been working hard to help children with cancer since Alex had her front yard lemonade stand. Over the years, they have donated more than $5 million and incorporated ALSF into countless campaigns to raise awareness for the cause. Their latest donation? What else, a car! And you could be the lucky winner if you purchase a raffle ticket for just $25 or 10 for $200.

**Call our office at 866-333-1213 to purchase your tickets or visit AlexsLemonade.org/campaign/win-brand-new-volvo to learn more.**

**Northwestern Mutual** and their offices across the country have donated more than $9 million to ALSF to help kids with cancer. To showcase how investing in research can make a difference, they recently dedicated a Rose Bowl Parade float in honor of a young cancer survivor whose life was saved by an ALSF-funded project. The theme of the parade was “Echoes of Success” and they chose to highlight how investments in research can lead to saving lives—the ultimate success! The float and the story that inspired it were recently featured on "CBS Sunday Morning."

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**GOING ABOVE AND BEYOND FOR CHILDHOOD CANCER!**

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**A CLUB FOR CURING CHILDHOOD CANCER**

ALSF founder, Alex Scott, believed that everyone could make a difference and that every gift would add up to a cure for childhood cancer. So far, our supporters like you have helped us fund over 690 research projects!

For the past five years, supporters in the **ALSF One Cup at a Time Club** have helped to make this funding possible by giving recurring gifts—one a month. These gifts have made an enormous impact and have enabled ALSF to fund innovative childhood cancer research. One Cup At A Time participants also receive special updates throughout the year showing how their donations are making an impact on children with cancer and their families.

The One Cup at a Time Club is perfect for everyone who wants to follow in Alex’s footsteps. Alex began with one lemonade stand—well, really, with one cup of lemonade. Each cup of lemonade and each donation (no matter how big or how small) adds up. ALSF-funded researcher, Dr. Jeffrey Huo, explains it like this: first, a few cups of lemonade funds an experiment, those experiments produce data and figures which lead to journal articles and eventually scientific breakthroughs. Each donation made is a building block that leads us closer to cures and recurring gifts add up quickly.

**Feeling inspired? Want to get involved? Learn more at AlexsLemonade.org/OneCupClub**

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**GO GOLD WITH US THIS SEPTEMBER! ONE MILE AT A TIME**

**Raise Awareness & Funds for Childhood Cancer by Teaming Up with ALSF**

Last year, throughout the month of September (Childhood Cancer Awareness Month), people across the country walked, ran and rode over 1 million miles to raise awareness for childhood cancer. This year, we want to do it again – with your help – and raise $1 MILLION to fund childhood cancer research.

Whether you are a marathon runner, a casual walker or an avid cyclist, you can log your miles on our website from September 1-30 all while fundraising to support important, life-changing research projects nationwide.

**Start a team, join one or participate on your own. Register at AlexsMillionMile.org!**

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**DONATE TODAY OR GET INVOLVED!**

**ALEXSLEMONADE.ORG**