Research Impact Highlights

September 30, 2022

Impact Highlights

- Results from the *St. Baldrick's Foundation Martha's BEST Grant for All were presented* at the recent American Association of Cancer Research (AACR) Special Conference. This research showed that when tested in models, a new drug candidate was 25 times stronger than current FDA approved drugs in trials for Ewing sarcoma treatment. See blog.

- St. Baldrick's Fellow Dr. Jessica Tsai and colleagues discovered that a gene called FOXR2 that is normally turned off in most tissues is activated in at least 70% of cancer types. Their study, recently published in Cancer Research, can help researchers understand how cancer develops. See blog.

- A new approach from researchers including St. Baldrick's Scholar Dr. Saba Ghassemi, has drastically cut the time it takes to alter patients' immune cells for infusion back into the body to find and attack cancer. This process typically takes 9-14 days, but as shown in a recent publication in Nature Biomedical Engineering, Dr. Ghassemi and colleagues generated functional CAR T cells in just 24 hours. See blog.

- The FDA approved the combination of 2 targeted drugs for the treatment of adults and children ages 6 years or older with nearly any type of advanced solid tumor that has a specific mutation in a gene called BRAF. Results from three clinical trials, including one with pediatric patients, laid the groundwork for the approval. Data from the pediatric trial was also used to adapt the use of Trametinib in a phase 2 trial for pediatric patients with relapsed or refractory Juvenile Myelomonocytic Leukemia (JMML). The St. Baldrick's Foundation is providing support for this JMML phase 2 COG study. See blog.

Summary Statistics – *As of June 2022*

- *A total of 1,674 grants,* to date, fueling an ongoing stream of research - from basic discovery, to translational research, to clinical trials testing new treatments for patients.

- *More than $322 million* in research projects funded since 2005, making St. Baldrick's the biggest grant-maker in childhood cancer research aside from the U.S. government.

- This includes support of *more than 336 clinical trials*, conducted at more than 230 research institutions across North America and beyond, through the Children's Oncology Group, the St. Baldrick's – Stand Up to Cancer Pediatric Cancer Dream Team and other groups.

- *More than 136,000* infants, children, teens, and young adults fighting cancer have been treated on more than 336 clinical trials supported by St. Baldrick's, since 2005. (With some enrolled in more than one trial, total *enrollments* are 232,379.)
    - Of these, 277 trials are through the Children's Oncology Group, with more than 232,000 trial enrollments. (Some patients are enrolled in more than one trial.)
    - Most *other* patients in North America and beyond are treated on protocols resulting from research supported by St. Baldrick's.
    - St. Baldrick's is a lead funder of Project:EveryChild, which *captures the biology and outcome of every child diagnosed with cancer* in the U.S. and COG partner countries, a foundation for new discovery and treatment.

- St. Baldrick's plays a vital role in *training the next generation*, having funded:
    - *148 St. Baldrick's Fellows* – funding to complete their training to become pediatric oncology researchers.
    - *141 St. Baldrick's Scholars* – funding for researchers early in their careers, to help them explore new ideas while establishing themselves for long-term success.

Past Highlights

- Researchers including St. Baldrick's-supported Dr. Paul Northcott have developed a test aimed at identifying residual disease sooner than other current methods in children with medulloblastoma. Currently, by the time doctors discover the cancer has returned – through MRI or spinal tap – it is usually advanced and difficult to treat, and almost all relapsed children ultimately die from the disease. Researchers believe this test would identify children who still have evidence of disease shortly after completing treatment and are at high risk of relapse. Additional studies are needed to validate their results before the test can be used for kids with medulloblastoma, but the hope is that this will ultimately give doctors precious time to treat these patients with more aggressive therapies, to save lives. See blog.
- Diffuse intrinsic pontine glioma (DIPG) and other diffuse midline gliomas are universally fatal pediatric brain tumors. Researchers on the St. Baldrick's Foundation Stand Up to Cancer Pediatric Cancer Dream Team are taking what they have learned from treating blood cancers with CAR-T cell immunotherapy and are applying it to these solid tumors. Results published in Nature from the first 4 patients enrolled in a clinical trial show consistent effectiveness. Some trial patients have seen their tumors shrink by 95% or more — a dramatic achievement never seen in DIPG. Though some have since died, most survived far longer than expected. While more research is needed, these findings provide much-needed hope for families. See blog.
- In what some researchers say is the biggest increase in survival rates seen from a single clinical trial, the 5-year survival rate of children with high-risk group 3 medulloblastoma increased from 54% to 73%. This COG trial did not use a new drug; it used existing treatments in a new combination, adding carboplatin during radiation therapy. The research also emphasizes the need to know the patient's risk group at diagnosis. On average, 20 more kids of every 100 diagnosed with this subtype will survive than before.

See blog.

- St. Baldrick's researcher Dr. Jack Shern was part of the largest-ever international study on rhabdomyosarcoma, which found that genetic testing of these patients can predict which patients will do well and which won't, allowing treatment plans to be personalized to each patient's risk level. Researchers hope this genetic testing will become part of the standard treatment plan for rare cancers like rhabdomyosarcoma. See blog.
- Recent discoveries reveal the potential to prevent Ewing sarcoma cells from spreading beyond the primary tumor site, with insights into what triggers the process allowing cancer cells to survive while traveling through the bloodstream. This research comes from Dr. Poul Sorensen, funded through a $1 million RFA supported by an anonymous donor. See blog.
- Two clinical trials are underway through the St. Baldrick's - SU2C Dream Team for patients with diffuse midline glioma (DMG), a currently fatal disease with no effective standard therapies. These immunotherapy trials offer hope where there has been none. See blog.
- Adding the drug gemtuzumab ozogamicin to standard chemotherapy significantly improved event-free survival (quality of life) for patients with a sub-type of pediatric AML, according to a COG trial as evaluated by St. Baldrick's Scholar Dr. Jessica Pollard. (Event-free survival rate was 29% without the drug, and 48% with it.) Also, of patients going into remission, fewer later relapsed. See blog.
- A viral immunotherapy has been developed by researchers including St. Baldrick's Scholar Dr. Gregory Friedman to be delivered directly into a childhood brain tumor. The overall survival rate of these patients was more than double the typical survival rate for children with high-grade glioma. The next step is to determine the best timing for the treatment and what therapies can be used along with the viral immunotherapy to maximize the anti-tumor immune response. See blog.
- A study including Dr. Sam Behjati, the first international recipient of the St. Baldrick's Robert J. Arceci Innovation Award, found that all neuroblastomas come from a single type of developmental cell called sympathoblasts, making these an attractive drug target. Sympathoblasts are not normally found in children after they are born. This discovery leads to hope for the development of less intrusive therapies targeting these cells. See blog.
- A study conducted by the St. Baldrick's - SU2C Dream Team found that pediatric patients who receive CART-cell immunotherapy for acute lymphoblastic leukemia suffer fewer relapses and are more likely to survive when treatment is paired with a subsequent stem cell transplant. CART-cell therapy results in complete remission for 60% or more of patients, but relapse rates are high. When combined with a subsequent

stem cell transplant, the relapse rate was less than 10% two years later. See blog.

- As a result of a COG clinical trial, the FDA approved crizotinib in January 2021 for pediatric patients aged one and older and young adults with relapsed or refractory anaplastic large cell lymphoma (ALCL) that is ALK-positive. This is a drug that has been used to treat lung cancer. See blog.
- In September 2020, the FDA granted rare pediatric disease designation for IVT-8086, a monoclonal antibody for the treatment of osteosarcoma. This study was partly the outcome of St. Baldrick's Scholar (and now board member) Dr. Jason Yustein, who studied a protein expressed in a variety of tumors including osteosarcoma and has since collaborated with a team at Innova Therapeutics. See blog.
- In April 2020, a study by the St. Baldrick's - SU2C Dream Team made the cover of Nature Medicine, outlining new advances in training immune cells in pediatric patients to target brain tumors called atypical teratoid/rhabdoid tumors (ATRT). These tumors develop in babies and toddlers, who typically survive an average of 17 months. Patients also experience catastrophic side effects from current therapies, so immunotherapy to target only cancer cells is crucial. The study addressed the discovery and targeting of a particular protein marker, and the testing of ways to overcome the challenges of getting the immunotherapy cells to travel from the bloodstream to the tumor site in the brain. See blog.
- In January 2020, Steven Vokes, Ph.D. and his colleagues published findings on a set of proteins and how they control gene expression in response to the "Hedgehog pathway." Mutations in this pathway or the genes it regulates can also cause a wide variety of birth defects and are present in about 25% of medulloblastoma tumors (the most common brain tumor type in children). With a better understanding of this fundamental process, we may not only unlock information about the genes that cause specific birth defects, but also new ways to target cancers, including medulloblastoma. This is an outcome of a St. Baldrick's Research Grant funded in 2016. See blog.
- Findings from St. Baldrick's Scholar Dr. Ben Stanton were published in Nature in February 2020, and already these discoveries have increased understanding of rhabdomyosarcoma, a highly aggressive cancer of the soft tissue and skeletal muscle. Chromatin is the material that packages our DNA, and researchers have been working for two decades to understand the three-dimensional chromatin landscape. Dr. Stanton and colleagues developed a method for this and used that tool to see that a class of drugs called HDAC caused tumor cells to lose the capacity to proliferate. This can now be applied to other research as well. See blog.
- St. Baldrick's Scholar Dr. Elias Sayour has been working on innovative personalized immunotherapy for pediatric high-grade gliomas, the primary cause of death in children with brain tumors. We've funded him since 2016, and now that investment has resulted

in a clinical trial funded at $2.5 million by another foundation, as announced on March 30, 2020. If this immunotherapy proves successful in treating high-grade gliomas, it may also translate to other pediatric and adult solid tumors.

- News from the St. Baldrick's - SU2C Dream Team: In August 2019, the FDA granted breakthrough therapy designation to an experimental immunotherapy being developed for B-cell acute lymphoblastic leukemia (ALL). This therapy targets cancer cells bearing a surface molecule called CD22, is intended for children and young adults whose ALL has relapsed after or is resistant to immunotherapies directed toward another surface molecule, CD19. St. Baldrick's is acknowledged as a funding source in the publication. (Breakthrough therapy designation expedites the development and review of drugs.)
- A July 30, 2019 report from PBS was titled, "Childhood cancer wipes out 11 million years of human potential each year." The source was a publication in The Lancet resulting from research supported by the St. Baldrick's Foundation, The study was led by Dr. Lisa Force, now a St. Baldrick's Fellow at St. Jude Children's Research Center. Also participating was St. Baldrick's Scholar Dr. Nickhill Bhakta, who has done other important research on the late effects of childhood cancer treatment.
- Discovery reported by Dr. Alex Kentsis, 2018 St. Baldrick's Robert J. Arceci Innovation Award winner: Elevated levels of a protein in the urine and tumors of children with Wilms' tumors may lead to relapse. This could help doctors identify children who are at risk for disease recurrence and precisely tailor treatment to overcome drug resistance.
- In May 2019, St. Baldrick's Innovation Award recipient Dr. Will Parsons reported that 24% of childhood cancer patients who had their tumors tested for genetic changes were eligible to receive one of the targeted therapies being tested (much higher than the 10% scientists had predicted) through the Pediatric MATCH trial (led jointly by the NCI and the Children's Oncology Group). This nationwide trial is treating patients on the basis of genetic alterations in their tumors, rather than the type or site of cancer.
- The first recipient of the St. Baldrick's Robert J. Arceci Innovation Award, Dr. Charles Mullighan, reported fundamental insights into the genetic basis of poorly understood subtypes of acute lymphoblastic leukemia (ALL), resulting in a revised classification of leukemia, identification of new therapeutic targets, and the establishment of new experimental approaches to understand how leukemia develops.
- Dr. Alex Kentsis , 2018 recipient of the St. Baldrick's Robert J. Arceci Innovation Award, co-led a study that found that the mutations behind certain pediatric blood cancers, including acute myeloid leukemia (AML) are different from those that trigger leukemia in adults, and helps explain why some leukemias in children are so difficult to treat. The study also suggests new approaches for more accurate diagnosis and better therapies.
- Because of a Children's Oncology Group clinical trial supported by St. Baldrick's, researchers now know that an accurate brain tumor diagnosis requires genomic analysis. Tumors that look exactly alike under a microscope can have very different biology and

require different treatment protocols; this study will result in more children surviving brain tumors.

- On November 26, 2018, the FDA approved the first drug developed to target a key genetic driver of cancer , rather than a specific type of tumor. These genetic fusions are rare, but are present in some patients with many cancers, including infantile fibrosarcoma, typically diagnosed before the age of one. Drs. Noah Federman and Erin Rudzinski credit St. Baldrick's for their early career funding that made it possible for them to participate in the development of this drug, Vitrakvi. Dr. Douglas Hawkins of Seattle Children's Hospital says, "I was approached to be part of this study because we have the phase I infrastructure necessary to conduct the study. We could not have built that infrastructure without St. Baldrick's support over the years."
- As an outcome of his 2014-2017 St. Baldrick's Fellowship, Dr. Elliot Stieglitz is now leading a Phase 2 clinical trial for kids with relapsed JMML (juvenile myelomonocytic leukemia), testing whether an oral targeted medication used in the treatment of melanoma in adults slows or even kills leukemia cells in kids with persistent JMML. He has also developed a test that predicts which JMML patients have the best prognosis and therefore need less intense therapy (thereby reducing late effects).
- Beckwith-Wiedemann syndrome (BWS) is a genetic disorder that affects thousands of children, up to 25% of whom develop cancer, most commonly liver and kidney cancer. The same genetic changes that cause BWS also cause other types of cancer. A St. Baldrick's Scholar since 2015, Dr. Jennifer Kalish is studying why this happens, and has helped develop national guidelines that healthcare providers can use with BWS patients to detect tumors before they have a chance to spread, boosting their chance to survive.
- In addition to the August 2018 graduation of the first four pediatric oncologists to be trained in Uganda, by 2020 at least 16 will have completed the program founded and directed by St. Baldrick's International Scholar Dr. Joseph Lubega.
- A groundbreaking study has revealed that Wilms tumor cells have the same characteristics of a normal developing kidney cell which may have gotten "stuck" during development. This could lead to an entirely new model for treating childhood cancer, by manipulating the development state of the cells instead of trying to kill them with chemotherapy. Dr. Sam Behjati says this was only possible because of the freedom afforded by his St. Baldrick's Robert J. Arceci Innovation Award.
- St. Baldrick's Scholar Dr. Elizabeth Stewart at St. Jude's was part of the most comprehensive analysis yet of rhabdomyosarcoma, identifying weaknesses to target and a promising precision medicine that is now in clinical trials.
- Discovery of a new protein on neuroblastoma cells, and a new immunotherapy already developed to target it. This protein is involved in many other childhood cancers and is moving quickly to clinical trials. This is a St. Baldrick's - SU2C Dream Team discovery.
- A genetically modified herpes virus showing promise in killing high-grade glioma (brain tumor) cancer cells, stimulating the immune system to attack the tumor. Dr. Gregory

Friedman, a St. Baldrick's Scholar, has opened a phase I clinical trial to test the therapy.

- A new cumulative burden metric developed by St. Baldrick's Fellow Dr. Nickhill Bhakta allowing researchers to measure, for the first time, the true magnitude of long-term effects and disease burden experienced by childhood cancer survivors. This data will save lives, by preventing or catching health issues before they get worse.
- In June 2018, a leading scientific journal announced exciting progress in the fight against DIPG, a type of pediatric brain tumor which has been incurable. St. Baldrick's support led to a phase I clinical trial to test a new drug delivery method. Early results show no serious side effects or dose-limiting toxicities, and the trial is expanding.
- Improved survival of a form of acute lymphoblastic leukemia (PH+) from 20% to 70%, with the FDA's approval of Gleevec in 2013.
- An increase in the survival of a form of acute lymphoblastic leukemia from 80% to 90%, by using an old drug (Methotrexate) in a new way.
- An increase from 30% to almost 50% in the survival of high-risk neuroblastoma, with the FDA's approval Unituxin, a new immunotherapy.
- Increased survival from 82% to 94% for children with high-risk non-Hodgkin lymphoma, using Rituximab, a drug previously approved for adult cancers.
- Accelerated discovery in rare cancers through a High Impact Initiative, encouraging Children’s Oncology Group members to open clinical trials for these rare conditions.
- Groundbreaking news with the FDA’s approval of Kymriah in 2017- the first gene therapy approved in the U.S. – saving the lives of more than 80% of relapsed childhood leukemia patients who had no other hope.