SPARK

THE TULLIE AND RICKEY FAMILIES
SPARK AWARDS FOR
INNOVATIONS IN IMMUNOLOGY

ANNUAL REPORT 2024


Thank you for your generosity and supporting the SPARK program!
David Pla
¡Muchas gracias! I am truly grateful for your belief in my research.
Rosa Isela Galvez
A huge thank you to all the SPARK donors for making our research ideas a reality!
Sloan Lewis

SPARK | THE TULLIE AND RICKEY FAMILIES SPARK AWARDS FOR INNOVATIONS IN IMMUNOLOGY

Innovation comes at a cost. Without proof-of-concept to convince highly competitive granting agencies to fund a novel project, many bold ideas never come to fruition.

This is especially challenging for early-career scientists who are still building their professional foundations. La Jolla Institute's Tullie and Rickey Families SPARK Awards for Innovations in Immunology are designed to overcome these hurdles.

This philanthropically funded program offers $25,000 per award in seed funding to support projects that may not secure traditional grant funding due to their innovative or "risky" nature. The program's goal is to help scientists generate enough preliminary data to support bold new approaches to diagnosing, treating, and potentially curing diseases that affect us today. This data is crucial for success in subsequent peer reviews, such as those conducted by the NIH, enabling researchers to attract additional funding to further their work and advance their careers.

In addition to funding cutting-edge research aimed at revolutionizing disease prevention and treatment, The Tullie and Rickey Families SPARK Awards program focuses on educating and promoting the professional development of the next generation of researchers. Finalists receive coaching on how to communicate their research to the public and present their ideas to funders. SPARK awardees also gain valuable experience in independently managing a research project. This experience is an important career milestone, as it helps young researchers develop critical skills in project planning, execution, and leadership, all of which are essential for their future success.

Each year, LJI receives numerous proposals from early-career investigators from its laboratories and core facilities, including postdoctoral fellows, graduate students, instructors, and research technicians. A panel reviews these proposals, narrowing the pool to finalists by ensuring that each project demonstrates scientific rigor, novelty, and potential significance to donors and stakeholders. These SPARK finalists then have the opportunity to pitch their ideas to a donor panel in the hopes of securing funding to pursue their projects.

We are incredibly grateful to all the donors, reviewers, volunteers, and scientists who empower our early-career investigators to take risks that bridge the gap between imagination and groundbreaking discoveries.

About the Tullie and Rickey Families

Left to right: Tom and Judy Tullie, Brenda and Dave Rickey

The Tullie and Rickey families hope that by ensuring the program's longevity, they will inspire other donors to contribute, enabling the funding of additional awards and helping as many innovative ideas as possible take flight.

Some of the most exciting and potentially life-saving immunology research never sees the light of day because it lies only in the imagination of early-career scientists who have no viable path to develop their innovative ideas.

Fortunately, at LJI, a pathway has been established to address the needs of our emerging researchers with innovative and compelling project ideas, thanks, in large part, to the support and generosity of LJI Board Director Tom Tullie, MBA, and his wife Judy, as well as LJI Board Director Dave Rickey and his wife Brenda, and their families.

Their belief and multi-year investment in the SPARK Awards program have been critical in ensuring the longevity of the program. In recognition of their dedication, LJI renamed the SPARK program to The Tullie and Rickey Families SPARK Awards for Innovations in Immunology in 2019.

In 2018, Tom Tullie served as one of the first SPARK pitch reviewers, an experience that inspired him to involve his family in the program. "I've been an entrepreneur and involved in innovation my entire career, but this is the most exciting program I've seen because the ideas these young scientists have are not only fascinating, they have the potential to generate breakthrough discoveries that will someday save lives," says Tom. Since then, Tom and his wife Judy and their daughters Jaqueline, Anna, and Samantha have all taken part in the pitch review process.

For the Rickeys, involvement in the SPARK program was spurred by the couple's belief in the Institute's mission itself. "Brenda and I love the idea of 'life without disease' because so many of our friends and family have suffered or died from cancer, heart problems, dementia, and other ailments," says Dave. "A lot of nonprofits don't have clear goals, but the Institute's mission is concise while being extremely bold and ambitious. It may not be fully realized in our lifetime, but we believe with the amazing talent of their scientists, the Institute's mission is achievable."

The Tullie and Rickey Families SPARK Awards program offers donors a chance to significantly impact the careers of young researchers and help ignite the next big breakthroughs in medical research. You can donate online at donate.lji.org/SPARK, or contact SPARK Program Manager, Sierra Felt-Morales, at 858-752-6667 to discuss giving opportunities.

SPARK

THE TULLIE AND RICKEY FAMILIES SPARK AWARDS FOR INNOVATIONS IN IMMUNOLOGY

We are pleased to present the 2024 Annual Report for the Tullie and Rickey Families SPARK Awards for Innovations in Immunology.

Within these pages, you will discover the results of the novel research projects of the 2023 SPARK awardees, representing the highest caliber of rising stars in immunology research.

As you continue reading, you will gain insights into this year's SPARK Progress Pitch winner and learn about the progress of the 2024 SPARK Award recipients. Additionally, you will find highlights from several SPARK alumni—our SPARK Stars—who have gone above and beyond in advancing the field of immunology.

The Tullie and Rickey Families SPARK Awards program thrives thanks to the generous support of our donors, whose contributions make it possible for us to fuel groundbreaking research and empower emerging scientists. Thank you for making impactful advancements in biomedical science possible. **Your philanthropy is the cornerstone of this program's success.**

Need to read this report in a flash?

Check out the new **"SPARK" Notes** section for a concise summary of all the updates covered for each SPARK Award winner.

Erik Ehinger

FUNDED / January 2023

FUNDED BY / The generosity of LJI Board Director Dave Rickey and the Rickey Family

What if we can hijack the immune system's rubbish-disposal system to toughen T cells against cancer?

"SPARK" Notes

Erik's project—focused on helping T cells fight cancer more effectively by using a special technique to remove proteins that make them "exhausted"—has opened the door to exploring new, more effective cancer treatments. Erik's career has also taken off in significant ways. He has submitted his research findings publication in a high-impact journal, and his project led to significant funding from Curebound—all while he completes the final stretch of his doctorate.

What was the goal of your SPARK project?

Immunotherapies such as checkpoint blockade and CAR T cell therapies can be effective for blood cancers, but these therapies struggle with solid tumors due to T cell "exhaustion," where T cells lose responsiveness. T cell exhaustion is caused by inhibitory receptors like PD-1 and CTLA4. To address this challenge, I focused on the intrinsic molecular mechanisms underlying T cell exhaustion, rather than solely targeting peripheral inhibitory receptors. **The goal of my SPARK project was to leverage the cellular degradation system to address the fundamental causes of immune cell exhaustion, aiming to develop the next generation of cancer therapies**.

THE MEANING OF SPARK FOR ERIK

"Winning a SPARK award was deeply validating and affirmed the potential of my ideas. It provided a unique opportunity to pursue independent research while honing my ability to communicate science effectively to the public. The experience also broadened my perspective, teaching me to consider the commercial implications of my research direction. The impact of receiving SPARK funding has significantly shaped my approach to research and science communication."

SPARK Project Results

In my studies, I found that NR4A transcription factors drive T cell exhaustion, hindering cancer immunotherapy. Using a proteolysis targeting chimera (PROTAC) called dTAG-13 to degrade NR4A proteins, I reduced exhaustion markers such as PD-1 and TIM3, restoring T cell function and boosting cytokine production. Animal models confirmed these findings, showing slower tumor growth and improved survival with systemic or T cell-specific NR4A depletion.

These promising results suggest that PROTACs could offer a new avenue for enhancing cancer immunotherapy by directly targeting the mechanisms of T cell exhaustion. This novel approach may allow us to shift from targeting surface receptors to degrading exhaustion-promoting transcription factors, offering reversibility, potential oral administration, and a stronger anti-tumor response. I aim to further explore this strategy to enhance cancer treatment.

What's next for this project?

My SPARK project started with the hypothesis that proteins overexpressed in tumor-infiltrating T cells cause exhaustion, impairing their tumor-fighting ability. Initially, I aimed to show these proteins induce exhaustion and that targeted degradation could mitigate this. Now, I'm investigating if these findings apply to human T cells and if degrading multiple exhaustion-related proteins enhances T cell tumor-fighting capacity. I'm also developing a therapeutic molecule to selectively target and degrade these proteins in human T cells. With this, I aim to bridge basic research and clinical applications, and advance this research from foundational science to therapy development.

What's next for Erik?

As a SPARK grant recipient and current Ph.D. candidate, I anticipate completing my degree by the end of 2024. In January 2024, I received a Curebound Discovery Grant, which will allow me to build on my SPARK project. I also have a scientific manuscript under review, marking a key career milestone. This project has enriched my academic journey and broadened my professional perspective.

Rosa Isela Gálvez, Ph.D.

FUNDED / January 2023

FUNDED BY / The generosity of various donors

What if immune "crosstalk" could make malaria partially protective against dengue fever?

"SPARK" Notes

Rosa's project—which focused on analyzing human samples collected in tropical regions where both malaria and dengue are endemic—has generated substantial preliminary data to address neglected infectious diseases in West Africa. Now as a staff scientist at the Bernhard Nocht Institute for Tropical Medicine in Hamburg, Germany, Rosa is concentrating on understanding the co-circulation, immunity, and clinical outcomes of dengue and Zika viruses in Africa. She is also building on her preliminary data from her SPARK project to enhance surveillance and research on neglected and emerging mosquite-borne infections in Africa.

What was the goal of your SPARK project?

Forty percent of the world's population live in tropical regions where mosquitoes and other arthropods, such as ticks, spread disease. People in these regions often suffer from multiple "arboviral" or mosquito-borne infections simultaneously, posing complex challenges for their immune systems. Unlike the controlled settings of laboratories, the intricacies of real-world co-infections cannot be fully replicated experimentally; therefore, to understand these dynamics, I analyzed human samples from these areas. In West Africa, children face high mortality rates due to malnutrition, respiratory infections, diarrheal diseases, and especially malaria. **The goal of my SPARK project was to challenge the assumption that dengue has minimal impact in Africa by exploring the immune reactions between malaria and dengue, despite the low reported incidence of dengue in the region.**

THE MEANING OF SPARK FOR ROSA

"My SPARK award has had a profound impact on my career, allowing me to conduct in-depth research into neglected tropical diseases and foster valuable collaborations. It has enhanced my scientific skills, problem-solving abilities, and resilience. The experience also broadened my professional network, increased my visibility within the scientific community, and solidified my commitment to addressing neglected global health issues."

SPARK Project Results

The impact of co-infections on disease severity and mortality is not well understood. Co-infections affect both innate and adaptive immunity and can complicate immune responses. I wanted to determine if co-infections worsen disease severity or modulate immune responses positively. To access patient blood samples, I established a collaboration between LJI and the Bernhard Nocht Institute for Tropical Medicine in Hamburg. I then analyzed 422 samples from children with acute malaria. I found that 13.5% of these children had also been exposed to dengue viruses. My findings challenge the belief that flaviviruses have minimal impact in West Africa and highlight the need for better surveillance and diagnostics in the region.

What's next for this project?

I am using my SPARK project results as the basis for two applications with major consortium funding. The first, under the Wellcome Trust Infectious Disease Award, is the DEZIWA project, focusing on dengue and Zika viruses in Africa. As lead PI for the immunology work package, I will work in Mali and Burkina Faso to generate data for public health interventions. The second project, ARBOVIR, funded by the German-African Cooperation in Infectiology, aims to enhance surveillance and research on arboviral infections in Africa. Collaborating with the Bernhard Nocht Institute and the Kumasi Centre, this project will implement rapid diagnostics and train health technicians in rural Ghana.

What's next for Rosa?

Over the past year, my career has evolved to include both teaching and research after starting my position at the Bernhard Nocht Institute for Tropical Medicine in November 2023. This transition allows me to inspire and mentor students while continuing my work in infectious diseases. Along with teaching, I am actively involved in collaborative research grant applications with colleagues in Hamburg and internationally. My goal is to expand research into adaptive immunity in infectious diseases and establish a research base in South America to advance this critical field further.

Sloan Lewis, Ph.D.

FUNDED / January 2023

FUNDED BY / The generosity of the Rosemary Kraemer Raitt Foundation Trust

What if we can identify new ways of diagnosing and treating milk allergy in children?

"SPARK" Notes

Sloan investigated how immune cells called monocytes respond to cow's milk in children with allergies—compared to those without allergies. Her work revealed that monocytes, a type of immune cell, from allergic children are more active and produce more inflammatory molecules, which could lead to new diagnostic methods and treatments for this common allergy. Sloan's research not only gained her attention in her field, but led to a career in industry. She is now working at a clinical-stage biotechnology company dedicated to advancing immunology therapeutics.

What was the goal of your SPARK project?

Cow's milk allergy is the most common food allergy in infants and young children, and its prevalence is increasing. Currently, the only management strategy is avoidance, which is challenging due to the widespread presence of cow's milk in food products. The absence of reliable diagnostic methods for food allergies highlights the critical need for research in this area. Monocytes, a type of immune cell, have been shown to exhibit hyper-inflammatory responses in food allergies, yet their specific responses to cow's milk have not been thoroughly investigated. **The goal of my SPARK project was to understand the role of monocytes in pediatric cow's milk allergy**.

THE MEANING OF SPARK FOR SLOAN

"Competing for and winning a SPARK award was an invaluable learning experience that significantly enhanced my leadership and communication skills. The process of presenting my research to a broad audience has made me a better scientist."

SPARK Project Results

To investigate monocytes in pediatric cow milk allergy (CMA), I stimulated blood immune cells from both CMA and non-CMA children with cow milk extract and analyzed the responses using spectral flow cytometry. This method revealed differences in cell surface markers and cytokine production. I optimized the procedure, developed a 29-marker panel, and tested blood samples from seven children. Results showed that CMA monocytes had higher activation levels and increased inflammatory cytokines IL-1β and IL-6 compared to non-CMA children. Additionally, CMA T cells produced more cytokines IL-4, IL-32, and TNFα, while non-CMA T cells showed more activation markers CD69 and HLA-DR. These findings highlight distinct immune responses in CMA, suggesting potential for new diagnostic tests and better understanding of food allergies.

What's next for this project?

The findings from my SPARK project indicate that monocytes in pediatric individuals with cow's milk allergy exhibit a distinctive response to cow's milk protein, which correlates with T cell responses. These results provide valuable preliminary data for a future grant proposal focused on further elucidating the role of monocytes in cow's milk allergy. This analysis could be expanded by including more subjects.

What's next for Sloan?

In the summer of 2024, I transitioned to a scientist position at a biotech company following the completion of my postdoctoral fellowship at La Jolla Institute for Immunology. In my new role, I will continue to pursue innovative immunology research, similar to my SPARK project, in the context of autoimmune and inflammatory diseases in industry.

Gregory Williams, Ph.D.

FUNDED / January 2023

FUNDED BY / The generosity of various donors

What if we can detect dangerous T cell responses in the blood of ALS patients?

"SPARK" Notes

Greg's SPARK project shed light on how immune responses in the blood of amyotrophic lateral sclerosis (ALS) patients differ from those in healthy individuals. He found signs of abnormal immune responses in ALS and uncovered potential new targets for treatment. Greg is now advancing his career in neuroinflammatory research in the biomedical industry.

What was the goal of your SPARK project?

Amyotrophic lateral sclerosis (ALS), formerly known as Lou Gehrig's disease, is a progressive and fatal neurodegenerative disorder. Although the exact causes of ALS remain unclear, it is known that several brain proteins misfold and become neurotoxic.

Recent research also suggests the immune system might play a role in ALS. **The goal of my SPARK project was to investigate the immune mechanisms in ALS by comparing immune responses of ALS patients with age-matched healthy controls**.

THE MEANING OF SPARK FOR GREGORY

"Earning a SPARK award was meaningful to my scientific career in several ways. Primarily, the award provided me with the confidence and experience needed to develop and execute my own research ideas. Additionally, my SPARK project offered me practical insights into the intricacies of grant management, including budgeting and time management. This experience has bolstered my ability to undertake independent scientific projects and helped me demonstrate to potential employers my capability to conceive and lead my own research endeavors."

SPARK Project Results

My project involved collecting blood samples from ALS patients and healthy donors, in collaboration with Emory ALS Center, UC Irvine MDA ALS Center, and the NIH Neurodegenerative Disorders Clinic. I obtained blood from 20 ALS patients and 9 healthy controls, exceeding my goal. I used previously collected PBMC samples for healthy controls and processed them at LJI's John and Susan Major Center for Clinical Investigation. I generated and screened ALS peptide pools using PBMCs from both groups to detect immune response differences, which led me to focus on pro-inflammatory cytokines IL-5 and IL-10. While no significant pro-inflammatory differences were found, increased anti-inflammatory responses related to the C9ORF72 gene were noted. These findings suggest abnormal immune responses in ALS and indicate that IL-5 and IL-10 may be potential targets for therapeutic interventions.

What's next for this project?

The data I generated through my SPARK project offered valuable insights into the role of the immune system in ALS. These findings supported the hypothesis that immune cells exhibit dysregulated signaling in ALS, particularly with regard to T cell reactions to ALS-related proteins. I have now transitioned to a new role as a scientist at Escient Pharmaceuticals, a local neuroinflammatory pharmaceutical company; however, LJI's Sette laboratory with LJI Adjunct Professor Cecilia Lindestam Arlehamn are continuing this important work. I hope future experiments can further enhance our understanding of the immune landscape in individuals with ALS.

What's next for Gregory?

I am excited about the opportunity to work in an industry role at a local company specializing in neuroinflammatory disorders. I am eager to advance my career by spearheading and managing projects aimed at innovative therapeutic solutions.

Dawid Zyla, Ph.D.

FUNDED / January 2023

FUNDED BY / The generosity of LJI Board Director Barbara Donnell, and Bill Passey and Maria Silva, in honor of Susan Donnell Budd and Elizabeth Donnell Morrison

What if we can use viruses to monitor the efficacy of our immune system?

"SPARK" Notes

Dawid aimed to improve how we detect and manage anelloviruses, which are usually harmless but can cause problems in patients with weakened immune systems. His project led to the development of new tools that better track certain viruses, and his findings may significantly improve the care of immunocompromised patients. He is now building on this groundbreaking research to tackle other viral diseases, including measles, as he pursues a career in academia.

What was the goal of your SPARK project?

The human body harbors many viruses that are typically kept in check by a balanced immune system. When illness or medications weaken this system, this shift can lead to elevated virus levels, which scientists call "viremia." My research focused on developing tools to monitor and manage anelloviruses, which are usually harmless, but pose risks to individuals with compromised immune systems.

The goal of my SPARK project was to identify the most immunogenic peptides of the anellovirus capsid protein and generate antibodies to detect these viruses directly from blood. Ultimately, I sought to create a diagnostic tool that would use anelloviruses as a metric for immune system status. This kind of tool may aid clinicians in the administration of immunosuppressive drugs, particularly during transplants.

THE MEANING OF SPARK FOR DAWID

"Being honored with a SPARK award provided me with a unique opportunity to develop an entire project from scratch—encompassing the conceptualization, experimental setup, funding acquisition, scientific evaluation, and reporting. This experience has been invaluable and has equipped me with expertise and essential skills for my scientific career."

SPARK Project Results

Identifying the average genetic sequence for each anellovirus subtype has provided new insights for better monitoring and managing these viruses, especially in transplant and cancer patients on immunosuppressive treatments who often have higher virus levels. I identified key peptides within anelloviruses and used them to generate antibodies by immunizing rabbits, with help from Genescript. Although some peptides had weaker responses, the data is valuable for further research. Purifying these antibodies is crucial for refining detection methods. Current PCR-based methods are complex and costly, so developing a simpler approach by focusing on common virus regions could improve detection and management of these viruses.

What's next for this project?

Through my SPARK project, I gained valuable experience in bioinformatics via collaboration with LJI's Bioinformatics Core, significantly enhancing my skills in sequence analysis and validation. Currently, I am focused on developing novel strategies to eradicate the measles virus, including antiviral and vaccination approaches. I aim to leverage the knowledge gained from my SPARK project to extend my research to devise effective strategies against other viral diseases. By integrating virology, structural biology, and bioinformatics, I am building a unique skill set that will support my career goal of becoming an assistant professor.

What's next for Dawid?

I am currently in my fourth year as a postdoctoral researcher in Dr. Saphire's laboratory, focusing primarily on measles virus research. Over the past year, I have deepened my expertise in virology and am now exploring opportunities to transition to an independent scientist role, particularly as an assistant professor. This role would enable me to pursue my own research while mentoring a team of researchers and driving innovative projects to expand our understanding of viruses.

Felix Nettersheim, M.D.

FUNDED / January 2023

FUNDED BY / The generosity of LJI Board Director Tom Tullie and the Tullie Family

What if we can enhance a heart disease vaccine by blocking regulatory molecules?

"SPARK" Notes

Felix's project aimed to boost the effectiveness of heart disease vaccines by blocking specific regulatory molecules. With SPARK funding, Felix discovered that simultaneous blocking of two regulatory molecules, called PD1 and CD73, substantially increased the response to a heart disease vaccine in mice. Before returning to Germany to conclude his physician training, Felix will test his findings in human cells to see if this approach can lead to better preventive treatments for heart disease.

What was the goal of your SPARK project?

Nearly 18 million people die from cardiovascular disease each year. This disease is often caused by an uncontrolled autoimmune attack on blood vessels. Preclinical evidence suggests that a vaccine containing cholesterol particles could reduce this autoimmune response. Animal studies have shown that a vaccine targeting the cholesterol protein ApoB can stimulate protective regulatory T cells. However, such vaccines have so far proven less effective compared with the efficacy of vaccines that target bacteria or viruses. **The goal of my SPARK project was to investigate whether blocking PD1 and CD73 can increase the effectiveness of a heart disease vaccine**.

THE MEANING OF SPARK FOR FELIX

"Receiving a SPARK award was a profound affirmation of my dedication to research and has given me further confidence in the potential of my ideas to improve treatment options for patients with heart disease. SPARK not only provided the necessary funding for this project but also served as a powerful motivator to pursue my career as a clinician-scientist."

SPARK Project Results

I compared immune cell responses to a virus particle with immune cell responses to cholesterol molecules. I found that PD1 and CD73 were potentially responsible for the weak vaccine response. I then tested whether blocking these molecules could improve the immune cell response to an experimental heart disease vaccine. I first looked at how the vaccine affected mice that lacked one of the two molecules.

Mice missing PD1 had a huge boost in vaccine response, while those missing CD73 showed no extra benefit. Then, I tested blocking both molecules together. This combo led to a six-fold increase in the vaccine's effectiveness. In a heart disease model, mice treated with both the vaccine and blockers had much less plaque buildup, which suggests this approach could significantly improve vaccine results.

What's next for this project?

After competing in the 2023 SPARK Progress Pitch competition, I won additional SPARK funding. With this funding, I plan to build on my promising findings by conducting a series of detailed experiments to further investigate the mechanisms driving vaccine efficacy. Specifically, I will investigate how the blockade of the two regulatory molecules enhances the immune response against heart disease and explore the underlying biological processes contributing to this effect. These studies will include in-depth analyses of immune cell interactions and the signaling pathways involved in the vaccine response.

What's next for Felix?

Currently, I am finalizing my postdoctoral projects and preparing manuscripts for publication. After completing my postdoc, I will return to Germany to conclude my clinical training and obtain board certification in cardiology. I plan to seek funding through grant proposals to establish my own laboratory and continue advancing my research. My long-term career objective is to become a clinician-scientist specializing in cardiovascular immunology.

2023 Progress Pitch Competition and Winner Progress

Recognizing and advancing promising research

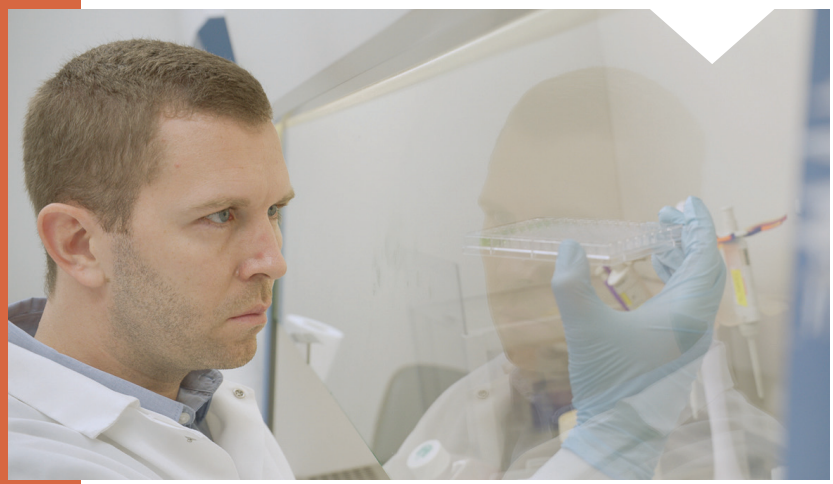
The 2023 Tullie and Rickey Families SPARK Award winners had the opportunity to compete for an additional $25,000 SPARK Award to further their research. This event, known as the Progress Pitches, aims to provide an extra boost to the most promising early-stage research funded by a SPARK Award.

The goal is to help scientists maintain their momentum in establishing proof-of-concept data and prevent potential funding gaps. During the Progress Pitches, the 2023 SPARK Award winners presented the advancements they made with their initial SPARK award and proposed a continued line of research.

A panel of SPARK program stakeholders and LJI Board Directors reviewed the presentations and selected this year's winner, Felix Nettersheim, M.D.

> "Your **generous contribution** through the Progress Pitches has been a tremendous boost to my research on cardiovascular immunology. With your support, we are **making significant strides toward developing more effective heart disease vaccines**. Thank you for your dedication to advancing medical science and for supporting our efforts to improve patient outcomes."

Felix Nettersheim, M.D.



What is the goal of this next phase of your SPARK project?

In this next phase, I will focus on evaluating the translational potential of the blocking strategy by working with human cells to determine if they respond similarly to the treatment. A key objective will be to identify patients who would particularly benefit from this approach. I am enthusiastic about contributing to this innovative field of research and am committed to overcoming the challenges ahead. The ultimate goal is to offer an effective preventive treatment for heart disease, potentially transforming the landscape of cardiovascular health.

What progress have you made so far and what comes next?

My results have been encouraging, showing that the blocking strategy I investigated has considerable potential to improve the effectiveness of a heart disease vaccine. While the recent findings are promising, I am still in the early stages of developing an effective heart disease vaccine. With these positive outcomes as a foundation, I am advancing my research with the aim of translating these findings into clinical applications.

SPARK Awards Program Timeline

Securing and executing a SPARK Award involves a multi-year process, spanning across two calendar years.

YEAR ONE: APPLICATION PHASE

This phase focuses on application submission and review, along with the launch of the fundraising campaign.

REQUESTS FOR PROPOSALS / SPRING
Postdoctoral fellows, graduate students, and research technicians are encouraged to apply.

SUMMER — **APPLICATION DEADLINE** /
The window for submissions closes.

APPLICATION REVIEW / SUMMER
LJI leadership, faculty, and members of the Tullie and Rickey families select the SPARK finalists.

SUMMER — **FINALISTS TRAINING** /
The finalists receive guidance in project communication through writing, video production, networking, and live-audience pitching.

FUNDRAISING CAMPAIGN / FALL
Donations of all sizes are accepted from individuals passionate about scientific research. The number of SPARK awards given will depend on the funds raised through this campaign.

FALL — **PITCH EVENT** /
Finalists present their projects in 15-minute sessions to a review panel. The panel ranks each presentation to decide who will receive a SPARK award.

WINNERS ANNOUNCEMENT / WINTER
The Tullie and Rickey Families SPARK Award recipients are announced.

YEAR TWO: PROJECT EXECUTION PHASE

This phase involves the completion of the awarded SPARK project, where awardees independently manage their projects—from conducting experiments to handling budgets.

GRANT MANAGEMENT TRAINING / WINTER
Awardees receive training to manage their $25,000 grant budgets effectively.

SPRING — **SPARK AWARDS CELEBRATION** /
This celebration honors SPARK winners and connects them with donors.

PROGRESS REPORTS / SUMMER
Progress reports are submitted for inclusion in that year's SPARK Annual Report.

FALL — **PROGRESS PITCH COMPETITION** /
SPARK awardees from the current year have the opportunity to present a continued line of research based on their project results. A review panel ranks each presentation and decides who will receive additional funding.

PROJECT COMPLETION / FALL
Final reports are submitted for inclusion in the following year's SPARK Annual Report.

2024 SPARK Awards Celebration

Left to right: 2024 SPARK winners Jingru Fang, Ph.D., Chen Sun, Ph.D., and Isaac López-Moyado, Ph.D., with LJI Professor, President & CEO Erica Ollmann Saphire, Ph.D, MBA, as well as SPARK winners Kazumasa Suzuki, M.D., Ph.D., Thomas Riffelmacher, Ph.D., and Rimjhim Agarwal

On June 4, 2024, LJI hosted a "sparkling" outdoor reception celebrating seven years of the Tullie and Rickey Families SPARK Awards for Innovations in Immunology.

Held on LJI's back patio, the event honored the 2024 SPARK award winners and recognized the generous SPARK donors who make this program possible. This year's event paid special tribute to Joani Nelson, whose philanthropic generosity through her estate provided program underwriting. Guests heard from 2023 SPARK Award winner Felix Nettersheim, M.D., about his cardiovascular health research, followed by reflections from LJI Board Director Barbara Donnell, MA, on Joani Nelson's longstanding support and connection to the SPARK Awards program. The event concluded with LJI Board Director Tom Tullie, MBA, sharing his vision for the program's future.

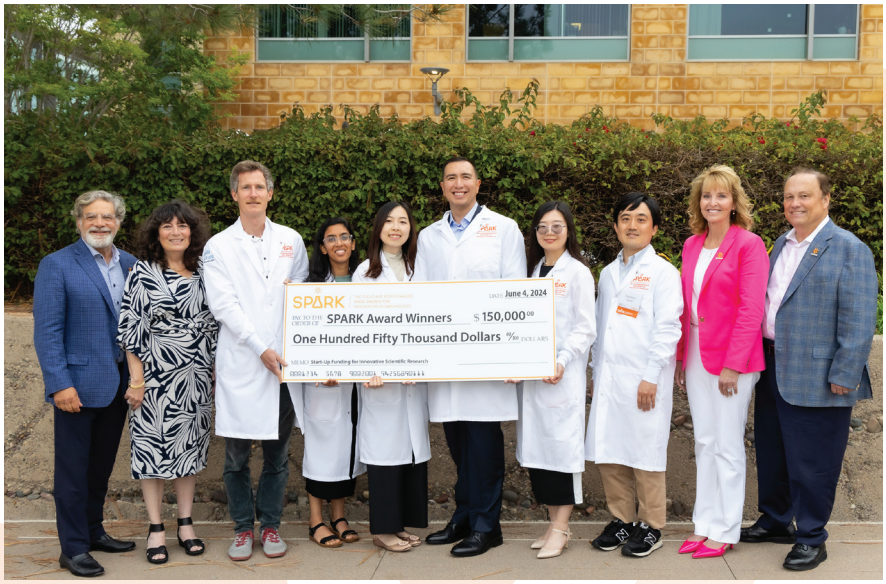
Left to right: Barbara and Ken Magid

Left to right: Carolyn Nelson, LJI Vice President of Advancement Kelsey Dale, CFRE, CSPG, Carol Streeter, and Curebound CSIO Karen Hooper

Left to right: Carol and Vann Parker

Left to right: Kamal Agarwal, with 2024 SPARK winner Rimjhim Agarwal, and Ashu Agarwal

Left to right: Lulu Hsu, Joshua Nelson, Min Hwang, and Woo Young Lin



Left to right: Tom and Judy Tullie, alongside 2024 SPARK winners Thomas Riffelmacher, Ph.D., Rimjhim Agarwal, Jingru Fang, Ph.D., Isaac López-Moyado, Ph.D., Chen Sun, Ph.D., and Kazumasa Suzuki, M.D., Ph.D., as well as Brenda and Dave Rickey

Left to right: Barbara Donnell and Joshua Nelson

Left to right: John Kraemer and 2024 SPARK winner Rimjhim Agarwal

Thank you, reviewers!

We are extremely grateful for the time and support of the application and pitch reviewers for the 2024 Tullie and Rickey Families SPARK Awards for Innovations in Immunology:

Ferhat Ay, Ph.D.

Michael Croft, Ph.D.

Kelsey Dale, CFRE, CSPG

Ted Dohmen

Barbara Donnell, MA

Brandon Fabritzky, MBA, CRA

Gina Kirchweger, Ph.D.

Robert Mahley, M.D., Ph.D.

Joani Nelson

Margaret Ng Thow Hing, J.D.

Sheila Noeth

David M. Rickey

Peter St. Clair

Raydene St. Clair

Tom Tullie, MBA

David Webb, Ph.D.

2024 SPARK Award Winner Progress

The following pages provide a brief progress update from the most recent SPARK cohort winners. For more in-depth updates, please visit: lji.org/sparkannualreport/progress-reports

FUNDED BY / The generosity of LJI Board Director Sandor Shapery and Rebecca Shapery

Jingru Fang, Ph.D.

How do bats tolerate viral infections that are otherwise fatal in humans?

My SPARK project explores why bat-associated viruses, like Ebola, are harmless in bats but deadly in humans. I aim to uncover how these viruses form structures in infected cells, known as viral factories. Preliminary experiments in both human and bat cells suggest that these viral factories can trap cellular mRNAs and make it harder for the host's immune system to fight infection. My ongoing analysis will help identify which mRNAs are trapped by the viral factories in human cells. My next steps will be to validate these findings in bat cells and measure the impact of mRNA trapping a cell's ability to produce antiviral proteins. Understanding how these viruses manipulate immune responses differently in bats and humans **could lead to new strategies for boosting immunity and developing effective treatments for infectious diseases** such as Ebola. So far, my research has also supported the continued use of a cutting-edge spatial transcriptomics technique called MERFISH to investigate viral factories. I'm currently using MERFISH to map and count over a hundred cellular antiviral mRNAs in human cells carrying Ebola viral factories.

Isaac López-Moyado, Ph.D.

Can we take advantage of a vulnerability in cancer cells to preferentially kill them?

Cancer cells accumulate more RNA-DNA hybrids than normal cells. My SPARK project explores whether scientists can actually increase these hybrids to kill cancer cells. Cancer cells form RNA-DNA hybrids during gene expression. Normally, a cell's RNase H enzymes step in to prevent hybrid buildup. I aim to block these enzymes and force cancer cells to accumulate RNA-DNA hybrids.

I began by using bone marrow cells from a mouse model of acute myeloid leukemia, and I found higher levels of RNA-DNA hybrids in these cancer cells. I then used CRISPR gene-editing techniques to delete RNase H genes and increased these hybrids. **I found that this change caused the cancer cells to stop growing within six days.**

My analysis showed that cancer cells without RNase H enzymes showed more DNA breaks, indicating that RNA-DNA hybrids cause harmful DNA damage—which spells trouble for a cancer cell. Mapping these breaks revealed they occurred at genomic enhancers, which regulate gene expression. Going forward, I am testing two drugs that inhibit RNase H enzymes on cancer cells and in mice with leukemia. **This approach could lead to new cancer treatments** that take advantage of RNA-DNA hybrids to kill cancer cells.

FUNDED BY / The generosity of LJI Board Director Tom Tullie and the Tullie Family

Kazumasa Suzuki, M.D., Ph.D.

How do regulatory T cells become corrupted to drive autoimmune disease?

FUNDED BY / The generosity of LJI Board Director Barbara Donnell, Bill Passey and Maria Silva, and various donors

Inflammation is a devastating force in autoimmune disease. Inflammation from wayward immune cells damages healthy cells and tissues. Normally, a protein called Foxp3 allows special regulatory T cells (Treg cells) to jump in and suppress this inflammation. When Treg cells lose Foxp3, they can transform into harmful ex-Treg cells. For my SPARK project, I am investigating the role of genetic material called transposable elements (TEs), once considered "junk" DNA, which are now recognized for their roles in inflammation and cancer.

I hypothesize that Foxp3 represses TEs in Treg cells. When Foxp3 is lost, TEs increase, leading to inflammation.

I found that Treg cells without Foxp3 convert to ex-Treg cells, which secrete inflammatory substances and have higher levels of TEs. Foxp3 binds near TE sequences on DNA, regulating their expression. My work so far shows that reintroducing Foxp3 has a direct role in suppressing TEs. Targeting ex-Treg cells may prevent Tregs from becoming harmful, which could lead to new autoimmune disease treatments. Going forward, I will test drugs and gene editing to suppress TEs and reduce inflammation—**aiming to develop innovative autoimmune disease therapies**.

FUNDED BY / The generosity of various donors

Chen Sun, Ph.D.

Can we design better receptors for CAR-T cell therapy?

Multiple myeloma is the second most common blood cancer, and while treatments have improved, a cure remains elusive. Since 2021, therapies developed with engineered immune cells, called CAR-T cell therapies, improved patient outcomes. My project aims to understand how CAR-T cells interact with cancer cells using cryo-electron tomography (cryo-ET). I am studying two FDA-approved CAR-T cells for multiple myeloma: Ide-cel and Cilta-cel. Both of these CAR-T therapies target the same protein on cancer cells, but they are not equally effective. Initial live cell imaging I've conducted shows that Cilta-cel binds to cancer cells faster than Ide-cel, which matches clinical data indicating Cilta-cel's superior performance. Cilta-cel is also more effective even at lower doses.

We need to know more about how these therapies work. By using cryo-ET, I will freeze and thinly slice cancer cells to analyze how CAR-T cells connect and attack cancer cells. My research aims to reveal why Cilta-cel works better—and **guide the development of more effective CAR-T therapies, offering new hope for cancer patients.**

Rimjhim Agarwal

Does chronic chikungunya infection resemble an autoimmune disease?

We need to understand why so many people infected with Chikungunya virus (CHIKV) develop chronic, arthritis-like disease. My SPARK project investigates if this mysterious arthritis-like disease resembles an autoimmune disease. I am examining whether T helper cells, a type of immune cell, may mistakenly begin to attack a person's own cells instead of taking aim at targets on CHIKV.

Using bioinformatics, I identified 15 self-antigens (sites on healthy cells) with high sequence similarity to CHIKV antigens (sites on the virus). I then stimulated T helper cells from chronic CHIKV patients with these self-antigens.

I found no immune response, suggesting no cross-reactivity; however, this finding doesn't rule out the possibility that T helper cells are mistaking healthy cells for viral targets. As a next step, I will further investigate by comparing the entire CHIKV proteome with the human proteome to find better sequence matches. I will also test for T helper cell cross-reactivity with other viruses, such as cytomegalovirus and Epstein-Barr virus. Understanding the role of T helper cells in chronic CHIKV disease **could lead to better vaccines and treatments for people affected with virus-induced autoimmune diseases around the world.**

FUNDED BY / The generosity of the Rosemary Kraemer Raitt Foundation Trust

Thomas Riffelmacher, Ph.D.

Are fat-addicted MAIT cells driving liver disease?

Fatty liver disease affects 30-40 percent of U.S. adults and often goes unnoticed in its early stages. Fatty liver disease is triggered by factors like alcohol consumption and poor diet, and can lead to severe conditions such as steatosis and liver cancer. My SPARK project investigates Mucosal Associated Invariant T (MAIT) cells, which produce the molecule IL-17, a key driver of the disease.

I developed a system to isolate MAIT cells from donor samples and assessed their responses under various conditions. By culturing these cells with labeled glucose, I measured their glucose consumption and metabolic activity, compared to CD8+ T cells. This analysis may help uncover metabolic factors that cause MAIT cells to contribute to disease progression.

Supported by SPARK, I'm analyzing MAIT cells from individuals with different body mass indices (BMI) and fatty liver disease. This research seeks to find targets to stabilize or repair liver tissue, **potentially leading to new treatments for fatty liver disease**.

FUNDED BY / The generosity of LJI Board Director Dave Rickey and the Rickey Family

SPARK Stars

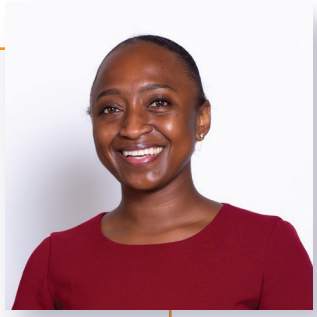
In addition to offering seed funding for innovative ideas, the Tullie and Rickey Families SPARK Awards program focuses on training and supporting the most promising early-career scientists.

Throughout 2024, we have highlighted the successes of our "SPARK Stars," previous SPARK Award recipients who have achieved remarkable milestones. Their achievements demonstrate how philanthropic investment in the SPARK program drives discovery and fosters the next generation of researchers. If you missed any updates, here are a few highlights:

Post-award scientific breakthroughs

Annie Elong Ngono, Ph.D.

2021 SPARK Award Winner



Annie Elong Ngono, Ph.D., discovered that common cold coronaviruses can train T cells to fight SARS-CoV-2. Her study, published in *Nature Communications*, found that mice previously exposed to a common cold coronavirus had partial protection against COVID-19. Dr. Elong Ngono is now advancing new vaccines that harness these T cells to provide broader immunity against COVID-19 and other coronaviruses.

Dawid Zyla, Ph.D.

2023 SPARK Award Winner

Dawid Zyla, Ph.D., has significantly advanced the study of the measles virus at LJI. Using cryo-electron microscopy, he captured detailed images of an antibody, mAb 77, binding to the measles fusion protein. These stunning images show how mAb 77 prevents the virus from entering human cells. Dr. Zyla's work, in collaboration with Columbia University, revealed how mAb 77 locks the measles fusion protein in place and stops infection. Dr. Zyla's research combined expertise in structural biology, cell biology, and virology, and paves the way for new strategies to combat measles and related viruses.

Securing prestigious follow-on funding

Thomas Riffelmacher, Ph.D.

2020 and 2024 SPARK Award Winner

The San Diego Digestive Diseases Research Center (SDDRC) awarded Thomas Riffelmacher, Ph.D., a $40,000 feasibility grant to support his innovative research into the underlying causes of digestive diseases. His project, titled "Targeting Metabolic Dependencies of MAIT Cells in Fatty Liver Disease," builds on his latest SPARK research project. Dr. Riffelmacher is working to better understand the role of immune cells called MAIT cells, which are abundant in the liver and rely on a metabolic process involving fatty acid oxidation to produce IL-17A, a molecule involved in inflammation. His ultimate goal is to adjust immune cell responses to address fatty liver disease.

Erik Ehinger

2023 SPARK Award Winner

In January 2024, Erik Ehinger was awarded a Curebound Discovery Grant of $250,000, for a project titled, "Improving Anti-Tumor Responses by Degrading Transcription Factors that Impose T Cell Exhaustion." This new funding allows Ehinger to build on findings from his 2023 SPARK project and may bring him closer to improving immunotherapy strategies against solid tumors.

Maria Inês Matias, Ph.D.

2022 SPARK Award Winner

Maria Inês Matias, Ph.D., was awarded a Curebound Discovery Grant of $250,000 in January 2024. Her project, titled, "Hijacking CD4+ Treg Cells into Cytotoxic T Cells: A New Strategy for Cancer Immunotherapy," aims to identify new therapeutic targets to enhance anti-tumor immunotherapies, which could open new avenues in cancer treatment.

Advancing through professional growth

Isaac López-Moyado, Ph.D.

2024 SPARK Award Winner

Isaac López-Moyado, Ph.D., is among eight postdoctoral awardees from across the United States selected for the 2024 Fred Hutch Cancer Center Dr. Eddie Méndez Scholar Award. This honor recognizes Dr. López-Moyado as an exceptional early-career scientist from an underrepresented background who is conducting impactful cancer research. Dr. López-Moyado presented his research at the Méndez Symposium at Fred Hutch in Seattle in July 2024.

Jingru Fang, Ph.D.

2024 SPARK Award Winner

In July 2024, Jingru Fang, Ph.D., began her role as a Postdoctoral Research Associate at Princeton University in New Jersey.

Rosa Isela Gálvez, Ph.D.

2023 SPARK Award Winner

In November 2023, Rosa Isela Gálvez, Ph.D., took a position as a Staff Scientist at the Bernhard Nocht Institute for Tropical Medicine in Hamburg, Germany.

Achieving new faculty roles

Melissa Meyer, Ph.D.

2022 SPARK Award Winner

In 2024, Melissa Meyer, Ph.D., accepted an Assistant Professor position in the Department of Microbiology and Immunology at Des Moines University in Iowa.

Daniela Weiskopf, Ph.D.

2023 SPARK Award Winner

In recognition of her outstanding research achievements, La Jolla Institute for Immunology (LJI) promoted Research Assistant Professor Daniela Weiskopf, Ph.D., to a tenure-track Assistant Professor position. Dr. Weiskopf's laboratory focuses on protective and maladapted immune responses to emerging infectious diseases. She has joined the LJI Center for Vaccine Innovation and the LJI Center for Sex-based Differences in the Immune System.

Estefania Quesada Masachs, M.D., Ph.D.

2020 and 2022 SPARK Award Winner

Estefania Quesada Masachs, M.D., Ph.D., accepted a faculty position as an Assistant Professor at the Diabetes Research Institute (DRI) at the University of Miami starting in February 2024. The DRI is renowned for its focus on diabetes research, particularly type 1 diabetes.

SPARK Donor Honor Roll

Philanthropy fuels the next generation of research

Thank you to all of the generous donors to the Tullie and Rickey Families SPARK Awards for Innovations in Immunology program. The donor list below includes all contributors to the Tullie and Rickey Families SPARK Awards program since its inception in the fall of 2017 through June 2024. Any donor with a SPARK icon (✳) after their name denotes they've given enough cumulatively to fund at least one whole SPARK Award.

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*In Memoriam

Meet the SPARK program architect and manager

CONTACT KELSEY AT:
kdale@lji.org / 858-752-6542

Kelsey Dale, CFRE, CSPG, *Vice President of Advancement*

The Tullie and Rickey Families SPARK Awards Program Architect

Kelsey Dale, CFRE, CSPG, is the visionary and architect behind The Tullie and Rickey Families SPARK Awards for Innovations in Immunology, established in 2017. Kelsey joined La Jolla Institute for Immunology (LJI) in 2016 as Deputy Director of Advancement and was promoted to Vice President of Advancement in 2022. Kelsey played a crucial role in launching this program and designing its structure, which has served as a model for other nonprofits. Although she no longer manages daily program operations, Kelsey continues to ensure the program's mission is upheld.

CONTACT SIERRA AT:
sfeltmorales@lji.org / 858-752-6667

Sierra Felt-Morales, *Advancement Associate*

The Tullie and Rickey Families SPARK Awards Program Manager

Sierra Felt-Morales took the helm as the program manager of The Tullie and Rickey Families SPARK Awards for Innovations in Immunology in late 2023. Since joining the Advancement team in 2023, Sierra has worked to connect the community with research in need of funding, bringing both a fresh perspective and a passion for advancing breakthrough research. As the program manager, Sierra oversees the program from start to finish, builds relationships with early-career scientists, and ensures that the program effectively links donors with cutting-edge research.

A program impact snapshot

Over the past seven years, **226 donor families** nationwide have fueled this vital program through their philanthropic support, **contributing over $1.2 million to fund 45 innovative projects**.

This support led to **promotions for 21 young scientists, with 11 successfully establishing their own independent laboratories**.

Tullie and Rickey Families SPARK awardees have collectively **published 62 papers and submitted 7 patent or intellectual property filings** based on the research they conducted for their SPARK projects. Early-career scientists can develop viable proof-of-concept data through a Tullie and Rickey Families SPARK Awards project—and this has **resulted in over $11.6 million in follow-on funding** to build on SPARK projects.

For more information on how to support the 2025 Tullie and Rickey Families SPARK Awards for Innovations in Immunology, scan the QR code or visit our website at **lji.org/SPARK**.

Thanks to the SPARK award, I can develop a project entirely independent and focus on a disease (ALS) that is in need of more study.

- Greg Williams

Thank you SPARK Donors for giving young researchers like me a chance to make an idea a reality!

- Erik Ehinger

Many thanks to all donors for supporting our research.

Felix Nebrich

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For more information about The Tullie and Rickey Families SPARK Awards for Innovations in Immunology, please reach out to:

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