SPARK

THE TULLIE AND RICKEY FAMILIES
SPARK AWARDS FOR
INNOVATIONS IN IMMUNOLOGY

Annual Report 2022

LJI scientists publish first head-to-head comparison of four COVID-19 vaccines

Daniela Weiskopf, Ph.D.
'18 Winner

New investigation reveals the strength of T cell, B cell, and antibody responses over time

Scan the QR code to read more:

Rethinking the rabies vaccine

Heather Callaway, Ph.D.
'22 Winner

LJI scientists, in collaboration with researchers from the Institut Pasteur in France, capture new high-resolution view of rabies virus, revealing potential vaccine targets

Scan the QR code to read more:

Putting the brakes on budding viruses

Michael Norris, Ph.D.
'21 Winner

New measles, Nipah research offers a window into viral assembly

Scan the QR code to read more:

Can your macrophages 'smell' infections?

Marco Orecchioni, Ph.D.
'19 Winner

With new funding, LJI and UC San Diego researchers will investigate how olfactory receptors in immune cells called macrophages respond to pathogens

Scan the QR code to read more:

Origin story: How T cell heroes and villains are made

Greet Verstichel, Ph.D.
'20 Winner

LJI Postdoctoral Fellow Greet Verstichel on how T cells learn their "fate"

Scan the QR code to read more:

The Conrad Prebys Foundation grants more than $1.5 million to support critical infrastructure—and a fascinating branch of immunology

Julie Burel, Ph.D.
'19 Winner

Grants to LJI scientists will open up new areas of study against infectious disease and more

Scan the QR code to read more:

Researchers track down metabolic enzyme that protects against inflammation

Ian Mathews, Ph.D.
'18 Winner

LJI study shows new link between metabolismand the immune system

Scan the QR code to read more:

THE TULLIE AND RICKEY FAMILIES SPARK AWARDS PROGRAM FOR INNOVATIONS IN IMMUNOLOGY:

Five Years of Fueling the Next Generation of Researchers

By: Kelsey Dale, Vice President of Advancement and The Tullie and Rickey Families SPARK Awards Program Manager

When the La Jolla Institute SPARK Awards was first conceived in 2017, we had high hopes for the program but it was the first of its kind that we were aware of, and of course there is always a risk to charting a new course. We were filled with questions about whether it would work.

The program was developed to meet two complementary needs at the Institute. First, young researchers often have fresh and innovative ideas, and their career advancement is dependent on them making their own contributions to the field of immunology, but they are often challenged with finding both the opportunity and funding to take their ideas from concept to solid data. Secondly, we had heard from our supporters that it could be difficult for them to feel like they were making an impact since full-scale research projects or equipment often require large amounts of funding and because it could take so long to see if their donation was contributing to progress or success. So we were tasked with how to make our research more accessible and inspiring to donors. In thinking about these needs we realized there was an opportunity to address both by connecting our supporters directly with our early career scientists eager to explore their big ideas with the help of seed funding.

Our initial goal was to fund at least two $25,000 awards to establish the program. We hoped the program would attract the interest of our postdocs and also resonate with our supporters, but only time would tell. Almost immediately, we saw there was indeed an appetite for this opportunity from our scientists when we received nearly 25 applications in response to the first request for proposals. We narrowed that pool to four finalists who we then trained in lay-friendly communication skills and prepared them to pitch their projects to prospective donors. Next, we needed to see if these scientists and their projects would appeal to donors.

We didn't have to wait long—that first year, thanks to an early first commitment from Board Member François Ferré, Ph.D. and his wife Magda Marquet, Ph.D., we moved into our fundraising campaign with momentum and secured enough funding for four initial projects and more. In fact, in 2018 we funded eight projects. This success confirmed there was indeed a desire for our supporters

We received nearly 25 applications in response to the first request for proposals.

In 2018, we funded eight projects.

In 2018, the Tullie and Rickey families made pledges to secure the program for the forseeable future, and it was renamed The Tullie and Rickey Families SPARK Awards for Innovations and Immunology in their honor.

to connect with our individual scientists and fund specific, short-term projects. But even then we were left with important questions. *Would we be able to sustain this interest? How could we ensure this program wouldn't fizzle out over time*? After all, it might take a couple years before we could really see if the program was going to be successful in helping these scientists use the data they collected from their projects to attract follow-on funding for their project or compete for critical career-advancing grants and fellowships.

In 2019, Dr. Rana Herro became the first SPARK Star when she secured a faculty position at Cincinnati Children's Hospital.

In 2020 and 2021, supporters funded 16 projects, all of which persevered through a global pandemic, and several actually focused on better understanding SARS-CoV-2.

After sitting on the pitch panel the first year in 2018, Tom Tullie saw the potential of the program, but he also recognized the delicate stage it was in. That was when he and his wife Judy came forward with an incredible $250,000 pledge to ensure the program could fund at least one award a year for the next 10 years. Not only this, but Tom reached out to his long-time friend Dave Rickey and invited him and his wife Brenda to learn about the program and get involved as well. Their joint commitments of $375,000 secured the program for the foreseeable future. To honor their visionary generosity, the program was renamed The Tullie and Rickey Families SPARK Awards for Innovations and Immunology.

With the security of the program in place, we were able to blaze boldly ahead. In 2019, we continued to attract donors to join the Tullies and Rickeys in supporting the program, and we successfully funded another six SPARK Award projects. That summer, LJI representatives and Tom Tullie took the program to a national stage at the Classy Collaborative conference in Boston, to share with others in the non-profit space how we were able to successfully connect donors to our mission through the program. And in the fall of 2019, our first "SPARK Star," Dr. Rana Herro, advanced her career by securing a faculty position at Cincinnati Children's Hospital, which she in part attributed to the experience and skills she gained from her involvement with the SPARK program.

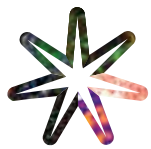
In those early years, SPARK winner feedback highlighted unexpected benefits about the program. For example, we had underestimated how valuable and unique the training we were giving our postdocs was for building their own confidence and preparing them to not only effectively convey their ideas during the award pitches, but also to communicate effectively in interviews for faculty positions or when writing grant applications for private foundations and individuals. These science communication skills were also valuable in helping our supporters feel a more personal connection with the Institute. Over time, SPARK winners have taken on true ambassador roles for LJI, participating in donor tours and events to provide their personal perspectives of amazing work underway at LJI.

By 2020, the program truly became an established gem of the Institute, featuring exciting new projects from LJI's best and brightest young researchers, as well as inspiring even more donors to become involved. Between 2020 and 2021, supporters funded an additional 16 projects, including several projects aimed at helping us better understand the virus behind the global COVID-19 pandemic. We also started to see the first cohorts of SPARK winners build on their SPARK projects, proving that investment in them and their ideas could result in scientific breakthroughs and career advancement. The first really large follow-on funding grants begin to materialize in 2021, when Dr. Marco Orecchioni and Dr. Abhijit Chakraborty each won six-figure awards from The Conrad Prebys Foundation to build on the data they collected from their SPARK projects. And later that spring, Dr. Ian Mathews, together with his P.I. Dr. Sonia Sharma, secured a $4.2M R01 grant from the National Cancer Institute, stemming from the data he produced with his SPARK award in 2018. Not only that, but in those two years six more SPARK Stars among the 2018–2021 winners went on to start their own labs (Dr. Daniela Weiskopf, Dr. Holger Winkels, Dr. Huy Dinh, Dr. Cecilia Lindestam Arlehamn, Dr. Vipul Shukla, and Dr. Michael Norris).

And now in 2022, our fifth year of awards, the program shows no sign of slowing down. Not only did we fund six new SPARK projects in January, but we've also had three more former winners, Dr. Greet Verstichel, Dr. Nicolas Thiault, and Dr. Julie Burel, secure six-figure awards from private individuals and foundations to continue their work.

Looking back over the past five years, we've seen SPARK project data contribute to the publication of at least 12 manuscripts in leading scientific journals and four applications for patents, demonstrating the innovative aspects of the projects being funded through this program. And as of writing this, there are roughly 20 papers or grant applications in progress by SPARK Award winners, indicating the number of publications and awards will continue to climb in the next five years.

We are so grateful to the approximately 200 supporters of this program who have helped us raise more than $1.1M since 2017. We are especially grateful for the investment and belief of the Tullie and Rickey families at such a critical time in this program's history. This partnership helped us confidently build this program to where it is today and has also allowed us to be nimble as we've piloted new aspects of the program. For example, in 2021 we implemented a $5,000 pitch bonus to the scientist with the top pitch—to further incentivise our scientists to find ways to make their pitch really stand out to donors. And in 2022 we look forward to giving our 2022 winners an opportunity to compete for



Drs. Marco Orecchioni and Abhijit Chakraborty became SPARK Stars when they each won significant follow-on funding from The Conrad Prebys Foundation.

SPARK project data has contributed to the publication of at least 12 manuscripts, four patent applications and there are currently 20 papers or grant applications in progress.

an additional $25,000 award after six months of progress, which would concentrate more award dollars behind the project showing the greatest promise.

As we look to the future of the Tullie and Rickey Families SPARK Awards program, we do still have questions. But we no longer wonder if the program will survive or be successful; instead, we are excited to imagine just how successful *it will be*.

We are so grateful to the approximately 200 supporters of this program who have helped us raise more than $1.1M since 2017.

SPARK donors Jackie, Tom and Judy Tullie with '21 winner Michael Norris, Ph.D.

'21 winner Payel Roy, Ph.D. with SPARK donor Carol Streeter

LJI Chief Scientific Officer, Mitchell Kronenberg, Ph.D. and '22 winners Heather Callaway, Ph.D., Maria Matias, Ph.D., and Melissa Meyer, Ph.D.

SPARK donor Tom Tullie giving remarks at the five year anniversary celebration in 2022.

LJI faculty members Sujan Shresta, Ph.D., and Chris Benedict, Ph.D. (center) with '21 winner Annie Ngono, Ph.D., Holly Sullivan, '19 winner Julie Burel, Ph.D., and '21 winner Simon Brunel, Ph.D.

SPARK

THE TULLIE AND RICKEY FAMILIES
SPARK AWARDS FOR
INNOVATIONS IN IMMUNOLOGY

It is our pleasure to present the 2022 Annual Report for The Tullie and Rickey Families SPARK Awards for Innovations in Immunology. In the following pages, we hope you enjoy reading the results of the 2021 SPARK winners' research projects.

Later in this report, you will find progress updates from our 2022 SPARK winners, as well as highlights about some of our former SPARK winners who have been promoted, earned follow-on funding and published significant findings.

We are grateful to all of the donors, volunteers and scientists who make this program possible!

Michael Norris, Ph.D.

What if we could act now to prevent a future, even deadlier pandemic?

FUNDED

JANUARY 2021

FUNDED BY

The generosity of LJI Board Director Tom Tullie and the Tullie family.

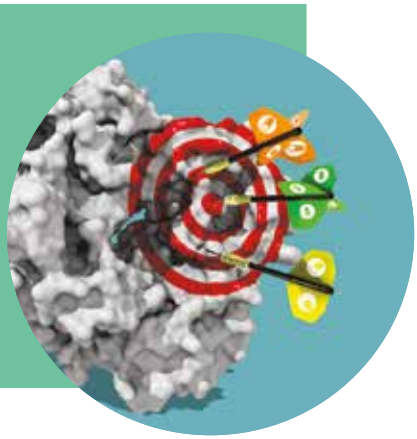
What was the goal of your SPARK project?

The emergence of viruses in the paramyxovirus family is a major concern for world health officials. These viruses are respiratory viruses with significant lethality and transmissibility—giving them pandemic potential. Included among paramyxoviruses are measles (infects over 7 million people/year), parainfluenza (causative agent of croup), multiple livestock pathogens, as well as the deadly Nipah virus (kills 9 of 10 people infected). Sadly, no therapies exist for any paramyxovirus.

To stop these viruses, we need to develop drugs that can target a key viral protein called the matrix protein. This protein is the critical field marshal that builds new viruses and releases them from infected cells to spread throughout a patient. My aim was to advance the development of an antiviral drug that can target the matrix protein and stop viral assembly, halting the spread of the virus.

Did you face any challenges?

Due to the COVID-19 pandemic and the ongoing war in Ukraine (location of Enamine, the company that provides over 70% of the world's stock of chemical building blocks and reagents), the synthesis of the compounds I identified in my work was significantly delayed. However, I was able to work with the SPARK program manager to obtain an extension and completed my project in May 2022.



SPARK
IMPACT STATEMENT:

"The SPARK program accelerated a novel project that could have important implications for the development of therapeutics against paramyxovirus infections. This could not only lead to life saving therapies against some of the deadliest viruses known to mankind, but it could also ensure that we have, at the ready, therapeutic drugs against any newly emergent paramyxoviruses."

SPARK project results:

Funds provided through the SPARK program gave me the opportunity to attend the High-Throughput Virtual Screening for Hit Finding and Evaluation course taught by world experts in virtual screening at Schrödinger. This six-week immersive course provided me with the critical skills and hands-on training in the use of the Schrödinger small molecule drug discovery suite of software, and ultimately accelerated the discovery of candidate molecules in this research project.

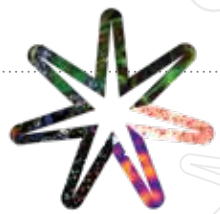
With these skills in hand, I used advanced computational algorithms to assess the druggability of key sites on measles and Nipah virus matrix proteins, called the dimer interface, the lipid-binding pocket, and the NTD pocket. Based on key characteristics of the sites such as size and enclosure from the environment, I concluded that both the lipid-binding pocket and the NTD pocket are highly druggable sites.

From there, I began narrowing down a group of potential drug candidates to find those that could best target these sites and inhibit matrix proteins. I used an approach called "molecular docking" to predict a drug's conformation, position, and its orientation within a protein binding site. This let me identify compounds with the best affinity and most favorablebtoxicity profiles for each site of interest on the matrix protein.

Next, I tested these promising compounds for their ability to block matrix-driven assembly and budding. To do this, I developed a novel cell-based budding assay for high-throughput screening at biosafety level 2.

What's next for this project?

The results of this project have already been instrumental in publishing a study which made the cover story in *Science Advances* in June 2022. This study is the first-ever look at a key stage in the life cycles of measles and nipah viruses and reveals how future therapies might stop these viruses in their tracks.



What's next for Michael?

I accepted a faculty position at the University of Toronto and started my lab there in Spring 2022.

My lab seeks to understand the structure and molecular assembly of pathogenic viruses, with special emphasis on paramyxoviruses and filoviruses. We combine structural biology, virology, molecular biology, and microscopy techniques to understand how the protein building blocks of these viruses interact with one another and self-assemble in a series of highly coordinated events that allow production of infectious viral particles. The three-dimensional molecular structures we reveal provide detailed information on the biological mechanisms driving viral assembly and will lay the foundation for the development of new, effective, and targeted therapeutic strategies.

Annie Elong Ngono, Ph.D.

What if we could halt the spread of dengue, the most prevalent mosquito-borne virus, through improved vaccine development?

FUNDED

JANUARY 2021

FUNDED BY

The generosity of Barbara Donnell, Bill Passey & Maria Silva, and various 2020 SPARK Donors.

What was the goal of your SPARK project?

Dengue virus affects 3.6 billion people worldwide, and the severe form of dengue has been known to kill thousands of children annually for decades. We aimed to identify how prior exposure to another flavivirus, called Japanese encephalitis virus (JEV), modulates disease severity in patients with acute dengue infection.

My SPARK project began as a first step to determine whether pre-existing immunity to JEV can modulate dengue infection and disease severity, and thus understand the influence of pre-exposure to closely related viruses on subsequent infection. We planned to collect suspected dengue cases in partnering hospitals in Nepal and perform laboratory experiments to confirm dengue infection.

The long-term goal of this research is to guide vaccine design by exploring the host immune response of individuals with prior immunity to a closely related virus and define which components of the immune response induced protection or pathogenesis.

Did you face any challenges?

Although we anticipated that the pandemic would delay patient enrollment or reduce the numbers of samples for the study, we did not expect that the second wave of COVID-19 in Nepal during 2021 would prevent the enrollment of dengue patients. All of our partnering hospitals were designated as COVID-19 centers, in addition lockdowns and illness among the staff added to the challenge of enrolling suspected dengue patients. However, I was able to pivot and use samples collected in 2017. These samples had some limitations but I was ultimately able to move forward with my project.

SPARK
IMPACT STATEMENT:

"This project emphasized the ability of our team at LJI and our partners in Nepal to screen and classify dengue infection from a patient cohort. This was the first study on dengue infection and pre-existing immunity to Japanese encephalitis virus carried out by our team and Nepalese researchers. Our findings provide valuable preliminary data for future grant applications."

SPARK project results:

Although, we were not able to conclude on the association between pre-existing immunity to JEV and dengue disease severity due to the small sample size, we were able to (1) detect and classify dengue infection in 2017 in Nepal, (2) determine and confirm the presence of prior-exposure to JEV in patients experiencing dengue infection, (3) establish and strengthen the collaboration between LJI and Nepal to successfully continue our research work (in terms of legal documents and experiments), (4) substantially advance our understanding of cross-reactive immunity, (5) generate meaningful preliminary data for grants, including NIH opportunities, (6) prepare the team in Nepal for the future dengue sample collection in 2022 (predicted outbreak year based on dengue cycle in Nepal). Nepal represents a unique model system to address many critical questions related to immunology controlling or exacerbating dengue virus, flaviviruses, and emerging infectious diseases.

What's next for this project?

My experience with the SPARK program allowed me to realize how ambitious the project I proposed was and the different steps (paperwork and technical adjustments) needed to start working on a pathogen such as JEV. The SPARK award set up a critical framework for this new type of research at LJI. The results generated during this project are important and will be used as preliminary data to apply for NIH grants and write a manuscript.

What's next for Annie?

I would like to continue studying infectious diseases, with a focus on emerging and neglected viruses. My expertise right now is on flaviviruses and coronaviruses, but I do not intend to restrict my research interests to only these virus families in the future. I am open to opportunities, but ultimately I would like to establish my own lab that focuses on host immune responses to viral infection.

Mehdi Benkahla, Ph.D.

What if viral infections could trigger type 1 diabetes?

FUNDED

JANUARY 2021

FUNDED BY

The generosity of the donors to the Sierra Shapery Memorial SPARK Award.

What was the goal of your SPARK project?

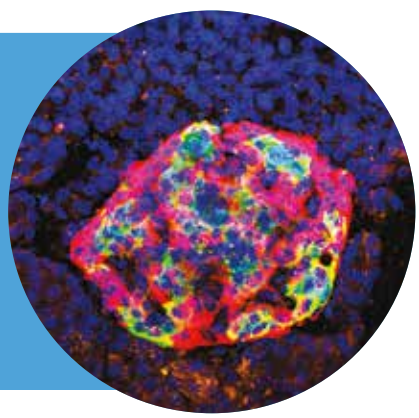
The incidence of type 1 diabetes (T1D) has been increasing over the years, and this can only be explained by changes in the environment. Decades of research have provided epidemiological evidence for an association between T1D and viruses, particularly coxsackieviruses of the *Enterovirus* genus. We just don't know how these viruses are implicated in the crime.

I set out to shed light on this mystery by using a newly developed model of human pancreatic slices (HPS), which can be kept alive *in vitro*. The goal was to infect the HPS using a coxsackievirus B3 genetically engineered to express an enhanced green fluorescent.

I wanted to know: Which cell types in the pancreas are susceptible to infection? What is the impact of viral infection on beta cell function? Which inflammatory responses are induced and do they correlate with beta cell function? What is the effect of viral infection on islet-resident macrophages and other immune interactions? What is the effect of viral infection on HLA class I expression and autophagy in islet pancreatic cells?

Did you face any challenges?

Yes, the challenge I faced was the scarcity of human pancreatic slices. Our supplier had very low inventory; we would get one donor every six months or so, which is not enough for our experiments. Now, we get samples of human pancreas from a different supplier, Prodo Labs, and slice it ourselves with the help of our colleagues at Moores Cancer Center at UC San Diego Health.



SPARK
IMPACT STATEMENT:

"This project has shown the value of a new model for studying type 1 diabetes. We've been able to generate valuable preliminary data for follow-on funding from NIH. This SPARK award has been a great opportunity for me. We were able to study viral infections in a live human pancreas slices, generate important preliminary data and apply for follow-on funding. It's a great experience because you manage the entire project by yourself, not just the experiments but the finances as well, which is helpful training for any future scientist."

SPARK project results:

We followed the fluorescent protein markers to see how infection spread in the HPS. After 3 days of infection, the green fluorescent protein (GFP) was detected by high resolution confocal microscopy in the insulin-producing beta cells. These infected beta cells were also expressing HLA-I, which is a molecule by which cells present antigen to the immune system to trigger an immune response. HLA-I is also a hallmark of T1D.

We also observed that tissue-resident macrophages (an immune cell type that eliminates infected cells) were also infected by CVB3. Our 3D analysis shows that HLA-I is hyperexpressed in the CVB3-infected slices compared to the controls.

Since the HPS have tissue-resident immune cells, we wanted to study the impact of the infection on CD68+ macrophages. Do they become attracted to islets during CVB3 infection? We quantified the number of macrophages in CVB3-infected and non-infected islets, and we observed that in our model at day 3 post-infection, macrophages were not more attracted to the islets during CVB3 infection.

What's next for this project?

More effort is needed to generate a better understanding of the consequences of viral infections in the pancreas and its role in the onset of type 1 diabetes. We plan to evaluate the impact of CVB3-GFP infection on beta cells and tissue-resident macrophages and if the infection could lead to an immune destruction of beta cells when cocultured with PBMCs. Tissue-resident macrophages will be characterized by single-cell RNA-seq and their interaction with PBMCs will be assessed.

Using the preliminary data generated during my SPARK project, we've applied for follow-on funding from NIH in the form of an R21. We've also secured other sources of human pancreatic tissues from City of Hope and Prodolabs, as well as initiated a collaboration with Moores Cancer Center for slicing pancreas tissue samples.

What's next for Mehdi?

I will continue to further this research as I complete the last year of my post doc at LJI. For the next steps in my career, I hope to move to industry and obtain a position at a biotech that studies type 1 diabetes. I'm also open to moving into new research areas where I can continue to learn new skills.

Nicolas Thiault, Ph.D.

What if there is a new immune cell that could be engineered to safely kill tumor cells and cure cancer?

FUNDED

JANUARY 2021

FUNDED BY

The generosity of the LJI Board Director Emeritus Larry Spitcaufsky and Tiki Spitcaufsky

What was the goal of your SPARK project?

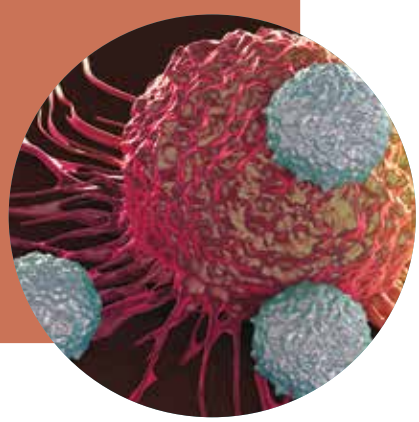
Recently, we discovered a new cellular actor in the immune system. These cells, called DNT, possess unique features that distinguish them from ones currently used in immunotherapies. Indeed, we have strong evidence showing that these cells are potent killer cells without inducing tissue damage or organ failure. However, before this DNT cell-based therapeutic approach can be tested in clinical trials, we critically require proof-of-concept in mouse models.

A cutting-edge technology, chimeric antigen receptor (CAR) T cells, has shown interesting promise in the field of cancer immunotherapy, allowing us to hijack resistance mechanisms developed by solid tumors. Unfortunately, CAR T cells are often associated with severe toxicity and a high failure rate in certain types of cancers when associated with the mainstream immune cells, currently used in immunotherapies.

My goal is to apply existing CAR T cell technology to new immune cells, discovered at LJI, called double negative T (DNT) cells in order to design a superior therapeutic strategy aiming to eliminate solid tumors with a lower toxicity.

Did you face any challenges?

Unfortunately, because of the COVID-19 pandemic and multiple reagent shortages, the *in vitro* experiments I needed to run were delayed, so I was granted a six-month extension in January 2022. During this period, I have received all critical components for the *in vitro* and *in vivo* experiments to validate our working hypothesis. I can now address whether engineered DNT cells can safely kill tumors and cure cancer *in vivo*. I look forward to providing a final update this fall.



SPARK
IMPACT STATEMENT:

"Anti-cancer immunotherapies are a major breakthrough in the treatment of neoplastic disease. Nevertheless, major roadblocks still persist, notably the cancer-killing cells themselves which exhibit poor efficiency-facing resistance mechanisms developed by solid tumors and trigger the appearance of toxicity leading to dramatic side effects. The SPARK program has given me the opportunity to test the anti-tumor potential of newly identified potent killer cells. Moreover, the preliminary outcome being promising, this novel project could provide new insights for translational research to develop new and effective immunotherapies for cancer patients."

SPARK project updates:

One of the main challenges facing CAR T cell technology is the engineering of the DNT cells as carriers of the exogenous receptor. As such, my first operation was to perform a retrovirus-based transduction protocol to integrate an exogenous DNA construction coding for an anti-CD19 CAR into DNT cells genome. I also worked on engineering the target of anti-CD19 CAR DNT cells. Although the optimization of these different protocols doesn't represent any potential clinical relevance, they are yet essential to conduct the main upcoming *in vitro* and *in vivo* experiments. Nonetheless, such characterization of the DNT cell biology has never been described in fundamental nor translational research and would be worth considering for further investigation.

The second step consisted of testing the anti-tumor capacity of the anti-CD19 CAR DNT cells *in vivo* and compared their suspected efficiency to the mainstream killer CD8 T cells, which are profusely used in current Adoptive Cell Transfer (ACT) therapies against cancer. I have observed that DNT cells bearing the anti-CD19 CAR-injected six days after tumor implantation have tremendously controlled the growth of the melanoma tumor cells expressing the CD19 protein. This greatly enhanced the survival of mice bearing tumors compared to the untreated group. Remarkably, the unique injection of these cells has even led to a partial remission of cancer. Moreover, I have observed that anti-CD19 CAR DNT treatment exhibits a superior ability to eradicate tumors than the one using mainstream killer CD8 T cells. These preliminary results might represent a hope for the development of better therapeutic strategies to treat cancer in a global fashion, given the versatility of the DNT cells.

What's next for this project?

Thanks to my SPARK award, I may have generated some very promising data, which suggest that DNT cells are a new player in anticancer immunotherapies. Nevertheless, the B16 melanoma mouse model, although useful, is physiologically distant from human cancer. Therefore, it is essential to confirm these preliminary results into other mouse models that reflect more human disease. As such, I will repeat these experiments using human-derived cells transplanted into transgenic "humanized" mice and DNT cells obtained from healthy donor blood draws. Moreover, together with Dr. Hilde Cheroutre, I secured a $350,000 grant from a private family in January 2022 to build on this work in the context of glioblastoma (brain cancer) in mice and humans.

What's next for Nicolas?

I wish to pursue finishing the *in vitro* experiments in order to prove a direct lethal hit to the tumor cells by DNT cells and address the toxicity in genetically mismatched settings. I also would like to start implementing the framework to test our hypothesis using human samples.

Finally, with our new funding, I have started to repeat this set of experiments in glioblastoma cancer (mouse and human), and we are already showing encouraging results.

Artem Romanov, Ph.D.

What if we could improve treatment for severe cases of COVID-19 to save lives?

FUNDED

JANUARY 2021

FUNDED BY

The generosity of various 2020 SPARK donors.

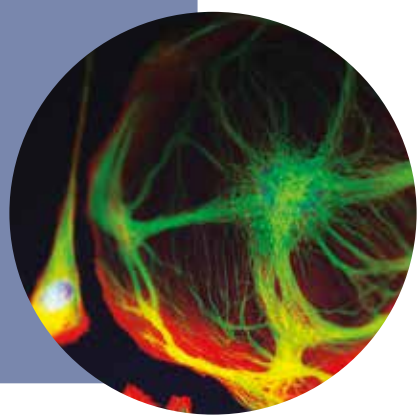
What was the goal of your SPARK project?

What if it would be possible to change the outcome of severe COVID-19 into a mild-case scenario, or avert long-term damage by changing the levels of certain molecules present in the blood?

The aim of this project was to apply state-of-the-art, high-resolution mass spectrometry to characterize the blood metabolic profile of patients with severe COVID-19, with a focus on vulnerable populations including cancer patients, patients with cardiovascular disease, type II diabetes or obesity, or with different ethnic backgrounds. I was also interested in seeing if there were any male-specific metabolites in the context of severe COVID-19, because men are more vulnerable to severe disease worldwide.

Did you face any challenges?

Yes. My main challenge was organizing the collaborative and analytical work with our off-site collaborator groups during a time when many people were working remotely. Sample preparation and data acquisition were also considerably slower and more time-consuming than I anticipated. I would like to add that learning to properly pace the work over the past year has taught me a lot about deadlines.



SPARK
IMPACT STATEMENT:

"My SPARK project revealed for the first time that there are specific changes in blood metabolite profiles in mild versus severe COVID-19 patients, and that these changes are different in males and females. Surprisingly, more metabolites were elevated in patients with mild COVID-19 cases than with severe COVID-19 cases, which was actually opposite to our initial hypothesis. On the other hand this might be even more interesting because these so-called 'protective' metabolites could be used as therapeutic metabolites."

SPARK project results:

My analysis showed that 27,875 metabolites were detectable in most of the samples (~95%), but only one metabolite was significantly associated with developing severe COVID-19. In contrast, most metabolites were specifically associated with developing mild COVID-19. These results demonstrate that the presence or absence of specific blood-borne metabolites are predictive of mild COVID-19 disease, as opposed to predictive of severe COVID-19 disease. This finding was surprising and different from my original objective of identifying severe COVID-19 metabolites. However, this is also more promising and potentially exciting because mild COVID-19 metabolites can be further developed as biomarkers of mild COVID-19 disease or as immune-stimulatory therapeutic compounds to prevent severe COVID-19 disease.

Regarding sex-specific metabolites, I uncovered metabolites that were specifically associated with the development of either severe or mild disease in males. These results demonstrate that circulating metabolites are a good indicator of sex-specific differences in COVID-19 disease severity, and may be useful in developing sex-specific biomarkers of COVID-19 disease severity or therapies.

What's next for this project?

Based upon these exciting findings, I would like to validate and extend the initial observations I made during the course of this SPARK project by 1) expanding my metabolite analysis to additional patient cohorts to see if they replicate in other COVID-19 patients; 2) identifying the chemical nature of the mild COVID-19 metabolites and the male-specific COVID-19 metabolites; 3) exploring the use of these metabolites as bio-marker predictors or modulators of COVID-19 disease outcomes.

I am applying for R21 or R00/R99 funding from the NIH/NIAID, and coordinating with my PI, Dr. Sonia Sharma, to apply for a collaborative R01 grant from the NIH/NIAID. Additional patient cohorts can be obtained from key collaborations between myself, Dr. Sharma, and Dr. Sujan Shresta at LJI.

What's next for Artem?

Ultimately, I hope to contribute to the development of new translational approaches in the field of immune-metabolism and immune-therapy. Whether that will be in academia or industry doesn't matter so much to me as long as I can keep working on developing new metabolite-based treatments for cancer and other immune diseases, including COVID-19. I feel lucky that during my time as a graduate student and as a postdoc there has been a true "renaissance" for understanding how metabolism and metabolites interface with immune diseases.

Payel Roy, Ph.D.

What if we could screen for heart disease earlier and improve patient outcomes?

FUNDED

JANUARY 2021

FUNDED BY

The generosity of Dave Rickey and the Rickey Family.

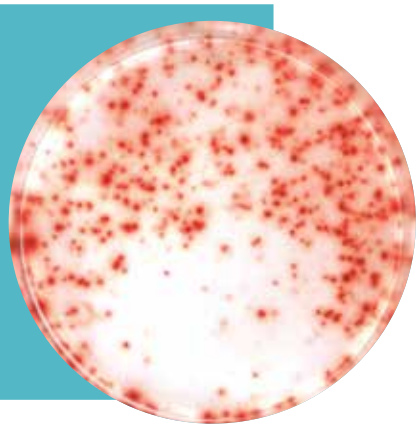
What was the goal of your SPARK project?

A T cell response is not a random event, but is directed towards specific molecules known as "antigens." Normally, T cells respond only to foreign antigens, such as markers on bacteria and viruses. But in the case of heart disease, some rogue T cells recognize self-antigens, i.e., molecules that are present in our own bodies. In mouse models, researchers have shown that apolipoprotein B, the protein that forms the backbone of low-density lipoprotein (LDL), is a major inducer of heart disease-related harmful immune responses. Therefore, I focused my attention on this protein and began to set up experimental strategies to examine whether human T cells similarly respond to this self-antigen.

My goal was to optimize and validate re-stimulation-based protocols that can detect and characterize autoimmune T cell responses to human apolipoprotein B. My goal was to shed light on heart disease by developing assays that can detect, as well as reveal, the biological identities of the harmful T cells.

Did you face any challenges?

Overall, LJI managed the pandemic situation extremely well and the net negative impact on my research workflow was minimal. However, the patient samples that I was expecting to receive through University of California, San Diego (UC San Diego) Health could not be acquired until late 2021, due to COVID-19-related restrictions. Despite this, I was able to complete my SPARK project by managing to receive patient samples through our collaborators at University of Virginia (UVA) Health.



SPARK
IMPACT STATEMENT:

"The SPARK program helped me to establish an immune-based screening strategy for human cardiovascular diseases that can selectively detect those immune cells that have gone rogue. My research identified those specific T cells that accumulate with progressing heart disease. Using diverse immunological assays and cutting-edge sequencing techniques, I unraveled their detailed molecular signatures, thereby facilitating not only their early detection but also paving the way for the development of precise intervention strategies for heart disease."

SPARK project results:

I optimized my immunological assays and achieved high levels of sensitivity that allowed detection of rogue T cells in the blood of study subjects. These T cells exhibited an inflammatory phenotype, concordant with their postulated role in triggering chronic inflammation that characterizes the long latent phase of heart disease. I discovered that six specific regions, known as "epitopes," in the human apolipoprotein B self-antigen have predominant roles in inducing the rogue T cells.

Next, I wanted to explore the potential of my immunological assays as a screening tool. To do this, I adopted two different strategies. First, I collected blood samples from donors from different age groups (range 20 – 66 years). One part of the sample was sent to clinical labs at UC San Diego to measure lipid risk factors, such as triglyceride, total cholesterol, LDL-cholesterol, etc. The other part of the sample was used to run my immunological tests. None of these donors had a known condition of heart disease.

I found that donors who had elevated levels of lipid risk factors also showed increased responses in my assays. Such heightened immunological responses were detectable even in donors who were in their 20s and 30s.

Second, I obtained blood samples from patients undergoing coronary angiography at the UVA. They were divided into low and high severity groups based on their heart disease burden (standard angiographic scores). Rogue T cell responses were significantly higher in patients who were angiographically determined to have high cardiovascular disease burden.

In the end, I showed that my assays can detect heart disease-related inflammatory T cell responses in young and middle-aged people who have abnormal levels of blood lipids and cholesterol. A strong correlation exists between my assay scores and angiographic scores of heart disease. This signifies the tremendous potential of this workflow in evaluating early signs of the disease.

My work was recently published in *Circulation Research*, one of the top journals related to heart disease. This work also led to a patent application covering TCR-based cardiovascular diagnostics and therapeutics which was submitted in June 2022.

What's next for this project?

We have acquired more samples from patients recruited through Scripps Health, UC San Diego, and the UVA. Our plan is to explore whether similar associations between APOB-specific T cell responses, cardiovascular lipid risks and disease severity exist in multiple cohorts. In-depth statistical analyses will be performed to determine whether my assay readouts can be developed as a biomarker. I will also undertake transcriptomic profiling of these APOB-specific T cells to learn more about their functional states and to identify any potential modifiable targets for intervention. Together these studies will facilitate immunological assessment of cardiovascular risks and will shed light into the pathophysiological nature of autoimmune-related cardiovascular disease.

What's next for Payel?

While my P.I., Klaus Ley, Ph.D., has accepted a new position at the Medical College of Georgia, I will continue to work with Dr. Ley and complete my post doc at LJI through the end of 2023. I would like to continue in academia and wish to one day open my own lab. I intend to continue to study heart disease, but would also like to broaden my horizons by also looking at related disorders and understanding inter-disease relationships.

Simon Brunel, Ph.D.

What if we had one therapy that could cure all autoimmune diseases?

FUNDED

JANUARY 2021

FUNDED BY

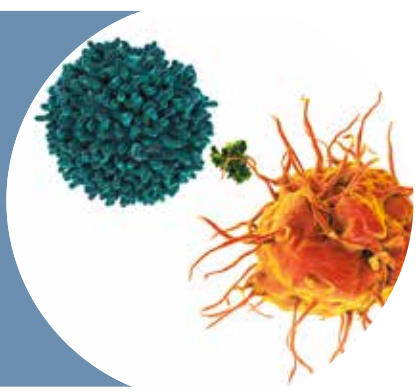
The generosity of The Rosemary Kraemer Raitt Foundation Trust, John and Cim Kraemer and 2020 Various Donors.

What was the goal of your SPARK project?

The overall aim of this project is to validate a new cell therapy protocol in mice to induce immune tolerance to a given antigen using the thymus as a target. This tolerance could be used to counteract the immune response that occurs in some gene therapy protocols or to reinitiate thymic tolerance to self-antigens. Given the well-established role of the chemokine receptor CCR9 in directing migration of peripheral dendritic cells (DCs) to the thymus and their role in tolerance induction, we hypothesized that the expression of an antigen conveyed in the thymus by genetically-modified DCs will impact T cell selection in the thymus, hence the immune response to this antigen in the periphery.

Did you face any challenges?

The global world shortage of goods did not spare science reagents and supplies. Delivery delays impacted the schedule of my experiments. Using a mouse model for my experiments required a lot of ethical writing and protocol approval that also significantly impacted my timeline and scheduled experiment. Due to these delays, I was granted a six month extension on my project and look forward to providing a final update this fall.



SPARK
IMPACT STATEMENT:

"My SPARK award enabled novel research into a cure for autoimmune diseases. My project revealed that we can successfully engineer cells to co-express a specific antigen and a chemokine receptor, allowing cells to migrate to immunologic areas where they can induce immune tolerance for antigens involved in autoimmune diseases."

SPARK project update:

Preliminary results indicate the working hypothesis might prove correct. As of today, we have obtained the functional proof *in vitro* that CCR9 expression on genetically-modified BMDC (bone marrow dendritic cells derived) improves their migration in response to the CCL25 ligand. With that knowledge, we undertook *in vivo* experiments with modified DCs injected into congenic mice. We observed a higher thymus to spleen ratio in terms of frequency of BMDC cells of donor origin if those were modified by a CCR9-expressing vector, suggesting that modified DCs preferentially migrated to the thymus compared to unmodified DCs. Although the numbers of detected cells are still low, we think that the protocol can be improved. Notably, we began our investigation using the luciferase reporter gene to monitor cell migration *in vivo* in live animals. The therapeutic phase of this project has been challenging, but encouraging results should be available soon and I look forward to providing a final update this fall.

What's next for this project?

More experiments on preclinical models are currently running. We are expecting very encouraging results soon, and we believe they will extend the diversity of preclinical models. Those results combined will hopefully lead to a breakthrough publication that will attract more grant funding. In the long term, I'm hoping biotech companies will be interested in developing this methodology of immune system editing.

What's next for Simon?

I am now starting my fourth year as postdoc at LJI. This is usually the year that entails publication and finalizing projects. In order to carry my SPARK project as far forward as possible, I'm currently building skills that will be required to lead this project at a company or startup.

2022 SPARK AWARDS CELEBRATION

On April 12, 2022, La Jolla Institute for Immunology (LJI) hosted guests at a dazzling reception celebrating five years of The Tullie and Rickey Families SPARK Awards for Innovations in Immunology. The event was held on LJI's back patio, in part to honor the brilliant '22 SPARK winners, but also to recognize the donors and supporters of the program. Guests sipped on "spark"ling cocktails while hearing from LJI leadership about current LJI endeavors and from former SPARK winners about their ongoing research projects.

SPARK Program Manager Kelsey Dale with the '22 Tullie and Rickey Families SPARK Award winners

'19 SPARK winner Julie Burel, Ph.D. and Anne Hill

'22 SPARK winner Melissa Meyer, Ph.D., and SPARK donor, Sylvia Liwerant

From left to right: Richard Stryjewski, Peter St Clair, Raydene St Clair, Sam Myers, Ph.D.

From left to right: SPARK donor Barbara Donnell, Michael Croft, Ph.D., and Matthias von Herrath, M.D.

Center: Tom and Judy Tullie with the 2022 Tullie and Rickey Families SPARK Award winners

JULIE BUREL, PH.D.

'19 SPARK WINNER

Earlier this year, Dr. Burel was awarded $415,000 from The Conrad Prebys Foundation that will allow her to build on her SPARK project data and potentially help develop a completely novel area of infectious disease research. Dr. Burel, now an instructor in the Peters Lab, has pioneered the study of doublets. Doublets occur when two immune cells are stuck together. For decades, researchers thought doublets were an accidental artifact of certain laboratory procedures commonly used for analyzing clinical samples. Burel's work, in collaboration with the LJI Flow Cytometry Core, has shown that some doublets do have a role in the body—they may even be a sign that the immune system is fighting an infection.

At the SPARK Awards Celebration this year, Dr. Burel spoke about her success and how critical her SPARK award was in being able to apply for and win this significant follow-on funding.

RANA HERRO, PH.D.

'18 SPARK WINNER

In 2020, Dr. Herro accepted a faculty position at Cincinnati Children's Medical Center in the Division of Immunobiology, where her goal is to develop effective therapeutics and novel prognostic biomarkers for fibrotic diseases. Dr. Herro returned to LJI to speak at this year's SPARK Awards Celebration about how her SPARK award was a springboard for her career as an independent researcher.

THANK YOU, REVIEWERS

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

Barbara Donnell

François Ferré, Ph.D.

Cheryl Hammond

Gina Kirchweger, Ph.D.

Christopher Lee, MBA

Bob Mahley, Ph.D.

Sylvia Liwerant

Samuel Myers, Ph.D.

Margaret Ng Thow Hing, J.D.

Dave Rickey

Ingrid Stuiver, Ph.D.

Tom Tullie

David Webb, Ph.D.

Daniela Weiskopf, Ph.D.

Sharleen Wollach

PROGRESS REPORTS FROM THE **2022 SPARK WINNERS**

The ambitious and talented 2022 cohort is tackling problems as bold as improving cancer patient outcomes, advancing vaccine development, and shedding light on diseases such as asthma, type 1 diabetes, and COVID-19. These dedicated scientists have already been working away on their projects for six months. Now, for the first time, they will have the chance to make a competitive pitch for one additional $25,000 award in August to take their research even further. Here are the six-month progress reports for the winners of the 2022 Tullie and Rickey Families SPARK Awards for Innovations in Immunology:

Heather Callaway, Ph.D.

WHAT IF WE COULD DESIGN LONGER-LASTING VACCINES?

My project aims to test a stabilized form of rabies glycoprotein as a vaccine candidate and to identify anti-rabies antibodies that may be used as therapeutics to treat rabies infection. To date, I have completed preliminary experiments to optimize conditions for vaccinating mice and testing their immune response, mouse vaccinations, and the first Beacon experiment to isolate anti-rabies antibodies from mice. I am currently conducting work to collect blood from vaccinated mice and quantify immune cells in order to measure the longevity of the antibody response after vaccination.

The anti-rabies antibodies that I have isolated from my first Beacon experiment could be used as new therapeutics to treat rabies infection, and could be engineered to target multiple different lyssaviruses, including rabies.

Priyanka Saminathan, Ph.D.

WHAT IF WE COULD UNCOVER THE BIOLOGICAL MECHANISM THAT MAKES MEN MORE VULNERABLE TO COVID-19?

My SPARK project set out to identify why men are more vulnerable to COVID-19 infectivity. We have so far identified that men tend to have increased adenosine deaminase (ADA) activity in their serum. Now rigorous training and protocol preparation that is required to work in the BSL-3 units with SARS-CoV-2 is underway. In the meantime, we have designed, prepared, and tested immune cell isolation from tissues and intra and extracellular immune cell flow cytometric panels that we will be using for our mouse studies. Also ongoing is our dosage-curve pilot experiment to test multiple ADA concentrations to identify optimal and non-lethal dosages of ADA that can be supplemented in mice.

These experiments thus far have implicated that endogenous retroviral elements (ERVs) in the blood cannot be used as a proxy for ADA activity. Our next goal is to identify how this translates to levels of IFNβ at the tissue levels which we believe is one step closer in identifying why men are more vulnerable to not only COVID-19, but to several other respiratory tract infections such as influenza, pneumococcal disease, and common colds.

Gurupreet S. Sethi, Ph.D.

WHAT IF WE COULD CURE ASTHMA BY ERASING THE IMMUNE SYSTEM'S MEMORY OF ALLERGENS?

I've made progress in developing a mouse model to study immune cell memory of allergens. I've worked with Foxp3 GFP reporter mice subjected to the multiple exposures to house dust mites extract (human allergen), which leads to the development of memory T cells in their lungs. By staining their lung tissue with fluorochrome antibodies, I've tracked down a particular subset of lung-localized memory T cells. These memory T cells were sorted out and further processed for RNA extraction and single-cell RNA sequencing.

The next half of the project is critical as the single-cell RNA sequence data will be analyzed using different bioinformatics tools to help us understand the allergic memory T cells. In addition, by comparing the allergic memory T cells with memory T cells of naïve mice, we will try to find out the differentially expressed genes responsible for the long-lasting persistence of these allergic memory T cells.

Melissa Meyer, Ph.D.

WHAT IF WE COULD TARGET PRO-TUMORAL IMMUNE CELLS WHILE LEAVING INFECTIOUS DISEASE-FIGHTING IMMUNE CELLS UNHARMED?

My SPARK award supports work to understand how immune cells that prevent infection differ from immune cells that support tumor progression in melanoma patients. To do this, I am utilizing new technology, CITE-seq, to understand the markers present on the outside of cells and associate them with an anti-bacterial or pro-tumoral phenotype.

Over the past four months, I have made progress in optimizing the process of performing and analyzing the CITE-seq experiment. In addition, working with a larger group, I have designed a custom reagent necessary for the proposed experiments. The custom reagent has finally arrived and will allow me to now begin the large-scale proposed experiment soon. I have also been working with our computational team to prepare for the downstream analysis. We previously generated a CITE-seq mouse bone marrow data set that included neutrophils. We are working through the pipeline with this data set to optimize the analysis for neutrophil detection. Working with the mouse data set will better prepare us to analyze the human data set once it becomes available.

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

WHAT IF A PERSON'S INSULIN-PRODUCING BETA CELLS ARE ORCHESTRATING THEIR OWN DEMISE?

Type 1 diabetes (T1D) is a chronic disease that results from the autoimmune destruction of insulin-producing beta cells. My hypothesis for this SPARK project is that beta cells may directly present self-antigens to autoreactive CD4+ T cells, and hence, I am now investigating whether pancreatic beta cells can directly communicate to CD4+ T cells and the effects of this cross communication.

Using an innovative platform with 3D human islet microtissues, I co-cultured those islet spheroids with human CD4 T cells from HLA matched donors and monitored changes in islet shape and size, and overall CD4 T cell infiltration. I also studied functional changes with the GSIS (glucose stimulated insulin secretion test). Additionally, I am obtaining high-resolution images with confocal LSM 780 to precisely quantify CD4 T cell infiltration and the expression and colocalization of markers of interest. The high quality of the stainings allows us to precisely locate the infiltrating T cells and locate and quantify the expression of our markers of interest. Using SPARK funds, I have improved our methods to process the islet spheroids after staining them, and now I can preserve their 3D structure, create 3D iso-surfacing of the whole structure using Imaris, and perform 3D image analysis. I anticipate having preliminary data very soon.

Maria Inês Matias, Ph.D.

WHAT IF WE COULD CONVERT PRO-TUMOR CELLS INTO TUMOR-FIGHTING CELLS?

With my SPARK project, I aim to understand how nutrient availability in a tumor can impact killer T cells differentiation and function. Ultimately, I want to know how we can transform pro-tumoral cells into tumor-fighting cells by modulating nutrient availability.

The last few months have been dedicated to characterizing and optimizing differentiation protocols for these cells. I was able to optimize protocols to derive an expected and an unexpected killer immune cell type that share common anti-tumor features. The cells generated from these two protocols display features that might influence their persistence and tumor-killing capacity once injected into patients. I am now working toward performing deep molecular characterization of these two cell populations and comparing them with the objective cells identified in the small intestine. The outcome of this molecular profiling will guide efforts to identify the impact of nutrient availability in tumor-killing functions in T cells.

SPARK STARS ARE TAKING THEIR RESEARCH AND CAREERS TO NEW HEIGHTS

In addition to providing seed funding for innovative ideas, the Tullie and Rickey Families SPARK Awards program also aims to prepare promising early-career scientists to take the next steps in their research and careers. We regularly share stories of our "SPARK Stars" who are demonstrating that donor investment in SPARK is helping to ignite discoveries and field the next generation of researchers. Here are a few highlights from the past year.

GREET VERSTICHEL, M.D., PH.D.

'20 SPARK WINNER

Together with her P.I., Dr. Hilde Cheroutre, Dr. Verstichel has been awarded $400,000 from the **Praespero Foundation** to continue her SPARK-funded research where she examined gene expression and T cell fate in human cells She has now confirmed that the phenomenon she discovered in mice holds true in humans. Whether a self-reactive T cell is good or bad is determined through gene expression changes very early on. Dr. Verstichel hopes scientists can use these findings to better manipulate T cells and prevent disease.

lji.org/blog/origin-story-how-t-cell-heroes-and-villains-are-made/

PROMOTIONS TO INSTRUCTOR

TOM RIFFELMACHER, PH.D.

'20 SPARK WINNER

In January, 2022, Dr. Riffelmacher was promoted to Instructor in the Kronenberg Lab. "The SPARK program certainly provided fantastic training in independently conducting research. As an instructor, I am applying what I learned during my SPARK project as I am writing NIH grants and applying to faculty positions in order to continue my work."

SARA LANDERAS-BUENO, PH.D.,

'20 SPARK WINNER

Dr. Landeras-Bueno was promoted to Instructor in the Saphire Lab in May 2022. "I was the first person in my lab to win a SPARK award and after me, three other people in my lab were selected as finalists. I like to think that I inspired them to participate by telling them what the SPARK awards is about. At the end of the day, being an Instructor is not only a recognition of our scientific successes but also a responsibility to mentor and inspire others. My SPARK award helped me to visualize myself as a leader, to manage my own research budget and to propose an independent research project, so I am sure it really contributed to my promotion!"

MICHAEL NORRIS, PH.D.

'21 SPARK WINNER

Dr. Norris, now faculty at the University of Toronto, and an international team of collaborators have published the first-ever look at a key stage in the life cycles of measles and Nipah viruses. Their new study, published as the cover story in *Science Advances*, reveals how future therapies might stop these viruses in their tracks.

Scan the QR code to learn more about each researcher

MARCO ORECCHIONI, PH.D.

'19 SPARK WINNER

In addition to receiving a grant from The Conrad Prebys Foundation in 2021 to further his research on the role of olfactory receptors in disease, Dr. Orecchioni has also received the prestigious American Heart Association Career Development Award. This award in March 2022 provides $231,000 to Dr. Orecchioni to pursue this line of investigation through March 2025. In July 2022, the Program in Immunology at LJI and the University of California, San Diego, also awarded Dr. Orecchioni $50,000 to further this research in collaboration with a faculty member at UC San Diego. As a result of his outstanding work, Dr. Orecchioni was promoted to Instructor in the Ley Lab earlier this year.

NICOLAS THIAULT, PH.D.

'21 SPARK WINNER

Dr. Thiault's $25,000 award helped him and his PI, Dr. Hilde Cheroutre, to secure $350,000 in follow-on funding from a private family in January 2022. Based on the data from his SPARK project, which underscores the unique and potent functional capacity of the DNT cells, Dr. Thiault and his Dr. Cherourtre, are using this new funding to investigate whether they are the ideal T cell type to develop a rational-designed immunotherapy to safely and effectively cure glioblastoma (brain cancer) This novel work could have implications for other cancer types as well.

DANIELA WEISKOPF PH.D.

'18 SPARK WINNER

Dr. Weiskopf's SPARK-funded dengue virus research had direct impacts on her recent work with the SARS-CoV-2 virus, leading to significant discoveries regarding COVID-19 in her own laboratory at LJI which she established in 2020. Earlier this year, Dr. Weiskopf published results from the first investigation in history to compare how three different types of vaccines trigger an immune response against the same pathogen.

DONOR HONOR ROLL

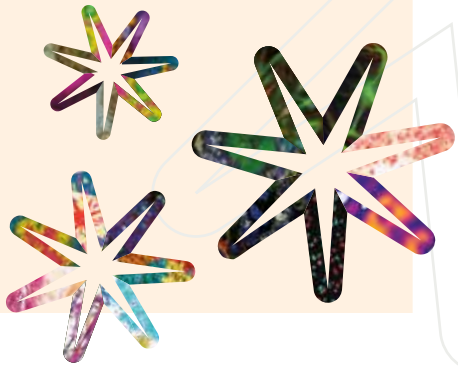
PHILANTHROPY FUELS THE NEXT GENERATION OF RESEARCH

Thank you to all of the generous donors to the Tullie and Rickey Families SPARK Awards for Innovations in Immunology. The donor list below represents all donors to the Tullie and Rickey Families SPARK Awards for Innovations in Immunology since the beginning of the program in Fall 2017 through June 2022. Any donor with a SPARK icon after their name denotes they've given enough cumulatively to fund at least one whole SPARK award.

Anonymous
Anonymous
Anonymous
Anonymous
Acre Investment Real Estate Services
Amnon and Claire Altman
David Anderson
Applied Materials
Jessica and Adrian Ayala
Nicholas Backer
Claudia Baird
Edward and Susan Ball Family Foundation
The Bank of America Charitable Fund
Rita Baudewijn-Vanryckeghem
Becton, Dickinson and Company
Lynn Berman
Richard S. and Karna S. Bodman
The Mark and Katie Bowles Family Foundation
Catherine Boyer
David Brenner and Tatiana Kisseleva
Peegan Brosnan
Thomas Butch
Robert Butterfield
C.R. Bard Foundation
Douglas and Lenore Cameron
Megan Carolan
Anthony R. Carr
The Center for Wealth and Legacy
Check Family Foundation
Ellen and David Cohen
Maurits Cheroutre* and Marie-Louise Cheroutre-Vanryckeghem*
Maxine and Harvey Colchamiro / Colchamiro Charitable Fund
Robert and Lynne Copeland
Kenneth and Adriane Coveney
Ken and Kathleen Croff
Cushman Foundation
Kelsey and Patrick Dale
Suryasarathi Dasgupta
Frank and Elizabeth Deni
Peggy Dinan
Barbara Donnell
Andrew Dremak
Ashley Durkin
Ecke-Meyer Family Foundation
James and Jewel Edson
Marc and Michelle Effron
Robert Eggold and Mary Mills
Matt Ellenbogen
Robert L. and Dominga Enich
Derry and Lois Eynon
Sally Fallon
Thomas and Karen Ferguson
François Ferré and Magda Marquet
L. Michael and Pamela Foley
Craig and Meredith Garner
Amy Geogan
Ayumi Gillespie
Mary Anne and Dave Gladyszewski
Gleiberman Family Fund of the Jewish Community Foundation
Daniel P. and Patricia C. Gold
Jessica Gonzalez
Caitlin Gould
Stuart Gross
Dave and Carol Hall
Erin Hall
Wilson and Jenna Hambrick
J. and Marla J. Harrigan
Reese Harris
Barbara and James Hartung
Lewis C. Haskell
Katya and James Hazel
Holly Heaton
Rebecca Helbig
David and Nancy Herrington
Christopher Himes
Breda Hing
Peter and Dawn Holman
Gary and Jeri Horton
Ali Houry
James B. Isaacs, Jr.
Niles Johanson
Franklin and Catherine Johnson
Terry and Linda Kaltenbach
Andrew Kaplan
Carol and Mike Kearney
Gina Kirchweger and Jan Karlseder
Chad Koelling
John and Cim Kraemer
Gale Krause
Mitchell Kronenberg and Hilde Cheroutre
Kevin and Julie Krumdieck
Ralph T. and June K. Kubo
John J. Lamberti
Cecelia Lance
Gene Lay
Christopher A. and Stephanie Elizabeth Lee
Gary & Lisa Levine Fund of the Jewish Community Foundation
Richard S. and Patricia Levy
Gene Lin
Shao-Chi and Lily Lin
Craig Linden
Aaron and Andrea Ling
Jaime* and Sylvia Liwerant Fund of the Jewish Community Foundation
Shannon London

We'd like to specifically recognize the supporters who have believed in this program from the very beginning and have given to the **SPARK** program every year for the past five years:

Amnon and Claire Altman
David Brenner and Tatiana Kisseleva
Kenneth and Adriane Coveney
Kevin and Julie Krumdieck
Robert and Linda Mahley
Vann and Carol Parker
Larry and Tiki Spitcaufsky
Peter and Raydene St. Clair
Tom and Judy Tullie
Aaron Tyznik



Michelle Lord
Chelsea and Erik Luedeke
Annette Luetzow
Morag and Kenneth Mackay
Robert and Linda Mahley
Richard* and Carol Markus
Ashley Marquez
Joel Martin and Pam Reynolds
Rodney McClendon
Dympna McFadden
Christa McReynolds
Than and Cindy Merrill
Joseph Meyer
Miller-Bowes Giving Fund
The Miller Family Fund
Ernest C. Miller* and Tung-Fen Lin Miller
Jeffrey E. Miller
Dave Mitchell and Judy Bradley
Cherry Miyake
Kevin and Pingya Moore
Daniel Morgan
Eleanor Mosca
Shin Mukai
Lauren Murphy
Gail K. Naughton
Carolyn and Jeffrey Nelson
Joani Nelson
Margaret Ng Thow Hing
Larraine Nobes
Kenneth and Linda Olson
Robert D. and Mary-Lou M. Orphey
Donald Osborne
Renee and Sidney* Parker
Vann and Carol Parker
PartnersFinancial Charitable Foundation
William Passey and Maria Silva
Ramamohan Paturi
Bonnie and Bill Payne
Rachel and Robert Perlmutter
Hunt and Laura Pettit
Pillsbury Winthrop Shaw Pittman, LLP
Gary Powell
Precision Oncology
Patrice Purtzer
Charles Puskas
Amogh Rajanna
Erin Randolph
Ray and Jenifer Raub
The Brenda and Dave Rickey Foundation Charitable Trust
Ira and Kathleen Robb
Paulette Roberts
Dan and Laura Roos
Rosemary Kraemer Raitt Foundation Trust
Rotary Club of Del Mar
The Samuel Lawrence Foundation
San Diego Advisor of the Year / Paul and Lori Thiel
Denny Sanford
Herbert Schnall
Justin and Connie Seng
Sandor and Rebecca Shapery
Thomas and Candace Sharkey
Jack Shevel
Larry and Tiki Spitcaufsky / Spitcaufsky Memorial Fund
Peter and Raydene St. Clair
Todd Steele
John and Diana Stillwagen
Carole Streeter
Ken and Sharon Strong
Studio L
Janet Stull Baumgartner Foundation
Joseph and Joan Tarnowski
Lolly Tharp
The Thomas C. Ackerman Foundation
TIGER 21
Eileen and Robert Timken
Tom and Judy Tullie / Tullie Family Foundation
Aaron Tyznik
Claire Van Ryswyk
Nancy L. Vaughan
Mark Veta
Matthias and Natalie von Herrath
Mark B. Wallner Foundation
J. Mark and Paula Waxman
David and Lila Webb
Carolyn Wheeler
Joanna Wilkinson
Loie Williams
Herman Winick
Richard T.* and Lucy F. Wold
Beverly Wolgast
Andrew Yuen and Elisabeth Wolcott-Yuen

The donor list above represents all donors to The Tullie and Rickey Families SPARK Awards for Innovations in Immunology specifically as of June 30, 2022.

*Deceased

Why Bio-Pharma Industry Leader David Webb, Ph.D., is a Committed SPARK Supporter

David Webb together with his wife, Lila, at a recent La Jolla Institute for Immunology event. Photo credit: Melissa Jacobs

As soon as David Webb, Ph.D., heard about preliminary plans for La Jolla Institute's SPARK program, the concept had his full support. With a background in both academia and research, and then biotech start-ups, he knew what this could mean for early career scientists.

Dr. Webb is the Founding CEO of Synbal, Inc., a platform technology company that is commercializing CRISPR-based breakthrough active genetic technologies developed at the University of California, San Diego. In his spare time, he is also Adjunct Professor in the Department of Integrative Structural and Computational Biology at Scripps Research and serves on various boards, including La Jolla Institute's Board of Directors.

The concept of treating postdocs as independent thinkers, and not just worker bees who support their PI's research, is inherent to the SPARK program model and this resonated with Dr. Webb right away. He remembers being immediately impressed by the proposals put forward by the postdocs for SPARK funding in the very first year.

Since then, Dr. Webb has not only supported the program financially, but he has also served on the application review committee and pitch panel every year. He finds SPARK applications satisfying to review because they are innovative research questions that are finite and short-term, focused yet comprehensive

The pitch process, though, is the secret sauce.

"In both an academic and industrial setting, you have to be able to think on your feet and present well. Yes, writing is important, and of course execution in the lab is critical - but presenting in front of your peers and colleagues in a way that's believable and convincing and that makes people want to fund it is an acquired skill. It's something that everybody needs to work on."

From a donor's perspective, Dr. Webb has found the program to be a great investment with tangible results. "This is an opportunity to directly support a talented young scientist and see them develop before your eyes in a very specific way. You know the input and you know the output and that's unique."

Dr. Webb commends the Tullie and Rickey families for their driving support of this program and the impact it has had in jump-starting the careers of so many young scientists over the past five years. He intends to stay involved and encourages others to consider it too. "We're taking some of the best and brightest that the Institute has to offer and giving them an opportunity to show what they can do. That's unusual and worth celebrating."

"This is an opportunity to directly support a talented young scientist and see them develop before your eyes in a very specific way. You know the input and you know the output and that's unique."

5 years of awards*

*Based on donations and pledges received from 2017–22 and SPARK Awards given between 2018–22.

$835,000 awarded to early-career scientists exploring bold ideas

192 donors have made more than **450** **gifts/pledges to the** Tullie and Rickey SPARK Awards Program, raising more than **$1.1M** **for the program.**

32 awards given

The SPARK award winners represent **19** **different labs at LJI**

4 years of results*

*Based on 27 SPARK projects funded between 2018–21

Since receiving their awards, former SPARK winners have won **11 new grants**, totaling more than **$6.3M** in follow-on funding for their projects or career advancement from a mix of private individuals, foundations and government agencies.

40% of SPARK Award winners have earned a promotion, with **7 SPARK Award** winners staying in research academia to start their own labs.

20 papers or grant applications are currently in progress by SPARK Award winners related to their project or career advancement.

12 manuscripts have been published related to research generated by the SPARK projects.

There are currently **4 Intellectual Property** filings related to patents for discoveries made in SPARK projects.

About the Tullie and Rickey Families

From left to right: Judy and Tom Tullie, Dave and Brenda Rickey

We'd like to thank and recognize the incredible support and generosity of LJI Board Director Tom Tullie and his wife Judy, as well as LJI Board Director Dave Rickey and his wife Brenda and their families. Their joint commitments to the SPARK program made in 2019 meant LJI has the assurance that this program will have funding in place for several awards a year for the next decade. That year, LJI honored their commitment by renaming the SPARK program to The Tullie and Rickey Families SPARK Awards for Innovations in Immunology.

Tom Tullie was one of the first SPARK pitch reviewers in 2018, and that was what drove him to get his family engaged 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 an invitation from Tom and also 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," Dave says. The Rickeys were attracted to the SPARK program largely due to its structure and opportunity to drive research forward. "In the philanthropy world, we like to give money where there will be a return. This program is really tangible and it's good to see."

The Tullie and Rickey families hope that by ensuring the program's longevity, other donors will be inspired to contribute to the program to fund additional awards and get as many of these ideas off the ground as possible. "I'd love to see people join us," shares Tom, "I guarantee you that it will be well worth our investment because these ideas are unbelievable and they need to get funded."

The Tullie and Rickey Families SPARK Awards for Innovations in Immunology represents an opportunity for donors of all levels to have a profound impact on the future of early-career researchers and also help ignite the next big breakthroughs. You can donate online at donate.**lji.org/SPARK** or reach out to **Kelsey Dale** at **kdale@lji.org** or **858-752-6542** if you'd like to discuss other giving options.

Strange DNA structures may drive cancer development

Vipul Shukla, Ph.D.
'20 Winner

LJI researchers shed light on the role of TET enzymes in genomic stability and cancers

Scan the QR code to read more:

Macrophages in the artery wall 'smell' their surroundings

Marco Orecchioni, Ph.D.
'19 Winner

Immune cells can sniff out octanal in blood, triggering dangerous inflammation and atherosclerosis.

Scan the QR code to read more:

Scientists uncover new targets for treating Parkinson's disease

Cecilia Lindestam Arlehamn, Ph.D.
'20 Winner

LJI study suggests therapies could stop T cells from attacking brain cells in Parkinson's

Scan the QR code to read more:

New research gets to the roots of type 1 diabetes

Estefania Quesada-Masachs, M.D., Ph.D.
'20 and '22 Winner

discusses her most recent findings, published in the February 2022 issue of *Diabetologia*

Scan the QR code to read more:

Fighting Zika? Call in the T cells

Annie Elong Ngono, Ph.D.
'21 Winner

Stopping emerging viruses could depend on getting T cells and antibodies to work together

Scan the QR code to read more:

The Conrad Prebys Foundation grants more than $450,000 for studies into childhood cancer, cardiovascular disease

Abhijit Chakraborty, Ph.D.
'20 Winner and
Marco Orecchioni, Ph.D.
'19 Winner

New funding will support high-risk, high-reward projects led by two early-career scientists

Scan the QR code to read more:

LJI team gets first-ever look at a rare but vital stem cell in humans

Huy Dinh, Ph.D.
'19 Winner

New understanding of immune cell origins may offer cancer and COVID-19 drug targets

Scan the QR code to read more:

SPARK

THE TULLIE AND RICKEY FAMILIES SPARK AWARDS FOR INNOVATIONS IN IMMUNOLOGY

9420 Athena Circle, La Jolla, CA 92037

Non-Profit Org
U.S. Postage
PAID
Permit 2256
San Diego CA

About The Tullie and Rickey Families SPARK Awards for Innovations in Immunology

Innovation doesn't come cheap. But without proof-of-concept to convince highly competitive granting agencies to fund a daring project, many bold ideas are never put into action. This is a particular challenge for younger scientists, who are still establishing their career. La Jolla Institute's Tullie and Rickey Families SPARK Awards program is designed to overcome these hurdles.

The Tullie and Rickey Families SPARK Awards for Innovations in Immunology provides $25,000 in flexible start-up funding that enables LJI's early career investigators to act on their promising projects for bold new approaches to diagnoses, treatments, and possibly even cures for diseases that afflict us today. It fills the gap between scientists' imagination and that first solid set of data that allows them to attract additional funding to further their research and ultimately make life-saving discoveries.

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

Kelsey Dale
Vice President of Advancement
La Jolla Institute for Immunology
kdale@lji.org | 858-752-6542