

LA JOLLA INSTITUTE FOR IMMUNOLOGY



SPARK

THE TULLIE AND RICKEY FAMILIES
SPARK AWARDS FOR
INNOVATIONS IN IMMUNOLOGY

2019 ANNUAL REPORT



PHILANTHROPY FUELS THE NEXT GENERATION OF RESEARCH



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

Through their generous gifts to the Tullie and Rickey Families SPARK program, donors are directly empowering young investigators to take risks and fill the gaps between imagination and groundbreaking discoveries.





THE TULLIE AND RICKEY FAMILIES SPARK AWARDS FOR INNOVATIONS IN IMMUNOLOGY

La Jolla Institute's SPARK program was designed to break down inherent barriers in research funding for early career scientists. The innovative design of this philanthropically financed program provides flexible seed funding for bold new approaches to diagnoses, treatments, and possibly even cures for diseases that afflict us today.

In addition to funding high-risk, high-reward research, the SPARK program also helps train and advance the careers of the next generation of researchers. SPARK applicants receive coaching in how to communicate their research to the public, and specifically how to present their ideas to funders. And the SPARK award winners ultimately get the experience of running an independent research project.

Each SPARK award is \$25,000 and must be spent within one year. The goal is to enable scientists to generate enough preliminary data to attract additional funding to further their research and career.

Since fundraising began in the fall of 2017, private donations have funded 14 SPARK projects that range in focus from autoimmune diseases and cancer, to infectious disease diagnostics and vaccine development. It is our pleasure to present this annual report and share the results of the first cohort of the SPARK award recipients from 2018.

We'd like to sincerely thank the nearly 100 donors who believed in the vision of this program in its very first year, helping us raise more than \$200,000 in 2017. Your support

was game-changing and fueled the success of this program. As you can see on each SPARK report, we have listed the supporters who helped make each project possible. (For a more complete listing of all SPARK donors please see the back cover.)

We'd also like to give a special thanks to David and Diane Steffy, whose generous multi-year pledge in 2017 propelled the program forward into its second year, and gave us the assurance that this program would continue for several years to come.

Our 2018 SPARK donors helped continue our momentum as we were able to fund an additional six awards in January 2019. We look forward to providing full reports on those projects in our 2020 SPARK Annual Report, but we do have some quick highlights at the back of this report on page 18.

And, most notably, 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 Dave and Brenda Rickey and their families. With their joint commitment to the SPARK program made this year, we now have the assurance that this program will have funding for at least four awards per year for the next 10 years. Their impact on the early-career researchers at La Jolla Institute will be profound, as will the knowledge we gain from the projects that are seeded by the SPARK awards. We have honored their commitment by renaming the SPARK program The Tullie and Rickey Families SPARK Awards for Innovations in Immunology. ✨



Building on Breakthroughs in Cancer Immunotherapies

Ian T. Mathews

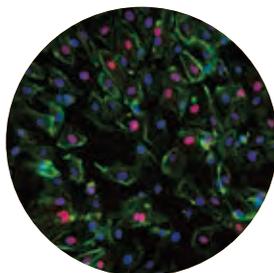


What was the goal of your SPARK project?

Immunotherapies are a novel class of cancer-targeting drugs that reawaken the immune system against a patient's own tumors. These treatments have shown remarkable clinical success, treating melanoma and some of the most advanced tumors known with efficacy never before shown against these forms of cancer. However, some patients either do not respond to therapy or get worse because of immunotherapy, developing autoimmune-like side effects. Immunotherapy can be miraculous for some and horrendous for others, underscoring the potency of this class of drug. Understanding which patients to give immunotherapy and how we can improve a patient's response to treatment, therefore are important clinical questions. Under this SPARK award, we set out to measure the tens of thousands of molecules in the blood of cancer patients treated with immunotherapy, in the hope that we could detect molecules that can predict who will respond to therapy, and potentially find signatures that suggest how we might improve patient response.

SPARK project results:

In melanoma patients treated with the immunotherapy ipilimumab (Yervoy), we found molecules that, when high in a patient's blood, could predict whether that patient would respond to therapy. In addition, we found molecules that either increased or decreased in patients' blood while on therapy, some of which were only changed in patients who developed autoimmune side effects.



These latter molecules may be a window into understanding the still unknown mechanisms by which some patients develop severe side effects while other individuals do not. This study was an important first step in a project we hope to continue all the way to developing a simple blood test for predicting and improving cancer patient response to immunotherapy.



IMPACT STATEMENT:

“My SPARK award has really blossomed into something special. It’s led to a well-funded project of its own, with immense potential for clinical benefit in immune oncology. The excitement surrounding our work and the support we have received, has given me personally a great deal of courage to pursue a career around predictive and surrogate biomarkers for immunotherapy patients. It’s incredibly heartening to follow research questions which begin with initiatives like SPARK—and include engaged community members supporting inquiries into accessible, important clinical questions and discoveries.”

FUNDED

FEBRUARY 2018

FUNDED BY

The generosity of LJI Board Member Gail Naughton

What’s next for this project?

Following the SPARK award, I was able to successfully apply for and receive an F31 Predoctoral Fellowship from the National Cancer Institute (NCI), more than quadrupling the initial funding provided for this project. Additionally, we completed an R01 and an U01 application to the NCI using predominantly data generated over the course of this SPARK-funded study. Both grant applications scored well but didn’t receive funding. However, we were encouraged to resubmit and plan to apply for another NCI R01 in October 2019.

We have expanded our immunotherapy blood sampling cohorts to include two additional cohorts, totaling thousands of blood samples from hundreds of cancer patients treated with immunotherapy. Using these cohorts, we were able to identify specific metabolites which associate with Grade III/IV irAEs, the severe side effects of immunotherapy that can take patients off of therapy.

We were able to study these metabolites in mice and reduce the severity of these side effects by modulating the levels of these same metabolites.

The next steps of this project are twofold: Firstly, we intend to greatly expand our immunotherapy blood sampling cohorts for screening by LC-MS/MS through collaborative efforts and access to preexisting biobanking. Secondly, we intend to further study some of the metabolites discovered in this project via *in vivo* tumor and irAE modeling, in an attempt to better understand these metabolites’ potential function in tumor and systemic immunity. Cumulatively, these next steps will require funding on the order of hundreds of thousands of dollars, for which we are preparing (and are optimistic in the preparation of) additional applications for funding.

What’s next for Ian?

I hope to graduate with my Ph.D. in Biomedical Sciences from UC San Diego in Summer of 2020, after which I plan to enter medical school to earn an M.D.. My ultimate career goal is one in academic medicine, following research questions in predictive and preventative care for cancer patients not dissimilar to what we pursued with our SPARK award.*

Probiotics or Antibiotics to Cure Allergy

Rana Herro, Ph.D.



What was the goal of your SPARK project?

Over the last decades, the incidence of chronic immune disorders such as food allergies, eczema, asthma, type 1 diabetes, and multiple sclerosis has skyrocketed. Through association studies in humans and experimental animal models, we know that chronic inflammatory disorders are linked to the microbiome in humans and that changes in microbiota (dysbiosis) can cause disease in animal experimentation models. The SPARK project was designed to profile the microbiome in patients during the “atopic march”, a term referring to the typical progression of allergic diseases from skin (atopic dermatitis) to gut (food allergy) to lung (asthma) during early life. The overarching goal is to identify a “protective” versus “pathogenic” microbial signature that can be targeted in therapies to halt allergic diseases.

SPARK project results:

We sequenced stool samples of four atopic march patients matched with healthy controls and were able to see a striking 6.54-fold decrease in alpha diversity in the allergic patients as compared to healthy controls. This indicates a decrease in microbial diversity with predominant microbe species abundantly present in allergic stools compared to healthy ones.

Regarding the skin, we observed a clear dysbiosis within the same atopic march individual (history of eczema, asthma) that had contact urticaria on the left arm but not on his right arm, which didn't develop an allergic reaction. Interestingly, the same dysbiosis was amplified in eczematous skin with three predominant microbes abundantly homing the skin. These results are very

encouraging, as it clearly indicates a direct relationship between dysbiosis and allergy, observed in localized contact urticaria and amplified in eczema.

What's next for this project?

In addition to expanding our human studies, we will introduce pathogenic microbiomes into allergy-resistant rodents to study whether dysbiosis alone is sufficient to promote atopic diseases. Vice versa, we will treat allergy-sensitive strains with antibiotics that suppress the pathogenic microbiome, or promote beneficial dysbiosis by supplementing their diet with probiotics to test for disease reversal when a healthy microbiome is restored. Finally, we will use Multiple Reaction Monitoring mass spectrometry technology to profile the microbiome and immune responses at the protein level (complementing the genomic approach we will first adopt). The idea is to form a library of microbial metabolites that could potentially serve as drug targets in human therapies to halt allergic diseases, with little to no side effects considering



their prokaryotic origin. If successful, the follow up study should confirm the hypothesis that microbial dysbiosis can exacerbate if not cause atopic diseases, and whether developing selective therapies to change the microbiome can benefit patients with allergies.

What's next for Rana:

Next spring, I will start a position as Assistant Professor at the Cincinnati College of Medicine/Cincinnati Children's Hospital Medical Center. The data I collected as part of my SPARK project allowed me to successfully compete for a Mucosal Immunology Study Team grant from the National Institutes of Health and will form the basis for a larger NIH grant, which I plan to submit as soon as I move to Cincinnati. ✨

SPARK

IMPACT STATEMENT:

“The SPARK grant turned out to be a crucial springboard for my career as an independent researcher. But the implication of this work for human allergic disorders is even bigger. We hope to be able to cure allergy by manipulating the microbiome through antibiotic treatment or probiotic administration. I believe that if we can correct dysbiosis, we can restore health.”

FUNDED
JANUARY 2018

FUNDED BY
The generosity of LJI Board Member Larry Spitcaufsky and Tiki Spitcaufsky



Can the Environment Give You Cancer?

Nadine Hartmann, Ph.D.

What was the goal of your SPARK project?

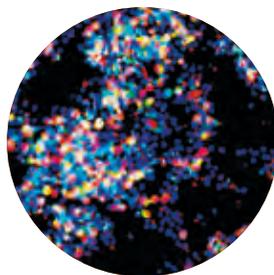
In the United States, every three minutes somebody gets diagnosed with blood cancer and every nine minutes, somebody dies from it, making it one of the most fatal cancer types. Yet, we still do not fully understand the causes and factors that contribute to the disease. Mutations in certain genes like TET2 are often found in leukemia patients,

but, there are healthy individuals harboring these mutations without developing leukemia. Thus, secondary factors might be necessary to trigger the disease. Similar to humans, we found a mouse model of TET2 mutant mice, which develop several types of cancer in some animal facilities while staying healthy in others. Therefore, the aim of our study was to determine

whether environmental influences like infections or chronic inflammation are involved in cancer development in these mice. The SPARK award was used to purchase and maintain wildtype (WT) and TET2 mutant mice at the LJI facility, sequence their gut microbiome, and perform pilot infectious experiments.

SPARK project results:

The first step of our project was to sequence the gut microbiome of wildtype mice and healthy TET2 mutant mice in LJI's facility to establish whether they would have similar microbiomes. Dr. Bana Jabri, at the University of Chicago had recently published that their wildtype mice and sick TET2 mutant mice harbored a similar microbiome, so it was



important for us to confirm whether the same was true for the mice in LJI's facility. Once this was established, we were then interested in comparing the difference in the gut bacteria between the healthy TET2 mutant mice at LJI and the sick TET2 mice at the University of Chicago. This comparison found that our healthy TET2 mutant mice

have a more diverse microbiome and lack certain bacteria that are known to promote gut inflammation.

To further analyze if inflammation-causing bacteria can trigger cancer development in TET2 mutant mice, we colonized these and wildtype mice either with an acute inflammation-causing bacteria species or chronic but mild inflammation-causing bacteria species and then compared them to control groups that received saline. Interestingly, only the TET2 mutant mice infected with the acute inflammation-causing bacteria showed elevated myeloid cell levels in their blood four weeks after infection. This suggests a strong inflammatory signal might be involved as a first step in triggering cell expansion during disease onset.

What's next for this project?

The SPARK Award was crucial in obtaining preliminary data suggesting acute gut inflammation plays a role in cell expansion during leukemia

development. The next steps are to validate the findings of this experiment. Future experiments will address whether repeated infection with the acute inflammation-causing bacteria and other strong proinflammatory stimuli contribute not just to cell expansion but also to secondary mutations, gut barrier function deficiency, and, finally, tumor development. It's our hope that our studies will shed light on whether preventing infections and chronic inflammation might suppress cancer development and provide new insight into the therapeutic potential of targeting the microbiome of patients carrying a TET2 mutation.

What's next for Nadine:

Recently, I've taken the next step in my career by accepting a new position as a Non-Clinical Scientist at Intercept Pharmaceuticals, a company specializing in progressive, non-viral liver disease. At Intercept, I design and manage non-clinical studies at CROs, collaborate with external research departments, and focus on exploratory sub-studies from Intercept's clinical trials. ✨



SPARK

IMPACT STATEMENT:

“For me, SPARK equals opportunity—it allowed me to work on a meaningful project of my own that will help shed light on how our gut can influence our risk for cancer. This experience also prepared me for the next steps in my career, as many institutions and companies want to hire researchers with the skill of communicating science to the general public.”

FUNDED

FEBRUARY 2018

FUNDED BY

The generosity of Rachel and Robert Perlmutter and The Thomas C. Ackerman Foundation



New Immune Cells in Atherosclerosis

Holger Winkels, Ph.D.

What was the goal of your SPARK project?

The immune system plays a pivotal role in the progression of atherosclerosis, the underlying cause of fatal cardiovascular events, including myocardial infarction and stroke. In previous work, I analyzed the immune cell landscape in aortas of atherosclerotic mice at different stages of disease. During the analysis of these data sets I identified a new aortic immune cell population, which appears to consist of T cell progenitors. T cell progenitors, so called thymocytes (CD4CD8 cells), are thought to only reside in the thymus. Finding them in the aorta may indicate that the thymus, where T cells develop, might have a leak allowing progenitors to escape. This could be potentially dangerous, as uncontrolled T cells responses can lead to autoimmunity. The SPARK award was used to further characterize and describe these new aortic immune cells.

SPARK project results:

I first screened 16 organs of non-atherosclerotic mice and was able to confirm the presence of CD4CD8 cells not only in the thymus as expected, but also the mediastinal fat and the aortic arch.

Using state-of-the-art 3D whole mount fluorescence microscopy of tissue blocks containing the thymus, mediastinal fat, and the aortic arch I confirmed the presence of these cells in all three tissues. Interestingly, CD4CD8 cells in the arch were

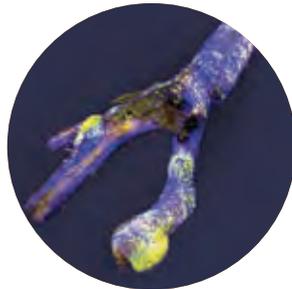
localized in clusters, whereas fat CD4CD8 cells were aligning along the vasculature in fat tissue. This points to an organization of these cells and argues against a random distribution. A significant amount of the SPARK award was used to gain further insight into the functionality and identity of these cells.

To do so, I isolated CD4CD8 cells from the thymus, mediastinal fat, and aortic arch by flow cytometry and subjected those cells to an extremely low input

sequencing protocol to assess their transcriptome. I could demonstrate that CD4CD8 cells isolated from the mediastinal fat and aortic arch could develop into functional T cells in a tissue culture experiment. However, in exploring their gene expression landscape, I found that extra-thymic CD4CD8 cells seem to be impaired in forming particular T cell responses. Further transcriptomic analysis revealed that extra-thymic CD4CD8 cells express factors, which are important for the maintenance of neurons. A functional innervation of the vasculature, among others, is essential to sense, integrate, and regulate blood pressure. Dysregulated blood pressure can lead to heart disease. Extra-thymic CD4CD8 cells might thus nurse nerves in vessels, a hypothesis I will test in future experiments.

What's next for this project?

The SPARK award was instrumental in obtaining preliminary data regarding the presence and function of extra-thymic CD4CD8 cells. Based on these findings, I will soon write a manuscript describing for the first time the presence of CD4CD8 cells outside of



the thymus. Future experiments will address how CD4CD8 cells leave the thymus to accumulate in mediastinal fat and the aortic arch, whether these cells occur in humans, how they survive in the extra-thymic environment and what their precise function *in vivo* is.

What's next for Holger:

Beginning in 2020, I will start my own group as a W2/Assistant Professor in the Cardiology Department of the Medical Faculty at the University of Cologne. The findings and data from this SPARK project will be the basis for an independent research grant proposal that I plan to submit to the German Research Council (DFG). With the follow-up grant I would like to study the functionality and escape mechanisms of these cells in my own research group. ✨

SPARK

IMPACT STATEMENT:

“The SPARK award helped me to gain valuable insights into these cells and set me on my path of academic independence. Exciting work lies ahead.”

FUNDED
JANUARY 2018

FUNDED BY
The generosity of San Diego Advisor
of the Year Awards Program

Development of a Diagnostic Test to Predict Disease Severity After Infection with Dengue Virus

Daniela Weiskopf, Ph.D.



What was the goal of your SPARK project?

Dengue virus (DENV) is the most significant mosquito-borne viral disease in humans. The virus, which actually has four serotypes or strains (DENV1-4), causes a wide spectrum of clinical disease ranging from asymptomatic infection, undifferentiated fever, to dengue fever and dengue hemorrhagic fever (DHF). Currently there is no vaccine or specific treatment available to prevent or treat dengue, which poses a serious risk since as many as 400 million dengue infections occur

worldwide annually, of which 96 million manifest clinically. The most serious reaction to dengue, DHF, occurs in a minority of patients and is characterized by bleeding and plasma leakage. Plasma leakage may lead to shock and can result in death if not managed appropriately in a timely fashion. Treatment is largely supportive in nature and relies on diagnosis by a highly trained physician. Interestingly, only a minority of patients will actually progress to severe dengue but

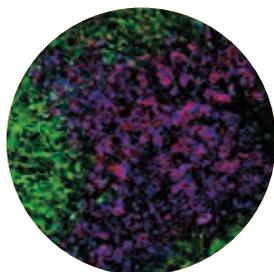
currently physicians are unable to identify those patients reliably, requiring careful attention to fluid management and proactive treatment of hemorrhage of most patients. To be able to predict plasma leakage on the basis of a simple blood test is thus a key issue in the study and management of dengue fever. My SPARK project aimed to collect preliminary data to support the development of a diagnostic test that can predict disease severity in dengue patients.

SPARK project results:

For my SPARK project, I studied blood samples from dengue patients with different disease severity outcomes and defined transcriptional profiles of genes that are up- or down-regulated in these individuals. Interestingly, we identified a panel of genes that clearly predicted the development of bleeding and plasma leakage in this patient subset. We are now in the process to further validate these genes in more detail in an independent study cohort as well as develop a diagnostic test based on establishing short DNA segments, so called primers, that can be used to amplify these genes of interest in basic clinical settings. This diagnostic test to assess genes associated with disease progression to plasma leakage has the potential to identify patients at risk for severe disease and will be invaluable in the management of dengue virus infection and associated clinical disease. Our findings are expected to make an important, innovative, and original contribution to advancing solutions relevant to military and public health and ultimately lead to an improved outcome for the general public.

What's next for this project?

I used the preliminary data that I was able to obtain thanks to my SPARK



award to submit an independent proposal “Cellular and transcriptional immunosignatures to predict development of plasma leakage in acute dengue infection” to the Accelerating Innovation in Military Medicine (AIMM) mechanism of the Department of Defense. Although it was favorably reviewed and received an excellent score, it was unfortunately not recommended for further funding. We used that feedback to amend the application, including adding new additional data from the independent cohort, which yielded inconclusive results after repeated sequencing. Currently, we are sequencing the third cohort as a “tie breaker”.

The amended application was resubmitted as an R21 application to the National Institutes of Health. Though the proposal was not chosen for funding, this was an invaluable experience for my career and professional development. These experiences have inspired continued grant applications and have reaffirmed my dream of having my own laboratory one day. ✨

SPARK

IMPACT STATEMENT:

“The SPARK program has an immediate impact on the research of young scientists like me. It empowered me to pursue my own ideas and helped to create enough preliminary data to seek additional independent funding—which is critical to advancing in a scientific career. The program also plays a vital role in supporting high-risk, high-reward projects like mine that might otherwise go unfunded.”

FUNDED
JANUARY 2018

FUNDED BY
The generosity of LJI Board
Member François Ferré
and Magda Marquet

Nanoparticles to Deliver Cancer Immunotherapy?

Yuan Lin, Ph.D.

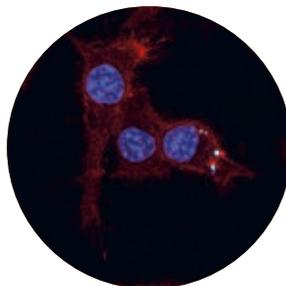


What was the goal of your SPARK project?

With solid tumor cancers, the challenge for the immune system is both to identify and then successfully attack the tumor. Recent cancer immunotherapies involving immune checkpoint inhibitors have had success in yanking away tumor cells' "invisibility cloak". However, one of the protective molecules deployed by tumors, adenosine, accumulates in such high concentrations that it can render the immunotherapy ineffective. This suggests that multiple immune suppression mechanisms co-exist and there might be a benefit to combining adenosine blockers (ARIs) with existing check-point immunotherapies. There are several ARI drugs in development, however the challenge remains to design a tool that delivers these drugs in a manner that allows them to counteract the high concentration of adenosine. This SPARK project was to determine if nanoparticles could be used as an effective delivery mechanism for ARIs.

SPARK project results:

For this project, we wanted to test our hypothesis that by using nanoparticles to deliver ARIs, we could more effectively deliver high amounts of ARIs to tumors to shrink and ultimately kill them. We used SPARK funding to combine a particular ARI (SCH58261) with a fluorescent dye and encapsulate them together in a biodegradable polymer to create drug-eluting



nanoparticles, which, once injected into a tumor, result in a slow, localized drug release. We then used fluorescence microscopy and flow cytometry to visualize the fluorescent dye first in cell culture to help determine which immune cells take up nanoparticles, and then *in vivo* in tumor-bearing mice to determine its effectiveness in reducing tumor size.

When we analyzed the uptake of nanoparticles in mouse immune cells and then human immune cells, we identified phagocytic macrophages as the primary target for nanoparticle uptake in both. We then moved on to investigating *in vivo* uptake of nanoparticles, and found that virtually all of the particles remained at the site of injection and that no fluorescence could be detected outside of the tumor, suggesting that intratumoral injection of nanoparticles could be used to localize drugs within tumors to improve potency and reduce toxicity. Further studies found that our ARI-loaded nanoparticles could more effectively reduce tumor size in mice.

What's next for this project?

The findings from this SPARK-funded experiment have great potential for clinical translation since encapsulation of ARI drugs into nanoparticles may prove to be safer and more effective than orally administered ARIs currently in clinical trials. The future work is to test more nanoparticles to find the best composition used for drug loading. I applied for a grant for follow-up studies with the National Institutes of Health as a result of the preliminary results from this project. ✨



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IMPACT STATEMENT:

“The SPARK award was critical because my research was stalled at an early stage and finding other support was very difficult. In the near future our goal is to develop a drug that can cure cancer.”

FUNDED
JANUARY 2018

FUNDED BY
The generosity of various
2017 SPARK Donors



Flaviviral Infections in Nepal

Melanie McCauley, M.D.

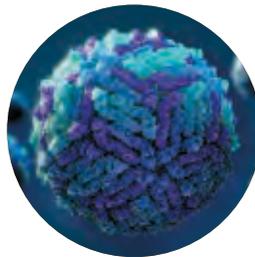
What was the goal of your SPARK project?

Dengue virus has circulated in tropical countries for decades. Now, the virus and its mosquito vector are moving into regions at higher elevations classically associated with cooler temperatures. This means millions more people are going to be at risk of this disease. As new populations of people become vulnerable to diseases like dengue virus for the first time, we have the opportunity to learn how a naïve immune system responds when an individual

is first infected. In addition, we wanted to compare viruses from two separate climactic regions within Nepal to elucidate any genomic differences that may give dengue virus a selective advantage at cooler climate regions. Our goal was to gain valuable data on the immune system's response to primary and secondary infection that could be used to design a safe vaccine for dengue.

SPARK project results:

In order to get started, it was crucial to bring much-needed supplies and training to our partners in Nepal so that we could strengthen our clinical research protocol and train new team members in experimental design and implementation to increase the accuracy and speed of our data collection. I used the SPARK funding to travel to Nepal for this critical stage and bring the much-needed supplies to make the sample collection a success.



I was also able to purchase and supply our collaborators in Nepal with electronic tablets that can securely store patient data and allow our team at La Jolla Institute to keep track of the collection in real time. While there, I trained the team to use these tablets; discussed procedures for the year's collection; and enrolled several patients who presented with suspected dengue illness in our study. One of the most important purchases the SPARK grant made possible was a

temperature-controlled multipurpose centrifuge, which is critical to study human blood samples and preserve cell lines that are crucial to the study of the immune response to dengue virus infection.

Another vital component to the study was providing access to very expensive diagnostic kits that help us look for dengue virus IgM antibody, IgG antibody and nonstructural protein 1 (NS1) antigens. SPARK funds allowed me to purchase enough kits to analyze banked samples from 2016 and 2017. These diagnostic studies allowed me to distinguish between patients who have no disease, a primary infection, or a secondary infection. We now know that 27 of our samples are positive for NS1, and from those we have isolated dengue virus and are planning to do full genome sequencing.

Further analysis of samples collected in Nepal demonstrated that people in Nepal exhibit immunity to one or multiple serotypes of dengue virus, supporting our hypothesis that these viruses are more widespread in the country than previously observed. We did not find evidence of Zika virus infections.

What's next for this project?

Information regarding circulating serotypes of both dengue and Zika virus give us valuable information

regarding how the human immune response is shaped as viruses become endemic in a country, which could help several countries, including the United States, be better equipped to help protect people from these viruses. Currently, we still have several samples from the 2018 data collection season in Nepal that we plan to analyze once additional funding is secured for this project. My colleagues and principal investigator, Dr. Sujan Shresta, continue to seek grants and private funds to build on this data collected from this SPARK project and support our lab's broader goal of developing a universal vaccine for dengue and Zika.

What's next for Melanie?

I recently finished my infectious diseases fellowship at UC San Diego and La Jolla Institute and accepted a permanent position as a Research Physician with The Henry M. Jackson Foundation for the Advancement of Military Medicine supporting the Emerging Infectious Disease Branch at Walter Reed Army Institute of Research in Bethesda, M.D.. In this role, I will continue to study neglected tropical diseases in resource-poor countries, working to improve local capacity and infrastructure by conducting large-scale clinical trials. ✨



SPARK

IMPACT STATEMENT:

“My SPARK award made it possible for me to gather and analyze patient samples in order to help us better understand the immune system's response when a naïve population has been newly introduced to dengue virus. In addition, it allowed me to directly help strengthen our collaboration with our partners in Nepal. In this way, the SPARK award will continue to have a positive ripple effect on our goal of understanding various aspects of the immune response as it pertains to vaccine development long after the conclusion of my project.”

FUNDED
FEBRUARY 2018

FUNDED BY
The generosity of LJI Board
Member Hunt Pettit and
Laura Pettit

CATHERINE CROSBY, PH.D.

Catherine 'Catie' Crosby, Ph.D., a SPARK Award winner in 2018, leveraged her experiences at the Institute, including with SPARK, to continue her career at a biopharmaceutical company in the fall of 2018. Being part of SPARK was an important stepping stone in her career, as it provided the opportunity to pursue and resourcefully communicate her independent research interests. Catie left LJI to take on her new job before completing her SPARK project, therefore her unused award funds were put back into the SPARK fund pool to be awarded in 2019.

The SPARK Award winners of 2019 made great progress in the first six months of pursuing their projects. The immediate impact of SPARK is already clear from novel research findings to critical career milestones for these ambitious researchers.

HUY DINH, PH.D.

Early findings by Huy Dinh, Ph.D., observed several important and cancer-related genes that are specific to cancer patients. This pilot data is instrumental in the application for potentially significant follow-on funding from the National Institutes of Health.

JULIE BUREL, PH.D.

Becoming a contributor to a novel field of research and achieving a major career milestone were already accomplished by Julie Burel, Ph.D., as her preliminary observations of immune cell complexes were published in the renowned journal *eLife*. She's made great progress in studying the sensitivity of commercially available testing kits for the clinical diagnosis of tuberculosis and dengue fever.

DAN GILES, PH.D.

An artificial intelligence solution with 90 percent accuracy was developed by Dan Giles, Ph.D., to determine how inflammatory bowel disease (IBD) patients may respond to a specific biologic treatment option. Working with clinical collaborators, Dan also used this algorithm to predict patient responses to another popular IBD drug. This could have notable impact on the over 1 million Americans afflicted with IBD, including Crohn's disease and ulcerative colitis, with limited and frequently ineffective treatment options.

SARA McARDLE, PH.D.

Sara McArdle, Ph.D., achieved highly specialized expertise in the recently developed super-resolution imaging technique, DNA-PAINT, to better understand the interactions between cancer cells and immune cells. This competitive expertise will have significant collateral impact at the Institute, as it will be applied to previously not possible analysis focused on a range of diseases.

MEHDI BENKAHLA, PH.D.

A novel discovery surfaced for Mehdi Benkahla, Ph.D., as preliminary data comparing type 1 diabetes (T1D) samples to non-diabetic control samples indicated that a viral protein, specifically the human herpesvirus-6 gB viral protein, is more expressed in the T1D samples. This finding may just be an important lead, as the triggers of T1D are still unknown, though lines of evidence suggest that environmental factors, such as viruses and genetic susceptibility both play important roles.

MARCO ORECCHIONI, PH.D.

A possible lead in heart disease research was identified by researcher Marco Orecchioni, Ph.D.. His preliminary data confirmed the importance of olfactory receptors in mediating the function of macrophages exposed to "Western-style" high fat diets. The data also confirmed that blocking olfactory receptors might be a promising target for drug development to prevent and treat atherosclerosis-based cardiovascular diseases, the leading cause of death worldwide. ✨

We hope this report on The Tullie and Rickey Families SPARK Awards for Innovations in Immunology has inspired you. We are excited to announce this year's finalists vying for a Tullie and Rickey Families SPARK Award. You can read more about their projects on our website at lji.org/donate/giving-opportunities/spark-program/ or by following us on Facebook or Instagram. This November we will be launching our 2019 fundraising campaign to help fund all of these transformative projects and we hope we can count on your support.



Abhijit Chakraborty, Ph.D.



Katia Faliti, Ph.D.



Sara Landeras
Bueno, Ph.D.



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