Making a Difference

MENDEZ NATIONAL INSTITUTE OF TRANSPLANTATION FOUNDATION
Dear friends,

Welcome to the latest edition of the MNITF magazine! As 2020 draws to a close, we look back on a year defined by a devastating global pandemic and civil unrest, the effects of which are still being felt. While looking back shines a light on many unforeseen challenges and the difficulties those challenges have brought, it also underscores the need to look forward, and to cultivate new and different ways to make things better. For this reason, our magazine’s theme is Making a Difference.

In this issue, we are excited to share how MNITF is making a difference in both research and education activities. Earlier this year, we opened up our Research Grant Program to help fund projects that are specifically related to COVID-19, and in September, the MNITF awarded two grants. One project explores creating a “pseudovirus” to dissect the effects of the coronavirus on the human immune system, and the other involves creating a “lung-on-a-chip” to explore how the coronavirus causes lung injury. Three of our Research Advisory Board members are involved in these projects.

MNITF is once again at the forefront of creating targeted education that directly addresses the needs of a vulnerable population. The prevalence of COVID-19 has further illuminated the significant racial and health-care disparities that exist for African-Americans, who are...
disproportionately affected by kidney disease. Following the success of the multi-award-winning digital series Fixing Paco, MNITF is now developing its next edutainment project, An African-American Family Story about Kidney Disease (working title). With so many people wanting to find a way to make a difference these days, we hope that you’ll consider becoming a Project Sponsor. You can learn all about this groundbreaking project and the fundraising campaign in this issue.

You’ll also get to read about the grant MNITF awarded to United Network for Organ Donation to help the transplant community better understand the role of biopsies on kidney transplant outcomes, in order to decrease the instance of donated organs being discarded instead of transplanted. In addition, you’ll be introduced to the work of Dr. Phillip Halloran, who recently joined MNITF’s Research Advisory Board. The recipient of three grants through the Research Grant Program, Dr. Halloran’s area of research focuses on changing care in lung transplantation by reading biopsies through measuring molecules, and interpreting the results using machine learning/artificial intelligence.

In other developments, we are excited to announce that Enrique Lopez has joined our Board of Directors. An accomplished finance and accounting professional and educator, Enrique also has had personal experience with family members suffering from kidney disease. You can read about Enrique and how he’s hoping to help advance MNITF’s mission, given his unique perspective.

As we focus our efforts on making a positive impact on even more lives during this trying time, we want to thank you for your ongoing support. With your help, we are making a difference. We hope you enjoy this issue!

Nicole Mendez
Executive Director

COVID-19 has had a devastating impact on society, and vulnerable populations continue to be most acutely affected. While individuals who suffer racial and economic disparities have been most heavily hit, those who suffer from organ failure or who are immunocompromised due to living with a transplant are also extremely vulnerable. The medical and scientific communities are racing to better understand the virus in hopes of finding a cure. There is an urgent need for the transplant field to investigate how the virus impacts the body, how to prevent organ injury, and how to ensure the ongoing health and well-being of transplant recipients.

As the rate of infection continues to surge at an alarming rate around the country, MNITF has been at the forefront of promoting research that can lead to solutions. Through its Research Grant Program (RGP), MNITF has recently funded two projects that target COVID-19 and its impact: SARS CoV-2-Pseudotyped Vectors for Immune Response Evaluation and Vaccine Development and Non-synthetic Lung-on-a-Chip COVID-19 Modeling Platform. The studies are progressing under the direct guidance of MNITF Research Advisory Board (RAB) members, who are dedicated to making a difference in the lives of those who are suffering.

Engineering a “Pseudovirus”

Dr. Nori Kasahara, of the University of California, San Francisco (UCSF), is a member of the MNITF RAB who has proposed engineering “pseudoviruses” that mimic the SARS-CoV-2 virus. SARS-CoV-2 is the virus that causes COVID-19 disease, and it requires highly specialized facilities with strict biosafety requirements for handling. “My usual research on gene therapy and immunotherapy involves reengineering viruses to serve as delivery vehicles to carry genetic material into cells. But what if we could create a virus-like particle that mimics SARS-CoV-2?” Kasahara said. “This would allow us to study the virus in a less specialized setting, which could greatly accelerate our understanding of how the virus works and how to fight it.”

The first project, SARS CoV-2-Pseudotyped Vectors for Immune Response Evaluation and Vaccine Development, will involve creating a vaccine that mimics the SARS-CoV-2 virus to test its effectiveness in protecting against the actual virus. The second project, Non-synthetic Lung-on-a-Chip COVID-19 Modeling Platform, will involve creating a lung model that can be used to test the effectiveness of potential treatments for COVID-19.

Through its Research Grant Program (RGP), MNITF has recently funded two projects that aim to advance our understanding of the COVID-19 pandemic. These projects represent just a small fraction of the research being conducted to find a cure for this devastating disease.

Daniel Cheng, Ph.D.
Noriyuki Kasahara, M.D., Ph.D.

MNITF Fast-Tracks Funding for Two Pivotal COVID-19 Studies
vehicles for therapeutic genes and to stimulate immune responses against cancer,” he said. “I wanted to find a way that my laboratory’s expertise and technology might be able to make some contribution to the global effort to fight this pandemic.”

The “pseudovirus” is a virus-like particle that is encased with the “spike” protein from the coronavirus. But the rest of the particle comes from a different virus, which is disabled by removing key elements of its genome so that it can no longer make copies of itself. Part of the disabled virus’s genome that is removed is then replaced by splicing in genes that make infected cells glow under UV light (this is called a “reporter gene”). The result is that the pseudovirus essentially mimics the real coronavirus, and is easily traceable, but it’s not harmful and is safe to use in the lab for testing and research.

Once engineered, the pseudoviruses can be safely used as a surrogate for the actual virus in most laboratory settings. These surrogate viruses can then be used to dissect the effects of SARS-CoV-2 on the immune system. In addition, having these pseudoviruses will allow a large-scale survey of the ability of antibodies from patient serum to functionally neutralize virus infection, or conversely, the potential for patient antibodies to enhance the infection of immune cells (a phenomenon previously reported in other virus infections, known as “antibody-dependent enhancement”). Dr. Kasahara and his team will also evaluate these pseudoviruses’ potential to serve as a unique vaccine platform. “People are succumbing to this disease every day, and we need to make progress quickly in developing better diagnostic tests, to improve our understanding of the disease, and to develop vaccines and therapies,” he said. “We hope to be able to better evaluate whether real immunity against the virus develops, either after a natural infection or after vaccination, or whether the virus can subvert the immune system to cause more serious disease, and to use this knowledge to develop better vaccines.”

The project may also provide insights into how viral infection might activate cytokine storm responses in some patients. Cytokines are proteins that are released in response to infection, and they act as signals that activate the immune system. However, sometimes the body overreacts, and too many of these cytokines are released, which hyperactivates the immune system and causes it to go haywire. This reaction is called a “cytokine storm,” and it can be life-threatening and even lethal. “There is still a critical lack of knowledge about how our immune systems can effectively fight this coronavirus. Some people can be infected but show no symptoms or only very mild symptoms. But even then, they may develop significant problems with their heart or lung function, or cognitive disorders,” Kasahara said. “Other people develop a severe disease that affects their lungs, and in many cases, also their kidneys and other organs, to the extent that it is lethal. We still don’t know whether these differences in the severity of the disease are because, in some cases, their immune systems are not reacting enough, or because they are reacting too strongly and causing a cytokine storm.”

It’s theorized that the coronavirus triggering a cytokine storm might be why some individuals have a more serious COVID-19 illness than others and why such responses contribute to life-threatening complications of COVID-19, including acute kidney injury (AKI). According to Kasahara, US/UK/EU studies report that 26-85% of ICU patients with COVID-19 develop AKI, and these patients show ~75% mortality rate, which is 5.3 times higher than COVID-19 patients without AKI. “So, overall, COVID-19 patients are at significant risk for AKI, and developing this complication appears to be a marker of the severity of COVID-19 infection. Mortality is higher for these patients, and even if they recover, 1 in 3 patients with COVID-19-related AKI continue to have low kidney function after discharge from the hospital,” he said.

The virus’s effect on kidney function could create a long-term impact on the field of transplantation. Not only are immunosuppressed kidney transplant recipients at high risk for infection with SARS-CoV-2, but the ongoing pandemic could result in increased numbers of patients who develop kidney injury and may eventually require dialysis and transplantation. “We believe that our study will have significant implications for our transplantation community. People with kidney disease and other medical conditions are at higher risk for more severe illnesses. And people who are on dialysis or post-transplant immunosuppression (i.e., anti-rejection medications) have weaker immune systems, making it harder for them to fight infections. Also, concerning the longer-term implications of AKI in COVID-19 patients, because their risk of developing chronic- and end-stage-kidney disease is higher, there is the possibility that more patients will need kidney transplants as a result of this pandemic,” said Kasahara. Accordingly, understanding how COVID-19 might affect the immune system is particularly important for the transplantation community. Developing new testing methods that contribute to assessing vaccination effectiveness and new vaccine technologies are critical steps.

By investigating the interactions of SARS-CoV-2 with the immune system, Dr. Kasahara and his team think it may be possible to identify targets for a therapeutic intervention to prevent or mitigate these consequences of COVID-19 in the future. Dr. Marek Nowicki, also a member of the MNITF RAB and a consultant on the project, echoes this belief. “Dr. Kasahara’s project is a valuable, multifaceted use of the pseudovirus model to evaluate response to the CoV-2 (neutralizing antibodies), test antivirals, and investigate the potentially harmful antibody-dependent enhancement of the CoV-2 infection potential. His project will increase our understanding of CoV-2 pathophysiology and enable us to design treatments that are uniquely tailored to the needs of solid organ recipients,” he said.

Having the opportunity to work on the pseudovirus project is exciting for Dr. Kasahara, and he’s grateful for the support of MNITF. “The most exciting thing to me is that thanks to this funding from MNITF, we are now in a position to contribute to the effort against this global pandemic, which has caused so much death and suffering worldwide and affects all of humanity,” he said. With MNITF’s support,
Dr. Kasahara believes that the best possible outcome would be if his team’s efforts lead to a better understanding of how COVID-19 affects the immune system, which may help illuminate better methods of treatment. If a broad-based vaccine platform can be developed that is useful against this coronavirus, there is the possibility that it could be deployed in future pandemics.

Creating a “Lung-on-a-Chip”

The MNITF Research Advisory Board (RAB) has a strong legacy of supporting young investigators’ career development to help continue innovating solutions and advancing the science and practice of transplantation. As the rate of COVID-19 infections rises in the U.S., supporting the groundbreaking work of this next generation of investigators has never been more critical. Dr. Daniel Cheng, of IVIVA Medical Inc., is one such investigator, and he works under Dr. Harald Ott, a member of the MNITF Research Advisory Board (RAB).

The ongoing and tragic COVID-19 pandemic has been a reminder of how vulnerable we are as individuals and as a society. SARS-CoV-2, the virus that causes COVID-19, has infected more than 50 million individuals worldwide to date and led to over 1 million deaths. SARS-CoV-2 causes a broad spectrum of disease manifestations ranging from mild cold symptoms to devastating organ failure, requiring transplantation. Despite all the global efforts that have been poured into COVID-19-related research to date, the scientific community still doesn’t understand the exact mechanism of injury.

One major gap in enabling studies of the effects of SARS-CoV-2 and discovering novel therapies is the lack of models of human lungs. Dr. Cheng’s project involves developing a viable model of human lung tissue on a chip to address this problem. A “lung-on-a-chip” is a miniaturized 3D cell culture system that recapitulates or mimics key aspects of lung function, and it can be used for the \textit{in vitro} (laboratory) study of cell biology. One of the significant benefits of such a system is to enable research on cells in a physiologically relevant context that is less expensive than animal studies and provides more accurate experimental conditions than traditional \textit{in vitro} methods. “Aspects such as cell type, vascular flow conditions, and soluble factors can be independently controlled in our engineered systems while simultaneously measuring cell responses in real-time,” said Cheng. “All of these factors are extremely complicated to control in humans or animals; thus, a lung-on-a-chip model enables the ability to study biological processes, as well as cell responses to therapeutic drugs or other stimuli, in a highly controlled yet physiologically relevant setting.”

Dr. Cheng and IVIVA will leverage their scaffold technology to build a model that allows for the simulation of critical steps of initial viral infection, immune response, and discovery, and the evaluation of treatment strategies. “At IVIVA Medical, we are developing fully biological scaffolds using emerging complementary technologies in tissue engineering, 3D additive manufacturing, and stem cell biology. We fabricate fully biologic scaffolds onto which live human cells can be seeded while providing the necessary conditions to stimulate key cellular functions,” Cheng said.

Although the mechanisms of SARS-CoV-2 infection are not yet well understood, the symptoms are synonymous with the disruption of the air-to-blood barrier in the lung across which air exchange occurs. Infected patients may show decreased blood oxygenation levels and a leakage of fluid from the blood vessels across the thin membrane and into the airway spaces. The lung-on-a-chip will utilize human-induced pluripotent stem cell (iPSC)-derived alveolar epithelial and endothelial cells to mimic real-world lungs as closely as possible and enable moderate throughput experiments on a small and resource-efficient scale. Induced pluripotent stem cells are human cells...
that can be derived from skin or blood cells and then reprogrammed into an embryonic-like state. These cells can then be cultured under specific protocols to differentiate them into other cell types, such as alveolar epithelial and endothelial cells. Alveolar epithelial cells are the cells that line the inner surface of an alveoli, where most of the air exchange in the lung occurs. Endothelial cells line the walls of blood vessels that are separated from the alveoli air compartment by a thin membrane across which air is exchanged.

Producing the lung-on-a-chip will be a crucial step forward in better understanding SARS-CoV-2 infection. “While most lung-on-a-chip devices to date have been constructed using synthetic polymers that may not accurately recapitulate the cellular environment, our lung-on-a-chip is entirely non-synthetic,” Cheng said. “We will populate our lung-on-a-chip with human-derived stem cells and measure functional lung outcomes such as oxygen transfer from an airway to a vascular channel network. After validating our system by comparing several functional lung metrics to native lung tissue, we plan to simulate viral infection of lung cells by SARS-CoV-2 in the system.”

Dr. Harald Ott, who has been consulting on the project, sees great promise in the study. “The current COVID-19 pandemic highlights the critical need for a broadly available, low-tech, affordable, scalable, and yet physiologically relevant platform to study the effects of viral infection on human airway epithelium and distal lung tissue,” he said. “With the help of MNITF funding, we will build a physiologically relevant 3D model to study SARS-CoV-2 infection. This model will enable the study of the direct effects of viral infections on lung tissue.”

Having the opportunity to support Dr. Cheng’s work on the lung-on-a-chip project has also been exciting for Dr. Ott. “Young investigators are our most valuable yet most vulnerable resource. Early-stage grants that are provided by the MNITF RAB help young investigators to bring novel and sometimes high-risk ideas closer to realization, and they play an important role in building early careers in research,” he said. “MNITF funding provides vital support at a stage too early for conventional funding mechanisms such as NIH or DOD grants.”

Dr. Cheng’s work at IVIVA Medical will also make a difference in the field of transplantation. “A long-term goal of our company is to develop artificial lab-grown organs for transplantation,” he said. “While developing a miniaturized lung-on-a-chip that maintains key lung functions such as gas exchange and blood flow, we will gain a great deal of knowledge that can later inform the development of larger functional tissues and organs.”

Putting It All Together

The next step for Dr. Cheng and IVIVA on the lung-on-a-chip project is to partner with Dr. Noriyuki Kasahara’s laboratory at UCSF to use genetically engineered forms of SARS-CoV-2 to learn more about the mechanism of injury and how the immune system contributes to the effects of the virus. “After developing and validating our lung-on-a-chip model, we hope to study SARS-CoV-2 infection in our system using the pseudovirus developed by Dr. Noriyuki Kasahara,” said Cheng. “This will be particularly relevant as vaccines emerge, and a large portion of the global population will develop an ‘immune memory’ of this disease.”

The partnership represents a powerful bridge of collaboration between RAB members and RGP recipients in their shared goal of understanding the impact of SARS-CoV-2. It’s also a meaningful fulfillment of MNITF’s mission to promote the work of young investigators. Dr. Cheng appreciates this unique opportunity. "We at IVIVA Medical are a small but energetic team," he said. "We are thankful and excited to generate impactful work with MNITF’s support.”

Scientific Registry of Transplant Recipients

<table>
<thead>
<tr>
<th>Race/Ethnicity</th>
<th>All Transplants</th>
<th>Deceased Donors</th>
<th>Living Donors</th>
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<tbody>
<tr>
<td>White</td>
<td>45.9%</td>
<td>38.2%</td>
<td>64.7%</td>
</tr>
<tr>
<td>Hispanic</td>
<td>18.1%</td>
<td>19.2%</td>
<td>15.3%</td>
</tr>
<tr>
<td>Black</td>
<td>26.9%</td>
<td>32.7%</td>
<td>12.5%</td>
</tr>
</tbody>
</table>


In the U.S., the African-American community suffers most disproportionately from kidney disease:

- **CHRONIC KIDNEY DISEASE IS 25% HIGHER THAN IN WHITES**
- **THEY ARE 10 TIMES MORE LIKELY TO DEVELOP HYPERTENSION-BASED KIDNEY FAILURE**
- **THEY ARE 3 TIMES MORE LIKELY TO PROGRESS TO KIDNEY FAILURE, AS COMPARED TO WHITES**

The health disparities that African-Americans face are caused by barriers to preventive care, higher rates of developing kidney disease, and lower access to optimal treatments including renal transplants from living donors. Additionally, the dual impact of COVID-19 and civil unrest has thrust these disparities into the national spotlight. As African-Americans’ struggle with ongoing racial inequalities has become illuminated, it has elevated the public awareness of their experience in an undeniable way.

Paramount to MNITF’s mission is finding ways to specifically address the unique needs of underserved communities, and to provide help, guidance, support, and education to individuals and families who are affected by kidney disease. In 2019, MNITF awarded Charles Drew University of Medicine and Science (CDU) a grant to conduct the Development of Media-Based Intervention to Increase African-Americans’ Use of Paired Kidney Transplant study. The study is Phase 1 of MNITF’s next edutainment project, An African-American Family Story About Kidney Disease (working title). Already in progress, the study is extremely timely, given current national circumstances.

As with MNITF’s multi-award-winning Fixing Paco series, An African-American Family Story About Kidney Disease will present transplant and living donation information using a fictional story about a family that is facing end-stage renal disease (ESRD). The project is unique in that scientific research will be used to guide, support, and educate individuals and families who are affected by kidney disease.
Two-Way Paired Kidney Exchange  Domino-Paired Donation


The goal of Phase 1 includes summarizing the current evidence on barriers and facilitators to care and the use of scripted narrative for film, television, and web-based media as a health intervention. This phase also involves engaging stakeholders, including paired donors and recipients, transplant care providers, content experts, and scripted narrative writers, in an effort to develop content that creates awareness and increases the participation of African-Americans in paired donation and donor chain efforts.

According to the Terasaki Institute for Biomedical Innovation, in 2018, in the U.S., 6,442 patients received a living donor kidney transplant (LDKT), and 4,004 patients died while waiting for a kidney from a deceased donor—nearly half of the patients who died were African American or Latinx. African-Americans continue to have a disparate amount of end-stage renal disease and a disproportionately longer time for having to stay on dialysis due to lack of successful kidney transplantation. Paired-kidney transplant donor exchange programs offer a unique opportunity to increase access to living donor in kidney transplants, which can in turn help reduce these inequities. The programs are also associated with better outcomes and a longer life for those who are currently on dialysis.

Leading the Phase 1 study at CDU is Dr. Roberto Vargas, who is hoping that a framework for a culturally sensitive and relevant narrative can be created that will help African-Americans better understand their care options. “Phase 1 will have several important outcomes. An authentic, reliable storyline will be more likely, as our project includes the input of themes from individuals who have actually gone through this process or been faced with these challenges as African-American patients or potential donors. Moreover, having stakeholders who are physicians, social workers, and researchers adds the perspective of what the system-level challenges are that the patient may not be aware of, which also contributes to African-American disparities in receiving kidney transplants,” said Vargas.

“Finally, having the involvement of those who develop and produce scripted narrative content provides insight into the process of developing media content that may inform strategies for targeted messaging. When this all comes together, we will have not only a compelling story, but hopefully, an effective educational product.”

Phase 1 will also determine if a digital series or a feature-length film is the most effective format for communicating the vital health information of the project.

With Phase 1 scheduled to be complete by the end of 2020, MNITF is poised to begin Phase 2 in early 2021. Phase 2 goals include script development based on data from Phase 1, focused on relevant themes for African-Americans. A focus group review of the script will be conducted before it is finalized to ensure that the characters, storyline, and messaging are specifically targeted, relatable, educationally appropriate, and provide clear examples of how patients can be proactive with their health. Phase 2 will culminate with producing and completing the series or film.

Phase 3, planned as a post-study, is targeted for 2022 and will involve conducting a scientific study to determine the effectiveness of using an entertainment format to educate about health issues, specifically kidney transplantation and organ donation. In addition, Phase 3 will seek to determine if An African-American Family Story about Kidney Disease is successful in reaching out to the African-American population, to
kidney patients and their families, and to the general population. “Our ability to communicate messages to change behavior is one of the most rapidly changing aspects of modern society. The advent of social media and the ability to connect to the internet through the use of handheld devices and streaming services have made scripted narrative content ubiquitous,” said Vargas, when asked about the need for a post-study on the project. “If we are really interested in changing behavior to improve health, every available modality should be considered.”

Producing An African-American Family Story about Kidney Disease is an exciting next step for MNITF and a logical progression in its mission to serve the transplant community, address disparities, and develop non-biased content that can make a difference. “I’ve wanted to create a project that specifically targets the needs of the African-American population since we finished the Fixing Paco series eight years ago,” said Nicole Mendez, MNITF’s Executive Director. “No one could have predicted how the events of 2020 would unfold, especially when it comes to the racial inequalities and health-care disparities that are coming into national awareness, as never before, for African-Americans. It’s exciting to think that we can create an edutainment project that has the potential to reach and help so many, including those in other communities. There’s never been a more perfect time, and it’s truly time to tell this story.”

YOU CAN MAKE A DIFFERENCE!

Currently in development, An African-American Family Story about Kidney Disease will tell the relatable, culturally relevant story of a family struggling with kidney disease. It will also provide targeted education that is desperately needed and long overdue. We hope that you will help us take immediate action in addressing the significant racial and health care disparities that exist within the African-American population, and consider becoming a Sponsor.

IT’S TIME TO TAKE ACTION.

African-Americans have a prevalence of chronic kidney disease that is 25% higher than whites, and they are 10 times more likely to develop hypertension-related kidney failure and 3 times more likely to develop kidney failure. COVID-19 has further exposed the significant health-care disparities that exist within this population.

IT’S TIME TO MEET THE NEED.

Phase 1 brought together stakeholders, including African-Americans who have received kidney transplants, kidney donors, entertainment professionals, physicians, nurses, social workers, and researchers, to provide perspectives on developing a culturally-sensitive story line about kidney transplantation with relatable characters. Using a Delphi method process, the group identified key themes they felt would improve patients’, donors’, families’, and caregivers’ understanding of the personal and system-level challenges that contribute to African-American disparities in receiving kidney transplants and how to overcome them.

IT’S TIME TO TELL THE STORY.

In 2012, MNITF broke new ground when it launched the multi-award-winning Fixing Paco edutainment series in response to the alarming rates of kidney disease in the Hispanic population. In Phase 2, MNITF will apply its proven track record of creating compelling, engaging, non-biased content to writing and completing production on An African-American Family Story About Kidney Disease. To watch Fixing Paco, visit www.FixingPaco.org.

IT’S TIME TO SHARE WHAT WORKS.

The ability to communicate messages to change behavior is one of the most rapidly changing aspects of modern society, and every available modality should be considered when it comes to improving health. To this end, Phase 3 will be a post-study to measure the effectiveness of An African-American Family Story About Kidney Disease as an intervention in helping African-Americans who are affected by kidney disease to access transplantation and be proactive in improving their health.

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COMING SOON!
AN AFRICAN-AMERICAN FAMILY STORY
ABOUT KIDNEY DISEASE (WORKING TITLE)

Sponsorship Levels

☐ EXECUTIVE PRODUCER (maximum of 4) $100,000
Credit as Executive Producer (EP) in opening and end credits of film; EP credit on IMDb, the world’s most popular Film, TV, and celebrity content site; EP credit on MNITF’s websites and in newsletter; lunch on set; and invitation to wrap party

☐ CONTRIBUTING PRODUCER (maximum of 6) $50,000
Credit as Contributing Producer (CP) in opening and end credits of film; CP credit on MNITF’s websites and in newsletter; lunch on set; and invitation to wrap party

☐ ASSOCIATE PRODUCER (maximum of 8) $25,000
Credit as Associate Producer (AP) in end credits of film; AP credit on MNITF’s websites and in newsletter; and invitation to wrap party

☐ CAMEO SPEAKING ROLE (maximum of 2; one line for each) $10,000
Character credit in end credits of film; listed as a Featured Contributor on MNITF’s websites and in newsletter; and invitation to wrap party

☐ WALK-ON ROLE (maximum of 2; no lines) $7,500
Listed as a Contributor in end credits of film; listed as a Contributor on MNITF’s websites and in newsletter; and invitation to wrap party

☐ CONTRIBUTOR $10,000–$1,000
Listed as a Contributor in end credits of film; listed as a Contributor on MNITF’s websites and in newsletter

Sponsorship Levels: Your contribution will go directly to the production of An African-American Family Story About Kidney Disease (working title), an edutainment project that will provide information to the public about kidney transplantation, living donation, and kidney disease prevention. Your contribution is considered a sponsorship only, and there will be no involvement with actual production. Film production is expected to be complete in 2021. All contributions are tax-deductible to the full extent of the law; please discuss with your accountant or tax professional. (501c3, Tax ID #95-445-0030)

For more information please contact Nicole Mendez at 424.358.4450

Mendez National Institute of Transplantation Foundation

SAFE, PRECISE, & SAVING LIVES

MNITF’s Newest Research Advisory Board Member Develops a Groundbreaking System for Improving Clinical Decisions in Lung Biopsies

The gift of transplantation is life-changing, and it can be a new beginning for transplant recipients. But the work of living with a transplant and sustaining an improved state of health creates another new life for the recipient, one that involves an ongoing commitment to managing the risk of organ rejection through the use of medication, in addition to being closely monitored for signs of rejection.

Improving the lives of transplant recipients and supporting groundbreaking approaches in the field of transplantation is the primary goal of the MNITF Research Advisory Board (RAB). Since its inception, the RAB has been dedicated to advancing research that directly impacts the health and well-being of those who suffer from organ failure and need a transplant. As the RAB works to promote even more research that can lead to solutions in the transplant field, they are excited to announce the addition of their newest member, Dr. Phillip Halloran, who has devoted his career to researching innovative methods for accurately diagnosing and preventing transplant rejection and organ injury.

Dr. Halloran, a Distinguished Professor of Medicine at the University of Alberta, Canada, and the Muttart Chair in Clinical Immunology, felt drawn to the field of transplantation early in his career. “As a young physician, I was eager to deliver new hope to extremely ill patients with organ diseases, and transplantation offered the most opportunity,” he said. “In many ways, it still has that potential.” Dr. Halloran’s research has focused on the molecular phenotype of organ transplant rejection and organ injury (measuring the molecules that change in disease states and interpreting and classifying those diseases in new ways) to create diagnostic systems to transform care. He has published 355 original peer-reviewed papers throughout his career and has trained many fellows who are now on
Not only does this method pose the risk of serious complications for patients, but TBB pathology assessments have poor reproducibility (the results from repeated tests often don’t match), and they can’t assess antibody-mediated rejection. Sometimes, all pieces of the TBB tissue are not assessed and the tissue is dangerous to biopsy and very difficult to interpret the results using machine learning/artificial intelligence. To this end, Dr. Halloran’s team has established and validated a new system for reading biopsies through measuring molecules, and interpreting the results by their ability to stick to tiny squares on a silicon chip (a microarray, similar in some ways to a computer chip). This generates 50,000 measurements, and we have developed computer algorithms to turn those numbers into reports, which we send back to the patient’s doctor.”

"We take a tiny piece of a biopsy and stabilize it to protect the "messages," the messenger RNA (mRNA). There are tens of thousands of different mRNAs, and they change in diseases," said Halloran. “We label them and read them by their ability to stick to tiny squares on a silicon chip. This generates 50,000 measurements, and we have developed computer algorithms to turn those numbers into reports, which we send back to the patient’s doctor.”

The MMDx, when fully developed, will be able to diagnose rejection more accurately and with more reproducibility than pathology, and it will greatly improve patient safety. Dr. Halloran and his team have also found that MMDx has promise for assessing MBs, and it offers an even greater improvement in safety, especially for sickest patients. “Lung tissue is dangerous to biopsy and very difficult to read by histology [tissue organization or structure]." MMDx can read rejection in lung tissue with fewer requirements for dangerous bites of the tissue, and it can also read tissue from sites that are safer to biopsy, like the bronchus. MMDx offers safety as well as precision,” said Halloran.

The 2020 grant from the MNITF RGP has opened the doorway for phase 3 of the MMDx project’s mission, which is changing care in lung transplantation by reading biopsies through measuring molecules, and interpreting the results using machine learning/artificial intelligence. To this end, Dr. Halloran’s team has established and validated a new system for reading biopsies that is safer, more precise, and more accurate than current tests. “MMDx offers a new look at biopsies that is changing the whole way we classify the diseases and a far more accurate and precise basis for making clinical decisions. But it is also helping to develop new treatments,” Halloran said. “Our goal is not just to recognize problems, but to find new ways of fixing them based on the molecular changes in the tissue.” In phase 3, the work is to define the clinical meaning for doctors who are using the new tests and monitor the tests’ ability to predict future events.

In the future, the focus will be on making MMDx biopsy assessments available to patients whose transplants have problems, all over the world. Dr. Halloran’s group has already licensed the system to the One Lambda division of Thermo Fisher Scientific, which will allow transplant centers everywhere to benefit from changing patient care through MMDx. “MMDx joins many other molecular initiatives to make clinical assessments less dependent on human opinion and more precise and accurate as a basis for clinical decisions,” said Halloran. "It adds a dimension that will help us to understand troubles in transplants and deliver better care by giving exactly the right treatments with less guesswork. Understanding the molecular changes in human disease is really the best basis for making progress in medicine—progress we all need to stay healthy and fight diseases."

Dr. Halloran is grateful for MNITF’s ongoing support of his research, and he welcomes the opportunity to join the RAB and help MNITF make a difference in the science and practice of transplantation. “I will most enjoy seeing new initiatives that address important questions and helping to see that these are recognized and supported, possibly with suggestions for enhancements,” he said. “Getting to work with the other RAB members will be very enjoyable. . . . MNITF follows a pathway that allows researchers to explore potential funding with a minimum of wasted effort, compared to the low success rate of other agencies . . . It is a very well-run organization.”

Dr. Halloran and his team at Alberta Transplant Applied Genomics Centre
Researchers aim to address the gap in scientific knowledge about the association between kidney biopsy results and transplant survival outcomes.

By Anne Dreyfuss
Corporate communications strategist,
United Network for Organ Sharing

The Mendez National Institute of Transplantation Foundation recently awarded a $100,000 grant to United Network for Organ Sharing researchers to help the transplant community better understand the role of biopsies on organ transplant outcomes. The research further aims to improve the tools that inform kidney offer acceptance decisions.

A kidney biopsy is often taken after a kidney is recovered from a deceased donor to help transplant surgeons assess the organ’s quality and predict how well the organ will function once transplanted. “The results of biopsies have significant measurement error and the degree to which biopsy findings affect how well the organ will do after transplant remains unclear,” said UNOS principal research scientist Darren Stewart.

With support from the grant, Stewart will partner with co-investigators Gaurav Gupta, M.D., and Layla Kamal, M.D., both from Virginia Commonwealth University School of Medicine to clarify the associations between kidney-specific prognostic markers and long-term, post-transplant outcomes. Through their research, the researchers aim to ultimately reduce the national kidney discard rate. Stewart and UNOS colleagues will lead the research and statistical analysis, while the VCU co-investigators will provide clinical guidance and data analysis support.

The work was motivated by a UNOS Labs project in which researchers studied the role of biopsies in decision-making.

“We hope that our collaborative research efforts can help in reducing kidney discard and optimize the kidney allocation process to benefit patients with kidney failure,” Gupta said.

An atmosphere of uncertainty

A January 2019 report by the National Kidney Foundation found that the number of kidneys procured only to later be discarded prior to organ transplantation had risen to 20 percent. The report, which was led by MedStar Georgetown Transplant Institute director of kidney and pancreas transplantation and UNOS Board of Directors president-elect Matthew Cooper, M.D., published in the journal Clinical Transplantation, the Journal of Clinical and Translational Research. According...
to the National Kidney Foundation, approximately 12 people die each day waiting for a kidney transplant, while about ten kidneys are discarded daily.

“Every year, hundreds of kidneys are discarded that were potentially usable and could have extended the lives of our kidney failure patients,” said Gupta, who practices transplant nephrology at the VCU Health Hume-Lee Transplant Center.

Biopsy findings are often cited by transplant surgeons as the reason for kidney discards. “Kidney biopsies appear to be a strong driver of non-usage of transplant-quality kidneys due to concerns—perhaps overstated or not fully justified—about the association between biopsy findings and transplant outcomes,” Stewart said. “Decisions are being made about whether or not to transplant kidneys in an atmosphere of uncertainty. We aim to reduce that uncertainty by studying biopsies and transplant outcomes in new ways through a large-scale study that will help address this significant knowledge gap.”

Improving survival outcomes by reducing uncertainty

The research involves collecting and analyzing kidney biopsy data as it relates to long-term survival rates, as well as conducting a kidney offer simulation study to examine behavioral effects of sharing biopsy results and other kidney prognostic markers in new ways.

“Current decision-making tools, such as the kidney donor profile index, are incomplete because they don’t take into account organ-specific parameters such as biopsy results,” Stewart said, adding that the incomplete decision-making tools may compel transplant surgeons to rely more on subjective viewpoints. “Some people in the transplant community feel that biopsies, despite the measurement uncertainty and inconsistent association with outcomes in the literature, are valid reasons by themselves for turning down a kidney offer, while others firmly insist that we should do away with biopsies altogether, reasoning that they’re not needed for decision-making and they do more harm than good.”

Stewart and his research colleagues postulate that more information has the potential to be better than less, “but only if it is used appropriately to make sound decisions,” he said. “If biopsies are going to be referenced during the organ offer process, we should work to improve the way they are used for decision-making by better understanding how they influence patient outcomes and integrating results into decision-making tools.”

A legacy of improving kidney utilization

The Mendez National Institute of Transplantation Foundation was founded as part of the vision of Robert Mendez, M.D., and Rafael Mendez, M.D., who are twin brothers and transplant surgeon pioneers. The pair led the kidney transplant program at St. Vincent’s Medical Center in Los Angeles for more than 35 years.

“Throughout their careers, both Drs. Rafael and Robert Mendez were focused on exploring ways to reduce the organ shortage by utilizing organs that were previously not used in an effort to decrease the long wait times and number of deaths of people waiting for a lifesaving organ,” said MNITF executive director Nicole Mendez. Her uncle, Robert Mendez, served as president of the UNOS Board of Directors in 1991 and has served on numerous Organ Procurement and Transplantation Network committees since 1987, including the Ad Hoc International Relations Committee, the Executive Committee and the Membership and Professional Standards Committee.

“This is an important and timely study that aims to evaluate the impact of biopsy findings on kidney utilization versus discard rates, and aims to discern if biopsy findings might correlate with patient outcomes after transplantation,” said Noriyuki Kasahara, M.D., Ph.D., who is a professor of neurological surgery at University of California, San Francisco and a MNITF research advisory board member. “New insights derived from this study could even be incorporated into the development of metrics, like the kidney donor risk index score, to predict and improve transplantation outcomes. This would have significant impact for the field of transplantation.”
The MNITF is excited to announce the appointment of Enrique Lopez to its Board of Directors (BoD). With more than 25 years of experience in leading restaurant finance and field operations teams at Pizza Hut, Panda Restaurant Group, and Porto’s Bakery & Cafés, Enrique is an accomplished finance and accounting professional who is also the founder of Elo Restaurant Advisors, a restaurant consulting practice focused on providing fractional CFO, operations, and analytical support services to growing restaurant concepts. In addition, he is a Professor of Accounting at Santa Monica College, where he is entering his second year of a five-year tenure track, and he looks forward to sharing his distinguished skillset with MNITF in its next phase of growth and beyond. “I hope that my diverse leadership experience in accounting and financial roles across varied industries can help bring valuable insights into furthering our mission in a more impactful, funds-effective manner,” he said.

Enrique also has a personal connection to MNITF and its mission of helping others. After receiving a bachelor’s degree in accounting, with honors distinction, from California State University, Northridge, he attended the Stanford University Graduate School of Business, where he earned a master’s degree in business administration. It was during his time at Stanford that he met fellow classmate Justin Dooley, MNITF’s Chairman, and the two eventually became united by their mutual commitment to helping others. “Enrique and I were classmates when the LA riots happened in 1992, and he organized a group to go down and help. I joined Enrique, and that’s where we got to know each other well, through living and working together, 24/7,” said Dooley. “We not only met people on the street but also the Mayor. We used our expertise and connections to help get financial aid to the local businesses that had been destroyed. So, our relationship started with volunteering, and it continues on to this day.”

A spirit of volunteerism has led Enrique to participate in many other community activities, including the Riordan Programs at UCLA, which provide a range of leadership and management training to diverse individuals all over the country. The programs include the Scholars Program, the College to Career Program, and the MBA Fellows Program, and they work to develop tomorrow’s leaders by providing a transformational experience through the use of mentors, educational workshops, and community service. An alumnus of the program, Enrique serves as a mentor in the College to Career Program as well as a coach in the Stock Market Competition for the Scholars Program.

Other volunteer posts include being involved in the Hispanic Scholarship Fund as a student mentor at youth leadership conferences and serving as a scholarship reader. He is also a youth business alliance speaker at inner-city high schools and represents his alma mater Stanford as a volunteer at Homeboy Industries.

But it’s Enrique’s family connection to kidney disease that gives him a profoundly unique perspective as a member of the BoD. Married to Grace Lopez, an elementary school teacher, he has two grown children, and his entire family has had the painful experience of watching loved ones suffer. “Unfortunately, we have been impacted by two cases of kidney failure,” he said. “My wife’s cousin was diagnosed with diabetes as a teenager. It steadily worsened over the years, and we watched her struggle with trying to lead a normal life. She was unable to get a transplant, and at the age of 33, she lost her battle and died of kidney failure, leaving a husband and two boys. I also have a brother-in-law who received a kidney transplant a few years ago, and he continues to maintain his medical regime, but he has lost sight in his right eye and is losing vision in his left eye.”

Having the opportunity to continue making a difference in the community while blending his professional expertise with his personal experience of kidney disease makes his new role with the BoD an exciting venture for Enrique. “Being a part of a tenured group of dedicated board members who have a servant’s heart in seeking to better the lives of those with dire medical needs is something I look forward to,” he said. “No doubt, the mission is personal to me as kidney disease has impacted my family, and this makes my involvement much more fulfilling. I am humbled and honored to be joining the board, and I thank Justin, Nicole Mendez, and the other board members for their support. I look forward to learning more about the awesome things that are being done to better the lives of others.”

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Research Grant Program Awards 34 Grants

In December 2014, MNITF launched the Research Grant Program and awarded four grants during its first cycle. To date, MNITF has awarded 34 grants, both nationally and internationally, surpassing $2.5 million.

“This program continues to seek and inspire the transplant community and improve the quality of transplant medical practice in an effort to help organ transplant recipients live better lives,” said Claudia Chincilla-Reyes, a member of the MNITF Research Advisory Board (RAB). The RAB is comprised of senior investigators and experts in transplantation research who review the grant proposals and provide recommendations to the MNITF Board of Directors, who then make the final decision on awarding each grant. Due to the number and high quality of submitted proposals, the Board has awarded more than the budgeted amount from the Endowment. Contributions to the MNITF from supporters have made this possible.

WAYS TO GIVE

The Gift of Making a Difference

You can be an important part of continuing the mission of MNITF and helping to save and improve the lives of so many. Financial giving to MNITF creates unique opportunities for us to devote necessary resources to further advancing research and education. Below is a list of ways that you, your family, and friends can help keep the flame of hope alive for potential transplant recipients.

Gift of Cash

This is the simplest and most common type of support. You can make a one-time gift, monthly payments, or pledge to donate over a one- to five-year period.

Life Income Gifts

Donating a no longer needed policy entitles you to an immediate tax deduction for the policy’s current cash value. This applies to whole life and term life insurance policies.

Life Insurance

The most common type of life income gifts are charitable gift annuities and charitable remainder trusts.

Directed Giving

With a planned giving strategy, you can earmark your contribution for any area of MNITF’s work that you choose, including the Research Grant Program and Education projects.

Senior Investigator

15 51.7%

Junior Investigator

14 48.3%

The MNITF website (www.MNITF.org) allows you to donate with a credit card by clicking on “Donate” near the bottom of the homepage. If you would like to discuss giving, please contact Nicole Mendez, Executive Director, at (424) 358-4450 or via email at Nicole@MNITF.org.
WANT TO MAKE A DIFFERENCE IN THE LIFE OF SOMEONE WHO IS SUFFERING FROM KIDNEY DISEASE OR KIDNEY FAILURE?

1. Text the word KIDNEY to 21000 to make a tax-deductible donation of any amount to MNITF!

2. Go to MNITF.org and click on the DONATE tab!

Your generosity makes our work possible!

WANT TO GO GREEN?
Visit MNITF.org and register to receive the Newsletter by email, www.MNITF.org/newsletter/newsletter-sign-up/