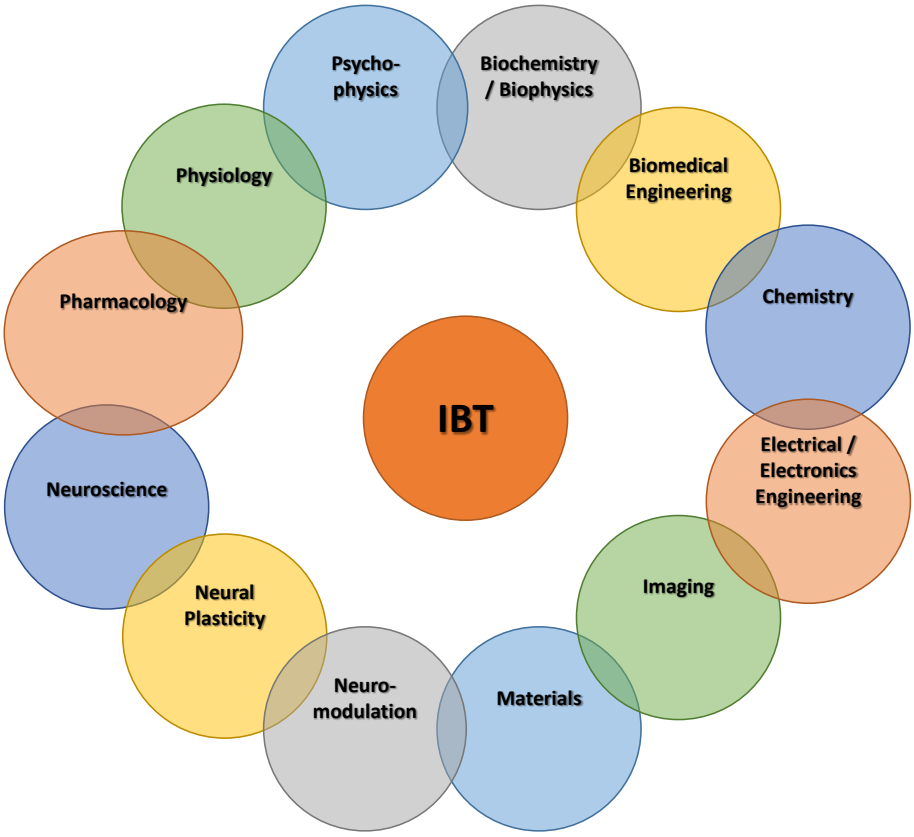
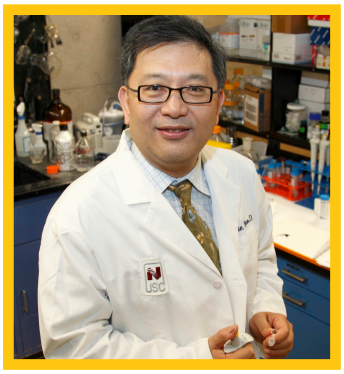
NEWSLETTER NOVEMBER 2020

USC Ginsburg Institute for Biomedical Therapeutics

Demonstrating the Power of Interdisciplinary Research



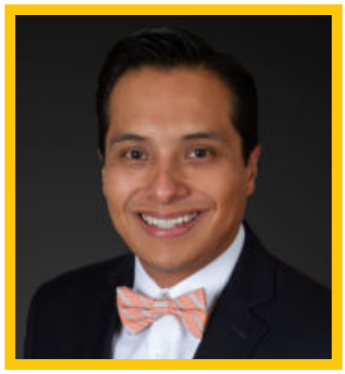
USC Ginsburg Institute for Biomedical Therapeutics in partnership with the USC School of Pharmacy and the USC Institute for Technology and Medical Systems Innovation submit for Foundation Fighting Blindness Funding.



Stan Louie, PharmD

Mark Humayun, MD, PhD

Isaac Asante, PhD



Juan Carlos Martinez, MD

Principal Investigator, Professor of Pharmacy, and Deputy Director of the USC Ginsburg Institute for Biomedical Therapeutics (GIBT), Stan Louie, PharmD, recently submitted an interdisciplinary proposal to the Foundation Fighting Blindness to move an exciting compound, EMX151, closer to patient impact. Co-investigators on this important project include GIBT director Mark Humayun, MD, PhD and GIBT members Isaac Asante, PhD, and Juan Carlos Martinez, MD.

Retinitis pigmentosa (RP) is an inherited eye condition that can lead to blindness. Over 60 genes and 200 mutations have been associated with RP. Despite these genetic differences, recent scientific advances have shown increased ocular inflammation plays an important role in promoting RP progression.

Normally, inflammation is self-limiting, where the affected tissue returns to the pre-inflammatory state, which is called "homeostasis." However, in RP, the ocular inflammation is persistent, progressive, and can lead to photoreceptor injury and ultimately blindness. Humans produce a lipid molecule called "Lipoxin" which plays a vital role in reducing chronic inflammation and restoring the affected tissue back to homeostasis. This suggests that lipoxin may be a potential treatment for diseases like RP. However, lipoxin is quickly removed by the body and therefore is not a good drug candidate. Our team has developed a chemical that retains the important biological activity(ies) similar to lipoxin, but is not removed quickly by the body, and is therefore capable of promoting restoration to homeostasis. This compound, called EMX151, is able to eliminate Neutrophils, a white blood cell that

activates and sustains inflammation. EMX151 is also able to activate macrophages, another type of white blood cell that eliminates neutrophils and therefore reduces the pro-inflammatory source.

In addition to reducing inflammation associated with neutrophils, we tested EMX151 in preclinical models of RP, where it was able to preserve photoreceptors and their function. Building on these exciting findings, this study proposes to 1) determine the safety of EMX151, 2) identify the EMX151 dose needed to maximally preserve the highest number of and greatest function of photoreceptors, and 3) determine how EMX151 exerts its pharmacologic activity. If our team is successful, we will submit an application to the FDA to start first in-human studies. Our hope is that EMX151 is able to delay and/or prevent vision loss and blindness in patients with RP.

Ocular persistent inflammation is not restricted to RP and has been implicated in other retinal diseases, such as age-related macular degeneration (AMD) and proliferative diabetic retinopathy (PDR). Similar to what is seen in RP, ocular inflammation in other eye diseases is related to the presence of neutrophils that has localized in the blood vessels of the affected eyes. These neutrophils can stick onto the blood vessel walls, thereby stimulating and sustaining ocular inflammation that can cause photoreceptor injury. Since EMX151 can reduce ocular inflammation, which corresponds to preservation of photoreceptors, EMX151 may also be useful for these eye conditions. The data from this proposal may give further insights as to whether EMX151 can also benefit these diseases.

The FFB TRAP III funding will allow our team to develop EMX151, where our next step will be to apply for FDA approval for an investigator new drug (IND) application. This will allow our team to test EMX151 in humans and ultimately deliver this treatment to patients with RP. With the FFB support, we anticipate the development to start human studies in three years, which will accelerate a new therapy for patients with RP for whom there is no cure for the foreseeable future.

USC GINSBURG INSTITUTE FOR BIOMEDICAL THERAPEUTICS AWARDS INAUGURAL MORDECHAI "MORT" ARDITTI AWARD FOR EXCELLENCE

On November 20, 2020, the USC Dr. Allen and Charlotte Ginsburg Institute for Biomedical Therapeutics awarded its inaugural Mordechai "Mort" Arditti Award for Excellence to Alejandra Gonzalez-Calle, PhD, a postdoctoral researcher working to develop vision science innovations at the USC Ginsburg Institute. Gonzalez-Calle grew up in Medellín, Colombia, and earned a BS in biomedical engineering at La Escuela de Ingenieria de Antioquia. As an undergraduate student, she planned to dedicate her career to developing affordable prosthetic limbs. After an accident that caused her to lose vision in her right eye, however, she redirected her energy toward advancing the field of vision science.

In 2009, Gonzalez-Calle reached out to Mark Humayun, MD, PhD, with the hope that she could pursue a research internship at his team's USC lab. Humayun and his colleagues had an impressive record of churning out engineering-based solutions to address the biological anomalies causing vision loss, and Gonzalez-Calle aspired to join the ranks of this innovative team. That internship ultimately blossomed into over a decade and counting of collaboratively pioneering interdisciplinary, translational approaches to address some of the most confounding challenges in vision science. During that time, Gonzalez-Calle received one of the USC Viterbi School of

> ***"He was such a special person for all of us. Besides being a mentor, Mort was also a friend to all the PhD students. I'm grateful to receive this award."***
>
> ~ Alejandra Gonzalez-Calle

Engineering's highest research awards to support her pursuit of a master's degree in biomedical engineering, and she later went on to earn a PhD in biomedical engineering in 2017.

Some of Gonzalez-Calle's most meaningful experiences working with the USC Ginsburg Institute team include fine-tuning the Argus II retinal prosthesis to restore eyesight to patients suffering from complete retinal blindness and contributing to the development of a novel stem cell-based retinal implant for patients with AMD. Recently, she worked with a multidisciplinary team that was able to demonstrate, for the first time, that noninvasive electrical stimulation could be used to slow retinal degeneration in pre-clinical models.

Throughout the years spent working on these remarkable feats in biomedical engineering, Gonzalez-Calle has remained continuously inspired by seeing how the projects to which she has contributed can tangibly enhance patients' lives. "Being able to see our projects evolve from the basic research stage to the point where they are implanted in patients, and then ultimately seeing how much of a difference these interventions can make in patients' lives, is what makes me so passionate about what I'm doing," Gonzalez-Calle says.

Receiving the inaugural Mordechai Arditti Award for Excellence carries special meaning for Gonzalez-Calle due to the fact that the late Arditti was an important mentor of hers throughout her training. Arditti, an electrical engineer by training, often contributed to and enhanced Gonzalez-Calle's projects by helping to build circuits and essential electrical components of the biomedical devices on which Gonzalez-Calle worked. "He was such a special person for all of us," Gonzalez-Calle remembers. "Besides being a mentor, he was also a friend to all the PhD students. I'm very grateful to receive this award and to feel like it's coming from him, even though he's not here with us anymore."

USC Virtual Symposium

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4 Sessions - 20 Expert Presenters - Poster Session

Jan. 21-22, 2021 • 7:00-11:30am PST

Registration & Info: ibt.usc.edu/symposium

National Eye Institute
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USC Ginsburg Institute for Biomedical Therapeutics

The *Super Doctors* list will be published in *Super Doctors Southern California Magazine*, delivered in January with the Los Angeles Times, and will also be available online at

www.superdoctors.com.