# 2020 SUMMER UPDATES CENTER FOR NEUROREGENERATION

**DEPARTMENT OF NEUROSURGERY** 

# **MISSION STATEMENT:**

Our mission is to generate therapies for people who suffer from chronic paralysis and neurologic loss due to devastating injury, stroke, or degenerative disease.

The Center for
Neuroregeneration focuses on
collaborative problem solving
and bioengineering
approaches that are incubated
not only within our research
laboratories, but also through
strategic partnerships with
clinical and biotherapeutic
entities.



#### MESSAGE FROM THE DIRECTOR

Welcome to the 2020 summer newsletter from the Houston Methodist Academic Institute's Center for Neuroregeneration. As we quickly enter the second half of 2020, I am very proud of our Center and how we have continued to work together and conduct exciting research during a very challenging time. Our faculty and researchers have made significant progress towards the research mission of our Center, despite the various obstacles and complications that have arisen as COVID-19 has permeated both the city of Houston and the world at large. We began this year with our annual Center for Neuroregeneration retreat, where we reflected on our first five years and engaged in discussions on how to improve communication, productivity, and education in the Center. The energy and inspiration gleaned from this retreat was crucial in how we responded to COVID-19. As a unit, we have quickly learned how to navigate our workflow and interactions with one another; while, at the same time, carrying on our innovative research that is supported by the public trust to develop cures. Our faculty members continue to excel in their respective research fields, as evidenced by the prestigious multi-million-dollar R01 grants from the National Institutes of Health they have received, the new collaborations they have established, and the numerous peer-reviewed articles they have published in prominent journals. In addition, COVID-19 has not impacted the Center's growth and communication. We are delighted to welcome our new NeuralCODR Fellow this year: Dr. Betsy Salazar. And, we are excited to announce that the third biennial Patricia Levy Zusman International Workshop (formerly known as the CNS Neuroregeneration Strategies: Discovery and Implementation Symposium) is scheduled to occur, through the use of technology and virtual conferencing, March 3rd to March 6th of 2021!

If you have an interest in collaborating with our program and/or contributing to our mission of research and training, please contact us.

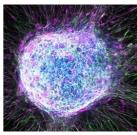
Sincerely,

Philip J. Horner, PhD

Director, Center for Neuroregeneration, Houston Methodist Academic Institute

Vice Chair Research, Department of Neurosurgery

#### CENTER FOR NEUROREGENERATION LAB HIGHLIGHTS



3D neural sphere comprised of astrocytes differentiated from human pluripotent stem cells.

So far in 2020, the **Astrocellular Therapeutics Lab** has been working on several focused research projects that involve their improved experimental model of the human brain. Specifically, this model combines several new biotechnologies into stem cells. Projects involving this technology aim to understand Alzheimer's disease and to discover drugs for Parkinson's disease. In addition, Dr. Krencik participated as a grant reviewer for the National Institutes of Health (NIH) in their first-ever fully

virtual meeting. Also, one of the lab's postdoctoral fellows, Dr. Caroline Cvetkovic, had her research <u>highlighted</u> as part of the Cell Picture Show on 3D imaging, which is hosted by a premiere scientific journal.

Research in the **Neurodegeneration & Brain Hemorrhage Research Lab** has focused on delineating the molecular insights into the involvement of genome damage/repair responses in disorders of the human brain (e.g. neurodegeneration, brain hemorrhage, and injury) and on

# 2020 CENTER FOR NEUROREGENERATION SEMINAR SERIES SPEAKERS:

Tuesday February 11: Kathryn Cunningham, PhD (University of Texas Medical Branch)

"Defining and Mining Targets for Therapeutics in Addiction"

Tuesday February 18: Mark Burns, PhD (Georgetown University)

"Frequency Matters – Mild Head Impact Exposure and the Development of Cognitive Impairments"

developing novel mechanism-based treatment strategies for human brain disorders. The lab specializes in utilizing state-of-the art molecular biology/CRISPR/Cas9 mediated gene editing technologies, human induced pluripotent cell derived neuronal models, and relevant mice models. Notably, the Neurodegeneration & Brain Hemorrhage Research Lab was awarded three new NIH grants in 2020, making it a total of four concurrent NIH awards!

The **Neuroepigenetics Lab** has focused its research on proximity-dependent labeling methods for subcellular proteomic profiling. Specifically, they have concentrated on developing collaborations and submitting grant applications, both aimed at identifying proteomic changes that modulate neuron and astrocyte plasticity. As such, the Neuroepigenetics Lab recently obtained funding from the Golfers Against Cancer foundation to explore how RNA changes link to tumor development and to translate their findings into a novel treatment. Further, based on his competitive pre-application, Dr. Yi-Lan Weng was selected to apply for the Pew Scholars Program as the Houston Methodist Academic Institute's representative. Excitingly, **Dr. Weng recently received his first RO1 from the NIH**, and he was awarded a Career Cornerstone Award from the Houston Methodist Academic Institute!

The Neuroplasticity & Repair Lab hosted four summer students in a virtual workshop focused on a team-based assessment of rodent forelimb function. The online workshop met weekly with students training in the rigorous assessment of forelimb kinematics from videos of rats performing skilled reaching movements. The team used an iterative process to refine assessment criteria in order to improve inter-rater consistency and reliability. The group also explored the use of artificial intelligence for assessment of skilled movements. The online workshop proved to be an effective way to engage summers students who could not physically work in the lab due to the pandemic, and results of the process improvements for skilled forelimb assessment are in the planning stages for publication. New research funded through a collaborative grant from the Cancer Prevention and Research Institute of Texas shared between the Horner and Rostomily laboratories got off to a good start. Gaby Walker has successfully isolated multiple lines of adult stem cells from the pig spinal cord and brain. These adult, pig neural stem cells have rarely been isolated and will be a critical resource to model repair and plasticity in a large mammalian brain as well as serve as a model for how stem cells produce brain tumors. Expanding on the laboratories interest a deeper understanding of how electrical stimulation promotes plasticity, a new collaboration between Drs. Hogan and Stigliano has developed whereby they will explore how neural activity cooperates with the immune system. Along with several manuscripts under review, a report exploring mechanisms of neuromodulation has been published in Trends in Neuroscience, with the lead author being Dr. Hogan!

Given the limited capability for human subject research these past few months, the **Neuromodulation & Recovery Lab** has focused primarily on communicating with their fellow researchers across the globe, sharing their knowledge, receiving feedback from others, and looking at their existing data from different angles. Specifically, their research relationships have strived with colleagues from other institutions thanks to teleconferencing. For example, **Dr. Sayenko and Dr. Masani (University of Toronto) received a collaborative grant from the Wings for Life Foundation to explore their novel non-invasive approach for regaining self-assisted standing after spinal cord injury. Additionally, a new collaboration has emerged with the Computational Neuromechanics Lab at Rice University via virtual channels. Finally, based on previously collected data, the Neuromodulation & Recovery Lab has initiated several projects with experts in computational science, biomechanics, and bioengineering (all from different institutions), and they have published several research papers in peer-reviewed journals.** 

The **Neurorestoration Lab** has continued to submit manuscripts and grant applications. In addition, they have maintained their preclinical work, carrying out animal research and provisionally establishing a behavior room that will be pertinent to all research in the Center for Neuroregeneration. Still, COVID-19 has substantially impacted their clinical trials and research. Dr. Villapol is now actively involved with the multi-institutional consortium, COVID-19 International Research Team (cov-irt.org). Also, she is collaborating with Weill Cornell Medical College to analyze the microbiome samples and viral load in COVID-19 patients. In fact, the **Neurorestoration Lab recently restructured one of their research projects to focus instead on helping COVID-19 patients**. Specifically, they are investigating gut microbiome changes in COVID-19 patients, as half of COVID-19 patients go through an initial phase of infection with intestinal symptoms (diarrhea, abdominal pain, vomiting). These changes appear to affect disease development in the second phase, characterized by respiratory or cardiovascular problems that can even lead to a stroke. Ultimately, they are seeking to determine whether the gut microbiome can help reduce the severity of COVID-19.

# NEUROREGENERATION IN THE CLINCS POTLIGHT



Dr. Mas Takashima

We are pleased to announce an exciting initiative that is quickly bringing the field of neuroregeneration into the clinic. In 2019, Mas Takashima, MD, FACS joined Houston Methodist Hospital to serve as Chair of the Department of Otolaryngology. In this role, Dr. Takashima is currently recruiting faculty who specialize in spatial nerve and auditory regeneration. One goal, mandated by Houston Methodist, is to combine our neuroregeneration clinical trials with those of the Department of Otolaryngology, thereby further propelling neuroregeneration research in the clinic.

#### NEURAL CONTROL OF ORGAN DEGENERATION AND REGENERATION (NeuralCODR) FELLOWS



*Dr. Betsy Salazar* NeuralCODR Fellow

The NeuralCODR fellowship program, which formally launched in 2018, welcomes it's third Fellow: **Dr. Betsy Salazar**. This innovative program trains the next generation of basic science researchers focusing on the intersection of neural development, engineering, and communication between the injured brain and peripheral organs. It also provides our fellows with rare, but much needed, hands-on clinical experience and long-term clinical advisement. Dr. Salazar's funding is made available via a generous endowed gift from Paula and Joseph C. 'Rusty' Walter III. Additionally, the Center is working vigilantly to grow this training progam. For example, in June, we submitted a federally funded T32 training grant application to help support an additional two to four NeuralCODR fellows.

# CENTER FOR NEUROREGENERATION ANNUAL RETREAT

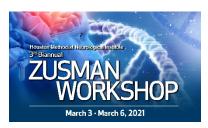
On Febraury 14th, members of the Center for Neuroregeneration convened for our Annual Retreat. 2020 marks the fifth annivary for the Center. Therefore, Dr. Horner took this opportunity to begin the retreat by reflecting on the milestones we have achieved during this exciting period of development as we set to chart our goals and aspriations for the next five years. Faculty and trainees presented their 2019 milestones and deliberated on their big ideas for 2020. We had exciting guest speakers: Dr. Jessica Logan and Dr. Jessica Uriarte who spoke on emotional intelligence and engaged our center members with some educational, but fun, interactive group activities. Center members also participated in a fun group activity where they were divided into three groups and had to work together to develop and present to guest judges an innovative improvement for the Center for Neuroregeneration. Needless to say, the judges were hard pressed to pick a winner as our Center members' proposed some truly innovative ideas. Finally, we ended the day with some bowling!



Center for Neuroregeneration Annual Retreat Highlights. Members of the Center for Neuroregeneration engaging in the emotional intelligence interactive activity. (b) Invited speakers (from left to right): Dr. Jessica Uriarte-Wright, Natalie Zuniga, and Dr. Jessica Logan; (c, f, g) Members of the Center for Neuroregeneration discussing potential innovative improvement ideas; (d,e) Members of the Center for Neuroregeneration presenting their innovative improvement ideas (h) a lively debate between the Center Director, Dr Philip Horner (far right) and our invited guest judges: Dr. Robert Rostomily, Dr. Francesca Taraballi, and Dr. Henry Pownall (from left to right).

#### PATRICIA LEVY ZUSMAN INTERNATIONAL WORKSHOP ON NEUROREGNERATION

We are actively planning and preparing for the third biennial Zusman International Workshop, which is scheduled to occur on March 3rd to March 6th of 2021. Given COVID-19 social distancing requirements, we are working to incorporate innovative virtual and teleconferencing elements into our program to allow the workshop to continue without delay. This workshop was purposefully built to create a new collaborative regeneration network, stimulating new ideas among scientists and encouraging innovative



multidisciplinary research projects. Targeted recruitment of early-stage, rising star investigators and underrepresented minorities is an important strength that contributes to a motivating environment. Our goal is to drive new ideas and relationships that will lead to a cure for paralysis. Currently, we have twenty-nine confirmed speakers. This including our three keynote speakers: 1) Dr. Vance Lemmon, a distinguished Chair and Professor at The Miami Project, whose research focuses on axon regeneration, cell adhesion molecules, ontology development and informatics, and vaccine development; 2) **Dr. Wolfram Tetzlaff**, a Professor at the University of British Columbia and Director of the International Collaboration on Repair Discoveries. His research focuses on cell transplantation, diet, myelin, neuroprotection, and regeneration; and, 3) **Dr. Jerry Silver**, a Professor at Case Western Researve University, whose research focuses on biology that underlies axonal dieback and regeneration failure in the adult spinal cord. We are proud to announce that funding for this workshop is made possible by the Patricia Levy Zusman Endowment and a recently awarded NIH grant to the Center Director, Dr. Philip Horner. Additionally, we anticipate the Wings for Life Foundation and the Neilsen Foundation will contribute additional funds towards attendee and speaker travel. For more information on this Workshop and to register to attend, please visit: <a href="mailto:events.houstonmethodist.org/neuroregeneration">events.houstonmethodist.org/neuroregeneration</a>

#### **ADAPTING TO COVID-19**

Although the past few months have been an unexpectedly difficult time for the Houston Methodist Academic Institute and the world at large, the Center for Neuroregeneration has remained positive and busy. The Center strives to successfully develop new innovative research programs and to expand the wealth of knowledge of our research faculty. In the face of COVID-19, our labs have received continued support from our students and trainees through careful planning and practiced social distancing via a combination of on-site and work-fromhome shifts. In addition, we have maintained communication and designed at-home projects with computational analyses. These strategies have helped us remain operational and productive during the difficult period. Further, COVID-19 has presented us with a unique opportunity to slow down and revisit potential ideas and projects that can be realized within the lab or in partnership with our collaborators. The idea that the break in research activity can be indefinite, and the urge to keep being productive has brought us together and forced to value the expertise of others. In fact, the amount and quality of work that can be done in virtual space is indeed fascinating. COVID-19 seems to have solidified a new Era of virtual scientific collaboration.

# Snapshot stories:



Research Coordinator
Neuromodulation

March 12th, 2020 – a date I am not likely to forget anytime soon. I was told I should take everything I needed from my office home and begin teleworking the following day. The virus everyone was buzzing about finally was hitting Houston and, seeing as I am at increased risk, I was more than happy to follow those directions! Little did I know, that would be my last day in the office until June 17th.

Transitioning to working from home was not super difficult for me. I've worked from home part-time at a couple of my previous jobs, so I know to stick to a routine, and I have a desk set-up at home for this purpose. In addition, our lab members communicate really well normally and it's not unusual for us to have group texts and WhatsApp messages going on when we're all in the office – having your lab and office in different buildings and the Magnetic Resonance Imaging (MRI) Core in a third make this necessary.

& Recovery Lab The biggest challenge for us was navigating our participant visits. These must be done in our lab or MRI, and almost all our studies involve populations at risk for COVID-19. At first, I was fielding quite a few calls from participants cancelling because they trusted us but were not comfortable coming to a hospital. Thankfully, after the first couple weeks, we have been able to shift things around and focus on participants who are not at increased risk or those who are but trust our precautions. This break in participant visits also allowed for a focus on finalizing publications and getting several grants out the door without quite so many interruptions.

Despite the relatively simple transition to working from home, it was great to be back in the office and see coworkers in person. It is especially nice to get through a conversation without the internet glitching or worrying about my dog barging in to join!

Working from home has presented itself with its own unique challenges. When we initially began to work from home towards the beginning of March. I was anxious what the future might bring. Unsure of when I may be back at the office, I took home my laptop along with other essentials needed for my day-to-day activities, as all administrators tried to stay away from the hospital staff in order to help them keep our patients safe. As the COVID-19 situation worsened, we realized we were in this for the long haul, consisting of at least three to four months. I realized we had no choice but to accept the current situation and move forward with the best possible way we knew how - constant communication and hard work. Our team adapted and developed ways to stay in touch and conduct weekly meetings effectively. We utilized Microsoft Teams to allow us to finish projects and tasks in a timely manner and video-conferenced with each other to discuss current plans of action for ongoing projects and future steps to ensure that productivity in our Center remains high throughout this difficult time. At Center for Neuroregeneration



Program Project Manager

times, I missed being in the office and being able to maneuver easily along my desk to maximize my productivity - notebooks on my right, laptop on my left, and two screens in front of me. I could go in and out of meetings smoothly, carrying my laptop in one hand and a coffee on the other. Now, in front of me is an altered environment, a different desk, and unique challenges. Not being able to pop my head in and ask quick questions to those around me has presented itself as the greatest challenge. I find myself having to send an email for the most minor question or comment, realizing that communication takes a lot more effort now than it did when we were physically in our offices and labs. However, looking back to the last three to four months, I can say with certainty that I am lucky to be a part of a team that is extremely understanding, patient, and hardworking. I am happy that our Center has been able to push through challenges successfully. I am proud of our trainees and assistants who have remained persistent, diligent, and hard-working even through a pandemic, which proves that, in the end, it is all about the love and passion we have for the science we strive to do.

# 2020 METRICS OF SUCCESS

#### Publications:

- Derry PJ. Hegde ML, Jackson GR, Kayed R, Tour JM, Tsai AL and Kent TA. Revisiting the intersection of amyloid, pathologically modified tau and iron in Alzheimer's disease from a ferroptosis perspective. Prog Neurobiol., 2020 Jan, 184, 101716. PubMed PMID: 31604111
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- Wang XW, Yang SG, Zhang C, Hu MW, Qian J, Ma JJ, Zhang Y, Yang BB, Weng YL, Ming GL, Kosanam AR, Saijilafu, Zhou FQ. Knocking out non-muscle myosin II in retinal ganglion cells promotes long-distance optic nerve regeneration. *Cell Reports*, 2020 Apr, 31(3), 107537. PubMed PMID: 32320663
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- Mitra J,\* Hegde ML\*. The Role of TDP-43 in Genome Repair and beyond in Amyotrophic Lateral Sclerosis. IntechOpen Open Access book, "Amyotrophic Lateral Sclerosis - Recent Advances and Therapeutic Challenges" edited by Dr. Muralidhar L. Hegde, 2020 Jun, DOI: 10.5772/intechopen.92696
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- Mitra J, Wang H, Kodavati M, Mitra S,\* Hegde ML\*. Emerging roles of non-canonical RNA binding proteins in repair of genome damage linked to human pathologies. Royal Society of Chemistry (UK) Book on DNA Damage, Repair and Disease, edited by M. Didzagaralu and Lloyd S. 2020 (In Press).

#### **Grants Awarded:**

February: Golfers Against Cancer. Druggable pathways to RNA m6A remodeling complex in cancers.

(Weng-Principal Investigator)

April: NIH/NIA R03AG064266. A new conditional TDPΔNLS knock-in mouse model generated using

CRISPR/Cas9 technology to study the linkage of TDP-43 pathology to motor and cognitive

defects in ALS, FTD and ADRD (**Hegde**-Principal Investigator)

NIH/NINDS R01NS094535. Novel carbon nanozyme mechanisms for traumatic brain injury.

(Hegde-Multiple Principal Investigator)

NIH/NINDS-NIA RF1NS112719. Defining the altered FUS-PARP1-DNA Ligase III axis and its implications to nuclear and mitochondrial genome damage response in motor neuron disease.

(Hegde-Principal Investigator)

Wings for Life Spinal Cord Research Foundation. Novel non-invasive approach for regaining self-assisted standing after SCI: combining transcutaneous spinal stimulation and functional

electrical stimulation. (Sayenko-co-Principal Investigator)

June: NIH/NIEHS R01ES031511. Systems-wide analysis of oxidative stress-responsive m6A

epitranscriptome. (Weng-Principal Investigator)

NIH/NINDS R13NS118763-01. The Patricia Levy Zusman international workshop on

neuroregeneration at Houston Methodist. (Horner-Principal Investigator)

# Patent/Invention Disclosures:

February: Pharmacological neuromodulation by A1 adenosine antagonists to synergize with electrical

spinal cord stimulation and improve functional deficit after neuromotor disturbances

(Sayenko)

June Cell-specific activation within all-inducible multi-cellular sphere cultures (Krencik)

# Awards:

June: Dr. Yi-Lan Weng – Career Cornerstone Award, Houston Methodist Academic Institute