

# 2019 YEAR IN REVIEW

## CENTER FOR NEUROREGENERATION

### DEPARTMENT OF NEUROSURGERY

#### MESSAGE FROM THE DIRECTOR

#### 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.



Welcome to the 2019 year in review of the Houston Methodist Research Institute's Center for Neuroregeneration. As we close out the Center's first five years, I am overwhelmed by the progress that we have accomplished together.

We have established a core group of talented and energetic faculty members, with the addition of Dr. Robert Krencik (*Astrocellular Therapeutics Lab*), Dr. Sonia Villapol (*Neurorestoration Lab*), Dr. Yi-Lan Weng (*Neuroepigenetics Lab*), and Dr. Dimitry Sayenko (*Neuromodulation & Recovery Lab*) to the Center. Each member brings with them innovative approaches to regenerate the brain (e.g., cell culture, neuroanatomy, clinical trials), the result of which has been the development of several innovative and advantageous devices and methods in the Center.

We have built a strong educational component to our Center that stemmed from our annually held, transdisciplinary, and always fully packed, Neural Control Course, and evolved into our first-of-its-kind transdisciplinary postdoctoral NeuralCODR fellowship program (see below) that provides fellows with much needed, and often overlooked, hands-on clinical experience. We have been fortunate to attract outstanding trainees and technical support that are the life blood of our research program. Some of their achievements are highlighted in the following stories.

And, we have made significant contributions to the scientific community not only through numerous published research articles, but also by growing and evolving our bi-annual "Patricia Levy Zusman International Workshop on Neuroregeneration" (we are currently planning the 3rd Workshop for 2021!).

This is an exciting period of transition in our Center as we move onwards to the next five years. Thanks to a significant endowment from the Walter Neurorestoration Program, we will focus on a common goal of further strengthening our signature research and translational medicine program that targets neural systems repair.

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

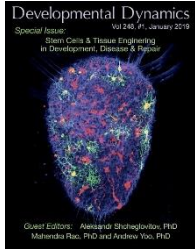
Sincerely,

A handwritten signature in black ink, appearing to read "Philip J. Horner".

Philip J. Horner, PhD

Director, Center for Neuroregeneration, Houston Methodist Research Institute  
Vice Chair Research, Department of Neurosurgery

## 2019 CENTER FOR NEUROREGENERATION LAB HIGHLIGHTS



The innovative “mini-brains” from the **Astrocellular Therapeutics Lab** were highlighted in various platforms, including the front cover of a special issue in the Journal of “Developmental Dynamics” and in-depth [feature article](#) in the Texas Medical Center magazine, “TMC pulse.” Mini-brains are three-dimensional brain organoids that hold similar properties to the human brain, making them *a great model system to study how neural connections are formed, damaged, and repaired*. The lab uses mini-brains to uncover novel methods to repair the nervous system, while also creating the next generation of brain organoids – with hopes of better mimicking the actual brain. In doing so, they have disclosed novel inventions to the patent office (*listed below*), which will enable the Astrocellular Therapeutics Lab to expand their research endeavors in 2020 and make new breakthroughs in the field of neuroregeneration.

The **Neuroepigenetics Lab** collaborated with Emory University and Baylor College of Medicine to better understand how a specific enzyme (DDX3X) can engage the RNA of neurons and modulate synaptic plasticity. This study was supported by The Brain & Behavior Research Foundation, which nominated (and recently awarded!) the lab’s Principal Investigator, Dr. Yi-Lan Weng, a [2019 NARSAD Young Investigator Grant](#). The Neuroepigenetics Lab seeks to advance our understanding of brain epitranscriptome as it instructs neurophysiology and a variety of neurological diseases. Therefore, it also collaborated with the Zhou lab at Johns Hopkins University to explore which molecular programs can be exploited to promote regeneration. As a result, the researchers discovered that a combination of overexpressing the RNA-binding protein Lin28 with a myosin IIA/B knockout can *lead to remarkable synergistic effects in axon regeneration*.

The **Neuroplasticity & Repair Lab** made significant strides forward in developing innovative devices to help improve outcomes following spinal cord injury (SCI). The lab designed *an ultra-flexible spinal stimulation system to deliver therapeutic stimulation to the spinal cord in ways not previously possible*. Very little is known about how spinal stimulation improves outcomes after injury. Moreover, the patterns and routes of spinal stimulation may be critical to achieve the best outcomes. Thus, this new technology will allow researchers to examine the route and pattern of spinal stimulation and their impact on improving outcomes after injury. This system will improve our understanding of electrical stimulation and provide critical knowledge to direct and guide new translational therapies for those suffering from spinal injuries. In addition, thanks to TRI funding, the lab developed a neurostimulation induced molecular (nSIM) protective therapy for advanced stroke care, wherein *a standard endotracheal tube is converted into a powerful non-invasive neurostimulator that can deliver adjuvant protective therapy during surgery and emergency care*. The Neuroplasticity & Repair lab is currently applying for 513(g) documentation for said nSIM device.

### 2019 CENTER FOR NEUROREGENERATION SEMINAR SERIES SPEAKERS:

**Tuesday January 22:**

Jacob Robinson, PhD (Baylor College of Medicine)

*“Nanotechnology to Study Neuroregulation and Develop New Therapies”*

**Tuesday February 19:**

Jiaqian Wu, PhD (The University of Texas Health Science Center at Houston)

*“Integrative Analysis of Long Noncoding RNA and Transcription Factor Regulation in Glial Cells and Spinal Cord Injury”*

**Tuesday March 26:**

Yury Gerasimenko, PhD (University of California, Los Angeles)

*“Nonfunctional Spinal Circuits into Functional States After the Loss of Brain Input”*

**Tuesday April 16:**

Claudia Robertson, PhD (Baylor College of Medicine)

*“Cerebrovascular Dysfunction after Traumatic Brain Injury”*

**Monday June 10:**

Aileen Anderson, PhD (University of California, Irvine)

*“To Go or Not to Go? A Novel Role for Neuroimmune Signaling in Defining Neural Stem Cell Function”*

**Monday June 10:**

Brian Cummings, PhD (University of California, Irvine)

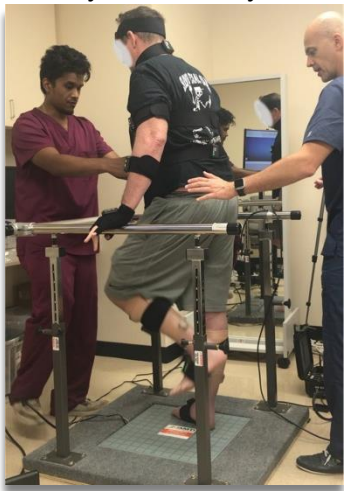
*“Stem Cell Therapies for Neurotrauma : Separating Hope from Hype”*

**Tuesday September 17:**

Michael Sofroniew, MD, PhD (University of California, Los Angeles)

*“Astrocyte Roles in CNS Repair and Regeneration”*

The **Neuromodulation & Recovery Lab** welcomed two new members – Ms. Rachel Markley, Research Coordinator and Dr. Gerome Manson, Postdoctoral Fellow. The lab is focused on bringing advanced neuromodulatory strategies that promote functional recovery and mobility after neuromuscular disorders and injuries to



*A stroke survivor is independently standing and performing motor activities while undergoing non-invasive spinal neuromodulation.*

eager neurological populations. In 2019, the team initiated an acute study where *the effects of invasive and non-invasive spinal stimulation approaches were directly compared in individuals with SCI*. This rigorous mechanistic research is essential in delineating the underlying mechanisms of spinal stimulation in order to drive the evolution of individual and combinatorial therapies to maximize restorative plasticity after neurological injuries and disorders. Further the lab expanded its collaborative ties and partnerships locally, nationally, and internationally, and it increased connections with the local disability communities (including local multiple sclerosis society support groups and stroke survivors), forming new relationships that will allow for more studies and data collection efforts, ultimately helping patients regain function during self-assisted standing and stepping.

The **Neurorestoration Lab** focused on three main research directions; 1) the role of peripheral organs in the neurorestoration and neuroinflammation of the injured brain, 2) the manipulation of microbiota to induce recovery and neuroregeneration of the damaged brain, and 3) the role of aging and Alzheimer's pathology in inflammatory processes and microbiome composition. The lab established three clinical research projects in patients with stroke, concussions, and traumatic brain injury to better study the connection between the gut and the brain. Notably, the lab is poised to begin a collaborative clinical study with Rice University investigating the long-term impact of sports-related concussions and intestinal changes (i.e., microbes found in the gut), thereby *stimulating the development of novel treatments that will prevent the consequences of concussions*. Finally, the Villapol lab welcomed two new lab members: Dr. Sirena Soriano (Postdoctoral Fellow) and Dr. Manoj Dandekar (Research Associate).

## NEUROREGENERATION IN THE CLINIC SPOTLIGHT

The Department of Neurosurgery encompasses several interconnected and collaborative centers (such as the Center for Neuroregeneration). Of note, the **Spine and Peripheral Center** offers a comprehensive, multi-disciplinary approach to the management of a wide variety of disorders affecting the spine. Spinal neurosurgeons work in collaboration with neurologists, neuroradiologists, orthopedic surgeons, pain management specialists, and rehabilitation experts to provide the most accurate diagnosis and appropriate treatment plan for every patient. In addition, some spinal neurosurgeons also perform neuroregenerative research.

**Dr. Sean Barber** is one such clinician-scientist whose research focuses on neuroregeneration after nervous system injury. He is focused on further evaluating the role of neuromodulation and stem cell therapy in functional recovery after SCI by studying the effect of neuromodulation on synaptic density and other variables in a rat model of chronic SCI. He also plans to design and implement a new spinal cord stimulation electrode for neuromodulation of patients with SCI related to spinal tumors and fractures of the spine, which could help with pain control and hopefully assist with recovery of motor and autonomic function after SCI. Finally, Dr. Barber has begun a collaborative research project with Dr. Francesca Taraballi, Director of the Center for Musculoskeletal Regeneration, to study spinal metastatic disease, including the pathophysiology underlying tumor metastasis to bone, the factors leading to epidural tumor growth from an intraosseous location, and several therapies (medical and surgical) to treat spinal metastatic disease.



## SPEAKERS CONT.:

**Tuesday October 15:**  
Jeffrey Tabor, PhD (Rice University)

*“Bacterial Two-Component Systems as Sensors for Synthetic Biology Applications”*

**Tuesday November 19:**  
Kevin Park, PhD (University of Miami)

*“Cell Type Specific Axon Regeneration and Target Reinnervation”*

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



The NeuralCODR fellowship program was formally launched in 2018 with the appointment of **Dr. Caroline Cvetkovic** and **Dr. Matt Hogan** to lead our inaugural class. 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. The expansive evolution of the NeuralCODR program that has occurred in

2019 is evidenced not only by the success of our [fellows](#), but also by [the addition of two additional Walter fellows](#), thanks to a generous endowed gift from Paula and Joseph C. 'Rusty' Walter III. Additionally, in May, 2019, we submitted a National Institutes of Health/National Institute of Neurological Disorders and Stroke T32 training grant application that will help support an additional two to four NeuralCODR fellows.



## 2019 CNS NEUROREGENERATION STRATEGIES: DISCOVERY AND IMPLEMENTATION WORKSHOP

The Center for Neuroregeneration hosted the second bi-annual international workshop centered on the application of neural stimulation and brain computer interfaces for the treatment of neurologic injury, stroke, and degenerative disease workshop on March 6<sup>th</sup> – 8<sup>th</sup>, 2019. This workshop series began in 2017 as an 'experiment' aimed at driving innovative ideas and catalyzing the communication and functional cooperation across sub-disciplines in neurobiology, engineering, and physiology in order to bring regenerative therapies to people who suffer from chronic paralysis, cognitive decline, and other neurologic impairments. In 2019, Dr. Karim Fouad, Professor at the University of Alberta and Canada Research Chair for Spinal Cord Injury, joined as a steering committee co-chair. A hallmark of the meeting is the inclusion of a facilitator who generates 'live' summaries (see [image below](#)) during the lectures and working discussions. These summaries can later be modified not only to generate grant proposals and meeting notes, but also to galvanize collaborative ideas. The workshop series is highly focused on the gap between molecular regeneration and electrophysiology, and it is concept driven by clinician and experimentalists who are currently problem solving in human therapy and focused on the establishment of cross training and expertise development in graduate and clinical fellows. We are excited to announce that in recognition and honor of the support bestowed upon our workshop series, it has been renamed the ["Patricia Levy Zusman International Workshop on Neuroregeneration"](#) (a.k.a., [Zusman Workshop](#)). We are currently in the beginning stages of organizing the 2021 Zusman Workshop. If you would like more information and/or are interested in attending, please feel free to contact us!

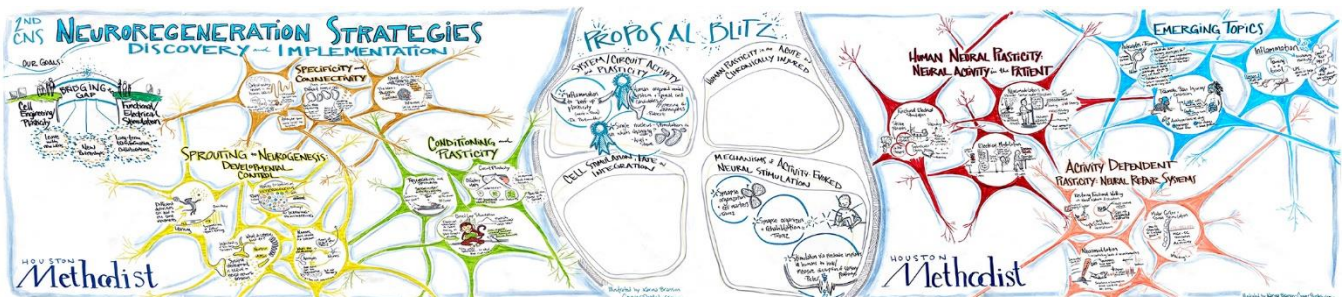


Photo credit: Karina Branson

## COLLABORATIVE RESEARCH OPPORTUNITIES

We welcomed Dr. Giuliano Taccola as the Center for Neuroregeneration's first Visiting Scholar and it was very productive. Dr. Taccola brought to the Center the innovative concept of combining neurostimulation with pharmacologic neuromodulation in the spinal cord. Working with Dr. Dimitry Sayenko, Dr. Betsy Salazar, and Dr. Matt Hogan, Dr. Taccola collected some exciting data and fostered new training. Dr. Taccola is currently

finalizing a review article with Dr. Sayenko that is based on their in-depth conversations that took place during Dr. Taccola's tenure with the Center.

The development of an exciting collaborative translational research program supported by the Dow Dagmar Dunn Innovator Award was established through the leadership of Dr. Philip Horner and Dr. Marcia O'Malley at Rice University. The three collaborative teams of researchers will focus on unique translational projects that exemplify the cutting edge of science. Specifically, they seek to: 1) generate a working algorithm for faster, superior, and precise interpretation of neurologic disorders, 2) create a versatile and practical mobile device for assessing the function and mechanisms of implanted neural stimulators, and 3) identify candidate brain and peripheral organ signals that could unveil novel pathways and mechanisms through which the body and brain communicate. These projects will leverage the unique engineering expertise of Rice University with the clinical expertise of Houston Methodist.

## POSTDOC SPOTLIGHT

**Dr. Sirena Soriano**, a postdoctoral fellow in the Neurorestoration Lab, *received awards for her presentations at the MAPTA Summer Science Symposium in July 2019 and at the TIRR Foundation Mission Connect Annual Scientific Symposium in December 2019.* Her research investigates the link between Traumatic Brain Injury (TBI) and Alzheimer's disease (AD). In 2019, she collected preliminary data that indicates changes in the gut microbiota of AD mice detrimentally effect recovery after TBI. These findings will help elucidate the role of gut microbiota in AD pathology after TBI and provide the foundation for exploring the manipulation of gut microbiota as a novel therapeutic avenue.



**Dr. Caroline Cvetkovic**, a postdoctoral fellow in the Astrocellular Therapeutics Lab, received a *Career Development Award* from the Biomedical Engineering Society, providing her with the support to attend the Annual Biomedical Engineering Society Meeting in October 2019. There, she presented her work on the development of a three-dimensional coculture system to examine the interaction of human neurons and astrocytes in a developing neural circuit (a.k.a., mini-brains). As a preclinical platform, this system may be effective in investigating the impact of stimulation paradigms or drug intervention on neural activity and neuroregenerative outcomes.



**Dr. Gerome Mason** is a postdoctoral fellow in the Neuromodulation & Recovery Lab. In 2019, his collaborative research project with the MRI Core at Houston Methodist revealed an increase in activation in task-related sub-cortical sensorimotor networks in response to non-invasive spinal stimulation compared to both no-stimulation and sham stimulation conditions. These results provide a basis for the investigation of the central effects of spinal stimulation, and data for future comparisons with neurologically-impaired populations. Dr. Mason recently presented this work at the Mission Connect Annual Scientific Symposium where he was recognized as the *best poster presentation in the Spinal Cord Injury Category.*



**Dr. Matthew Hogan**, a postdoctoral fellow in the Neuroplasticity & Repair Lab, was awarded a *one-year fellowship from the Morton Cure Paralysis Fund* to improve methods of electrical spinal stimulation for recovery after SCI. He also received a *two-year fellowship from the Nielsen Foundation* to determine how ventral spinal stimulation may be applied to enhance neural graft migration to a target, thereby improving synaptic integration into host spinal circuitry. He presented some of the exciting results from this work at the annual Biomedical Engineering Society meeting in October 2019!



## COMMUNITY INVOLVEMENT



### Houston Heart Walk | Nov. 9, 2019

Center members participated in the American Heart Association's 5K Heart Walk at the University of Houston in Houston, Texas. This event both celebrates heart disease and stroke survivors and raises funds to that are essential in supporting the research programs which drive scientific advancement in the heart and stroke fields (e.g., first artificial heart valve, crucial pediatric heart, and stroke research).

## FOCUS ON THE FUTURE

The **Neuromodulation & Recovery Lab** is on schedule to establish the first neuromodulation clinical trial at Houston Methodist Hospital. If you have interest in this study, please contact Rachel Markley at [rmarkley@houstonmethodist.org](mailto:rmarkley@houstonmethodist.org).

The **Neurorestoration Lab** is currently recruiting for a collaborative clinical trial with Rice University that explores the long-term impact of sports-related concussions and intestinal changes. For more information on this study, please contact [svillapol@houstonmethodist.org](mailto:svillapol@houstonmethodist.org)

## 2019 METRICS OF SUCCESS

### Publications:

- Patel R, Muir M, **Cvetkovic C**, **Krencik R**. Concepts toward directing human Astroplasticity to promote neuroregeneration. *Developmental Dynamics*. 2019 Jan, 248(1):21-33. PMID: 30016584
- Peeler DJ, Thai SN, Cheng Y, **Horner PJ**, Sellers DL, Pun SH. pH-sensitive polymer micelles provide selective and potentiated lytic capacity to venom peptides for effective intracellular delivery. *Biomaterials*. 2019 Feb, 192:235-244. PMID: 30458359
- Washington PM, **Villapol S**, Burns, MP. Polypathology and Dementia After Brain Trauma: Does Brain Injury Trigger Distinct Neurodegenerative Diseases, or Should They Be Classified Together as Traumatic Encephalopathy? *Concussion and Traumatic Encephalopathy: Causes, Diagnosis and Management*. Cambridge: Cambridge University Press. 2019, Chapter 13, pp 573-581.
- **Manson GA**, Blouin J, Kumawat AS, Crainic VA, Tremblay L. Rapid online corrections for upper limb reaches to perturbed somatosensory targets: evidence for non-visual sensorimotor transformation processes. *Experimental Brain Research*. 2019 Mar, 237:839–853. PMID: 30610265
- Tomilovskaya E, Shigueva T, **Sayenko D**, Rukavishnikov I, Kozlovskaya I. Dry Immersion as a ground-based model of microgravity physiological effects. *Front Physiol*. 2019 Mar, 10:284. PMID: 30971938
- Wicker E, Benton L, George K, Furlow W, **Villapol S**. Serum Amyloid A1 protein as a potential biomarker for severity and acute outcome in traumatic brain injury. *BioMed Research International*. 2019 Apr, Article ID 5967816. <https://doi.org/10.1155/2019/5967816>
- **Manson GA**, Tremblay L, Lebar N, de Grosbois J, Mouchnino L, Blouin, J. Auditory cues for somatosensory targets invoke visuomotor transformations: behavioral and electrophysiological evidence. *PLoS One*. 2019 May, 14(5): e0215518. PMID: 31048853
- Milosevic M, Masugi Y, Sasaki A, **Sayenko DG**, Nakazawa K. On the reflex mechanisms of cervical transcutaneous spinal cord stimulation in human subjects. *Journal of neurophysiology*. 2019 May, 121(5):1672-1679. PMID: 30840527

- Cheng R, Sui Y, **Sayenko D**, Burdick JW. Motor control after human SCI through activation of muscle synergies under spinal cord stimulation. *IEEE Trans Neural Syst Rehabil Eng*. 2019 Jun, 27(6):1331-1340. PMID: 31056504
- **Villapol S**, Faivre V, Joshi P, Moretti R, Besson VC, Charriaut-Marlangue C. Early sex differences in the immune-inflammatory responses to neonatal ischemic stroke. *Int J Mol Sci*. 2019 Aug, 20(15). pii: E3809. PMID: 31382688
- Wang XW, Yang SG, Zhang C, 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. *BioRxiv*. 2019 Sept, 625707. <https://doi.org/10.1101/625707>
- Blouin J, Saradijian A, Pialasse JP, **Manson GA**, Mouchnino L, Simoneau M. Two neural circuits to point towards home position after passive body displacements. *Frontiers in Neural Circuits*. 2019 Oct, 13:70. PMID: 31736717
- Calvert JS, Manson GA, Grahn PJ, **Sayenko DG**. Preferential activation of spinal sensorimotor networks via lateralized transcutaneous spinal stimulation in neurologically intact humans. *J Neurophysiol*. 2019 Nov, 122(5):2111-2118. PMID: 31553681
- Robinson-Whelen S, Hughes RB, Taylor HB, **Markley R**, Vega JC, Nosek TM, Nosek MA. Promoting psychological health in women with SCI: development of an online self-esteem intervention. *Disability and Health Journal*. 2019 Nov, 7:100867. PMID: 31757776
- Bested S, **Manson GA**, Tremblay L. Combining unassisted and robot-guided golf putting optimizes motor learning. *Journal of Motor Learning and Development*. 2019 Dec, 7(3):408-425. <https://doi.org/10.1123/jmld.2018-0040>

#### Patent Disclosures:

- May 15<sup>th</sup>: Microfluidic Device for 3D Sensing and Manipulating Organoids (**Krencik** and Banerjee)
- September 19<sup>th</sup>: StarGlue: Human Astrocyte-Inspired Functional Biomaterial (**Krencik**)
- November 7<sup>th</sup>: Biomimetic Targeting of Neural Cells with Nanoparticles (**Cvetkovic**, Zinger, Tasciotti, **Krencik**)

#### Awards:

- January: **Dr. Matt Hogan** – Postdoctoral Fellowship (Morton Cure Paralysis Fund)  
**Dr. Dimitry Sayenko** – Effects and mechanisms of transcutaneous and epidural spinal stimulation to recover sensorimotor function in individuals with multiple sclerosis (HMS Performance Grant)
- February: **Dr. Matt Hogan** – Postdoctoral Fellowship “*Spinal Cord Injury Research on a Translational Spectrum*” (Craig H. Neilsen Foundation)
- March: **Dr. Dimitry Sayenko** – Central Effects of Task-Specific Spinal Neuromodulation in Individuals with Spinal Cord Injury (Jerry Johnston Andrew Award)
- July: **Dr. Caroline Cvetkovic** – BMES Career Development Award (Biomedical Engineering Society)
- August: **Arya Shetty** (undergraduate) – First Place, poster presentation at the 2019 Summer Research Symposium (Institute of Biosciences and Bioengineering)  
**Dr. Sirena Soriano** – Second Place on podium presentation (MAPTA Summer Science Symposium)  
**Dr. Sirena Soriano** – Travel award (MAPTA Summer Science Symposium)
- September: **Arya Shetty** (undergraduate) – Best Presentation in Neuroscience (5th annual Fall Undergraduate Research Symposium at UT-Austin)
- October: **Dr. Robert Krencik** – Career Cornerstone Award (Houston Methodist Research Institute)

**Dr. Gerome Manson** – Franklin Henry Young Scientist Award – National Research Award for thesis-related research contributions to the field of motor learning and sports psychology (Canadian Society for Psychomotor Learning and Sport Psychology)

December:

**Dr. Yi-Lan Weng** – NARSAD Young Investigator Grant (Brain & Behavior Research Foundation)