2020 ANNUAL NEWSLETTER
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.

UPDATES FROM THE CENTER FOR NEUROREGENERATION

Welcome to the 2020 annual newsletter from the Center for Neuroregeneration. As we say goodbye to 2020, I find myself reflecting on the many successes our Center has made this past year. First and foremost, I am extremely proud of how our faculty and researchers came together to conduct exciting research in spite of COVID-19. They have received several prestigious multi-million-dollar R01 grants from the National Institutes of Health, formed many new exciting collaborations and published numerous peer-reviewed articles in prominent journals. As part of our commitment to translating ideas into therapies, the Center was also granted its second Translational Research Initiative (TRI) Award.

In addition, I am pleased to report that with the addition of Dr. Muralidhar Hegde to our faculty this year, Phase I of our Center's development ends; and, we now focus on our future strategic growth. Most notably, as part of our commitment to excellence, we have built an external scientific advisory board, made up of renowned experts in their fields (e.g., Aileen Anderson, Karim Fouad and James Guest). This advisory board will provide much needed support, aiding us to surpass our strategic goals and keep an eye toward building a national reputation in regeneration research. Committee members will provide our faculty with much needed advice, will help enhance our training plan and will guide our grant applications in support of growing our training program.

Lastly, I am excited to announce that our first fully virtual (and third overall) biennial Patricia Levy Zusman International Workshop (formerly known as the CNS Neuroregeneration Strategies: Discovery and Implementation Symposium) will occur virtually from 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

2020 DEPARTMENT OF NEUROSURGERY RESEARCH LAB HIGHLIGHTS

The **Barber Lab**, led by the spinal neurosurgeon and clinician-scientist Dr. Sean Barber, has worked towards gaining a better understanding of neuroregeneration after nervous system injury. In fact, Dr. Barber was awarded a Clinician Trialist award from the Houston Methodist Academic Institute to study the role of epidural and transcutaneous spinal cord stimulation on motor recovery, bladder function and peripheral immunity after spinal cord injury. This project will begin enrolling in the next few months. In addition, **the Barber Lab** is working on projects to evaluate spinal cord stimulation in patients with foot drop as a means to promote more rapid peripheral nerve regeneration and motor recovery after surgical decompression. Finally, the Barber lab is in the very early stages of developing a new endoscopic/robotic tool to be used in the minimally invasive resection of metastatic spinal tumors.

Research from the **Hegde lab** in the Center for Neuroregeneration was directed at 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 developing novel mechanism-based treatment strategies for human brain disorders. This exciting research led to not only ten exciting research articles in high impact journals and an entire book, but also three new grants from the National Institutes of Health! The **Hegde 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. Excitingly, the lab will soon be bringing this expertise to the 11th floor of the Research Institute! Lastly, but in no means least, Dr. Muralidhar Hegde was recognized for his hard work and dedication to his research through his promotion to full professor in the Department of Neurosurgery.

The **Horner Lab** received a TRI Award to support an MRI-based imaging technology to visualize myelin in people and animals. The invention is called SHIFT MRI and will be used to assist clinicians in the assessment of nerve fiber health in order to diagnose disease and guide surgical decisions. The new technology was developed over the past five years by a group that included **Horner Lab** engineers and international collaborators. The basis for the invention was published this October in the *Journal of Magnetic Resonance Imaging*. The **Horner Lab** also spent a significant amount of effort to improve the rigor and speed of a critical motor performance assay that is used to determine the extent of regeneration in rodents after a spinal cord injury. Functional assessment of motor behavior in rodents is a challenging but vital cornerstone of translational research. The team took a group approach that involved a virtual workshop where summer students, engineers, technicians and fellows designed a robotic assistive technology, a new camera system and a paired scoring approach that is now being applied to multiple regeneration projects. Dr. Horner and Dr. Rostomily built on their teams long-standing collaborative research that explores the role of glial cells in brain plasticity and cancer to acquire a new research award from the Cancer Prevention and Research Institute of Texas (CPRIT). Leaders among the two laboratories, including Dr. Chaboub from the Horner Lab, have made significant progress toward the development of a porcine model of brain cancer in order to ask important translational questions that cannot be addressed in small animal models. Finally, a new growing effort is seeking to uncover the link between the immune system and neuronal plasticity after spinal cord injury. Led by two senior Horner Lab members, Dr. Hogan and Dr. Stigliano, this project expands on a report exploring mechanisms of neuromodulation that Dr.

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"

Tuesday September 29:
Louise McCullough, MD, PhD (Memorial Hermann Hospital)

"Translational Stroke Research: Age and Sex"

Tuesday October 30:
Jens Christian Schwamborn, PhD (University of Luxembourg)

"Usage of Patient Specific Midbrain Organoids for In Vitro Modeling of Parkinson's Disease"

Tuesday November 17:
Marco Capogrosso, PhD (University of Pittsburgh)

"Spinal Cord Stimulation for the Recovery of Reaching & Grasping"

Hogan published in *Trends in Neuroscience*. These efforts resulted in multiple grant applications submitted in 2020 and exciting preliminary data that revealed candidate pathways to be targeted in 2021.

The **Krencik Lab** optimized their innovative technology to generate and interrogate experimental models of human neural networks. This technology, funded by the National Institute of Aging, consists of combining genetic engineering and bioengineering technologies into stem cells. They are now applying this towards the study of Parkinson's disease with the Michael J. Fox Foundation. Further, the Astrocellular Therapeutics Lab recently received a new grant from CPRIT to study functional interactions between neural cells and glioblastoma cancer stem cells. They have also begun several collaborative projects to accelerate their research. With funding from Mission Connect (a program of The Institute for Rehabilitation and Research [TIRR] foundation), the **Krencik Lab** is conducting preclinical testing of nanotherapeutics. Also, they recently started a collaborative effort with Rice University Department of Bioengineering to improve effectiveness of cellular transplant therapy. Throughout COVID, they have continued to communicate virtually and interact outside of the laboratory. For example, in November, Dr. Krencik was the plenary speaker for the annual regenerative medicine meeting at the University of Illinois at Chicago. Altogether, with these newly established technologies and collaborations, the **Krencik Lab's** goal in 2021 is to publish their findings and identify drugs with the highest potential for effective clinical therapy.

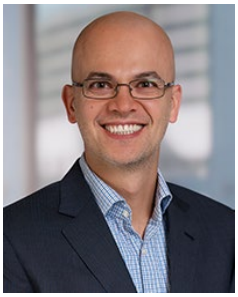
The **Rostomily Lab** focused on translating their novel understanding of the basic mechanisms of glioblastoma and brain metastasis malignancy to clinical applications, with an end goal of improving patient outcomes. Specifically, their research explored several different avenues such as, but not limited to, a) molecular mechanisms that regulate TWIST1 mediated glioma malignancy and invasion, b) microfluidic platforms for pre-clinical drug screening in patient derived samples, c) large animal glioblastoma models, d) pre-analytic variables that impact detection of MGMT promoter methylation in glioma, e) intra-tumor molecular and proteomic heterogeneity and f) aging and glioma malignancy. To achieve this, the **Rostomily Lab** worked with several new and well-established collaborators. For example, CPRIT awarded Dr. Rostomily and Dr. Krencik funding to support their collaborative work exploring a novel organoid platform that modulates human neural networks integrated with glioblastoma stem cells. In addition, Dr. Rostomily and Dr. Horner were awarded one of the inaugural NeuroSpark grants for their collaborative project which explores the neurorestoration of treatment induced myelin injury in a preclinical glioma model. Further, Dr. Rostomily obtained funding from that National Institutes of Health to support his research with Dr. Bomsztyk (University of Washington) that seeks to define pre-analytical procedure variables for glioblastoma biospecimens in order to minimize *ex-vivo* MGMT promoter methylation changes while preserving tissue integrity and his research with Dr. Wong (Houston Methodist Cancer Center) that studies the therapeutic benefit of disrupting novel signaling between resident astrocytes and metastatic cancer cells. Finally, the **Rostomily Lab** has published several exciting manuscripts. Of note, in collaboration with the Folch lab at the University of Washington, they recently published on the technical development and translational application of the microfluidic drug delivery device using xenograft and patient derived cancer slice cultures.

The **Sayenko Lab** continued working on clinical and preclinical studies aimed at exploring the effects of non-invasive and minimally invasive spinal neuromodulation on sensorimotor system. Specifically, they investigated and completed a study of the effects non-invasive spinal stimulation in individuals with multiple sclerosis (*publication in preparation*). In collaboration with neurosurgeons and the pain management clinic, they also initiated a study comparing neural targets of transcutaneous and epidural spinal stimulation via percutaneous lead electrodes in individuals with neuropathic pain. In collaboration with physical and occupational therapists, they are prepared to initiate sponsored clinical trials on evaluating the effects of spinal stimulation on upper limb function, as well as the effects of spinal stimulation combined with lower limb exoskeleton robotics, in individuals with spinal cord injury. In addition, the **Sayenko Lab** validated an electrophysiological assessment protocol in Yucatan pigs to test the integrity and viability of circuits and pathways at different levels of the neuroaxis. This protocol is now readily available to be applied in various models of acute and chronic neurological injuries, as well as during studies of combinatorial effects of different neuromodulation approaches (e.g., electrical and pharmacological). Finally, the **Sayenko Lab** identified and interviewed several candidates for a postdoctoral position and are expecting them to join the lab in 2021.

This year, the **Villapol Lab** has worked intensively to continue moving their research projects, both preclinical and clinical, forward and on schedule. Notably, they completed their clinical investigation of concussion in athletes from Rice University, the results of which will help identify bacteria as novel biomarkers for traumatic brain injury. Also, they wrapped up collaborative projects with Texas Children Hospital and Baylor that focused on the role of probiotics in brain damage recovery. In addition, they also established exciting new collaborations with the Taraballi lab at Houston Methodist to develop new technology to administer treatments using nanoparticles after brain damage, with Indunors and the Hospital Clinic in Buenos Aires (Argentina) to study how changes to the microbiome could help with recovery from COVID-19 and with Great Basin Scientific to incorporate their pathogen analyzer in the laboratory. Further, Dr. Villapol was named a standing member at the Molecular Neurogenetics (MNG) Study section at the National Institutes of Health for the next 4 years - a very prestigious accomplishment for a scientist, and Dr. Soriano was named Outstanding Postdoc of the Year by Houston Methodist's Office of Graduate Studies and Trainee Affairs. Additionally, the **Villapol Lab** decided to do their part to combat the COVID-19 pandemic, as they felt the lab's research could be beneficial. Therefore, they joined an international COVID-19 research team (cov-irt.org), which focuses on the dissemination of scientific information about treatments, vaccines or ways of protection that can save lives. Dr. Villapol has participated in numerous national and international TV news, newspapers and radio, and she has given multiple talks to schools about the pandemic. Finally, moving forward into 2021, the Villapol lab looks to expand its group, to push their promising projects forward and to continue their momentum with respect to high productivity and establishing a network of local and international collaborators.

The **Weng Lab** focused its research on characterizing the "m6A remodeling complex." A better understanding of how m6A RNA methylation is generated by the METTL3-METTL14 RNA methyltransferase complex will significantly advance the field's understanding of hitherto unknown novel epitranscriptomic regulations, thereby not only shedding light on the role of the m6A methyltransferase complex in normal and pathological settings, but also providing important mechanistic insights that can be exploited for the diagnosis and treatment of human diseases. As such, The **Weng Lab** has leveraged biotin-based proximity labeling approaches (APEX and TurboID) to determine *in situ* compositions of the m6A methyltransferase complex at different cellular types and states. Systematic analysis in a disease database has revealed that many m6A complex subunits are substantially mutated across different brain disorders, underscoring a driving role of aberrant residual m6A remodeling complex in pathogenesis of neurological diseases. Thus, the **Weng Lab** is poised to navigate the functional dependency of each subunit and explore how its dysregulation affects neuronal function. In addition, the **Weng Lab** received a grant 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, Dr. Weng was not only awarded with a Career Cornerstone Award from the Houston Methodist Academic Institute, but he received his first R01 from the NIH!

NEUROREGENERATION IN THE CLINC



Dr. Dimitry Sayenko

Dr. Dimitry Sayenko, MD, PhD is leading the Center for Neuroregeneration's first industry-sponsored clinical trial: EXASTIM Pilot Feasibility Clinical Validation Study. This clinical trial is a collaboration with Niche Biomedical, a multi-disciplinary bioelectronics medical device company that brings with it over three decades of research and a perpetual desire for bringing solutions to help suffers in need. Niche Biomedical's distinctive approach centers on applying neuromodulation via their extensively researched and precisely developed technology (e.g., EXASTIM) to address a variety of chronic diseases and injuries that up until now have defied conventional medical treatment. Thus, Dr. Sayenko will investigate the feasibility of noninvasive transcutaneous spinal cord stimulation to enhance upper extremity function in individuals with cervical spinal cord injury, specifically using Niche Biomedical's EXASTIM.

The first subject in the clinical trial undergoes occupational therapy in the Sayenko Lab with therapist Catherine Martin, PT

In July 2020, Dr. Sean Barber was awarded a Houston Methodist Academic Institute Clinician Trialist Faculty Development Award for his project "Ventral epidural spinal cord stimulation for enhancement of motor recovery and modulation of peripheral immunity after spinal cord injury." Specifically, this project will elucidate the advantages and disadvantages of ventral epidural spinal cord stimulation and transcutaneous spinal cord stimulation on patients with acute spinal cord injury, with a particular focus on how each procedure modifies the global inflammatory response and improves post-injury motor rehabilitation. Overall, this project could significantly improve our understanding of how spinal cord stimulation influences neurophysiological networks above and below the site of injury and peripheral immune/inflammatory states after spinal cord injury.

Dr. Sean Barber

NEURAL BIOREPOSITORY

Dr. Robert Rostomily

The **Glioblastoma and Brain Metastasis Research Lab** oversees the Neural Biorepository to collect tissues of interest to researchers within the department and the Houston Methodist Research Institute. Samples from approximately 100 patients are collected yearly since its inception in 2018. In addition, Dr. Rostomily oversees comprehensive retrospective and prospective clinical databases related to brain and spinal metastases and gliomas.

THE PAULA & JOSEPH C. 'RUSTY' WALTER III NEURORESTORATION INITIATIVE

Thanks to a generous endowed gift from Paula and Joseph C. 'Rusty' Walter III, the Department of Neurosurgery has significantly expanded on its Neurorestoration Initiative, the goal of which is to develop a signature research and translational medicine program devoted to neural systems repair. This is achieved by providing an unparalleled environment for multidisciplinary collaborative research at Houston Methodist that connects basic and clinical teams across departments, all with a common goal of reversing neurologic damage in patients. In 2020, we have established and expanded on key components of this environment and existing resources in order to create a leading restorative neuroscience research community.

Education:

The Neural Control of Organ Degeneration and Regeneration (NeuralCODR) Fellowship program, which formally launched in 2018, 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 a rare, but much needed, hands-on clinical experience and long-term clinical advisement. Funding from Paula and Joseph C. 'Rusty' Walter III allowed us to expand our fellowship program through the addition of our third Fellow: **Dr. Betsy Salazar**. As a Walter fellow, Dr. Salazar will be researching the therapeutic effects of electrical stimulation on sensorimotor function after a spinal cord injury. More specifically, she will examine the mechanisms associated with spinal cord injury and bladder dysfunction first by assessing the spinal circuitry regulating the neural control of bladder voiding following spinal cord injury and second by defining electrical stimulation protocols that improve both motor and bladder function after spinal cord injury. The ultimate goal of her research is to reduce and/or reverse the severity of spinal cord injury urinary and locomotor challenges in animal models and translate this knowledge into the clinical setting to implement novel therapies. Further, Dr. Salazar has built a mentorship team wherein each advisor can provide her with critical guidance in key research areas: the nervous system and peripheral organ disorders (**Dr. Philip Horner** – Scientific Director,

Dr. Betsy Salazar
NeuralCODR Fellow

Center for Neuroregeneration), the neuromodulatory effects of electrical stimulation of motor function pathway plasticity (**Dr. Dimitry Sayenko** - Assistant Professor of Neurosurgery, Center for Neuroregeneration) and the neural control of autonomic function and micturition (**Dr. Rose Khavari** - Associate Professor of Urology, Center for Restorative Pelvic Medicine). The long-lasting mentor-mentee relationships Dr. Salazar establishes through her tenure as a Walter Fellow will ultimately transform her research innovation and career opportunities.

External Steering Committee:

We have established an external scientific advisory board, which consists of the following notable experts in their fields: Dr. Aileen Anderson, PhD (University of California Irvine), Karim Fouad, PhD (University of Alberta), Jim Guest, MD, PhD (University of Miami), Susan Howley (Christopher & Dana Reeve Foundation), Linda Noble, PhD (The University of Texas at Austin) and Huda Zoghbi, MD (Texas Children's Hospital). The purpose of this committee is to help support and promote the mission of the Neurorestoration Initiative. They serve as advisors and as critics to our faculty, to our grant applications and to our education and training programs. Most recently, this external steering committee helped review and select the first two Neurospark funded projects (see below). In addition, we are excited to announce that on March 8th, 2021, the External Steering Committee will be making their first virtual visit to the Center for Neuroregeneration. After hearing from the Center faculty members and the Center Director, committee members will provide guidance on the spending priorities, recruitment candidates and strategies and overall program development. In addition, they will review the Center's progress in achieving key milestones and provide advice on the Center's growth opportunities and progress. The formation of an internationally recognized external advisory committee is a critical step for ensuring that regeneration research at Houston Methodist Hospital and the Walter Neurological Restoration Initiative is on track to become recognized for scientific rigor and innovation and is globally competitive in regeneration research.

Dr. Aileen Anderson | Dr. Karim Fouad | Dr. Jim Guest | Susan Howley | Dr. Linda Noble | Dr. Huda Zoghbi

Collaborative Research:

We have launched the NeuroSpark Seed Funding, which aims to cultivate an environment for multidisciplinary, collaborative research at Houston Methodist that will drive the development of restorative therapies for patients impaired by neurological disease and injury who currently have no viable option. We are pleased to report that we received a significant number of applications and the following two promising projects were selected for funding:

1. **Neurorestoration of Treatment-Induced Myelin Injury in a Preclinical Glioma Model**

The principal investigators of this project are **Dr. Robert Rostomily**, a world-renowned expert in cancer models, and **Dr. Phillip Horner**, who brings with him a wealth of expertise in cell therapy development and application. Together, this interdisciplinary team will address how standard cancer therapy treatments partially damage nerve fiber insulation (myelin) and deletion of the natural repair capacity of myelin precursor cells, ultimately harming the integrity of white matter tracts. Specifically, they hypothesize that the use of innovative, cell-based restorative strategies can significantly improve white matter injury and impaired cognitive function in brain cancer patients. Results from these studies will not only define the characteristics of cancer-induced and cancer-related therapy-induced white matter injury, but they will also produce the first clinically relevant test that can determine the capacity of myelin precursor cells to replenish the natural repair capacity of injured white matter tracts. This project leverages expertise in stem cell biology and transplantation to pursue a much-needed therapy that will restore damaged cells in the aftermath of cancer therapy.

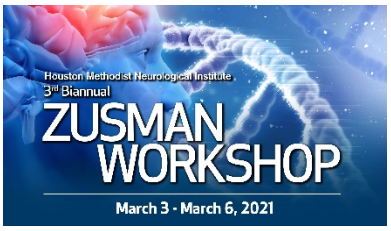
2. **Functional Reorganization of Brain-Spinal Connectivity After Stroke Using Noninvasive Neuromodulation and Robotic Upper Limb Exoskeleton for Neuromotor Rehabilitation**

The principal investigator of this project is **Dr. Sayenko**, an expert in spinal neuromodulation and electrophysiology. He is joined by two co-investigators: (1) Dr. Kaldis, Chief of Physical Medicine and Rehabilitation at Houston Methodist, who will serve as the study clinician and (2) Dr. Marcia O'Malley, professor of Mechanical Engineering and Computer Science at Rice University, who provides expertise in rehabilitation robotics, human-machine interfaces for human-assisted movement and the modeling of human-robot interactions. This interdisciplinary team seek to improve upon the traditional methods for post-stroke motor rehabilitation that currently do not provide enough specificity to target damaged neural networks and restore connections between the brain and periphery. Specifically, the investigators hypothesize that synergistic functional reorganization of the brain-spinal connectome after stroke depends on how much task-oriented and functional voluntary efforts are used in parallel with electrical neuromodulation of the cervical spinal cord. Therefore, they will develop a combination of novel robotic exoskeleton technologies and non-invasive spinal neuromodulation to facilitate the recovery of upper limb motor control in individuals with sensorimotor impairments after stroke. Gaining a better understanding of the underlying mechanisms of this combinatorial approach will not only help stroke patients but may also impact individuals with other forms of neurologic dysfunction and neurodegenerative disease (e.g., cerebral palsy, multiple sclerosis and Parkinson's disease).

NEURAL CONTROL OF ORGAN DEGENERATION AND REGENERATION (NEURALCODR) COURSE

In 2020, we held our first fully virtual **NeuralCODR course**. Led by Dr. Philip Horner, this team-taught, graduate level course was developed to promote new ideas and collaborations in the area of how the brain and peripheral organs communicate in disease and to break down barriers between related, but traditionally siloed, disciplines. Twenty-eight faculty members and clinicians from various institutions throughout the Texas Medical Center participated in this course. The maximum number of students for this course was originally ten; however, upon opening the registration process for the course, this number was met within 24 hours! As a result, we increased the cap and ended up with fifteen total students. Of the fifteen students, there was a mix of graduate students, postdoctoral fellows, biomedical engineers and research assistants. The **NeuralCODR course** incorporated brief speaker presentations with moderated, yet lively, conversations on a variety of exciting topics (e.g., "fixing your body with neural engineering", "curbing cell and system stress in stroke", "neural control of feeding and digestion" and "versatility of the extracellular matrix"), the goal of which was to catalyze new research concepts and identify roadblocks to communication and progress. Feedback from students has been exceptionally positive, with students stating the strengths of this format include "the open exchange of ideas," "having a clinicians present help[s] to better see how research ties into treatments for patients" and "very interesting topics and insights." The NeuralCODR course serves to seed collaborative ideas within trainees and mentors with Houston Methodist Hospital and throughout the Texas Medical Center.

PATRICIA LEVY ZUSMAN INTERNATIONAL WORKSHOP ON NEUROREGNERATION



We are actively planning and preparing for the third biennial Zusman International Workshop, which will occur March 3rd to March 6th of 2021. Given COVID-19 social distancing requirements, the Zusman workshop will be fully virtual this year. 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 under-represented 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, an NIH R13 grant and the Wings for Life Foundation. For more information on this Workshop and to register to attend, please visit: events.houstonmethodist.org/neuroregeneration

BUILDING NEW INDUSTRY CONNECTIONS

Thanks to Dr. Sonia Villapol, Great Basin Scientific has provided the Center for Neuroregeneration with a free demo/placement of their Great Basin System Benchtop Analyzer. The Benchtop Analyzer is a machine for pathological analysis. More specifically, it features: 1) on-demand testing; no batching to delay results, 2) sample-to-result, closed system simplicity so all shifts can run and report results, 3) definitive results in about 90 minutes, 4) wi-fi or wired connectivity, USB to download reports and 5) low-plex test and multiplex panel processing. Access to this machine will allow the Neurorestoration lab to analyze the bacteria in the stool samples from mice after traumatic brain injury and from control mice. Therefore, the lab will be able to determine which bacteria increase or decrease at several times post-brain injury!

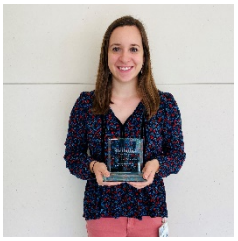
ADMINISTRATION SPOTLIGHT

Dr. Gillian Hamilton

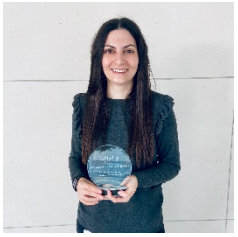
Gillian Hamilton, PhD serves as the Scientific Writer for the Center for Neuroregeneration. She provides broad support to both faculty and postdoctoral fellows in the Center for Neuroregeneration. Specifically, she aids in the planning, development, writing and editing of research manuscripts, grant proposals and fellowship applications. In addition, she leads a monthly journal club and offers additional mentorship and guidance to postdoctoral fellows, helping them strengthen project planning for manuscript and grant development. Her impact is far reaching. For example, Dr. Hogan, a postdoctoral fellow in the Horner Lab, took full advantage of access to a scientific writer, meeting regularly with Dr. Hamilton. These meetings ultimately led to the successful submission of a review article, on which they are both authors. Dr. Hamilton has also helped several faculty members and postdoctoral fellows obtain research funding. In addition, Dr. Hamilton leads a monthly Lunch and Learn seminar series that fosters discussions centered on the generation of new ideas, collaborations and problem solving. It also allows trainees and mentors to discuss relevant themes, topics, techniques or challenges. The topics of the seminars are based on suggestions from attendees. As such, this year topics have included: work/life balance, procrastination, implicit bias and happiness. Response to this seminar series has been overwhelmingly positive, with attendees providing a pool of suggestions for future topics and with feedback such as “great, fun and informative format!”

TRAINEE SPOTLIGHT

Monika Vishnoi, PhD is a Research Associate II in the Glioblastoma and Brain Metastasis Research Lab. Her abstract “Matrisome Signatures in GBM Heterogeneity” was selected for presentation as a Short Talk at the Keystone Symposia on Proteomics in Cell Biology and Disease, September 21, 2020. Additionally, she authored their comprehensive treatise on a book chapter entitled the “Basic biology of brain metastasis” in Central Nervous System Metastases. Springer, Cham edited by lab alumnus, Dr Rohan Ramakrishna.



Caroline Cvetkovic, PhD, a postdoctoral fellow in the Astrocellular Therapeutics Lab, received the "Excellence in Mentoring Award" from Houston Methodist's Office of Graduate Studies and Trainee Affairs in September 2020 for her dedication to providing guidance and leadership to research trainees in their lab or beyond. Since joining the Astrocellular Therapeutics lab in 2017, she has mentored three undergraduate students in the Houston Methodist Research Institute Summer Internship Program as well as one ongoing undergraduate student for the past three years. Dr. Cvetkovic also participates in the Mentor Matching Engine and, in 2020, she volunteered as a virtual mentor for Camp Talaria through the ATHENA program by Women in STEM at University of Chicago Lab Schools. Through her mentorship, Dr. Cvetkovic hopes to "impart not only scientific knowledge, research training and technical skills, but also (and just as importantly in [her] opinion) professional development, emotional intelligence and lifelong lessons."



Sirena Soriano, PhD, a postdoctoral fellow in the Villapol lab, received the "Outstanding Postdoc of the Year Award" from Houston Methodist's Office of Graduate Studies and Trainee Affairs, in collaboration with MAPTA. In 2020, she published a first author paper in *Cellular and Molecular Neurobiology*, with four more manuscripts currently in preparation for submission. Furthermore, she has established a behavioral core for the Center for Neuroregeneration, which allows for the characterization of motor, cognitive and anxiety-like behaviors in rodents. In addition to being involved in pre-clinical research, she is also coordinating clinical studies, including a project aiming at evaluating the effect of COVID-19 on the gut microbiome.

TEAMBUILDING IN TIMES OF COVID-19

This fall, members from the Center for Neuroregeneration met up for a socially distanced hike at Spotts Park in Houston, Texas. The group found its way to the Waugh Bridge "Bat Colony," where they witnessed thousands of Mexican free-tailed bats emerging from their bridge crevices for their nightly excursions that involve stretching their wings and hunting insects.

2020 METRICS OF SUCCESS

Publications:

- Atkinson DA, **Sayenko D**, D'Amico JM, Mink A, Lorenz DJ, Gerasimenko YP, Harkema S. Interlimb conditioning of lumbosacral spinally evoked motor responses after spinal cord injury. *Clinical Neurophysiology*, 2020 Jul, 131(7), 1519-1532. PubMed PMID: 32403065
- **ATLAS Investigators**. Pivotal trial of the neuroform atlas stent for treatment of anterior circulation aneurysms: one-year outcomes. Stroke, 2020 Jul, 51(7), 2087-2094. PubMed PMID: 32568654
- Austerman R, Rajendran S, Lee J & **Britz G.** The July effect and its impact on external ventricular drain placement by neurosurgical trainees - analysis of the national inpatient sample. *World Neurosurgery*, 2020 Oct, 142, e81-e88. PubMed PMID: 32585386
- Bacolla A, Sengupta S, Ye Z, Yang C, Mitra J, De-Paula RB, **Hegde ML**, Ahmed Z, Mort M, Cooper DN, Mitra S & Tainer JA. Heritable pattern of oxidized DNA base repair coincides with pre-targeting of repair complexes to open chromatin. *Nucleic Acids Research,* 2020 Dec, 9, gkaa1120. PubMed PMID: 33300026
- Beck L, Veith D, Linde M, Gill M, Calvert J, Grahn P, Garlanger K, Husmann D, Lavrov I, **Sayenko D**, Strommen J, Lee K, Zhao K. Impact of long-term epidural electrical stimulation enabled task-specific training on secondary conditions of chronic paraplegia in two humans. *The Journal of Spinal Cord Medicine*, 2020 Mar, 23, 1-6. PubMed PMID: 32202485

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Grants Awarded:

January: Michael J. Fox Foundation. Midbrain asteroids to interrogate human astrocyte function within neural networks. (**Krencik**- Principal Investigator)

HMRI Advances in Restorative Medicine. StarGlue: neurorestorative biomaterial from human astrocytes. (**Krencik**- Principal Investigator)

February: Golfers Against Cancer. Druggable pathways to RNA m6A remodeling complex in cancers. (**Weng**-Principal Investigator)

March: HMRI Orthopedics Pilot Project. Conditioning gut microbiome to reduce the degeneration effect in post-traumatic osteoarthritis animal model (**Villapol**-co-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/NCI U01CA246503. Influence of pre-analytical factors in glioblastoma MGMT promoter methylation biomarker assay. (**Rostomily**-co-Principal Investigator)

HMRI Golfer's Against Cancer. Druggable pathways to RNA m6A remodeling complex in cancers (**Weng**-Principal Investigator)

July: Clinician Trialist Faculty Development Award. Ventral epidural spinal cord stimulation for enhancement of motor recovery and modulation of peripheral immunity after spinal cord injury. (**Barber**- Principal Investigator)

HMRI TRI Award. Signal isolation magnetic resonance imaging (siMRI) for quantification of myelin integrity in humans. (**Horner**-Principal Investigator)

August: NIH R01. Elucidating spinal sensorimotor network components that underlie recovery of motor functions via lumbosacral epidural electrical stimulation in humans with spinal cord injury. (**Sayenko**-sub-Investigator)

CPRIT. A novel organoid platform to modulate human neural networks integrated with glioblastoma stem cells. (**Krencik**- Principal Investigator)

September: Siemens Healthineers. Evaluation of 7T angiography for follow-up of small cerebral aneurysms. (**Britz**-Principal Investigator)

Siemens Healthineers. Performance evaluation of an artificial-intelligence-based method for rotational angiography with single rotation of C-arm during image-guided neuro-interventional procedures. (**Britz**-Principal Investigator)

Siemens Healthineers. In vivo magnetic resonance spectroscopy (MRS) of meningioma patients at 7T for the differential diagnosis of grade-I and grade-II (Atypical) tumors. (**Pichumani**-Principal Investigator)

December: Mission Connect (TIRR Foundation) Nanoparticle-based therapeutics for traumatic brain injury. (**Villapol** -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:

January: **Dr. Yi-Lan Weng** – 2019 NARSAD Young Investigator
March: **Dr. Robert Krencik** – NIH Competitiveness Award, Houston Methodist Academic Institute
June: **Dr. Yi-Lan Weng** – Career Cornerstone Award, Houston Methodist Academic Institute

Sponsored Clinical Trials:

February: Ekso Bionics, Inc. Training with Exoskeleton and Transcutaneous Spinal Stimulation in SCI. (**Sayenko** - Principal Investigator)

October: Niche Biomedical, Inc. EXASTIM Pilot Feasibility Clinical Validation Study. (**Sayenko** - Principal Investigator)