# 2022 ANNUAL NEWSLETTER DEPARTMENT OF NEUROSURGERY

MESSAGE FROM THE DEPARTMENT CHAIR AND DIRECTOR OF THE CENTER FOR TRANSLATIONAL NEUROPROSTHETICS AND INTERFACES



#### **MISSION STATEMENT:**

Our Mission is to build a collaborative environment of clinician and bench science researchers focused on translational discoveries in neuro-oncology, neuroregeneration and neuroprosthetics.

#### **Mission Statement**

2022 marked another year of exciting progress for the Department of Neurosurgery. Clinically, we welcomed two new neurosurgeons to the Texas Medical Center. Dr. Alex Hoang joined as a cerebrovascular surgeon in August and Dr. Yevgeniy Freyvert joined as a spine surgeon in September. In the community hospitals we welcomed Dr. Jason Wilson in the Woodlands and Dr. Silky Patel at Houston Methodist West. In addition, we welcomed Dr. Farhaan Vahidy to the department. Farhaan's expertise in cerebrovascular outcomes and population health coupled with his model for outcomes research integration across other disease models will provide new research and training opportunities across the Neurological Institute. Finally, we welcomed Dr. Rai D'Ambrosio as Sr. Program Manager to oversee projects under our strategic partnership with Rice University. We continue to see tremendous growth with our research faculty. Dr. Robert Krencik achieved his first National Institutes of Health (NIH) R01 investigating proteins that may be used to therapeutically modulate abnormal brain activity due to neurodegenerative diseases, such as Parkinson's disease. Robert adds this to a National Institutes of Aging R21 and a grant from Mission Connect. Robert joined the department in 2017 and is a great example of our commitment to build junior faculty. 2022 also brought great progress in the Center for Translational Neural Prosthetics and Interfaces with the successful conclusion of participant recruitment for the Department of Defense-funded "Sleeping Cap" project. We successfully recruited thirty participants and completed testing in

seven different modalities to inform design during Phase II of cap development. Construction of the physical space for the new Center is currently underway with expected completion mid-2023. Finally, the year was marked with significant progress in strengthening our commitment to an exceptional training environment with the award of the NIH T32 NeuralCODR postdoctoral fellowship training program and the launch of the Houston Methodist campus Weill Cornell Medicine Neuroscience Graduate Program, both led by Dr. Phil Horner.

As we close 2022, Neurosurgery research is continuing to build a program focused on education and collaborative translational research in three core areas of research focus – neuro-oncology, neuroregeneration and now neuroprosthetics. Together with the team of outstanding clinicians, I feel a sense of pride and excitement as we look forward to continued growth and innovation in 2023 and beyond.

Sincerely,

Gavin W. Britz MD, MPH, MBA, FAANS
Candy and Tom Knudson Distinguished Centennial Chair in Neurosurgery
Professor and Chairman, Department of Neurosurgery
Director, Neurological Institute
Houston Methodist Hospital
Professor of Neurological Surgery, Weill Cornell Medical College, NY

# RESEARCH LAB HIGHLIGHTS FROM THE CENTER FOR TRANSLATIONAL NEUROPROSTHETICS AND INTERFACES



Dr. Gavin Britz

The **Britz lab** was awarded an NIH R21 grant to study **cerebrospinal flow** (CSF) and its potential impact in improving outcomes post injury. The team will leverage the drainage system of the CSF flow to decrease **hydrocephalus** and clear the cellular metabolic waste. They will investigate whether percutaneous electrostimulation of the mouse neck muscles accelerate CSF flow. This project's results will provide new therapeutic venues for the treatment of hydrocephalus and potentially other neurological diseases in which the glymphatic pathway is impaired. In addition, they completed Phase I of their Department of Defense-funded project in collaboration with Rice University where they collected multiple modalities in 30 participants to

inform the design and development of the "Sleep Cap" to improve CSF flow in humans.









Dr. Amir Faraji

In 2022, the **Faraji lab** pioneered the use of precision magnetic resonance (MR)-guided drug delivery to the brain with real-time visualization of infusion in large animal models. They demonstrated that mechanomyography provides objective intraoperative guidance to determine the extent of **nerve decompression**. They aim to develop central and peripheral nerve-interfaces, harnessing novel technology in the surgery room and emerging feedback strategies. To achieve this, they joined a leading neurosurgical peripheral nerve research network and are a part of a multicenter Department of Defense-funded clinical trial to advance nerve transfer outcomes following spinal cord injury. Further, the Faraji lab had a significant appearance at the Congress of Neurological Surgeons 2022 Annual Meeting in San

Francisco, CA with five abstract presentations including an oral presentation that was delivered by Dr. Khaled Taghlabi about the novel use of mechanomyography for neuromonitoring in peripheral nerve decompression surgeries. In addition, Lokeshwar S. Bhenderu won first place at the Texas A&M College of Medicine Senior Research Showcase and second place in the MAPTA 3MT competition for his research on **electrokinetic convection-enhanced delivery** to the brain. Notably, the Faraji lab recently published their innovative work on "Upper Limb Nerve Transfer Surgery in Patients with Tetraplegia" in the highly-competitive and distinguished *Journal of the American Medical Association (JAMA)*. The lab aims to develop the next generation of neural interventions by converging the research areas of precision agent delivery to the brain, real-time intraoperative visualization, and precise **nervous system stimulation**.









The Sayenko lab

The Neuromodulation and Recovery Sayenko lab continues to expand and evolve as they welcomed four new team members this year. Catherine Martin, PT, NCS (Senior Physical Therapist) joined from the Rehabilitation Department, bringing with her over 12 years of experience in a clinical setting. She specializes in neurological physical therapy and is now focusing exclusively on research. Michelle Scheffler, OTR, MOT (Senior Occupational Therapist) joined in January 2022 and has been practicing as an occupational therapist since 2013. Michelle has a particular interest in the

treatment of neurologic conditions in adults. Jenny Dinh (Clinical Research Specialist) is responsible for recruitment and coordinating the research studies. Remington (Cole) Crossnoe (Research Technician I) is currently processing data for the lab. Congratulations to Rachel Markley, MPH who has been promoted to

Clinical Trials Manager and to Dr. Dimitry Sayenko who has been promoted to Associate Professor and received the title Paula and Joseph C. "Rusty" Walter III



In 2022, the Department of Neurosurgery published 57 peerreviewed journal articles, 3 review article, 5 book chapters, and 2 editorials Associate Professor title from the Endowed Positions and Awards Committee! In collaboration with their industry partner, ANEUVO (Los Angeles, CA) (former Niche Biomedical), the Sayenko lab is preparing to start a pivotal multicenter clinical trial on the effects of cervical transcutaneous spinal stimulation on upper limb motor function in individuals with cervical spinal cord injury. Also, the Sayenko lab is fostering their collaboration with Dr. Argyrios Stampas at Memorial Hermann TIRR (Houston, TX) on multiple projects and recruitment of research participants.



https://sayenko.hmailabs.org/

# RESEARCH LAB HIGHLIGHTS FROM THE CENTER FOR NEUROREGENERATION

The **Horner lab** had a very successful and productive year advancing their electrode system that is capable of stimulating multiple spinal sites in rodents for the purpose of restoring function after **spinal cord injury**. First described in a *Scientific Reports* article published last year, this innovative electrode system was designed by Dr. Matthew Hogan and resulted in





Joy Mitra, PhD, a member of the Hegde lab, published a review article in *Ageing* Research Reviews, entitled "SARS-CoV-2 and the central nervous system: Emerging insights into hemorrhageassociated neurological consequences and therapeutic considerations." This article has been highlighted in various national and international media including The Week, News9 Live; Medical Xpress; Hindustan Times; and The Economic Times.



The Horner lab

numerous successfully funded grants in 2022, including one from the Wings for Life foundation to determine how electrical stimulation can be used to promote neural transplant stimulation and one from the Neilsen Foundation to take the lab in a new direction. Further, in 2022, Dr. Horner received a President's Award for Excellence in Education for his stellar and enduring contributions to high quality innovations in trainee education. Notably, over the past few years Dr. Horner has pioneered an exciting and unique postdoctoral training program, NeuralCODR, which received the support of the NIH this year in the form of a highly competitive, and first-of-its-kind at Houston Methodist, 5-year T32 training grant (see Neurosurgery Education for more details). Also, Dr. Cinzia Stigliano published in Advanced Therapeutics her impactful study where she demonstrated a new technique to selectively target inflammatory cells and convert them to lesion-repairing cells. Julio Mejia joined the lab as one of

the inaugural Weill Cornell Physiology, Biophysics & Systems Biology graduate studies class. He will be using big data tools to better understand the role of inflammatory cells in spinal cord injury by examining the immune system's role in activity-depended plasticity. Finally, the Horner lab is excited to bring a new technology called Lightsheet Microscopy to its functional state in the Center for Neuroregeneration. This new tool will allow researchers to image large regions of the rodent nervous system without having to cut the tissue.





https://horner.hmailabs.org/

**Dr. Sean Barber** is a rising-star spinal neurosurgeon who specializes in complex spinal pathologies (e.g. trauma, tumors, and degenerative). He has a strong research interest in the recovery of motor function via neuroregeneration after nervous system injury. Currently, Dr. Barber is recruiting patients for his clinical trial evaluating the role of ventral spinal cord stimulation in

motor recovery after spinal cord injury. The inaugural participant was enrolled in October and has successfully completed the interventional portion of the study and

has entered the follow-up phase. He is also pursuing a new large animal model of spinal metastatic



Dr. Sean Barber

tumors. In addition, Dr. Barber has published eight peer-reviewed journal articles thus far in 2022, two of which he was listed as the first author.





In 2022, the

Department of

Neurosurgery

received 11 new

grants to fund its

innovative research



In August 2022, Lola Montalvo Parra, PhD joined the **Krencik** lab where she has already become a key player in a collaborative research project between the Krencik and Taraballi labs (both at Houston Methodist) that aims to use Lipo-nanoparticles to target specific phenotypes of central nervous system cells.

Research from the Hegde lab continued their longstanding focus on the investigations into the involvement of genome damage/repair responses in disorders of the human brain, with a focus on neurodegeneration and brain hemorrhage, and on mechanism-based developing novel treatment strategies for human brain disorders. In addition to ongoing NIH awards, the Hegde lab has been awarded the Parkinson's Disease Research Challenge Fund sponsored by Houston Methodist and The Sherman Foundation. The purpose of the Parkinson's Disease Research Challenge Fund is to provide one-to-one matching opportunities designed to motivate other



The Hegde lab

contributors to support Parkinson's Disease research activities.





In 2022, the **Krencik lab** published their innovative technology to generate and

interrogate experimental models of human neural networks. The designed neural organoids contain both mature neurons and astrocytic glial cells in relative proportions as the human brain and open many research applications. This study was highlighted by news agencies including *Technology Networks* and *EurekAlert*, and Dr. Krencik can be seen describing the findings on the Houston Methodist Neurological Institute's <u>Youtube page</u>. Currently, the Krencik lab has started three major new projects. First, funded by the National Institute on Aging, they



The Krencik lab

are inventing and testing new nanomedicines that specifically target brain cells in **Alzheimer's disease**. Second, funded by the National Institute of Neurological Disorders and Stroke, they are investigating proteins that may be used to therapeutically modulate abnormal brain activity due to neurodegenerative diseases, such as **Parkinson's disease**. Third, funded by Mission Connect (a program of TIRR Foundation), they will create new therapeutic approaches to reduce inflammation and dysfunction after **neurotrauma**. Their goal in the next year is to move these projects towards translational therapies for clinical testing.







https://krencik.hmailabs.org/



The Rostomily lab

The **Rostomily lab** continued its research to develop new therapeutic strategies for lethal adult **glioblastoma** (GBM). Supported by an National Cancer Institute U01 grant, they are working to quantify MGMT gene promoter methylation which is the most robust predictor of GBM patient outcome and response to standard of care temozolomide (TMZ) chemotherapy. Supported by Golfers Against Cancer, Dr. Andrei Mikheev and Svetlana Mikheeva identified the inhibition of DYRK1A kinase as a promising therapeutic approach that overcomes TMZ resistance in concert with

inhibiting the oncogenic TWIST1 protein. Funded by the Cancer Prevention Research Institute of Texas, Dr. Monika Vishnoi is exploiting high-throughput screens and novel reporters of GBM cancer stem cell membrane potential and cell-cycle states to identify

novel "electroceuticals" to reprogram GBM cancer stem cells to less malignant and treatment-responsive states. To address the challenge of translating progress from small animal rodent models to human, the Rostomily lab collaborated with the **Horner** and **Faraji** labs to spearhead development of a novel large animal syngeneic pig model of glioma as a platform critical for translation of



discoveries, therapies (including immunotherapies), surgical techniques and imaging to human. Through collaborative efforts of neurosurgery resident Dr. J.D. Patterson, Dr. Joe Masdeu (HMRI), and Paolo Zanotti-Fregonara (NIH), the Rostomily lab completed a first in kind positron emission tomography (PET) study of Translocator protein (TSPO) detection in metastatic brain cancer. Neuropathology Fellow Dr. Oluwaseun Ogunbona joined the Rostomily lab to assay TSPO expression in human brain metastases and with assistance from Dr. Aboud Tahanis, established correlations with TSPO PET imaging expected to serve as a tool to for precision brain metastasis treatment. Additionally, the lab continued to build and maintain the Neural Biorepository, which provides fresh and frozen samples of human blood, cerebrospinal fluid and tissue for the study of nervous system diseases, including stroke and cancer.



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https://rostomily.hmailabs.org/

There is a lot of exciting news to report for the **Villapol lab** in 2022. They have strengthened their projects to study drug delivery in the damaged brain. This allowed them to establish collaborations with HMRI researchers and be awarded with an NIH R21 grant to study the role of **nanoparticles** in helping to recover from brain trauma. They have also received grants in collaboration





Hannah Flinn has been working in Villapol lab for more than a year. Since joining the lab, she has demonstrated strong mentoring skills with summer students, helping them to learn many of lab techniques in a short time frame. She has also been a beacon that helps keep everything on track and up to date in the lab, working very hard until all tasks are complete and coming up with innovative solutions to problems.



The Villapol lab

with Baylor and HMRI laboratories to explore different approaches to finding treatments for Alzheimer's disease. Their brain-gut-microbiome studies are ongoing, and some of the published work on the study of concussions and changes in the microbiome in Rice University football players have had a big media impact. This year they have also published five scientific articles and three book chapters and presented their work at several conferences and meetings. This success is due to the lab's fabulous team: Morgan Holcomb (lab manager), Dr. Sirena Soriano (postdoctoral researcher), and Hannah Flinn (research assistant). Also, they have been fortunate to incorporate four excellent medical students from different institutions to the lab: Jessica López

(Tecnologico University, Mexico), Peter Park (Texas A&M University), Leo Cruz-Pineda (Tecnologico University, Mexico), and Valerie DeLeon (University of Houston), as well as two brilliant undergraduate students from Rice University, Serena Wang and Donovan Butler.







https://villapol.hmailabs.org/



Dr. Yi-Lan Weng

The **Weng lab** is interested in how **epigenetics** and **RNA modifications** shape cell behavior and function, as well as how dysfunction of these mechanisms in response to the genetic and environmental risk factors could be linked to **brain disorders**. Currently, they are setting up proximity-dependent labeling methods for subcellular proteomic and RNA profiling to identify the origin endogenous immunogenic RNA. This innovative methodology allows researchers to better understand the signaling cascades that lead to inflammation and necroptosis. These results will reveal unprecedented pathogenic mechanisms underpinning **neurodegenerative diseases** and elucidate potential therapeutic applications to prevent neuroinflammation.





https://weng.hmailabs.org/

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NewScientist

#### Trainee Spotlight: Abdulaziz Bako, PhD

PhD Abdulaziz Bako. recently joined the Vahidy team where his research investigates intracerebral hemorrhage demographics to quantify differences in patient outcomes. Intracerebral hemorrhage is the deadliest form of stroke, but it is not as widely researched as other types of stroke. His publication, "Contemporary Trends in the Nationwide Incidence of Primary Intracerebral Hemorrhage" (Stroke) was featured in 42 news outlets including US News and World Report.

# RESEARCH LAB HIGHLIGHTS FROM THE CENTER FOR NEUROINFORMATICS AND NEUROSURGICAL OUTCOMES

The **Vahidy team** had a successful year building a team of researchers focused on analyzing population health systems to measure clinical decisions. Currently, the team is examining the incidence of intracerebral hemorrhage in the United States among different demographic populations. Other notable projects include longitudinal clinical studies that will study the efficacy of craniotomy compared with minimally invasive surgeries. The Vahidy team published extensively on the long-term effects of COVID-19, which have

gained national media attention. Of note, Dr. Farhaan Vahidy joined the editorial board of Neurology, the flagship medical journal of the American Academy of Neurology and a very well-respected journal in the field. In addition, Dr. Jonika Tannous continued her studies on how disruptions in care impacts Alzheimer's patients.









### RESEARCH LAB HIGHLIGHTS FROM THE KENNETH R. PEAK BRAIN AND PITUITARY TREATMENT CENTER



Dr. David S. Baskin

**Dr. David S. Baskin,** Director of the Peak Center, leads a team of brilliant scientists who are leading medicine by exploring and defining new scientific breakthroughs focused on novel treatments for **brain tumors**. The suffering that brain tumor patients experience is great, and their goal is to develop new and effective treatments for patients, taking new and important discoveries from the bench to the bedside. In 2022, the Baskin lab had several successful projects that achieved this goal, including the use of **oscillating magnetic fields** to kill brain cancer cells that have come from cell cultures to human trials, and a number of novel drugs that have been developed starting in silico to synthesize and use in animal models that produce powerful results. They have also unraveled the mystery of how brain cancer evades

the immune system and have found a number of targets to attack to remove the immune privilege that gliomas have produced and allow the immune system to eradicate malignant gliomas. Metabolic studies using MRI spectroscopy have provided new insight into how tumor cells alter their metabolism and provide new methods to kill cancer cells by attacking their unique and altered metabolism.





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houstonmethodist.org/research/our-faculty/labs/baskin-lab/

The **Baskin lab**: Dr. Martyn Sharpe played a key role in several papers published in 2022 that identified mitochondria as the primary target and the induction of reactive oxygen species as the driver of cancer cell death by the novel **Oncomagnetic device** that uses oscillating magnetic fields to kill cancer cells. As a trained biochemist with decades of **early-stage drug discovery** experience, Dr. Sharpe was the first to recognize the potential of the overexpressed catalytic enzyme monoamine oxidase B in gliomas, and successfully demonstrated its potential in **cancer chemotherapy** by developing two prodrugs, PAM-OBG and MP-Pt(IV) that have been remarkably successful in curing GBM in xenograft mice brain



Dr. Martyn Sharpe

tumor models. PAM-OBG analogs and MP-Pt(IV) were funded by the Translational Research Initiative at Houston Methodist Hospital for preclinical development. Dr. Sharpe's work explores how cancers modulate expression of sex-specific pathways for growth, and how these pathways could be exploited for vaccine development against /martyn-sharpe-88696650



cancers.

Dr. Kumar Pichumani

The **Baskin lab**: Dr. Kumar Pichumani is collaboratively working to understand the metabolic landscape of **meningioma**, which is the most commonly diagnosed central nervous system tumors in adults, results of which were recently published in *Neuro-Oncology*. He is pursuing **energy metabolism** of **malignant brain tumors**, including both low grade gliomas and glioblastoma (GBM), with the goal of identifying new therapeutic targets and non-invasive

diagnostic and prognostic biomarkers. For the first time ever, his team has demonstrated that both GBM and meningioma patients efficiently utilize ketone body (BHB) as an alternate nutrient to meet their bioenergetic requirements. Further, they identified MCT1 as the key enzyme involved in the transport of BHB and tested the effect of MCT1 inhibitor (AZD3965) on patient-derived primary cultures of GBM and meningiomas. Dr. Pichumani presented these results as an oral



presentation at the Annual Meeting of the International Society of the

Magnetic Resonance in Medicine, held in London, UK.



Dr. Santosh Helekar

The Baskin lab: Dr. Santosh A. Helekar, along with Dr. Shashank Hambarde and Dr. Arvind Pandey, has shown that patterned spinning oscillating magnetic field (sOMF) stimulation kills glioblastoma (GBM), diffuse intrinsic glioma, lung cancer, breast cancer and pancreatic cells in culture while sparing normal healthy cortical neurons, astrocytes, astroglial cells, and bronchial epithelial cells. They characterized the optimally effective range of frequency and timing parameters of sOMF and published a report where they show that sOMF is safe under in vivo conditions. These findings strongly support the use of oncomagnetic device and its safety for cancer patients. In 2022, they developed a fully functional human use Oncomagnetic helmet device prototype and used it to treat five end stage

recurrent GBM patients under an FDA-approved expanded access treatment program with promising results.



#### PATRICIA LEVY ZUSMAN INTERNATIONAL WORKSHOP ON NEUROREGNERATION

We are proud to announce that our fourth biennial Patricia Levy Zusman International Workshop on Neuroregeneration will occur from March 7-10, 2023. This workshop was built to develop a collaborative network that stimulates new ideas among scientists and encourages collaborations and research together in a hyper-focused environment with an incubator set-up. During the workshop, participants are encouraged to discuss novel concepts with other investigators and receive effective feedback, followed by an incubation period where they are urged to collaborate on the projects based on the ideas they had exchanged during the workshop, and lastly, have the chance to present their work at the next meeting. Targeted



"My research focus is in prospective and retrospective outcomes research in GBM and pituitary tumors. I am currently working on



Clinical Research Specialist

the outcomes analysis of Genemediated cytotoxic immunotherapies in combination with standard of care for the Herpes Simplex Virus-Thymidine Kinase clinical trial. Additionally, I am assessing the outcomes of multi-modal treatment approaches to patients with pituitary tumors. I am passionate about providing in-depth insights from data to investigate complex neuro-surgical inquiries."

recruitment of early-stage, rising star investigators and underrepresented minorities is an important strength that contributes to a motivating environment. We are proud to announce that funding for this workshop is made possible by the Patricia Levy Zusman Endowment and an NIH R13 grant. For more information and to register to attend, please visit: https://attend.houstonmethodist.org/event/zusman

#### DR. ROBERT GROSSMAN'S LEGACY CONTINUES



Dr. Robert Grossman

**Dr. Robert Grossman** is considered a pioneer in both neurosurgery and spinal cord injury research. Throughout his career, he discovered that the community lacked an accurate stereotactic atlas. Specifically, the quality of the histology in the few existing atlases was poor and there was no accurate representation of the lumbar and sacral region of the spinal

cord, which he realized would be critical for specific targeting of the spinal cord. As a result, it became his passion project to curate human spinal cord samples at Houston Methodist and explore fixation and staining protocols to produce a high quality lumbosacral spinal cord atlas. Over many years, he acquired twenty adult human spinal cord samples, processed those samples, and began to assemble an atlas. Sadly, he was not able to see this atlas published in his lifetime. However, his Research Associate Xiufeng "Hanna" Tang and colleague **Dr. Philip Horner**, worked together to complete and publish Dr. Grossman's labor of love. Per Dr. Grossman's wishes, this first-of-its-kind, high quality lumbosacral spinal cord atlas was published in *World Neurosurgery*. The creation of the only lumbosacral spinal cord atlas is a remarkable legacy

# ADMINISTRATION SPOTLIGHT: Bryan Santos



"Having the opportunity to be a part of such a prestigious institution has been an amazing experience so far. Although I'm relatively

Financial Analyst

new, I have already felt and seen how the environment creates a positive effect on everyone who walks through these doors. The energy that the faculty and staff bring every day on wanting to help make a difference in other people's lives has been inspirational for me to want to do the same. It feels great being surrounded by others who share the same passion and love for what they do, which is why I'm excited to join this journey in

creating a difference as part of

the Houston Methodist team!"

for Houston Methodist and for Dr. Grossman that will likely have an overreaching impact in the care and treatment of people with spinal cord injury.

#### 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 2022, we have established and expanded on key components of this environment and existing resources in order to create a leading restorative neuroscience research community.

#### **Collaborative Research:**

In 2022, the NeuroSpark Seed Funding helped to sponsor some internal collaborations that will build the really big ideas needed to drive the development of restorative neurological therapies. In addition, it continued to support several collaborative basic and clinical research teams who are seeking to reverse neurological damage in patients. Notably:



Dr. **Dimitry Sayenko** is working with Dr. Marcia O'Malley, a professor of Mechanical Engineering and Computer Science at Rice University, to improve upon the traditional methods for post-stroke motor rehabilitation by developing a combination of novel robotic exoskeleton technologies and non-invasive spinal neuromodulation. Results from this study 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).



Drs Horner and Rostomily are working to address how standard cancer therapy treatments ultimately harm the integrity of white matter tracts, which are made up of myelinated axons that enable signals to be sent up and down the spinal cord. 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.



Dr. Yi-Lan Weng is working with Dr. Francesca Taraballi, Director of the Center for Musculoskeletal Regeneration at Houston Methodist, to develop new therapeutic strategies to treat peripheral nerve injuries and neuropathies. Specifically, they are utilizing innovative tools to examine whether alterations in RNA methylation can promote and accelerate axon regeneration. Results from this study will open the door for many new therapeutic strategies by providing novel insights into the and ultimately provide novel insights into the regenerative mechanisms to encourage axon regeneration.

#### **Education:**

Further, thanks to the generosity of the Walter family, we were able to formally launch our innovative postdoctoral training program: Neural Control of Organ Degeneration and Regeneration (NeuralCODR). Specifically, NeuralCODR provides postdoctoral fellows with mentoring and training in the intersection of neural development, engineering, and communication between the injured brain and peripheral organs. It provides trainees with unique, and often rare, hands-on clinical experience and longterm clinical advisement. The success of the NeuralCODR program is not only exemplified by our two alums now in faculty positions, but also by our recently awarded, highly prestigious, and first-of-its-kind for Houston Methodist, NIH training grant (T32NS126115) that will enable us to further expand this education program. For more information see Neurosurgery Education below.



#### **Current Walter funded NeuralCODR trainees:**

As a NeuralCODR fellow, Dr. Sirena Soriano is exploring the therapeutic effect of fecal microbiota transplantation to restore the gut microbiota and improve recovery after traumatic brain injury in a mouse model of Alzheimer's disease. The results from her research will help elucidate the role of the brain-gut-microbiota in the association of traumatic brain injury and Alzheimer's disease. Further, they will provide the foundation for pursuing novel therapies based in manipulating the microbiota for Alzheimer's diseaserelated pathologies consequence of traumatic brain injury. In 2022, Dr. Soriano presented her research at the Gulf Coast Consortium Mental Health, Mission Connect and Society for



Dr. Sirena Soriano 2021 Walter Fellow

Neuroscience annual conferences and has published two first author and one co-author journal articles.

Since becoming a NeuralCODR fellow, Dr. Laura Montier has honed her networking skills as co-organizer of the Neuroregeneration lecture series and has developed several specialized technical skills. Of note, she has been trained in several surgical procedures that will be essential to performing her proposed research project that explores the role of mitochondria as a theraputic target in spinal cord injury. She has also taken operational ownership of maintaining the lab's Lightsheet microscope and mastered acquisition of high quality 3D images. This expertise allowed her to contribute images of injured mouse cortex for co-authorship of a book chapter with Dr. Villapol, as well as initiate a collaboration examining structural vascular and glial responses to injury using inovative tissue-clearing techniques.



2022 Walter Fellow

#### **NEUROSURGERY EDUCATION**

A major focus in the Department of Neurosurgery is a strong commitment to developing the next generation of clinician scientists and basic scientists. The Department's education initiatives are aimed at undergraduate, graduate, and postdoctoral trainees as well as clinical residents. We are happy to report that thanks to the generosity of the Paula and Joseph C. 'Rusty' Walter III family, we have established strong educational partnerships with various institutions (notably Weill Cornell) and have expanded our impact on the future generations of basic scientific and clinical researchers.

#### **Residency Training Program:**

The Department of Neurosurgery is fully committed to training tomorrows physicians and clinician-scientists. In 2022, we have 14 residents in our program, several of whom are currently performing their own research projects. Of note, Dr. Jaime Guerrero, a neurosurgical medical resident, received a Burroughs-Wellcome research fellowship that supports biomedical scientists at the beginning of their careers in areas of science that are poised for significant advancement but are currently undervalued and underfunded. He is currently conducting research under the mentorship of Drs. **Amir Faraji** and **Dimitry Sayenko**.



Dr. Jaime Guerrero

#### NIH-funded NeuralCODR T32 funded slots:

Through the generosity of the Paula and Joseph C. 'Rusty' Walter III family, we have created a solid foundation for our innovative postdoctoral training program: NeuralCODR, which offers trainees new perspectives on how the brain and organ systems interact in disease and repair. Further, it seeks to drive collaborations and training across the disciplines of molecular neuroscience, neural modulation, and organ function. We are pleased to announce that we received a first-of-its-kind for Houston Methodist and highly prestigious training grant (T32NS126115) from the NIH that will enable us to further expand this education program. In fact, we are currently in the middle of recruiting our inaugural NIH-funded class who will join our



Walter Fellows in the NeuralCODR program. To ensure proper governance and oversight for all NeuralCODR fellows, we formed a Leadership and Advisory Committee. This committee oversees and monitors all aspects of the NeuralCODR program, ensures each NeuralCODR trainee receives outstanding mentorship and guidance, and establishes/alters and implements appropriate guidelines as needed to assure success of the NeuralCODR program. If you would like to learn more about this program, please visit <a href="mailto:neuralcodr.org">neuralcodr.org</a>

















NeuralCODR Leadership and Advisory Committee members include (from left to right): Dr. Philip Horner (Program Director), Dr. Mary C. (Cindy) Farach-Carson (Program Co-Director); Dr. Jeannie Chin (faculty member); Dr. Rose Khavari (faculty member), Dr. Mario Romero-Ortega (faculty member), Dr. Benjamin Arenkiel (faculty member), Dr. Farhaan Vahidy (faculty member) and Dr. Matthew Hogan (trainee representative).

#### Weill Cornell Graduate Program:

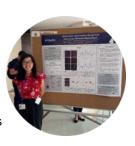
2022 marked an exciting milestone in furthering our education mission with the Weill Cornell Graduate School of Medical Sciences expanding their PhD program to the Houston Methodist campus. The Neuroscience graduate program will challenge students to develop their expertise beyond neuroscience, including organ and brain interactions, systems level physiology, engineering, in vivo imaging, and computational biology. Our inaugural roster of faculty includes Dr. **Phil Horner**, Dr. **Yi-Lan Weng**, Dr. **Murali Hegde**, and Dr. **Dimitry Sayenko**, with four additional neuroscience faculty under consideration next year. These faculty conduct internationally recognized research in models of aging, neuroregeneration, neurodegeneration, and injury within cell, animal, and human systems. A promising pool of candidates are currently under consideration for the 2023-24 academic year.

#### 2022 Summer Interns

The Department of Neurosurgery in collaboration with the Houston Methodist Academic Institute welcomed six undergraduate students to participate in a 10-week long summer internship program. Students were paired with faculty and postdoctoral fellows as they focused on a single research project. Also, they had the opportunity to attend weekly didactic lectures given by mentors, invited speakers, and others. The program is a vital component of the Department's commitment to training the next generation of scientists.

#### Rosemarie Le (Britz Lab)

My favorite part of this experience was presenting results to my lab and having small victories here and there! After this program, I am 100% sure I would like to continue research in whatever capacity it may be. I am still considering the physician-scientist pathway, but it seems more appealing now! Truly, I have learned so so much from basic lab skills like pipetting to immunohistochemistry and tractography to subarachnoid hemorrhages. Above all, I have learned how to troubleshoot and persist through obstacles as well as develop logical reasoning. My mentors all come from Europe, so it was interesting to hear about what their research experiences were like over there versus in the United States.



#### ADMINISTRATION SPOTLIGHT: Devon Miller

"I have been with Houston Methodist for about 6 years with a brief 3vear hiatus but have been back for about 3 months. lt's nice being back with

familiar



Research Operations Manager

faces and great meeting new team members and colleagues. Since returning, I have enjoyed the comfort of coming back to a great and supportive organization but joining a new department and learning new skills is always a and welcomed pleasure challenge. I am looking forward to growing and being a part of a team with ambitious, attainable goals to further science and discovery."

#### Scotland Inia Carter (Horner Lab)

My focal project explored whether delivery of therapeutic agents with nanoparticles could improve upper limb motor performance in rats with spinal cord injury. To do this, rats performed a forelimb reaching task where they grabbed a piece of chocolate. My task was to analyze and score those videos. The video scoring process was quite tedious, at times, but I felt delighted once the data were arranged in ways that one can use to derive meaning.

I feel much more empathy for researchers now, who watch their projects grow from an idea into a tangible entity that can help others. It was helpful to understand the dynamics of scientific research workspaces, like the Center for Neuroregeneration. It reminded me of the ways that ableism works against individuals who suffer damage to their motor skill functions—and how my school can work to help those in need. Lastly, I saw the importance of continuing to promote Diversity and Inclusion in spaces that have historically not had either. I feel even more strongly about uplifting youth—of every identity—so each student experiences a leveled playing field.

#### **Continuing Medical Education**

Dr. **Sonia Villapol** collaborated with Michael Dougan, MD, PhD and John P. Haran, MD, to develop a Continuing Medical Education module for MedScape on "The Role of Microbiome Modulation in COVID-19." The activity, aimed for clinicians who practice in infectious diseases, pulmonology, primary care, and gastroenterology, was built on her research on changes in the gut microbiome in COVID-19 patients. The CME & Education module represents one aspect of the Department of Neurosurgery's commitment to developing translational research.

#### IN THE MEDIA



Several of the Department of Neurosurgery faculty have been featured on the Houston Methodist Neurological Institute's YouTube Channel! The Neurological Institute is one of Houston Methodist's six centers of excellence, emphasizing medical care, research, and academics. To see Dr. Robert Krencik, Dr. Sonia Villapol, Dr. Sean Barber, and others speak on their most recent research

findings, visit the Houston Methodist Neurological Institute Lectures Series.

Dr. **Sonia Villapol**'s research on COVID-19 received extensive media coverage, including articles in Time, MSN, and Google News. Dr. Villapol was interviewed for <u>National Geographic</u> in March regarding her expertise on inflammation and COVID-19, where she commented that "there are virus reservoirs that can cause chronic inflammation." The article summarizes findings from her research, noting that "SARS-CoV-2 genetic material could persist for up to 230 days in the body and brains of COVID-19 patients, even in those who harbored only mild or asymptomatic infections."



Dr. Sonia Villapol

# houston foodbank

#### IN THE COMMUNITY

Houston Food Bank | October 17, 2022

Department members from the **Vahidy team** volunteered at the Houston Food Bank as part of Houston Methodist's I CARE in Action program. The Houston Food Bank serves 18 southeast Texas counties, where around 1 million people are considered food insecure.

Drs. Robert Krencik and Dimitry Sayenko spoke to trainees on their current research as part of Houston Methodist's Association for Postdoctoral and Trainee Affairs (MAPTA) on October 14. Their joint presentation, titled "Bridging the Gap: Neuroregeneration After Injury & Disease," addressed the current challenges and opportunities for translational research for patients with spinal cord injuries.



#### **METRICS OF SUCCESS**

#### **Grants Awarded:**

February: NIH/National Institutes of Aging R21AG075189. "Human Astrocyte-Based Nanovesicles to

Target Neuroinflammation in Alzheimer's Disease Networks." (**Krencik** – Principal Investigator)

GT Medical, STaRT Registry. "A Multicenter Observational Study of GammaTile™ Surgically Targeted Radiation Therapy (STaRT) in Intracranial Brain Neoplasms." (Baskin - Principal

Investigator)

May NIH/National Institute of Neurological Disorders and Stroke T32NS126115. "Training in

Neural Control of Organ Degeneration and Regeneration (NeuralCODR)." (Horner - Principal

Investigator)

June NIH/Office of the Director R21NS125509. "Methods and Devices to Assist and Improve

Cerebrospinal Fluid Drainage." (**Britz** – Principal Investigator)

July Department of Defense-DARPA G10000012) "Neurotechnology Responders to

Unconventional Brain Injuries (UBI)." (Villapol - Co-Principal Investigator)

The Sherman Foundation Parkinson's Disease Challenge Fund (Hegde - Principal Investigator)

Mission Connect, TIRR Foundation #022-105 "AstroCapsules: A Novel Tool to Detect and

Modulate the Neurotrauma Microenvironment." (Krencik - Principal Investigator)

August: Wings for Life Spinal Cord Research Foundation. "Neuromodulation for Enhanced Functional

Integration of Alginate Encapsulated Pre-organized and Networked Neural Stem Cell Ribbon

Grafts." (Horner – Principal Investigator)

September: NIH/National Institutes of Aging R01NS129788 "Relationship of the Human Astrocyte

Matrisome with Synaptic Networks." (**Krencik** – Principal Investigator)

NIH/National Institute of Neurological Disorders and Stroke R21NS127265. "Intranasal Delivery of Telomerase Reverse Transcriptase mRNA for Therapy of Traumatic Brain Injury."

(Villapol - Multi-Principal Investigator)

**December:** NIH/National Institute of Neurological Disorders and Stroke R13NS130938. "Patricia Levy

Zusman International Workshop on Neuroregeneration." (Horner – Principal Investigator)

#### **Peer-reviewed Publications**

#### January

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#### **Review Articles**

- Khan, S. U., Yedlapati, S. H., Khan, M. Z., Virani, S. S., Blaha, M. J., Sharma, G., Jordan, J. E., Kash, B. A., Vahidy, F. S., Arshad, A., Mossialos, E., & Nasir, K. (2022). Clinical and economic profile of homeless young adults with stroke in the United States, 2002-2017. Current Problems in Cardiology, 101190. https://doi.org/10.1016/j.cpcardiol.2022.101190
- Mitra, J., Kodavati, M., Provasek, V. E., Rao, K. S., Mitra, S., Hamilton, D. J., Horner, P. J., Vahidy, F. S., Britz, G. W., Kent, T. A., & Hegde, M. L. (2022). SARS-CoV-2 and the central nervous system: Emerging insights into hemorrhage-associated neurological consequences and therapeutic considerations. Ageing Research Reviews, 80, 101687. https://doi.org/10.1016/j.arr.2022.101687
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#### **Book Chapters**

- Villapol, S. (2022) Fisiopatología de las alteraciones gastrointestinales y hepáticas durante la infección por SARS-Cov2. In: Portela, E. B., editor. Fisiopatología de la COVID-19 en diferentes órganos y sistemas. Elsevier.
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- Villapol, S. (2022) Chapter 6. Gastrointestinal Disorders." In: Jason, L.A., & Lapp, C., editors. Understanding the Behavioral and Medical Impact of Long COVID: An Empirical Guide to Assessment and Treatment of Post-Acute Sequelae of SARS CoV-2 Infection. New York, NY: Routledge.
- Austerman, R.J., Rajendran, S., Faraji, A.H. (2022). Robotics in Functional Neurosurgery. In: González Martínez, J.A., Cardinale, F. (eds) Robotics in Neurosurgery. Springer, Cham. <a href="https://doi.org/10.1007/978-3-031-08380-8">https://doi.org/10.1007/978-3-031-08380-8</a>
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- Flinn, H., Cruz-Pineda, L., Montier, L., **Horner, P. J.** & **Villapol, S.** (2022) iDISCO tissue clearing whole-brain and light sheet microscopy for high-throughput imaging in a mouse model of traumatic brain injury. In: Borsello, T., editor. Neuroprotection: Methods and Protocols. Springer Nature.

#### **Editorials**

- Sadowsky C.L., Sayenko D.G. Harnessing neuroplasticity in the injured central nervous system using spinal neuromodulation. Front Rehabil Sci. 2022 Apr 27;3:841014. doi: 10.3389/fresc.2022.841014.
- Tannous J., Vahidy F.S. The collateral damage of COVID-19. Neurology. 2022 Feb 8;98(6):219-220. doi: 10.1212/WNL.00000000013196.

#### **Presentations and Invited Lectures**

#### January

• S. Villapol (January 11, 2022) "The role of the gut microbiome in the neuropathology of brain injury." Neuroscience Seminar via Zoom, organized by Baylor College of Medicine (BCM) and the Department of Neuroscience.

#### February

- S. Villapol (February 11, 2022) "Changes in the microbiota during aging and in patients with COVID-19." via Zoom, Mexican Association of Studies in Dementia.
- A. H. Faraji (February 17, 2022) "Why neurosurgeons need engineers." RICE Neuroengineering Initiative, Spring 2022 Seminar Series.

#### March

- S. Villapol (March 11, 2022) "COVID-19 SYMPOSIUM "Reflecting on 2 years of scientific accomplishments since the start of the COVID-19 pandemic" via Zoom, organized by Organized by the Ken Kennedy Institute, and Computer Science Department at Rice University.
- **D. Sayenko**, "Spinal cord stimulation after spinal cord injury." 17th Annual Meeting of the Korean American Spine Society, Austin, TX, USA.

#### April

• M. Hegde (April 7, 2022) "A new era of genome damage response at the forefront of brain health and therapy." International Brain Research Organization (IBRO) workshop on brain health awareness, K L University, India

- S. Villapol (April 9, 2022) "Two years of COVID-19: Lessons and improvements." MARC / RISE UPR- Río Piedras funded by NIH, Puerto Rico.
- S. Villapol (April 12, 2022) "Microbiome and brain damage: modulating neuroinflammation from the periphery." Department of Molecular Virology and Microbiology. CMMR Seminar Series.
- S. Villapol (April 27, 2022) "Modulating the gut microbiota to improve brain recovery." Department of Neurobiology and Anatomy, Drexel University, Philadelphia, PA.
- **S. Villapol** (April 29, 2022) "The role of the gut microbiome in the neuropathology of brain injury." American Association of Neural Therapy (ASNTR) 29th Annual Conference, FL.

#### May

 D. Sayenko, "Targeting cervical spinal sensorimotor networks using location-specific non-invasive spinal stimulation." The American Spinal Injury Association (ASIA) Meeting, New Orleans, LA, USA

#### June

• R. Krencik (June 25, 2022) "Astrocellular therapeutics." <u>Houston Methodist Neurological Institute Youtube Channel</u>

#### July

- M. Hegde (July 25, 2022) "A new era of DNA repair mechanisms based therapeutics for ageing and neurological disorders." International Meet on DNA Damage and Repair in Human Health- Scientific breakthroughs, Mangalore University, India
- S. Villapol (July 9, 2022) "Creating therapies for people with brain injuries" Houston Methodist Neurological Institute Youtube Channel

#### September

- Baskin Lab, K. Pichumani and O. Ijare (Sept. 2022), "Metabolomics of human meningiomas." 11th Annual Metabolism in Cancer Symposium, organized by MD Anderson Cancer Center.
- F. Vahidy (Sept. 2022) Neurosurgery Grand Rounds, Houston Methodist Hospital
- S. Villapol (Sept. 21-22, 2022) "Brain-periphery axis, establishing connections for better treatments." 4th Annual GCC Mental Health Research Conference. Rice University.
- **S. Villapol** (Sept 25, 2022) "Mechanisms of the Long-Covid." Post COVID World Health Network Virtual Symposium, online.
- S. Villapol (Sept. 26-28, 2022) "What the gut microbiome can tell us about concussion?: a football player story." Neurotrauma Symposium. University of California, UCLA.

#### November

- S. Villapol (Nov. 8-9, 2022). "What can DNA sequencing and the gut microbiome tell us about concussions?" Al in Health Conference, Ken Kennedy Institute at Rice University, Houston, TX.
- S. Villapol (Nov. 15, 2022) "Gut-brain interactions." Press Conference Neuroscience 2022: SfN Neuroscience, 2022. San Diego, CA.
- S. Barber (Nov. 29, 2022) "Intramedullary spinal cord tumors." <u>Houston Methodist Neurological Institute YouTube Channel.</u>
- R. Krencik (Nov. 30, 2022) "Neuromodulation of bioengineered organoids with reactive human astrocytes" Baylor College of Medicine, Huffington Center on Aging
- M. Hegde, "DNA damage-repair in brain health and disease: From mechanisms to innovative therapies." Houston Methodist Neurological Institute Lecture Series.

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