2021 ANNUAL NEWSLETTER
DEPARTMENT OF NEUROSURGERY

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

I joined Houston Methodist in 2013 with the vision to continue the legacy set by Dr. Robert Grossman in Houston Methodist being ranked as one of the top neurology and neurosurgery programs in U.S. News and World Report. We identified the need to build critical mass in our and clinical and research programs. In the last 8 years, we have expanded from 6 academic neurosurgeons to 20 academic neurosurgeons in addition to the 7 private neurosurgeons. Sixteen additional vital faculty in Neurocritical care, rehabilitation, pain, neuropsychology and neuro oncology make 36 total clinical faculty. In regard to the research, we started with one laboratory. The Kenneth R. Peak Brain & Pituitary Treatment Center was started by Dr. David Baskin who now has 6 PhDs running different research laboratories. The next major shift in expanding our research program was the recruitment of Dr. Phil Horner in 2017 and the development of the Center for Neuroregeneration. The Center for Neuroregeneration now is a team of five bench scientists focused on collaborative problem solving and bioengineering approaches to generate therapies for people with chronic paralysis and neurologic loss. My deep commitment to building a translational research program brought the opportunity to extend this research focus with the development and launch of the Center for Translational Neural Prosthetics & Interfaces in 2021. This program is in partnership with Rice University and will provide a human laboratory where neurosurgeons, neuroengineers and neurobiologists can work together to solve biomedical problems in the brain and spinal cord. Three basic science laboratories outside of the Rice engineers core faculty of 7, currently run collaborative projects in the Center for Translational Neural Prosthetics & Interfaces with the focus to recruit up to an additional three research teams.

As we close 2021, Neurosurgery research is building with fourteen dedicated research scientists and clinicians and nearly 75 research staff who support three core areas of research focus – neuro-oncology, neuroregeneration, and now neuroprosthetics. As Chair and 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 2022 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
Co-Director, Cerebrovascular Center
Co-Director, Skull Base Program
Houston Methodist Hospital
Professor of Neurological Surgery, Weill Cornell Medical College, NY

MISSION STATEMENT:

At Kenneth R. Peak Brain & Pituitary Treatment Center research laboratories, Dr. David Baskin along with a team of specialized scientists are developing exciting new treatment strategies to fight brain tumors. At this center, doctors and scientists collaborate to bring together multidisciplinary research approaches, translating into clinical outcomes as novel treatments to improve patient quality of life – with the ultimate goal to kill cancer.

At the Peak Center, we are committed to bench to bedside research and treatment. As Director, I encourage and recruit ideas, studies, and scientists that represent novel interventions that "think out of the box." The outcome for treatment of brain cancer has remained dismal for many years despite many millions of dollars being invested into work by brilliant scientists. Our philosophy is to support and encourage disruptive technology that brings new ideas and new ways of thinking to the problem. I am very proud of our team and our many accomplishments, including the inclusiveness and collaboration that occurs both within our group and also while working with many other brilliant scientists and clinicians. In 2021, we saw many of those innovative collaborations and promising studies flourish despite the COVID-19 restrictions. I am pleased to share with you an overview of some of those advancements (see *Updates from the Kenneth R. Peak Brain and Pituitary Treatment Center* for more details).

Sincerely,

David S. Baskin, MD, FACS, FAANS
Kenneth R. Peak Presidential Distinguished Chair
Vice Chairman and Residency Program Director
Department of Neurosurgery
Director, Kenneth R. Peak Brain and Pituitary Tumor Treatment Center
Professor of Neurosurgery, Weill Cornell Medical College

UPDATES FROM THE CENTER FOR NEUROREGENERATION

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.

As I reflect on not only the last year, but also the growth of the Center for Neuroregeneration since it's founding in 2015, I am amazed to recognize all that we have accomplished in such a relatively short time. We have assembled a cohesive, bedrock of neuroscientists who each provide a unique, established expertise, but who all have a common interest in innovative neuroscience with a strong translational focus. Together, this group of researchers has authored countless peer-reviewed journal articles, book chapters, and patents. They have developed new and exciting technologies, such as a first-of-its-kind neural stimulation chip and multi-electrode array system that can be implanted for over six months in neuromodulation experiments! Furthermore, they are educating the next generation of neuroscientists, with four of our postdoctoral fellows now established, independent faculty members at top ranking institutions (e.g., University of Illinois, Urbana-Champaign).

In 2021, this growth culminated with an upwards move - literally, as the Center moved from the 10th to the 11th floor of the Research Institute. We also saw our faculty members grow into their roles, with Dr. Muralidhar Hedge receiving an appointment as the Everett E. and Randee K. Bernal Centennial Endowed Director of DNA Repair. Further, despite COVID-19 restrictions, we were able to hold the third biennial Patricia Levy Zusman International Workshop (formerly known as the CNS Neuroregeneration Strategies: Discovery and Implementation Symposium), albeit 100% virtual. The warm reception and growing number of attendees at this National Institutes of Health (NIH) funded workshop epitomizes not only the emerging success of the Center for Neuroregeneration, but also its growing credibility and recognition on a national scale. And now, as I look forward to 2022 and beyond, I am full of enthusiasm to see how we will build on this strong foundation that we have established and not only further elevate our innovative research programs, but also positively impact both the social and the scientific communities.

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
Vice Chair Research, Department of Neurosurgery
Director, Center for Neuroregeneration, Houston Methodist Academic Institute
Professor of Neurosurgery, Weill Cornell Medical College

RESEARCH LAB HIGHLIGHTS FROM THE CENTER FOR NEUROPROSTHETICS

Dr. Gavin Britz

The **Britz Lab:** In 2021, the Britz lab published over ten peer-reviewed articles, In addition, we are pleased to announce a very exciting feat for 2021: the *forged partnership between the Britz lab (representing Houston Methodist) and Rice University to launch the Center for Translational Neural Prosthetics and Interfaces*, a collaboration that brings together scientists, clinicians, engineers and surgeons to solve clinical problems with neurorobotics. We fully believe this Center will be an accelerator for discovery. In fact, the first project seeded with this new collaboration seeks to develop a "sleeping cap" to analyze the cleansing flow of fluid that drains the brain of common metabolic waste during sleep. The potential of this project is illustrated by *the competitive research grant from the Medical Technology Enterprise Consortium (MTEC) the U.S. Army that was awarded to the project's principal investigators: Dr. Gavin Britz and Dr. Eugene Golanov.*
Website: https://britz.hmailabs.org/
Twitter: @gwb777

Dr. Amir Faraji

The **Faraji Lab**: In this first year at Houston Methodist, our functional neurosurgery program has made exciting leaps. We have built a busy deep brain stimulation and movement disorders program utilizing surgical robotics and advanced imaging for improved accuracy of lead placement. We have built a robust program in pain neuromodulation and spinal stimulation utilizing innovative neurophysiological assessment for accurate placement of electrodes combined with a strong clinical research program. *We have built a comprehensive translational program in peripheral nerve transfers to restore function lost by spinal cord injury, with Houston Methodist as the primary enrolling site for the southern United States in a multicenter clinical trial funded by the Department of Defense*. We are also building the groundwork for the Neural Electrokinetics Laboratory with work on drug delivery and understanding how electric fields move fluid through brain tissue and how peripheral nerve stimulation may enhance recovery as part of the Center for Translational Neural Prosthetics and Interfaces and in collaboration with the Center for Neuroregeneration.
Website: https://www.amirfaraji.com/
Twitter: @AmirHFaraji

The Sayenko Lab

The **Sayenko Lab**: The Sayenko lab is continuing to grow! A Postdoctoral Fellow, Dr. Jeonghoon Oh, two Research Technicians, Blesson Varghese and Madison Simmons, and a Research Assistant, Alexander Steele, have all joined our team in 2021. Further, our collaboration with our industry partner ANEUVO (Los Angeles, CA) (former Niche Biomedical) is growing, and we are wrapping up a pilot clinical trial on the effects of cervical transcutaneous spinal stimulation on the upper limb motor function in individuals with cervical spinal cord injury. In 2022, *we will continue working with ANEUVO and start an FDA-regulated pivotal multicenter clinical trial aimed to investigate the effects of cervical transcutaneous spinal stimulation on the upper limb motor function and quality of life in a larger spinal cord injury population,* together with Kennedy Krieger Institute (Baltimore, MD) and Shirley Ryan AbilityLab (Chicago, IL). In addition, several collaborative interinstitutional agreements have been signed between our team and (1) researchers from Dr. O'Malley's laboratory at Rice University (Houston, TX) to study the combinatorial effects of non-invasive spinal stimulation with an upper limb robotic exoskeleton and (2) Drs. Sheynin and Liberzon from Texas A&M University (Houston, TX) to investigate the effects of spinal stimulation on functional MRI of the brain. *Finally, a crowning achievement of 2021 is the funding of our first NIH grant to study the effects of non-invasive neurostimulation in people with paralysis.*
Website: https://sayenko.hmailabs.org/

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

Dr. Sanatosh A. Helekar

The **Baskin Lab**: One notable project, led by Dr. Santosh Helekar, was the development of our new Translational Research Initiative-funded Oncomagnetic Device, which is intended to treat glioblastoma and other solid malignant tumors. In 2021, we performed various pre-clinical studies to determine the mechanism of action underlying the anticancer effects of the spinning oscillating magnetic field (sOMF) generated by the device and characterized in detail the precise patterns of stimulation that are optimally effective in anticancer treatment. In doing so, we confirmed that sOMF selectively kills glioblastoma, diffuse intrinsic pontine glioma, lung cancer and breast cancer cells, but not normal neurons, astrocytes, and bronchial epithelial cells. Given the success we saw using the optimized sOMF parameters to treat mouse models of glioblastoma, we obtained an FDA approved compassionate use treatment protocol to treat three end-stage recurrent glioblastoma patients with a human use Oncomagnetic Helmet Device employing optimized sOMF stimulation parameters for two hours up to three times a day. ***Remarkably, all three patients showed more than 30% shrinkage of their contrast-enhanced tumors in the T1-weighted post-contrast MRI scans within the initial two to four weeks of treatment***. These promising results have so far led to three published papers and one manuscript currently under review. Of note, our published first-in-humans oncomagnetic treatment study case report in *Frontiers in Oncology* received world-wide press, internet, and social media coverage. Finally, the world and european versions of our "method and apparatus for oncomagnetic treatment" patent applications were published this year.

Website: https://www.houstonmethodist.org/research/our-faculty/labs/baskin-lab/
Twitter: @davidsbaskin1

Dr. Kumar Pichumani

The **Baskin Lab**: In 2021, we performed a series of studies led by Dr. Kumar Pichumani that focused on understanding the altered metabolism of brain tumors, given that tumorigenesis associated metabolic alterations are one of the core hallmarks of human cancers. Most studies to date on cancer metabolism have utilized isolated cultured cell lines, whose clinical relevance may be limited and uncertain and may not be optimal for developing targeted therapies or predicting treatment response. As such, we recently established the technology, using 13C Nuclear Magnetic Resonance spectroscopy, to safely study in vivo metabolic pathways in cancer patients***. Using this novel technology, we have discovered key differences in glucose metabolism between benign and atypical meningioma patients that will be of therapeutic interest to develop targeted therapies and non-invasive MRI diagnostics.*** Specifically, several currently ongoing clinical trials are based on the rationale that brain cancer cells do not oxidize ketone bodies. However, the results from our recent first-in-human pilot study indicate that glioblastomas and meningiomas are avidly oxidizing ketone bodies at a much higher rate than glucose. Ketone bodies rely on a monocarboxylate transporter, MCT1, for their rapid transport across the cell membrane, which is overexpressed in gliomas and meningiomas. Therefore, this discovery provides a unique opportunity to block the metabolism of ketone bodies using a small molecule MCT1 inhibitor. Finally, in 2021, we published a peer-reviewed article in the prestigious journal Neuro-Oncology on the role of glutamine in the growth and proliferation of meningiomas.

Website: https://www.houstonmethodist.org/research/our-faculty/labs/baskin-lab/
Twitter: @davidsbaskin1

Dr. Omkar Ijare

The **Baskin Lab**: Dr. Ijare is a trained Bioanalytical Chemist who, in collaboration with Drs. David Baskin and Kumar Pichumani, is investigating the metabolism of brain tumors (pituitary, gliomas, meningiomas) through the analysis of surgically resected tumor tissues and blood specimens. Specifically, this collaboration focuses on unravelling the metabolic pathways and genetic modulation that regulates the growth and control of pituitary tumors. They use nuclear magnetic resonance spectroscopy to establish novel metabolic pathways specific for pituitary tumors, as well as perform extensive studies of the genetic modulation and control of tumor growth. As a result, they have collected over 200 pituitary tumors harvested from patients during surgery, which permits many novel studies. The laboratory has published work regarding tissue and serum based novel biomarkers to differentiate various histopathological subtypes of pituitary adenoma, including Rathke's cleft cyst (RCC). The research on RCCs has earned the prestigious Integra Award from the American Association of Neurological surgeons in 2020. ***Currently, the laboratory is working on the comprehensive analysis of pituitary tumors and RCCs to develop the "Pituitary Tumor Metabolome," which will have immense applications in the diagnosis/prognosis of pituitary tumors and RCCs***. The laboratory also seeks to develop metabolomes of meningioma and glioblastoma tumors. Lastly, they recently published their preliminary study on meningioma tumors in *Neuro-Oncology*.
Website: https://www.houstonmethodist.org/research/our-faculty/labs/baskin-lab/
Twitter: @davidsbaskin1

The **Baskin Lab:** One exciting research avenue of the Baskin lab, led by Drs. Martyn Sharpe and Sudhir Raghavan, seeks to develop novel therapies for glioblastoma-drug design and new modalities of treatment. A key to anti-metabolite drug therapy development is to find an individual enzyme, or an enzymatic pathway, that is present in cancer, but not in normal tissues. Therefore, our group has focused on the ability of cancers to fuel their growth via metabolic systems that are normally only found in utero or in infancy. As a result, we have recently demonstrated that glioblastoma cells are highly efficient in taking up and catabolizing galactose, which is derived from lactose and that we normally ingest as babies. Glioblastomas can import galactose because they express high levels of the sugar transporters Glut3 and/or Glut14 which, unlike other sugar transporters, can efficiently transport both glucose and galactose. Glioblastomas also express all the enzymes needed for the metabolism of galactose, utilizing what is known as the Leloir pathway. No tissue in the normal adult body is capable of efficiently both importing galactose and metabolizing it. Therefore, a galactose based anti-metabolite that makes use of Glut3/14 importation and Leloir pathway enzymic activation will be non-toxic toward normal cells to have toxicity in glioblastomas. In 2021, we performed a series of experiments that ***led to the synthesis of the galactose-based anti-metabolite, 4-deoxy-4-fluorogalactose (4DFG), as a lead compound for a new class of galactose-based drugs.*** Our results show that treatment of glioblastoma cells with 4DFG can block glucose metabolism. Further, by examining patient GBM xenografts in immunosuppressed mice, ***we were able to show that low levels of 4DFG causes GBM flank tumors to shrink.***


Dr. Martyn Sharpe


Dr. Sudhir Raghavan

Website: https://www.houstonmethodist.org/research/our-faculty/labs/baskin-lab/
Twitter: @davidsbaskin1

RESEARCH LAB HIGHLIGHTS FROM THE CENTER FOR NEUROREGENERATION

Dr. Sean Barber

The **Barber Lab**: Led by Dr. Sean Barber, who is a rising-star spinal neurosurgeon and clinician-scientist, research in the Barber lab is geared towards gaining a better understanding of neuroregeneration after nervous system injury. Further, as a Clinician Trialist at Houston Methodist, Dr. Barber has spent the past year studying the role of epidural and transcutaneous spinal cord stimulation on motor recovery, bladder function, and peripheral immunity after spinal cord injury. In addition, not only has the Barber lab published five peer-reviewed journal articles thus far in 2021, but ***Dr. Barer has established an innovative and exciting collaborative project with Drs. Philip Horner and Tatiana Wolfe on a new large animal model for spinal cord injury***. In fact, they recently performed a successful trial experiment and are currently analyzing the results for publication.
Website: https://www.houstonmethodist.org/faculty/sean-m-barber/

The Hegde Lab

The **Hegde Lab:** We are very happy to announce that in November 2021, the principal investigator, ***Muralidhar Hegde, PhD, was appointed as Director of the newly-formed Division of DNA Repair Research within the Center for Neuroregeneration***. In 2021, researchers in the Hegde Lab continued their long-standing 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. Further, they worked on developing novel mechanism-based treatment strategies for human brain disorders. In addition to their ongoing NIH funding, the Hegde lab was awarded a sponsored research agreement with 'BridgeBio', a drug discovery company to develop new nucleic acid- for TDP-43-ALS in November. Finally, we are excited to welcome Mr. Vincent Provasek, an MD/PhD student from the Texas A&M University-Houston Methodist joint program, who joined the Hegde lab in August. As a member of the Hedge lab, Mr. Provasek will be performing his dissertation research which seeks to elucidate the role of TDP-43 in motor neuron disease and beyond.
Website:https://www.houstonmethodist.org/faculty/muralidhar-hegde/
Twitter: @mlhegde

2021 CENTER FOR NEUROREGENERATION SEMINAR SERIES SPEAKERS:

Tuesday March 16:
Jason J. Kutch, PhD (University of Southern California)

"Motor Cortical Treatment Targets for Chronic Pelvic Pain: Big Data, Small Data and Clinical Trials"

Tuesday April 20:
Michael E. Ward, MD PhD (National Institute of Neurological Disorders and Stroke, National Institutes of Health)

"Using iPSCs and 'omics to Unravel Mechanisms of Neurodegenerative Disease"

Tuesday May 25:
Yubin Zhou, MD, PhD (Texas A&M University)

"Engineering Signaling Proteins and Designer Cells for Biomedical Applications"

Tuesday September 21:
Ralph M. Garruto, PhD (Binghamton University, SUNY)

"Natural Foci of Neurodegenerative Diseases in the Western Pacific"

Tuesday October 19:
John P. Donnelly, PhD, MSPH, MS (University of Michigan Medical School)

"Implementation of Evidence Based Care for Life-threatening Infection"

Tuesday November 16:
Won-Suk Chung, PhD (KAIST)

"Role of Glial Cells in Synapse Elimination"

The Horner Lab

The **Horner Lab**: This year, we focused on our team approach to discovering the mechanisms of activity-dependent plasticity. The laboratory discovered an exciting link between stimulation of the spinal cord and master regulators of inflammation. These studies and collaborative research led to seven publications and a new grant from the Craig H. Neilsen Foundation. In addition, *the Horner Lab received an NIH grant to build a new rat model system that can be used to track any neural cell lineage after injury and stimulation*. We also published a series of manuscripts on a novel approach to replace damaged circuity after neural injury. In collaboration with the Paluh laboratory, we developed a stem cell-derived, pre-organized motor neuron network that can be engineered to replicate the natural columnar shape and organization of spinal motor networks. We refer to these human motor neuron columns as 'ribbons' and have shown they can be scaled and transplanted into an injury site. We are extremely proud of two of our post-doctoral fellows who have advanced to academic research positions; Dr. Betsy Salazar has been appointed Research Scientist in the Department of Urology at Houston Methodist and Dr. Tatiana Wolfe has joined the research faculty in the Department of Radiology at the University of Arkansas. Finally, *the lab director Dr. Horner was honored to be selected to present the G. Heiner Sell Distinguished Lecture at the 2021 American Spinal Injury Association annual meeting.*

Website: https://horner.hmailabs.org/

The Krencik Lab

The Krencik Lab: This year, we are excited to report that we have produced five new publications so far, including "*Humanized Biomimetic Nanovesicles for Neuron Targeting,*" which reports on a novel therapeutic tool to deliver drugs and genetic material to human brain cells. This tool was granted a patent and is planned to be utilized in upcoming research targeting Alzheimer's disease. Also, we are continuing to interact with the community outside of the research institute, including hosting two undergraduate research interns this summer and presenting at external research conferences, such as the Mission Connect annual symposium (a program of The Institute for Rehabilitation and Research). Further, *Dr. Krencik recently presented the lab's progress internationally to Utretcht University Brain Center in the Netherlands, and he participated as an external advisor to a National Science Foundation-funded traineeship titled "Understanding the Brain: Training the Next Generation of Researchers in Engineering and Deciphering of Miniature Brain Machinery."* In the upcoming year, we plan to continue ongoing grants awarded by the Michael J Fox Foundation to understand the cause of Parkinson's disease and by the Cancer Prevention and Research Institute of Texas to generate a new method to test therapies against glioblastoma stem cells.

Website: https://krencik.hmailabs.org/

Twitter: @krencik_lab

Dr. Robert Rostomily

The **Rostomily Lab**: In 2021, the Rostomily laboratory identified Dyrk1a kinase as a potential therapeutic target that inhibits the malignant functions of TWIST1 protein and its binding partners. These findings supported an NIH grant submission (R01) wherein we proposed, in collaboration with Dr. Dan Kiss, to directly inhibit TWIST1 with RNA therapeutics. We also characterized glioblastoma matrix proteins (the "matrisome"), which are hypothesized to modify predicted responses of glioma cancer stem cells (GSCs) to therapy. By combining public glioblastoma gene expression with our lab's proteomic data, we identified novel candidates undergoing testing via high-throughput drug screens and 3D modeling. Additionally, *we obtained a grant from the Cancer Prevention and Research Institute of Texas (CPRIT) that enabled us to initiate studies of repurposing ion channel drugs to inhibit GSC malignancy through modulation of electrophysiology.* Further, with CPRIT funding,

we generated a first-in-kind pig preclinical glioblastoma model to advance surgery, imaging, and treatments, including immunotherapy. We plan to submit future NIH proposals to establish its relevance as a new mammalian cancer model. We are pleased to report that our collaboration with the University of Washington (U01 grant) to identify pre-analytic factors that modify MGMT promoter methylation quantification, a predictive glioblastoma response marker, was renewed by the NIH. Finally, we 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. *Notably, in 2021, we had 384 eligible patients of whom 317 consented to participate*. From those 317 volunteers, we collected a total of 408 specimens, specifically 101 fresh tissue, 81 frozen tissue, and 226 blood samples (some patients had multiple tubes).
Website: https://rostomily.hmailabs.org/


The Villapol Lab

The **Villapol Lab**: There is lots of exciting news to report for the Villapol lab in 2021: new projects, funding, publications, team members, and even a new lab location. Notably, we have established a collaboration and obtained a grant from the Defense Advanced Research Projects Agency (DARPA) with the Department of Bioengineering at Rice University to study the first biological responders to brain injury. We have also secured two new grants to study Alzheimer's disease in collaboration with the Houston Methodist Department of Nanomedicine and with Baylor College of Medicine. Finally, our projects have led to the study of nanomedicine for drug delivery and brain injury thanks to a grant obtained from Mission Connect, Overall, we have established a very powerful line of research that combines nanomedicine and neuroscience. In large part, this success is thanks to our fabulous team: Morgan Holcomb (lab manager), Dr. Sirena Soriano (postdoctoral researcher), and, our most recent member, Hannah Flinn (research assistant). Also, we have been fortunate to collaborate with several undergraduate students from Texas A&M, University of Houston, and Rice University: Kristen Curry, Maria Wang, Serena Wang, Pranjal Sheth, Elsbeth Chow, and Eric Wang, and Donovan Butler. Thanks to their hard work and effort, *we have published thirteen scientific articles and presented our work at sixteen conferences and congresses this year alone!* For this effort, our publication on nanoparticles received an award from the Houston Methodist Academic Institute with the Award for Excellence in Peer-Reviewed Publication.
Website: https://villapol.hmailabs.org/
Twitter: @svillapol


The Weng Lab

The Weng Lab: In 2021, research from the Weng lab focused on Alzheimer's disease (AD) and Alzheimer's disease-related dementias (ADRD), which are the most common forms of dementia. ADRD causes devastating personal, familial, societal, and economic burdens. Both genetic and environmental factors and their interplays contribute to the increase of ADRD risks. Our laboratory identified per- and polyfluoroalkyl substances (PFAS), a category of stable manmade chemical that becomes drinking water contaminants, can alters the epigenomic landscape and subsequently reprograms brain cells to be more susceptible to disease. We are currently setting up single-cell epigenomics profiling technique by combining CUT&Tag and the ligation-based combinatorial barcoding system to reveal the epigenomic changes in each subtypes of microglia. This methodology also allows us to better understand the transcription factor competition and/or coordination of active/repressive histone marks in cellular states. *We believe this sequencing platform will be a great resource in the Center for Neuroregeneration and will foster more collaborative research.*
Website: https://weng.hmailabs.org/

PATRICIA LEVY ZUSMAN INTERNATIONAL WORKSHOP ON NEUROREGENERATION

This year we held the third (but first fully virtual) biennial Zusman International Workshop. The event, which took place on March 3rd to March 6th of 2021, was purposefully built to provide a unique hyper-focused environment with an incubator set-up that cultivates collaborations across previously siloed niches. Targeted recruitment of early-stage, rising star investigators and under-represented minorities is an important strength that contributes to said environment. In addition, we provided a wide array of speakers (we had 29 speakers this year) whose lectures aim to drive new ideas and relationships that will ultimately lead to a cure for paralysis. This included 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 Reserve University, whose research focuses on biology that underlies axonal dieback and regeneration failure in the adult spinal cord. Finally, one exciting aspect that sets the Zusman Workshop apart is our Catalyst Awards. Specifically, participants are encouraged to team up and brainstorm potential projects based on the ideas exchanged during the Zusman Workshop. Those ideas are then presented to the group, and the most promising are awarded Catalyst Awards that help propel the projects into fruition. *We are proud to announce that funding for this workshop was made possible by the Patricia Levy Zusman Endowment, an NIH R13 grant and the Wings for Life Foundation*.

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

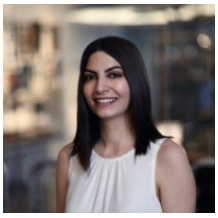
Thanks to a generous endowed gift from Paula and Joseph C. 'Rusty' Walter III, the Department of Neurosurgery has significantly expanded on its Neurorestoration Initiative, the goal of which is to develop a signature research and translational medicine program devoted to neural systems repair. This is 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 2021, 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 2020, we 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 two projects were selected for funding in 2020. In 2021, we have received a significant number of applications and they are currently under review by our External Advisory Committee.

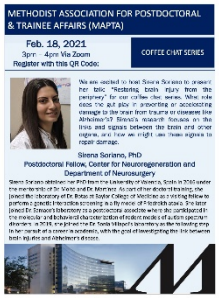
Education:

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. Thanks to the generous support from the Paula and Joseph C. "Rusty" Walter III Neurorestoration Endowment, we have been able to further formalize the training program by funding "Walter Fellows" in this program.



Dr. Sirena Soriano
2021 Walter Fellow

Most recently, **Dr. Sirena Soriano** was selected to be the 2021 NeuralCODR fellow. Dr. Soriano has established a mentorship team that consists of Dr. Villapol, Dr. Hegde, and Dr. Quigley. Her research aims to ***restore the gut microbiota in a mouse model of Alzheimer's disease in order to reduce neurodegeneration that occurs following a traumatic brain injury***. More specifically, she will determine whether gut microbiota restoration through fecal microbiota transplant can improve recovery after traumatic brain injury and the related Alzheimer's disease pathology. 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 disease-related pathologies consequence of traumatic brain injury. Notably, not only did ***Dr. Soriano publish two first author journal articles and two co-authored journal articles in 2021***, but she delivered a highly received and well-attended lecture on her research to the Methodist Association for Postdoctoral & Trainee Affairs (MAPTA).



Dr. Betsy Salazar
2020 Walter Fellow

As a NeuralCODR fellow, Dr. Salazar explored the therapeutic effects of electrical stimulation on sensorimotor function after spinal cord injury. More specifically, she sought to 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. ***She now has a faculty appointment as a Research Scientist in the Urology Department at Houston Methodist***. Her work focuses on studying the bladder-brain connection and utilizing noninvasive neuromodulation techniques to treat neurogenic and nonneurogenic bladder in humans. Notably, she recently presented data collected during her tenure as a NeuralCODR fellow at Mission Connect where her poster was awarded 1st place.

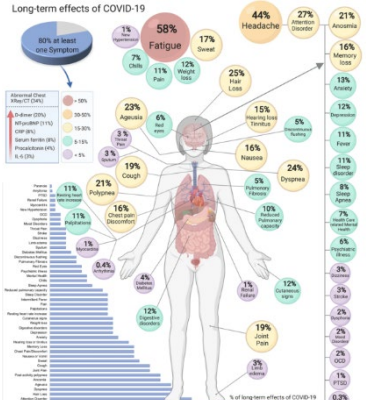
Dr. Caroline Cvetkovic
2020 Walter Fellow

As a NeuralCODR fellow, Dr. Cvetkovic sought to engineer biomimetic nano-scale vesicles applicable for central nervous system targeting and therapeutics by combining lipid-based nanoparticles with human stem cell-derived neural cells. Her project bridged multiple research fields with the potential for extensive collaboration as well as translation to other organ systems outside of the central nervous system. During her tenure as a fellow, she was awarded the Excellence in Mentoring Award (2020 Houston Methodist OGSTA) as we all both the Juror's Choice Winner and the People's Choice Winner in the NeuroArt Image Contest (2020). Additionally, she published one first author and one co-authored journal article. ***Currently, she is a Teaching Professor of Bioengineering at the Grainger College of Engineering, University of Illinois, Urbana-Champaign***.

IN THE MEDIA

Dr. Sonia Villapol

Of note, in response to the COVID-19 pandemic, the Villapol laboratory has focused on research aimed at helping COVID-19 patients. Specifically, the lab is studying the connection between changes in the microbiome and the severity of COVID-19. Based on this work, Dr. Villapol suggests that a person's microbiome holds the answer to whether they're likely to develop a more severe or moderate form of COVID-19 and if they are high risk for suffering from long-haul COVID-19. Further, Dr. Villapol recently published a systematic review and meta-analysis on this topic, which explores the more than 50 long-term effects of COVID-19. *This review paper has been picked up by 78 news outlets (e.g., SciTechDaily, Rolling Stone, ABC News, MSN, Yahoo, and Psychology Today), tweeted about more than 11,000 times, and its publication was listed as a significant scientific even in the 2021 in science Wikipedia page. Finally, a figure from this review article is featured in the Long_COVID Wikipedia page.* We are extremely proud to see the work from our Center having an impact in this COVID-19 world.



Taken from Dr. Villapol's review paper, and highlighted in Wikipedia, this figure illustrates the many long-term effects of COVID-19 as well as their estimated prevalence.

ADMINISTRATION SPOTLIGHT

Center for Neuroregeneration:

Two integral members of the Center for Neuroregeneration are our Research Assistants: Allison Frazer and Frances Humes. Both Allison and Frances helm the Center for Neuroregeneration's Animal Core. Not only are they trusted with the well-being and overall oversight of the animals themselves, but they serve as surgery coordinators for the Center. Briefly, they ensure that before a surgery happens, all the supplies are stocked and the people who need to be there are. In addition, they help center members stay within animal IACUC guidelines and guide the study coordinators in proper animal care, getting CMP veterinarians involved in their treatment when needed and staying within important guidelines. Further, they must ensure they not only stay abreast of new surgery procedures, post-operative care, and behavioral paradigms; but, they also must train center members on those same procedures, as needed.

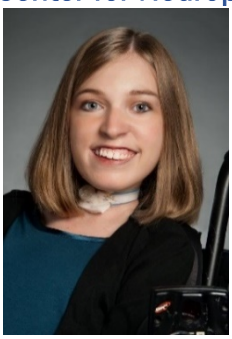
Allison Frazer
Research Technician

Allison, originally a veterinary technician, has been with the Center from Neuroregeneration since 2017. She brings with her an appreciation for both veterinary science and scientific research, which has enabled her to participate in more scientific veterinary studies. As part of the Center for Neuroregeneration, she has helped perform countless experiments (including a large pig study), participating in the *animal behavior, surgery (her favorite thing to do), data collection and analysis, and overall animal care,* though her main love remains pathology and anatomy.

Frances Humes
Research Technician

Frances, whose background includes clinical animal care, field research, and mitochondrial function, joined the Center for Neuroregeneration in 2019, where she primarily assists on pre-clinical projects examining spinal cord injury and motor function outcomes. Frances helps maintain our animal colonies, and she has quickly become adept at surgery procedures and behavioral paradigms. Overall, she has learned that *she loves contributing to the research projects. Specifically, she has found herself diving into the nuts and bolts of the research projects in order to support the big idea!*

Center for Neuroprosthetics:



Rachel Markley
Clinical Trials Manager

Rachel Markley was recently promoted to Clinical Trials Manager where she will lead coordinator staff and work to build and strengthen the Center for Neuroprosthetic's clinical research infrastructure. Rachel joined Houston Methodist in January 2019 to support Dr. Dimitry Sayenko's research program. During her tenure, she has shown continuous success in supporting the development of investigator initiated and industry sponsored human subjects research. In addition, she has expanded her expertise to providing guidance and support for FDA regulated device development trials, working closely with our Regulatory Affairs and Translational Management team to ensure successful IRB and FDA integration. In her new role, ***Rachel would like to strengthen resident and trainee education on clinical research start up and implementation, while continuing to assist faculty in growing their research programs.***

TRAINEE SPOTLIGHT

Morgan Holcomb is Research Assistant & Lab Manager from the Villapol laboratory where she has had a significant impact on the laboratory's research. In 2021, she has contributed to multiple projects, overseen administrative tasks, and mastered several techniques. Further, she has served as an excellent mentor to all the undergraduate students in the Villapol lab. As a product of her leadership, she produced enough data to present her research in a poster at the Mission Connect annual symposium.

Samira Ahglara-Fotovat is a Rice University Department of Bioengineering graduate student in the Krencik laboratory. She received a 1st place award at the 2021 Mission Connect Annual Symposium for her research poster presentation.

Shashank Hambarde is a Research Associate in the Baskin lab specializing in the detection of DNA damage. In 2021, he published a first author paper, which reported on the discovery of an ATR regulated EXO5-BLM protein complex that plays a crucial role in DNA replication restart, in the highly prestigious journal *Molecular Cell.* Further, Dr. Hambarde was invited to present his work at the 2021 Gordon Research Conference on Mammalian DNA Repair, where it was very well received.

Vincent Provasek is one of the first to take advantage of an exciting new collaborative education opportunity between Texas A&M and Houston Methodist. Specifically, as a Texas A&M MD/PhD student, he can complete his doctoral thesis work with a faculty member at HMRI. Mr. Provasek selected Dr. Hegde, in whose lab he hopes to elucidate the roles of TDP-43 in DNA repair and delineate the molecular basis of TDP-43 pathology mediated DNA repair defects in central nervous system/non-central nervous system disorders.

Yating Cheng is a Postdoctoral Fellow in the Weng laboratory. In 2021, she was awarded the Audience Choice Award for Best Podium Presentation and the Medical Resident/Postdoctoral Fellow Podium Presentation at the MAPTA Summer Science Symposium.

METRICS OF SUCCESS

Publications:

- Aghlara-Fotovat S, Nash A, Kim B, **Krencik R**, Veiseh O. Targeting the extracellular matrix for immunomodulation: applications in drug delivery and cell therapies. *Drug Delivery and Translational Research*. 2021 Dec;11(6):2394-2413. https://doi.org/10.1007/s13346-021-01018-0
- Austerman RJ, Sulhan S, Steele WJ, Sadrameli SS, Holman PJ & **Barber SM**. The utility of intraoperative neuromonitoring on simple posterior lumbar fusions—analysis of the national inpatient sample. *Journal of Spine Surgery*. 2021 Jun;7(2):132-140. https://doi.org/10.21037/jss-20-679
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- **Barber SM**, Sadrameli SS, Lee JJ, Fridley JS, Teh BS, Oyelese AA, Telfeian AE, Gokaslan ZL. Chordoma—current understanding and modern treatment paradigms. *Journal of Clinical Medicine*. 2021 Mar 4;10(5):1054. https://doi.org/10.3390/jcm10051054
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- Desai, VR, Lee, JJ, Sample, T, Kleiman, NS, Lumsden, A & **Britz, GW**. First in man pilot feasibility study in extracranial carotid robotic-assisted endovascular intervention. *Neurosurgery*. 2021 Feb 16;88(3):506-514. https://doi.org/10.1093/neuros/nyaa461
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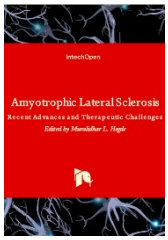

The book Dr. Muralidhar Hegde edited has been downloaded over 2,500 times to date. This achievement demonstrates the reach and usage of his publication:

- *Visibility*: more than 2500 researchers worldwide read, downloaded and interacted with his published content.
- *Impact*: Dr. Hegde's research clearly has influence within the scientific community.
- *Connectivity*: Researchers around the world have been able to connect with Dr. Hegde's research to further develop their own projects.

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Notable Lectures/Presentations:

January: "*Neuromodulation of spinal networks to recover motor function: Underlying mechanisms and clinical translations*." (virtual): Cellular to Clinically Applied Rehabilitation Research and Engineering (CARE). The University of Texas at Austin. (**Sayenko**)

February: "*Restoring brain injury from the periphery*". (virtual): Methodist Association for Postdoctoral and Trainee Affairs (MAPTA). Coffee Chat Series. (**Soriano**)

March: "*Neuromodulation of spinal sensorimotor networks using invasive and non-invasive spinal stimulation*" (virtual): 3rd Biennial Patricia Levy Zusman International Workshop on Neuroregeneration. (**Sayenko**)

"*Neuromodulation of spinal sensorimotor networks using invasive and non-invasive spinal stimulation*." (virtual): 11th Annual Trends in Spinal Cord Rehabilitation Symposium at

Kennedy Kreiger Institute. (**Sayenko**)

May: "*Can a concussion change your gut microbiome?*" (virtual): Sports Neuropsychology Society 9th Annual Symposium, Neuropsychology Society. (**Villapol**)

June: "*Sex differences in experimental neurotrauma: tips, advice, and live Q&A*". (virtual): Round Table. National Neurotrauma Society. Panelist Speaker. (**Villapol**)

July: "*The physiologic and molecular consequences of spinal cord stimulation after cervical spinal cord injury: Does electrode position matter?*" (virtual): American Spinal Injury Association Annual Meeting Sell Lecture. (**Horner**)

September: "*A new era of genome damage response at the forefront of brain health and therapy*" (virtual): Keynote Talk in the Vebleo Webinar on Materials Science, Engineering and Technology. (**Hegde**)

"*Microassembly of Bioengineered, Rapid, All-Inducible Neural System (μBRAINS) from Human Pluripotent Stem Cells*" (virtual): Utretcht University, Brain Center, Netherlands. (**Krencik**)

"*Leading medicine with the comprehensive treatment of movement disorders*" (virtual): HMNI Lecture Series: Movement and Functional. (**Faraji**)

Grants Awarded:

January: TIRR Foundation. "Astroparticles: A Human Astrocyte-Based Nanotechnology for Neuroregeneration." (**Krencik** – Principal Investigator)

CPRIT High Impact/High Risk Award RP190587. "Development of A Mini-pig Glioma Model and Validation of Human Clinical Relevance. (**Rostomily** – Principal Investigator)

February: Wings for Life Spinal Cord Research Foundation. "A Novel Non-Invasive Approach for Regaining Self-Assisted Standing after Spinal Cord Injury: Combining Transcutaneous Spinal Stimulation and Functional Electrical Stimulation." (**Sayenko** – co-Principal Investigator)

NIH/National Institute on Aging R21AG064567. "MicroBRAINS: Bioengineered Human Neural Circuits for Aging Research." (**Krencik** – Principal Investigator)

March NIH/National Institute of Environmental Health Sciences R01ES031511. "Systems-Wide Analysis of Oxidative Stress-Responsive m6A Epitranscriptome." (**Weng** – Principal Investigator)

Houston Methodist Translational Research Initiative Award. "MP-Pr(IV) - A Monamine Oxidase B Specific Mitochondrial 'Smartbomb' for the Treatment of Glioma." (**Baskin** – Principal Investigator)

June: Craig H. Neilsen Foundation: Neilsen Pilot Research Grant. "Non-invasive spinal neuromodulation and robotic exoskeleton to recover upper limb function after SCI." (**Sayenko** – Principal Investigator)

Craig H. Neilsen Foundation: Neilsen Pilot Research Grant. "Neuromodulation and the Neuroimmune Axis of Repair." (**Horner** – Principal Investigator)

NIH/National Institute of Neurological Disorders and Stroke R21NS106640. "The Role of the Gut Microbiome in the Neuropathology of Traumatic Brain Injury" (**Villapol** – Principal Investigator)

July: Craig H. Neilsen Foundation: Neilsen Pilot Research Grant. "Stimulation to Enhance Migration and Synaptic Integration of Neural Grafts." (**Horner** – Principal Investigator)

NIH/National Institute of Neurological Disorders and Stroke R01NS088645. "Etiological Linkage of DNA Damage/Repair Deficiency in Neurodegenerative Diseases." (**Hegde** – Principal Investigator)

NIH/National Institute of Neurological Disorders and Stroke R21NS117983. "A Versatile Reporter for Visualization of Myelin Plasticity in the Genetically Modified Rat." (**Horner** – Principal Investigator)

August: Department of Defense W81XWH-17-1-0331. "4-Aminopyridine Promotes Extensive Recovery in Acute Spinal Cord Injury" (**Horner** – Site-Principal Investigator)

September: NIH/National Cancer Institute U01CA246503-02. "Influence of Pre-Analytical factors in Glioblastoma MGMT Promoter Methylation Biomarker Assay." (**Rostomily** – co-Principal Investigator)

Department of Defense-DARPA G10000012. "High-Speed Biophysical and Biochemical Monitoring to Discover Early Markers of Unconventional Brain Injury" (**Villapol** – co-Principal Investigator)

October: Department of Defense. "Upper Extremity Nerve Transfers in Spinal Cord Injury Patients." (**Faraji** – Site-Principal Investigator)

BridgeBio Industry Sponsored Research Agreement. "Inhibition of TDP-43 Aggregation and Toxicity by Targeted Oligonucleotides in Cell-Based Models of TDP-43 Proteinopathy." (**Hegde** – Principal Investigator)

NIH/National Institute of Neurological Disorders and Stroke R01NS094535. "Novel Carbon Nanozyme Mechanisms for Traumatic Brain Injury Therapy." (**Hegde** – co-Principal Investigator)

CPRIT High Impact/High Risk Award RP210144. "Leveraging Glioma Stem Cell Electrophysiology for Therapy" (**Rostomily** – Principal Investigator)

November: Department of Defense MTEC. Rice University. "Translational Technologies for Detection and Restoration of Glymphatic Flow." (**Britz** – co-Principal Investigator)

NIH/National Institute of Neurological Disorders and Stroke R01 NS115877-01. "Elucidating spinal sensorimotor network components that underlie recovery of motor functions via lumbosacral epidural electrical stimulation in humans with spinal cord injury." (**Sayenko** – co-Investigator)

December: NIH/National Institutes of Aging 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/National Institute of Neurological Disorders and Stroke R01NS119587. "Harnessing Neuroplasticity of Postural Sensorimotor Networks Using Non-Invasive Spinal Neuromodulation to Maximize Functional Recovery After Spinal Cord Injury" (**Sayenko** – Principal Investigator)

Patent/Invention Disclosures:

February: Method and Apparatus for Oncomagnetic Treatment. Patent application No. WO2020102312A8. (**Helekar**, **Baskin**, **Sharpe**, and **Pichumani**)

May: Neurosome/Astrosome Compositions and Methods of Use. Patent No. WO2021091582. (**Krencik**)

September: Method and Apparatus for Oncomagnetic Treatment. Patent application No. EP3880299A1. (**Helekar**, **Baskin**, **Sharpe**, and **Pichumani**)

December: Closed Loop Sensor-based System for nSIM. Disclosure filed as additional intellectual property for a prior patent. (**Horner, Britz**).

Awards:

July: **Dr. Phil Horner**: Invited to give prestigious Sell Lecture at the 2021 American Spinal Injury Association annual meeting.

November: **Dr. Sonia Villapol**: President's Award for Excellence in Peer-Reviewed Publication, HMAI.