CENTER FOR NEUROREGENERATION 2017 YEAR IN REVIEW

DEPARTMENT OF NEUROSURGERY I HMRI REGENERATIVE MEDICINE PROGRAM

Volume 1 / Issue 1

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 within our research laboratories but also through strategic partnerships with clinical and biotherapeutic entities.

MESSAGE FROM THE DIRECTOR

Welcome to the inaugural year in review of the Houston Methodist Research Institute's Center for Neuroregeneration. We've confidently stepped toward our goal of creating an energetic group of collaborators that work to develop innovative approaches to regenerate the brain. We're thrilled that Dr. Robert Krencik joined our center as a laboratory director, and we expect further growth in the coming year that will add to our breadth of regeneration expertise. The appointment of Dee Woodson as our Program Manager has energized and focused our center goals. We've been fortunate to attract outstanding trainees and technical support that are the life-blood of our research program. Some of their achievements are highlighted in the following stories.

This is an exciting period of hope for translation of new approaches to repair the damaged nervous system. As our group grows and expands our collaborative network, we anticipate important contributions to report on the fundamental mechanisms of nerve regeneration and, importantly, how these ideas can be ushered to the bedside.

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

Sincerely,



Pro-

Philip J. Horner, PhD Director, Center for Neuroregeneration, Houston Methodist Research Institute Vice Chair Research, Department of Neurosurgery

LAUNCHING PROJECTS

In January 2017 we launched a New York State funded grant project in partnership with Dr. Victor Arvanian at the Northport Veterans Affairs Medical Center in Northport, New York. The objective of this project is to develop a viable, translational combination treatment integrating hiPSCs, to further maximize the beneficial effects of non-invasive repetitive electromagnetic stimulation and exercise.

In April 2017 Dr. Lesley Chaboub joined the lab as a Cullen Fellow generously

supported by the Cullen Trust for Health Care. Her project will focus on increasing the health of key cells responsible for making myelin to improve regeneration in central nervous system injuries.

In September 2017 the Center was awarded a grant from the Craig H. Neilsen Foundation in partnership with Dr. Chet Moritz from the University of Washington. We propose an innovative but technically challenging program to non-invasively stimulate spared host fibers in concert with transplanted neurons to create targeted connections.

TRAINING PROGRAM DEVELOPMENT

A core tenet of the Center for Neuroregeneration is to develop a world-class training program for postdoctoral fellows in the fields of neural stem cell biology, neural activity and stimulation, robotics, cell growth, myelin and the genetic regulation of plasticity. To that mission, we have developed relationships with academic partners at Baylor College of Medicine, McGovern Medical School and Rice University with the vision to develop a consortium for postdoctoral training in this emerging field. Our sights are set on May 2018 for submission of an NIH NINDS T32 training grant to fund the *Neural Control Fellowship Program*.

2017 NEUROREGENERATION SYMPOSIUM

In March 2017 Houston Methodist Hospital and The Center for Neuroregeneration hosted a NIH NINDS R13 supported international symposium centered on the application of neural stimulation and brain computer interfaces for treatment of neurologic injury, stroke and degenerative disease. The inaugural biannual workshop, *CNS Neuroregeneration Strategies: Discovery and Implementation*, focused on the intersection of electrical activity, brain connectomics and molecular neural plasticity with an eye toward clinical implementation to bridge the gap from the bench to the bedside. The two-day symposium welcomed 27 presenters from programs around the country representing this leading edge of neuroregenerative research. This symposium addressed the major opportunity for clinical/basic research partnerships to accelerate discovery of the mechanisms of stimulation but also inject exciting concepts from the field of neural regeneration to create combinatorial approaches that will further the efficacy of patient therapy. The 2017 Symposium was a huge success and planning for 2019 is currently underway.

COLLABORATIVE TRAINING OPPORTUNITIES

The Center for Neuroregeneration launched the Neural Control of Organ Disease and Regeneration Course in the spring of 2017. Our inaugural class consisted of 19 graduate and post graduate fellows from across the Texas Medical Center. This course complements research in organ regeneration, stem cell biology and tissue engineering by addressing the gaps in our knowledge of how the nervous system influences not only organ development, but also disease evolution and organ degeneration. The course is structured with each session pairing a clinical faculty with a basic science faculty to explore both perspectives on development and disease followed by an introduction to specific organ system regeneration approaches. Each session provided attendees the opportunity to learn about current research from leading faculty followed by dynamic discussion focused on problem-solving to identify gaps in knowledge and opportunities for future research. A diverse faculty has been incorporated into the training program, featuring labs from Baylor College of Medicine, Rice University, McGovern Medical School, University of Houston and the Houston Methodist Research Institute. Enrollment for our spring 2018 course is currently open with sessions beginning on February 12.

January 2017

Dee Woodson joins the Center as Program Manager to aid in program growth and development.

April 2017

Lesley Chaboub, PhD joins the Center as a Cullen Postdoctoral Fellow with research focus in oligodendrocytes and myelin biology in development and disease repair.

Betsy Salazar, PhD joins the Center as a Postdoctoral Fellow with research focus in effects of neuregulin-1 isoforms on regenerated myelin and the resulting impact on motor and autonomic function.

June 2017

Caroline Cvetkovic, PhD joins the Center as a Postdoctoral Fellow with research focus in bioengineering 3D neural cell culture systems or "mini brains" that can be used as a clinical model to study various aspects of development and regeneration.

2017 Summer Interns

Saba Barlas – Texas A&M Amanda Altenhofen – Baylor University Jocelyn Nikita Campa – Tec de Monterrey, Monterrey, Mexico Drew Levy – Duke University John Boom – St. John's School

July 2017

Caio Quini, PhD joins the Center as a Visiting Postdoctoral Fellow from the University of Sao Paolo, Brazil. His research focuses on the development of a technique that utilizes specifically designed magnetic nanoparticles to track biomarkers of neural regeneration

Leslie Rojas joins the Center as a Visiting Undergraduate Research Fellow from the University of Houston Downtown as an Engineering major with focus to learn basic science laboratory techniques.

August 2017

Avery Brightwell joins the Center as a Research Assistant to support the animal surgery core

September 2017

Joy Mosley joins the Center as a Secretary III.

December 2017

Allison Frazier joins the Center as a Research Assistant to provide rodent surgical support.

POSTDOC SPOTLIGHT

Dr. Caio Quini and Dr. Tatiana Wolfe were awarded for their work at the *TIRR Foundation Mission Connect Annual Scientific Symposium*. Their research has developed an enhanced white matter MRI contrast to study the quality of the myelin in the human brain and spinal cord. They named it myelin signal isolated MRI (siMRI). This advanced quantitative imaging modality employs a big data reconstruction model and processes the images offline using the institutional supercomputer cluster. The final images return to the lab benchtop for further research use. Preliminary data indicate that siMRI is capable of measuring normal aging and degeneration of human myelin. We have also piloted siMRI for visualization of traumatic brain injury. In November a selection of main results were presented at the *International Symposium on Neural Regeneration Conference (ISNR)* where we highlighted findings of global brain demyelination in people with multiple sclerosis. The Houston Chronical has reported the experience of a volunteer going through the siMRI scanning process and described the innovative aspect of this new imaging modality that is being developed in the Horner Lab. More on that story can be found <u>here</u>.

"WE NAMED IT MYELIN SIGNAL ISOLATED MRI (siMRI). THIS ADVANCED QUANTITATIVE IMAGING MODALITY EMPLOYS A BIG DATA RECONSTRUCTION MODEL AND PROCESSES THE IMAGES OFFLINE USING THE INSTITUTIONAL SUPERCOMPUTER CLUSTER...PRELIMINARY DATA INDICATE THAT SIMRI IS CAPABLE OF MEASURING NORMAL AGING AND DEGENERATION OF HUMAN MYELIN." DR. CAIO QUINI

Dr. Matthew Hogan presented his work at the International Symposium on Neural Regeneration (ISNR) in November 2017 and gave an invited talk at the TIRR Foundation Mission Connect Annual Scientific Symposium in December 2017. His project focuses on developing a novel spinal stimulation system designed for wireless control of nerve excitation. The system provides surgical advantages for implantation and can be operated remotely through a computer. This approach allows for increased flexibility and is capable of more precise stimulation than other therapeutic options.

FOCUS ON THE FUTURE

In 2018 we will initiate the design and prototype of a new device to treat acute stroke generously supported through the Houston Methodist Translational Research Initiative (TRI). The collaborative team members from the Department of Neurosurgery of Dr. Gavin Britz, Dr. Eugen Golanov, Dr. Tatiana Wolfe and Dr. Philip Horner will work with the Houston Methodist Research Institute GMP Core facility to design and manufacture an interventional device that meets FDA regulations. The project's mid term goal is to establish a limited clinical trial in 2020.

Faculty Recruitment – In 2018 our faculty recruitments will focus on two key initiatives. First, to increase our expertise in advanced neural rehabilitation methodologies and second, to recruit expertise in the molecular control of axon development and regeneration.

COMMUNITY INVOLVEMENT



Barbara Bush Literacy Foundation | May 11, 2017

Volunteers sorted and bagged nearly 10,000 books selected by children in three Houston area schools – Blackshear Elementary, Browning Elementary, and Treasure Forest Elementary School through the Foundation's My Home Library initiative. 2017 Metal and Muscle Regional Paralympic Sport Tournament | December 9, 2017

Our team helped out and cheered on the Shirley Ryan Ability Lab Chicago Bears Quad Rugby team. In addition to the rugby tournament, the 3 day event included wheelchair basketball, power soccer, sit volleyball, and other adaptive sports. This yearly event, hosted by the Houston Parks and Recreation Department's Adaptive Recreation division, brings teams from all over the country, and even internationally, together to compete.



2017 PUBLICATIONS

Krencik R, van Asperen JV, Ullian EM. Human astrocytes are distinct contributors to the complexity of synaptic function. Brain Research Bulletin. 2017 Mar;129:66-73. doi: 10.1016/j.brainresbull.2016.08.012.

Cheng Y, Sellers DL, Tan JY, Peeler DJ, **Horner PJ**, Pun SH. Development of switchable polymers to address the dilemma of stability and cargo release in polycationic nucleic acid carriers. Biomaterials. 2017 May;127:89-96. doi: 10.1016/j.biomaterials.2017.02.036. Epub 2017 Mar 1. PMID: 28284104

Nguyen H, Parvez Arnob MM, Becker AT, **Wolfe JC, Hogan MK, Horner PJ**, Shih WC. Fabrication of multipoint side-firing optical fiber by laser micro-ablation. Opt Lett. 2017 May 1;42(9):1808-1811. doi: 10.1364/OL.42.001808. PMID: 28454166

Nivison MP, Ericson NG, Green VM, Bielas JH, Campbell JS, **Horner PJ**. Age-related accumulation of phosphorylated mitofusin 2 protein in retinal ganglion cells correlates with glaucoma progression. Exp Neurol. 2017 Oct;296:49-61. doi: 10.1016/j.expneurol.2017.07.001. Epub 2017 Jul 3. PMID: 28684211

Zhao T, Sellers DL, Cheng Y, **Horner PJ**, Pun SH. Tunable, Injectable Hydrogels Based on Peptide-Cross-Linked, Cyclized Polymer Nanoparticles for Neural Progenitor Cell Delivery. Biomacromolecules. 2017 Sep 11;18(9):2723-2731. doi: 10.1021/acs.biomac.7b00510. Epub 2017 Aug 25 PMID: 28813139

Farina M, Ballerini A, Fraga D, **Hogan M**, Nicolov E, Demarchi D, Scaglione F, Sabek O, **Horner P**, Thekkedath U, Gaber O. 3D printed vascularized device for subcutaneous transplantation of human islets. Biotechnology journal. 2017 Sep 1. PMID: 28734022

Kondiles BR, Horner PJ. Myelin plasticity, neural activity, and traumatic neural injury. Dev Neurobiol. 2017 Sep 19. doi: 10.1002/dneu.22540. [Epub ahead of print] Review. PMID: 28925069

Krencik R, Seo K, van Asperen J, Basu N, Cvetkovic C, Barlas S, Chen R, Ludwig C, Wang C, Ward ME, Gan L, Horner PJ, Rowitch DR, Ullian EM. Systematic three-dimensional coculture rapidly recapitulates interactions between human neurons and astrocytes. Stem Cell Reports. 2017 Dec 12;9(6):1745-1753. doi: 10.1016/j.stemcr.2017.10.026. Epub 2017 Nov 30. PMID: 29198827

Krejciova Z, Alibhai J, Zhao C, **Krencik R**, Rzechorzek N, Ullian E, MansonJ, Ironside J, Head M, Chandran S. Human stem cellderived astrocytes replicate human prions in a PRNP genotype-dependent manner. Journal of Experimental Medicine J Exp Med. 2017 Dec 4;214(12):3481-3495. doi: 10.1084/jem.20161547. Epub 2017 Nov 15. PMID: 29141869

Yeh E, Dao D, Wu Z, Kandalam S, Camacho F, Tom C, Zhang W, **Krencik R**, Rauen K, and Ullian E, Weiss L. Patient-derived iPSCs show premature neural differentiation and neuron-type specific phenotypes relevant to neurodevelopment. Mol Psychiatry. 2017 Nov 21. doi: 10.1038/mp.2017.238. PMID: 29158583

Tan JY, Sellers DL, Pham B, Pun SH, Horner PJ. Non-Viral Nucleic Acid Delivery Strategies to the Central Nervous System. Front Mol Neurosci. 2016 Nov 1;9:108. eCollection 2016. Review. PMID: 27847462