The KSCIRC Report • Fall 2015

KENTUCKY SPINAL CORD INJURY RESEARCH CENTER

Director's Column

Collaboration and Translation, Keys to our Continued Success

Scott R. Whittemore, Ph.D. – KSCIRC Scientific Director

A great deal has occurred at KSCIRC since our last newsletter came out in April 2014. We have added new faculty, received numerous grants from the federal government and private foundations, and initiated exciting new research collaborations. To bring everyone up to date on our current faculty, we have provided short descriptions of their ongoing research. However, there is a twist to those descriptions. Ruth O'Bryan, KSCIRC Executive Administrative Associate and a lifelong lay person, collaborated with the faculty to write those paragraphs with the intention of making KSCIRC science understandable to all. She worked closely with our scientists and clinicians on their information and has done an outstanding job getting across both the direction and significance of the work that they do. I trust you will find them enlightening. If anyone has any questions regarding the research presented, I refer you to our webpage (http://louisville.edu/kscirc) where you can find individual contact information for our faculty. The scientists and clinicians who have recently joined our faculty are Robert James, M.D., Teresa Pitts, Ph.D., Enrico Rejc, Ph.D., and Fidias Leon-Sarmiento, M.D., Ph.D.

A major theme that runs through this newsletter is translational research. The foundation of KSCIRC continues to be outstanding basic science, rehabilitation and clinical research coupled with strong clinical neurosurgical and rehabilitation programs. Most importantly, there is continued crosstalk between these groups of scientists and physicians. Thus, results from the basic science laboratories drive new directions in patient care and questions raised by the clinicians are brought back to the basic science laboratories to address mechanism and/or new treatment paradigms. The former is often called 'bench to bedside' and the latter 'bedside to bench'. These are very important concepts that run through the entirety of the KSCIRC research portfolio. A good example, highlighted in this issue, is the work of two Ph.D. students, Darryn Atkinson and Amanda Pocratsky, investigating the same spinal cord

nerve pathway, in humans and experimental animals, respectively. Amanda's results have helped Darryn explain his data and the clinical questions that Darryn is asking are driving the next set of Amanda's experiments in the laboratory.

The KSCIRC faculty have developed extensive collaborations with faculty from other departments on both the Health Sciences and Belknap Campuses. To highlight a few of these, the Speed School of Engineering is intimately involved in the research of KSCIRC. Andrea Behrman Ph.D. and Dena Howland Ph.D. have been working with Tommy Roussel Ph.D. from the Bioengineering Department to design new devices for the Pediatric NeuroRecovery project which have resulted in major grants from the Coulter Foundation and Helmsley Charitable Trust. Moreover, these devices are being used clinically on a daily basis. Maxwell Boakye M.D. is collaborating with Robert Cohn Ph.D. from Electrical and Computer Engineering to develop new infrared sensors to measure blood flow in acute SCI patients in the operating room. This project will directly benefit SCI patients in the very near future. We are excited about these new partnerships

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SPOTLIGHT on Darlene Burke, M.S. — Research Coordinator

Darlene has worked for 23 of her 25 years at UofL on the Health Sciences Center campus in the Department of Neurological Surgery. She was one of the original members of the Department after it branched out from the Department of Surgery. She was brought on board as a biostatistician to analyze the data from experiments. However, since there were only a couple researchers and staff at that time, everyone was involved with all aspects of the research, from performing the experiments and collecting and analyzing data, to maintaining and ordering medical and office supplies. The Kentucky Spinal Cord Injury Research Center was established in 2000 and in just 15 years, has grown from just a handful of employees to over 120. Darlene interacts with many of them.

Darlene helps the faculty in their research by assisting with experimental design, analyzing data, and helping with experiment assessments and grants. She enjoys working with the large group of faculty because they are involved in so many different types of research. Because of this variety, the work doesn't become too routine or boring. In fact, there is such a broad range in the types of research conducted here that when new experimental research analysis problems sometimes arise, she enjoys the challenge of developing new and creative solutions.

Besides the faculty, Darlene works with the many trainees in the department seeking Master's, Ph.D. and M.D. degrees, as well as Postdoctoral Fellows and visiting summer students. She believes it is extremely important to help teach them the proper ways of collecting and analyzing the data. A publication of hers in 2013 (Burke, DA, Whittemore, SR and Magnuson, DSK, Journal of Neurotrauma, 30:797-805) emphasized how important is it to handle research data properly and carefully analyze it to make sure the results aren't over interpreted. She showed the consequences of overestimating positive results which can slow down progress of the research in the field.

Although Darlene may work with numbers all day, in her leisure time she has a creative side. She likes to draw, paint on wood and glass and enjoys wood burning and even writes poetry. She enjoys her job very much and hopes that the research here someday will help people with spinal cord injury.

"As the Scientific Director of KSCIRC, I can speak for all faculty who recognize the very significant contribution that Darlene makes to all of our research programs and we all appreciate her keeping us on our statistical toes" – SRW.

DIRECTOR'S COLUMN

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and will be discussing them in detail, as well as additional productive collaborations, in future newsletters.

Darryn and Amanda's research highlights another important aspect of KSCIRC. We have outstanding trainees that include Ph.D., M.S., medical, and undergraduate students as well as postdoctoral and clinical fellows. These trainees are the lifeblood of future scientific research and the KSCIRC faculty take very seriously the responsibility of their training and pride in their accomplishments. That is why every KSCIRC newsletter has a section devoted to their achievements. For this newsletter, congratulations to Starlyn Okada Ph.D., Amanda Pocratsky M.S., Anastasia Keller M.S., April Herrity Ph.D, D.C., Andrew Bankston Ph.D., Lynnette Montgomery Ph.D., Kelsey Stipp M.S., Grace Wainwright M.S., Justin Hallgren Ph.D., and Emily Martin and Alyssa Hoeper – undergraduates, who all won research awards or received advanced degrees. It is indeed an exciting time to be part of KSCIRC.

The 21st Annual Kentucky Spinal Cord and Head Injury Research Trust symposium was held in Louisville, May 20, 21st, 2015. There were 160 participants, speakers and participants who came together from all over the world to learn and share their most current research.

Those attending: **Front Row:** Rick Morimoto, Ph.D., Northwestern University; Scott R. Whittemore, Ph.D., symposium chair, University of Louisville; Marjorie Woollacott, Ph.D., University of Oregon; Amanda Bolton (trainee University of Kentucky);

2nd Row: Ronald Harris-Warrick, Ph.D., Cornell University; Tatiana Deliagina, Ph.D., Karolinska Institute, Sweden, Carolyn Meyer (trainee University of Kentucky); Chun-Li Zhang, Ph.D., University of Texas Southwest; Bonnie Ditterline (trainee University of Louisville);

3rd Row: Marc Freeman, Ph.D., University of Massachusetts (keynote speaker); Abdel El Manira, Ph.D., Karolinska Institute, Sweden; Stefan Stamm, Ph.D., University of Kentucky; Kathryn DeVeau, (trainee University of Louisville); Michael O'Donovan, Ph.D., Section on Developmental Neurobiology NIH/NINDS;

4th Row: Paul Kubes, Ph.D., University of Calgary; Christopher Power, M.D., University of Alberta; Jiaqian Wu, Ph.D., University of Texas;

5th Row: Carolyn Machamer, Ph.D., Johns Hopkins University; Ralph Nixon, M.D., Ph.D., New York University;

Picture not included: Lena H. Ting, Ph.D., M.S.E., Emory University

What's really going on at the KSCIRC?

A perspective from a long-time non-scientist.

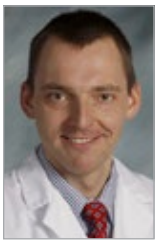
When you hear about the Kentucky Spinal Cord Injury Research Center (KSCIRC), your first thought is probably, "they only do research on spinal cord injury" (SCI). The thing is, research on SCI encompasses a wide variety of basic biological processes, and while the work starts out focused on SCI, it can end up affecting other biomedical issues that are related to SCI. There are millions of electrical wires in the body and when they are disrupted, it causes great damage to mobility, bowel and bladder function and a myriad of other bodily functions.

There are 19 basic science and clinical faculty members who are part of the KSCIRC. There are also 15 affiliated faculty members who are also basic scientists and clinicians who use the Center Core facilities to complete their research as well as collaborate with Center faculty. "Although each one has a single focus, the members expertise encompasses many aspects of scientific research which help SCI patients and may help others with stroke, Alzheimer's Disease, traumatic brain injury (TBI), and other neurological disorders, such as bowel and bladder issues, cardiovascular and breathing problems, the ability to cough and swallow, and mobility difficulties. Like the space program, there are many "spin offs" that come out of the Center research endeavors. Each lab within the Center is not an island. Collaborations between the labs at KSCIRC and labs in other institutions is the norm rather than the exception.

BASIC SCIENCE LABORATORIES

Laboratory of Molecular Neurobiology – Scott R. Whittemore, Ph.D., Scientific Director, KSCIRC

The main focus of Dr. Whittemore's research projects are how to protect cells in the spinal cord immediately following SCI. This is done by getting to the cells during the "acute" period which is less than "12 hours" after injury and the "sub-acute" period which is "1-3 days" after the injury. These time periods are critical and are when "many neurons and oligodendrocytes die." There is a means by which all cells are protected after stress or injury called proteostatis or "protein homeostatis." The Whittemore lab has focused over the past 5 years to identify targeted signaling pathways that enhance functional recovery after SCI. He is currently identifying new therapeutic targets in these pathways and screening FDA approved drugs to discover new treatments. A second major project is investigating how proteostasis mechanisms function in normal oligodendrocyte development – which could be therapeutically important to restore myelin lost after SCI. "This latter project has direct implications to multiple sclerosis and other myelin diseases."



Laboratory of Neural Signaling – Michal Hetman, M.D., Ph.D.

After SCI, cells around the injury begin to die, and how to keep this from happening is paramount for a patient so as to not lose more of their mobility or other bodily functions than what the original trauma caused. Dr. Hetman's labs works on cell death has direct implications for ALS, Alzheimer's disease, and TBI where there is also cell death.

Laboratory of Locomotor Systems and Rehabilitation – David S.K. Magnuson, Ph.D.

Dr. Magnuson's lab is working on the implications of gain and loss of locomotor function (stepping) after SCI. One of the lab mottos is "Exercise fixes everything." They have found that stretching and immobility may not be good for patients after a SCI, while increasing activity may be very good. People use wheel chairs for practical reasons, but no one has ever posed the question if using one is good, bad or indifferent for their recovery and health. The Magnuson lab also collaborates with several other labs to investigate cardiovascular issues, and they have discovered that the injury level, whether it be high (neck) or low (back) makes a big difference in how the cardiovascular system responds to and recovers from the injury. They are investigating if exercise, in this case swimming, can help improve function after an injury. "Much of this work may also be important for stroke, TBI or other neurological conditions."

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Glossary of Terms

Neurons – (also known as nerve cells) are the cells of the brain, spinal cord, and nerves which use electrical impulses to control various functions. They are connected to one another and also to all other tissues of the body. Interestingly, they don't touch, but communicate across a special gap known as synapse.

Dendrites – The part of a neuron which brings the information to the cell body

Axons – The "wires" of the neurons. They carry the information away from the cell body to other neurons or to cells like muscle cells.

Oligodendrocytes – Cells which provide the myelin (insulation) around the axons in the CNS.

Myelin – The material made bv the oligodendrocytes surrounding the axon to protect it, speed conduction velocity, and act as an electrical insulator.

White Matter – Any large collection of axons in the brain or spinal cord.

Translational Research – Taking the outcomes of the research endeavors the basic scientists find and translating those findings to the clinical and rehabilitation scientists.

Bench to Bedside – Taking what the basic scientists find in their research and translating it to the clinicians to use with patients.

Epidural Stimulator – This is a device that is surgically implanted in to a patient with a SCI with the expectation to stimulate movement.

SCI – Spinal Cord Injury

TBI – Traumatic Brain Injury

CNS – Central Nervous System

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Laboratory of Oligodendrocyte Function – Sujata Saraswat Ohri, Ph.D.

Oligodendrocytes, astrocytes and neurons are the main cellular building blocks of the CNS. Myelin that is secreted by oligodendrocytes wraps around the axons of the neurons which are the wires of the nervous system. Dr. Saraswat Ohri's lab focuses on ways to save and get the oligodendrocytes to work and function better after SCI by characterizing the basic regulation mechanisms in oligodendrocytes that are disrupted. The work from these studies will result in a better understanding of the complex functional changes that results after SCI and identify additional molecules that could be medically targeted. These basic studies are critical and lay the groundwork to be translated for clinical intervention and to other CNS injury models.

Laboratory of Advanced Optical Imaging – David P. Stirling, Ph.D.

The Stirling Laboratory uses a powerful imaging technique called two-photon excitation microscopy to visualize the spinal cord and white matter disintegration in "real time." After injury, they study how the response of the immune system to the SCI affects the "electrical system" of the body by watching the interaction of immune cells and axons that transmit information from the brain to the rest of the body. This lab is devising ways to stop the progression of the damage to the white matter in the spinal cord. These studies may also translate in to what happens in stroke, multiple sclerosis (MS) and other diseases that result in white matter loss.

Laboratory of Neural Plasticity, Repair and Functional Recovery – Dena R. Howland, Ph.D.

Dr. Howland's laboratory investigates the difficulties associated with walking and, in many cases, inability to walk following SCI. In addition to seeking to understand the basic processes that underlie the difficulties in walking and standing following SCI, this group's work also includes research into possible treatments to improve walking after SCI. These approaches rely on the nervous system's "plasticity," or its ability to adjust or adapt following trauma. Their lab's current approaches take advantage of the nervous system's plasticity range from attempting chemically to make the nervous system more likely to change and grow after injury to using training strategies to "teach" the spinal cord how to send correct "walk" signals to the legs and trunk. Some training requires subjects to practice various walking tasks of different levels of complexity, from simple treadmill stepping to ladder, stair and incline walking. Each of the more complex tasks requires the subject to evaluate and adapt to the sensory demands of the task that go beyond mere treadmill walking. This adaptation to the demands of the environment will be essential, making any restoration of walking following SCI have practical value for patients to operate in their communities. It will not only enhance their ability to get around but will also vastly improve their independence. By conducting work that ranges from the benchtop to studies with humans, Dr. Howland's overall research endeavors are designed to move information to the clinic level as quickly as possible and help patients. This research can also help patients with other neurological problems.

Laboratory of Airway Protection – Teresa Pitts, Ph.D.

Dr. Pitts is a speech pathologist who moved from bedside to bench following her Ph.D., and joined the faculty of the KSCIRC in January of 2015. Her lab concentrates on the interaction of cough, swallow and breathing disorders. Trauma to the CNS (such as SCI) and/or neurodegenerative diseases often result in disorders of swallow (dysphagia) and cough (dystussia). The co-occurrence of these clinical symptoms puts a patient at significant risk for pneumonia, a leading cause of death in these populations. Her lab's current projects focus on a full spectrum of research from basic experiments recording from the neural circuits in the brain stem that control these behaviors to clinical studies in SCI and the effect of respiratory strength training on airway protection. Dr. Pitts' long-term goal is to translate these findings to better equip clinicians (speech-language pathologists and physicians) to diagnose and treat disorders of the airway and devise protective measures.

Laboratory of Neural Physiology and Plasticity – Jeffrey C. Petruska, Ph.D.

Dr. Petruska's lab works on how nerve cells change (i.e., "neural plasticity") after SCI. Their focus is on axons, the wire-like parts of neurons which carry information. Axons that are spared can begin to make new connections naturally, a process called collateral sprouting. They hope to understand and control this process and "try to make what's left work better." The outcome of axons making new connections by collateral sprouting result in good effects or bad effects. An example of a good effect would be where the few spared axons make new connections so they can do the job of all of the similar axons that were injured. Examples of bad effects are symptoms such as pain, hypertension, and other associated conditions after SCI. Particularly troublesome is the condition called "autonomic dysreflexia," where people can have bouts of very high blood pressure that could even lead to a stroke. This condition is triggered by activity in pain-sensing neurons that have made improper new connections in the spinal cord. One of the goals of Dr. Petruska's lab is to manipulate the axons to make "good" outcomes, and prevent the pain and other issues. They have discovered many new genes controlling axon growth which may become targets for therapies. Importantly, they have also discovered other things that can be translated to the clinic for patients with SCI and other issues – notably

a possible new local anesthetic agent and a new treatment which may prevent development of chronic post-surgical pain.

Laboratory of Integrative Systems – Charles H. Hubscher, Ph.D.
Dr. Hubscher's laboratory is working on understanding how the CNS contributes to the functioning of the pelvic organs. Bladder, bowel and sexual dysfunctions consistently rank among the top disorders drastically affecting patient quality of life after SCI. Over the past decade, his lab's major focus has been on how the functioning of these organs is altered after SCI.

Novel therapies including exercise and epidural stimulation are currently being examined in an attempt to improve the functioning of all three organ systems. The lab is also examining ways to reduce chronic pain. In all experimental studies, the lab utilizes a variety of functional outcome measures to document improvements in the promising therapeutic interventions that are being tested. The discovery-driven insights of how these therapies affect pelvic organ function not only will lead to imminent treatments for those suffering with SCI; but could also influence the treatment of other neurological disorders such as multiple sclerosis, Parkinson's disease, and stroke.

CLINICAL LABORATORIES AND REHABILITATION LABORATORIES

Laboratory of Clinical Cardiovascular and Pulmonary Neurophysiology – Alex Ovechkin, M.D., Ph.D.
Dr. Ovechkin's laboratory investigates pulmonary and cardiovascular complications brought about by SCI. They are working on developing methods for improving these deficits. This research can also translate its findings to assist those with Chronic Obstructive Pulmonary Disease or (COPD) which is also a deficit in the ability to breathe properly.

Pediatric NeuroRecovery Lab – Andrea Behrman, PT, Ph.D.
Dr. Behrman's laboratory is examining ways to improve outcomes for children with severe and chronic SCI. Locomotor training is a developing therapy for use in this population. The therapy promotes activation of the neuromuscular system below the level of the lesion by repetitive practice of the tasks of walking and standing. This is done in a special environment with a treadmill, partial body weight support and manual trainers who facilitate the pattern of walking to provide the sensorimotor experience of walking. Some children have gained the ability to sit, to breathe better, to initiate steps, improved bladder control, and to walk. While the degree of improvement varies, the achievements are new when compared to current, traditional therapies. This therapy may have particular benefit to other pediatric populations with neurologic conditions such as children with severe cerebral palsy, head injury, stroke, or tumors in the brain or spinal cord.

Laboratory of Neural Plasticity – Susan J. Harkema Ph.D., Rehabilitation Director, KSCIRC and **Claudia Angeli, Ph.D. Senior Researcher, Human Locomotor Research Center, at Frazier Rehab Institute**
This lab has built on decades of basic science research models of SCI to develop the human epidural stimulation project. Currently, the research involves two main projects. "The first combines voluntary movement and locomotor training (standing and stepping) and epidural stimulation to produce improved motor function in individuals with injuries resulting in no motor function below the level of injury." There have been four individuals who have volunteered to be enrolled in this research study and they have "regained voluntary function after they were implanted with an epidural stimulator device." Two of the four who have no motor or sensory function below their injuries are now able to stand "over-ground" and able to bear their full body weight without any "external assistance," while they use only their hands for balance. The other two individuals, who had no motor function below their sustained injuries, are able to now stand with "minimal external assistance for extension of their hips."

The second project uses stimulation specifically targeted to improve cardiovascular issues to help "promote positive changes in heart rate and blood pressure through daily training, followed by a period of voluntary movement training (repeated attempts to move joints of the legs with stimulation), and then a period of stand training." These research projects help the research team understand the fundamentals of how the spinal cord controls movement; and in addition, things that are important to those with SCI like controlling bowel and bladder, sexual function, cardiovascular and respiratory function, and temperature regulation. These are all issues that SCI patients deal with on a daily basis. As these functions are being addressed with the "therapeutic methods" they are also able to collect data on the "safety and effectiveness of epidural stimulation and the training process which is the goal of a larger 36 participant research endeavor."

"This collaborative work in epidural stimulation shows that one of the primary problems in SCI may be the level of excitability of the spinal cord." In other words, "If the spinal cord circuitry can become more effective even without repair of the injury, then they can promote functional recovery even years after injury." This research also "lays the groundwork for understanding other movement disorders given that the spinal cord could be used as a gateway for positive changes through rehabilitation. That said, there could be potential for epidural stimulation to treat other neurological problems."

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Laboratory of Neuromuscular Control and Plasticity - Enrico Rejc, Ph.D.

One of the primary research aims of Dr. Rejc's lab is its concentration on helping the patient to recover their ability to stand after an SCI. Dr. Rejc's research "explores the communicating effects of the use of spinal cord electrical stimulation (epidural stimulation), while gaining sensory information originating from the skin, tendon and other receptors, and the rehabilitation outcomes on the nervous system." His goal is to find the correct combination of parameters while using the epidural stimulation regarding where the sites are located, the frequency and intensity to use in order to help the patient to stand by "enabling the spinal circuitry to activate the lower 'limbs' muscles 'naturally', rather than forcing them to act."

The lab's second project is looking at different levels of SCI and probing the effects on the spinal cord injured patient and the effects of different types of rehabilitation techniques on muscle function. He stated, "In spite of the trauma suffered by the paralyzed skeletal muscles, they can be reconditioned." It's important to examine different kinds of "rehabilitative protocols" regarding the muscles, their mass, strength, endurance and metabolic function to find ways to reverse the damage. This important research in improved muscle function can "be very useful to track and counteract any eventual health issues due to severe physical inactivity brought about by SCI as well as other conditions like stroke, COPD, and Parkinson's disease."

Laboratory of Human Neurophysiology and Neural Circuits – Fidias E. Leon-Sarmiento, M.D., MSc, Ph.D.

Dr. Leon-Sarmiento has been here at the University since June 2015. He collaborates with other faculty members examining injuries of the spinal cord to find what functions still work. His research is focused on understanding the "sensory, somatosensory, sensory-motor and motor control of individuals with SCI." Dr. Leon-Sarmiento is developing and supporting methods to "probe neural circuits using state-of-art non-invasive brain and spinal cord methods and tools. These include "transcranial magnetic stimulation, somatosensory evoked potentials, human brain and spinal cord neural responses, early and late spinal cord responses, autonomic system evaluation, and galvanic vestibular stimulation." These are non-invasive techniques which allow his group to study brain and spinal cord circuits that will ultimately help to improve neural function.

THE SCI CLINICAL AND TRANSLATIONAL RESEARCH PROGRAM

Laboratory of Spinal Cord and Brain Injury Research. Maxwell Boayke, M.D., Clinical Director, KSCIRC

The SCI clinical and translational research program supports the clinical studies with patients who have suffered a SCI, which are being conducted through UofL and Kentucky One's Frazier Rehabilitation Hospital. This program oversees the neurophysiology and imaging labs and is currently developing a porcine model of SCI. The program provides the neurosurgical preoperative services in the evaluation of best candidates for implanting the epidural stimulators in patients enrolled in the epidural research program. The program is assembling its infrastructure for building the coalition of translational research which include: "rehabilitation scientists, imaging scientists, neuroradiologists, engineers, basic scientists and electrodiagnosticians at the UofL." The program is a multidisciplinary program which includes clinical trials in patients with SCI in determining where the "gaps" are in treatments and then inform the basic scientists of those shortcomings so that they can address these issues in their research endeavors and translate those findings back to the clinicians to assist in their studies and their patients. The "program runs and manages the UofL participation in the North American Clinical Trials network (NACTN) which is the largest SCI research registry in the United States. The program also supervises UofL participation in the most promising clinical trials."

The first study by the porcine SCI research team will likely in January 2016. "The model will expand translational research opportunities to test mechanisms of epidural stimulation, spinal electrophysiological surrogate markers of recovery, biomarkers and therapeutics in a large research model of SCI. This is a multidisciplinary collaborative effort including Dr. Maxwell Boakye (clinician-scientist), Dr. Leslie Sherwood (Veterinary scientist), Dr. Susan Harkema (basic scientist), Dr. Dena Howland (basic scientist), Dr. Robert Cohn and Dr. Scott Cambron (Engineering) and Dr. Fidias Leon-Sarmiento (neurophysiologist) and the rest of our neurophysiological and translational research team."

The Cerebrovascular and Traumatic Brain Injury Clinical Research Laboratory (CTBI-CRL) - Robert F. James, M.D.

Dr. James joined the faculty at UofL in 2014. His lab is focusing on "translational and human clinical research methods to understand and prevent cerebral injury after trauma and stroke." The goal of his lab is to incorporate what has been learned from the basic scientist's research on neuroprotection and translate the methods to human patients who have suffered from devastating TBI or stroke. Efforts in his lab are an example of basic science faculty findings being able to be translated to the clinical faculty for use with humans.

Dr. James's group is currently involved in three clinical trials (see www.clinicaltrials.gov) 1) MISTIE-II, the primary focus of which is to decrease the negative impact of patients suffering from hemorrhagic stroke. 2) ASTROH which focuses on whether low-dose intravenous infusion of heparin (LDIVH) is safe and effective in patients with ruptured brain aneurysms. 3) PREDICT

which involves the Louisville Emergency Medical Services (EMS) and at least three other like services throughout the US. The goals of this study are to help EMS providers understand and determine whether patients are having the most severe type of stroke (ELVO) so they can be transported to the hospital as soon as possible in order to remove the blood clot to minimize the damage and restore brain function.

Physical Medicine and Rehabilitation – Darryl Kaelin, M.D.

Dr. Kaelin specializes in Physical Medicine and Rehabilitation. Also known as a "physiatrist," these doctors have trained in a specialized area of medicine treating loss of function and pain, whether it's "neuromuscular and musculoskeletal rehabilitation, pediatrics, sports medicine, pain management, geriatrics or neurology, among other areas." He evaluates the patients who may have suffered a neurological injury, a sports injury, dealing with cancer affecting various parts of the body, musculoskeletal conditions and spinal cord injuries, and then prescribes the proper treatment or medicines tailored to the patients' specific needs. Dr. Kaelin takes what the basic scientists have found in their research in movement, pain management, and bowl and bladder dysfunction and translates those findings to his patients. He is the "bedside" in the "bench to bedside" mission of KSCIRC and clinicians working together to help patients have a better life after injury or disease.

Assistive Technology Service – Mary Ellen Buning, Ph.D., OTR, ATP Department of Neurological Surgery

Dr. Buning works with patients who have many different kinds of diagnoses. Being able to move about independently is a "key focus" for this lab, as Dr. Buning works with patients who have "congenital or traumatic neurological injuries that include: SCI, Spina Bifida, Cerebral Palsy and other progressive diseases such as ALS, Muscular Dystrophy and Multiple Sclerosis." Working with patients/clients is paramount for her to come up with solutions tailored specifically to each patient's daily needs which are created by the environments they are in or their specific "life goals." She is also interested in the prevention of secondary disabilities that can arise in the "form of pressure ulcers, postural collapse with worsening curvatures and joint changes." "It's important to meet the patient where they are in their recovery or adaptation," she states, "some have clear goals and options while others are struggling to reorganize their lives and reestablish their priorities. Family support is often a key factor in this process."

Educating patients and making them aware of the resources available to them is an important component of her work with patients. "While it is important to learn about the technologies of rehabilitation: pressure management, postural support, and making the best choice of ultralight manual or powered wheelchairs, she believes that it is just as important to learn about community supports as well." She informs them of services available such as the "Office of Vocational Rehabilitation and the benefits provided by the American's with Disabilities Act and special education law." When patients go home they are armed with suggestions on how a "supportive environment can be created with the help of home modifications, personal care assistance, and wireless technologies to control the environment, communication devices, accessible and safe public or private transportation, finding resources and controlling things in the environment."

As you can see, all of these faculty members are working diligently together to help patients using what the basic scientists learn in their labs and forwarding that information on to the clinical and rehabilitation faculty to help patients with SCI and other neurological disorders have a better life.

KSCIRC Funding Received 2014 – 2015

Investigator(s)	*Funding Source*	*Amount*	*Start - End Dates*
Jeffrey Petruska	National Institutes of Health	$1,557,500	09/01/15 - 07/31/20
Charles Hubscher, Susan Harkema	Department of Defense	$744,159	09/30/15 - 09/29/18
Charles Hubscher	KSCHIRT	$299,846	01/15/15 - 01/14/18
Lynnette Montgomery (Charles Hubscher Post-doc)*	Paralyzed Veterans of America	$100,000	01/01/15 - 12/31/16
David Stirling	Craig H. Neilsen Foundation	$300,000	09/30/15 - 09/30/17
Teresa Pitts	National Institutes of Health	$730,889	04/01/15 - 12/31/18
Susan Harkema	Helmsley Foundation	$6,000,000	04/01/15 - 03/31/18
	National Institutes of Health	$250,000	09/23/14 - 05/31/19
	Department of Defense	$330,121	09/31/14 - 09/30/17
	Christopher and Dana Reeve Foundation	$93,843	10/15/14 - 10/14/15
Dena Howland	US Department of Veterans Affairs	$7,163	07/01/14 - 06/30/15
Andrea Behrman	Helmsley Foundation	$1,050,000	TBA
David Magnuson, Scott Whittemore	National Institutes of Health	$1,994,035	02/01/15 - 01/31/20

** Highest rated Fellowship proposal reviewed by PVA in 2015 funding round.*

Bench to Bedside:

Parallel clinical and experimental studies lead to novel insights in both.

As one of the leading Centers of its kind in the world, the Kentucky Spinal Cord Injury Research Center (KSCIRC) provides the unique opportunity for basic scientists, physicians, neurosurgeons, and physical therapists to work collaboratively with the common goal of curing paralysis. This continuum of research has facilitated a "bench-to-bedside" and "bedside-to-bench" approach where basic science questions are examined from a translational perspective, and findings in the clinical setting enlighten or guide future basic scientific studies. This enriching and integrative environment provides trainees the opportunity to experience a broad range of expertise and perspective in spinal cord injury (SCI) research. Since its inception in 2001, KSCIRC faculty have mentored, and continue to mentor, outstanding graduate students and postdoctoral fellows. Two of our current trainees were invited to speak at the 19th Annual Kentucky Spinal Cord and Head Injury Research Trust Symposium in Lexington, KY. http://www.mc.uky.edu/scobirc/symposia/symposia2014.html

Darryn Atkinson is a Ph.D. candidate in the Department of Anatomical Sciences and Neurobiology working in the laboratory of Dr. Susan Harkema. Darryn earned his Bachelors of Science in Exercise Science at Harding University (Searcy, AR), a Master's of Physical Therapy at the University of Texas Southwestern Medical Center (Dallas, TX), and a Master's of Science at the University of Louisville. Darryn's graduate work aims to identify spared neuronal connections between the brain and the spinal cord below the level of injury in patients. Recent studies in the Harkema lab have shown that during spinal epidural stimulation in humans with SCI, completely paralyzed individuals can move their legs voluntarily. The possible explanation is that some connections exist between the brain and spinal cord after human SCI that could not be activated previously. Darryn is using novel neurophysiological techniques to investigate the existence and nature of these connections. Determining the neuronal pathways by which descending signals cross the injury zone in humans will aid in understanding how the nervous system accomplishes the task of voluntary movement during epidural spinal stimulation.

Amanda Pocratsky is also a Ph.D. candidate in the Department of Anatomical Sciences and Neurobiology. She earned her Bachelors of Science in Neurobiology and Physiology at Purdue University (West Lafayette, IN) and a Master's of Science at the University of Louisville. Amanda is collaboratively working in the laboratories of Dr. Scott Whittemore and Dr. David Magnuson. Training in both laboratories has provided her the unique opportunity to combine the use of molecular and behavioral techniques to study neuronal pathways in the spinal cord that are thought to be spared after SCI. Using a sophisticated set of 'molecular tools,' she is able to transiently "silence" or functionally remove neuronal pathways from the spinal cord to determine their role in locomotion. After SCI, this technique can help identify spared pathways and their contribution to functional recovery acutely or chronically. Amanda hopes to identify a time window post-SCI where rehabilitation can be applied to enhance the recovery of function through the use of these spared connections.

Importantly, the spinal pathway that Darryn is studying in humans is the same pathway that Amanda is examining in the basic science model. Together, Darryn and Amanda represent one facet of the Center's seamless approach to SCI research where fundamental questions are simultaneously examined from a basic science and clinical perspective. The results in Amanda's basic science studies of spinal cord anatomy and physiology will aid in the interpretation of Darryn's clinical data. Darryn's data in humans will help Amanda interpret the functional significance of her basic science results. Better understanding the roles of these pathways gained through basic science research can help clinical scientists design new therapeutic strategies to target and optimize the use of these spared pathways after injury. Additionally, an improved understanding of the time-course of recovery after SCI is valuable to clinical scientists in the design and implementation of novel therapeutic intervention studies.

Amanda and Darryn are two of our very talented trainees, and represent the next generation of scientists. They discuss each other's data often and their scientific interaction is a perfect example of how translational research works.

"This enriching and integrative environment provides trainees the opportunity to experience a broad range of expertise and perspective in spinal cord injury (SCI) research."

Todd Crawford Foundation Walk/Run/Roll June 2015

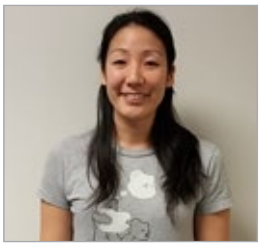
Pictured left are participants who came out to support the Todd Crawford Walk/Run/Roll event this past June helped raise money for the Crawford Kids. The Foundation does a myriad of fundraising events and those monies go towards helping kids with SCI be able to be treated at Frazier Rehabilitation Hospital. Since 2007 the Foundation has given KSCIRC over $77,000.

Right is Clare Conroy and her son Evander with Todd. Evander is the 2015 “Crawford Kid.” He was born with a malignant tumor in his chest and even with chemo therapy treatments being administered, the tumor damaged his spinal cord. His family was told he would never walk and would be bound to a wheelchair. Evander was enrolled in the research program being conducted at UofL whose focus looks for ways to better understand how the nervous system after injury responds to various therapies. This research is done in collaboration with the Kosair Charities Center for Pediatric NeuroRecovery and the KSCIRC led by Drs. Behrman and Howland and the Pediatric NeuroRecovery Team. For future events and support go to http://toddcrawfordfoundation.org/

Friends for Michael Foundation Events

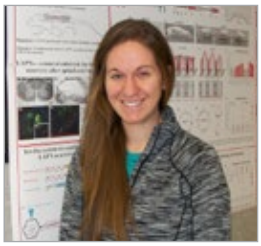
The Friends for Michael Foundation has provided research funds to the KSCIRC for over 14 years with donations of over $143,000. The funding goes towards supporting the research of one of KSCIRC’s trainees in Dr. David Magnuson’s laboratory. Dr. Magnuson holds the Friends for Michael Endowed Chair in Spinal Cord Injury Research. This year funds are supporting Ph.D. candidate Katie Harman. The FFM Foundation has multiple fundraising events during the year. (Left) Pictured at this year’s golf scramble are Linda Brent Berry, Michael’s mom, Coach Denny Crum who is a huge supporter of FFM and supporter Trish Osborn. Right, the FFM Foundation has also built a handicapped accessible playground in a community park in New Castle, KY. These are wonderful ways to remember Michael. For future fundraising events and support go to http://www.friendsformichael.org

Trainee Awards Research!Louisville 2014



Starlyn Okada, Ph.D. – Mentor David Stirling, Ph.D., received 2nd place in the postdoc category. The title of her poster was: "Effects of toll-like receptor 2 (TLR2)-mediated polarization of microglia following spinal cord injury" This research showed that after SCI, stimulation of the innate immune receptor TLR2 using a synthetic peptide treatment tended to lead to more anti-inflammatory responses by the tissue resident microglia.

April N. Herrity, D.C., Ph.D., – Mentor, Charles Hubscher, Ph.D., was the only student invited who gave a lecture at the Neuroscience Day Event called "What's happening in our backyard." The title of her lecture was "The impact of spinal cord injury on vagal afferents."



Amanda M. Pocratsky, M.S., Ph.D. candidate, — Mentors Drs. Scott R. Whittemore, Ph.D. and David S.K. Magnuson, Ph.D., won 1st place in the doctoral graduate student category. The title of her poster was "Hopping rats: a short tale of long ascending propriospinal neurons and locomotion." Amanda's project is identifying what role specific neurons play during locomotion. To do this, she uses a set of molecular tools that allows her to "silence" or inactivate pathways in the spinal cord and see how it affects stepping. She found that inactivating an ascending pathway that links the hindlimbs to the forelimbs (called long ascending propriospinal neurons) caused rabbit-like hopping during stepping. Her data has identified a novel pathway that plays a key role in locomotion. Ongoing studies in the laboratory will determine what role this pathway has in functional recovery following SCI

Amanda also won a University of Louisville Doctoral Basic Science Graduate Student Travel Award in September of 2014 for Research Louisville.

Anastasia Valerievna Keller, M.S., Ph.D. Candidate – Mentor David S.K. Magnuson. Ph.D.. Dr. Magnuson's laboratory has been collaborating tightly with Bioengineering Students from University of Louisville Speed School of Engineering. The highlight of this collaboration was an award winning poster at Research!Louisville 2014 by Anastasia (3rd year Ph.D. student in Physiology) with the title "Muscle stretch reduces locomotor function after a spinal cord injury: Implications for Physical Therapy." Among the authors were bioengineering students Grace Wainwright who has done a large portion of the analysis for that study and Erik Seibt, whose force sensing glove design and pilot study (measurement of forces during stretching of the leg muscles of their research model) have made it possible to draw out very important translational implications from our current basic research study for stretching rehabilitation in the clinics.

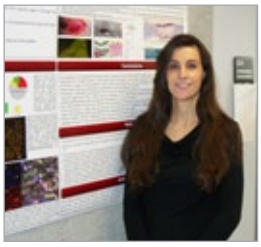
Degrees Received 2014

Kelsey Stipp M.S., Department of Anatomical Sciences and Neurobiology, Mentor, David S.K. Magnuson, received her Master's degree, August 2014. The title of her thesis was "Effects of passive immobilization on locomotor recovery after spinal cord injury in adult rats." Kelsey's studies examined the relationship between housing conditions (single vs double, large cage vs small cage), stress (using an open field assessment), overnight in-cage activity and locomotor recovery after SCI in rats. She developed a single-housing system where two animals occupy the same cage separated by a divider that allowed interactions with the other animal, but reduced the amount of overnight activity. This was found to be a stressful housing condition for the animals.

Trainee Awards Neuroscience Day 2015

Andrew N. Bankston, Ph.D., Postdoctoral Associate – Mentor Scott R. Whittemore, Ph.D., won 1st Place in the Postdoctoral category. The title of his poster was "Autophagy regulates the final stages of CNS myelin development." Andrew's project is researching the formation of myelin, the protective wraps around neurons, by oligodendrocytes in the central nervous system, which involves extensive cellular remodeling. He found that activity of autophagy, the process cells use to recycle their components, increased in oligodendrocytes during myelin formation and could be used to regulate the extent of myelin formation. Results found provide insight into novel functions of autophagy in oligodendrocyte and myelin development and identify autophagy as an attractive target to promote myelin repair after injury.

Emily Martin and Alyssa Hoeper (both bioengineering students) – Mentor David S.K. Magnuson, Ph.D., placed 1st in the E-Expo Student Research Competition. This is an event put on by the J.B. Speed School of Engineering at UofL. They also placed first at Neuroscience Day in the graduate student category. The title of their poster was "A novel continuous pool for investigating cardiovascular dysfunction after spinal cord injury." They also won the Diebold Award, which is an award that is judged during the E-Expo Student Research Competition.



April N. Herrity, D.C., Ph.D. – Mentor, Charles Hubscher, Ph.D., won 3rd place in the doctoral basic science graduate category with her poster titled "The effect of spinal cord injury on the neurochemical properties of vagal neurons." Her research showed: Since the vagus nerve does not travel directly through the spinal cord, its neurocircuitry is often considered intact following SCI. However, her research found that SCI induced a neurochemical change (an increase in P2X3 expression and a decrease in IB4 binding) in the cell bodies of the vagus nerve, including the cell bodies that innervate the bladder. These findings may have important clinical applications, such as helping understand reports of altered sensations stemming from internal organs below the level of injury as well as changes in visceral homeostatic mechanisms and nociceptive signaling that spinal cord injured patients may experience.

Degrees Received 2015

Grace Wainwright M.S., Mentor, David S.K. Magnuson, Ph.D., received a non-thesis Masters in Bioengineering August 2015. The title of her research was "Blood Pressure-Derived Respiration Rate During Exercise Swimming Challenges." She used filtering and data transformations to extract a breathing rate from blood pressure and heart rate signals captured from rats using a telemetry system. She showed that under some circumstances, but not all, a reliable breathing rate can be extracted and confirmed using cross-correlation. The main goal was to show how the breathing rate changed during the exercise challenge of swimming, and she accomplished that.

Justin Hallgren, Ph.D., Mentor, Michal Hetman, M.D., Ph.D. Justin successfully defended a Ph.D. thesis entitled "The Role of the Nucleolus in Neurodegeneration." Justin's thesis reported two major studies including (i) demonstration of ribosomal DNA instability in brains of patients with Lewy body dementia, and, (ii) identification of ribosomal protein L11 as mediator of neuronal apoptosis in response to disruptions of ribosomal biogenesis. Justin will continue his research career as a postdoctoral fellow at Thomas Jefferson University where he will study pathogenesis of amyotrophic lateral sclerosis.

Lynnette Montgomery, Ph.D., Postdoctoral Associate — Mentor, Charles Hubscher, Ph.D., received the Fritz Krauth Award from Paralyzed Veterans of America in Phoenix for being the highest ranked fellowship application in 2015. Lynnette also received the 1st Place Postdoctoral Fellow Award at Research!Louisville 2015.

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Kentucky Spinal Cord Injury Research Center

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