



**2005 PROGRESS REPORT FOR THE
SPINAL CORD AND BRAIN INJURY RESEARCH CENTER
(SCoBIRC)**

UNIVERSITY OF KENTUCKY

SUBMITTED TO THE

Kentucky Spinal Cord and Head Injury Research Trust

and

the Dean of the University of Kentucky College of Medicine

DECEMBER 31, 2005

EDWARD D. HALL, PH.D.

SCoBIRC DIRECTOR



This report describes our progress in achieving the goals for 2005 outlined in the 2004 Progress Report. Also presented are related SCoBIRC activities including the Invited Lecture Series, a full listing of publications, archived abstracts, and new grants for SCoBIRC Faculty and Faculty Associates. Lastly, we present the main SCoBIRC goals for 2006.

HIGHLIGHTS OF 2005

- SCoBIRC Core Faculty and 4 of the Faculty Associates moved into the newly completed Biomedical & Biological Sciences Research Building. SCoBIRC occupies approximately 30,000 square feet of space. This concentration of 11 SCoBIRC researchers into contiguous space has greatly enhanced communication and collaboration within the Center.
- Kathryn E. Saatman, Ph.D., formerly Research Associate Professor of Neurosurgery, University of Pennsylvania joined UK and SCoBIRC in January, 2005 as a Core Faculty Member and Associate Professor of Physiology.
- Addition of three new Faculty Associates: Melanie L. McEwen, Ph.D., Research Assistant Professor of Physical Medicine and Rehabilitation, Mark A. Prendergast, Ph.D., Associate Professor of Psychology and Karin R. Swartz, M.D., Assistant Professor of Neurosurgery
- Recruitment of Stephen M. Onifer, Ph.D. from the University of Louisville as a Senior Scientist III and Supervisor of the SCoBIRC Animal Surgery & TBI/SCI Models and Behavioral Testing Core Facilities.
- Acceptance of 5 new graduate students into SCoBIRC laboratories.
- Recruitment of 6 new post-doctoral fellows into SCoBIRC laboratories.
- SCoBIRC Faculty and Faculty associates published 57 full CNS injury-related publications.
- New CNS injury-related grants attributed to SCoBIRC Faculty and Faculty Associates included an NINDS Center Core Grant (\$2,256,211 over 5 years), Dr. Saatman's transferred grants and 4 KSCHIRT grants.
- Held first biannual SCoBIRC Faculty Retreat at Natural Bridge State Park on August 8-9, 2005.
- SCoBIRC Core Faculty organized and taught new graduate course on the "Neurobiology of CNS Injury" to 12 graduate students. The course will be offered every other year.
- With the help of Cardinal Hill Rehabilitation Hospital, we organized and hosted 3rd Biannual KSCHIRT Neurorehabilitation Symposium on September 30, 2005 at Hyatt Regency/Lexington Convention Center.

PROGRESS RELATED TO 2005 GOALS OUTLINED IN 2004 SCoBIRC PROGRESS REPORT

• GOAL 1: RECRUIT ADDITIONAL FACULTY/ SENIOR SCIENTIFIC STAFF

Kathryn E. Saatman, Ph.D.- Dr. Saatman joined SCoBIRC in January, 2005 as SCoBIRC Core Faculty member #7. She was formerly a Research Associate Professor of Neurosurgery and Associate Director of the Head Injury Center, University of Pennsylvania School of Medicine. She is an Associate Professor of Physiology (Tenure track, Regular Title Series). Her research is focused on cytoskeletal damage mechanisms in acute traumatic brain injury. She transferred her NINDS R01 grant and a PPG project to UK. Her laboratory has been fully functioning for several months and includes 3 newly recruited technicians and 2 postdoctoral fellows. In addition, Dr. Saatman has assumed Directorship of the SCoBIRC Behavioral Testing Core facility.

Stephen M. Onifer, Ph.D.- We were very pleased to recruit Dr. Stephen Onifer, formerly Assistant Professor of Neurosurgery at University of the Louisville (Kentucky Spinal Cord Injury Research Center, KSCIRC), to SCoBIRC as a Scientist III and Supervisor of the SCoBIRC Animal Surgery & TBI/SCI Models and Behavioral Testing Core Facilities. He has been actively involved in SCI research for many years as an NINDS-funded investigator. Dr. Onifer joined SCoBIRC in October, 2005, and has already made many improvements in the operation of our core facilities and is becoming involved as a co-investigator with some of the SCoBIRC Core Faculty.

New SCoBIRC Faculty Associates: Three new Faculty Associates have been added to the SCoBIRC ranks:

- **Melanie L. McEwen, Ph.D.-** Research Assistant Professor of Physical Medicine & Rehabilitation. Dr. McEwen's research interests include the role of apoptotic mechanisms in post-SCI secondary injury and develop of improved methods for assessing motor recovery in spinal cord-injured rodents.
- **Mark A. Prendergast, Ph.D.-** Associate Professor of Psychology. Dr. Prendergast's research involves the use of organotypic slice cultures for studying neurodegeneration.
- **Karin R. Swartz, M.D.-** Assistant Professor of Neurosurgery. Dr. Swartz, in addition to her clinical focus on spinal cord neurosurgery is also actively involved in investigating gender differences and the effects of estrogen on post-SCI secondary injury in rodent models.

Updated Listing of SCoBIRC Core Faculty and Faculty Associates:

The following is an updated listing of our SCoBIRC Core Faculty and Faculty Associates including their research interests arranged according to Basic-Plasticity/Regeneration/Remyelination, Basic-Secondary Injury Mechanisms/Neuroprotection and Clinical/Rehabilitation categories.

SCoBIRC Core Faculty:

Edward D. Hall, Ph.D., Director and Professor of Anatomy & Neurobiology,
Neurology and Neurosurgery

James W. Geddes, Ph.D., Associate Director and Professor of Anatomy & Neurobiology

George M. Smith, Ph.D., Professor of Physiology

Patrick G. Sullivan, Ph.D., Assistant Professor of Anatomy & Neurobiology

Alexander (Sasha) Rabchevsky, Ph.D., Assistant Professor of Physiology

Jinhui Chen, M.D., Ph.D., Assistant Professor of Anatomy & Neurobiology

Kathryn Saatman, Ph.D., Associate Professor of Physiology

Core Faculty Opening: 8-to be recruited in FY 2006

Core Faculty Opening: 9-to be recruited in FY 2006

Faculty and Faculty Associate Arranged According to Research Category:

- **Basic-Plasticity/Regeneration/Remyelination:**

Jinhui Chen, M.D., Ph.D., Assistant Professor
Dept. Anatomy & Neurobiology, College of Medicine
Control of post-traumatic neurogenesis

Pamela E. Knapp, Ph.D., Professor
Dept. Anatomy & Neurobiology, College of Medicine
Control of CNS glial development and myelination

Tim McClintock, Ph.D., Professor/Dept. Physiology, College of Medicine
Functional genomics of neuroregeneration and adult neurogenesis

Alexander (Sasha) G. Rabchevsky, Ph.D., Assistant Professor
Dept. Physiology, College of Medicine
Interventions to enhance functional recovery and reduce tissue damage following spinal cord injury; role of microglia in modulation of regeneration; mechanisms of autonomic dysreflexia

David C. Randall, Ph.D., Professor/ Dept. Physiology, College of Medicine
Autonomic control of cardiovascular function

George M. Smith, Ph.D., SCoBIRC Endowed Professor
Dept Physiology, College of Medicine
Cellular and molecular mechanisms involved in CNS wound healing and axonal regeneration; gene therapy of spinal cord injury

Diane M. Snow, Ph.D., Associate Professor/Dept Physiology, College of Medicine
Neuronal outgrowth inhibitory molecules, specifically chondroitin sulfate proteoglycans (CSPGs) during development and following CNS injury

Randal S. Voss, Ph.D., Associate Professor
Dept. Biological Sciences, College of Arts and Sciences
Microarray analysis of gene expression during amphibian spinal cord regeneration

Basic-Secondary Injury Mechanisms/Neuroprotection:

Annadora Bruce-Keller, Ph.D., Associate Professor
Dept. Anatomy & Neurobiology, College of Medicine
Inflammatory mechanisms in traumatic brain injury and neuroprotective effects of estrogen

James W. Geddes, Ph.D., Admiral Sheeley Endowed Professor/Dept. Anatomy & Neurobiology, and SCoBIRC Associate Director, College of Medicine
Cytoskeletal disruption following neuronal insult and calpain as a therapeutic target for spinal cord injury

Edward D. Hall, Ph.D., SCoBIRC Endowed Professor/ Departments of Anatomy & Neurobiology, Neurology, Neurosurgery, and SCoBIRC Director, College of Medicine
Reactive oxygen and cytoskeletal damage mechanisms in acute CNS injury; pharmacological neuroprotection; gender differences in CNS injury pathophysiology

Kurt F. Hauser, Ph.D., Professor/Dept. Anatomy & Neurobiology, College of Medicine
Role of opiate receptor mechanisms in acute CNS injury

Melanie L. McEwen, Ph.D., Research Assistant Professor/Dept. Physical Medicine & Rehabilitation, College of Medicine
Role of apoptotic mechanisms and novel methods for assessing motor recovery in spinal cord injury models

James R. Pauly, Ph.D., Associate Professor/Dept. Pharmaceutical Sciences, College of Pharmacy
Pharmacological neuroprotection and cognitive enhancement following traumatic brain injury

Mark A. Prendergast, Ph.D., Associate Professor/Dept. Psychology, College of Arts & Sciences
Investigation of neurodegenerative mechanisms in organotypic slice cultures

Kathryn E. Saatman, Ph.D., Associate Professor/Dept. Physiology, College of Medicine
Cytoskeletal damage mechanisms in acute brain injury

Stephen W. Scheff, Ph.D., Endowed Professor/Dept. of Anatomy & Neurobiology, College of Medicine; Associate Director, Sanders-Brown Center on Aging
Synaptic plasticity and recovery of function following head trauma and spinal cord injury

Joe E. Springer, Ph.D., Cardinal Hill Endowed Chair and Professor and Vice Chair for Research/Dept Physical Medicine & Rehabilitation, College of Medicine
Apoptotic cell death in traumatic spinal cord injury and neurorehabilitation research

Patrick G. Sullivan, Ph.D., Assistant Professor/Dept Anatomy & Neurobiology
Mechanisms and role of mitochondrial dysfunction in CNS injury

Clinical/Rehabilitation:

Franca Cambi, M.D., Ph.D., Associate Professor/Neurology, College of Medicine
Neurogenetics and mechanisms of demyelination in spinal cord disease

Jody Clasey, Ph.D., Assistant Professor/Dept Kinesiology and Health Promotion
Body composition analysis, and the relationship of body composition measures, physical activity and hormone function

Jimmi Hatton-Kolpek, Pharm.D., Associate Professor
Dept Pharmaceutical Sciences, College of Pharmacy
Organization, design and monitoring of traumatic brain and spinal cord injury trials; clinical pharmacokinetics of neuroprotective agents

Patrick Kitzman, Ph.D., Assistant Professor
Dept Rehabilitation Sciences, Division of Physical Therapy
Neuronal plasticity and spasticity following spinal cord injury.

Gerald Klim, D.O., Associate Professor and Chairman
Dept Physical Medicine and Rehabilitation, College of Medicine and Director, Brain Injury Rehabilitation Program, Cardinal Hill Rehabilitation Hospital
Rehabilitation after traumatic brain injury

Terry Malone, Ed.D., P.T., Professor and Director
Dept Rehabilitation Sciences, Division of Physical Therapy
Sports medicine and orthopedic injuries

Susan McDowell, M.D., Associate Professor/Dept Physical Medicine and Rehabilitation, College of Medicine and Medical Director, Spinal Cord Injury Unit, Cardinal Hill Rehabilitation Hospital
Rehabilitation after spinal cord injury

Karin R. Swartz, M.D., Assistant Professor/Division of Neurosurgery, College of Medicine
Gender differences in the pathophysiology of acute SCI

Byron Young, M.D., Professor and Head/Division of Neurosurgery, College of Medicine
Clinical trials in traumatic brain injury; cyclosporin A treatment of human TBI

- **GOAL 2: RECRUIT ADDITIONAL POSTDOCTORAL RESEARCHERS AND GRADUATE STUDENTS**

With the help of KSCHIRT-provided fellowship funding, we have recruited 5 new graduate students and 6 new post-doctoral fellows into SCoBIRC laboratories:

New Graduate Students

Mr. Lesley Gilmer	Laboratory of S. W. Scheff
Mr. Christopher Trimby	Laboratory of G.M. Smith
Mr. Aashish Joshi	Laboratory of J. W. Geddes
Mr. Robert Page	Laboratory of S.R. Voss
Mr. Jordan Clark	Laboratory of A. Bruce-Keller

New Post-doctoral Fellows

Liang Guan, M.D., Ph.D.	Laboratory of K. E. Saatman
Sindhu Madathil, Ph.D.	Laboratory of K. E. Saatman
Yanzhang Li, Ph.D.	Laboratory of J. W. Geddes
Kranthi Kumari Naga, Ph.D.	Laboratory of J. W. Geddes
Shaoping Hou, Ph.D.	Laboratory of A. G. Rabchevsky
Wongil Cho, Ph.D., M.D.	Laboratory of J. Chen

- **GOAL 3: CONTINUE TO BUILD EXTRAMURAL FUNDING BASE**

For the 2005 Fiscal Year alone, the SCoBIRC Core Faculty alone were responsible for \$3,062,229 in grant support. In addition, SCoBIRC was awarded an NINDS Center Core Grant which will run for 5 years. This grant has provided needed funding for equipping, maintaining and staffing 5 new SCoBIRC Core Facilities. The first funding year began in May, 2005. At this time, all of the cores have been established.

NIH/NINDS P30 NS051220 "UK Spinal Cord & Brain Injury Research Center Core Grant"

Direct Costs (full 5 years): \$2,256,211

PI: E.D. Hall

- Administrative & Bioinformatics Core- **J.W. Geddes, Core Director**
- Animal Surgery & TBI/SCI Models Core- **S. W. Scheff, Core Director; S.M. Onifer, Asst. Core Director**
- Behavioral Testing Core- **K.E. Saatman, Core Director; S.M. Onifer Asst. Director**
- Microscopy, Imaging & Stereology Core- **P.G. Sullivan, Core Director; A.G. Rabchevsky, Asst. Core Director**
- Pharmacokinetics & Biomarker Core- **E.D. Hall, Core Director; J. M. Bosken, Asst. Core Director**

Dr. Saatman, who joined SCoBIRC in 2005, transferred the following NINDS funding to UK-SCoBIRC

NIH NINDS R01 "Pathology of Traumatic Injury to CNS Axons"

Annual direct costs \$150,000

12/01/02-11/30/07

P.I. K.E. Saatman

NIH NINDS P-50 Center grant "Mechanisms of Cell Death after Traumatic Brain Injury"

9/30/00 – 8/31/06

Project 2 "Calpain Activation and Neurofilament Damage after TBI"

Project Director: K.E. Saatman

Total direct costs transferred to UK \$73,759

SCoBIRC faculty also successfully competed for 4 new KSCHIRT grants which began in early, 2005

P.H. Kitzman

"Role of glutamatergic system in SCI-induced spasticity in axial musculature"

J. Chen

"Wnt signaling pathway and neural stem cell fate determination"

J. Geddes

"Therapeutic window for calpain inhibition in spinal cord injury"

J. Hatton-Kolpek

"Effect of cyclosporine on isoprostane and neuroprostane levels in severe traumatic brain injury"

Other grants awarded to SCoBIRC Faculty Associates Relevant to SCoBIRC Research:

F. Cambi and P. E. Knapp

European Leukodystrophy Association.

"Correcting PLP Driven Myelin Deficiencies in Mouse and Human"

12-01-05 to 11-30-10

Direct Costs: \$585,000

S.R. Voss

National Science Foundation (DEB-0515730)

"Collaborative Research: Gauging introgression: Variation across the genome in mode and tempo of natural selection in a tiger salamander hybrid zone"

9/05-8-07

Direct Costs: \$161,648.

• **GOAL 4: PURSUE OPPORTUNITIES FOR BASIC-CLINICAL TRANSLATION**

The following clinical projects are in progress:

Phase I/II evaluation of cyclosporin A in patients with severe TBI -Young/Hatton-Kolpek

The NINDS-funded phase I/II dose-escalation study with cyclosporin A up to a 5 mg/kg i.v./day for 3 days in severe TBI patients has been completed. The drug was shown to be safe over the dose range studied and the pharmacokinetics were defined. A significant reduction in the 24 hr post-TBI plasma levels of 8-isoprostanes, brain-selective lipid peroxidation-related biomarkers, was observed along with a trend toward an improvement in 6 month neurological recovery.

Evaluation of the lipid peroxidation products isoprostanes and neuroprostanes as potential biomarkers for studies in severe TBI -Hatton-Kolpek/Young/Hall

We have successfully developed and validated a highly sensitive gas chromatography/mass spectrometry method for measurement of 8-isoprostanes in CSF and plasma obtained from neurosurgical patients. We are nearly finished with the development of a similar assay for the brain-selective neuroprostanes.

The following preclinical therapeutic discovery projects are ongoing, and will hopefully lead to clinical trials in the future:

- **Assessment of novel mitochondrial protective agents as neuroprotectants for acute TBI and SCI**

- **Non-immunosuppressive cyclosporin A analog NIM 811 (Novartis)**– Springer/Sullivan/ Hall: It has been shown that the mitochondrial and neuroprotective effects of cyclosporin A can be duplicated in a TBI model by the non-immunosuppressive cyclosporin A analog NIM 811. In addition, the compound is more effective than cyclosporin A in producing mitochondrial and neuroprotection in a rat spinal cord injury model. It is anticipated that we will complete the preclinical analysis of the compound in TBI and SCI models over the next two years. If it continues to look promising, it could be a candidate for movement into clinical trials in acute SCI and TBI.
- **Peroxynitrite scavengers**-Hall/Sullivan/Rabchevsky: The evaluation of the neuroprotective effects of the peroxynitrite scavengers tempol and penicillamine in rodent TBI and SCI models is ongoing. Studies with the former compound have shown promising mitochondrial and neuroprotective effects in the injured rat spinal cord.
- **Mild mitochondrial uncoupling agents**-Sullivan: The Sullivan laboratory has been pursuing a variety of different types of compounds that protect brain or spinal cord mitochondria by the induction of “mild uncoupling. This very novel strategy continues to look promising.
- **Evaluation of newer calpain inhibitors**- Geddes/Saatman/Hall: The proteolytic enzyme calpain is one of the key factors in post-traumatic secondary injury in the injured spinal cord and brain, and represents one of the best targets for neuroprotective interventions. With the recent addition Dr. Saatman, who is a calpain expert, to the SCoBIRC Core Faculty, we have achieved a critical mass of calpain expertise. Accordingly, we are planning to submit an NINDS Program Project Grant, lead by Dr. Geddes, that will be focused on novel therapeutic strategies for inhibiting calpain-mediated secondary injury in TBI and SCI. Until recently, the discovery and development of calpain inhibitors with good pharmaceutical properties has been elusive. We are in the process of evaluating newer and potentially “druggable” calpain inhibitors, one that we are obtaining from Abbott Pharmaceuticals and another from the laboratory of UK faculty member, Dr. Rodney Guttman. Calpain inhibition as a neuroprotective strategy is also attractive because the therapeutic time window for inhibition of calpain-mediated damage may be longer than some of the other leading neuroprotective approaches.
- **Evaluation of glutamate release inhibitors gabapentin and/or riluzole for control of SCI spasticity**-Kitzman: Post-traumatic spasticity is a major problem for the majority of patients with spinal cord injuries. Most of the available drugs for controlling spasticity work by potentiating the action of the inhibitory neurotransmitter GABA. In contrast, Dr. Kitzman, using a rat model of post-SCI spasticity in a KSCHIRT-funded project, has shown that two commercially available drugs that reduce the release of the excitatory neurotransmitter glutamate, riluzole and gabapentin, can also inhibit spasticity and may represent a novel and more effective approach for the treatment of spasticity than the GABA potentiating compound baclofen. This work could lead to a clinical trial to evaluate one or both of these drugs for spasticity modulation in SCI patients.
- **GOAL 5: HOST 2005 3RD BIENNIAL KSCHIRT NEUROREHABILITATION SYMPOSIUM**

Dr. Joe Springer, Cardinal Hill Endowed Chair and Professor and Vice Chair for Research in Department of Physical Medicine and Dr. Edward Hall, SCoBIRC Director, together with staff based at UK and Cardinal Hill Rehabilitation Hospital, organized a very successful and well-attended neurorehabilitation symposium which was held at the Lexington Hyatt Regency/Lexington Convention Center on September 30, 2005. The program is attached at the end of the report as **Appendix A**.

- **GOAL 6: HOST 2005 SCoBIRC INVITED LECTURE SERIES**

We hosted fewer invited speakers than usual in 2005 due in large part to moving 11 of our SCoBIRC administration and laboratories into the newly completed BBSRB. This effort turned out to be much more time consuming than we had anticipated. However, we were able to host four leading CNS injury investigators.

April 2nd: Dale Pelligrino, Ph.D.; Professor and Director of Neuroanesthesia Research, University of Illinois at Chicago. *When Good Hormones Go Bad: Neuroinflammatory Effects of Estrogen Replacement Therapy in the Diabetic Female*

September 29th: John T. Povlishock, Ph.D.; Professor and Chairman, Department of Anatomy & Neurobiology, Medical College of Virginia. *Traumatically Induced Cell Membrane Perturbation and its implications for Neuronal Injury and Death*

October 20th: Christopher C. Giza, M.D.; Assistant Professor of Neurology, UCLA-David Geffen School of Medicine. *Pediatric Traumatic Brain Injury*

November 30th: Ramesh Raghupathi, Ph.D., Assistant Professor of Neurobiology and Anatomy, Drexel University School of Medicine. *Intracellular Signaling Mechanisms After Brain Injury: A Worthwhile Endeavor or a Sisyphean Effort?*

2. SCoBIRC GOALS for 2006

- **GOAL 1: RECRUIT ADDITIONAL FACULTY**

Our primary goal will be to fill our last two promised SCoBIRC Core Faculty positions. We are focusing on young scientists working in the regeneration/plasticity area. However, we are carefully considering all applications from promising young neurotrauma scientists who have fundable, translationally-focused research programs.

- **GOAL 2: RECRUIT ADDITIONAL POSTDOCTORAL RESEARCHERS AND GRADUATE STUDENTS**

We will continue to look for promising graduate students and post-doctoral fellows who are interested in careers in neurotrauma research for recruitment into SCoBIRC laboratories. Our success in building our extramural funding during the past two years will make this easier although having a continued annual investment from KSCHIRT continues to be critically important for pre- and post-doctoral fellowship support.

We are also preparing an application for an NINDS T32 Training Grant in response to the recent RFA for Training in Translational Research in Neurobiology of Disease which will be submitted in late February.

- **GOAL 3: CONTINUE TO BUILD EXTRAMURAL FUNDING BASE**

We are continuing in our aggressive efforts to add to our extramural funding. Although we will still continue to pursue individual investigator funding (e.g. R01s, R21s), we will submit an application for an NINDS Program Project Grant focused on the neuroprotective effects of calpain inhibitors in acute CNS injury.

- **GOAL 4: PURSUE OPPORTUNITIES FOR BASIC-CLINICAL TRANSLATION**

Based upon the encouraging results obtained in the phase I/II studies with cyclosporin A in severe TBI patients, we have submitted an application for an NINDS Clinical Trial Planning Grant (P.I. B. Young) to develop a multi-center phase III clinical trial to evaluate the neuroprotective efficacy of CsA

in severe TBI. If we are awarded the planning grant, we hope to be in a position to submit a full NINDS R01 application for the actual trial for the June 1 NIH deadline. This trial is being organized in collaboration with Drs. A. Marmarou and R. Bullock at the Medical College of Virginia who have also completed a phase I/II trial of CsA in severe TBI patients.

- **GOAL 5: HOST 12TH ANNUAL KSCHIRT SYMPOSIUM**

The 12th Annual KSCHIRT Symposium will be held on June 15-16, 2006 at the Lexington Hyatt Regency and Convention Center. The Organizing Committee has completed the development of a very exciting scientific program, and all invited speakers have accepted. The final program is attached as **Appendix B**.

- **GOAL 6: HOST 2006 SCoBIRC INVITED LECTURE SERIES**

Now that we are settled into our new laboratory space, we are organizing a more complete seminar series for 2006 which will bring in speakers at least on a monthly basis. Thus far, 6 speakers are scheduled during the first half of the year.

3. CNS INJURY-RELEVANT FULL PUBLICATIONS (Papers, Chapters or Reviews) by SCoBIRC Faculty and Faculty Associates in 2005 (57)

- Anderson KJ, Miller KM, Fugaccia I, **Scheff SW** (2005) Regional distribution of fluoro-jade B staining in the hippocampus following traumatic brain injury. *Exp Neurol* 193:125-130.
- Arlotta P, Molyneaux BJ, **Chen J**, Inoue J, Kominami R, Macklis JD (2005) Neuronal subtype-specific genes that control corticospinal motor neuron development in vivo. *Neuron* 45:207-221.
- Brown MR, Bondada V, Keller JN, Thorpe J, **Geddes JW** (2005) Proteasome or calpain inhibition does not alter cellular tau levels in neuroblastoma cells or primary neurons. *J Alzheimers Dis* 7:15-24.
- Brown, M.R., **Sullivan, P.G.**, **Geddes, J.W.** (2005). Synaptic Mitochondria are more Susceptible to Ca²⁺ Overload than Non-synaptic Mitochondria. *J. Biol. Chem.*, In Press.
- Cai J, Peng X, Nelson KD, Eberhart R, **Smith GM** (2005) Permeable guidance channels containing microfilament scaffolds enhance axon growth and maturation. *J Biomed Mater Res A* 75:374-386.
- Cameron A. A., G. M. Smith, D. C. Randall, D. R. Brown and **A. G. Rabchevsky**. Genetic manipulation of intraspinal plasticity after spinal cord injury alters the severity of autonomic dysreflexia. *J. Neurosci.* (In Press)
- Clasey JL**, Gater DR, Jr. (2005) A comparison of hydrostatic weighing and air displacement plethysmography in adults with spinal cord injury. *Arch Phys Med Rehabil* 86:2106-2113.
- Crow BB, Borneman AF, Hawkins DL, **Smith GM**, Nelson KD (2005) Evaluation of in vitro drug release, pH change, and molecular weight degradation of poly(L-lactic acid) and poly(D,L-lactide-co-glycolide) fibers. *Tissue Eng* 11:1077-1084.
- De Jong MJ, **Randall DC** (2005) Heart rate variability analysis in the assessment of autonomic function in heart failure. *J Cardiovasc Nurs* 20:186-195; quiz 196-187.
- Dimayuga FO, Reed JL, Carnero GA, Wang C, Dimayuga ER, Dimayuga VM, Perger A, Wilson ME, Keller JN, **Bruce-Keller AJ** (2005) Estrogen and brain inflammation: effects on microglial expression of MHC, costimulatory molecules and cytokines. *J Neuroimmunol* 161:123-136.
- EI-Hage N, Gurwell JA, Singh IN, **Knapp PE**, Nath A, **Hauser KF** (2005) Synergistic increases in intracellular Ca²⁺, and the release of MCP-1, RANTES, and IL-6 by astrocytes treated with opiates and HIV-1 Tat. *Glia* 50:91-106.
- EI-Wazir YM, Li SG, Williams DT, Sprinkle AG, Brown DR, **Randall DC** (2005) Differential acquisition of specific components of a classically conditioned arterial blood pressure response in rat. *Am J Physiol Regul Integr Comp Physiol* 289:R784-788.
- Emery DL, Fulp CT, **Saatman KE**, Schutz C, Neugebauer E, McIntosh TK (2005) Newly born granule cells in the dentate gyrus rapidly extend axons into the hippocampal CA3 region following experimental brain injury. *J Neurotrauma* 22:978-988.

- Empey PE, McNamara PJ, **Young B**, Rosbolt MB, **Hatton J**. Cyclosporin A disposition following acute traumatic brain injury. *J Neurotrauma*, in press.
- Gabbita SP, **Scheff SW**, Menard RM, Roberts K, Fugaccia I, Zemlan FP (2005) Cleaved-tau: a biomarker of neuronal damage after traumatic brain injury. *J Neurotrauma* 22:83-94.
- Garcia M, Bondada V, **Geddes JW** (2005) Mitochondrial localization of mu-calpain. *Biochem Biophys Res Commun* 338:1241-1247.
- Hall ED**, Gibson TR, Pavel KM (2005a) Lack of a gender difference in post-traumatic neurodegeneration in the mouse controlled cortical impact injury model. *J Neurotrauma* 22:669-679.
- Hall ED**, **Sullivan PG**, Gibson TR, Pavel KM, Thompson BM, **Scheff SW** (2005b) Spatial and temporal characteristics of neurodegeneration after controlled cortical impact in mice: more than a focal brain injury. *J Neurotrauma* 22:252-265.
- Hauser KF**, Aldrich JV, Anderson KJ, Bakalkin G, Christie MJ, **Hall ED**, **Knapp PE**, **Scheff SW**, Singh IN, Vissel B, Woods AS, Yakovleva T, Shippenberg TS (2005) Pathobiology of dynorphins in trauma and disease. *Front Biosci* 10:216-235.
- Keller JN, Schmitt FA, **Scheff SW**, Ding Q, Chen Q, Butterfield DA, Markesbery WR (2005) Evidence of increased oxidative damage in subjects with mild cognitive impairment. *Neurology* 64:1152-1156.
- Kitzman P** (2005a) Changes in vesicular glutamate transporter 2, vesicular GABA transporter and vesicular acetylcholine transporter labeling of sacrocaudal motoneurons in the spastic rat. *Exp Neurol*.
- Kitzman P** (2005b) Alteration in axial motoneuronal morphology in the spinal cord injured spastic rat. *Exp Neurol* 192:100-108.
- Korde AS, **Sullivan PG**, Maragos WF (2005) The Uncoupling Agent 2,4-Dinitrophenol Improves Mitochondrial Homeostasis following Striatal Quinolinic Acid Injections. *J Neurotrauma* 22:1142-1149.
- Lenzlinger PM, Shimizu S, Marklund N, Thompson HJ, Schwab ME, **Saatman KE**, Hoover RC, Bareyre FM, Motta M, Luginbuhl A, Pape R, Clouse AK, Morganti-Kossmann C, McIntosh TK (2005) Delayed inhibition of Nogo-A does not alter injury-induced axonal sprouting but enhances recovery of cognitive function following experimental traumatic brain injury in rats. *Neuroscience* 134:1047-1056.
- Lifshitz, J., **Sullivan, P.G.**, Hovda, D.A., McIntosh, T.K., (2005). Mitochondrial Damage and Dysfunction in Traumatic Brain Injury. Invited Review, *Mitochondrion*, 4, 705-713.
- Longhi L, **Saatman KE**, Fujimoto S, Raghupathi R, Meaney DF, Davis J, McMillan BSA, Conte V, Laurer HL, Stein S, Stocchetti N, McIntosh TK (2005) Temporal window of vulnerability to repetitive experimental concussive brain injury. *Neurosurgery* 56:364-374; discussion 364-374.
- Mattiasson, G. and **Sullivan, P.G.**, (2005). The Emerging Roles of UCP2 in Health and Disease. Invited Review. *Antioxidants and Redox Signaling*, In Press.
- McEwen ML, **Springer JE** (2005) A mapping study of caspase-3 activation following acute spinal cord contusion in rats. *J Histochem Cytochem* 53:809-819.
- Nukala VN, Singh IN, Davis LM, **Sullivan PG** (2005) Cryopreservation of brain mitochondria: A novel methodology for functional studies. *J Neurosci Methods*.
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5. INVITED LECTURES OR SEMINARS

Geddes

“Calpain Inhibition Strategies for Neurotrauma” India Neurotrauma Society, Kolkata, India, August, 2005.

“The four C’s of Mitochondria: Calpain, Cyclophilin, Cyclosporin, and CNS.” University of Kentucky NIA-Aging Symposium, Lexington, KY (Symposium Speaker).

Hall

“Newer Concepts of Oxidative Damage Mechanisms and Antioxidant Approaches for Acute CNS Injury”, Colloquium in Neuroscience, University of Texas-Houston, Houston, TX, June 2, 2005.

“Basic Science Priorities for TBI Research”, International Symposium: Finding a Cure for Brain Injury: Improving Outcomes, Johnstown, PA, October 14, 2005.

Hatton

"Research Project Development in the Clinical Setting" – April 2005 – American College of Clinical Pharmacy – Myrtle Beach, SC

"Developing Advanced Research Skills for Graduate Training and Competitive Funding" – April 2005 – American College of Clinical Pharmacy – Myrtle Beach, SC

"Do Placebo Groups Have a Role in Clinical Trials" – A Debate – April 2005 – American College of Clinical Pharmacy – Myrtle Beach, SC

Keller

"Neuroinflammatory Mechanisms in Central Nervous System Injury". 35th Annual Society for Neuroscience – Minisymposium. Washington, DC. "Complex Actions of Estrogen on Traumatic Brain Injury-Induced Inflammation" November 14, 2005

"Gender and Steroid Regulation of Glial Function". Great Lakes Glia Meeting. Thompsonville, MI. ; Session Co-Organizer and speaker, "Estrogen, Gender and Traumatic Brain Injury-Induced Inflammation" October 9, 2005

Kitzman

"Skills Enhancement Training II: Spinal Cord Injury (2005)". Kentucky Office of Vocational Rehabilitation, Frankfort, KY.

"Theoretical Basis of Motor Control (2005)". American Physical Therapy Association Meeting, Washington, DC.

"Changes in excitatory and inhibitory synapses on sacrocaudal motoneurons in the SCI-induced spastic rat (2005)". Thematic Poster Session at the American Physical Therapy Association Combined Sections meetings. New Orleans, LA.

Rabchevsky

The 1st Translational Neuroscience Conference, April 27-29, Lexington, KY "Spinal cord injury and neural prostheses." (Co-Chair)

"Pathways influencing autonomic reflex dysfunction following spinal cord injury." *The 4th Congress of the International Society for Autonomic Neuroscience*, Marseille, France.

July 12-16, Marseille, France. Also chaired session on "Spinal cord injury, autonomic nervous system and dysfunction"

Saatman

"Calpain in Neural Degeneration: Assassin or Tombstone?" National Neurotrauma Symposium, Washington, D.C., November 2005.

Sullivan

"Variables affecting outcome in experimental models of spinal cord injury" Ludwig Boltzmann Institute, Vienna, Austria 3/2005

"Designing a therapy for traumatic brain injury: mitochondrial involvement" Ludwig Boltzmann Institute, Vienna, Austria 3/2005

"Developing a therapy for CNS trauma: Experimental TBI and SCI" University of Pittsburgh, Pittsburgh, PA 8/2005

"Developing a therapy for CNS trauma: Experimental TBI and SCI" University of Louisville, Louisville, KY 9/2005

"Novel Approaches to Altering Mitochondrial Permeability as a Neuroprotective Intervention following Traumatic Brain and Spinal Cord Injury".Burke Medical Research Institute, Cornell University, White Plains, NY (Research Seminar).

"Novel Therapeutic Interventions for the Treatment of Head and Spinal Cord Injury: Taking Aim at the "Powerhouse" of the Cell"Robarts BioTherapeutics Research Center, University of Western Ontario, London, Ontario (Research Seminar)

Mitochondrial Dysfunction in Acute CNS Injury.23rd Annual National Neurotrauma Society Symposium, Washington, DC (Symposium Speaker).

"Novel Therapeutic Interventions for the Treatment of Head and Spinal Cord Injury: Taking Aim at the "Powerhouse" of the Cell"; Barrow Neurological Institute and St. Joseph's Hospital & Medical Center, Phoenix, AZ

"Chronic Exposure to Trichloroethylene Directly Inhibits Mitochondrial Complex-I Activity and Induces Parkinsonism in Rats" University of Kentucky NIA-Aging Symposium, Lexington, KY (Symposium Speaker).

"Therapeutic Interventions for the Treatment of Head and Spinal Cord Injury"; Brain Injury Association of Kentucky, Brain Injury Summit, Cardinal Hill Rehabilitation Center, Lexington, KY (Symposium Speaker).

Voss

"Genome Resources For Model Amphibians: Ambystomatid Salamanders".October 2005 – Invited presentation, Aquatic Models of Human Disease. Athens, GA.

"How KBRIN Helps My Research Program." October 2005 – Invited presentation, Kentucky Bioinformatics Research Infrastructure Network Steering Committee Meeting. Lexington, KY

*"Ambystoma: A new aquatic model for gene expression analysis of environmental factors"*July 2005 - Invited presentation, Oak Ridge Center for Advanced Studies Workshop: "Assessing Environmental Health and Ecosystem Function Using Molecular Tools. Oak Ridge National Laboratory, TN.

*"Ambystoma: A new aquatic model for gene expression analysis of environmental factors"*May 2005 – Invited presentation (by the Ecology and Evolution Graduate Students), University of California, Irvine).

6. HONORS, AWARDS OR ELECTIONS TO SOCIETY OFFICES DURING 2005

J.W. Geddes

Appointed as Section Editor, **Experimental Neurology**

E. D. Hall

Appointment as a regular member to NINDS CND Study Section

Appointed to Editorial Board, **Restorative Neurology & Neuroscience**

Served as Vice President, National Neurotrauma Society

J.R. Hatton

Awarded Fellowship Status in American College of Critical Care Medicine

T.S. McClintock

Chairman, Chapters Committee, Society for Neuroscience
Served on Program Committee, Association of Chemoreceptive Sciences
Served on Program Committee, CNS Section, American Physiological Society

K.E. Saatman

Served as Secretary/Treasurer, National Neurotrauma Society

S.W. Scheff

Appointed as a University of Kentucky "University Professor"

J.E. Springer

Elected President, Society for Neuroscience Bluegrass Chapter

7. GRADUATE COURSE DEVELOPMENT

The SCoBIRC faculty developed a novel and much needed graduate course entitled "**Neurobiology of CNS Injury & Repair**" (ANA 605) which was offered for the first time in Fall, 2005. The course attracted 12 graduate students, most of whom are pursuing Ph.D.s in Neurotrauma research. It was a team taught course that was very well received by the students. The plan is to offer the course every other year. The syllabus for the 2005 course is attached as **APPENDIX C**.

Appendix A

KENTUCKY SPINAL CORD & HEAD INJURY RESEARCH TRUST

Presents

**SPINAL CORD & BRAIN INJURY NEURO-REHABILITATION SYMPOSIUM
AND SPINAL CORD INJURY ASSOCIATION OF KENTUCKY SUMMIT**

Lexington Hyatt Regency Hotel & Convention Center
Lexington, Kentucky

SEPTEMBER 29-30, 2005

Hosted By: University of Kentucky Spinal Cord & Brain Injury Research Center & Cardinal Hill Rehabilitation Hospital

THURSDAY, September 29, 2005

Cardinal Hill Rehabilitation Hospital

6:00 p.m. – 6:30 p.m.

Registration for Symposium

6:30 p.m. – 8:00 p.m.

Opening Remarks ~ Kerry Gillihan, President & CEO
Cardinal Hill Rehabilitation Hospital

Feature Speaker:

Gerald Klim, D.O.
Associate Professor & Chairman
UK Physical Medicine & Rehabilitation

Topic: “Current State of Neuro-Endocrine Dysfunction in
Traumatic Brain Injury”

FRIDAY, September 30, 2005

Hyatt Regency Hotel & Convention Center

(Morning Session)

Thoroughbred Room 2/3

Morning Moderator:

Russell Travis, M.D.
Cardinal Hill Rehabilitation Hospital

7:15 a.m. – 7:45 a.m.

Registration & Continental Breakfast
Foyer

7:45 a.m. – 8:00 a.m.

Opening Remarks ~ Ed Hall, Ph.D., Director, SCoBIRC

Welcome ~ Senator Tim Shaughnessy

8:00 a.m. – 9:00 a.m.

Christopher B. Shields, M.D.
University of Louisville
“Treatment of Spinal Cord Injury: Past, Present and Future”

9:00 a.m. – 10:00 a.m.

Susan Harkema, Ph.D.
University of Louisville
“Activity-Based Interventions for Recovery of Function After
Neurologic Injury”

10:00 a.m. – 10:15 a.m.

BREAK/Posters/Exhibits

10:15 a.m. – 11:15 a.m.

David Gater, Ph.D.

University of Michigan
“Metabolic Syndrome in Spinal Cord Injury”

11:15 a.m. – 12:00 p.m.

Special Presentation to Mr. Tony Goetz by Dr. Jim Shaughnessy,
Chairman of KSCHIRT/Lunch

Note: The afternoon is broken into two Concurrent Sessions: 1) Spinal Cord & Brain Injury Neuro-Rehabilitation Symposium (Thoroughbred Room 2/3) and 2) Spinal Cord Injury Association of Kentucky Summit (Thoroughbred Room 1).

Spinal Cord & Brain Injury Neurorehabilitation Symposium

FRIDAY, September 30, 2005
(Afternoon Session)

**Hyatt Regency Hotel & Convention Center
Thoroughbred Room 2/3**

Afternoon Moderator:

Joe Springer, Ph.D.
Cardinal Hill Endowed Chair
UK Physical Medicine & Rehabilitation

12:00 p.m. – 1:00 p.m.

David Burke, M.D.
Spaulding Rehabilitation Hospital/Harvard
“Rehabilitation of Patients with Brain Injury”

1:00 p.m. – 2:00 p.m.

David Hovda, Ph.D.
University of California/Los Angeles
“Challenges for Experience-Dependent Plasticity Following A
Traumatic Brain Injury: A Road Block for Rehabilitation”

2:00 p.m. – 2:15 p.m.

BREAK/Posters/Exhibits

2:15 p.m. – 3:15 p.m.

John Povlishock, Ph.D.
Virginia Commonwealth University
“Advances in Our Understanding of Neurorehabilitation in the
Context of Traumatic Brain Injury”

3:15 p.m. – 4:15 p.m.

Exhibits & Research Poster Presentations

4:15 p.m. – 4:30 p.m.

Evaluations/Receive Certificates

4:30 p.m. – 5:30 p.m.

Wine & Cheese Reception

Spinal Cord Injury Association of Kentucky Summit

FRIDAY, September 30, 2005
(Afternoon Session)

**Hyatt Regency Hotel & Convention Center
Thoroughbred Room 1**

12:00 p.m. – 1:00 p.m.

Mike Schlappi
“If You Can’t Stand Up, Stand Out!”

1:00 p.m. – 2:00 p.m.

Ann E. Cody
“The Power of Individual and Community Advocacy”

2:00 p.m. – 2:15 p.m.

BREAK/Posters/Exhibits

2:15 p.m. – 3:15 p.m.

Coach Jim Hayes
“A Journey of Survival: Spinal Cord Injuries in the 60’s
Through Modern Realities and the Tools We have to
Achieve Quality of Life”

3:15 p.m. – 4:15 p.m.

Cheryl L. Vines, M.S.
“Making a Quilt: A 30-Year Perspective of Serving People
With Spinal Cord Injury in the Community”

4:15 p.m. – 4:30 p.m.

Evaluations/Receive Certificates

4:30 p.m. – 5:30 p.m.

Wine & Cheese Reception

APPENDIX B

Thursday 12th KENTUCKY SPINAL CORD & HEAD INJURY RESEARCH TRUST SYMPOSIUM June 15, 2006 Heritage Hall; Lexington, KY	
7:15 - 8:00 am	REGISTRATION and Continental Breakfast
8:00 – 8:10	Welcome and Opening Remarks Edward D. Hall, PhD, Director, UK Spinal Cord & Brain Injury Research Center
SESSION 1 NEUROGENESIS Jinhui Chen, Ph.D., M.D., Session Chair	
8:10 – 8:50	Jeffrey D. Macklis, M.D.-Harvard University <i>Molecular Development and Cellular Repair of Corticospinal Motor Neuron</i>
8:50-9:30	Samuel J. Pleasure, Ph.D., M.D.- University of California, San Francisco <i>Forced Differentiation of Neuronal Precursor Cells by Transcriptional Networks</i>
9:30-10:10	Hongjun Song, Ph.D.- Johns Hopkins University <i>Mechanisms Regulating Neural Stem Cells and Neurogenesis in the Adult Mammalian CNS</i>
10:10-10:40	COFFEE BREAK
SESSION 2 VASCULAR DYSFUNCTION IN CNS INJURY Edward D. Hall, PhD, Session Chair	
10:40 – 11:20	Douglas S. DeWitt, Ph.D.- University of Texas-Galveston <i>Peroxyne Nitrite, Gap Junctions and Traumatic Cerebral Vascular Injury</i>
11:15 – Noon	Paula Dore-Duffy- Wayne State University <i>The Role of the Pericyte in Microvascular Response to Traumatic Brain Injury</i>
Noon – 1:30 pm	LUNCH
SESSION 3 REGENERATION AND PLASTICITY George M. Smith, Ph.D., Session Chair	
1:30 – 2:10	Melitta Schachner, Ph.D.- University of Hamburg <i>A Role for Neural Cell Adhesion Molecules in Spinal Cord Regeneration</i>
2:10 – 2:50	Zhigang He, Ph.D., Harvard University
2:50 – 3:05	BREAK
3:05 – 3:45	John D. Houle, Ph.D.- Drexel University <i>Activity-Dependent Plasticity and Transplant-Mediated Repair in the Injured Spinal Cord</i>
3:45-4:30	James W. Fawcett, M.D., Ph.D.- Cambridge University <i>Intrinsic and Extrinsic Control of Axon Regeneration and Plasticity</i>
SPECIAL PRESENTATION	
4:30-5:15	Danny Heumann, Attorney at Law- Heumannly Capable
5:15-7:00	POSTER SESSION AND RECEPTION
7:00 – 9:00	DINNER

Friday June 16, 2004 Heritage Hall

8:00 – 8:30 am REGISTRATION and Continental Breakfast

**SESSION 4 GLIAL RESTRICTED PRECURSORS
Alexander G. Rabchevsky, Ph.D.- Session Chair**

8:30 – 9:15 Robert Miller, Ph.D.- Case-Western Reserve University
Control of Glial Cell Fate in Development and Disease

9:15 – 10:00 Hans Keirstead, Ph.D.- University of California, Irvine
Human Embryonic Stem Cell-Derived Oligodendroglial Precursors for the Treatment of Spinal Cord Injury

10:00 – 10:30 COFFEE BREAK

10:30 – 11:15 Clive N. Svendsen, Ph.D. – University of Wisconsin-Madison
Combining Stem Cells and Gene Therapy for ALS

11:15 - 12:00 Open

12:00 – 1:30 pm LUNCH

**SESSION 5 TRANSLATION OF THERAPEUTIC STRATEGIES FOR SCI INTO CLINICAL TRIALS
Edward D. Hall, Ph.D. Session Chair**

1:30 – 2:15 Joe E. Springer, Ph.D.- University of Kentucky
Paradigm Shifts in SCI Translational Research: From the Bench to the Bedside and Beyond

2:15 - 3:00 W. Dalton Dietrich, Ph.D.- University of Miami, Miami Project to Cure Paralysis
Replication of Preclinical Studies on Therapeutic Strategies for Spinal Cord Injury

3:00 – 3:15 COFFEE BREAK

3:15-4:15 John Steeves, Ph.D.- University of British Columbia
Challenges of Translational Research in SCI: Who, What, Where, When, Why, and Let Us Not Forget, How!

4:15 – 4:30 CLOSING REMARKS
James W. Geddes, Ph.D., Associate Director UK Spinal Cord & Brain Injury Research Center

APPENDIX C

ANA 605: Principles of Neurobiology: Neurobiology of CNS Injury and Repair (4 Credits)

Fall Semester, 2005

Syllabus

Class meetings:

This course meets once per week for 3.5 hrs (Wednesday, 1:00- 4:30 pm)

Location BBSRB 202A

<u>Course Director:</u>	<u>Office</u>	<u>Telephone</u>	<u>e-mail</u>
Edward D. Hall, Ph.D.	383 BBSRB	323-4678	edhall@uky.edu
<u>Course Co-Director:</u>			
Jinhui Chen, Ph.D., M.D.	369 BBSRB	323-5688	jchen@uky.edu

Other Faculty:	Office	Phone	Email
Kathryn E. Saatman, Ph.D.	BBSRB 367	323-5145	k.saatman@uky.edu
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George M. Smith, Ph.D.	BBSRB 373	323-3541	gmsmith@uky.edu
Stephanie Thompson, Ph.D.	Cubicle across from B367	323-1148	snott2@uky.edu
Pamela Knapp, Ph.D.	MS 209	323-3517	peknapp@uky.edu
Franca Cambi, M.D.	L445 Kentucky Clinic	323-6702	franca.cambi@uky.edu
Patrick H. Kitzman, Ph.D.	Wethington 126G	323-1100 (x80580)	phkitz1@uky.edu

Faculty will give lectures, assign readings, evaluate class discussions and grade midterm and final exam.

Objectives:

1. Introduce students to major concepts and issues of general importance with respect to the degenerative and reparative response of the brain and spinal cord to mechanical injury.
2. Provide students with a broad state of the art background in regards to the pathophysiology and therapeutic approaches for traumatic brain and spinal cord injury so that they will be able to interpret and evaluate research findings in the neurotrauma literature and integrate this information into their own laboratory research.
3. Enhance appreciation for basic and clinical efforts in neurotrauma research.
4. Develop understanding of the process of translation of basic neurotrauma research into clinical trials.

Course Description:

The course will consist of weekly didactic presentations (3 hrs with 10 min. breaks each hour) by faculty and open discussions (60 min) led by class members regarding assigned readings of relevance to the faculty presentation. Active participation by all class members is expected. Each weekly faculty presentation is designed to provide a general overview of the current state of knowledge in a given area of neurotrauma pathophysiology and therapeutic approaches. The course will provide a strong working background concerning the issues, techniques and frontiers of neurotrauma therapeutic discovery research aimed at reducing acute post-traumatic neurodegeneration in the injured brain or spinal cord or enabling regeneration and repair.

Prerequisites:

This course is a graduate level course intended for students who are in their second or subsequent years of graduate study and who are pursuing focused research training in neurotrauma research. No special prerequisites, other than graduate standing, are necessary. However, a background in neuroanatomy and neurophysiology is highly recommended.

Readings:

There is no textbook for this course. With the exception of the first class week, assigned readings will be handed out one week prior to class or will be accessible via Pubmed.

Course Expectations:

1. Attendance and participation in class discussions. Due to the nature of this course, there is no substitute for attendance and participation in class discussions. Students will be expected to compensate for both excused and unexcused absences in consultation with relevant faculty members.
2. Command of assigned readings. Because the course is designed to promote discussion of interdisciplinary research publications, students have a responsibility to the class as a whole to be prepared for discussion of assigned readings (1-3 papers) during class sessions.
3. There will be two written exams (mid-term and final) of equal weight. The final will only include material covered after the mid-term exam. Exams will consist of short answer and brief essay questions.

Grades:

Grades will be determined as follows:

	<u>% of grade</u>
Class Attendance	10
Discussion Participation	10
Mid Term Exam	40
Final Exam	<u>40</u>
	100

Weekly Course Outline:

1. **Wed., August 24th:** Introduction to CNS Injury (**Hall/Chen**):
 - Epidemiology of CNS Injury: SCI, TBI, Shaken Baby Syndrome, Ischemia and Hemorrhage
 - Basic Concepts of Post-Traumatic Pathology and Pathophysiology
 - i. Primary vs. secondary injury
 - ii. Apoptosis and necrosis
 - iii. Anterograde (Wallerian) vs. retrograde degeneration
 - iv. Demyelination and its functional consequences
 - v. Microvascular dysfunction
 - vi. Reactive gliosis
 - vii. Influence of secondary insults (e.g. shock, hypoxia, ischemia, hemorrhage)
2. **Wed., August 31st:** Overview of CNS Injury Animals Models
 - TBI Models (**Saatman**)
 - SCI Models (**Rabchevsky**)
 - Ischemic and hemorrhagic stroke models (**Hall**)
3. **Wed., September 7th:** Mechanisms of Secondary Neuronal Injury and Neuroprotective Strategies-Part 1
 - Excitotoxicity (**Hall**)
 - Reactive oxygen mechanisms (**Hall**)
 - Programmed cell death mechanisms (**Nottingham**)
4. **Wed., September 14th:** Mechanisms of Secondary Neuronal Injury and Neuroprotective Strategies-Part 2
 - Calcium-mediated injury mechanisms (**Saatman**)
 - Metabolic and mitochondrial dysfunction (**Sullivan**)
5. **Tues., September 20th:** Mechanisms of Secondary Neuronal Injury and Neuroprotective Strategies-Part 3 (**Hall**) (*Class will be from 2:00-4:00 PM for this day*)
 - Inflammatory mechanisms
 - Intracellular signaling mechanisms
 - Influence of growth/trophic factors
 - Integration of secondary injury mechanisms
6. **Wed., September 28th:** Midterm Exam
7. **Wed., October 5th:** History of and Lessons Learned from Neuroprotective Clinical Trials
 - SCI (**Hall**)
 - TBI (**Hatton**)
 - Pharmacological principles of neuroprotective therapy evaluation (**Hall**)
8. **Wed., October 12th:** Post-Traumatic Demyelination and Remyelination (**Knapp/Cambi**)
9. **Wed., October 19th:** Mechanisms of Post-Traumatic Plasticity and Regeneration- Part 1 (**Smith**)
10. **Wed., October 26th:** Mechanisms of Post-Traumatic Plasticity and Regeneration- Part 2 (**Chen**)
11. **Wed., November 2nd:** Mechanisms of Neurogenesis and Stem Cell /Progenitor Cell Transplantation Strategies (**Chen**)

Wed., November 9th: No class due to conflict with Neurotrauma Symposium

Wed., November 16th: No class due to conflict with Society for Neuroscience Meeting

12. **Mon., November 21st:** Neurological Sequelae of SCI (***Class is on Monday since this is Thanksgiving week***)
 - Neuropathic pain (**Smith**)
 - Autonomic dysfunction (**Rabchevsky**)
 - Spasticity (**Kitzman**)
13. **Wed., November 30th:** Overview of Worldwide Research in CNS Injury: Who are the Other Players (**Hall**)
14. **Wed., December 7th:** Final Exam: covering material since midterm exam