



**2006 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

JANUARY 19, 2007

EDWARD D. HALL, PH.D.

SCoBIRC DIRECTOR



This report describes our progress in achieving the goals for 2006 outlined in the 2005 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 2007.

HIGHLIGHTS OF 2006

- **Jonathan Lifshitz, Ph.D.**, formerly a Postdoctoral Fellow at the Medical College of Virginia, joined UK and SCoBIRC in January 1, 2007 as a **Core Faculty Member** and Assistant Professor of Anatomy & Neurobiology.
- Appointment of **five new SCoBIRC Faculty Associates: Walter M. High, Ph.D.**, Cardinal Hill Associate Professor of Physical Medicine & Rehabilitation; **Kimberly Nixon, Ph.D.**, Assistant Professor of Pharmaceutical Sciences; **Rodney P. Guttmann, Ph.D.**; Assistant Professor of Gerontology and Physiology and **Richard D. Andreatta, Ph.D.**, Associate Professor of Rehabilitation Sciences and **Indrapal N. Singh, Ph.D.**, Research Assistant Professor of Anatomy & Neurobiology.
- Obtained a 5 year NIH Translational Neuroscience T32 Training Grant **“Therapeutic Strategies for Neurodegeneration”** which funds 5 graduate students, a postdoctoral fellow and a clinical fellow each year. This grant and four others awarded to SCoBIRC Faculty totaled \$1,581,127 in multi-year direct costs
- Appointment of Dr. Patrick G. Sullivan as an Associate Director of SCoBIRC joining Associate Director Dr. James W. Geddes
- Acceptance of 2 new graduate students into SCoBIRC laboratories.
- Recruitment of 5 new post-doctoral fellows into SCoBIRC laboratories.
- SCoBIRC Faculty and Faculty associates published 41 full CNS injury-related publications, 1 patent application and 20 invited lectures/seminars.

1. PROGRESS RELATED TO 2006 GOALS OUTLINED IN 2005 SCoBIRC PROGRESS REPORT

• **GOAL 1: RECRUIT ADDITIONAL FACULTY/ SENIOR SCIENTIFIC STAFF**

New SCoBIRC Core Faculty Member: Dr. Jonathan Lifshitz joined the SCoBIRC Core Faculty as an Assistant Professor of Anatomy & Neurobiology on January 1, 2007 bringing to UK and SCoBIRC a wealth of training and research experience in traumatic brain injury. Dr. Lifshitz received his B.S. for UCLA from where he first became involved in traumatic brain injury research, completing his senior thesis project in the laboratory of Dr. David Hovda, Director, UCLA Brain Injury Center. He then moved to the University of Pennsylvania School of Medicine where he completed his Ph.D. in Neuroscience in the laboratory of Dr. Tracy McIntosh. Following an initial postdoctoral fellowship with Dr Sean Grady, Professor and Chairman of Neurosurgery at Penn, he moved to the Medical College of Virginia where he received additional postdoctoral training under Dr. John Povlishock, Professor and Chairman of Anatomy & Neurobiology. He has published 14 refereed papers. His current research interests concern the mechanisms and discovery of potential neurorestorative treatment strategies. Specifically, he is exploring the pathophysiology of diffuse TBI in a rodent model and using the somatosensory whisker-barrel circuit to evaluate neural circuit disruption, impaired circuit activation and possible rehabilitation strategies in order to understand the neural mechanisms underlying injury-induced circuit alterations that define post-traumatic morbidity and effect the potential for recovery.

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

- **Richard D. Andreatta, Ph.D.**, Associate Professor of Rehabilitation Sciences-Dr. Andreatta is interested in motor control, sensory physiology, somatosensory psychophysics, and psychophysiology of the lower face in humans during dynamic and skilled orofacial force control tasks.
- **Rodney P. Guttmann, Ph.D.**, Assistant Professor of Gerontology & Physiology- Dr. Guttmann who joined the UK faculty several years ago is an expert on the regulation of the proteolytic enzyme calpain that is critically important in secondary injury mechanisms after SCI and TBI. He has been working closely with other SCoBIRC faculty members for the past few years.
- **Walter M. High, Ph.D.**, Cardinal Hill Associate Professor of Physical Medicine & Rehabilitation- Dr. High was recently recruited to UK from the Baylor University College of Medicine. He is a leading authority on neuropsychometric assessment of outcome in pediatric and adult TBI patients and factors that influence post-traumatic recovery. His expertise will be important in the design and analysis of future clinical trials in TBI.
- **Kimberly Nixon, Ph.D.**, Assistant Professor of Pharmaceutical Sciences- Dr. Nixon joined the UK College of Pharmacy in 2005. Her research interest concerns the neurodegenerative effects of alcohol, which is a contributing factor in occurrence and pathophysiology of many CNS injuries.
- **Indrapal N. Singh, Ph.D.**, Research Assistant Professor of Anatomy & Neurobiology- Dr. Singh joined UK in 2001. He is a biochemist who has published over 30 papers on lipid biochemistry and other topics. Most recently, he has been working on mitochondrial pathophysiology and on the possible role of lipid mediators in secondary injury mechanisms.

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

Patrick G. Sullivan, Ph.D., Associate Director and Associate Professor of Anatomy &
Neurobiology

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

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

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

Kathryn E. Saatman, Ph.D., Associate Professor of Physiology and Neurosurgery

Jonathan Lifshitz, Ph.D., Assistant Professor of Anatomy & Neurobiology

Core Faculty Opening: 9-to be recruited in FY 2007

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. Anatomy & Neurobiology, 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

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

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

Rodney P. Guttman, Ph.D., Assistant Professor/Gerontology and Physiology, College of Medicine
Role of calpain in post-traumatic pathophysiology and design of novel calpain inhibitory strategies

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

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

Jonathan Lifshitz, Ph.D., Assistant Professor/Anatomy & Neurobiology, College of Medicine
Mechanisms and the discovery of potential neuroprotective and neurorestorative treatment strategies related to disruption of brain functional circuits

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

Kimberly Nixon, Ph.D., Assistant Professor of Pharmaceutical Sciences/College of Pharmacy
Neurodegenerative mechanisms associated with alcohol intoxication and alcoholism

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/Depts. Physiology and Neurosurgery, College of Medicine
Cytoskeletal damage mechanisms in acute brain injury; pathobiology of traumatic axonal 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

Indrapal N. Singh, Ph.D., Research Assistant Professor of Anatomy & Neurobiology, College of Medicine
Roles of mitochondrial dysfunction and lipid mediators in post-traumatic neurodegeneration

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., Associate Professor/Dept Anatomy & Neurobiology and SCoBIRC Associate Director, College of Medicine
Mechanisms and role of mitochondrial dysfunction in CNS injury

Clinical/Rehabilitation:

Richard D. Andreatta, Ph.D., Associate Professor/Rehabilitation Sciences, College of Allied Health Sciences
Neurophysiology of orofacial dysfunction after traumatic brain injury

Jody Clasey, Ph.D., Assistant Professor/Dept Kinesiology and Health Promotion, College of Education
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

Walter M. High, Ph.D., Cardinal Hill Associate Professor/Physical Medicine & Rehabilitation and Neurosurgery, College of Medicine
Assessment of neurorehabilitation outcomes after traumatic brain injury and clinical trial design

Patrick H. Kitzman, Ph.D., Associate Professor/Dept Rehabilitation Sciences, Division of Physical Therapy
Neuronal plasticity and treatment of 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 post-doctoral fellows and 2 new graduate students into SCoBIRC laboratories:

New Post-doctoral Fellows

Mubeen Ansari, Ph.D.	Laboratory of S.W. Scheff
Hanad Duale, Ph.D.	Laboratory of A.G. Rabchevsky
Samir Patel, Ph.D.	Laboratory of A.G. Rabchevsky
Evelyn Perez, Ph.D.	Laboratory of P.G. Sullivan
Michael Pizzi, Ph.D.	Laboratory of K.E. Saatman

New Graduate Students

Mr. Andrew Sauerbeck	Laboratory of P.G. Sullivan
Mr. Ayman G. Mustafa	Laboratory of E.D. Hall

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

During 2006, the SCoBIRC Core Faculty and Faculty Associates obtained new multi-year extramural grant funding for neurotrauma-related research totaling \$1,581,127:

NIH-NIDA 1T32 DA 022738-01
"Therapeutic Strategies for Neurodegeneration Training Grant"
PI and Program Director: E.D. Hall
9/26/06-9/30/11
Total Direct Costs \$1,240,734

NIH-NIMH 1 R25 MN079332
"Mechanisms of Neurologic Disease Course"
PI: J.W. Geddes
9/25/06-8/31/08
Total Direct Costs \$115,569

Paralysis Project of America
"Inhibition of ERK1/2 Signaling for Spinal Cord Injury"
PI: J.W. Geddes
3/1/06-2/28/07
Total Direct Costs: \$50,000

NIH – SBIR Grant,
"Cell-Permeant Peptides for Modulating Neuronal Growth Cone Behavior"
Co-PI: D. Snow
8-1-06 to 7-31-07
Total Direct Costs \$35,000

ELA (European Leukodystrophy Association)
"PLP/DM20 alternative splicing: studies on regulatory sequences, splicing factors and mutations affecting splicing in PMD patients".
PI: F. Cambi
12/01/06-11/30-08
Total Direct Costs \$139,824

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

The following translational projects are in progress:

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 CSF levels of neuroprostanes, brain-selective lipid peroxidation-related biomarkers, was observed along with a trend toward an improvement in 6 month neurological recovery. An NIH clinical trial planning grant is under review aimed at the organization of a multi-center phase III trial of cyclosporin A in severe TBI patients.

Measurement of the lipid peroxidation-related isoprostanes and neuroprostanes as potential biomarkers for studies in severe TBI -Hatton-Kolpek/Young/Hall (remove bold for consistency)

We have successfully developed and validated highly sensitive gas chromatography/mass spectrometry methods for measurement of oxidative damage-related isoprostanes and neuroprostanes in CSF and plasma obtained from neurosurgical patients. We are currently completing the analysis of these markers in CSF samples from the phase II Cyclosporin A clinical trial patients. This method will also be employed in the planned phase III TBI trial.

Investigation of the glutamate release inhibitor gabapentin for control of SCI spasticity-Kitzman/Hall (remove bold for consistency)

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 the commercially available drug gabapentin (Neurontin[®]) which reduces the release of the excitatory neurotransmitter glutamate 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 ongoing work could lead to a clinical trial to evaluate this drug alone or in combination with the GABA agonist baclofen for spasticity control in SCI patients.

Friday | June 16, 2006 Lexington Convention Center

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 Scott Whittemore, Ph.D.- University of Louisville
Stem Cell Repair of the Injured Spinal Cord

12:00 – 1:30 pm LUNCH

**SESSION 5 | TRANSLATION OF THERAPEUTIC STRATEGIES FOR SCI INTO CLINICAL TRIALS
James Geddes, 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

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

2006 SCoBIRC Seminar Schedule

January, 17th: Tom Hering, Ph.D., Associate Professor of Orthopaedics & Anatomy, Department of Orthopaedics Case Western Reserve University, Cleveland, Ohio, *“Recombinant Aggrecan: A model for CS-Proteoglycan Biosynthesis, Structure, Function & Degradation”*

***February 2nd:** Cynthia Camarilli, Post-Doctoral Fellow, Department of Neuroscience & Experimental Therapeutics. The Texas A&M University System HSC College Station, TX, *“Pre-*

exposure to Alcohol Disrupts the Proliferation and Subsequent Differentiation of Cerebral Cortical Stem Cells"

***February 15th:** Simone Di Giovanni, M.D., Ph.D., Instructor, Georgetown University Medical Center, Department of Neuroscience, Washington, D.C. *"The Role of the Tumor Suppressor p53 in Neurite Outgrown and Axonal Regeneration"*

***February 16th:** Michael A. Pizzi, Post Doctoral Candidate, Cell Biology, Neurobiology and Anatomy, Medical College of Wisconsin, Wauwatosa, WI. *"Transduced fibroblasts over-expressing MMP-3 promote axonal regeneration and functional recovery after spinal cord injury"*

March 2nd: Philip J. Horner, Ph.D., Assistant Professor, Department of Neurosurgery, University of Washington, Seattle, WA. *"Trauma-induced fate restriction of the adult stem cell and the failure of spinal cord regeneration"*

March 10th: Thomas H. Mareci, Ph.D., Associate Professor of Biochemistry, Biomedical Engineering & Physics, Director, Center for Structural Biology, University of Florida. *"The Study of Spinal Cord Injury with Magnetic Resonance Imaging"*

***March 14th:** Bradley Kerr, Ph.D., McGill University, Center for Research in Neuroscience, Montreal General Hospital, Livingston Hall, Montreal Quebec, Canada. *"Cytokines and their suppressors: Pro- and anti-inflammatory pathways in models of spinal cord injury"*

March 28th: Stephen Leinenweber, M.D., Assistant Professor, Pediatrics Department of Critical Care Medicine, University of North Carolina, Chapel Hill, *"Insulin Growth Factor its role in brain development: a case for protection after traumatic brain injury"*

***March 30th:** Jonathan Lifshitz, Ph.D., Post-Doctoral Fellow, Department of Anatomy and Neurobiology, Virginia Commonwealth University, Medical College of Virginia Campus, Richmond, VA. *"Focal neurodegeneration vs. diffuse neural circuit disruption: impact on post-traumatic morbidity"*

April 6th: Samuel David, Ph.D., Professor, McGill University, Department of Neurology and Neurosurgery, Montreal, Quebec Canada, *"Iron homeostasis in the CNS and its involvement in spinal cord injury"*

***April 19th:** Candace Floyd, Ph.D., Assistant Professor, Department of Neurological Surgery, University of California, Davis, California, *"Astroglia: Important mediators of traumatic CNS injury"*

May 4th: Itzhak Fischer, Ph.D., Professor and Chair, Department of Neurobiology and Anatomy, Drexel University College of Medicine, Philadelphia, PA, *"Transplantation of neural stem cells in spinal cord injury: The Promise and Challenges"*

***May 5th:** Julia Herrmann, Postdoctoral Fellow, University of California, Los Angeles, Department of Neurobiology, Los Angeles, CA. *"Roles of reactive astrocytes after crush spinal cord injury"*

May 9th: Gerd Kempermann, M.D., Volkswagenstiftung Research Group, Department of Experimental Neurology, Charité, University Medicine Berlin, Berlin Germany. *"Genes and environment in the regulation of adult hippocampal neurogenesis"*

May 12th: John M. McCall, Ph.D., Senior Consultant PharMac LLC, Boca Grande, FL. *"Compendium on Drug Discovery and Development"*

May 31st: Billie Jean Huskey, M.S. Physical Therapy, Ph.D. Student, Virginia Polytechnical University Bluefield, West Virginia. *"What would a day be like if every body acted just like you?"*

June 9th: Kochupurackal Mohanakumar, Ph.D., Scientist F & Deputy Director
Indian Institute of Chemical Biology, Division of Cell Biology & Physiology Head,
Business Development Group Laboratory of Experimental & Clinical Neuroscience
India. *"Neurodegeneration and Neuroprotection in Parkinson's Disease"*

***June 22nd:** Gregory M. Holmes, Ph.D., Assistant Professor, Division of Nutrition and the Brain
Pennington Biomedical Research Center, Baton Rouge, LA. *"Impaired supraspinal control of
gastrointestinal reflexes after spinal contusion injury"*

***June 29th:** Chalk Talk - Jonathan Lifshitz, Ph.D., Post-Doctoral Fellow, Department of Anatomy and
Neurobiology, Virginia Commonwealth University, Medical College of Virginia Campus, Richmond,
VA. *"Somatosensory Circuit Disruption and Rehabilitation after Diffuse Brain Injury"*

July 10th: Alexander Velumian, Ph.D., DSc, Neuroscience/Cellular Electrophysiology and Imaging.
Division of Neurosurgery, Toronto Western Hospital UHN, Toronto, ON. *"The Functional Aspects of
Myelin in the CNS: What do we know and what we assume we know"*

July 14th: Patrizio Blandina, Ph.D., Professor of Pharmacology, Dipartimento di Farmacologia
Clinica e Preclinica, Universita di Firenze (1) School of Pharmacy
Dean of the Students of the School of Pharmacy, Firenze ITALY. *"Histamine in the brain: new roles
for an old actor"*

October 5th: Lyn B. Jakeman, PhD., Department of Physiology and Cell Biology Ohio State University
College of Medicine and Public Health, Spinal Trauma and Repair (STAR*) Lab. Columbus, OH 43210,
"Remodeling and Recovery after Spinal Cord Injury: Insights from Murine Models"

October 10th: Brian Webb, University of Kentucky 1998 College Graduate, Lexington, KY. *"Don't Give
Up, Don't Ever Give Up: A Young Man's True Story of Tragedy, Patience and Hope"*

October 12th: L. Jackson Roberts, II, M.D., Professor of Pharmacology & Medicine Department of
Pharmacology, Vanderbilt University, Nashville, TN, *"Biochemistry and Pharmacology of
Isoprostane, Neuroprostane and Isofuran Pathways of Lipid Peroxidation"*

November 2nd: Barclay Morrison III, Ph.D., Assistant Professor, Biomedical Engineering,
Columbia University, New York, NY. *"Is post-Traumatic, Intra-Hippocampal, Regional Vulnerability a
Function of Biomechanical Heterogeneity?"*

December 7th: Gregory A. Dekaban, Ph.D., Professor, Dept. of Microbiology & Immunology,
Research Scientist and Co-Director/Director of the BioTherapeutics Research Group London,
Ontario Canada, *"The Role of the CD11d Integrin in the Cellular Inflammatory Response to Spinal
Cord Injury"*

*** Faculty or Post Doctoral Candidate**

2. SCoBIRC GOALS for 2007

• GOAL 1: RECRUIT ADDITIONAL FACULTY

We will fill our last SCoBIRC Core Faculty position (# 9) this year. We have narrowed the field of candidates gleaned from our last international advertisement to a single person who is a highly experienced scientist who works in the SCI regeneration/plasticity arena.

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

We will continue to recruit promising graduate students and post-doctoral fellows who are interested in careers in neurotrauma research into SCoBIRC laboratories. Our success in building our extramural funding during the past two years will make this easier. However, we very much appreciate the continued annual investment from KSCHIRT for pre- and post-doctoral fellowship support. Moreover, our recently funded NINDS T32 Training Grant has also increased our training opportunities .

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

We are continuing in our aggressive efforts to add to our extramural funding. Our 5 year NINDS Program Project Grant (1 P01 NS058484) entitled "*Calpain Inhibitory Strategies for TBI*" was submitted on June 1, 2006, and received a score of 130. This is recommended for funding, pending approval by the NINDS Council which meets in February. Jim Geddes is the PI and Project Leader for one of the component Projects. The other project leaders are Kathryn Saatman, Rodney Guttmann and Ed Hall.

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

As noted above, 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 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 6: HOST 2007 SCoBIRC INVITED LECTURE SERIES**

Thanks to the generous KSCHIRT support, we hosted twenty six speakers in 2006. In addition, we have we have filled most of our monthly seminar slots through June, 2007.

- **GOAL 7: DEVELOP PUBLIC RELATIONS MATERIALS STRATEGY**

During the coming year, we will be committed to improving our Public Relations for the purpose of increasing our funding base. In the past year, we developed a SCoBIRC tri-fold handout for distribution at various sites (e.g. hospitals, doctor's offices, etc.). Moreover, we have greatly improved our SCoBIRC website (www.mc.uky.edu/scobirc/) which was recently chosen for an Award of Excellence by the District III (southeastern U.S.) Council for the Advancement of and Support of Education (CASE III). We are also continuing to work with the Brain Injury Association of Kentucky (BIAK) in which SCoBIRC Director E.D. Hall is an Honorary Board Member and Associate Director P.G. Sullivan is a Regular Board Member. However, during 2007, we will work more aggressively with UK Public Relations staff to improve our visibility among the general public. As part of that, we will develop a more complete Public Relations Brochure to advertise our research and draw the attention of potential donors.

- **GOAL 8: INCREASE FUNDRAISING EFFORTS**

Although SCoBIRC has enjoyed considerable success in competing for extramural research funding over the past 4 years, we have not been very effective in raising support from private organizations or individuals. In particular, we need to identify significant funding with which to match the past three annual \$500,000 KSCHIRT endowment investments with which we have created SCoBIRC Professorships 6, 7 and 8. The Dean of the College of Medicine and Vice President of Clinical Affairs Dr. Jay A. Perman and the Executive Vice President for Health Affairs, Dr. Michael Karpf are actively working with SCoBIRC Director E. D. Hall to find matching funds for the currently unmatched \$500,000 seed endowments provided by KSCHIRT in 2004, 2005 and 2006. It is our goal to aggressively solve this problem and to identify funds. Beyond this immediate need, we desire to build

up a pool of discretionary funds to help support pilot research studies and other research costs that are difficult to obtain through granting agencies.

3. CNS INJURY-RELEVANT FULL PUBLICATIONS (Papers, Chapters or Reviews) by SCoBIRC Faculty and Faculty Associates in 2006-SCoBIRC Faculty indicated in bold

- Beaumont E, **Onifer SM**, Reed WR, Magnuson DSK (2006) Magnetically-evoked inter-enlargement response: An assessment of ascending propriospinal fibers following spinal cord injury. Exp Neurol 201:428-440.
- Brown MR, **Sullivan PG**, **Geddes JW** (2006) Synaptic mitochondria are more susceptible to Ca²⁺ overload than nonsynaptic mitochondria. J Biol Chem 281:11658-68.
- Bruce-Keller AJ**, Dimayuga FO, Reed JL, Wang C, Angers R, Wilson ME, Dimaygua VM, and **Scheff SW** (2006) Gender and estrogen manipulation do not modulate TBI in mice. J Neurotrauma, in press.
- Burke DA, Magnuson DSK, Nunn CD, Fentress KG, Wilson ML, Shum-Siu AH, Moore MC, Turner LE, King WW, **Onifer SM** (2006) Use of environmentally enriched housing for rats with spinal cord injury: The need for standardization. J Amer Assoc Lab Animal Sci in press.
- Cameron A.A., **Smith G.M.**, **Randall D.C.**, Brown D.R. and **Rabchevsky A.G.** (2006) Genetic manipulation of intraspinal plasticity after spinal cord injury alters the severity of autonomic dysreflexia. J. Neuroscience 26(11): 2923-2932.
- Chaudhry N, de Silva U, **Smith GM**. (2006) Cell adhesion molecule L1 modulates nerve-growth-factor-induced CGRP-IR fiber sprouting. Exp Neurol. 202:238-249.
- Chen, Q., S. Wang, S.N. Thompson, **E.D. Hall** and **R.P. Guttman**. Identification and characterization of PEBP as a calpain substrate. J. Neurochem. 99:1133-1141, 2006.
- Cook, AM, **Hatton J**. "Neurological Impairment" In: American Society of Parenteral and Enteral Nutrition Adult Nutrition Support Science and Practice: An Interdisciplinary Core Curriculum, in press.
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4. PATENTS

Smith, G.M. and Rabchevsky, A.G. "Methods of inhibiting pain and autonomic dysreflexia with semaphorin 3A" Pending at US patent and Trade Mark Office. Serial # 11/343,160

5. INVITED LECTURES OR SEMINARS

Cambi, F.

- First International ELA symposium: The vital function of myelin: Development and Maintenance. Paris October 5-7, 2006. "Correcting PLP mutations"
- "PLP workshop" at the American Society for Neurochemistry meeting, March 10-15, 2006. "Is PLP necessary for brain development and function? The human perspective"

Chen, J.

- "Neural stem cell and neuroregeneration in the adult brain". University of Kentucky Grand Rounds, 9-2006.
- "Stem cell and induced neurogenesis in adult brain" Chinese Academy of Science. Invited speaker 7-06

Geddes, J.W.

- Indiana University/Purdue University, Indianapolis "Mitochondrial Ca²⁺ and Calpain: New Tricks for an Old Dog" December 12, 2006
- Indian Institute of Chemical Biology, Calcutta; International Workshop on Neurochemical Techniques, Invited Faculty, December 29 2006 to January 9, 2007

Hall, E.D.

- "Current Concepts of Oxidative Damage and Antioxidant Neuroprotection in Acute CNS Injury", Plenary Lecture at Rachidian Society Meeting, Kailua-Kona, Hawaii, February 6, 2006.
- "Role of Peroxynitrite in Secondary Damage in Traumatic Brain and Spinal Cord Injury", Seminar, Medical College of Virginia; Richmond, VA April 12, 2006.
- "Pathophysiology of Traumatic Brain Injury: Opportunities for Pharmacological Neuroprotection" and "Pathophysiology of Traumatic Spinal Cord Injury: Opportunities for Pharmacological Neuroprotection", University of Alaska-Fairbanks; Fairbanks, Alaska, August 28, 2006.

Onifer, SM

- "Axonal Sprouting and Regeneration after Spinal Cord Injury", Department of Biological Sciences, Phi Sigma, POE in Neuroscience and Behavior, Illinois State University, Normal, IL, October, 2006.

Pauly, J.R.

- Neuronal Nicotinic Acetylcholine Receptors as Targets For Therapeutic Drug Discovery, Centre College, Department of Chemistry, March 20, 2006
- Gender-dependent Outcomes in a Mouse Model of Prenatal Nicotine Exposure and Behavioral Teratogenicity. World Conference on Tobacco or Health, July 13, 2006, Washington, DC
- Neuronal Nicotinic Receptors: The Good, The Bad, And The Unknown. University of KY, Dept. of Physiology, November 15, 2006

Rabchevsky, A.G.

- Drexel University College of Medicine, Department of Neurobiology and Anatomy, Philadelphia, PA "Plasticity of both sensory axons and propriospinal neurons influences the severity of autonomic dysreflexia after complete spinal cord injury." November 1, 2006
- Beckman Center, Irvine, CA, The National Academies Keck's Future Initiative, Smart Prosthetics: Exploring Assistive Devices for the Body and Mind, "Perspectives on neuroprosthetics from the view of a neuroscientist and user." November 9, 2006

Smith, G.M.

- "Directing Axonal Growth from Neuronal Transplants to Specific Target Locations", Reeve-Irvine Center, Univ. Of California, Irvine
- "Remaking Connections: Sprouting and Regeneration of Sensory Afferents", University of Michigan, Ann Arbor MI

Snow, D

- "Axonal Growth in the Complex Environment Surrounding Spinal Cord Injury", Amer. Soc. Neurochem. Symposium invited speaker, Portland, OR; March, 2006.
- "Neuronal growth cones detect subtle variations in chondroitin sulfate proteoglycan structure". 24th Annual Neurotrauma Symposium, Invited speaker, Session 6: Injury and ECM, St. Louis, MO; July 2006.

Voss, S.R.

- "Genetic and genomic architecture of salamander metamorphosis and regeneration", January 2006 – Invited seminar, Department of Physiology, University of Kentucky.

6. HONORS, AWARDS, NEW EDITORIAL BOARD APPOINTMENTS OR ELECTIONS TO SOCIETY OFFICES DURING 2006

Hall, E.D.

- Elected President of the National Neurotrauma Society for 2007-2008
- Appointed to Editorial Board of **Biochemical Pharmacology**, 2006-Present

Pauly, J.R.

- Outstanding Second Year Instructor, Univ. of KY, College of Pharmacy
- Rho Chi Pharmacy Honor Society, Univ. of KY, College of Pharmacy (Honorary Membership)
- Senior Class Award for Outstanding Faculty Member, Univ. of KY, College of Pharmacy

Rabchevsky, A.G.

- Abraham Flexner Master Educator Award for "Outstanding Teaching Contribution", Center for Excellence in Medical Education, University of Kentucky

Saatman, K.E.

- Elected as Vice President, National Neurotrauma Society, to serve 2007-2008

Snow, D.M.

- Served as President of the Women in Neurotrauma Research (WINTR) 2006-2007

Sullivan, P.G.

- Promoted to Associate Professor of Anatomy & Neurobiology with tenure and appointed as a SCoBIRC Associate Director
- Appointment to the Board of the Brain Injury Association of Kentucky (BIAK)

7. MISCELLANEOUS

- SCoBIRC Associate Director J.W. Geddes organized a new graduate course for students working in SCoBIRC laboratories and other UK laboratories involved in neurological disease research. The development of the team-taught course, "Mechanisms of Neurologic Disease," is being funded by a recently awarded NIH R25 grant.
- We recently received word that the SCoBIRC website (www.mc.uky.edu/scobirc/), designed by Gisele Rabchevsky of DigiZel Graphix, LLC, was chosen to receive an Award of Excellence from District III (southeastern U.S. states) the Council for the Advancement and Support of Education (CASE III). The website was chosen from 22 nominees for the award and was cited for a "nice clean design" and "excellent use of white space". The Award will be accepted at the CASE III convention in Nashville, TN in February by Kristin Cruser, Manager of UK Communications.
- SCoBIRC faculty member Dr. A.G. (Sasha) Rabchevsky (a T5 paraplegic), in collaboration with Cardinal Hill Rehabilitation Hospital, organized a "Day in a Wheelchair" experience for SCoBIRC personnel in the fall of 2006. The SCoBIRC Director, the SCoBIRC Core Faculty, their laboratory personnel, postdoctoral fellows and graduate students took turns spending a day at work in a wheelchair. It was a tremendously enlightening experience for the able-bodied SCoBIRC personnel concerning the kinds of difficulties and challenges SCI people face in their everyday lives. The hope was that the time spent living life in a wheelchair would enhance not only our sensitivity to what it is like to live with the lasting effects of a spinal cord injury, but also provide us with a stronger sense of mission in regards to helping to find neurorestorative and life-improving treatments to help SCI (and TBI) patients.

8. 2006 DONORS

We are extremely grateful to the following donors who made generous donations to SCoBIRC during the past year.

- Kentucky-Indiana Chapter of the Paralyzed Veterans of America
- Atlas Metal Products Co., Inc. (Louisville, KY)
- Cognosci, Inc. (Research Triangle Park, NC)
- Centre for Neuro Skills (Irving, TX)
- Mark Robert Bartella Scholarship Fund
- Cardinal Hill Rehabilitation Hospital