



**2004 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, 2004

EDWARD D. HALL, PH.D.

SCoBIRC DIRECTOR



This report describes our progress in achieving the goals for 2004 outlined in the 2003 Progress Report. Also presented are related SCoBIRC activities including the Invited Lecture Series, the 2004 Kentucky Spinal Cord and Brain Injury Research Symposium, a full listing of publications, archived abstracts, and new grants for SCoBIRC Faculty and Faculty Associates. As is apparent from this document, 2004 has been a wonderfully productive year for SCoBIRC on several fronts. Finally, we present the main SCoBIRC goals for 2005.

HIGHLIGHTS OF 2004

- Recruitment of new SCoBIRC Faculty: Kathryn E. Saatman, Ph.D., Research Associate Professor of Neurosurgery, University of Pennsylvania, who will join UK as a SCoBIRC Core Faculty Member and Associate Professor of Physiology.
- Appointment of SCoBIRC Core Faculty James W. Geddes, Ph.D. as SCoBIRC Associate Director
- Appointment of SCoBIRC Faculty Associate Byron Young, M.D. as SCoBIRC Clinical Director
- Appointment of SCoBIRC Faculty Associate Joe E. Springer, Ph.D. to be the Cardinal Hill Endowed Chair and Professor and Vice Chair, Physical Medicine & Rehabilitation
- Addition of two new Faculty Associates: David Randall, Ph.D., Professor of Physiology and Randal Voss, Ph.D., Associate Professor of Biological Sciences
- Acceptance of three new graduate students into SCoBIRC laboratories: Lamin Mbye, Yiqin Xiong and Laurie Davis.
- Completion of Ph.D. by two SCoBIRC graduate students: Tomoko Senjoku, Ph.D. and Stephanie Nottingham, Ph.D.
- Recruitment of 8 new post-doctoral fellows into SCoBIRC laboratories: Bing Zhao, Ph.D., Xiong Gao, Ph.D., Jignesh Pandya, Ph.D., Gabrielle Curinga, Ph.D., Stephanie Nottingham, Ph.D., Xinhua Hu, Ph.D., Erming Wang, Ph.D. and Neviana Dimova, M.D.
- SCoBIRC Faculty and Faculty associates published 26 full CNS injury-related publications and one patent application.
- New CNS injury-related grants attributed to SCoBIRC Faculty and Faculty Associates included 8 NIH R01s, 4 new KSCHIRT grants and 3 grants/contracts from private foundations or industry. These totaled \$8,623,617 in multi-year funding. In addition, an NIH Center Core grant was very favorably reviewed with funding anticipated to begin in Spring 2005 (\$2,256,211), bringing the new grant funding to \$10.8 million in direct costs.
- Hosted 12 speakers from various U.S. and Israeli universities in the SCoBIRC Seminar Series.
- Hosted the 2004 KSCHIRT Symposium in June. Participants included 15 speakers from U.S., Canadian, British and Swedish Universities and 145 attendees.

PROGRESS RELATED TO 2004 GOALS OUTLINED IN 2003 SCoBIRC PROGRESS REPORT

- **RECRUIT ADDITIONAL FACULTY**

Appointment of James W. Geddes, Ph.D. as SCoBIRC Associate Director: Dr. Jim Geddes, who previously served as Director of SCoBIRC during its first three years (1999-2002) has accepted the position of SCoBIRC Associate Director. Since the arrival of Dr. Edward Hall at the Spinal Cord and Brain Injury Research Center at the University of Kentucky, and his assumption of the Directorship in

July, 2002, Dr. Geddes has been a consistent source of encouragement, information, help and support. In his new role he will be responsible for the following:

- Fill in for Director during latter's absence including signing authority for purchases
- Direct Administrative and Bioinformatics Core facility in regards to database management
- Assist Director with recruitment of faculty and post-doctoral fellows
- Direct maintenance and updating of website
- Organize seminar series/mini-symposia
- Co-Chair planning committee for biannual KSCHIRT Symposia
- Assist Director in fundraising and public outreach activities
- Assist Director with leadership and organization of multi-investigator program project grants

As noted later in this report, during the past year Dr. Geddes has received a new NINDS R01 grant, a new KSCHIRT grant, and is a Program Director on a newly awarded National Institute of Aging Program Project Grant.

Appointment of A. Byron Young, M.D. as SCoBIRC Clinical Director: In September, 2004, Dr. Byron Young, Professor and Head of Neurosurgery, accepted the appointment as SCoBIRC Clinical Director. Dr. Young is nationally and internationally respected for his clinical research in traumatic brain injury and currently is PI on an NINDS R01 grant involving a Phase II trial of cyclosporin A in severe TBI patients. Dr. Young has been an investigator of many, if not all, of the past phase II and III clinical trials of various pharmacological agents carried out during the past 15-20 years. There could be no better person to direct the design and implementation of future UK-SCoBIRC trials in TBI and SCI. In that regard, he will Chair the newly instituted SCoBIRC Clinical Trials Committee.

Recruitment of Kathryn E. Saatman, Ph.D.: We are most pleased to have successfully attracted Dr. Kathy Saatman, Research Associate Professor of Neurosurgery and Associate Director of the Head Injury Center, University of Pennsylvania School of Medicine to become a SCoBIRC Core Faculty member. She will also be an Associate Professor of Physiology (Tenure track, Regular Title Series). Kathy will begin at UK on January 24, 2005. She will be joined by three research technicians who are moving with her. Her research is focused on cytoskeletal damage mechanisms in acute traumatic brain injury. She has spent her entire professional career at the University of Pennsylvania where she received her Ph.D. in Biomedical Engineering and completed her post-doctoral fellowship in the Department of Neurosurgery. Subsequently, she joined the faculty in the Department of Neurosurgery. She presently holds an NINDS R01 grant which will transfer with her.

Appointment of Joe E. Springer, Ph.D. as Cardinal Hill Endowed Chair and Professor and Vice Chair for Research in Department of Physical Medicine and Rehabilitation: Dr. Joe E. Springer, who has been a Faculty Associate and one of our most productive and well respected SCoBIRC scientists since its inception, was appointed this fall to the Cardinal Hill Endowed Chair and promoted to Professor and Vice Chair for Research in the Department of Physical Medicine and Rehabilitation. In addition to continuing his well-funded research in spinal cord injury neuroprotection, Joe is in the process of building a neurorehabilitation research group which includes recruitment of two Cardinal Hill Endowed Professorships. That group will continue to work closely with SCoBIRC to achieve successful translation of new therapies for SCI and TBI into clinical trials. Dr. Springer is currently funded by two NINDS R01 grants.

New SCoBIRC Faculty Associates: Two new faculty associates have been added to the SCoBIRC ranks:

- **David C. Randall, Ph.D., Professor of Physiology.** Dr. Randall is actively collaborating with SCoBIRC faculty on mechanisms of autonomic dysfunction after spinal cord injury.

- **Randal S. Voss, Ph.D., Associate Professor of Biological Sciences.** Dr. Voss works with the Mexican axolotl salamander which can regenerate its spinal cord after injury, and is attempting to define differences in post-traumatic gene expression in axolotls versus mammals in which spinal cord regeneration is limited.

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-Neuroprotection and Clinical/Rehabilitation categories).

SCoBIRC Core Faculty:

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

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

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

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 K. Knapp, Ph.D., Associate 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 Associate 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-Neuroprotection:

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

D. Allan Butterfield, Ph.D., Professor/Dept. Chemistry, College of Arts and Sciences
Role of reactive oxygen mechanisms in neurodegeneration

James W. Geddes, Ph.D., Admiral Sheeley Endowed Associate 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

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

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

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

- **Departure of Three SCoBIRC Faculty Associates:** During the past year, Dr. Greg Barnes, Assistant Professor of Neurology, moved to Vanderbilt University. Dr. Debra Blades, Assistant Professor of Neurosurgery, moved back home to Barbados to be closer to family. Moreover, Dr. Sue Queen, Assistant Professor of Physical Therapy in the Department of Rehabilitation Sciences, has recently resigned from UK to become Director of the Physical Therapy at the University of New Mexico. In the case of Drs. Barnes and Queen, these moves were to pursue career advancement. We are grateful for the contributions of these excellent faculty to SCoBIRC, and we wish them all the best in their future lives and careers.
- **RECRUIT ADDITIONAL POSTDOCTORAL RESEARCHERS AND GRADUATE STUDENTS**

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

Graduate Students

Ms. Yiqin Xiong	Laboratory of E.D. Hall
Mr. Lamin Mbye	Laboratory of E.D. Hall
Ms. Laurie Davis	laboratory of P.G. Sullivan

Post-doctoral Fellows

Stephanie Nottingham, Ph.D.	Laboratory of E.D. Hall
Jignesh Pandya, Ph.D.	Laboratory of P.G. Sullivan
Xinhua Hu, Ph.D.	Laboratory of G.M. Smith
Gabrielle Curinga, Ph.D.	Laboratories of D. Snow and G.M. Smith
Bing Zhao, Ph.D.	Laboratory of J. Chen
Xiong Gao, Ph.D.	Laboratory of J. Chen
Erming Wang, Ph.D.	Laboratory of F. Cambi
Neviana Dimova, M.D.	Laboratory of F. Cambi

- **Continue to Build Extramural Funding Base**

The following is a list of new CNS injury-related grants awarded to SCoBIRC Faculty or Faculty Associates during 2004. We have obtained \$7,249,881 (Direct Costs) in new NIH grants including **six** NINDS R01s, **one** NINDS R21 and a portion (**one** project) of a National Institute of Aging Program Project Grant (P50). In addition, we have received \$1,137,434 in new KSCHIRT grants and \$236,302 in new Foundation or Industry grants. The indirect cost income to the University of Kentucky for the **eight** new NIH grants will be \$3,429,194. Adding this amount to the NIH direct costs and to the KSCHIRT and Foundation/Industry brings the total new multi-year extramural funding awarded to SCoBIRC Core Faculty and Faculty Associates during 2004 to **\$12,052,811**.

National Institutes of Health

NINDS R01 NS045726; **PI: J.W. Geddes**
"Calpain Inhibition Strategies for Spinal Cord Injury"
Direct costs: \$1,000,000; 01/01/04-12/31/08

NINDS R01NS046566; **PI: E.D. Hall**
"Peroxynitrite-Induced Oxidative Damage in TBI"
Direct costs: \$925,000; 04/01/04-03/31/08

NINDS R01 NS046380; **PI: J.E. Springer**
"Cyclooxygenase Pathophysiology in Spinal Cord Injury"
Direct costs: \$925,000, 4/01/04-3/31/08.

NINDS R01 NS048191; **PI: P.G. Sullivan**
"Mitochondrial Uncoupling as a Therapeutic Target in TBI"
Direct costs: \$1,125,000, 2/1/04-1/31/09

NINDS R01 NS040592; **PI: G.M. Smith**
"Axon Growth and Guidance in Nervous System Repair"
Direct costs \$1,216,131, 1/1/05 - 12/31/09

NINDS R01 NS049901 **PI: A.G. Rabchevsky**
"Role of Intraspinal Plasticity in Autonomic Dysreflexia"
Direct costs: \$1,156,250, 5/1/04-4/30/09

AG P5010836 **Project 4 Leader: J.W. Geddes**
"Mitochondria, ROS, Ca²⁺, and Calpain in the Aging CNS"
Direct Costs \$625,000 for Project 4. 9/30/04-8/31/09

NINDS R21 NS046426; **PI: P.G. Sullivan**
"Oxidative Stress and the Ketogenic Diet"
Direct Costs: \$277,500, 7/1/04-4/30/06

Total New NIH Funding: \$7,249,881

Pending NIH Funding:

NIH/NINDS P30 NS051220; **PI: E.D. Hall**
"UK Spinal Cord & Brain Injury Research Center Core Grant"
Direct Costs: \$2,256,211

This application received a priority score of 145 and a percentile score of 3.5% with no recommendations for reduction of the budget; 5 year funding anticipated beginning spring 2005.

KSCHIRT Grants

E.D. Hall

“Novel Pharmacotherapy for Traumatic Brain Injury”
\$287,093; 1/15/04-1/14/07

A.G. Rabchevsky

“Influence of Neurotrophins on Intraspinal Plasticity Modulating Autonomic Dysreflexia”
\$297,000; 1/15/04-1/14/07

J.E. Springer

“COX-2 Induction in Traumatic Spinal Cord Injury”
\$253,341; 1/15/04-1/14/07

S.R. Voss

“Microarray and *In Situ* Hybridization Analyses of Natural Spinal Cord Regeneration”
\$300,000; 2/01/04 – 1/31/07

Total New KSCHIRT Funding: \$1,137,434

Foundations/Industry:

A.G. Rabchevsky

Geron Corporation, Menlo Park, CA
“Transplantation of Human Embryonic Stem Cells into the Injured Rat Spinal Cord”
\$99,730; 2/1/04-6/30/05

P.H. Kitzman

Paralyzed Veterans of America Spinal Cord Research Foundation
“Suppression of SCI-induced Spasticity by Inhibition of Glutamate Release”
\$136,572; 1/1/05-12/31/06.

• **Pursue Opportunities for Basic-Clinical Translation**

The following clinical projects are in progress:

- Phase II evaluation of cyclosporin A in patients with severe TBI -Young/Hatton-Kolpek
- Evaluation of the lipid peroxidation products isoprostanes and neuroprostanes as potential biomarkers for studies in severe TBI -Hatton-Kolpek/Young/Hall
- Participation in a multi-center Phase III study of the combination glutamate NMDA receptor antagonist/antioxidant dexanabinol (Pharmos, Israel) in severe TBI patients- Young/Hatton-Kolpek

The following preclinical therapeutic discovery projects are in progress, 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
 - Peroxynitrite scavengers-Hall/Sullivan
 - Mild mitochondrial uncoupling agents-Sullivan
 - Mitochondria-penetrable antioxidant peptides (collaboration with Cornell University)-Hall/Sullivan

- Evaluation of novel delivery systems for the calpain inhibitory protein calpastatin- Geddes
- Evaluation of glutamate release inhibitors gabapentin and/or riluzole for control of SCI spasticity- Kitzman/Hall
- **2004 Spinal Cord and Brain Injury Research Center (SCoBIRC) Invited Lecture Series**
 - January 6
KATHRYN E. SAATMAN, PH.D. (Faculty Candidate)
University of Pennsylvania
"Trauma-induced alterations in the neuronal cytoskeleton"
 - January 20
STEFANO SENSI, Ph.D.
University of California, Irvine
"Glutamate and Neuronal Injury: THINK ZINC"
 - February 18
CLIVE SVENDSEN, Ph.D.
University of Wisconsin-Madison
"Combining Growth Factor, Gene and Stem Cell Therapy for Neurodegenerative Disorders"
(Co-sponsored with the Department of Physiology)
 - February 25
MICHAEL CRAGGS, PH.D.
University College London, United Kingdom
"Spinal Cord Injury: The Restoration of Pelvic Function by Implantable Devices"
(Co-sponsored with the Department of Physiology)
 - March 15
REBECCA ELLIS (SCoBIRC candidate)
University of Florida
Informal Seminar Presentation
 - April 5
GANG CHEN, PH.D. (Postdoctoral Candidate)
Rutgers University
Informal Seminar Presentation
 - April 28
SHUXIN LI M.D., PH.D. (Faculty Candidate)
Yale University School of Medicine
"Axonal Regeneration in the Injured CNS by Targeting Myelin-derived Inhibitions"
 - May 12
KIMBERLY ANDERSON, Ph.D. (SCoBIRC candidate)
University of California, Irvine
"Targeting Recovery: Priorities of the Spinal Cord Injured Population"

June 23

BING ZHAO (Postdoctoral Candidate)
University of Kentucky

"Development and projections from serotonergic reticular formation cells to the optic tectum of *Rana pipiens*"

October 6

JIGNESH PANDYA, PH.D. (Postdoctoral Candidate)
State University of NY at Buffalo
"Role of dietary manipulation for treatment of Obesity"

October 19

ESTHER SHOHAMI, PH.D.
Hebrew University, Jerusalem, ISRAEL
"Targeting Intracellular Pathways as a Novel Therapy for TBI"
"Roundtable Discussion: "The Importance of Timing in the Treatment of TBI"

December 13

CHEN-GUANG YU, M.D., Ph.D. (Research Assistant)
University of Florida
"ERK1/2 Signaling Cascades and Therapeutic Strategies for Spinal Cord Injury"

- **Host 2004 KSCHIRT Symposium**

UK-SCoBIRC hosted the 2004 Kentucky Spinal Cord & Head Injury Research Trust Symposium on June 10th and 11th at the Keeneland Race Course. The planning committee consisted of E.D. Hall (Chair), J.W. Geddes, P.G. Sullivan, G.M. Smith, A. Rabchevsky, D. Snow, Z. Frye and S. Malley. There were 145 attendees (including invited speakers) from the University of Kentucky, University of Louisville and various U.S. and Canadian universities. The program is listed below.

Thursday	June 10, 2004 Phoenix Room - Keeneland Clubhouse
7:15 – 8:00 am	Registration and Continental Breakfast
8:00 – 8:10	Opening Remarks Edward D. Hall, Ph.D. , Director, UK Spinal Cord & Brain Injury Research Center
SESSION 1	SCI AND TBI CLINICAL DRUG TRIALS Edward Hall, Ph.D., Session Chair
8:10 – 9:05	Michael Bracken, Ph.D. <i>Yale University</i> Clinical Trials in SCI: Why are we not doing more?
9:05 – 10:00	Raj Narayan, M.D. <i>University of Cincinnati</i> Clinical Trials in TBI
10:00 – 10:30	BREAK
SESSION 2	CNS INJURY BIOMARKERS James Geddes, Ph.D., Session Chair
10:30 – 11:15 am	Ronald Hayes, Ph.D <i>University of Florida</i> Development of non-invasive biochemical markers of acute brain

11:15 – 12:00 noon	Frank Zelman, Ph.D. <i>University of Cincinnati</i> C-tau biomarker of spinal cord and traumatic brain injury: translational studies.
12:00 – 1:30 pm	LUNCH (1 st Floor Clubhouse)
SESSION 3	THE ROLE OF MITOCHONDRIA IN NEURONAL INJURY Patrick Sullivan, Ph.D., Session Chair
1:30 – 2:20 pm	Gary Fiskum, Ph.D. <i>University of Maryland</i> Mitochondrial mechanisms and targets for neuroprotection in ischemic and traumatic brain injury.
2:20 – 3:10	Tadeusz Wieloch, Ph.D. <i>University of Lund, Sweden</i> Uncoupling protein 2 as an inducible neuroprotectant derived from gene expression analysis.
3:10 – 3:45	Patrick Sullivan, Ph.D. <i>University of Kentucky</i> Neuroprotective potential for mild mitochondrial uncoupling in CNS injury.
SESSION 4	POSTER PRESENTATION and RECEPTION (Phoenix Room)
4:00 – 6:00	
6:00 – 8:00	DINNER - 1st Floor Clubhouse
Friday	June 11, 2004, Phoenix Room - Keeneland Clubhouse
8:00 – 8:30 am	Registration and Continental Breakfast
SESSION 5	CLINICAL ASPECTS AND NEUROBIOLOGY OF AUTONOMIC DYSFUNCTION IN SCI PATIENTS Alexander Rabchevsky, Ph.D., Session Chair
8:30 – 9:15	Lawrence Schramm, Ph.D. <i>Johns Hopkins University</i> Neurobiological studies on the mechanisms of hypertensive crises after spinal cord injury.
9:15 – 10:00	Andrei Krassioukov, M.D., Ph.D. <i>ICORD and University of British Columbia</i> Does a neurologically complete spinal cord injury also mean a complete injury of the descending autonomic pathway in man?
10:00 – 10:30	BREAK
10:30 – 11:15	Christopher Mathias, DPhil DSc FRCP FMedSci <i>Imperial College London at St. Mary's Hospital and University College London, UK</i> Evidence based therapy of autonomic malfunction in spinal cord injuries.

11:15 – 12:00	William deGroat, Ph.D. <i>University of Pittsburgh</i>
	Reorganization of visceral reflex pathways following spinal cord injury.
12:00 – 1:30 pm	LUNCH (1st Floor Clubhouse)
SESSION 6	AXON GUIDANCE MECHANISMS AND THE TRANSPLANTATION OF OLFACTORY ENSHEATHING CELLS IN SCI George Smith, Ph.D. and Diane Snow, Ph.D., Session Chairs
1:30 – 2:15	Geoffrey Raisman, M.D., Ph.D. <i>National Institute for Medical Research, London UK</i>
	Repair of spinal cord injury by transplantation of olfactory ensheathing cells.
2:15 – 3:00	Jane Roskams, Ph.D. <i>University of British Columbia</i>
	Olfactory ensheathing cells and CNS repair: myth or reality?
3:00 – 3:30	BREAK
3:30 – 4:15	Paul Letourneau, Ph.D. <i>University of Minnesota School of Medicine</i>
	Guidance mechanisms of axonal growth cones.
4:15 – 5:00	Jerry Silver, Ph.D. <i>Case Western Reserve University School of Medicine</i>
	Regeneration beyond the glial scar.
5:00	Adjourn

2004 Refereed Publications by SCoBIRC Faculty and Faculty Associates (Faculty Names Bolded):

Brown M.R., **Geddes J.W.** and **Sullivan P.G.** Brain region-specific, age-related, alterations in mitochondrial responses to elevated calcium. *J Bioenerg Biomembr.* 36:401-406, 2004.

Brown M.B., **Sullivan P.G., (co-first author)**, Dorenbos K.A., Modafferi E.F., **Geddes J.W.**, Steward O. Nitrogen Disruption of Synaptoneurosomes: An alternative method to isolate total or synaptic brain mitochondria. *Journal of Neuroscience Methods*, 137, 299-303, 2004.

Brown M.B., **Geddes J.W., Sullivan, P.G.** Brain region-specific, age-related, alterations in mitochondrial responses to elevated calcium. *Journal of Bioenergetics and Biomembranes*, 36, 401-406, 2004.

Cai J., Peng X., Nelson K.D., Eberhart R., **Smith G.M.** Synergistic improvement from bioresorbable filaments and human heregulin-1 on cellular and axonal migration across sciatic nerve lesion gap. *J. Biomedical Materials Research.* 69A:247-258, 2004.

Chen J, Magavi SS, Macklis JD. Neurogenesis of corticospinal motor neurons extending spinal projections in adult mice. *Proc Natl Acad Sci U S A.* 101(46):16357-16362, 2004.

Hall E.D., Detloff, M.R., Johnson K. and Kupina N.C. Peroxynitrite-mediated protein nitration and lipid peroxidation in a mouse model of traumatic brain injury. *J. Neurotrauma* 21:9-20, 2004.

Hynds D.L., Rangappa N, Beest J.T., **Snow D.M.**, **Rabchevsky A.G.** Microglia enhance dorsal root ganglion outgrowth in Schwann cell cultures. *Glia* 46:218-226, 2004.

Jin Y., McEwen M.L., Nottingham S., Maragos W.F., Dragicevic N.B., **Sullivan P.G.**, and **Springer J.E.** The mitochondrial uncoupling agent 2,4-dinitrophenol improves mitochondrial function, attenuates oxidative damage and increases white matter sparing in the contused spinal cord. *J. Neurotrauma* 21(10):1396-1404, 2004.

Karakashian A.A., Giltiay N.V., **Smith G.M.**, and Nikolova-Karakashian M.N. Expression of neutral sphingomyelinase-2 (NSMase-2) in primary rat hepatocytes modulates IL-b-induced JNK activation. *FASEB Journal* 18:968-970.

Knapp P.E. and Adams M.A. Epidermal growth factor promotes oligodendrocyte differentiation and enhances survival and regrowth after injury. *Exp. Cell Res.*, 269 (2): 135-144, 2004.

Pauly J.R., Charriez C.M., Guseva M.V. and **Scheff, S.W.** Nicotinic Receptor Modulation for Neuroprotection and Enhancement of Functional Recovery Following Brain Injury or Disease. *Annals New York Academy of Sciences* 1035: 1-19, 2004

Putta S., Smith J.J., Walker J., Rondet M., Weisrock D., Monaghan J., Kump K., King D.C., Maness N.J., Habermann B., Tanaka E., Bryant S.V., Gardiner D.M., Parichy D.M., **Voss S.R.** From Biomedicine to Natural History Research: Expressed Sequence Tag Resources for Ambystomatid Salamanders. *BMC Genomics* 5:54, 2004.

Ravikumar,R., Flora G., **Geddes J.W.**, Hennig B., and Toborek M. Nicotine attenuates oxidative stress, activation of redox-regulated transcription factors and induction of proinflammatory genes in compressive spinal cord trauma. *Brain Res Mol Brain Res.* 124:188-198, 2004.

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Patents by SCoBIRC Faculty:

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2. SCoBIRC GOALS for 2005

- **MOVE INTO NEW LABORATORY SPACE IN BIOLOGICAL AND BIOMEDICAL RESEARCH BUILDING**

The SCoBIRC Core Faculty and certain Faculty Associates will move into new contiguous laboratory and office space on the third floor of the recently completed Biological and Biomedical Research Building (BBSRB) in January and February, 2005. We will create three Core facilities on the third floor. The first of these will be the Administrative & Bioinformatics Core directed by SCoBIRC Associate Director, James Geddes and will include our SCoBIRC Administrator, Administrative Assistant and server for data storage. The second will be a Microscopy, Stereology & Image Analysis Core directed by Patrick Sullivan and Alexander Rabchevsky. The third will be our Pharmacokinetics & Biomarker Core directed by SCoBIRC Director Edward Hall. SCoBIRC will also have space on the ground floor within the BBSRB vivarium that will house two additional core facilities: Animal Surgery & TBI/SCI Model Core directed by Dr. Stephen Scheff and Behavioral Testing Core directed by Drs. Jim Pauly. It is expected that moving into this space will greatly enhance collaboration and research efficiency.

- **RECRUIT ADDITIONAL FACULTY**

SCoBIRC has been promised two additional Core tenure track faculty, #8 and #9. The 8th slot was to have been filled in FY 2005. However, due to fiscal constraints imposed by state budget cuts, the Dean of the College of Medicine delayed our recruitment of faculty #8 until at least FY 2006. It is hoped that we will be able to proceed with the completion of our recruitment effort including both slots 8 and 9 in FY2006 which begins in July, 2005. We have one very strong TBI-

focused candidate on hold for #8 who would bring multiple extramural grants with him. However, we are going to re-advertise for candidates for slot #9 and will aim that position toward a spinal cord regeneration-focused scientist.

- **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.

- **HOST 2005 REHABILITATION SYMPOSIUM**

Dr. Edward Hall, SCoBIRC Director, Dr. Joe Springer, Cardinal Hill Endowed Chair and Professor and Vice Chair for Research in Department of Physical Medicine, and Rehabilitation and Dr. Gerald Klim, Associate Professor and Chairman of the Department of Physical Medicine and Rehabilitation, will direct the efforts to organize this symposium together with SCoBIRC Faculty and staff based at UK and Cardinal Hill Rehabilitation Hospital.

- **CONTINUE TO BUILD EXTRAMURAL FUNDING BASE**

We are continuing in our aggressive efforts to add to our extramural funding. We are extremely gratified to have recently received word that our NINDS Center Core Grant submitted on June 1, 2004 entitled "UK Spinal Cord & Brain Injury Research Center Core Grant" (NIH/NINDS P30 NS051220) received a priority score of 145 and a percentile score of 3.5% with no recommendations for reduction of the budget. We have been told that this 5 year grant totaling \$2,256,211 in direct costs will be funded in the spring. This grant will provide full time technical support and major equipment for each of our SCoBIRC Core Facilities (vide supra).

Although we will continue to pursue individual investigator funding (e.g. R01s, R21s), we also plan to submit one or two program project grants during 2005. We have now reached critical mass in at least two areas making these multi-investigator proposals more feasible. Possible themes for these include strategies to inhibit calpain-mediated cytoskeletal damage, inhibition of reactive oxygen damage, strategies for mitochondrial protection and mechanisms and inhibition of aberrant post-SCI neural plasticity.

In addition, we have recently received word that four additional KSCHIRT grants have been approved for funding in 2005. These are:

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"

- **PURSUE OPPORTUNITIES FOR BASIC-CLINICAL TRANSLATION**

Biomarker Development: An important part of the SCoBIRC mission is to translate basic science discoveries concerning the pathophysiology and treatment of SCI and TBI into improvements in clinical care. During the coming year, we will continue to conduct preclinical and clinical studies involving the measurement of two chemically similar classes of lipid peroxidation products known as “isoprostanes” and “neuroprostanes” which show promise as biomarkers for monitoring of the secondary pathophysiology of CNS injury. During the past year, we have successfully implemented the GC-MS technology for measuring these and made significant improvements to tissue sample extraction procedure and have succeeded in making measurements in TBI patient CSF samples. In 2005, we will utilize this methodology to measure isoprostanes and neuroprostanes in biofluids from severely injured TBI rats and UK TBI patients. The development of this and other biomarkers is critically important to allow us to monitor the time course and severity of secondary injury mechanisms and the effects of novel neuroprotective agents in future clinical trials.

Cyclosporin A Neuroprotection for TBI: An ongoing NIH-funded UK Phase II clinical trial of CsA pharmacokinetics in severe TBI patients being lead by Drs. B. Young and J. Hatton-Kolpek will be completed in 2005. Discussions about possible phase III studies are ongoing.

Discovery of Novel Neuroprotective Agents for SCI and TBI: As mentioned earlier, we are actively involved in preclinical discovery work to evaluate the neuroprotective potential of several pharmacological strategies. These include novel antioxidants, non-immunosuppressive cyclosporin analogs and mitochondrial protectants. All of these studies are being done with an eye toward providing practical information necessary for clinical translation. During 2005, this overall effort may result in the identification of a compound that can subsequently be moved toward clinical trials.