



Neuroscience Newsletter

3 New Students Join Neuroscience Program

Todd Robinson grew up in Hamburg, Pennsylvania. He received his Bachelors degree in the liberal arts from St. John's College in 2004, where his studies focused primarily on philosophy. Todd's work at St. John's College culminated in an analytical essay on the civil philosophy of Thomas Hobbes. Through St. John's, he was provided an opportunity to work in Dr. Brian McCarthy's lab in the Dept. of Pharmacology at USU in the summer of 2003. In the summer of 2004, Todd returned to Dr. McCarthy's lab as an ASPET intern where he explored the role of Sar1 in vesicular budding from the endoplasmic reticulum. Todd appreciates neuroscience for its dynamic implications across biology as well as philosophy. His outside interests include reading/writing fiction and poetry, painting, running, and a lifelong dedication to the martial arts.



Please welcome (pictured from left to right) Todd, Jeremy and Danette.

Jeremy Henriques was born in New Orleans, LA, where still claims residence, despite growing up all over the southern and eastern U.S. He obtained his B.S. in Chemistry and minor in Mathematics at Northwestern State University in Natchitoches, LA (if you've ever seen Steel Magnolias, you've seen Natchitoches). Jeremy has many research hours under his belt. In the summer of 2002 he was a recipient of an NSF REU (Research Experience for Undergraduates) Fellowship from the University of California at Santa Cruz. His undergraduate thesis research in biophysical chemistry at UC-SC focused on the small neuroprotein, alpha-synuclein. Alpha-synuclein comprises ~90% of the tissue in Lewy Bodies and Lewy Neurites, which are inclusions in the mid-brain thought to cause or contribute to neurological disorders such as Parkinson's Disease, Alzheimer's Disease, and dementia. Jeremy also was a recipient of the NASA-JOVE (Joint Venture) research scholarship throughout his tenure at NSU for which he did inorganic and organometallic synthesis. His future interests are broad, but hopes to find some specificity in the coming years. Though Jeremy did not go to LSU, he has been brainwashed to bleed purple and gold for the rest of his life and is looking for anyone who shares the same passion for college football viewing. He enjoys doing almost any outdoors or sports related activity.

Danette Cruthirds is from Delaware, Ohio and is a Major in the United States Army. Danette attended Austin Peay State University on a ROTC scholarship and received her Bachelors Degree in Nursing in 1992. She then worked as a staff nurse in the newborn nursery and intensive care unit at Ft Benning, GA before returning to school to obtain a Masters Degree in Nurse Anesthesia from the US Army Graduate Program in 1999. Danette's masters' thesis research was performed at Tripler Army Medical Center in Hawaii and her project was to determine the affect of dilution on the onset time of Rocuronium, an intermediate paralytic agent, as defined by intubating conditions and Train of Four. While stationed in Hawaii for an additional 4 years after graduation, she progressed from staff nurse anesthetist, to adjunct faculty in the US Army Graduate Nurse Anesthesia Program, to associate professor in the graduate program. Danette arrives at USU from Ft Leavenworth, Kansas where she attended the Command and General Staff College (a senior military school). Danette is a novice in the lab but is looking forward to her experience at USU. Her interests in Neuroscience are varied and range from glial cell development to pain response. Other interests include learning the joys of parenthood (Danette and her husband Eddie have a daughter, Nicole Ellen, who is 3 months old), exercise, music, movies, scrapbooking and travel.

USUHS Neuroscience Student Graduates

A. Tamara Crowder completed her Ph.D. in Neuroscience on February 2, 2004 under the direction of Thomas E. Cote, Ph.D., Associate Professor of Pharmacology and Neuroscience. Tammy came to the Neuroscience program after receiving a M.S. in Microbiology at USU in February 1999. She is currently pursuing her postdoctoral studies with Dr. Kirk Druey at NIAID, NIH.

CO-EXPRESSION OF REGULATOR OF G PROTEIN SIGNALLING 4 (RGS4) AND THE MU OPIOID RECEPTOR IN REGIONS OF RAT BRAIN: EVIDENCE THAT RGS4 ATTENUATES MU OPIOID RECEPTOR SIGNALLING

A. Tamara Crowder

Directed by Thomas E. Cote, Ph.D., Associate Professor of Pharmacology and Neuroscience

Regulators of G protein Signalling (RGS) proteins influence G protein-coupled receptor signal transduction by enhancing the intrinsic GTPase activity of G proteins. The RGS-enhanced GTPase activity of G proteins may be responsible for the desensitization of certain G protein-coupled receptors, including the mu opioid receptor. The goal of this research was to evaluate the ability of recombinant RGS4 to affect mu opioid receptor-mediated cellular signalling and to identify regions of the rat brain in which both RGS4 and the mu opioid receptor are co-expressed.

We evaluated the ability of recombinant RGS4 to affect [D-Ala², N-Me-Phe⁴, gly-ol] enkephalin (DAMGO)-mediated inhibition of adenylyl cyclase activity in membranes of SH-SY5Y cells, a cell line that express endogenous mu receptors. Recombinant RGS4 caused a concentration-dependent attenuation of DAMGO-mediated inhibition of adenylyl cyclase activity.

RGS4 diminished the efficacy, but not the potency, of DAMGO in inhibiting adenylyl cyclase activity. In contrast, RGS4 had no effect on the ability of GTPγS, a nonhydrolyzable analogue of GTP, to inhibit adenylyl cyclase activity. RGS4 also had no effect on DAMGO stimulated [³⁵S]GTPγS binding in SH-SY5Y membranes. Additionally, RGS4 was tested for its ability to affect [³H]DAMGO binding to the mu receptor. RGS4 failed to affect either the K_D of the B_{max} of [³H]DAMGO in saturation binding experiments.

Antibodies generated against rat RGS4 and the rat mu opioid receptor were used in immunohistochemical staining to identify specific regions of rat brain where the two proteins are co-expressed. Both RGS4 and mu opioid receptor proteins were present in many of the same regions of the brain. Further, we demonstrated that RGS4 is primarily localized to the nucleus, but that administration of fentanyl, a potent mu opioid agonist, induces translocation out of the nucleus, to the cytoplasm in the hippocampal CA3 pyramidal neurons.

Together, these findings are consistent with the proposal that RGS4 can desensitize mu opioid receptor by increasing the intrinsic GTPase of Gi-type G proteins associated with the mu opioid receptor and that, *in vivo*, RGS4 and the mu opioid receptor are co-expressed in many of the same regions of the rat brain.

Student Fellowships

Comprehensive Neuroscience Program

The objective of the CNP is to develop and support translational research related to nervous system events that cause pain and degeneration of neurological function. The focus of the CNP is the neuroscience of dysfunction, damage, and repair, with the understanding that knowledge of these issues gives researchers and clinicians the power to develop better ways to manage and treat pain, headache, seizures, neurodegeneration, and stroke. Graduate Student Fellowships provide up to \$25,000 / year for 2 years and were awarded based upon competitive peer-review of the applications.

This years recipients are: **Tara Romanczyk and Thomas McFate**

Tyler Best is the recipient of 2 fellowships.

The Jerome Lejeune Foundation (Paris France) awarded Tyler a three year fellowship (renewable each year) for his proposal entitled "PIP2 modulation of GIRK current in Down syndrome".

The Henry M. Jackson Fellowship in Medical Sciences awarded Tyler a one year fellowship for his thesis research.

Joseph O'Sullivan was awarded an 2 year fellowship from the **Tri-Service Nursing Research Program** for his proposal entitled " Effect of Diazoxide on Hemorrhagic Shock ".

Your Graduate Student Representative

is currently **Tyler Best**. Each USUHS graduate program has a Student Program Representative whose role is to serve as liaison between administration/faculty and graduate students through the dissemination of pertinent information. This position also allows students to raise concerns and issues that can then be addressed through more formal channels. If you have any questions, comments or concerns, please contact Tyler .

Neuroscience Open House

Wednesday, November 17, 2004 from 3:30-5:30 pm.

In Memory of Dr. Cinda Helke

Dr. Cinda J. Helke, Associate Dean for Graduate Education and Professor of Pharmacology and Neuroscience at USUHS, passed away on Sunday June 13, 2004.

Dr. Helke was a native of Iowa, and retained a Midwestern sense of practicality and grounding throughout her life. After graduating from St. Joseph's Academy in Des Moines, Iowa, she entered Creighton University in Omaha, Neb., graduating summa cum laude from the School of Pharmacy in 1974. While at Creighton, she met and married her husband, Joel. Dr. Helke obtained a PhD in pharmacology from Georgetown University in Washington, D.C., in 1978, receiving an award for her outstanding dissertation research on central serotonergic neurons and autonomic function. Her research at Georgetown laid the foundation for her lifelong interest in understanding the structure and function of the autonomic nervous system and its regulation by the central nervous system. She was offered a prestigious PRAT Fellowship for post-doctoral training at the National Institute of Mental Health, where she spent two years in the laboratory of Dr. David Jacobowitz.



Dr. Helke was recruited from NIMH to the Department of Pharmacology at USUHS in 1980. She rose to Associate Professor with tenure in just 4 years and then to Professor. She also quickly established a highly productive research laboratory that concentrated on co-localization of neuropeptides and classical neurotransmitters in autonomic neurons. Her research received continuous funding from NIH for 22 years and produced over 120 publications, numerous national and international presentations and membership on editorial boards and NIH study sections. Dr. Helke's commitment and contributions to medical education were recognized with six awards for excellence in teaching and appointment to the USMLE Step 1 Test Material Development and National Board of Medical Examiners Pharmacology Test Committee. Her contributions to graduate education began during this period with expert training in neuroscience and pharmacology to graduate students and post-doctoral fellows from many countries. It continued when in 1993, Dr. Helke took over the directorship of the graduate program in neuroscience and transformed the program into a model for all interdisciplinary graduate programs at USUHS and other medical schools our size. She very successfully expanded student recruitment and increased institutional financial support. Her success with the neuroscience program led to her appointment as Associate Dean for Graduate Education in 2001. The graduate programs flourished under her highly professional leadership and her efforts consistently were geared towards championing the needs of graduate students. Dr. Helke strove to increase stipends, establish fellowships, increase the level of training excellence, and promote growth, diversity and modernization of the graduate programs. Throughout her career, Dr. Helke also was an active and involved member of the Society for Neuroscience and the American Society for Pharmacology and Experimental Therapeutics (ASPET), serving as the Secretary/Treasurer of ASPET at the time of her death. Her distinguished career led to her being honored with the Carol Johns Award, the highest award based on teaching excellence at USUHS.

Dr. Helke's contributions extend well beyond a listing of her biography. As one of seven Assistant professors recruited to the Department of Pharmacology in the early 1980s, Dr. Helke's successes became the yardstick by which the rest were measured and by which they measured themselves. As a senior faculty member, Dr. Helke served as a role model and an objective, firm, yet compassionate mentor to many USUHS junior faculty. She was generous with her time, energy, support and counsel and was genuinely happy for the successes of those she mentored. As an administrator, students, staff, faculty and administrators alike sought out Dr. Helke's wisdom and advice. Dr. Helke's personal and professional commitment to faculty development, student education and issues related to women in science was longstanding and unwavering and her service in these areas brought great credit to USUHS. Dr. Helke was personally known and loved by many students, scientists and educators both locally and nationally. Both USUHS and the larger communities of pharmacology and neuroscience have sustained a significant loss with her untimely death. She is dearly missed.

Compiled from contributions from Drs. Regina Armstrong, Brian Cox, Jeffrey Harmon and Ajay Verma of USUHS and Dr. Linda Werling of George Washington University.

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In memory of Dr. Helke:

The graduate student fellowships awarded by the Defense Brain and Spinal Cord Injury Program were re-named the **Cinda J. Helke Fellowships**

The USUHS Graduate Education Fund was renamed the **Cinda J. Helke Memorial Graduate Education Fund for USUHS**

The USUHS Center for Health Disparities Research and Education awarded the **Cinda J. Helke, Ph.D. USUCHD Summer Research Internship Award** to their summer intern with the best research presentation.

Monthly Lunch Group for Graduate Students & Student-run Neuroscience Journal Club

The goals of the monthly lunch group for USUHS Neuroscience graduate students (NSL) are to discuss issues important to graduate students and to facilitate peer support. The Neuroscience Journal Club (JC) aims to keep students abreast of current literature, offers an opportunity to discuss Neuroscience topics and provides an informal setting to practice presenting research. The combination NSL/JC Meetings will be held the 2nd Tuesday of each month. These are informal, student run meetings designed to help graduate students get through their graduate careers. If you have suggestions for a meeting or journal club topic, please contact Alisa Schaefer (aschaefer@usuhs.mil) or Tara Romanczyk (tromanczyk@usuhs.mil).

2004/2005 SCHEDULE (Topics and dates subject to change)

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| September: | noon-1:30pm | <i>NSL topic:</i> Orientation to Grad School: Choosing a Lab, Mentor & Rotations <i>JC:</i> Sean Manion will present: Nature Neurosci 6:119-126. |
| October: | noon-1:30pm | <i>NSL topic:</i> Attending Conferences and Presenting a Poster <i>JC:</i> To be determined |
| November: | noon-1 pm | <i>NSL topic:</i> Finances <i>JC:</i> To be determined |
| December: | noon-1 pm | Holiday Luncheon |
| January: | noon-1 pm | <i>NSL topic:</i> Applying for Grants & Fellowships |
| February: | noon-1 pm | <i>NSL topic:</i> Thesis Writing |
| March: | noon-1 pm | <i>NSL topic:</i> Oral Presentations |
| April: | noon-1 pm | <i>NSL topic:</i> The Qualifying Exam |

2004/2005 Neuroscience Program Executive Committee

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