Molecular & Integrative Physiology

Newsletter December 2011

Greetings from the Head

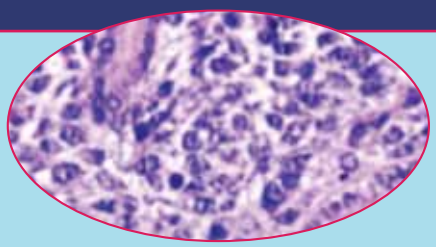
Byron Kemper

As I enter my fifth year as head of The Department of Molecular and Integrative Physiology, I am pleased and excited to be able to report for the first time in all those years that we are poised for growth. I look back on a tenure marked by an unprecedented financial crunch for the nation, the State of Illinois, and the University of Illinois. The university responded with the Stewarding Illinois program, an intense self-evaluation of essentially all university activities with the emphasis on optimizing the use of our resources. To reduce expenditures, hiring was limited to meet essential needs and a voluntary retirement program was instituted. This environment, combined with the demographics of our department, resulted in a decrease in MIP faculty size from 20 to 15, in spite of 4 new hires in the last 4 years. These vigorous and sometimes painful efforts are now paying dividends. For the first time in 5 years the College of Liberal Arts and Sciences is operating in the black and is looking forward to substantially increase hiring in the next few years. As I have discussed in previous newsletters, I believe physiology will be a key discipline in the next couple of decades as complex systems, functional analysis in whole animals, and translational research become the forefront of biological research. The next five years should be an exciting time for MIP.

A picture of C. Ladd Prosser is on this page to highlight a 5-year effort to raise $125,000 to establish an endowment to support our annual C. Ladd Prosser Lecture. Ladd came to Illinois in 1939, was instrumental in the formation of the physiology department in 1949, and was head for 10 years. He retired in 1975, but was active into the '90s. He was a cornerstone of comparative physiology worldwide and was a member of the U.S. National Academy of Sciences. MIP has been sponsoring an annual lecture honoring Ladd for more than 15 years, but a lack of dedicated funds has limited our ability to make it the premier annual lecture of the department. Seed donations and pledges of about $25,000 have been received from a small group of donors. If 200 of you put a quarter from your loose change in a jar each morning for 5 years for the Prosser Lecture, we would reach our goal. Easier would be a 5-year pledge/donation (see donation form inside) of $500 or more or less depending on your ability. I hope you will find this lecture named for Ladd a fitting tribute and worthy of your support.

In this issue, Dan Llano, a new faculty member in the College of Medicine and MIP introduces himself. Also, Charles (Lee) Cox and Milan Bagchi, two senior faculty members, write about their research. For the second year, we are fortunate to have a feature article contributed by Dr. Jeanne Bullock Goldberg, a U of I alumna and MIP supporter, describing hormonal-dependent cancer research in MIP. I hope you enjoy the news from MIP, and as always, we would love to hear from you—email us at mip-news@illinois.edu.

C. Ladd Prosser



In This Issue

About the Newsletter

The Molecular and Physiology Newsletter is an annual publication of the Department of Molecular and Integrative Physiology in the School of Molecular and Cellular Biology at the University of Illinois, Urbana-Champaign. The newsletter is written by MIP faculty and friends, and designed by William Gillespie.

Our alumni are important to us. We want to hear from you. Send us your latest news, and we'll include it in the next newsletter's MIP Family News.

We also welcome suggestions for future newsletters. Here's how to reach us:

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UNRAVELING COMPLEXITIES OF ENDOCRINE-DEPENDENT CANCERS

by Jeanne Bullock Goldberg

Cancers that depend on hormones secreted by the endocrine system have been diagnosed in over 500,000 Americans this year and represent a major cause of death in our country. Breast cancers in women and prostate cancers in men are second only to cancers of the lung and bronchus as the most common causes of cancer-related deaths. Over 230,000 cases of breast cancer and 240,000 cases of prostate cancer will be newly diagnosed this year in the U.S., representing approximately 30% of all newly diagnosed cancers in women and men respectively. Cancers of the uterus (endometrium) and ovary will be diagnosed in an additional 68,460 women and together make up 9% of newly diagnosed female cancers and 9% of cancer deaths among women.

Research scientists at MIP are making great strides in deciphering how complex gene networks, which are intimately associated with hormones, not only promote normal cell development and function, but can also be causative factors in the development and spread of cancer. Interestingly, although a given MIP project may focus on one hormone, hormone receptor, or organ, the research findings often contribute to our understanding of other cancers and components of the endocrine system because the "operating systems" are similar.

Prostate cancer is the most frequently diagnosed male cancer in our country and is a focus of research in Assistant Professor Eric Bolton's laboratory. Androgens are responsible for the development of male reproductive organs and secondary sexual characteristics, but interestingly also play a key role in the development of the female ovaries and breasts. The androgen receptor (AR) binds to testosterone and dihydrotestosterone and then influences the expression of genes, and also interacts with signal transduction proteins in the cell's cytoplasm which causes changes in cell functions, such as ion transport.

Bolton's research program is aimed not only at defining gene networks that control normal androgen action, including prostate development and homeostasis, but also at dissecting the signaling pathways that play a role in prostate cancer. Androgen deprivation (castration) has been a mainstay in treatment of prostate cancer, but almost all prostate cancers eventually develop resistance to androgen deprivation via several mechanisms such as overexpression of AR, AR mutations enabling activation of it by other hormones, or production of androgens by the tumors themselves. It is believed that many advanced tumors require AR signaling for growth, and, using a mouse model, Bolton's laboratory has demonstrated that this AR signaling can be inhibited by hormone-independent non-competitive AR antagonists. A highly desirable feature of these antagonists is that they may bind to other "pockets" in the AR and can have a significant impact in the treatment of prostate cancer. This novel strategy may impact future treatments for other endocrine-dependent cancers.

Milan Bagchi

Eric Bolton

Benita Katzenellenbogen

Ann Nardulli

Research from the laboratory of Professor Milan Bagchi has not only shed new light on the development of ovarian cancer, but it also has the potential to lead to the discovery of new diagnostic and treatment tools for this deadly malignancy, which kills over 15,000 women in the U.S. each year. Collaborators Professor of Veterinary Biosciences Indrani Bagchi, Mary Laws, and others in the laboratory have developed an animal model of estrogen-dependent ovarian cancer by studying mice that lack ERα expression in the pituitary, resulting in a dysregulation of systemic estrogen signaling and resultant ovarian cancer. The results of these studies could potentially lead to the development of biomarkers for the early detection of ovarian cancer.

Breast cancer is the most frequently diagnosed cancer in women and has been the focus of research in several MIP and MIP-affiliated laboratories.

Of great public interest is the biological role of botanical estrogens which have been extensively marketed as cancer preventives, aids to relieve menopausal symptoms, and as promoters of healthy aging. Sources of botanical estrogens—soy, licorice root, wild yam, and dong quai—are consumed by a large number of women in our country. However, there is currently only sketchy scientific understanding of how they act and their safety, including their role in estrogen-dependent cancers. In the new NIH-supported Botanical Research Center at the U of I, a multidisciplinary team of researchers at the U of I and other institutions, including Swanlund Professor of Molecular and Integrative Physiology and Cell and Developmental Biology Benita Katzenellenbogen, is conducting studies to provide sound physiological data concerning botanical estrogens. These studies will be useful both in formulating recommendations regarding their use, and in designing future clinical trials to determine their effectiveness.

Katzenellenbogen's laboratory is also doing genomic profiling of the estrogen hormonal pathway for breast cancer prevention and treatment. The signaling pathways by which estrogens regulate the gene transcriptional and proliferative programs of hormone-dependent cancers involve dynamic interplay between alpha and beta estrogen receptors (ERs) and between nuclear-initiated and extranuclear-initiated kinase pathways. In Professor Katzenellenbogen's words, "Hormonal regulation of breast cancer involves cooperation between ERs and protein kinases." The crucial level at which the ER and kinase-mediated signaling pathways converge is at the chromatin level, where regulation of gene expression and microRNAs occurs,

which alters cell properties. Katzenellenbogen's laboratory has demonstrated that up-regulation of kinase is a hallmark of resistance, which may provide a target for novel therapies for suppressing breast cancer progression and resistance to endocrine therapy. For example, a key discovery in her laboratory is the important role that the protein 14-3-3-zeta plays in development of resistance to endocrine treatments (Figure 1). By reducing the level of this protein, sensitivity of breast cancers to endocrine therapy was restored.

Professor Milan Bagchi and his students and associates have also discovered a very strong linkage between the expression of an estrogen-regulated gene, Cuzdl, and breast cancer development in mice, and are collaborating with investigators at Baylor College of Medicine to correlate their findings with analyses of human tissue samples at various stages of human breast cancer.

Professor Ann Nardulli, who was recently appointed co-PI of the new Midwest Cancer Nanotechnology Training Center, has also furthered our understanding of breast cancer with studies in her MIP laboratory. She has studied the progesterone receptor gene (PR) because of its crucial role in mammary gland development and reproductive health, and has used it as a marker for breast cancer. She and her associates and students have demonstrated the interesting finding that remote (distal) regions of the PR gene as well as proximal ones, by coordinated action, respond to changes in hormone levels to provide, in their words, "extraordinary versatility and sensitivity."

Her studies have also focused on the central role that estrogen, the intracellular ER, and the estrogen response elements in ER's target genes play in regulating gene expression. They have demonstrated, with others, that binding of either hormone or DNA to the ERα alters its form (conformation). In addition, Nardulli's laboratory has developed a novel method of identifying the complex networks of proteins (versus individual proteins) that are recruited by this bound receptor. This diverse array of proteins remodels chromatin and regulates cell cycles, protein turnover, signaling pathways, cell migration (possibly important in metastatic disease in cancer), and DNA repair, among other functions. In one case, their studies have suggested that oxidative stress proteins and DNA repair proteins not only protect normal cells from damage but also promote survival and actual growth of breast cancer cells. Hence, dysregulation of these protein networks is likely very important, but further studies will be necessary to determine if they cause cancer and whether targeting these proteins might allow new treatment strategies.

The endocrine system is complex and comprises many components and networks which must communicate effectively in a coordinated manner for optimum health. Mirroring this dynamic is the core of talented MIP research scientists who are collaborating among themselves and with other premier institutions such as UI College of Medicine, the Mayo Clinic, Carle Clinic, and the Baylor College of Medicine to share groundbreaking findings to bridge the traditional information gap between the laboratory and the bedside.

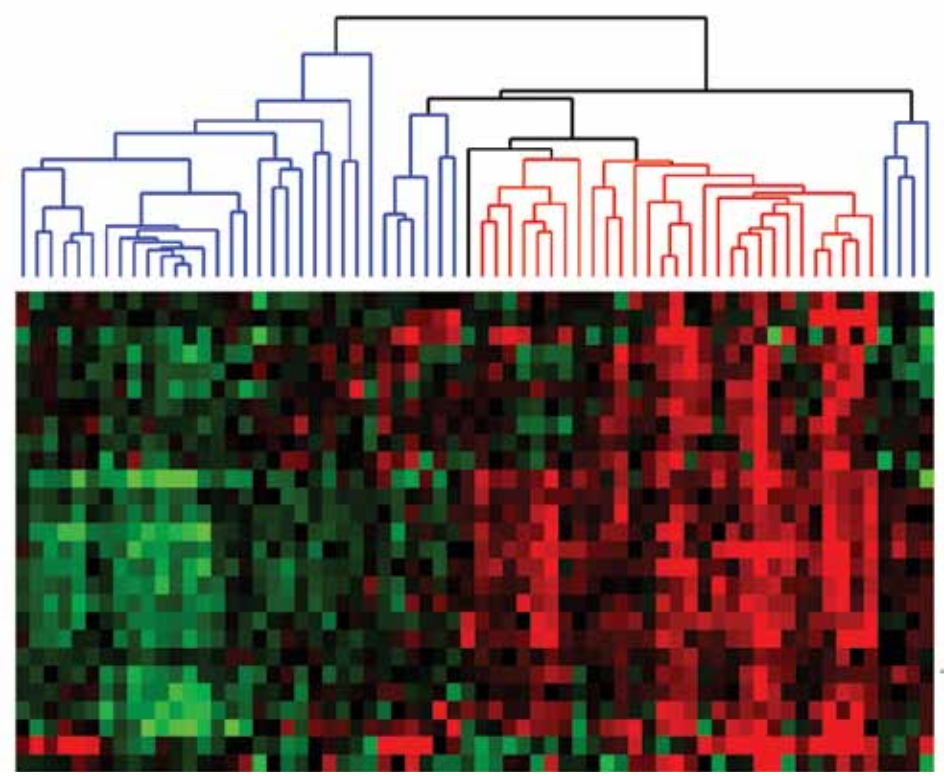


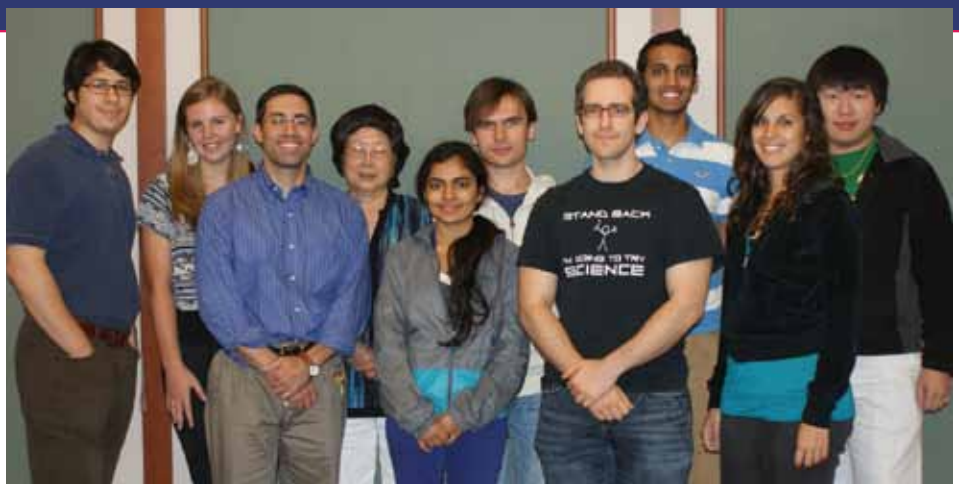
Figure 1. Identification of a 14-3-3ζ gene signature found to be associated with aggressiveness of breast cancers. High levels of 14-3-3ζ (red) correlate with elevated levels of mitosis related genes and are associated with poor prognosis. [From A. Bergamaschi, B.L. Christensen and B.S. Katzenellenbogen, *Breast Cancer Research*, 2011,13:R70.]

Auditory Physiology in Health and Disease

by Daniel Llano

I joined MIP as a faculty member in the Fall of 2010, and my lab is housed in the Beckman Institute. It's been a bit nostalgic for me to come back—I finished my Ph.D. in MIP in 2000 under Al Feng. After finishing my M.D. and Ph.D., I completed a neurology residency at the Massachusetts General/Brigham and Women's Hospital, and completed further research and clinical training at the University of Chicago. I then worked for Abbott labs, developing research programs for new Alzheimer's Disease therapeutics. I returned to the University of Illinois with the assistance of the Division of Biomedical Sciences to pursue my longstanding interest in bridging basic sciences with clinical medicine.

Our lab studies cortical-subcortical interactions in the auditory system, and how these interactions are modified by disease. It is known that the cortex



Llano lab (from left to right): Kevin Stebbings, Alex Lesicko, Daniel Llano, Dr. Wenyu Lin, Mili Patel, Gosha Yudintsev, B.J. Slater, Karthic Chandran, Kate Srikant, Luye Yang (not pictured, Elizabeth Rivera Cruz).

sends massive projections to lower centers, such as the thalamus and midbrain, and that these projections are critical for the normal functioning of the auditory system. In fact, we call on these systems whenever sound gets obscured by noise. Think of the last time you were on a noisy cell phone connection—you were probably still able to make out most of the conversation on the other end of the line by the use of context. That is, you had some idea of what the other person was saying based on their manner of speech, the subject of the conversation, even the types of words that the other person tends to use. We use these cues automatically to navigate our noisy and unpredictable world. And these systems tend to break down during disease processes and normal aging.

Therefore, our lab studies the circuitry of the top-down projections in both healthy and diseased animals. We use a variety of electrophysiological, laser stimulation and imaging techniques to study these systems. The lab has been up and running for about a year, and we have been making progress toward understanding these systems. For example, B.J. Slater, graduate student in the lab, has recently shown that there is previously unrecognized layer-specific heterogeneity in the descending projections from the auditory cortex to the auditory midbrain. This work was presented at the 2011 Society for Neuroscience meeting. We are also developing a novel transcranial imaging and stroke model to study the role of subcortical projections in neural reorganization after stroke. In addition, we have been collaborating with Drs. Don Caspary and Jeremy Turner at the SIU School of Medicine and have found significant changes in thalamocortical GABAergic circuitry with aging (Figures 1A and B).

It is hoped that this work will open up opportunities to intervene to ameliorate cognitive changes associated with aging, and to assist with the recovery of cognitive function after stroke. In addition to the laboratory work, I am the course coordinator for "Brain, Behavior and Human Development" in the College of Medicine, and I run a cognitive neurology clinic at Carle. As part of the work within the College of Medicine, we are actively seeking to build the relationship between Carle and the University to capitalize on the enormous strengths of the two organizations to further patient care.

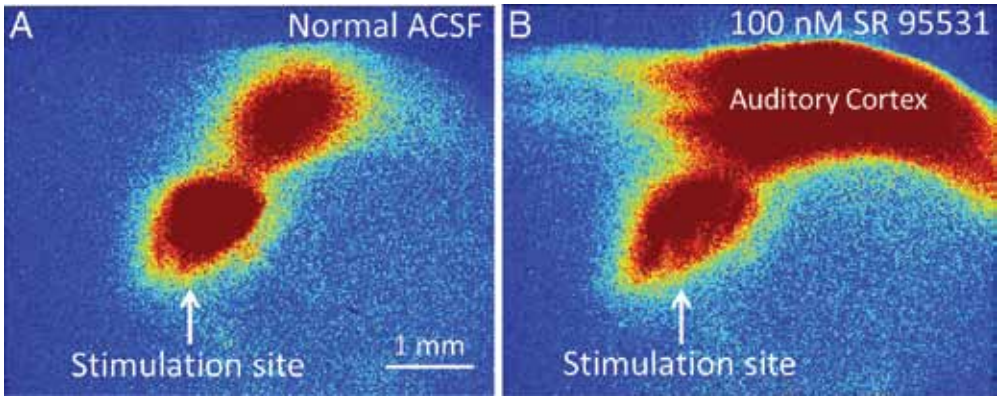


Figure 1, A and B: Flavoprotein autofluorescence image of thalamocortical activation in the aged mouse, in vitro. A: In normal artificial cerebrospinal fluid (ACSF). B: In 100 nM SR95531, a specific $GABA_A$ antagonist.

Dan received a B.S. in Biology in 1992, a Ph.D. in Molecular and Integrative Physiology in 1999 and an M.D. degree with honors from the College of Medicine at UIUC. After an internship and residency at Massachusetts General and Brigham and Women's Hospitals, he was a fellow in neurology with Steven Small and a postdoctoral fellow in neurobiology with Murray Sherman at the University of Chicago. He was then an associate medical director at Abbott Laboratories for 2 years. He joined MIP as an assistant professor in 2010.

Hormonal Control of Maternal-Fetal Interactions During Early Development

by Milan Bagchi

I began my career as a molecular biologist studying the mechanisms of gene regulation, and over the years, developed a strong interest in exploring the hormonal signaling mechanisms that control the gene networks regulating reproduction and early development. My laboratory has been studying the molecular and cellular mechanisms of action of the steroid hormones for the past twenty years. We are working to delineate the pathways regulated by the steroid hormones estrogen and progesterone during development and differentiation of key hormone-responsive tissues, including the female reproductive tract.

In humans, infertility is one of the most common disturbances of reproductive health, with 10–15% of couples finding it difficult or impossible to conceive. Despite significant advances in assisted reproductive technologies (ART), many couples experience infertility as a result of failed implantation of the fertilized embryos into the uterus (Figure 1) and

Research groups of Drs. Indrani and Milan Bagchi.

subsequent loss of these embryos. The implantation rates in ART remain low, even with high-quality embryos, pointing to the importance of uterine deficiency during implantation as a major cause of pregnancy failure and infertility. Therefore, in order to better address the clinical challenges of infertility, it is imperative to gain a clear understanding of the cellular and genetic mechanisms underlying embryo implantation. A major goal of my research program is to explore the hormonal signaling mechanisms that regulate maternal-fetal interactions during implantation and to identify factors that underlie early pregnancy loss and infertility.

Gene expression profiling analyses in my laboratory uncovered novel steroid-regulated pathways in the uterine tissue, providing important insights into the cellular mechanisms by which implantation is controlled. Combination of this new knowledge with functional analysis in gene knockout mouse models is providing a blueprint of the molecular networks that mediate the hormonal regulation of this process. A clear understanding of the gene pathways underlying the cell- and tissue-specific actions of estrogen and progesterone receptors will provide important insights that enable rational approaches toward clinical intervention when inappropriate endocrine actions occur, as in female reproductive tract dysfunctions leading to infertility. We believe that the translational aspects of our research, the flow of knowledge from the mouse model to the human and vice-versa, is of utmost importance in providing useful insights into molecular and cellular pathways that underlie normal physiology and are dysregulated in human diseases.

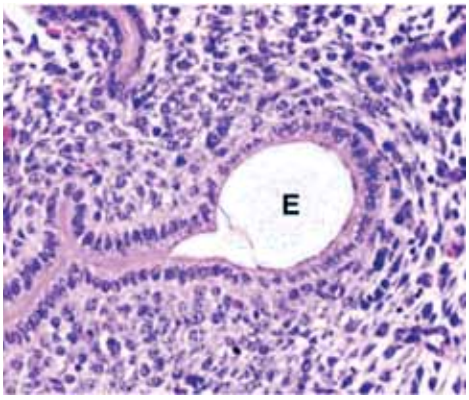


Figure 1: An implanted embryo (E) in the mouse uterus.

To extend the information obtained from basic cell biological studies and unique animal models to the clinical realm, we have started collaborating with Dr. Robert Taylor of the Emory University Medical School to understand the molecular basis of endometriosis, a common gynecologic disorder affecting millions of women in the U.S. and associated with reduced fertility. Our analyses of endometrial tissues obtained from women suffering from endometriosis will help identify factors that underlie this condition. The knowledge gained from our research will have direct impact on women's health by aiding in development of new molecular diagnostic tools for screening endometrial dysfunction and enabling targeted therapeutic strategies for the treatment of endometriosis.

Our laboratory is part of a Center for Research in Reproduction and Infertility funded by the National Institutes of Health at the University of Illinois, Urbana-Champaign. At this Center, my research group collaborates closely with those of Professor Benita Katzenellenbogen (Department of Molecular and Integrative Physiology) and Professor Indrani Bagchi (Department of Comparative Biosciences). The strength of this research group is that we work together collaboratively and synergistically to maximally benefit from the information generated from our research, and apply it to decipher hormone-regulated signaling pathways and assess their impact on fertility and reproductive health.

Milan joined MIP in 2001 and was promoted to professor in 2005. He is director of the National Center for Research in Reproduction and Infertility at the U of I. He has a Ph.D. in chemistry (University of Nebraska), was a postdoc with Bert O'Malley at the Baylor College of Medicine, and was a staff scientist and laboratory head at the Population Council and The Rockefeller University before joining MIP. His areas of research interest are mechanisms of modulation of nuclear hormone activity and the molecular basis of steroid hormone action in the uterus and ovary.

How Do Complex Neuronal Networks Function?

by Charles (Lee) Cox

A common feature of neurological disorders is altered communication between neurons that results in abnormal neural activities. Individual neurons must integrate thousands of synaptic inputs from other neurons, and pass this information to downstream neurons. These incoming synaptic signals can be mediated by many different molecules (neurotransmitters) and their different receptor subtypes that can lead to a large variety of responses. Although a daunting challenge, understanding the basic physiology of neural circuits will provide a solid foundation for understanding how the brain performs higher order computational tasks, and how pathophysiological and genetic changes can alter brain function.

The research in our lab focuses on a specific neuronal network in the mammalian nervous system: the thalamocortical circuit, a relatively simple circuit that plays a critical role in sensory processing, arousal, and attention, and neural diseases, such as epilepsy, autism, and certain psychoses. Historically, the thalamus has been thought of as a passive relay station for sensory information to the neocortex for processing; however, our laboratory and others have found that there is considerable processing of information within the thalamus itself. Our goal is to understand basic cellular and synaptic properties that underlie the organization of this circuit and its plasticity (long lasting changes in neuronal activity), particularly, the functional significance of these non-retinal inputs and how they influence visual information transfer through the thalamus (Figure 1).

Dr. Gubbi Govindaiah has been focusing on the contribution of inhibitory circuitry in the processing of information within the thalamocortical circuit. His work has focused on unique dendritic output of thalamic interneurons, and the modulatory actions of dopamine on thalamic activity. His studies have elucidated key mechanisms by which visual information can be shaped by distinct activities within the interneurons.

Traditional electrophysiological methods monitor the activity of single neurons, but with our recent acquisition of a 2-photon laser-scanning microscope, we measure the activity of a single synapse on a neuron. Shane Crandall, Neuroscience graduate student, has been studying the integrative properties of dendrites of thalamic neurons using this new technology, which allows direct measurements of activity within these small structures. Understanding these microcircuit type issues are important to our knowledge on how neural circuits can "focus" attention on specific information and possibly filter out "noise" in sensory information processing.

Along similar lines we are also studying how various neuromodulators alter synaptic integration within the neocortex. Dr. Kush Paul has been studying catecholamine modulation within the prefrontal cortex, a region important in decision-making. Aurora Cruz Torres, MIP graduate student, has been studying the complex modulatory activity of acetylcholine in auditory cortex.

Alterations in modulatory activity within the nervous system can be associated with a variety of neurological pathologies. We are also investigating neural alterations associated with Fragile X Syndrome (FXS), the leading inheritable form of mental retardation. To understand this condition, we are carrying out studies at multiple levels: molecular, cellular, network, and behavioral approaches. Dr. Deepa Venkitaramani is identifying alterations in intracellular signaling mechanisms and subsequent changes in synaptic structure and associated behavior in a mouse model of FXS. This work is supported by the technical assistance of Sulalita Chaki and Adrianna Guerrero. In conjunction, Drs. Govindaiah and Paul are studying alterations in synaptic activity associated with FXS. These studies will provide insight as to alteration in neuronal function associated with this disorder and thereby potentially provide key insight for future therapeutic intervention or treatment of FXS. Our research is funded by the National Eye Institute, National Institute of Mental Health, and National Institute of Child Health and Human Development from the NIH.

Lee received B.S through Ph.D. degrees from the University of California, Riverside. After postdoctoral work at Stanford University and the State University of New York, Stony Brook, he was appointed assistant professor in MIP and the Department of Pharmacology in the College of Medicine in 2000. He is a member of the Neurotech group at the Beckman Institute. He was promoted to professor in 2011 and has been head of the Department of Pharmacology since 2009.

MIP Family News

Katzenellenbogen Receives Mentor Award

Professor Benita S. Katzenellenbogen received the Mentor Award for 2011 from Women in Endocrinology at the Annual meeting of the Endocrine Society in Boston in June. This prestigious award is given to one person, male or female, "in recognition of outstanding contributions to the mentoring and training of endocrinologists."

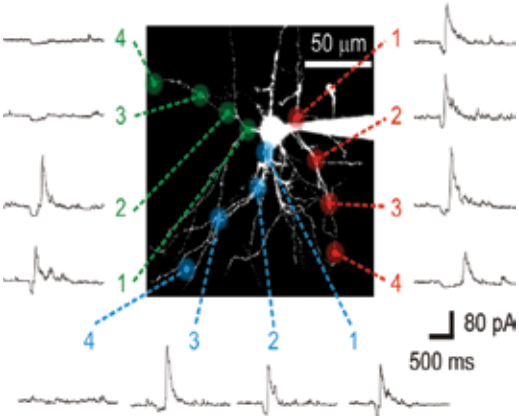


Figure 1: Somatically recorded responses to photo-uncaging of glutamate at distinct locations on different dendrites.

Cox Lab (left to right): Govindaiah Gubbi, Kathleen Louis, Deepa Venkitaramani, Kush Paul, Lee Cox, Sulalita Chaki, Shane Crandall, Aurora Cruz-Torres, Adriana Guerrero, Greg Stanton, and Ivan Jeanne Weiler.

New Ph.D.s '10-'11

Tyler Bowers Moran (Ph.D., 2010) "*Uncovering Novel Actions of Numb and Aryl Hydrocarbon Receptor in the Pituitary*" with Lori Raetzman. Tyler is finishing medical studies in the College of Medicine.

Pamela Monahan (Ph.D., 2010) "Notch Signaling and Cell Cycle Inhibitor Regulation in Pituitary Organogenesis" with Lori Raetzman. Pam is a postdoctoral fellowship at Northwestern University with Kelly Mayo.

Kyuri Kim (Ph.D., 2010) "Regulation of Estrogen Receptor-Alpha mediated Gene Expression and Endocrine Resistance through Estrogen Receptor-Alpha Phosphorylation and Micro-RNA in Breast Cancer" with Benita Katzenellenbogen. Kyuri is in Palo Alto, CA completing manuscripts for publication.

Jiyoung Lee (Ph.D., 2011) "Gene Selective Regulation by Hepatic Farnesoid X Receptor (FXR) in Health and Disease" with Jongsook Kim Kemper. Jiyoung is a postdoctoral researcher with Marsha Rosner at University of Chicago.

Sung Hee Park (Ph.D., 2011) "Repressor of Estrogen Receptor Activity (REA) is a Gene Dose-Dependent Coregulator Protein Affecting Estrogen Signaling and Cell Survival" with Benita Katzenellenbogen. Sung Hee is a postdoctoral researcher at Duke University Medical Center.

Ruijie Liu (Ph.D., 2011) "Post-Translational Modification Regulate ß2-Adrenoceptor Signaling in Cardiomyocytes" with Kevin Xiang. Ruijie is a postdoctoral fellow at Cincinnati Children's Hospital.

Vanessa Noboa (Ph.D., 2011) "Prey Avoidance Learning and Neuronal Elements Mediating Behavioral Switching in the Predatory Sea-Slug Pleurobranchaea Californica" with Rhanor Gillette.

Jie Sun (Ph.D., 2011) "The Intramolecular Domain Interactions and Phosphatase Activation Mechanisms of Shp2" with Yingxiao "Peter" Wang. Jie will continue as a postdoctoral fellow in Dr. Wang's lab.

Alumni News

H. Fred Downey (Ph.D., 1968, Biophysics) is Regents Professor of Physiology at the University of North Texas Health Science Center at Fort Worth. He was recruited to the Department of Physiology at Southwestern Medical School in Dallas in 1972 and moved to North Texas in 1985. He notes that he was one of a very few non-physics majors in the Biophysics graduate program and took all the courses required for the Ph.D. in physiology in case he "met a physics course I couldn't pass." While cardiovascular physiology has been his major research interest, a serendipitous observation resulting from placing a flow transducer on the thoracic lymph duct of a dog, in addition to the coronary artery, showed that osteopathic manipulation greatly increased lymph flow and increased leukocyte number in thoracic duct lymph. This observation led to 6 years of NIH support to study lymph, and a $1M grant for the Assistant Professor who counted the leukocytes and for whom he now works. He says that in all his projects "I have built on the foundation of education and training I gained during my doctoral studies at the University of Illinois."

June Aprille (Ph.D., 1969) retired as Provost and Professor of Biology from Washington and Lee University in May 2011. June moved to Washington and Lee in 2007 from Tufts University where she had joined the Department of Biology in 1977. She was appointed the Henry Bromfield Pearson Professor of Natural Sciences at Tufts in 1987 and was assistant clinical professor of pediatrics at Tufts University School of Medicine and a lecturer in biochemistry for pediatrics at Harvard Medical School. She serves on the advisory board of the National Reyes Syndrome Foundation. June received the MIP Distinguished Alumni Award in 2003.

William Kem (Ph.D., 1969) visited MIP in September on the way from presenting a seminar at Southern Illinois

Prosser Lecture Fund

Molecular and Integrative Physiology at Illinois

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University to personal business in Ohio. William is a long-time Professor in the Department of Pharmacology and Therapeutics in the College of Medicine, University of Florida in Gainesville. He continues to actively study naturally occurring marine toxins that affect cholinergic receptors and ion channels, including, amazingly enough, anabaseine, which he discovered while a graduate student here 40 years ago.

Bruce Koeppen (B.S. 1973, Ph.D. 1980; M.D. 1977, Univ. Chicago) was appointed the founding Dean of the new Quinnipiac University School of Medicine on November 1, 2010, upon retirement from the University of Connecticut, School of Medicine. Bruce will basically be building from scratch the new school, which will focus on educating primary care physicians. After receiving his Ph.D., Bruce was a postdoctoral fellow at Yale and then joined the faculty in the Department of Medicine at the University of Connecticut, School of Medicine, where he held the Albert and Wilda Van Dusen Professor of Academic Medicine endowed chair. In the early 90's, he moved to administration and was dean for academic affairs at the time of retirement.

Michael Friedlander (Ph.D. 1975) has been appointed to the position of senior dean for research at the Virginia Tech Carilion (VTC) School of Medicine in 2011 and was the founding executive director of the VTC Research Institute. He is also professor of biological sciences in the College of Science and adjunct professor in the School of Biomedical Engineering and Science at VTC. Prior to moving to Virginia Tech, he was the Wilhelmia Robertson Professor of Neuroscience, chair of the Department of Neuroscience, and director of the Neurosciences initiatives at Baylor College of Medicine. He is presently president of the Society for Experimental Biology and Medicine. His research focuses on synaptic plasticity in development, learning, and in response to brain injury. Mike received the MIP Distinguished Alumni Award in 1999.

Kyungjin Kim (Ph D, 1984) is a professor in the Brain and Neuroendocrinology Research Laboratory in the Department of Biological Sciences at the Seoul National University. He is also the director of the Brain Research Center for 21st Century Frontier Program on Neuroscience. In 2010, he received the highest award for a scientist in Korea from the Korean National Academy of Science. His research areas are molecular neuroendocrine approaches to the mammalian biological clock and developmental and neural plasticity of the hippocampus.

Nicholas J. Laping (Ph.D, 1989) has been been appointed director for pharmacology and discovery and early development at Endo Pharmaceuticals in Chadds Ford, PA. After a postdoc at the University of Southern California, Nick joined SmithKlineBeecham as an investigator, was appointed a manager at GlaxoSmithKline in 2000 and director of biology in 2004. He joined Endo Pharmaceuticals in 2009.

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