CenterPiece

A Quarterly Publication Featuring Achievements from Northwestern University Research Centers

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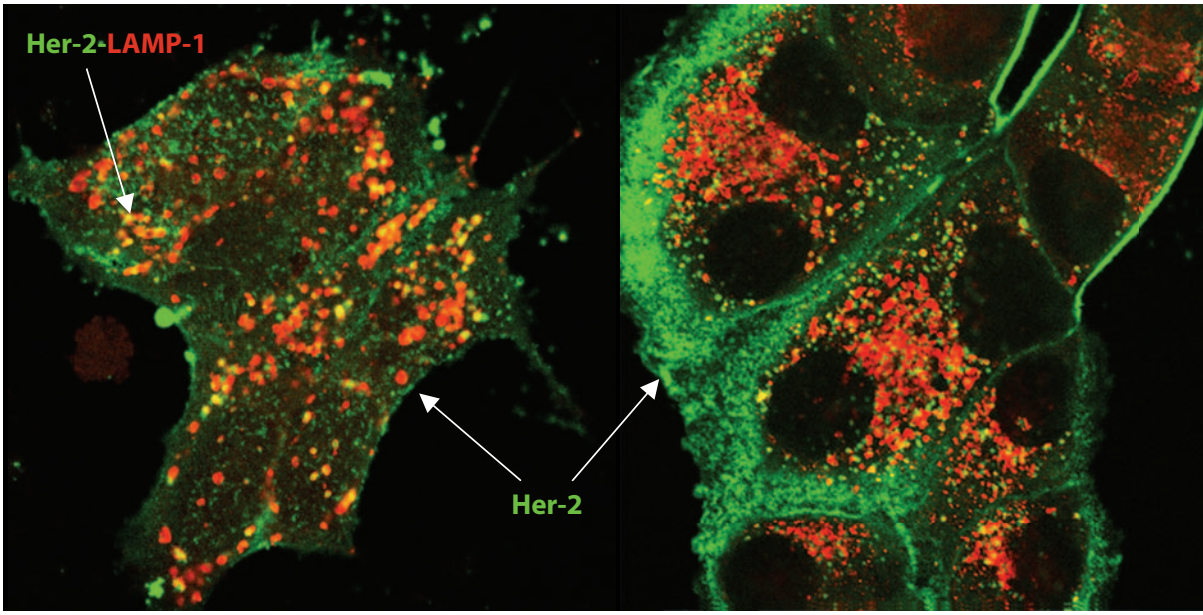
IN THIS ISSUE



Targeting breast cancers: These high-magnification confocal microscope fluorescent images show two human breast tumor cells being studied in Hamid Band's laboratory at the Evanston Northwestern Healthcare Research Institute. They show two cells that produce excessive amounts of Her-2/Neu, a protein over-expressed in 20 to 30 percent of breast cancers. The human breast tumor cell on the left is BT-474; on the right, SKBR-3. Both cells have been treated with inhibitors that affect HSP90, a heat shock protein necessary for the stability of Her-2/Neu. Her-2/Neu (stained in green) normally appears on the surface of the cell. HSP90 inhibitors cause the Her-2/Neu to be internalized and then destroyed in lysosomal compartments that contain digestive enzymes (stained in red). Band's studies show the effectiveness of HSP90 inhibitors, an emerging class of drugs, as novel therapeutics for treatment of breast cancers that produce excessive amounts of Her-2/Neu. This research is funded by the Department of Defense and the National Institutes of Health. Image courtesy of Srikumar Raja, medicine.

Breast Cancer Research at ENH Research Institute

More than a quarter of external funding at the Evanston Northwestern Healthcare (ENH) Research Institute supports research to prevent cancer, detect it earlier, and develop more effective treatments.

Vimla Band, medicine, and Hamid Band, medicine, lend international stature to ENH's growing cancer and medical genetics initiatives. Their research has far-reaching implications for understanding immune and inflammatory responses to cancer.

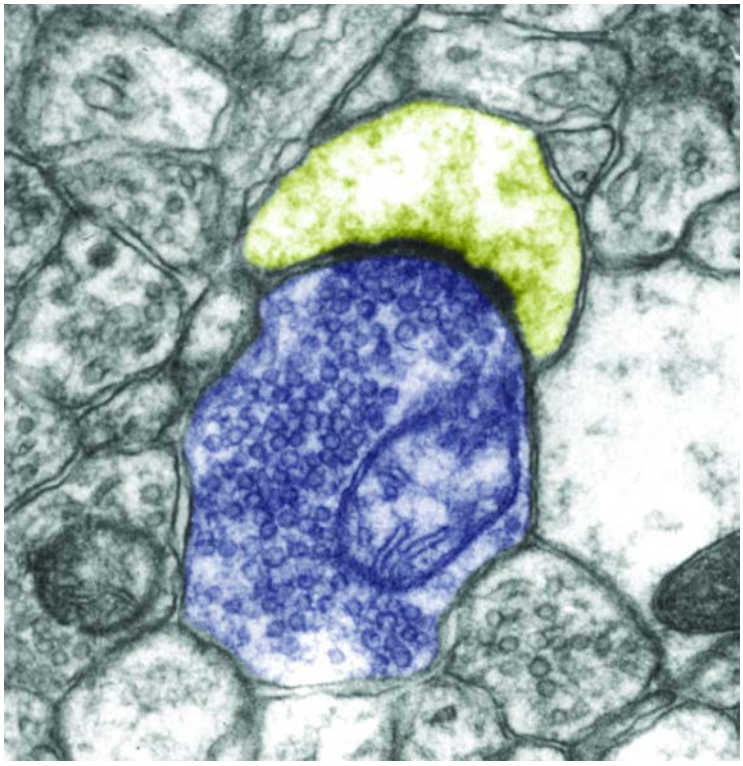
Vimla Band's focus is the molecular basis of tumor progression with emphasis on breast cancer. As head of the Division of Cancer Biology at ENH, she is working to identify novel genetic markers for early diagnosis and/or prognosis with an emphasis on

—see Cancer Research, continued on page 8

CENTERPIECE Q & A

Catherine Woolley

Catherine Woolley, neurobiology and physiology, has been using reproductive hormones as tools to understand brain plasticity and brain function since her earliest days as a doctoral researcher at Rockefeller University. She came to Northwestern in 1998 and in 2002 received a W. M. Keck Foundation Distinguished Young Scholar in Medical Research Award. The Young Scholar initiative is designed to support innovative research by young investigators who exhibit both extraordinary promise for independent basic medical research and a clear capacity for academic leadership. Under the program, Northwestern received an award of $1 million to support Woolley's research activities for five years. She sat down with *CenterPiece* to discuss the implications of her neurological research.



Electron micrograph of a brain synapse. In the center of the image, an axonal bouton (blue) packed with vesicles of neurotransmitter forms a synapse with the cup-like head of a dendritic spine (yellow). The region of the spine head where the synaptic connection is formed appears dark due to its high protein content.

You were Northwestern's first Keck Award winner. For what was it awarded?

It was given to allow us to extend our studies of estrogen's influence on neural circuitry related to cognition — and particularly to explore innovative ideas that are a little riskier than most funding mechanisms allow. That is one of the great things about the Keck Award: Investigators are allowed — even encouraged — to follow their noses; if the experiments take us in a different direction than we anticipated at first, that's okay, as long as we can make the case that a new direction is worth taking. Receiving the Keck Award has been tremendously valuable for my group.

We have certainly taken some new directions since 2002. We use a range of approaches in our work such as confocal and electron microscopy, electrophysiology, biochemistry, and behavioral studies. When we received the Keck Award, we were really focused on understanding how estrogen affects the postsynaptic side of synapses in the brain, particularly changes in the number of dendritic spines and synapses on hippocampal neurons. As we got deeper into the experiments, though, we began to see important things presynaptically and our focus shifted.

Most recently we've been studying estrogen receptors in axons and how they may mediate acute effects of estrogen on presynaptic neurotransmitter release. Ironically, the field of steroid action in the brain is emerging as a hot topic. I say ironically because the experiments that first suggested that steroids could act rapidly in the brain were done almost 30 years ago, but few people paid attention then. In the last couple of years, the concepts that steroid hormones are produced in the brain and can act locally and rapidly to alter neuronal physiology have gotten a lot of people really excited. The Keck Award has given us the freedom to study these issues.

How do steroid hormones influence the brain?

The answer to that question has gotten complicated because now we know that hormones act through mechanisms that go well beyond the classical effects mediated by nuclear receptors that regulate gene expression. Understanding how steroids act acutely via second messenger systems to influence ion channels or other effectors is a major focus of our current work.

For example, one of our projects asks how estrogen action in the hippocampus influences seizures in epilepsy. The hippocampus is important in cognition, but it is also frequently a focus of seizure activity in epilepsy. For about 30 to 40 percent of women with epilepsy, seizures fluctuate across the menstrual cycle, and this is due in part to estrogen. Importantly for basic epilepsy research, the effects of estrogen on seizure occurrence are similar in humans and animal models. We're using rats to study how estrogen alters the structure and function of hippocampal circuitry to determine what changes in that circuitry make the hippocampus more or less susceptible to seizure activity.

What causes seizures in epilepsy?

Seizures occur when a group of neurons fires excessively and synchronously; usually a seizure is a transient event. The behavioral manifestation of the seizure depends on the location and number of the neurons involved, whether and how the seizure spreads to other parts of the brain, and how long it lasts. Epilepsy — which occurs in 1 to 2 percent of the population — is defined as a tendency for recurrent seizures. It can be hereditary or acquired, for example, as the result of a head injury or an infection.

Can epilepsy be cured?

There are many antiepileptic drugs that are effective in controlling seizures, but they don't cure epilepsy. Brain surgery to remove the seizure focus can be an alternative when seizures are resistant to drug therapies, but understandably, surgery is a pretty scary option. Most antiepileptic drugs work by blocking ion channels or interfering with neurotransmitter function. But because these ion channels and neurotransmitters aren't specific to seizure activity, current antiepileptic drugs can have a lot of side effects.

A major focus of epilepsy research is to better understand the mechanisms of seizure initiation, propagation and termination so that we can develop drug therapies that affect seizures more specifically and thus have fewer side effects. That's where our estrogen studies come in. Estrogen itself does not cause seizures, but it does increase susceptibility to seizure initiation. If we can understand how that happens, we'll have a better way to target seizures specifically.

So what does estrogen do?

We have found that estrogen's effects on seizures are due, at least in part, to changes at the level of synapses. Estrogen first suppresses inhibitory synaptic function through a decrease in inhibitory transmitter release. This is followed by an increase in excitatory synapse number. Interestingly, the increase in excitatory synapse number also involves a physical change in the way neurons are wired together so that one presynaptic neuron can activate multiple postsynaptic neurons simultaneously. That wiring change is likely to increase synchronous firing.

"...strong parallels between human epilepsy and animal models of epilepsy make it possible to work out cellular mechanisms that could lead to novel therapies to control seizures. That's what we are working toward."

Recently, we've discovered that neuropeptides, which are released when neurons fire at high frequency, also play an important role in estrogen's effects on seizures. But in this case, the effect is to dampen seizure activity. So it turns out that, concurrent with increasing seizure susceptibility, estrogen also decreases seizure severity. It can get a little complicated, but the strong parallels between human epilepsy and animal models of epilepsy make it possible to work out cellular mechanisms that could lead to

—see Woolley, continued on page 10

CREATIVE COLLABORATION WITH MEDICAL AFFILIATES:
Evanston Northwestern Healthcare Research Institute

Evanston Northwestern Healthcare (ENH) has a well-established tradition of medical student and resident teaching dating back to 1930, when Evanston Hospital began its formal affiliation with what is today Northwestern's Feinberg School of Medicine. The ENH Research Institute is the research arm of Evanston Northwestern Healthcare that focuses on integrating leading-edge science into world-class care. As a fully integrated healthcare system, ENH is able to move the latest research findings into the hospital, into ambulatory settings, and even to the patient's home.

Researchers at ENH, who also serve as faculty at Northwestern University, conduct both clinical and translational research. The affiliation with the Feinberg School of Medicine and the University's basic sciences and biomedical engineering departments creates an ideal environment where clinical and scientific minds collaborate and innovate to advance medical research and bring new therapies to the patients who need them most.

HISTORY OF THE INSTITUTE

Although ENH Research Institute was founded only 10 years ago, ENH has had a long history of research discovery that dates back to the early 20th century. Exemplifying the devotion of its physicians to research and improved patient care, Louis W. Sauer developed the whooping cough vaccine at Evanston Hospital in the 1920s, and in the 1930s physicians George and Gladys Dick developed a toxin for the prevention of scarlet fever.

In 1940 the Abbott family donated land and money to Evanston Hospital to build the institute's first research facility, the Abbott Memorial Building. With the creation of ENH Research Institute in October 1996, ENH renewed its commitment to expand its research facilities by building new laboratories, including its flagship laboratory facility in the Northwestern University/Evanston Research Park in 2001 and the Charles R. Walgreen Jr. Building on the Evanston Hospital campus in 2005. In addition, ENH collaborated with Northwestern to establish the Arthur and Gladys Pancoe–Evanston Northwestern Healthcare Life Sciences

Mark R. Neaman, President and CEO, Evanston Northwestern Healthcare

"Research plays a critically important role at Evanston Northwestern Healthcare. Our relationships with Northwestern University and the Feinberg School of Medicine are at the core of our successes as a healthcare provider and an academic institution."

—Mark R. Neaman

Pertussis vaccines were first created in 1926 by physician Louis W. Sauer (right) of Evanston Hospital and Northwestern University.

[In this article, the departments in which ENH Research Institute scientists teach at Northwestern University appear after their names.]

Pavilion on the University's Evanston campus where ENH's translational researchers and Northwestern's basic scientists work side by side. ENH research now occupies more than 150,000 square feet.

Accompanying the investment in research facilities by ENH has been a notable increase in external research support from both federal sources such as the National Institutes of Health (NIH) and the Centers for Disease Control and Prevention (CDC) and an increasing variety of medical and pharmaceutical industry sponsors. Since its inception, the ENH Research Institute has seen its annualized external funding grow from $4 million in fiscal year 1997 to more than $33 million in 2006. Today, ENH is the top NIH-funded independent hospital in Illinois and is ranked 20th nationwide as an independent hospital system receiving NIH support and 10th among the nation's comprehensive independent research hospitals. Over the last decade, ENH Research Institute has been Northwestern's fastest-growing research component and affiliate.

ENH RESEARCH INSTITUTE PRIORITIES

The institute's mission is to add value to ENH's clinical care programs by enabling the corporation to recruit the best clinicians, and to integrate leading-edge research into clinical activities. In pursuit of this mission, ENH Research Institute has built an international reputation in seven areas of research with the greatest potential to benefit the people in its communities:

Advanced imaging: Evanston Northwestern Healthcare is host to some of the most advanced imaging technology in the region, with research-dedicated magnetic resonance imaging facilities separate from those used for patient care.

Cancer research: In frequent collaboration with the Robert H. Lurie Comprehensive Cancer Center, research is underway on prevention strategies for colon, ovarian, and prostate cancer and improved treatments for lymphoma. Clinical trials in thoracic oncology span the continuum from screening and early detection through new treatments for advanced disease.

Cardiovascular surgery and research: Investigators are developing greatly advanced ways to operate on the heart without opening the chest. They are also examining the biochemical and physiological basis of heart function in hopes of preventing the onset of heart disease.

Hemant Roy, an ENH gastroenterologist, and Vadim Backman, a biomedical engineer, work together to design highly sensitive optical screening devices that will identify tissue anomalies sooner and thereby enable earlier cancer diagnoses and treatments.

Medical genetics: Investigators and physicians are using the newest molecular methods to understand how medical disorders are inherited. With this information, ENH physicians are able to help patients understand and manage their risk for disease.

Neuroscience: Investigators at the ENH Movement Disorders Center have developed innovative surgical techniques to help a range of patients with tremors. The center offers a global approach in the diagnosis and treatment of Parkinson's disease and other movement-related disorders.

Outcomes: David Cella, psychiatry and behavioral science, has built the ENH Center on Outcomes Research and Education (CORE) into an internationally recognized resource for determining best practices across the continuum of medicine. CORE often partners with the Institute for Healthcare Studies at Feinberg.

Peri-neonatal medicine: Research on critical diseases of infants before and just after birth is helping to prevent and cure conditions that have eluded medical science for many years, thus improving outcomes for ENH's newborns.

One example of the beneficial cooperation between ENH and the University leading to improved clinical care is the work of Hemant Roy, medicine, and Vadim Backman, biomedical engineering, who are conducting clinical trials on a new optical technology to detect colorectal and

—see ENH Research Institute, continued on page 8

Spatial Intelligence and Learning Center: Perceiving Life in Three Dimensions

Human beings have developed specialized abilities to process information about the world around them in a number of ways. One of our most important mental abilities is spatial intelligence — the ability to perceive accurately and to recreate or transform aspects of the world. The Spatial Intelligence and Learning Center (SILC), Northwestern's new interdisciplinary center, brings together researchers from four leading universities in a collaborative effort to understand and solve scientific puzzles of spatial learning and to enhance the mental skills people need to compete in today's technological workforce.

Northwestern University scholars have joined with colleagues from Temple University, the University of Chicago, and the University of Pennsylvania to form SILC. The center draws together researchers who focus on spatial intelligence — a central arena of human mental processing. The goal is to gain a deeper understanding of human cognition and how it develops and to use this understanding to increase spatial ability in individuals and enhance the country's competitive edge.

Dedre Gentner, psychology and education, and director of the Cognitive Science Program at Northwestern, directs the new Spatial Intelligence and Learning Center. "Our research comprises three strands: foundational research on the mental processes that underlie spatial intelligence and how they develop; research on the effects of spatial symbols such as maps, graphs, and spatial language on spatial cognition; and research on how best to foster spatial learning from preschool through college and beyond," she says. An understanding of spatial relationships provides the foundation for a wide range of reasoning and communication skills as varied as designing buildings, solving mathematical problems, and forming mental abstractions.

NORTHWESTERN FACULTY INVOLVEMENT

Gentner's own research focuses on analogical processes in learning: e.g., how children learn to understand spatial models. She also studies language learning, including effects of spatial language on spatial cognition.

Researcher David Uttal, psychology and education, studies the role of map learning in fostering children's spatial understanding. For example, Uttal conducts studies both in the laboratory and in children's neighborhoods

Dedre Gentner, director, Spatial Intelligence and Learning Center

Courtesy of Spatial Intelligence and Learning Center

SILC researchers study the development of spatial pattern matching.

Courtesy of Spatial Intelligence and Learning Center

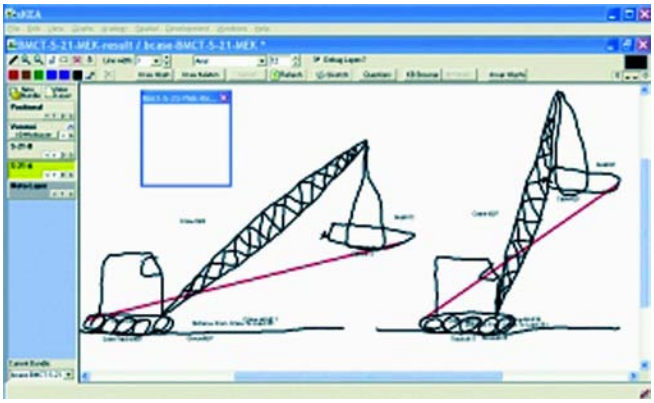
SILC research includes cross-cultural studies. Here, an Indonesian child is solving a spatial mapping task.




SILC faculty members: Ken Forbus, Louis Gomez, David Uttal, and Larry Hedges.

that assess how children come to think about the world beyond their immediate experience and how doing so influences their spatial thinking.

Ken Forbus, computer science and education, studies spatial processes by building intelligent artificial intelligence (AI) systems that can represent and reason about spatial relations. Forbus and his team are developing a unique research platform called CogSketch — a program that will be able to interpret sketches in a humanlike way. CogSketch will allow students to sketch on a screen and receive feedback on their work. Once installed on handheld computers, CogSketch could be used in classrooms to promote spatial learning or by engineers working out conceptual design issues.



Courtesy of Spatial Intelligence and Learning Center

A cognitive model, a precursor to CogSketch, reasoning through a problem. The system concludes that the crane on the left is less stable because the load is hanging farther out.

SILC researchers are collaborating to study how students' spatial reasoning skills influence their ability to learn from maps and other spatial representations and to see how their use of these representations contributes to their spatial analysis skills. Louis Gomez, education and computer science, studies how to improve students' use of charts, graphs, and other spatial media in science and math texts. Daniel Edelson, education and computer science, conducts research on Earth and environmental science education. He designs and studies curricula that engage students in investigations of real-world data using interactive mapping tools.

Other Northwestern faculty members who are central to SILC include Larry Hedges, statistics, education and social policy, a fellow of the Institute for Policy Research.

INTERPRETING AND USING SPATIAL TOOLS

Spatial insight extends beyond domains that directly involve spatial relations. Spatial analogies are used to portray abstract relationships across a range of disciplines, from economics (e.g., we speak of economic indices rising or falling) to ethology (e.g., we speak of a species whose evolutionary niche is shrinking or expanding); and these analogies often form the basis for graphs and predictions. Being able to interpret and use these spatial tools is becoming increasingly important in our highly technological society. People must be able to work with data and manipulate images mentally in reasoning about complex phenomena and systems.

STUDY RECRUITMENT

SILC members are always seeking families to participate in studies on the development of spatial learning and thinking. "The studies are fun for children, and parents can sign up for one visit or more, as they prefer," Uttal said. To sign up or to receive more information, parents should call 847-467-3045 or visit online at www.kids.northwestern.edu. SILC researchers also are interested in recruiting undergraduates, especially those with expertise in engineering or geology who would like to participate in studies of spatial learning.

For more information about SILC, go to http://spatiallearning.org/.

Unless otherwise noted, photographs in this article by Martin Woods Image Consulting, LLC.

— *ENH Research Institute, continued from page 5*

pancreatic cancer at the earliest stages. These researchers are using a miniature fiber-optic light probe, that employs technology called four dimensional elastic light-scattering fingerprinting (4D-ELF), to detect signs of colon cancer in tissue that are up to 50 times smaller than those detectable using conventional methods. This alternative to colonoscopy may one day be used routinely during a patient's annual physical in a doctor's office, dramatically reducing the incidence of colorectal cancer, the second leading cause of cancer deaths in the United States.

In another example of the many collaborations between ENH and Northwestern scientists, Joseph Bass, medicine and neurobiology and physiology, is working with Northwestern's Joseph S. Takahashi and Fred W. Turek, neurobiology and physiology, discoverers of the "sleep" gene for circadian rhythms, to explore the impact of circadian rhythms on metabolism and thus diabetes and obesity. Their 2005 publication in *Science* was judged by the journal *Nature Medicine* to be one of the year's top 15 in terms of impact on medical science.

ENH CLINICAL TRIALS CENTER

ENH physicians have been involved in clinical trial research for decades. Currently, more than 300 investigators and 30 study coordinators involved in more than 1,000 protocols participate in clinical trials research.

Additional information about ENH and the ENH Research Institute can be found at www.enh.org. ▮

— *Cancer Research, continued from page 1*

tumor suppressor genes. The reagents and techniques developed by her laboratory are used by cancer researchers around the world.

As head of the Division of Molecular Oncology at ENH, Hamid Band's focus is on how leukocytes are kept in check to protect against autoimmunity and how epithelial cells replicate without becoming cancerous.

Together, Hamid and Vilma Band's vision is to dissect the biochemical pathways of breast tumor progression to identify novel targets for therapy and genetic markers for early detection. ▮

SPOTLIGHT ON OTHER ENH RESEARCH INSTITUTE RESEARCH EXCELLENCE

Medical Genetics

Pablo Gejman heads the Center for Psychiatric Genetics at the ENH Research Institute in its studies of clinical and biological inherited factors in major psychiatric disorders, molecular genetic diversity, and psychopharmacology and pharmacogenetics. He is an internationally prominent researcher who discovered an important gene for schizophrenia and bipolar disorder. This finding, reported in the *American Journal of Human Genetics*, was based on the linkage studies of 192 families of European and African American ancestry that had a history of schizophrenia. Gejman received the largest NIH research grant awarded to a psychiatrist in the United States to collect a new sample of 4,500 schizophrenics and 4,500 control subjects necessary to conduct new studies that will improve the understanding of the biological mechanisms that lead to schizophrenia and how they interact with the environmental risks.

Neuroscience

ENH is one of only six nationwide sites selected by the National Institute of Neurologic Disorders and Stroke to study a new treatment for patients with stroke thanks to the work of Issam A. Awad, director of Neurovascular Surgery at ENH and neurosurgeon at the Feinberg School of Medicine. His NIH-funded basic research focuses on the molecular mechanisms leading to the genesis and growth of cerebrovascular anomalies, highly prevalent lesions that predispose patients to stroke and epilepsy.

Peri-neonatal Medicine

Michael Caplan, pediatrics, has won international acclaim for his NIH-funded research on the causes and treatment of neonatal necrotizing enterocolitis, a bowel-destroying disease that is the third leading cause of death of premature infants. To further ENH's efforts to provide superior clinical care for high-risk mothers and babies, other ENH Research Institute investigators are studying the genetic role in preterm labor, exploring new therapies for fetal growth retardation and preeclampsia, identifying markers of biochemical changes that are highly damaging to the neonatal brain, and developing strategies to prevent and treat lung disease and fetal birth defects.

Alumna Endows International Center

The Center for International and Comparative Studies will now be known as the Roberta Buffett Center for International and Comparative Studies, thanks to a series of significant gifts from alumna Roberta Buffett Bialek of Carmel, California. Buffett Bialek received a bachelor's degree in history from Northwestern in 1954. Her gifts are being used to create an endowment to support the center's research and educational programs.

The center was founded in 1994 to promote collaborative scholarship across the university on crucial world problems. With more than 180 affiliated faculty members, it is a hub of internationally focused research, education, and outreach at Northwestern.

The Roberta Buffett Center for International and comparative Studies (BCICS) brings scholars from around the world to Northwestern to build international relationships and provide educational opportunities for students. Through summer study abroad programs, student-organized conferences, and publications, BCICS provides undergraduates with a variety of opportunities to engage in international study and research.

Buffett Bialek has been a generous supporter of the center over the last several years. Her first gift, made in honor of her 50th reunion, created the Roberta Buffett Visiting Professorship in International Studies, which brings leading international scholars to the University.

Three Buffett professors have been in residence this year: Ales Debeljak, one of Eastern Europe's leading intellectuals, poets, and a cultural studies specialist, is at Northwestern for the entire year, teaching courses on the European Union, the Balkans, modernity and the arts, and on East European poetry and politics in 20th century. In the fall, Stephen Kinzer, an award-winning *New York Times* journalist and author, and Norwegian sociologist Frederick Engelstad spoke to students. Kinzer has been signed up for an additional three-year stint and the center expects to launch a joint program between the Department of Sociology and Englestad's research unit in Oslo as a result of his stay here.

More recent gifts from Buffett Bialek have supported the research and scholarly activities of the BCICS. Andrew Wachtel, director of the center, said, "The support of Roberta Buffett Bialek will help us to ensure that our students, faculty, alumni, and the broader community become and remain exemplary global citizens, aware of the complexity of the world around us."

For more information about BCICS, visit online at www.cics.northwestern.edu/.

BCICS Director Andrew Wachtel with Fall 2005 Roberta Buffett Visiting Professor Ariane Chebel d'Appollonia and Roberta Buffett Bialek.

Rwandan Genocide Expert to be Buffett Visiting Professor in 2007

Next fall, José H. Kagabo will be the Roberta Buffett Visiting Professor of International Studies. Kagabo teaches at the École des Hautes Études en Sciences Sociales in France, and is an internationally renowned expert on the Rwandan genocide. He has testified before the International Criminal Tribunal for Rwanda and has written numerous books and articles on crises in central Africa including *Islam and the "Swahili" in Rwanda* and *The Question of Rwandan Refugees.*

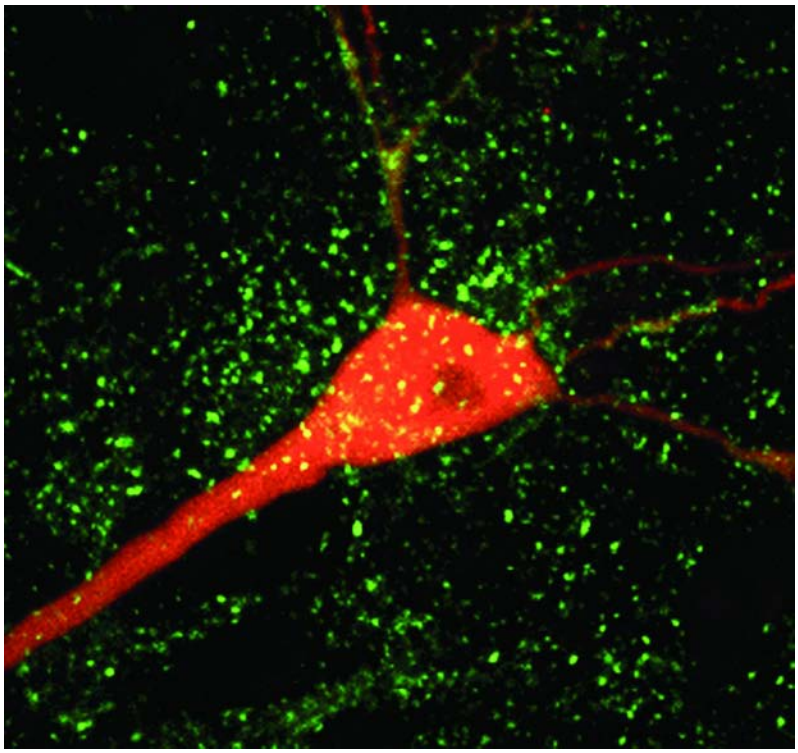
Kagabo is currently working on a book about the Rwandan genocide that will focus on how the network of conspirators was organized and examine the role of politicians, intellectuals, and businessmen in motivating ordinary citizens to become the perpetrators of violence. Building on his distinct knowledge of the Rwandan genocide, international justice programs, and the truth-seeking tribunals, Kagabo will develop and teach two courses while at Northwestern.

— *Woolley, continued from page 3*

novel therapies to control seizures. That's what we are working toward.

The effects of hormones in the brain raise the question: Do male and female brains work differently?

Unequivocally, the answer is yes. Androgens and estrogens act perinatally to organize neural circuits into the male and female patterns, and they act again in adulthood to activate those neural circuits. Most sexually dimorphic behaviors in adults require both the organizational and activational effects of hormones. Sexual dimorphism in the brain and behavior is most evident — and, I suppose, least controversial — in parts of the brain that control reproductive function. However, there are also sex differences in parts of the brain that are not directly related to reproduction. These are sometimes more controversial because they can be associated with value judgments. That is, "work differently" is too easily translated into "work better" or "work worse." This is a mistake. For example, studies show that there are differences in the way male and female rats solve mazes. As a result, whether males outperform females, or females outperform males, depends heavily on how the maze is designed.



Projected image from a stack of confocal micrographs showing a hippocampal neuron (red) in tissue that has been stained to visualize inhibitory axonal boutons (green). Points of overlap between the red and green (yellow) are likely sites of synaptic contact between inhibitory axonal boutons and the cell.

What other non-reproductive behaviors differ between males and females?

We are just beginning a new project to investigate sex differences in addiction. Behavioral studies show that estrogen interacts with underlying sexual dimorphisms in the brain to make females more susceptible to drug addiction. One hallmark of drug addiction is the potentially life-long propensity to relapse, which suggests that addiction involves permanent changes in brain wiring. So: do these changes in brain wiring differ between males and females, and are they affected by hormones? This is what we are trying to find out. Our preliminary studies on the nucleus accumbens, a part of the brain important in addiction, suggest that there are sex differences in the way neurons there are wired together. If that holds up, those may contribute to male-female differences in the process of addiction.

This addiction project is an example of a general theme in my laboratory. By determining how differences or changes in brain infrastructure correspond to variations in behavior — and especially by manipulating those distinctions — we can learn a lot about basic mechanisms of brain function. In this way, studies of sex differences and hormone effects in the brain can have very broad implications.

What are the advantages to working at Northwestern?

Oh, I think there are many. I would have to say that one of the biggest is the collaborative, can-do attitude of my colleagues. Let me give you an example of how this can be good for research. My work depends heavily on high-end (and expensive) microscopy, such as electron microscopy. This is the only way to visualize synaptic connections between neurons at nanometer resolution, which is critical for our research. When I came to the University, the only electron microscope suitable for biological imaging was on its last legs. Additionally, there was no available confocal microscope, which is necessary for high-resolution fluorescence imaging. I needed both, and some of my other colleagues did too. We decided to do something about it. I got together with other faculty in neurobiology and physiology; biochemistry, molecular

biology, and cell biology; and biomedical engineering and we formed what is now the Biological Imaging Facility (BIF).

BIF started with a grant that I wrote to the NIH for a confocal microscope and support from the office of the vice president for research to renovate space. Once it got off the ground, we hired an outstanding microscopist, William A. Russin, neurobiology and physiology, to run the facility and since then, we've added a beautiful new electron microscope, a high-end confocal microscope capable of single molecule imaging, and several other instruments as well. With support from multiple research centers and departments at Northwestern as well as foundation support (e.g., The Whitaker Foundation, the Howard Hughes Medical Institute, and the Daniel F. and Ada L. Rice Foundation), BIF has grown tremendously — serving over 450 users from 28 different departments at Northwestern — and continues to be an integral part of the life sciences research community. ▮

CenterPiece

The Office for Research promotes, facilitates, and enhances research at Northwestern University.

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To submit center news or request copies of *CenterPiece*, contact Kathleen Mandell at 847-491-3880 or by e-mail at kathym@northwestern.edu.

This publication is available online at www.northwestern.edu/research/publications/centerpiece/.

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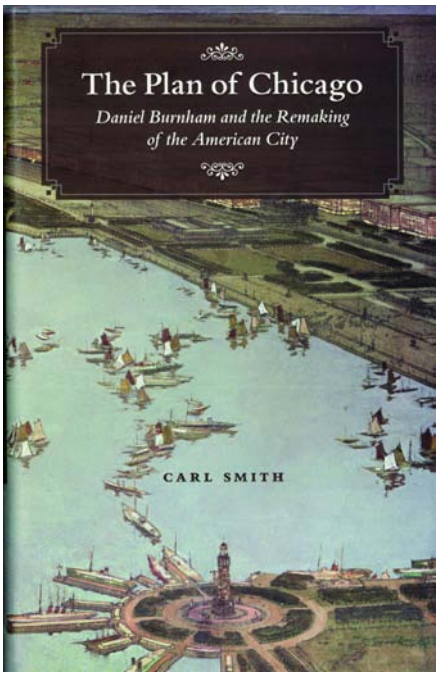
Spatial Intelligence and Learning Center
Dedre Gentner, director | http://spatiallearning.org

ON THE BOOKSHELF

The Plan of Chicago: Daniel Burnham and the Remaking of the American City by Carl Smith (University of Chicago Press, 2006)



Carl Smith, English and American studies, wrote his book *The Plan of Chicago* about an earlier book of the same name by Daniel Burnham. Burnham's book, published in a limited edition by the Commercial Club of Chicago in 1909, presented a vision of Chicago restructured in such a way that would make it the equal of Paris. Smith's book puts that vision in context, describing Chicago's haphazard growth before the plan, how Burnham became the city's most famous architect, and the Commercial Club and its audacious plan to reengineer a city of nearly 2 million inhabitants.

Burnham's *Plan of Chicago* became a seminal book in the history of urban planning — and of public relations: The way it was publicized, a story told in Smith's book, makes a fascinating saga in itself. Smith's *Plan of Chicago* is a succinct history that will delight Chicago history buffs as well as city planners, architects, political activists, urban historians, architectural historians, and reformers.

In addition to being an author of several books of urban history, Smith, who is a faculty associate at the Institute for Policy Research, is an experienced author and curator who collaborated with the Chicago History Museum and Northwestern's Academic Technologies division on the online exhibits *The Great Chicago Fire and Web of Memory* and *The Dramas of Haymarket* both of which may be viewed at www.chicagohistory.org. *The Plan of Chicago* is a revised version of his electronic entry for the online edition of the *Encyclopedia of Chicago*, which may be found at www.encyclopedia.chicagohistory.org. ▮

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