

CenterPiece

A Quarterly Publication Featuring the Northwestern University Research Centers

Winter 2005
Volume 4/Number 1



NORTHWESTERN
UNIVERSITY

IN THIS ISSUE

*Psycho-Legal Studies Program
research provides direction for
public health* 2

Study abroad reaps benefits 5

*International Institute for
Nanotechnology launched* 6

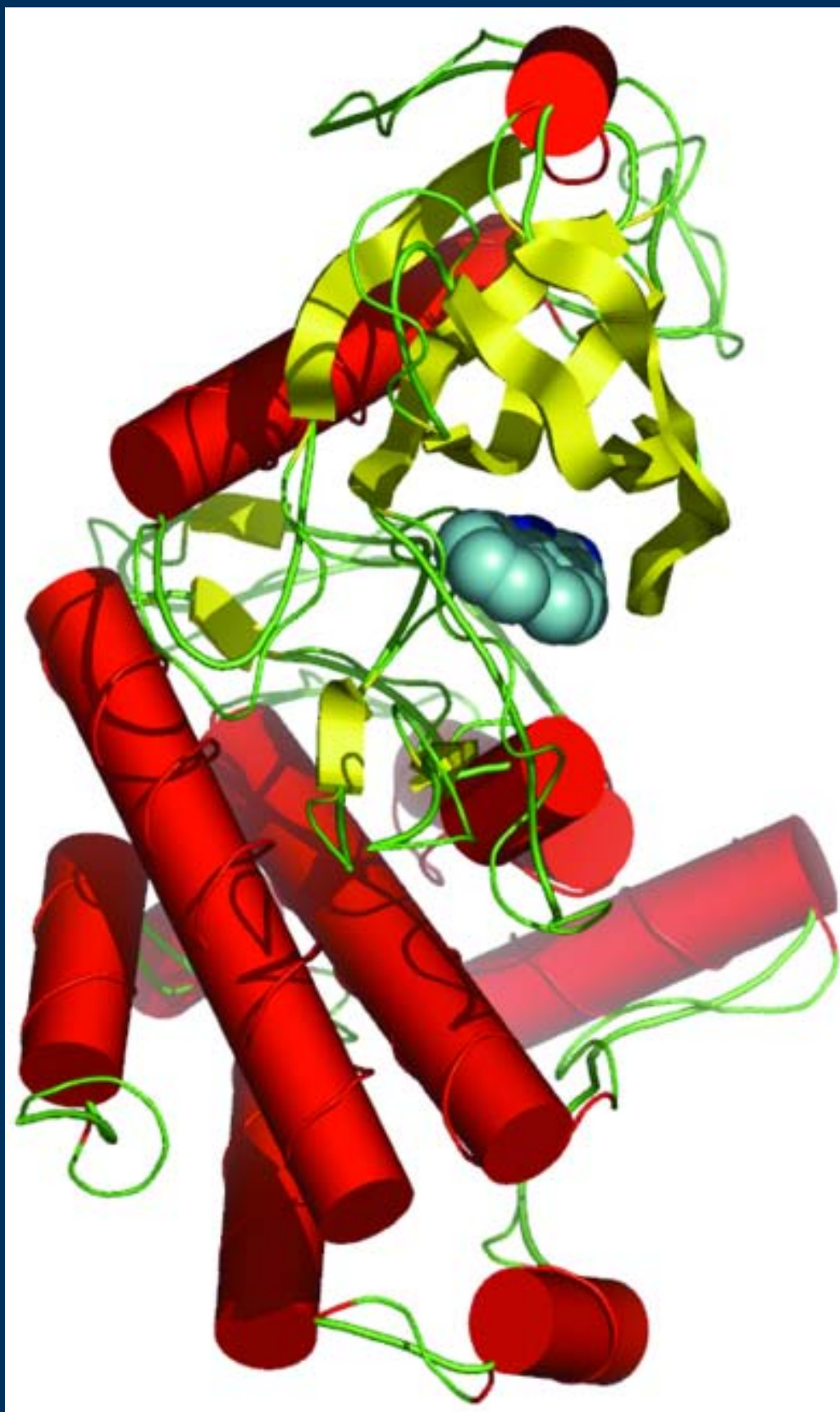
University research centers 7

*Molecular mechanism sheds
light on neurodegenerative
diseases* Back cover

Pictured at right is a schematic diagram of the 3-dimensional structure of a complex between a drug-like molecule (aqua) and an enzyme (yellow, red, and green). The enzyme is death-associated protein kinase (DAPK), a potential therapeutic target for attenuating disease progression in stroke and neurodegenerative diseases.

The structure of the target was determined and the drug-like small molecule was synthesized as part of collaborative studies involving faculty, students, and postdoctoral fellows of the recently established Center for Drug Discovery and Chemical Biology. Martin Watterson, molecular pharmacology and biological chemistry, and Linda Van Eldik, cell and molecular biology, are co-directors of this new University research center.

Figure courtesy of Laura Wing, a predoctoral trainee in Watterson's laboratory. ☺



Psycho-Legal Studies Program research provides direction for public health

“Unless you have good data, you can’t begin to allocate scarce mental health resources where they are needed,” responds Linda Teplin, director of the Psycho-Legal Studies Program, when asked about her pioneering research. For nearly 30 years, Teplin and her colleagues have studied the interface between the mental health and criminal justice systems. The results of their research have provided much needed empirical data to those who form policy about public health services at all levels of government.

The groundbreaking empirical studies conducted by the Psycho-Legal Studies Program have replaced conjectures regarding largely neglected populations – such as mentally ill jail detainees and juvenile delinquents – with rigorous research results. The multidisciplinary and multimethod approach employed in these studies reflects the interdisciplinary perspective of the Psycho-Legal Studies Program team.

In addition to her primary appointment as Owen L. Coon Professor of Psychiatry and Behavioral Sciences, Teplin holds joint appointments in the School of Education and Social Policy, Department of Sociology, Institute for Policy Research, and Center for Sleep and Circadian Biology. Karen Abram, associate director, is a clinical psychologist, and Gary McClelland, senior research analyst, is a sociologist.

The commitment to research that is multidisciplinary and policy-relevant led the Psycho-Legal Studies Program to investigate fields that are often avoided by others because of the methodological problems and access limitations. The Program focuses on

four broad areas: the criminalization of the mentally ill, epidemiologic characteristics of jail detainees, correlates of violence and victimization, and juvenile delinquency.

Landmark project

Teplin’s interest in these neglected areas of research began in 1975, when she was studying the relative effectiveness of different treatments for psychiatric emergency room patients referred by police; deinstitutionalization was still relatively new. Discovering that police never brought more than 50 mentally ill persons to the emergency room per month, she asked, “What happens to all the other persons with serious mental disorders? Are they arrested instead of treated?”

To answer this question, Teplin and five graduate students rode in squad cars with Chicago police over a 14-month period to observe how the officers managed persons with severe mental disorders. The findings of this initial study were striking: although mentally ill persons did not commit crimes more frequently than the non-ill, they were arrested nearly twice as often. Furthermore, most arrests took place when mental health treatment would have been preferred, but was not available. The study highlighted the failure of deinstitutionalization



Photograph courtesy of Feinberg School of Medicine.

Linda Teplin (above) rode in squad cars with Chicago police to observe how the officers managed persons with severe mental disorders.

policies as then implemented and suggested that jail had become the poor person’s mental hospital.

Relevant public health research

With this landmark project, Teplin achieved her goal of providing relevant public health research. Her findings were cited in amicus briefs to the U.S. Supreme Court and used to develop American Bar Association Criminal Justice Standards. The National Institute of Mental Health cited her research in reports to Congress to highlight the failure of deinstitutionalization policies and to justify increased funding for mental health programs. And the

Psycho-Legal Studies Program (previously just referred to as “Linda’s Research”) was formally launched.

In conferring upon Teplin the 1992 Award for Distinguished Contribution to Research in Public Policy, the American Psychological Association (APA) recognized that, “her widely cited studies of how police interact with citizens they perceive as mentally disordered have become the gold standard for research on police behavior.”

Study of jail detainees launched

If jails were becoming the hospitals for mentally ill persons in need of assistance, an obvious follow-up question for the Psycho-Legal Studies Program was, “Do we know how many persons in jails have severe mental disorders and need treatment?” Without numbers, jails could not plan the breadth and type of psychiatric services they were required to provide. So the Psycho-Legal Studies Program launched the largest epidemiological study of male jail detainees ever conducted to determine the prevalence of mental disorder. This study showed that rates of major mental disorders, such as schizophrenia and affective disorders, in jail detainees are two to three times those of the general population.

A follow-up study revealed that, once arrested, few persons with mental disorders – 45% of those with schizophrenia and only 7% of those with major depression – are treated in jail. These findings helped jails nationwide to develop programs to screen and treat mentally ill persons in custody.

Subsequent research examined the commonly held stereotype that mentally ill offenders are the most violent and are at particular risk for criminal recidivism. The study showed that psychiatric disorder was irrelevant to the probability of

re-arrest for violent crime, debunking the myth that persons with severe mental disorders are prone to violence.

Study extended to female jail detainees

Recognizing that the number of female offenders was increasing and that there was an absence of data on women in jail, the Psycho-Legal Studies Program undertook the largest epidemiologic study of female jail detainees ever conducted – a two-year study of 1,272 females who had been arrested and were awaiting trial. Over 80% of the group met criteria for one or more lifetime psychiatric disorder(s), with nearly 14% having severe depression, a major mental disorder.

In the first study to track treatment of mentally ill women in jail, Teplin and her group found that only 24% of women in jail who needed mental health services received them. Like the first study of male jail detainees, this research helped to influence public policy. The National Institute of Corrections developed a special program for jails nationwide to create services to address the unique needs of female detainees.

Northwestern Juvenile Project

The research on adults in jail had revealed that most mentally ill detainees have histories of early onset psychiatric disorders and juvenile arrest records. “Our prior studies suggested that juveniles with psychiatric disorders may be vulnerable to arrest, particularly if they are poor and cannot afford treatment,” Teplin explains. To learn more about this group, the Psycho-Legal Studies Program’s Northwestern Juvenile Project was launched, the first large-scale longitudinal study of psychiatric

disorders and outcomes among delinquent youth. The five-year study, sponsored by the National Institute of Mental Health and a consortium of other federal agencies and private foundations, looked at the prevalence of alcohol, drug, and mental disorders among 1,829 male and female detainees, ages 10 to 18, in the Cook County Juvenile Temporary Detention Center.

“Our data will help guide intervention strategies for delinquent youth.”

“Everybody else had studied general population kids to see who *becomes* delinquent,” Teplin notes. “But we purposely sampled only delinquent youth because they are at such high risk for poor outcomes, such as psychiatric disorders, HIV/AIDS risk behaviors, life-threatening problem behaviors, violent victimization, and early violent death. Our data will help guide intervention strategies for delinquent youth.”

Psychiatric and substance use disorders

In findings published to date, Teplin and her team have reported that over three-quarters of females and two-thirds of males in the study have one or more psychiatric disorders [Teplin, et al., *Archives of General Psychiatry*, 59, 1133-1143 (2002)]. This study clearly shows that youth with psychiatric disorders pose a challenge for the juvenile justice system and, after their release, for the larger mental health system. “Our findings have profound implications for understanding health disparities,” Teplin says. “Over 60% of detainees are racial or ethnic minorities.”

—see *Psycho-Legal Program*, continued on p. 4

—*Psycho-Legal Program, continued from p. 3*

A companion study focused on the comorbidity (overlap) of psychiatric disorders among juvenile detainees. Nearly 50% of females and more than 40% of males had two or more types of psychiatric disorders. As illustrated in the accompanying Venn diagrams, 22% of females and 17% of males had three or more types of disorders [Abram, et al., *Archives of General Psychiatry*, 60, 1097-1108 (2003)]. “Among juvenile detainees with psychiatric disorders,” Abram observes, “comorbidity is the rule, not the exception.”

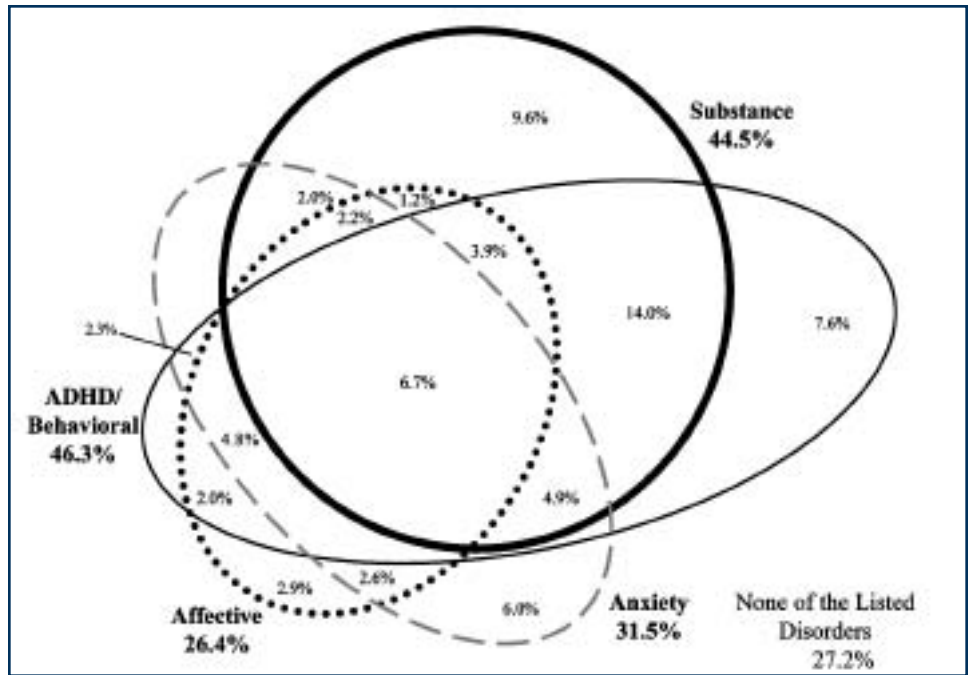
HIV/AIDS risk behaviors studied

The first comprehensive study of HIV/AIDS risk behaviors (drug and sex behaviors) in juvenile detainees revealed that 95% of the youth engaged in three or more risk behaviors, and 65% reported 10 or more risk behaviors. “Let’s remember that kids are detained an average of only two weeks,” McClelland comments. “Reducing HIV/AIDS risk behaviors in detained juveniles will reduce the spread of HIV in the community.”

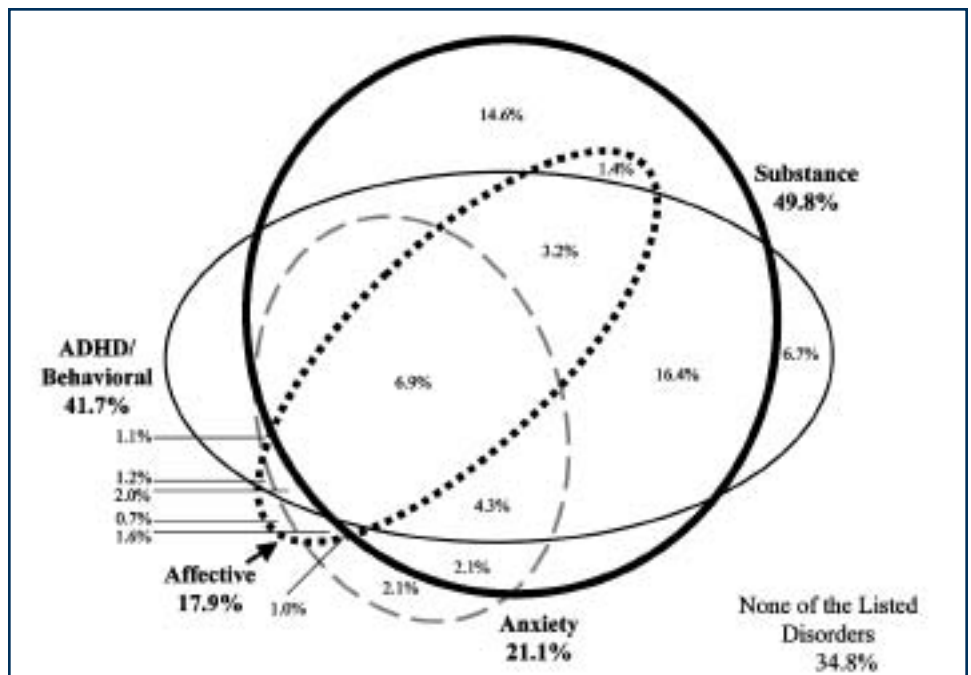
Violent death and violent victimization

Most recently, the Psycho-Legal Studies Program has focused on the risk of early violent death in delinquent youth and on violent victimization among persons with serious mental disorders who live in the community. Of the 1,829 youth who participated in the Northwestern Juvenile Project, 65 were dead within seven years.

A study to be published in *Pediatrics* [Teplin, et al., in press] reports that, even after controlling for demographic differences, mortality among delinquent youth is more than four times higher than in the general population; mortality among females is nearly eight times higher. More than 90% of deaths in delinquent youth are homicides, and 93% of the



Simultaneously diagnosed (comorbidity) types of disorder among females.



Simultaneously diagnosed (comorbidity) types of disorder among males.

homicides are from gunshot wounds. As in the general population, African American males have the highest mortality. “Early violent death is one of our country’s most profound health disparities,” Teplin asserts.

“Perhaps nothing underscores our failure to reach and rehabilitate at-risk youth more than their vulnerability to an early and violent death,” she continues. “It is ironic that mass

school shootings – which accounted for 52 deaths between 1990 and 2000 – have received far more attention than homicides of inner city youth. To put this into perspective, during the same period in New York City alone, there were 840 homicides among youth aged 14 to 17 years.”

The first large scale study of violent victimization among adults —see *Psycho-Legal Program, continued on p. 6*

Study abroad reaps benefits

For the United States to remain at the forefront of science and technology, the country needs an educated scientific workforce that is capable of operating in an international research environment and in a global market. Recognizing this need, the Nanoscale Science and Engineering Center (NSEC) of the Institute for Nanotechnology provides support for graduate students and postdoctoral associates to engage in short-term collaborative studies in nanotechnology-related research laboratories worldwide. The goal of this program is to strengthen international collaborations and provide students and junior researchers with global research experiences and educational opportunities.

Collaborative research

Tom Chiesl is a graduate student in the laboratory of Annelise Barron, chemical and biological engineering. His research involves the creation of novel materials and methods for the purification of biomolecules (DNA and proteins) by electrophoresis on microfluidic devices. These devices form the basis of a so-called “lab-on-a-chip” technology that can conduct highly sensitive analytical measurements. Microfluidic technologies enable the

fabrication of highly integrated devices for performing several different functions on the same chip substrate. Microfluidics research is a critical component in gene chip and protein chip development efforts.

Truly a collaborative project, the ultrasensitive nanotechnology-driven DNA sensing technology was developed in the laboratory of Chad Mirkin, Department of Chemistry and director of the International Institute for Nanotechnology; the microfluidic device was created by Chang Liu’s group in the Department of Electrical and Computer Engineering at the University of Illinois at Urbana-Champaign.

Chiesl has synthesized copolymers that can extract DNA from a complex sample (such as blood or a cheek swab) and adsorb unwanted cellular material. “The goal of the research is to be able put these polymers into a microfluidic device so that we can deliver a pure sample to an ultrasensitive detection technology,” Chiesl explains. “We are trying to make an automated device where you can take a drop of blood, put it on the chip, and get some genetic information out within a short time period, be it for clinical diagnostics or biological weapons detection.”

Chiesl went to Malmo, Sweden, and to Copenhagen, Denmark, where he worked with Jorg Kutter at the Danish Technical University. There he learned about several new microfluidic chromatographic techniques and detection technologies. He was also able to attend a conference on micro-total analytical systems to hear presentations on cutting-edge microfluidic technologies.

Computer simulation

Sharon Loverde, a graduate student working with Monica Olvera de la Cruz, materials science and engineering, is studying computer simulation techniques for polymeric and biological molecules. “In order to gain a better understanding of the physics behind the self-assembly processes and pattern formation seen in real-life systems,” Loverde points out, “it is often helpful to develop an idealized model of the interactions that the molecules of interest possess and mimic their real-life behavior on a computer.”

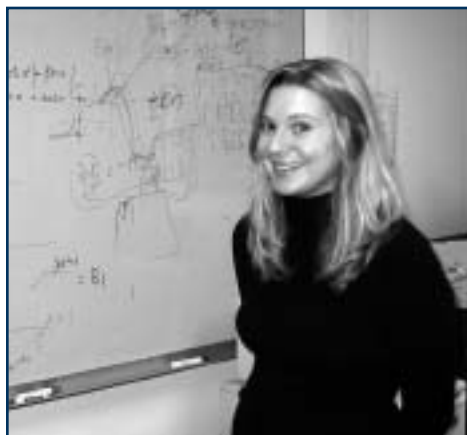
Research pursued in Germany

Loverde went to the Max Planck Institute for Polymer Research in Mainz, Germany, to pursue her research on the simulation of charged systems. “To have the experts in the

—see *Study abroad*, continued on p. 7



Erin McLellan, a graduate student in the laboratories of Richard Van Duyne and Kenneth Spears, is pictured with an electron beam deposition system used to deposit metal onto prepared surfaces to create nanoparticle arrays. Photograph by Anthony F. Abbinanti.



Sharon Loverde is in the laboratory of Monica Olvera de la Cruz. The group studies statistics, thermodynamics and dynamics of macromolecules, phase transformations, and soft matter theory. Photograph by Anthony F. Abbinanti.



Tom Chiesl is in Annelise Barron’s laboratory. He is pictured running a capillary electrophoresis experiment to measure the amount of protein adsorption onto copolymer matrices. Photograph courtesy of Tom Chiesl.

—*Psycho-Legal Program, continued from p. 4*

with serious mental disorders who live in the community revealed that nearly one-quarter of this extremely high risk population had been victims of a violent crime in the past year, more than 11 times general population rates even after controlling for demographic differences between the two samples [Teplin, et al., *Archives of General Psychiatry*, in press]. Depending on the type of violent crime, prevalence is 5 to 21 times greater among persons with serious mental illnesses than the general population.

“The results of this study make it clear that among persons with severe mental illness, violent *victimization* is far more prevalent than *perpetration* of violence,” Teplin emphasizes. “Yet, negative stereotypes of persons with severe mental illness dominate the public’s view, and behavioral scientists continue to focus on perpetration of violence. We need to recognize that crime victimization is a major health problem among persons with serious mental illnesses who are treated in the community. Since the advent of deinstitutionalization, most persons with serious mental illnesses now live in the community. We need to keep them safe.”

Worldwide recognition

The Psycho-Legal Studies Program’s ground-breaking research has gained worldwide recognition and garnered Teplin numerous prestigious awards, including a National Institutes of Health MERIT award. But, for Teplin, the knowledge that her work is used to guide public policy is more important than the awards. As expressed in the APA citation, “Her program of scholarship stands as testimony to the proposition that scientific excellence and policy influence can be simultaneously and successfully pursued.” 🐾

International Institute for Nanotechnology launched

Nanotechnology, the science and technology of controlling the structure of matter at the molecular level, is widely viewed as the most significant technological frontier currently being explored. Materials and devices at the nanoscale (a nanometer is one billionth of one meter) hold vast promise for innovation in virtually every industry and public endeavor, including health, electronics, transportation, the environment, and national security.

Researchers from Northwestern University and Argonne National Laboratory are collaborating on the establishment of the International Institute for Nanotechnology (IIN). This new venture unites all of the nanotechnology researchers and educational programs at Northwestern and Argonne under one umbrella, while encouraging and supporting collaborations at Argonne’s Center for Nanoscale Materials (CNM).

Currently, the nanotechnology efforts at Northwestern and Argonne represent more than \$300 million in state, federal, and University funding. In addition, Northwestern’s Institute for Nanotechnology has collaborative research and exchange agreements with Seoul National University and Ajou University in Korea. Nanoalliance, a student organization that serves as a gateway for students from many different fields to learn more about nanotechnology, will also be involved in IIN.

The steering committee includes representatives of CNM and faculty from the Feinberg School of Medicine, McCormick School of Engineering and Applied Science, Weinberg College of Arts and Sciences, and two University research centers – NUANCE Center and the Institute for BioNanotechnology in Medicine (IBNAM). Chad A. Mirkin has been appointed director of this new University research institute.

In addition to Mirkin, the steering committee for IIN includes:

- Annelise E. Barron, chemical and biological engineering;
- Catherine L. Brinson, mechanical engineering;
- Stephen H. Davis, engineering sciences and applied mathematics and mechanical engineering;
- Vinayak P. Dravid, materials science and engineering and director of NUANCE Center;
- Millicent A. Firestone, co-director of CNM nanoscience summer school;
- Eric D. Isaacs, director, CNM;
- John B. Ketterson, physics and astronomy;
- C. Bradley Moore, vice president for research;
- Mark A. Ratner, chemistry;
- Rodney S. Ruoff, mechanical engineering and director of Northwestern’s BIMat Center;
- Samuel I. Stupp, materials science and engineering, chemistry, medicine, and director of IBNAM; and
- Steven M. Wolinsky, infectious diseases. 🐾

CenterPiece

C. Bradley Moore, vice president for research, Northwestern University

CenterPiece is published by the Office of Research Analysis and Communication

Leila S. Edwards, executive director
Kathleen P. Mandell, senior editor

To submit center news or request copies of the newsletter, 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/.

©2005 Northwestern University.
All rights reserved.

—Study abroad, continued from p. 5

field, those who developed the techniques I was using, next door ready to offer advice or answer questions about computer language scripting was quite amazing,” Loverde replies, when asked about her two-month trip. “It is much easier to understand something when the person who wrote the paper is next door to you and not eight time zones away.

“The experience was vastly encouraging on both a scientific and social level,” she continues. “The people I worked with came from all over the world and were just as ready to give advice on how to make the best cappuccino or Dutch pancakes as to share insights on how to approach a particular research problem.”

Fabricating nanoparticle array surfaces

Erin McLellan is a graduate student in the laboratories of two chemists, Richard Van Duyne and Kenneth Spears. “The research I do here at Northwestern is in the broad category of nanotechnology,” McLellan notes. “More specifically, I fabricate different types of nanoparticle array surfaces to utilize their unique catalytic, optical, electrical, and structural properties.”

Work at a Swedish University

McLellan recently returned from a three-month trip to Göteborg, Sweden, where she worked with Bengt Kasemo, applied physics, and Mikael Käll, condensed matter physics, at Chalmers University of Technology. There she studied the effects of particle spacing on the localized surface plasmon resonance (LSPR) of lines of cylindrical nanoparticles produced by electron beam lithography (EBL).

Reflecting on her experience, McLellan observes, “By going to Chalmers, I expanded my knowledge in nanofabrication and improved my ability to pick and choose which methods to use for different projects. My work at Chalmers has also given me great contacts in other countries who are tops in their respective fields,” she adds. “These contacts will be beneficial if I need advice or help on future projects.”

Valuable experience

The students agree that their experiences were rewarding and provided extraordinary opportunities to make not only scientific discoveries, but also discoveries about other people and cultures. “I think everyone should study abroad for at least a short time,” McLellan declares. “You get to experience what it is like in another country and discover

Center for Applied Psychological and Family Studies

William M. Pinsof, director | e-mail: family-institute@northwestern.edu

Center for Catalysis and Surface Science

Peter C. Stair, director | www.northwestern.edu/catalysis

Center for Drug Discovery and Chemical Biology

D. Martin Watterson and Linda J. Van Eldik, co-directors
www.northwestern.edu/research/cddcb

Center for Functional Genomics

Joseph S. Takahashi, director | www.genome.northwestern.edu

Center for International and Comparative Studies

Andrew B. Wachtel, director | www.northwestern.edu/cics

Center for Reproductive Science

Kelly E. Mayo, director | www.northwestern.edu/research/crs

Center for Sleep and Circadian Biology

Fred W. Turek, director | www.northwestern.edu/cscb

Center for Technology Innovation Management

Michael Radnor, director | e-mail: m-radnor@kellogg.northwestern.edu

Chemistry of Life Processes Institute

Thomas V. O'Halloran, director | www.clp.chem.northwestern.edu/

Institute for BioNanotechnology in Advanced Medicine

Samuel I. Stupp, director | www.ibnam.northwestern.edu

Institute for Nanotechnology

Chad A. Mirkin, director | www.nanotechnology.northwestern.edu

Institute for Neuroscience

Enrico Mugnaini, director | www.northwestern.edu/nuin

Institute for Policy Research

Fay Lomax Cook, director | www.northwestern.edu/ipr

International Institute for Nanotechnology

Chad A. Mirkin, director | www.nanotechnology.northwestern.edu

Materials Research Center

John M. Torkelson, director | http://mrcemis.ms.northwestern.edu

Materials Research Institute

R.P.H. Chang, director | http://materialsresearchinstitute.northwestern.edu

Northwestern University Atomic and Nanoscale Characterization (NUANCE) Center

Vinayak P. Dravid, director | www.nuance.northwestern.edu

Program of African Studies

Richard A. Joseph, director | www.northwestern.edu/african-studies

Synchrotron Research Center

www.dnd.aps.anl.gov

The Northwestern Institute on Complex Systems

Julio M. Ottino and Daniel A. Diermeier, co-directors
www.nico.northwestern.edu

wonderful cultures. You also learn to appreciate what we have here in the U.S.”

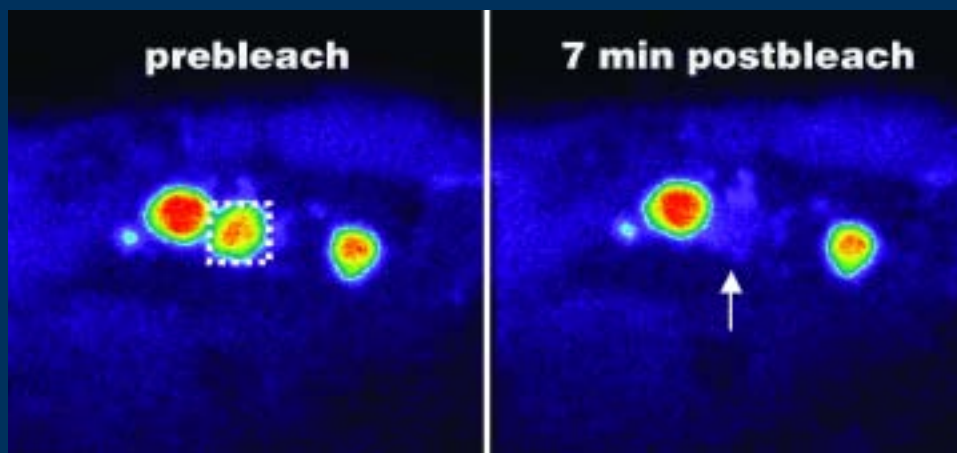
The program is supported primarily by the Nanoscale Science and Engineering Initiative of the National Science Foundation under NSF Award Number EEC-0118025. For more information about applying for an international research experience, contact Kathleen Cook (k-cook@northwestern.edu). 🌐

Molecular mechanism sheds light on neurodegenerative diseases

Millions of Americans are affected with neurodegenerative disorders, including Alzheimer's, Parkinson's, Lou Gehrig's, and Huntington's diseases. These diseases destroy neuronal function in different ways, but they appear to share some underlying molecular mechanisms. Recently, a team of researchers led by Richard Morimoto, biochemistry, molecular biology, and cell biology, discovered one such mechanism for Huntington's disease. The researchers found that the disease-causing protein – mutant Huntingtin – interferes with the activity of the proteasome, the machinery responsible for protein degradation in the cell.

The proteasome acts as a selective “garbage disposal.” It is a key player that regulates the clearance of proteins from the cell. Misfolded and otherwise damaged proteins and other proteins no longer required are eliminated by the proteasome. In certain cases, such as in the neurodegenerative diseases, the mutant disease-causing protein is not eliminated, but instead forms toxic aggregates. The reason for this is still an open question for investigators.

The Morimoto laboratory is the first to demonstrate in living human cells and in real time that aggregates of mutant Huntingtin irreversibly capture the normally highly mobile proteasomes, suggesting that the proteasomes are no longer available for protein degradation throughout the cell. The researchers discovered that the aggregating protein is inefficiently degraded and exhibits a close and stable association with the proteasome, indicating that the protein is trapped within the proteasome. The interference with the cell's degradation system results in a backlog of other proteins that should have been eliminated. The findings explain the



Fluorescence recovery after photobleaching (FRAP) analysis of the proteasome (LMP2-GFP) in a cell coexpressing mutant Huntingtin (Htt-Q65). The proteasome associated with Huntingtin aggregates is immobile, as there is no fluorescence recovery (arrow) after photobleaching of the white-boxed area.



Acceptor photobleaching experiments reveal that fluorescence resonance energy transfer (FRET) occurs between the proteasome (LMP2-CFP) and aggregated mutant Huntingtin (Htt-Q78-YFP), as indicated in the FRET efficiency image (arrow). Reprinted by permission from *EMBO Journal*, © 2004, Macmillan Publishers Ltd.

deleterious effects on the health of the cell in which disease builds over decades before symptoms occur. These results could lead to an understanding of how to prevent neurodegenerative diseases and to the development of effective drugs.

Published in “Inefficient degradation of truncated polyglutamine proteins by the proteasome.” C.I. Holmberg, K.E. Staniszewski, K.N. Mensah, A. Matouschek, R.I. Morimoto. *EMBO Journal* 23: 4307-18 (2004). This research is supported by the National Institutes of Health, Huntington Disease Society of America Coalition for the Cure, and the Daniel F. and Ada L. Rice Foundation. 🐾

CenterPiece

Office of Research
Northwestern University
633 Clark Street
Evanston, Illinois 60208-1108