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November 2006

NIEHS Spotlight

Science Notebook

Did You Know?

NIEHS Spotlight

New Clinical Research Unit to Open at RTP Campus

By Eddy Ball (with Robin Mackar)

The architect's rendering of the new facility. (Drawing courtesy of Williams-Scotsman)

Translational research at NIEHS took a major leap forward with the announcement in October of a new Clinical Research Unit (CRU) on the main campus. Construction is expected to begin early in 2007 on land that is now part of Lot F. The 11,500 square foot facility will be connected to Module F by a breezeway, and research activities there should begin in the summer. The NIEHS unit will be first of its kind at NIEHS, and it will be instrumental in helping NIEHS accomplish the goals of its Strategic Plan.

According to NIEHS Director of Translational Research William Martin, M.D., the CRU will encourage NIEHS scientists and grantees to develop protocols that will promote interdisciplinary research at various levels. "I think it's very important that the CRU become a metaphor for the changes that are happening within the institute in terms of the Strategic Plan. There's nothing quite like a building to say that we are going in a new direction."

NIEHS envisions the CRU as central in accomplishing three important goals. A clinical research program should enhance the impact of intramural research on understanding human health and disease in a "bi-directional" feedback process between basic science research and clinical research. It also will offer a model for applying basic science to problems in clinical environmental health. Finally, it will serve as a role model for extramural scientists, helping them to develop similar programs at NIEHS-supported research centers nationwide.

Initially, clinical staff at the facility will focus on environmental lung diseases such as asthma, for which there is abundant evidence of the role of exposure to air-borne materials. NIEHS researchers at the CRU will see outpatient research subjects only; the facility will not accommodate inpatient studies. The facility will offer routine subject evaluation, fluoroscopy, x-ray imaging, sample collection and processing, as well as specialized diagnostic capabilities such as pulmonary function testing, inhalation exposure, bronchoscopy and bronchial sampling.

Director of Translational Research William Martin, M.D. (Photo courtesy of Steve McCaw)

In addition to meeting the institute's immediate needs for clinical research, the facility will presage the construction of a larger clinical facility with inpatient capabilities, advanced imaging and other features. As the unit progresses, the National Advisory Environmental Health Sciences Council will advise and monitor clinical research efforts and help address questions about ways the CRU could expand beyond the institute's core competencies in pulmonary exposures and diseases. "Success in developing the latter facility, planned for some time around 2012, remains tied to our success at attracting a robust multi-disciplinary clinical scientific presence to the NIEHS campus," said Dr. Martin.

Along with the physician-scientists already on staff at NIEHS, two more have recently been recruited to staff the new facility. Dr. William Martin, himself a physician and well-known researcher in pulmonary diseases, joined the NIEHS in March 2006. Dr. Michael Fessler, also a physician-scientist who specializes in pulmonary and critical care medicine, recently joined NIEHS to serve as both a Clinical Investigator and head of the new Host Defense Group in the Laboratory of Respiratory Biology. As an example of how the basic and clinical arenas will merge to improve patient outcomes, Dr. Fessler says he will use a disease-oriented translational approach to develop clinical applications out of his group's work on the pulmonary and immune systems. A staff clinician is also being recruited to oversee day-to-day operations and management of the facility.

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NIEHS Celebrates ONES Award Winners

By John Peterson (with Eddy Ball)

NIEHS welcomed eight members of the next generation of environmental researchers on October 16 with an Outstanding New Environmental Scientist (ONES) Award ceremony in Rodbell. NIEHS Director David Schwartz, M.D., delivered a welcome address and program overview to a near-capacity audience of scientists and grant administrators. Individual ONES recipients then presented thirty-minute summaries of the research they are undertaking in a program moderated by Cellular, Organ and Systems Pathobiology Branch Chief, Pat Mastin, Ph.D.

Moderator Pat Mastin. (Photo courtesy of Steve McCaw)

When he announced the award winners in September, Schwartz emphasized the program's importance in nurturing new talent at NIEHS. "The ONES Program is designed to provide a strong foundation for outstanding scientists who are in the early, formative stages of their careers," he explained. "These grants will assist the scientists in launching innovative research programs that focus on human disease and the influence of the environment."

Totaling $3.6 million, the ONES Awards are part of an NIEHS initiative to bridge the gap between research in the basic sciences and applications in human health. As a component of the Strategic Plan, the awards will stimulate interdisciplinary research into diseases with close links to environmental exposures by recruiting and training the next generation of environmental scientists. By identifying exposures, biological impact and the interplay of genetics with environment, researchers will improve understanding of the risks of exposure to selected environmental agents, factors which make some populations more susceptible to developing disease than others, and potential interventions in the mechanisms of disease processes.

Grants were awarded to scientists engaged in research related to human disease. The titles of individual studies themselves reflect the increasing emphasis in NIEHS research on taking research from the laboratory bench into the development of preventive and treatment interventions to improve human health. The grants will support the eight researchers over a five-year period as they conduct their studies.

The eight awardees are pursuing research with promise of preventive and clinical applications:

Dr. Schwartz had questions for each of the ONES winners. Behind him, ONES winners Gokhan Multu and Donna Zhang listen. (Photo courtesy of Steve McCaw)

- Donna D. Zhang, Ph.D., University of Arizona, will study the mechanism by which cells protect themselves from the toxic effects of arsenic, a highly poisonous metal that can cause DNA damage and lead to an increased risk for certain cancers. "*The Protective Role of Nrf2 in Arsenic-Induced Toxicity and Carcinogenicity*"

- Thomas J. Begley, Ph.D., State University of New York at Albany, will examine the way in which damage to DNA from environmental exposures can trigger the production of certain proteins that help protect the cell from toxic agents. "*The Roles of Trm9 and tRNA Methylation in the DNA Damage Response.*"

- Patricia Lynn Opresko, Ph.D., University of Pittsburgh, will explore the effects of environmental agents on telomeres, small segments of DNA located at the ends of chromosomes, which help control aging and death of cells. "*Mechanisms of Telomeric DNA Loss and Repair.*"

- Sven-Eric Jordt, Ph.D., Yale University, will study the way in which certain airborne pollutants interact with sensory nerve cells in order to produce eye, nose and throat irritation. "*TRPA1 Channels in Sensory Neurons as Targets for Environmental Irritants.*"

- Michelle L. Bell, Ph.D., Yale University, will study the relationship between outdoor concentrations of ozone, a form of oxygen that is a primary component of urban smog, and the incidence of respiratory disease and death in exposed populations. "*National Assessment of the Mortality and Morbidity Effects of Tropospheric Ozone.*"

- Stephania A. Cormier, Ph.D., Louisiana State University, will conduct research on fine particle air pollution - microscopic particles of dust and soot less than 2.5 microns in diameter - to determine whether exposure to these tiny particles can produce changes in immune system function that could result in an increased risk for developing asthma. "*Combustion Generated PM0.1 and Predisposition to Asthma.*"

- Michael Borchers, Ph.D., University of Cincinnati, will examine the relationship between exposure to airborne chemicals from vehicle exhaust and industrial sources, and increased susceptibility to respiratory illnesses such as emphysema and chronic obstructive pulmonary disease. "*Shared Mechanisms of Pulmonary Lymphocyte Activation by Bacteria and Toxicants.*"

- Gokhan M. Mutlu, M.D., Northwestern University, will study the effects of fine particle exposure on blood flow and heart disease risk. "*Mechanisms of Airborne Particulate Matter Induced Thrombosis.*"

Following the morning presentations, ONES award winners gathered outside for photo. Shown (left to right) are Gokhan Multu, Stephania Cormier, Patricia (Patty) Opresko, Sven Jordt, Michael Borchers, Donna Zhang, Michelle Bell and Thomas (Tom) Begley. (Photo courtesy of Steve McCaw)

Following their presentations, the ONES recipients had lunch with DERT program administrators and met with DIR scientists engaged in investigations related to their research.

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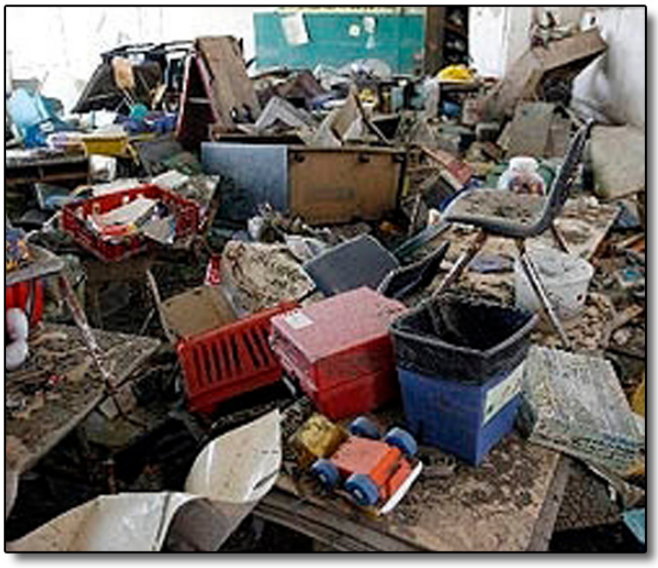
NIEHS to Help New Orleans HEAL

By Eddy Ball

In August 2005, the world watched as Hurricane Katrina devastated New Orleans and surrounding areas, displaced over half the city's population and drove an already disadvantaged population into crisis mode. NIEHS helped New Orleans then, and the institute plans to help again with an elegantly designed clinical intervention study set to begin recruiting participants in November. The 30-month collaborative Head-off Environmental Asthma in Louisiana (HEAL) study offers scientists an unprecedented opportunity to provide immediate help for New Orleans children with persistent or uncontrolled asthma, as well as refine and develop intervention protocols for treating the condition effectively at the community level.

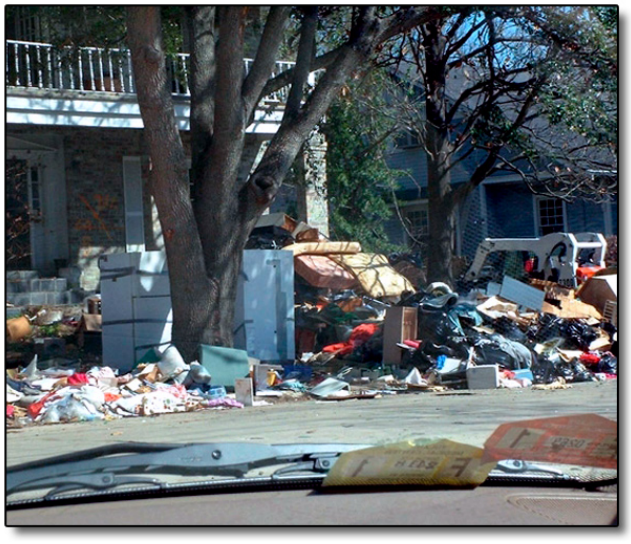


Katrina disrupted most of the city's educational infrastructure. (Photo courtesy of Tulane University researcher Sam Lehrer)

NIEHS Director for Translational Research William Martin, M.D., explained that the study builds upon what has been learned from a series of earlier studies of asthma in inner-city environments to improve the quality of intervention. "In NIH terms, this project is type two translational research," explained Martin. "It involves taking knowledge that we have learned from basic science, clinical studies and public health studies and applying it in practice to a community."

NIEHS Health Scientist Administrator Pat Chulada, Ph.D., has taken the lead in designing this study, in conjunction with health care professionals and scientists from the Tulane University School of Public Health and Tropical Medicine, the New Orleans Department of Health and private sector companies Constella Group and Rho, Inc., NIEHS-funded scientists will launch a major initiative to recruit, evaluate and test a study population of children with asthma. According to Chulada, researchers are especially interested in determining how effective outreach and educational efforts can be in moderating asthmatic children's response to exposures and elucidating the genetic/environmental interactions that exacerbate the condition.

Chulada emphasized that the goal of HEAL is to implement and test an expanded Asthma Counselor (AC) intervention model, which includes a comprehensive educational role in addition to conventional case management duties. The intervention model can then be replicated in conditions similar to those in New Orleans to enhance quality and continuity of care. Put simply, the assumption is that if the interventions work in New Orleans with its extreme damage and antigen-nurturing environment by reducing symptom occurrence, the enhanced AC model will be effective almost anywhere.



Trash piles throughout the city offered roaches and other vermin a perfect environment for reproducing, increasing the allergen levels in nearby homes. (Photo courtesy of Sam Lehrer)

Using a network of screening and referral sources, HEAL will recruit and enroll at least 450 children, aged four to twelve years, for the study. In addition to age requirements, participants must meet three other inclusion criteria:

uncontrolled or persistent asthma, current long-term asthma control therapy, and a parent or legal guardian willing to provide written informed consent.

The intake process will include questionnaires and interviews, clinical examinations, training on use of peak flow meters, and testing for pulmonary functioning and allergic reactions (prick skin testing). Participating laboratories will test blood samples for IgE and IgG antibodies, with a portion of the blood archived for future genetic testing.

The environmental intervention component of HEAL will involve visits to the homes of participants. Technicians will perform visual inspection, a home environment survey, air sampling, and indoor dust and allergen collection. The study will tailor AC intervention according to each participant family's risk assessment and needs, providing training, supplies and allergen-abatement equipment to improve the home environment.

With electricity off and moisture levels high, molds proliferated in abandoned housing. Children with allergies faced levels of exposure that were higher than ever before. (Photo courtesy of Sam Lehrer).

Chulada explained that the approximately 450 participants will be divided into two groups, which will both receive referrals for access to high-quality care for their condition. In addition, one group will receive AC intervention. Researchers will examine mean maximum symptom day difference between the groups as endpoints, testing their hypothesis that the combined intervention will improve patient outcomes. At the end of the study, children in group two (the control group with no AC) will receive intervention similar to that provided to group one participants. Parents of children in both groups will participate in follow-up phone surveys for asthma morbidity.

An adjunct component of HEAL will involve two rounds of school surveys administered to approximately 1,500 families with children in New Orleans schools, public and private. The survey will help analysts assess post-Katrina living conditions and stress levels of the families and establish the prevalence of children with asthma.

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NIEHS Library Initiatives to Aid Researchers

By Dav Robertson

The "digital revolution" has brought profound changes to the creation, organization and delivery of information, especially in the scientific realm. It is in this context of a changing technological world that the library is adopting new service models that not only take advantage of these technological advances, but also use staff expertise in targeted research areas.

Last year the library conducted a Needs Assessment Survey for library and information services. As a result of survey responses and discussions from focus groups, the NIEHS Library and Information Services Branch (LISB) has developed an exciting new vision and future direction.

In the upcoming months the LISB will begin implementing three new initiatives to meet the information needs of NIEHS staff. More details will be forthcoming regarding each of these programs.

Digital Library

The trend toward increased use of electronic resources is leading the library to enhance its "virtual" presence and reduce its print collection. Currently, NIEHS staff have electronic access to 4800+ journals and 150+ e-books. The Library will be increasing its partnership with the NIH Library to continue to build the online collection and streamline online reprint requests and delivery. The LISB will also provide more training opportunities on how to effectively use these resources.

The print collection will be reduced and arranged on new compact shelving. More details will be announced soon regarding the shelving installation and what it will mean for access to the library.

By expanding its online books and journals and introducing compact shelving for the remaining print collection, the library will conserve space and increase available resources for research at NIEHS. (Photo courtesy of Steve McCaw)

"Embedding" a Librarian in the Research Team

The library is creating, on a pilot basis, a Research Team Librarian. This concept of a librarian as an integrated member of the research team is similar to a journalist "embedded" with the troops or a clinical librarian on rounds. By participating in lab meetings, journal clubs and other group events, the librarian gains a better understanding of the context of the research. As a result, he or she can more effectively respond to the group's information needs and impact the process of scientific discovery. For further information, contact Larry Wright or Stephanie Holmgren (541-3426).

Senior Investigator Stephanie London, M.D., and Biomedical Librarian Stephanie Holmgren, M.S.L.S., demonstrate one of the ways the NIEHS Library is evolving to meet the needs of researchers. The Library's reference staff will be "embedding" themselves in research teams to enhance the information available to investigators for scientific discovery. (Photo courtesy of Steve McCaw)

Research Informatics

Finally, the survey indicated the need for a Ph.D.-level scientist with information science skills to provide service and development in the area of bioinformatics, computational biology, -omics, etc. This person would work in close collaboration with the National Center for Biotechnology Information at the National Library of Medicine. While the position is still in development, some of the proposed services being considered include resource consultation and development of predictive software, among others. An advisory group is being formed to craft this informatics position. Scientists who would like to participate should contact Dav Robertson (541-3426).

First Annual NIEHS Library Open House

We're gearing up for our first Open House. Join us for

Used Book Fair

Database Demos
QUOSA
Scopus
Web of Science (new version)

and lots more!
Date and time
to be announced soon!

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Extramural Researchers Honored

By Eddy Ball

Beate Ritz, winner of the Robert M. Zweig, M. D., Memorial Award. (Photo courtesy of University of California Los Angeles)

In two separate ceremonies on October 12, extramural grantees Beate Ritz, M.D., Ph.D., and Beverley Wright, Ph.D., were honored with prestigious awards for their extraordinary contributions to environmental health and justice. In Los Angeles, Ritz, an epidemiologist at the University of California Los Angeles, received the Robert M. Zweig, M.D., Memorial Award from the South Coast Air Quality Management District (AQMD), the air pollution control agency for Orange County and the urban portions of Los Angeles, Riverside and San Bernardino counties. Wright, a professor of sociology and the founding director of the Deep South Center for Environmental Justice (DSCEJ) at Dillard University in New Orleans, was honored in Scottsdale, Ariz. with a $120,000 National Robert Wood Johnson Gulf Coast Community Health Leadership Award.

AQMD praised Ritz for her work on the effects of air pollution on infants and fetuses in the South Coast Air Basin of southern California, a nearly 7,000 square mile non-desert area populated by approximately 15 million people. Her most recent study, supported by an NIEHS grant, investigated the possible links between pollutants and infant deaths in cases recorded between 1989 and 2000. The research examined both short-term (weeks before death) and longer-term (one to six months before death) exposures to specific air pollutants in 19,664 infant deaths. William A. Burke, Ed.D., chairman of AQMD's Governing Board, described Ritz and the other two top award winners as "our community's progressive leaders who have made a commitment to healthy air quality."

The award is especially meaningful to Ritz because it recognizes her career-long commitment to preventive medicine. As a young medical student at the University of Hamburg, Germany, Ritz had already realized her vocational mission. "I was less interested in taking care of sick patients," she said, "than in learning why they had become sick in the first place." After immigrating to America, she pursued advanced degrees at the UCLA School of Public Health and became an occupational and environmental epidemiologist. In addition to her NIEHS-supported work in air quality and respiratory health, Ritz is co-director of the UCLA Center for Gene-Environment Studies in Parkinson's Disease, also funded by NIEHS.

Beverly Wright (left) received the special Robert Wood Johnson Gulf Coast Community Health Leadership Award from Judith Stavisky, Senior Program Officer, the Robert Wood Johnson Foundation. (Photo courtesy of Susan Laine)

Wright's Community Health Leadership Program (CHLP) award recognizes her contributions in the aftermath of Hurricane Katrina. While working from temporary headquarters in Atlanta and Baton Rouge, Wright coordinated recovery efforts for her city and pressed for services to help poor residents. A Katrina evacuee who experienced great personal loss, Wright worked tirelessly to inform agencies involved in providing aid and recovery efforts about the seriousness of the disaster and to raise awareness of the environmental justice issues involved.

For the past ten years, she has administered NIEHS-funded minority worker training (MWT) programs and brownfields minority worker training programs with exceptional job placement rates. Administrators of the NIEHS Worker Education and Training Program praised the high level of collaboration and grass roots involvement in the "Safe Way Back Home" project conducted by the DSCEJ under her leadership and the United Steelworkers of America, who provided safety and health training for residents and workers striving to rebuild an East New Orleans neighborhood. In 2006, she co-authored the Russell Sage Foundation report on the disaster, "In the Wake of the Storm: Environment, Disaster, and Race After Katrina."

Wright was one of five recipients who each received $105,000 to continue their work, in addition to a $15,000 personal award. In presenting the awards, CHLP Director Catherine Dunham, Ed.D., underscored the importance of grass roots efforts to help victims of the disaster. "Last summer's devastating hurricanes brought into focus for all Americans the gaping holes in this country's safety net," she said. "It reinforced what we know to be true[,]… that local leaders taking the initiative are really the first and best responders. They deserve this special award as recognition of their extraordinary contribution to the recovery effort."

Both AQMD and CHLP have a history of recognizing accomplishments in the areas of environmental health and justice. 2006 marks the eighteenth year that South Coast AQMD has presented Clean Air Awards for outstanding contributions to air quality in the region. CHLP awards $1.2 million each year to health leaders who have surmounted substantial obstacles to improve the health of their communities. Since 1992, the program has distributed 140 awards in 47 states, Washington, D.C. and Puerto Rico.

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Parkinson's Researchers Hold Annual Meeting

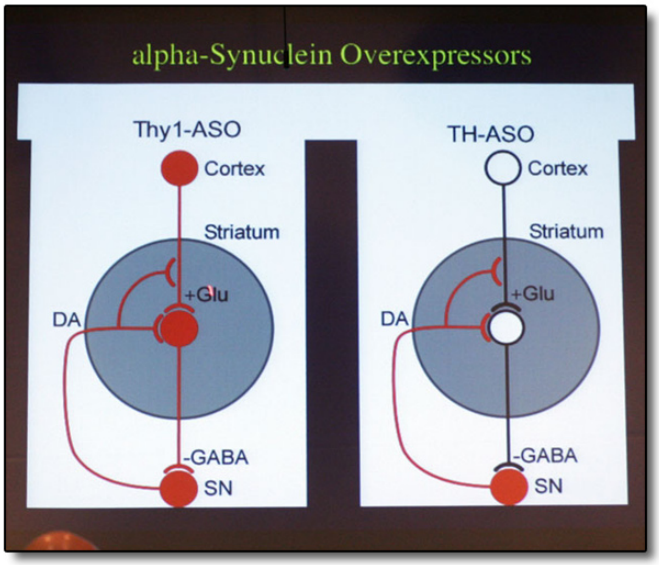
By Eddy Ball

On October 4, NIEHS hosted the annual meeting of the Collaborative Centers for Parkinson's Disease Environmental Research (CCPDER) Consortium at Rodbell A Conference Center. The consortium is composed of NIEHS-sponsored principal investigators affiliated with centers at Emory University in Atlanta, The Parkinson Institute (TPI) and the University of California Los Angeles (UCLA). The group has gathered each year since its founding in 2002 to discuss the highlights of ongoing research into the causes, risk factors, symptoms and treatment of Parkinson's Disease (PD).

UCLA Center Co-Director Marie-Francoise Chesselet smiles as she responds to a question from a colleague. (Photo courtesy of Steve McCaw)

Four years into a five-year grant, researchers were especially concerned with communicating their accomplishments. The goals of CCPDER (pronounced "sip-der") included three main objectives:

- Identifying genetic and environmental factors that interact to contribute to development of PD;
- Achieving an understanding of the mechanism of gene-environment interactions that trigger the disease processes that ultimately produce PD;
- Developing a knowledge base to enable translation of research findings into rational prevention and intervention strategies for PD.



Research by CCPDR investigators into over expression of α-synuclein may lead to interventions in Parkinson's. (Photo courtesy of Steve McCaw)

Each of the three centers presented a concise overview of the year's research, focusing on what meeting host Cindy Lawler, Ph.D., described as "breath-taking breakthroughs." Presenters described their successes in determining appropriate animal models for PD, producing PD symptom models using such environmental triggers as the pesticides Rotonone and Ziram, and studying extensively the metabolic mechanisms involved in the disease. They also discussed potentially useful interventions. According to TPI Center Director William Langston, M.D., CCPDER funding has given the centers an unprecedented opportunity to "integrate research across disciplines… [and] add strength to NIEHS programs" by drawing on the intellectual and financial resources of other groups interested in PD.

All of the principal investigators emphasized the value of the interdisciplinary research approach and the high level of collaboration the program has fostered. This spirit of cooperation inspired UCLA Center Co-Director Marie-Francoise Chesselet, M.D., Ph.D., to praise the "CCPDR synergy" that emerged. "Each of the centers has benefited from the interactions and intellectual collaboration," she said. Chesselet pointed out that PD groups throughout the country and around the world are communicating in ways they never were before.

NIEHS sponsorship helped the two California centers gain legislative approval for the California Parkinson's Disease Registry (CPDR). The CPDR will provide demographic data that may help uncover the rate of PD in the population and determine whether race, ethnicity, gender, age, environmental factors or place of residence influence the likelihood of getting the disease. In the course of developing the project, TPI and UCLA collaborated with the Parkinson's Action Network, American Parkinson's Disease Association, Young Onset Parkinson's Association, National Parkinson's Foundation, Team Parkinson and Parkinson's Resource Organization.

As investigators listened to their colleague, DERT program staff worked behind the scenes to make the meeting go as planned. Shown here is Program Analyst Mike Humble. (Photo courtesy of Steve McCaw)

NIEHS support also helped Emory investigators to collaborate with DeCode Genetics of Reykjavik, Iceland. The research project used data from over 1,000 subjects to study genes that may play a role in PD. Because of its unusually homogeneous population, Iceland was an especially promising site for the research. "Iceland's

national pastime is genealogy," said Emory's Allen Levey, M.D., Ph.D., "and the country has an accurate family tree that goes back over a thousand years." The collaboration helped researchers better understand the extent of familial clustering in late onset, idiopathic PD.

CCPDER operates under the administrative umbrella of the institute's Division of Extramural Research and Training (DERT). The consortium was inspired by a 2001 NIEHS-sponsored workshop held in Colorado Springs prior to that year's International Neurotoxicology Society's Annual Conference. The research findings and knowledge gaps identified at those meetings led the institute, then directed by Kenneth Olden, Ph.D., to formulate a five-year, $20 million grant under the Cooperative Agreement U54 Specialized Cooperative Center program award mechanism. CCPDER grants were awarded in August 2002. Currently, the grant is administered by a DERT team made up of Program Administrator Annette Kirshner, Ph.D., Program Coordinator Cindy Lawler and Program Analyst Mike Humble, Ph.D.

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NIEHS Centers - Moving Discoveries from the Bench to the Bedside

By John Peterson

At his recent meeting with the directors of the Institute's 25 Environmental Health Sciences (EHS) Core Centers, NIEHS Director David Schwartz outlined four major areas that will have the greatest impact on preventing disease and improving human health – basic science, disease-oriented research, global environmental health and training tomorrow's scientists. In order to support these and other new initiatives outlined in the NIEHS Strategic Plan, the current generation of NIEHS Centers will have a different focus – the translation of their basic science results to real-world applications with clinical benefits.

Schwartz has articulated his new vision for the centers programs. The Institute is realigning the centers to meet evolving challenges in environmental health science. (Photo courtesy of Steve McCaw)

In addition to the EHS Core Centers, which provide centralized resources and facilities that are shared by investigators with existing research projects, the NIEHS Centers Program includes 33 other centers, headquartered at major universities and medical centers, where scientists look for better ways to evaluate the impact of environmental exposures on many common diseases, including asthma and other respiratory illnesses, breast cancer, reproductive and developmental disorders, Parkinson's disease and childhood illnesses. (See text box) "Our ultimate goal is to develop clinical applications that will benefit highly-exposed populations in the United States and around the globe," said Schwartz.

A major step in this direction is the requirement that each competing core center include a core facility that will promote the translation of basic research findings into clinical or public health applications. "Some of our existing centers already have this translation requirement built into their mission statements," said Schwartz.

Another major initiative is the recent unveiling of the Institute's newest Centers program, the Disease Investigation through Specialized Clinically Oriented Ventures in Environmental Research (DISCOVER) Centers. The purpose of the DISCOVER Centers is to speed the translation of basic research results into clinical applications by bringing

together basic, clinical and population-based scientists to conduct research on the interplay between environmental and genetic factors in disease risk. The research will draw from many areas, including biomarkers, environmental genetics and genomics, patient-oriented research and epidemiology.

NIEHS has traditionally played a pivotal role in funding research on children's health, partnering with the U.S. Environmental Protection Agency over an eight-year period to support thirteen research centers devoted exclusively to children's environmental health and disease prevention. In order to identify the most effective ways of conducting research on the links between environmental exposures and childhood disease, the Institute is conducting an independent review of the many ways it can fund research on children's environmental health. "Children's health is a top priority, and NIEHS is committed to making the most of every research dollar," said Schwartz.

The Institute is also collaborating with the National Cancer Institute to fund four Breast Cancer and Environment Research Centers. The program will support research on the impact of prenatal, childhood and adult exposures that may predispose a girl to early onset of puberty, an accepted predictor of breast cancer risk. The research findings will be used to develop public health messages designed to educate young girls and women who are concerned about the causes of breast cancer, the roles played by environmental agents and the ways of reducing their exposures to these agents. The Institute is also sponsoring its third annual Early Environmental Exposures Meeting, November 2-3, 2006 in Berkeley, Calif., to allow community residents and breast cancer advocacy groups to participate in the presentation and discussion of the latest scientific findings.

Future plans also include some changes in the funding of the Institute's EHS Core Centers, where investigators with existing research grants share common resources and work on a collaborative agenda. Although the EHS Core Centers have been highly successful in supporting and promoting research on the environmental causes of disease, budgetary restrictions will result in a reduction in the number of core centers from 25 to 18 over a period of five years. "These core centers must continue to invest their research dollars into new areas and programs that will support our goals and objectives," said Schwartz.

Chief among these priorities is the Exposure Biology Program, one of two complementary research programs outlined in the Genes and Environment Initiative, a five-year, NIH-wide effort to identify the genetic and environmental underpinnings of human disease. The purpose of the program is to support the development of new technologies that will improve the measurement of environmental exposures that contribute to human disease. This program will include four new Biological Response Indicators of Environmental Stress Centers that will focus on the development of sensitive biomarkers that can reflect

NIEHS Centers Program

NIEHS Core Centers

Centers for Oceans and Human Health

Centers for Children's Environmental Health and Disease Prevention Research

Centers for Population Health and Health Disparities

Comparative Mouse Genomics Centers Consortium

Toxicogenomics Research Consortium

Breast Cancer and the Environment Research Centers

Collaborative Centers for Parkinson's Disease Environmental Research

Dietary Supplement Research Centers: Botanicals

subtle changes in inflammation, oxidative damage and other pathways that lead to disease, and the incorporation of these markers into field- and laboratory-based sensing devices.

As they prepare for the new challenges that lie ahead, the NIEHS Centers will continue to provide health educators, policy makers and the public with a better understanding of the complex relationship between environmental risk factors and human disease.

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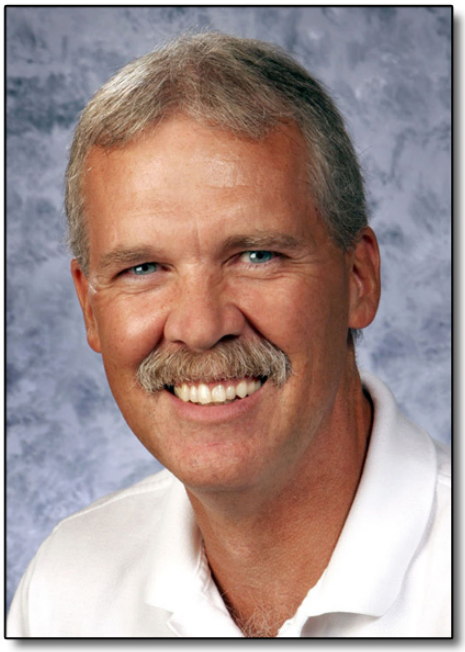
NIEHS Announces First Director's Challenge Award

By Eddy Ball



Director's Challenge Award Winner Steven Kleeberger. (Photo courtesy of Steve McCaw)

Transcending barriers in quality translational research is the overall theme of the Director's Challenge Award, a pilot program developed by NIEHS Director David A. Schwartz, M.D., that made its initial grant award in October. Laboratory of Respiratory Biology (LRB) Chief Steven Kleeberger, Ph.D., and his colleagues received the 2006 award for an interdisciplinary research program that promises to meet that objective – and set the direction for NIEHS translational studies to follow.

Kleeberger and colleagues proposed a five-year Integrative Research Program that cuts across the borders of disciplines, institutional divisions and specialties, as well as geography, culture and language, to produce an exemplary translational research model made up of three interactive projects and a training component supported by an Administrative Core. For the veteran researcher and former Johns Hopkins University professor, the award offers the satisfaction of pursuing translational research related to his long-standing interest in genetic susceptibility to respiratory diseases such as brochopulmonary dysplasia [BPD] among premature infants.

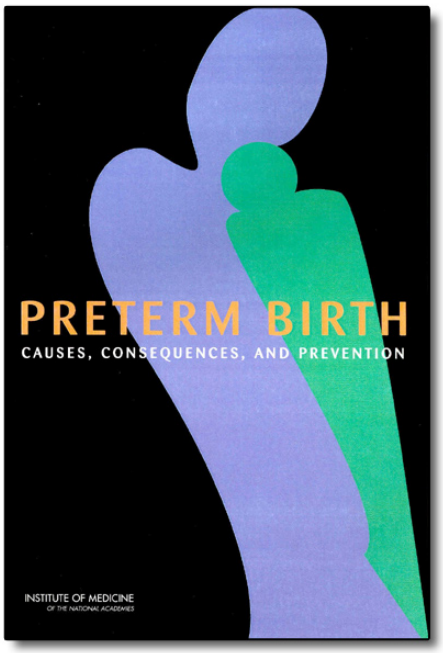
"The award allows us to bring together investigators who under normal circumstances might not be working with each other," Kleeberger explained. "We're addressing a very real public health problem with oxidant stress-induced diseases, and in the spirit of the Director's Challenge, we'll be moving forward and making some significant translational progress with BPD."

Under Kleeberger's direction, an interdisciplinary team of NIEHS scientists at main campus labs, researchers with the Pamerican Infant Translational Research Center at Johns Hopkins University and investigators at Fundacion INFANT in Buenos Aires, Argentina will collaborate in a feed-forward, feed-back process of research between basic science and clinical application. The researchers will work toward understanding more completely the role of specific genes that increase human susceptibility to oxidant stress-induced inflammatory diseases such as BPD. The program's central research interest may be respiratory biology and pulmonary conditions, such as asthma and BPD, but the results will be applicable to atherosclerosis, cancer, cardiovascular disorders and neurodegenerative diseases as well.

The interdisciplinary team's research will cross organizational divisions among labs, incorporating cell biology studies using several organisms, mouse models, genetic polymorphism, genomics, clinical research and patient samples from infants with BPD. In one component, directed by Principal Investigator Fernando Polack, M.D., of Johns Hopkins Bloomberg School of Public Health, researchers will establish a prospective cohort of 1200 case-parent triads in Argentina for the clinical component of the program.

The program will establish a highly collaborative research team uniting bench science with clinical research and patient outcomes. The team includes physician scientists, such as Polack and Co-Investigator Michael Fessler, M.D., LRB tenure-track investigator, as well as scientists representing other disciplines. DERT Program Analysis Branch Chief and Laboratory of Molecular Genetics Investigator Ben Van Houten, Ph.D., will be the Principal Investigator for a component of the study examining the role of mitochondrial reactive oxygen species in hyperoxia-induced tissue injury.

Other co-investigators from NIEHS are Laboratory of Molecular Genetics Senior Investigator Douglas A. Bell, Ph.D., Environmental Diseases and Medicine Program Biostatistics Branch Mathematical Statistician Clare Weinberg, Ph.D., and Environmental Toxicology Program and Laboratory of Molecular Toxicology Senior Investigator Rick Paules, Ph.D. Investigators will also collaborate with researchers at Duke University, the University of North Carolina, North Carolina State University and the University of Buenos Aires.



Kleeberger's project presentation included this compelling graphic from a new Institute of Medicine study on preterm birth. The image added aesthetic appeal to the proposal for addressing brochopulmonary dysplasia among preterm infants. (Cover graphic courtesy of Steve Kleeberger)

Supporting the program is an Administrative Core coordinated by Kleeberger, Bell and Administrative Support Specialist Sharyn Rigsbee. Office of the Scientific Director Program Director Joan Packenham, Ph.D., worked closely with Kleeberger in designing the program and will provide grant management services during its five years of funding. The training component of the program will recruit and train doctoral students and post-doctoral fellows in the area of translational research.

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Science Notebook

Distinguished Lecturer Outlines Hypertension Breakthrough

By Eddy Ball

On October 10 in Rodbell Auditorium, University of California at Davis Distinguished Professor Bruce Hammock, Ph.D., delivered the second talk in the Distinguished Lecture series. In a lecture titled "Herbicides to Hypertension: The Soluble Epoxide Hydrolase [sEH] as a Therapeutic Target for Hypertension, Inflammation and Analgesia," Hammock summarized a discovery process that he described as "circuitous and serendipitous," leading to the development of what could be the next generation of treatment for hypertension and inflammation in humans.

Bruce Hammock engaged the audience with his wit as he described his journey from caterpillars to people in a quest to understand the role of soluble epoxide hydrolase in insect and human metabolism. (Photo courtesy of Steve McCaw)

Hosted by William Suk, Ph.D., the lecture took an audience of NIEHS and local area scientists from Hammock's basic scientific research sponsored by a Superfund grant into insect control and xenobiotic metabolism to anticipated applications of sEH inhibitors in human health that may soon enter Phase Ia/Ib clinical trials. "I hope I can entertain you," Hammock told his audience at the start of the lecture, "with a nice story that goes from two aspects of very fundamental science towards something I think is getting very, very close to potentially helping patients."

With the NIEHS grant he received in 1973, Hammock began to study epoxide hydrolases (EH), enzymes that degrade xenobiotics and help keep people alive by rendering epoxides in pesticides and combustion byproducts less harmful. The early research discovered two forms of EH, microsomal and soluble, and the possibility that the soluble form might have a biological role. Hammock performed his early research on mice, which have high levels of sEH, rather than rats, which have very low concentrations of the enzyme. Because of its role in detoxification, Hammock and his colleagues found sEH in the liver, but they also discovered an unexpected distribution pattern of sEH outside the liver. High concentrations of the enzyme were found in the vascular endothelium, where sEH impacted vasodilation and inflammation.

By manipulating the transitional stage of sEH metabolism, Hammock soon discovered that preserving fatty acids in epoxide form could influence the course of the arachidonic acid cascade, shifting it from the production of inflammatory compounds to the production of anti-inflammatory compounds. He discovered that sEH inhibitors improved an organism's response to endoxins, such as lipopolysaccharides, by helping to maintain blood pressure at normal levels, enhancing airway response by down-regulating inflammation and acting to reduce pain perception. In a series of recent studies, Hammock and colleagues, including NIEHS Senior Investigator Darryl Zeldin, have demonstrated the therapeutic benefits of sEH inhibition and explored the synergistic effects of sEH inhibitors in combination with COX inhibitors. They also have identified one genetic polymorphism, K55R, that is associated with higher levels of sEH in affected individuals.

Over the course of his lecture, Hammock acknowledged the importance of NIEHS grants in his discovery process. "The work has been funded probably 10 percent by the Department of Agriculture and 90 percent by NIEHS," he explained. However, now Hammock faces the drug-development "valley of death," the funding gulf that stretches from government-sponsored pre-clinical research with laboratory animals to the initiation of human clinical trials funded by pharmaceutical manufacturers and venture capitalists.

LPC Supervisory Pharmacologist John Hong (left), LMC Tenure Track Investigator Paul Wade and LPC Pharmacologist Joyce Goldstein listen to Hammock's explanation of soluble epoxide hydrolase metabolism. (Photo courtesy of Steve McCaw)

An author of more than 625 peer-reviewed articles, Hammock is a leader in his fields of research. He was elected to the National Academy of Sciences in 1999 and has received a long list of awards and recognitions for his achievements. He has received the Frasch and Spencer Awards of the American Chemical Society and the Alexander von Humboldt Award, one of the most prestigious in the field of agriculture. If Hammock's work with sEH inhibition lives up to its promise of what he called "the first new target for anti-hypertension in twenty years," his work may emerge as a major contribution to the prevention of hypertension and its pathological effects throughout the body.

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New Exposure Biology Grants, Intramural and Extramural

By John Peterson

For the first time in NIEHS history, application eligibility for new extramural research grants includes scientists working in the Division of Intramural Research, in addition to researchers outside the institute. The new Exposure Biology Program request for applications, announced in mid-October, offers $74 million in grant opportunities for the development of new technologies that will improve the measurement of environmental exposures contributing to human disease. "Any individuals with the skills, knowledge and abilities required to carry out the proposed research, including scientists who work in NIH laboratories, are encouraged to submit an application for participation in the program," explained Brenda Weis, Ph.D., senior science advisor at NIEHS and program coordinator for the Exposure Biology Program.

The three grant opportunities will support research to develop portable, easy-to-use sensing devices that will accurately measure personal exposure to a wide variety of chemical and biological agents. The grants will also support the development of sensitive biomarkers, based on subtle changes in DNA structure, proteins, metabolites and other molecules that will enable scientists to study how the body responds to environmental stress.

Applicants should submit letters of intent no later than November 22, 2006 and applications by December 22. Peer review will take place during March and April 2007, with council review scheduled during May. The earliest anticipated start date for approved applications is July 2007.

The institute held an information meeting and videoconference on October 20 to allow potential applicants to obtain information and clarify any questions about the funding opportunities, which are part the Gene and Environment Initiative. Detailed information about the meeting and the new grant opportunities is available at the Exposure Biology Program website.

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Extramural Guest Lecturer on PD Risk Factors

By Eddy Ball

As part of the Laboratory of Pharmacology and Chemistry (LPC) 2006-2007 Seminar Series, Donato Di Monte, M.D., director of basic research at The Parkinson Institute (TPI), spoke on October 5 in F-193. Following an introduction by Host John Hong, Ph.D., supervisory pharmacologist in the LPC, Di Monte presented to a standing-room-only audience of NIEHS scientists his latest research findings on "Risk Factors for Human Parkinsonism: Clues from Experimental Work."

Extramural Guest Lecturer Donato (Dino) Di Monte. (Photo courtesy of The Parkinson Institute)

For several years, Di Monte, an internist with advanced training in toxicology and biochemistry, and his colleagues have been elucidating the mechanisms of toxicant-induced neuron damage. They have used models of Parkinson's Disease (PD) triggered by exposures to MTPT, an industrial toxin and by-product of street-lab drug production, and the pesticides Rotenone and Paraquat. Their findings in cellular, rodent and non-human primate studies show promise in the search for risk factor analysis, early warning and intervention.

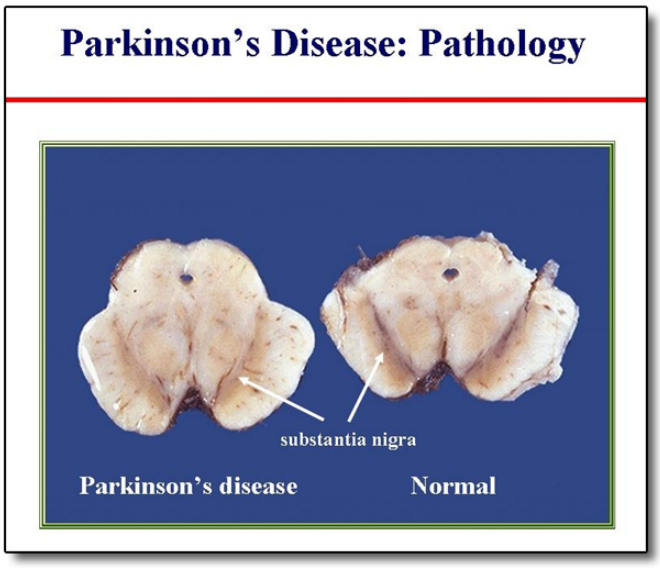
Epidemiological data indicate that risk for PD is age- and gender-dependent, with men more than two times as likely as women to develop the disease. Early onset of the disease is relatively rare, but incidence begins to spike at age 50 and continues to rise later in life. Di Monte and other PD researchers have hypothesized that early events may with time predispose a person to develop PD, and they are attempting to identify long-term latency risk factors for early warning signs.

Animal *in vivo* models using environmental inducers of PD-like symptoms demonstrated that the numbers of neurons decrease dramatically in older animals following exposures. Depending on the toxicant used, these reductions occurred in total dopamine (DA) count or in specific types of DA receptors. Age and toxicant exposure appeared to work synergistically to produce greater damage than either does by itself.

In mice studies using Paraquat, Di Monte observed a distinct sequence of exposure that suggested what Di Monte described as a "priming" effect that could be a potential target of intervention. Initial exposure activated microglial cells, which appeared to make DA neurons more susceptible to damage from a second exposure. If clinicians can

reverse activation, as they have by administering the antibiotic minocycline, then neuron damage may be reduced or prevented.

Di Monte's studies also indicated that two other risk factors, exposure to the endotoxin lipopolysaccharide and the up-regulation of the enzyme known as NADPH oxidase, precede the neuron damage that takes place in PD. Both stimulated oxidative damage by producing lipid peroxides. Theoretically, the oxygen free radicals produced as a result create an underlying inflammatory condition that sets the stage for significant cell death and damage in the nigra straitum. Research within the TPI and in other centers has identified yet another risk factor, elevated iron levels of infant formula, and potentially protective agents, nicotine and nicotinic receptor agonists.



Parkinson's disease causes the degeneration of pigmented neurons in the substantia nigra of the brain. (Slide courtesy of Donato Di Monte)

Within the past year, Di Monte and other PD researchers have taken a special interest in a "rogue" protein in the brain, α-synuclein (SNCA). SNCA appears to be initially protective when activated, but with continued up-regulation in response to toxicant exposure, it seems to trigger cell loss. SNCA up-regulation has been linked to gene mutations and may be the first major breakthrough in establishing a genetic link in PD, which accounts for approximately 10 per cent of cases. Blocking activation of SNCA could be a potentially effective intervention for patients with the disease.

During the lecture, Di Monte expressed his gratitude for institute sponsorship, noting that "NIEHS has contributed significantly to the field [of PD research]." TPI, one of three NIEHS-sponsored centers, offers unique opportunities by combining basic research and clinical settings under one roof at its Sunnyvale, Ca. headquarters. The Collaborative Centers Program for Parkinson's Disease Research has been funded since 2002 through the NIEHS Division of Extramural Research and Training.

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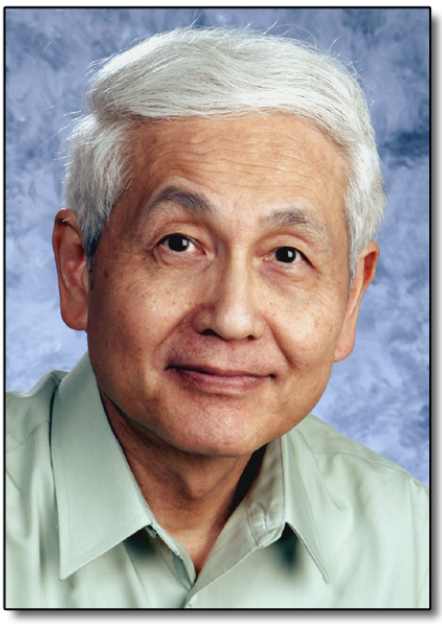
Intramural Lecturer Presents Combined Therapy Model for PD

By Eddy Ball

Laboratory of Pharmacology and Chemistry (LPC) Supervisory Pharmacologist John Hong, Ph.D., delivered a lecture on Parkinson's Disease (PD) on October 12 in F193 as part of the LPC Seminar Series. Hong, who was host for the LPC Seminar with guest lecturer Donato Di Monte the previous week, focused on the "Role of Inflammation in the Pathogenesis of Parkinson's Disease: Models, Mechanisms and Therapeutic Interventions." Introduced by Host John Pritchard, Ph.D., chief of the LPC, Hong's lecture explored a complementary model using the endotoxin lipopolysaccharide (LPS) to trigger the inflammatory cascade that induces damage to neurons in the substantia nigra. This inflammation is characteristic of PD and other neurodegenerative diseases. Experiments with the model have led Hong to develop a novel combined therapy for these disorders.

The mechanistic studies and the novel interventions Hong's lab has tested offer additional insights into PD and other diseases. The lab tested LPS treatment *in vivo* and *in vitro*, finding what Hong described as "delayed,

progressive and selective loss of dopaminergic (DA) neurons" in the substantia nigra following dosing. Hong and his colleagues found that age was an important variable in the results, with older animals experiencing a significantly greater response than younger animals to exposure.



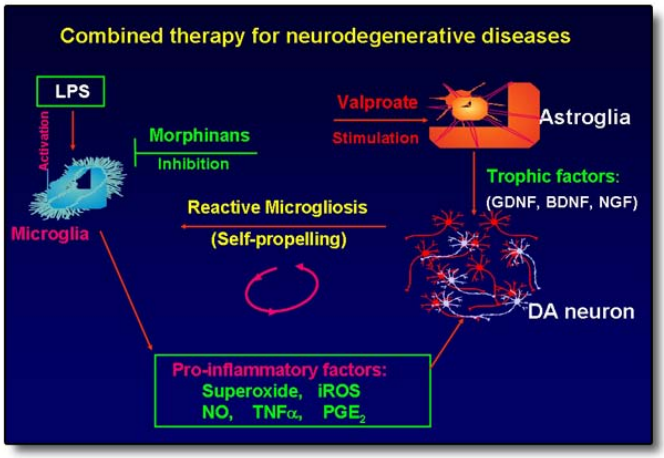
Intramural lecturer John Hong. (Photo courtesy of Steve McCaw)

Hong and his colleagues have used two types of toxins, LPS and MTPT, to study the possible mechanism underlying the progressive nature of neurodegeneration. They determined that LPS causes neuronal death indirectly through the activation of migratory nervous system cells called microglia, while MPTP can damage dopamine neuron directly. However, whether initiated by LPS or MPTP, neuronal death will cause "reactive microgliosis" to further activate microglia to release proinflammatory factors and induce further neuronal damage.

Hong's laboratory has developed a two-pronged therapy for PD. The therapy targets microglia, by inhibiting the over-production of multiple inflammatory factors and oxidative damage to neurons, and transport cells in the brain known as astroglia, by stimulating production and release of neurotrophic factors. Neurotrophic factors protect neurons by increasing their plasticity and their ability to rebound from assault by inflammatory compounds activated by the microglia.

Hong's lab built on previous research in a variety of neurodegenerative disease animal models demonstrating the neuroprotective effects of morphinans, a series of compounds that are structurally similar to morphine. Hong explored the possibility that morphinan neuroprotection was due to anti-inflammatory effects resulting from the prevention of microglia over-activation. Hong's colleagues tested several types of morphinans and finally selected an opioid receptor antagonist, naltrexone, which does not produce the pleasurable and often addicting side effects of many morphinans. Additional research demonstrated that dextromethorphan (DM), an active ingredient in cough mixtures, and its final metabolite, 3-hydroxy-morphinan, are safe, potent and inexpensive neuroprotective agents.

For the second prong of combined therapy, Hong's lab tested valproic acid (VPA), a short-chain fatty acid commonly used to treat bipolar disorder and seizures. VPA has been shown to activate cell survival factors and induce release of neurotrophic factors. Moreover, VPA promotes neuron outgrowth and DA uptake, helping neurons rebound after inflammatory insult. Hong's lab found that astroglia in the brain played a critical role in mediating VPA-induced neurotrophic and neuroprotective effects and constituted a potential target for intervention.



This slide illustrates the combined therapy model developed in Hong's lab. Morphinans inhibit reactive microgliosis while valproate stimulates production of protective factors. (Slide courtesy of John Hong)

Although the combined therapy model is still several steps away from testing in humans, it holds promise as an innovative treatment for PD and other neurodegenerative diseases. It utilizes existing therapeutic compounds that are commercially available, have few side effects and have demonstrated clinical utility. The therapy also operates both protectively, by strengthening neurons, and remedially, by down-regulating inflammatory compounds, to produce a synergetic therapeutic effect. Hong's work embodies the translational emphasis of innovative research at NIEHS in its efforts to connect basic scientific research and clinical interventions.

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DERT Papers of the Month

By Jerry Phelps

Chronic Treatment with Nicotine Protects Against Parkinsonian Symptoms in Primates

NIEHS-supported researchers at The Parkinson's Institute report that long-term oral administration of nicotine to squirrel monkeys protects against Parkinson-like symptoms induced by exposure to the dopaminergic neurotoxin MPTP. These findings mirror human epidemiologic studies that suggest that smokers are less likely to develop Parkinson's disease than non-smokers.

The primates were administered nicotine in drinking water to produce blood nicotine levels within the range seen in cigarette smokers. Laboratory results suggest that nicotine acts to restore or maintain dopamine production in the substantia nigra region of the brain. These data further support a protective role of nicotine and support future studies to explore nicotine or compounds that act similarly as possible therapeutic agents for Parkinson's disease.

Citation: Quik M, Parameswaran N, McCallum SE, Bordia T, Bao S, McCormack A, Kim A, Tyndale RF, Langston JW, Di Monte DA. 2006. Chronic oral nicotine treatment protects against striatal degeneration in MPTP-treated primates. J Neurochem 98(6):1866-1875.

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Functional MRI Demonstrates Impacts of Lead Exposure on Brain Organization

Bruce Lanphear and colleagues at the Cincinnati Children's Environmental Health Center report new findings related to childhood lead exposure. Using functional magnetic resonance imaging, they saw evidence of reorganization of the language centers of the brains of young adults with a history of childhood lead exposure.

Lead exposure is known to cause behavioral problems and learning deficits in children that persist into adulthood. The current study offers new findings that demonstrate a substantial adverse effect of lead on normal language centers and simultaneous recruitment of other brain regions. These results are among the first to suggest that lead exposure affects language ability and offer further confirmation of the deleterious effects of lead exposure on cognitive abilities.

Citation: Yuan W, Holland SK, Cecil KM, Dietrich KN, Wessel SD, Altaye M, Hornung RW, Ris MD, Egelhoff JC, Lanphear BP. 2006. The impact of early childhood lead exposure on brain organization: a functional magnetic resonance imaging study of language function. Pediatrics 118(3):971-977.

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CD63: A Tissue Inhibitor of Metalloproteinase

Previously it was thought tissue inhibitors of the enzyme metalloproteinase-1 (TIMP-1) suppressed cancer metastasis. However, subsequent clinical studies linked increased TIMP-1 expression with poor prognosis in certain malignancies, including metastatic breast cancer. This NIEHS-supported research team at Wayne State University addressed the issue by investigating the role of TIMP-1 during breast cancer progression.

Dr. Hyeong-Reh Choi Kim's laboratory was one of the first research teams to report TIMP-1 as an inhibitor of apoptosis. Since this discovery, many investigators have suggested TIMP-1 regulates cell survival through its interaction with an unknown cell surface receptor. Dr. Kim's team identified CD63 as a cell surface-binding partner for TIMP-1, which is critical for human breast epithelial cell survival.

The study team acknowledges that future studies aimed at unveiling the functions of TIMP-1 at the molecular level would greatly enhance the understanding of breast cancer progression. This information may also be useful in designing other interventions.

Citation: Jung KK, Liu XW, Chirco R, Fridman R, Kim HR. 2006. Identification of CD63 as a tissue inhibitor of metalloproteinase-1 interacting cell surface protein. EMBO J 25(17):3934-3942.

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DIR Papers of the Month

By Eddy Ball

High BMI and Male Infertility

In what may be the first study of its kind, scientists in the NIEHS Epidemiology Branch have found a significant correlation between reduced couple fertility and male obesity or overweight status. Previous studies have found diminished semen quality and hormone alterations among men with high body mass index (BMI), and overweight men may be at a greater risk of erectile dysfunction – all contributors to reduced fertility. However, to the researchers' knowledge until this NIEHS-sponsored study, which appeared in the September issue of *Epidemiology*, no researchers had presented data regarding the effect of male obesity and overweight on couple fertility.

This analysis of fertility data from the Agricultural Health Study on 2,111 couples supports the hypothesis that the obesity epidemic is associated with the personal and societal costs of male infertility and its treatment. If confirmed in subsequent studies, these results may offer an added incentive for men to make efforts to reduce weight.

Citation: Sallmen M, Sandler DP, Hoppin JA, Blair A, Baird DD. 2006. Reduced fertility among overweight and obese men. Epidemiology 17(5):520-523.

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Transcription Factor for Lung Inflammation

Investigators in the NIEHS Laboratory of Respiratory Biology, in collaboration with researchers from Duke University and the Durham Veterans Administration Medical Center, have identified a type II transcription factor, interferon-gamma (IFN-γ), that plays a critical role in the lung's response to inhaled endoxin. The research team evaluated wild type and IFN-γ-deficient mice exposed to the endoxin lipopolysaccharide (LPS), which is known to result in predictable inflammation of the lower respiratory tract. Appearing in the October issue of the *American Journal of Physiology-Lung Cellular and Molecular Physiology*, the study determined that complex transcriptional response to LPS, involving expression of many genes, is modified and regulated by other molecules, such as IFN-γ.

By identifying the role of the critical signaling molecule IFN-γ in LPS-induced inflammatory lung disease, this study has identified potential targets for pharmacological intervention to modify the progression and severity of such diseases as asthma, atherosclerosis and diabetes, which are associated with dysregulation of Nuclear Factor Kappa Beta and other transcription factors.

Citation: Burch LH, Yang IV, Whitehead GS, Chao FG, Berman KG, Schwartz DA. 2006. The transcriptional response to lipopolysaccharide reveals a role for interferon-γ in lung neutrophil recruitment. Am J Physiol Lung Cell Mol Physiol 291(4):L677-682.

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Soluble Epoxide Hydrolase and Cardiac Function

In a study published in the August issue of *Circulation Research*, a DIR-funded research team investigated the role of the enzyme soluble epoxide hydrolase (sEH) in recovery of heart contractile function following ischemia, which occurs during a heart attack. The investigators examined hearts of sEH knockout mice and wild type controls at baseline and following ischemia. They measured the abilty of hearts to contract and determined that hearts from sEH knockout mice recovered better function than hearts from control mice after ischemia. Moreover, the study found that disruption of the sEH gene resulted in increased availability of epoxyeicosatrienoic acids (EETs), endogenous fatty acids that are potent vasodilators and cardioprotective factors, by interrupting their conversion to less active downstream metabolites. Researchers also demonstrated that treatment with an EET-antagonist abolished the improved functional recovery following ischemia in sEH knockout hearts, indicating that the cardioprotective effects were mediated by EETs in this model.

The study's results suggest the possibility that sEH inhibition may represent a novel approach for the treatment of cardiac dysfunction associated with heart attacks.

Citation: Seubert JM, Sinal CJ, Graves J, DeGraff LM, Bradbury JA, Lee CR, Goralski K, Carey MA, Luria A, Newman JW, Hammock BD, Falck JR, Roberts H, Rockman HA, Murphy E, Zeldin DC. 2006. Role of soluble epoxide hydrolase in postischemic recovery of heart contractile function. Circ Res 99(4):442-450.

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BMP Signaling and Embryonic Development

In a collaborative study involving DIR investigators from the Laboratory of Reproductive and Developmental Toxicology and the Duke University Medical Center Department of Cell Biology, researchers examined the mechanism of bone morphogenetic protein (BMP) signaling in the development of mouse embryonic tissues (or organs) known as somites, which will form the vertebral column and segmented musculature of the developing organism. Published in the August issue of *Development*, the study reports on experiments with genetically altered mice that have modified expression of the gene *Bmpr1a*, demonstrating the critical role of BMP signaling, as well as its antagonistic relationship with fibroblast growth factor signaling in recruiting prospective cells correctly and directing normal somite development.

This research into mouse embryonic development may ultimately provide insight into the prevention of birth defects and failed embryonic development in humans.

Citation: Miura S, Davis S, Klingensmith J, Mishina Y. 2006. BMP signaling in the epiblast is required for proper recruitment of the prospective paraxial mesoderm and development of the somites. Development 133(19):3767-3775.

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Did You Know?

Party Time for Kids in Cincinnati Children's Study

By Eddy Ball

The Cincinnati Childhood Allergy and Air Pollution Study (CCAAPS) concluded its five-year study of the role of diesel exhaust particles (DEP) and allergy on a fun note by throwing a picnic and party for participants. The October 7 event was held at the Cincinnati Zoo and featured activities and puppets. It was the study's way to thank participants and their parents and remind them to comply with treatment plans and attend follow-up visits.

Funded by an NIEHS grant administered through DERT, the study focused on children living in the Cincinnati metropolitan region, where three interstate corridors intersect creating one of the busiest U.S. north/south and east/west commercial truck routes converging on a population of 1.9 million. The conversion of the three interstates causes traffic volumes to be one of the largest in the country. Researchers sought to determine if infants

Larger than life-size puppets take the stage for the picnic and party at the Cincinnati Zoo. (Photo courtesy of CCAAPS)

who are exposed to DEP via truck exhaust are at an increased risk for atopy and atopic respiratory disorders. They also wanted to determine if this effect is magnified in a genetically at risk population. According to CCAAPS, results of this study may ultimately result in finding a preventable cause of atopic disorders in children.

According to Epidemiologist Grace LeMasters Ph.D., principal investigator of the study, CCAAPS has made significant progress in identifying genetic and environmental influences on atopy and atopic respiratory disorders during early childhood. The study has led to greater understanding of the pathophysiology and provided more insight into the development of preventative measures for these common childhood disorders.

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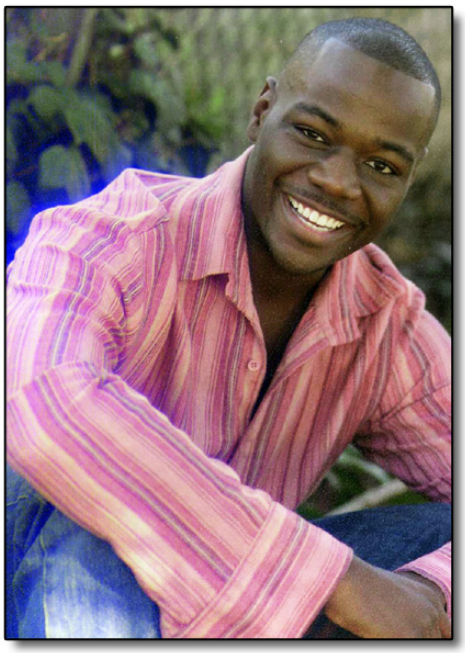
Durham Native Tours in Broadway Show

By Eddy Ball



Chris Lewis had his opportunity to serenade Nala before packed houses in Raleigh. (Photo courtesy Terry Lewis)

NIEHS employee Terry Lewis is a mom with good reason to be especially proud of her son during the Raleigh performances of the Broadway musical "Lion King." Durham native and Riverside High graduate Chris Lewis is a member of the Gazelle Company, which performed the musical to record crowds at Memorial Auditorium. He has been living his high school dream after landing a role as the understudy for the lead character Simba and member of the ensemble. Chris took over the role when S.J. Hannah went on vacation in late October.

A program assistant in the DIR Office of the Scientific Director, Terry Lewis spent five and a half weeks in September and October watching fellow employees make the connection between the shy mom and her handsome, talented son. "I told a few people when I found out Chris was coming [to the Triangle]," she said, "and the news began to spread like wildfire."

With his time in the limelight, Chris has already accomplished more than most performers. Now that he has a national tour to his credit, there's no telling how far Chris' talents will take him.

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(L to R) S.J. Hannah as "Simba" and Chauntée Schuler as "Nala" embrace in "Can You Feel The Love Tonight" from THE LION KING National Tour. ©2006, Disney. Photo Credit: Joan Marcus. (Photo courtesy of Rachel Gragg, Broadway Series South Press Representative)

Dancing Warriors Rock NIEHS

By Eddy Ball

The usually staid and heady Rodbell Auditorium filled with music, grunts and the sound of flesh hitting flesh and wood on October 10, as instructors and advanced students from the White Tiger TaeKwonDo School in Cary presented a special demonstration at NIEHS. Sponsored by the Fitness and Wellness Committee, the event gave NIEHS folks a chance to see what discipline and patience can do for young people.

Justin Chang and Harrison Lee (in glasses), prepare to confront one of the White Tiger instructors. (Photo courtesy of Steve McCaw)

According to school representatives and contrary to the pop images of film and television, martial arts are actually a form of mental, as well as physical training, and the goals of TaeKwonDo are the building of self-esteem, emotional control and respect for others. Self-defense, though an important consideration for kids when they sign up, is not really the central aim of the martial arts program.

"A lot of kids sign up for TaeKwonDo to become a Jackie Chan or a Crouching Tiger," explained Fitness Room Manager Stephanie Bullock-Allen. "But they soon discover that it takes much more physical effort than it looks on TV." Bullock-Allen schedules these kinds of events with one goal in mind: getting kids off the couch and away from the TV and computer screen long enough to learn how to enjoy exercise. Judging by the choreographed performance and airborne antics in Rodbell, her plan seems to be working. One of the performers, Justin Chang, is testing for his second-degree black belt, along with his friend, Harrison Lee. He is the son of Research Fellow Hye-Youn Cho of the Laboratory of Respiratory Biology.

Harrison Lee is airborne as he breaks a board with a disciplined kick. (Photo courtesy of Steve McCaw).

Justin and Harrison take their bows to the applause of their instructors and their audience. (Photo courtesy of Steve McCaw)

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Good Books at Good Prices

By Eddy Ball

Every fall and spring, the NIEHS Fitness and Wellness Committee puts a little twist on its recreational theme by sponsoring a two-day Book Fair to help employees exercise their minds as well as their bodies. This fall's event on October 11 and 12, like earlier Book Fairs, gave employees a chance to do some early shopping for solstice season celebrations – or just spend some free time looking for new hardcover books at discounted prices.

The Book Fair drew browsers and shoppers to the D-module mall. (Photo courtesy of Steve McCaw)

Because the vendor, Books Are Fun, a division of Reader's Digest, gives 10 percent of sales back to its sponsoring organization, the event was also a time for Program Manager Diane Crawford, Fitness Room Manager Stephanie Bullock-Allen and Fitness Specialist Jennifer Cordone to pick up some additional funds for incidental expenses and, most importantly, incentive prizes for such programs as the "Biggest Loser" competition.

Occupational Health Nurse Lindia Engram spent part of her lunch hour checking out new books. (Photo courtesy of Steve McCaw)

Visitors at the Book Fair browsed shelves in D-module filled with items priced as much as 70 percent less than retail. The event featured many books, puzzles, learning toys and games for children and young adults, in addition to best sellers, cookbooks, coffee table books and special interest titles for adults. The Fair also offered a selection of music CDs, DVDs, knick-knacks and book-related items.

Books Are Fun operates book fairs for schools and several area businesses and organizations, such a Sygenta, Rex Hospital and Duke Children's Hospital. According to company representative Sharon Bobbitt, organizations with 300 or more employees can sponsor book fairs with Books Are Fun, which operates from a warehouse in Raleigh. A ten-year veteran of the company, Bobbitt looks forward to the fairs as a break from her usual job as a contract accountant. "It's given me a chance to see people I've met year after year," she said. "I also get a chance to see what the books look like and discover what's new."

After working the Book Fair for a few years, Books are Fun representative Sharon Bobbitt has become a familiar face to NIEHS employees. (Photo courtesy of Steve McCaw).

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Program Manager Discusses Reasonable Accommodation

By Eddy Ball

As part of Disability Awareness Month activities, NIH OEODM Disability Program Manager Carlton Coleman addressed a group of NIEHS employees October 17 in Rodbell C. His talk, titled "Reasonable Accommodation in the Workplace," addressed the diverse needs of his mixed audience. Coleman spoke to the concerns of employees with physical and mental challenges, employee advocates, and individuals in management positions or with aspirations to join the ranks of management.

Speaker Carlton Coleman. (Photo courtesy of Steve McCaw)

DIR Administrative Officers Bruce Wiggins, Cindy Garrard and Lisa Rogers listen as Coleman makes a point about what is "reasonable" in terms of accommodations for employees with handicaps. (Photo courtesy of Steve McCaw)

Coleman began his talk with an overview and examples designed to sensitize the audience to the hierarchy of needs experienced by people with disabilities. "People want to be seen as people first — not as their disabilities," he said. An amputee as the result of a freak accident when he helped a stranded motorist one night, Coleman spoke from experience. "I thought nothing could happen to me," he observed. "Then suddenly I was in a hospital fighting for my life."

Coleman became one of the one out of seven people who find themselves disabled at some point in their lives. As he adjusted to using a wheelchair. Coleman discovered that one of his biggest challenges involved changing the attitudes of people who saw the chair first, and the man second. Noting the mounting casualties in the war in Iraq, Coleman observed that many of the men and women saved from death by advanced medical care there will come home with disabilities and face many of the same problems that he has encountered.

After the talk, Coleman discussed an individual question with Terry Nesbett, an administrator with the DERT Scientific Review Branch. (Photo courtesy of Steve McCaw)

The talk included advice for managers about current definitions of disability and reasonable accommodation. Coleman also gave people with disabilities advice about working with doctors to get the correct documentation for requesting reasonable accommodation and changes in status. He brought along information from the Department of Labor website on disabilities and government regulations. After the presentation, Coleman talked individually with several NIEHS employees with concerns or questions.

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Upcoming Distinguished Lecture

By Eddy Ball

Douglas R. Green, Ph.D., will deliver the Falk Lecture on November 14 at 2:00 PM on "Apoptosis: The Paths of Perdition." Green is the chair of Immunology at St. Jude's Children's Research Hospital in Memphis and Peter C. Doherty Endowed Chair of Immunology.

Apoptosis, or programmed cell death, is the body's way of fragmenting cells for elimination. In an *Essential Science Indicators Special Topics Interview*, Dr. Green explained the importance of understanding the process of apoptosis. "Apoptosis affects every cell type and organ system; it is an important part of normal development and homeostasis, and the major protection from spontaneous cell transformation leading to cancer," he said. "It is also the basis for degenerative diseases and many types of tissue damage. An in-depth understanding of apoptosis and how it can be controlled has wide-ranging implications for health and disease."

Green's talk will be the third in the institute's Distinguished Lecture Series. Program Analysis Branch Chief Ben Van Houten is the lecture host. He will join Dr. Green following the lecture for a roundtable with NIEHS fellows and scientists.

Lecturer Douglas Green. (Photo courtesy of St. Jude's Children's Research Hospital)

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Also Upcoming

- **November 2** in Rodbell beginning at 8:30 AM - The Fourth Annual NIEHS Science Awards Day honors outstanding scientific work, including a lecture (3:30-4:30 PM) by Scientist of the Year, Ronald P. Mason, Ph.D., "Do it Yourself Detection of Protein and DNA Free Radicals in Organelles, Cells, and Tissues: A 30 year Odyssey."

- **November 4 – 8** in Boston: NIEHS scientists present and facilitate at the American Public Health Association's 134th Annual Meeting. Abstracts and program are online.

- **November 8**, 8:30 – 5:30, in Rodbell: Environmental Health Sciences Review Committee (Open to the Public).

- **November 9**, 10:00 – 3:30, in Rodbell AB: SEMINAR: Native American Heritage Celebration.

- **November 14**, 2:00 – 3:30, in Rodbell: SEMINAR: "Apoptosis: The Paths of Perdition," by Distinguished Lecturer Doug Green.

- **November 16**, 10:00 – 12:00, in Rodbell C: Gwen Locklear, Native American Storyteller and Crafter (Open to the Public)

- **November 16**, 11:00 – 2:00, in D Mall: Annual Health Benefits Fair.

- **November 16**, 10:30 – 11:30, in F193: LPC/LMT Seminar with Dino Di Monte.

- **November 30** in Rodbell: Scientific Advisory Committee on Alternative Toxicological Methods (SACATM) meets. Registration required. Call 541-0530.

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