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WAYNE STATE UNIVERSITY

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— Dr. Hilary Ratner

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Letter from the Vice President for Research

At Wayne State University, we have long viewed our mission as embedded in the life of our community, one of America's great cities, which leads to a focus on urban issues and a commitment to social action. Wayne State University's urban mission is manifest in our history, location and tradition, and the commitment to this mission has been reaffirmed as part of the vision for WSU as the model research urban university for the 21st century. WSU has a rich history and long tradition of innovation - developing new knowledge and products, discovering "why" so we can know "how," offering creative solutions to real-world problems, and educating our students. Here at Wayne State, research serves as a bridge between access and excellence.

The research enterprise at Wayne State has undergone fundamental changes in the past decade, leading to significant success. Some of our success stories are shared here. Multi-disciplinary, multi-investigator, and multi-institutional projects; opportunities for commercialization and entrepreneurship; economic development; and translational research are just some of the influences that have shaped the work we do. Most important, however, is the fact that our achievements would not be possible without the talent, commitment, and investment of our exceptional faculty whose ideas are transformational.

In this issue of *New Science*, we offer you a sample of the groundbreaking advances in our research and scholarship, often conducted collaboratively with partners such as the University Research Corridor, Children's Hospital of Michigan, and the Henry Ford Health System. Alliances such as these not only create more opportunities for new ideas, but also support translating our research into action faster, better, and smarter.

Our faculty's commitment to foster teaching and research programs that educate future leaders provides many with the knowledge to improve the world in which we live. Wayne State University is at the forefront of pioneering approaches critical to economic growth, solving universal problems, and improving the quality of urban life here at home, across the nation, and around the world.

I hope you enjoy this issue of *New Science*.

Hilary H. Ratner, Ph.D.


William D. Lyman, Ph.D.
Director

Changing the Course of Children's Health

Michigan Alliance for the National Children's Study

By Julie O'Connor

As a nation, we have made great advances in improving the health and development of children over the past century. However, high rates of asthma, developmental disorders, obesity, preventable injuries and a host of other problems are still a challenge for our society. While studies in recent years have offered important insights into these conditions, most have been too small or too specific to analyze the wide range of environmental factors and relationships that may impact diseases and conditions afflicting today's child.

The National Institutes of Health (NIH) is leading the most ambitious nationwide children's health research project in history – the National Children's Study – which is designed to follow children from before birth to age 21 to study the impact of the environment, broadly defined, on their health and ultimately to seek out ways to prevent many of the diseases from which children suffer. In 2007, the NIH awarded $18.5 million to the Michigan Alliance for the National Children's Study (MANCS) for study work in Wayne County, and an additional $57 million in 2008 to study children in Genesee, Grand Traverse, Lenawee and Macomb counties. Through these awards, MANCS will monitor 5,000 children in Michigan to pinpoint the root causes of many of today's major childhood diseases and disorders and determine what aspects of the environment are harmful, but also what is helpful to children's health and development.

Growing up healthy in Michigan

As part of an alliance with Michigan's top research universities, health care systems and local health agencies, MANCS' role in this nationwide study is to provide researchers, health care providers, educators and others with a resource of data that will aid in the development of prevention strategies, health and safety guidelines, educational approaches, and the hope for new treatments and cures for health conditions. And, for the first time ever, this study will allow researchers to apply knowledge of the human genome on a large scale and understand the conditions that arise from many factors including gene/environmental interactions.

The alliance is made up of Michigan State University, University of Michigan, Wayne State University, Children's Hospital of Michigan, Henry Ford Health System and the Michigan Department of Community Health. Each institution brings unique leadership to the alliance with the following roles:

Building on the Michigan Alliance for the National Children's Study

Wayne State University and Henry Ford Health System have created an inter-institutional effort to bring together and integrate the research faculty of these institutions to develop an increased understanding of the biological and social basis for health disparities among populations of differing demographics, test alternative strategies to overcome reasons for these disparities, and develop health and information management systems to support efforts to eliminate disparities altogether.

The Institute for Population Sciences, Health Assessment, Administration, Services and Economics (INPHAASE), the core of these activities, aims to investigate the problems of disease prevention and management, and health promotion in large urban areas as epitomized by metropolitan Detroit. The goal is to change individual and population behavior related to health status, as well as the behavior of health care systems and providers through collaborative research programs funded by WSU and HFHS, ultimately leading to larger scale programs and projects in these areas.

In late 2008, INPHAASE awarded four research awards totaling nearly $400,000 to develop programs that would closely associate with the National Children's Study. Each of the funded projects involve faculty from both Henry Ford Health System and Wayne State University. Awardees include:

- Andrea Cassidy-Bushrow, Ph.D., epidemiologist, Department of Biostatistics and Research

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Epidemiology, Henry Ford Health System, for her project, *Maternal Coping with Environmental Stress: Influences on Pregnancy and Child Health Outcomes*. This study proposes to examine the independent and interactional effects of stress, coping and emotion on pregnancy outcomes, particularly how the role of racism has prenatal factors with long-lasting health effects that may reveal targets to the earliest possible primary prevention of chronic disease in adulthood.

- Catherine Jen, Ph.D., professor and chair, Department of Nutrition and Food Science, Wayne State University for her project, *Assessments of Healthy Status of Preschoolers: A Feasibility Study.* This study aims to obtain pilot data and describe preschoolers' body weight status, diet intake patterns, and physical activity proficiency and levels in two day care centers, one which serves mostly African American preschoolers and the other which serves mostly Caucasians. These are important data that will expand upon the National Children's Study, particularly when considering the childhood obesity epidemic that is emerging as a public health crisis.
- John Reiners, Ph.D., professor, Institute of Environmental Health Sciences, Wayne State University, for his project, *Environmental and Behavioral Risk Factors for the Asthma/Allergy Epidemic: Do they Impact the Epigenome*. This study will address critical issues in the field of asthma research. Dr. Reiners and his collaborators expect to detect both 'expected' and 'new' genes in their screens and use generated information for future design of high-throughput, targeted assays that utilize amounts of blood that can be safely drawn from very young children. These assays will facilitate longitudinal epidemiological studies that address how fetal and early life diet and environmental factors affect the epigenome, and the role epigenetic changes play in influencing asthma.
- Kimberley Woodcroft, Ph.D., bioscientific staff, Department of Biostatistics and Research Epidemiology, Henry Ford Health System, for her project, *Gene-Tobacco Smoke Interactions on Child Behavioral and Cognitive Development.* This study will examine broadly defined environmental influences, including genetic, on health and development of children in the United States, aiming to identify genetic biomarkers associated with tobacco exposure and adverse child cognitive development that may aid in identifying at-risk populations for intensive parental smoking cessation intervention. This study will be the first to examine the gene-environment interaction of polymorphisms in nicotine metabolism, neural nicotinic receptors and nicotine-activated signaling pathways involved in brain development on the adverse association between maternal smoking during pregnancy and behavioral and cognitive development in children.

"This collaboration between Henry Ford Health System and Wayne State University reflects our common goals in learning how to take better care of the health needs of our community," said Dr. Gloria Heppner, associate vice president for research at WSU. "Furthermore, this joint endeavor has allowed the two institutions to develop important research collaborations in support of the Michigan Alliance for the National Children's Study, ultimately shaping the research agenda for the next generation."

Children's Health continued

Robert Sokol, M.D., director of the C.S. Mott Center for Human Grown and Development

- Michigan State University will coordinate the overall work for the study and house the project at its East Lansing campus. MSU's extension center will help develop the community support for this project. Nigel Paneth, M.D., professor of epidemiology and pediatrics, is leading this effort.
- The University of Michigan is responsible for enrolling and interviewing study participants and

William D. Lyman, Ph.D., director of the Children's Research Center at Children's Hospital

assessing postnatal child development. This is led by Daniel Keating, Ph.D., professor of psychology.

- Wayne State University will oversee the assessment and care of pregnant women. This effort is led by Robert Sokol, M.D., director of the C.S. Mott Center for Human Growth and Development, and distinguished professor of obstetrics and gynecology.
- Children's Hospital of Michigan will manage biological samples, and is led by William Lyman, Ph.D., director of the Children's Research Center at Children's Hospital and associate department chair of pediatrics at Wayne State.
- Henry Ford Health System will manage environmental samples and perform medical examinations of children. These efforts are led by Christine Cole Johnson, Ph.D, MPH, senior staff epidemiologist and interim department chair, Department of Biostatistics and Research Epidemiology, Henry Ford Hospital and Health System and Charles Barone, M.D., FAAP, chair, Department of Pediatrics, Henry Ford Medical Group; division chief, Division of Pediatric Hospitalist Medicine, University Pediatricians/ Children's Hospital of Michigan; clinical associate professor of pediatrics, Wayne State University School of Medicine; and president, Michigan Chapter of the American Academy of Pediatrics.
- The Michigan Department of Community Health will provide information related to live birth characteristics and locations in the study, and is led by Violanda Grigorescu, M.D., director of the Division of Genomics, Perinatal Health and Chronic Disease Epidemiology.

"Working cooperatively with the other major biomedical institutions in the state allowed us to bring together a team of unmatched expertise," said Dr. Sokol. "It also assured that our joint efforts would be adequately funded so that we will be able to perform all portions of the study well," he added.

The National Children's Study will provide health and economic benefits through reduced illness and disability, as well as increased school and work productivity, ultimately profiting the nation well beyond the investment of creating and maintaining this important study. By evaluating environmental exposures in relation to genetic predispositions to health and disease among the 100,000 participating children nationwide, a more complete picture of what actually causes diseases and promotes health will be realized. The end result may not be prevention or treatment for every childhood health problem, but certainly a repository of data from which new preventions and treatments can be developed for today's most common health disorders.

"The National Children's Study will provide critical information to help guide the treatment, cure and, hopefully, prevention of many childhood diseases," said Dr. Lyman. "It is important to remember that these children will become adults and what we learn about their development can have profound implications for adult disease and well-being also. The results of this study will transform maternal and child health and development for the next 50 to 100 years. This is the most important research initiative that has ever taken place and will allow our children, grandchildren and great-grandchildren to reap many benefits in the future."

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Helping our Heroes

Investigating blast induced neurotrauma in U.S. troops

By Amy Oprean

From the machine guns and air raids of the World Wars to the lingering effects of Agent Orange in Vietnam, the threats that U.S. troops endure have continually changed with every era of war. No exception to this rule are the conflicts of Afghanistan and Iraq, which are the first in U.S. history to see improvised explosive devices (IEDs) – bombs detonated under artillery vehicles and on crowded streets, sometimes strapped to suicide bombers – as the primary mode of attack waged on U.S. soldiers. Young in their diagnosis but vast in impact, blast injuries from IEDs make up about 80 percent of injuries to U.S. troops returning from Iraq, and have earned the title *the signature injury* of these wars.

The prevalence of injuries from this weapon of choice has elicited an onslaught of questions that researchers are scrambling to answer: What are the long term effects of these close-range, frequent blasts? How do blast waves impact soldiers in artillery vehicles differently than those on foot? And perhaps the most perplexing, how are these blasts causing traumatic brain injury, or TBI, in 10 to 20 percent of returning troops?

Wayne State researchers, Dr. Cynthia Bir and Dr. Pamela VandeVord, and a team of collaborators are working to answer those questions with the project *Blast Induced Neurotrauma,* an investigation funded by a $790,000 grant from the Office of Naval Research and additional funding from the Department of Veterans Affairs. Using a state of the art blast tube – one of less than a dozen owned by U.S. universities – Bir and VandeVord are conducting an integrative investigation of "primary" blast injuries, or damages caused by the short duration, high amplitude pressure waves emitted from explosives. These injuries are now believed to be the reason behind the unprecedented number of soldiers that are returning from war with symptoms of mild to moderate traumatic brain injuries, many of whom don't recall being hit in the head.

> "We've realized that neurotrauma does occur from primary blast waves and that we need to investigate this. With such a strong history of neurotrauma research here at Wayne, it was an obvious choice to start looking at this."
>
> **— Dr. Cynthia Bir**

"There's been a lot of research trying to determine if primary blast neurotrauma is actually a phenomenon, because for a while it was felt that you needed to have other aspects of a blast as well," said Dr. Bir, associate professor of biomedical engineering in the College of Engineering at WSU and lead investigator of the project. "But now we've realized that neurotrauma does occur from primary blast waves and that we need to investigate this. With such a strong history of neurotrauma research here at Wayne, it was an obvious choice to start looking at this."

A new kind of brain trauma

Until recently, soldiers were considered to have blast injuries if they had some sort of tangible mark, such as cuts from shrapnel or burns from the fireball. For brain trauma, hemorrhages and edema were long established indicators of injury. Yet, there is a large portion of soldiers returning from war without any of the traditional indicators of brain trauma who still suffer memory lapses, speech problems, difficulties with decision making, and other telltale signs of TBI.

"The soldiers that are really close to the explosion will get blown down and probably fall and hit their head," said VandeVord, assistant professor of biomedical engineering in

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Helping our Heroes continued

the College of Engineering. "But the ones that are coming back with the mild TBI, they say that they didn't fall. They may have felt as if something weird was going on, but they're not falling and hitting their head."

Though it's difficult to estimate the number of TBI cases that have gone undiagnosed, the Defense and Veterans Brain Injury Center estimated in 2008 that 10 to 20 percent of all soldiers on duty in Iraq and Afghanistan have suffered some form of TBI. A TBI study released by the RAND Corporation in April 2008 fell in at the higher end of that percentage, estimating 19 percent or 320,000 soldiers experienced traumatic brain injury while deployed.

The startling prevalence of this form of mild TBI, coupled with the lack of understanding of how it works, is what prompted Bir and VandeVord to procure the blast tube. The twenty-foot long blast tube can be manipulated to simulate the pressure wave of an explosive without the additional elements of heat or shrapnel – allowing Bir and VandeVord to assess the effects of the pressure wave alone.

One of the main objectives for the blast tube is assessing how pressure waves cause brain damage – the types of cells that are damaged, how they become damaged, and the pathways by which the blast energy transfers through the brain. Equally important is establishing the threshold, either of pressure intensity or number of repeated exposures required for damage to occur.

Dr. Cynthia Bir, associate professor of biomedical engineering

The ultimate goal, Bir said, is to be able to recognize a soldier that has undergone mild traumatic brain injury through yet-to-be discovered biomarkers and provide treatments. "I think the thing this research is going to promote, especially within the Department of Defense, is the use of prophylactic medicine; giving soldiers some sort of medication either prior to going out in the field or directly after being exposed to prevent this injury from occurring," she said.

Before treatment or preventative medicine can be developed for mild TBI, however, researchers must first learn how to diagnose it. In addition to the blast tube, Drs. Bir and VandeVord are partnering with Dr. Mark Haacke, professor of radiology in the School of Medicine at Wayne State, to utilize a number of MRI methods that may provide information on how to recognize a brain with mild TBI. Using arterial spin labeling, or ASL, for instance, Bir and VandeVord are measuring blood flow rates in the brain before and after mild TBI has occurred. Susceptibility-weighted imaging, another type of MRI, detects micro-hemorrhaging. Lastly, using Magnetic Resonance Spectroscopy, they can assess possible changes in the levels of different kinds of metabolites and neurotransmitters due to blast waves.

The first cells hit

It is not certain which of these aspects of the brain will provide the best indicator that mild TBI has occurred, VandeVord said, but there have been hints that the initial change caused by pressure waves is a biochemical one. Funded by a $300,000 grant from the Department of Veterans Affairs, VandeVord exposed individual brain cells to pressure waves, to see which ones are

> "We believe that we are going to make a big difference."
> **— Dr. Pamela VandeVord**

affected by overpressure. She subjected neurons to immense pressures, but saw little negative effect. "We've gone to very high pressures, and neurons are surviving, which was strange to us," she said. She then turned her attention to glial cells, supporting cells of the brain that provide many different functions, including balancing nutrients, fighting infection and maintaining neurons' local environment. Over-active glial cells have been linked to neural damage in several neurodegenerative diseases, including Parkinson's disease. VandeVord ran the trial again, and found that unlike neurons, glial cells become activated in response to pressure waves, secreting molecules that can be toxic to neurons at high concentrations.

VandeVord's next step in research will be funded by a four-year, $600,000 TBI Intramural Investigator Award from the Congressionally Directed Medical Research Programs of the Department of Defense. With this award, she hopes to determine whether or not the toxic secretions are causing neuron apoptosis – or programmed cell death. "With these research efforts, if the neurons do die after being exposed to overpressure, we may begin to understand why," she said.

Dr. Pamela VandeVord, assistant professor of biomedical engineering

Regardless of whether glial cells turn out to be the turning point in understanding blast injuries, VandeVord is confident that Wayne State will be at the forefront of new developments in blast injury research in both imaging and blast simulation. "We believe that we are going to make a big difference," VandeVord said. "Other researchers in the field of blast injury seemed to be really impressed with how we are going about our research. We have spent a lot of time understanding blast physics, which is extremely important when entering this field. We made a point to train ourselves well in order to establish our group as leaders."

About Dr. Cynthia Bir:: Dr. Bir received a B.S. in nursing from Nazareth College, an M.S. in bioengineering from the University of Michigan, an M.S. in mechanical engineering and a Ph.D. in biomedical engineering from Wayne State University. Dr. Bir serves as the lead scientist on the Emmy award winning show, *Sports Science*, on the Fox Sports Network. She joined Wayne State University in 2000.

About Dr. Pamela VandeVord: Dr. VandeVord received a B.S. in physiology from Michigan State University, an M.S. in basic medical sciences and a Ph.D. in biomedical engineering from Wayne State University. She is an active member of the Society for Biomaterials, Biomedical Engineering Society, and Society of Women Engineers. She joined Wayne State University in 2002.

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Protecting the Mature Mind

by Julie O'Connor

One of the major unsolved mysteries of aging is why some people age gracefully with little to no memory or cognitive dysfunction, while others are afflicted with debilitating diseases such as Alzheimer's and other forms of dementia.

An adult brain contains about 100 billion nerve cells – neurons - that branch out and connect to more than 100 trillion points. Signals traveling through the neurons form the basis of thoughts, feelings and memories. It is these cells that are destroyed by Alzheimer's disease, leading to tissue loss throughout the brain, affecting nearly all of its functions.

Dr. Scott Moffat's research is focused on understanding these complex elements of the mind which may one day lead to new solutions to slow or stop debilitating diseases such as Alzheimer's.

Dr. Moffat, associate professor in the Institute of Gerontology, and his research team are investigating two principal areas of research associated with aging. The first which is conducted in his Neuroscience of Aging Lab, seeks to understand the cognitive, structural and functional brain changes associated with aging. He has developed virtual reality technology that incorporates functional MRI studies to assess the behavioral and neural mechanisms of age-related decline in human spatial cognition.

His second area of research focuses on human behavioral endocrinology, which is examining two hormones thought to influence the brain's health and functions: testosterone and cortisol. By understanding how some hormones may affect people's brain functions, Dr. Moffat may one day have an answer to the causes of brain atrophy and loss of brain function.

A virtual – reality approach to studying spatial memory

Throughout our lives, we must navigate on a daily basis, whether driving to work or finding our way to someplace new. As people age, navigation becomes more difficult. Using real-world situations to evaluate this problem is complicated according to Dr. Moffat. Problems include the fact that navigation takes place over relatively large spaces; physical limitations make it difficult for many older individuals to walk long distances; learning a new route often takes repeated tries; and researchers cannot control the location and placement of landmarks.

Through virtual reality technology, these barriers are eliminated, and allow simulations to explore a variety of three-dimensional environments. It also allows researchers to design the environments including cues and landmarks the study participants will see, and also to record detailed analyses of their behavior during the study. Dr. Moffat's studies of young and elderly individuals solving a virtual navigation task in the lab and later in a functional MRI scanner reveal that older participants had significant challenges in performing the spatial memory task, and had different patterns of brain activation while solving the task.

"Our results demonstrate that elderly individuals may encounter greater difficulty learning the layout of unfamiliar environments than younger individuals," said Dr. Moffat. "Because navigating successfully is a necessary activity for people of all ages, our research has important implications for understanding how navigation skills may change with age," he added.

Dr. Moffat and his research team may one day understand wandering in Alzheimer's disease, in which people with the disease become lost and disoriented. Wandering affects up to 60 percent of patients with Alzheimer's and is often one of the early warning signs of the condition.

Understanding the role of hormones in brain health

Dr. Moffat is interested in understanding how some hormones may negatively and positively affect people's brain functions. In earlier research, Dr. Moffat and his colleagues found that higher levels of circulating testosterone may have a broad range of positive influences on the brains of aging men. Moreover, the loss of testosterone may play a key role in the development of certain types of memory loss and Alzheimer's.

In the Baltimore Longitudinal Study of Aging, Dr. Moffat investigated age-associated decreases in testosterone concentrations and neuropsychological performance of more than 400 men ages 50 to 91 for ten years. The study showed that men with higher testosterone levels had higher scores on visual and verbal memory, and visual spatial function. Dr. Moffat and his research team are currently conducting placebo-controlled testosterone intervention studies in elderly men to test whether administering testosterone to men with low levels may enhance cognitive brain function.

Dr. Moffat recently began studying cortisol, a stress hormone thought to influence the brain's health and functions, funded by a grant from the National Institutes of Health's National Institute on Aging. A high level of cortisol – produced by the adrenal gland – has been found in animals to be associated with poor cognitive abilities. "Researchers believe that cortisol attacks certain brain regions and causes some atrophy and loss of brain function," said Dr. Moffat. "In humans, we think that exposure to stress and high levels of cortisol may cause memory loss and ultimately increase the risk for dementia."

While early in the research stage, Dr. Moffat's studies may be the key that reveals additional risk factors for age-related declines in cognitive and neural function, someday leading to new treatments to eliminate or delay these debilitating and often deadly dysfunctions.

About Dr. Scott Moffat: Dr. Moffat received his B.S. from the University of Toronto where he studied psychology and neuroscience. He received his Ph.D. in neuropsychology from the University of Western Ontario in London, Ontario, Canada. He was a visiting fellow at the National Institute of Aging. He joined Wayne State University in 2002.

Dr. Scott Moffat, associate professor, department of psychology and the Institute of Gerontology

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Two Part Harmony:

Beginner music students learn the strings as undergrads make teaching debut

by Amy Oprean

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Ever since she was 12 years old, Dr. Laura Roelofs, assistant professor of music in Wayne State University's College of Fine, Performing and Communication Arts, knew she wanted to be a performer, but it took a few more years to discover she also wanted to teach. "I planned right away on playing the violin professionally, but I realized within a few years that performing and teaching go hand in hand, and that you learn even more from teaching someone else than you do by practicing."

Roelofs hopes some of Wayne State University's music students will experience a similar moment of discovery during their time as teachers in the String Project @ Wayne, an intensive teacher-training program that began its first semester in September 2008. The program offers three levels of lessons for the violin, viola, cello and bass for Detroit-area children grades three to five, taught by WSU music performance or music education undergraduate students under the supervision of a master teacher. Classes are small – no more than 10 students to a teacher – and range from $4 to $5 per session, depending on the class. For 2008-09, the project is funded by WSU's President's Research Enhancement Program and the NAMM Foundation through the National String Project Consortium. The String Project @ Wayne has also formed a collaborative partnership with the Detroit Symphony Orchestra; the project classes serve as the foundation level of the DSO's Power of Dreams Program, a project that provides children with little to no access to string education the opportunity to participate in string classes.

There are more than 30 string projects nationwide, all of which have the overarching goal of increasing the number of well-qualified string teachers in the country while providing exemplary string education to children in underserved areas. The Wayne State program stands out as one of very few string projects located in large urban centers. Roelofs sees the String Project @ Wayne as an opportunity to expand Detroit's arts and culture community. "I see it as a way to bring all of the disparate constituencies in the area together around educating kids on strings," she said.

Although the string project concept has been around for decades, only a single research paper has been published assessing the impact that such programs have on the college-age interns and the elementary music students they teach. Roelofs believes Wayne State's program is an ideal place to conduct additional studies, and will begin implementing her research in the program's second semester.

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>
> **— Dr. Laura Roelofs**

One of the major questions Roelofs wants to answer is the extent to which string project participation can inspire music undergraduates to pursue careers in teaching. For decades in the U.S., more string teachers have retired than have entered the field, a trend that has resulted in what the National Association for Music Education estimated in 2005 to be about 5,000 unfilled job vacancies

Dr. Laura Roelofs, assistant professor of music

per year. While this can be traced back to serious string students preferring to perform rather than teach, and even to a subtle cultural stigma attached to string teaching, Roelofs attributes the disparity at least partly to simple lack of teaching exposure.

"Once you get it the first time, it becomes almost addictive; that 'a-ha' moment when the kids are picking it up, it's working, and you can see that you're having a real life-changing impact on other people," she said. "That's one of the big things that I want to do with this program – connect strong performance skills with a love of teaching to show how rewarding it is." Advising the interns throughout the process is inaugural master teacher William Starnes, the same string instructor who inspired Roelofs in her youth to become a teacher. Since beginning his career as a professional violinist at age 14, Starnes has been a member of the El Paso Symphony Orchestra, the San Antonio Symphony Orchestra, the United States Air Force Strings in Washington, D.C, the Pittsburgh Opera, the Pittsburgh Ballet and the Pittsburgh Civic Light Opera. He's taught as an adjunct professor at Catholic University, American University, and the Academy of Musical Arts in the Washington, D.C. area and served as assistant director for music and instruction at the D.C. Youth Orchestra Program for more than 20 years. Roelofs hopes Starnes' extensive experience and unparalleled enthusiasm for orchestra teaching will help the interns stay focused as they take on many new responsibilities, including lesson planning, communicating with

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Two Part Harmony continued

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> — **Dr. Laura Roelofs**

parents and school administrators and recruiting new students. "He is the role model that I want for them," she said. "As he says, music is caught, not taught, and so that's what I want to convey. Your own passion about the music and your passion about doing it exactly right is what will get them."

Another research topic Roelofs is interested in investigating is how many of the program's students will continue taking instrument lessons past their first year. Recruited largely through concerts at local elementary schools, the program's inaugural class of 93 is full of enthusiastic beginners whose retention will be tracked. "We're targeting third to fifth graders because it's the perfect time to catch their interest," she said. "They're old enough to have the attention span to grasp the concepts and pay attention for the hour-and-a-half classes, and they're still so open. Not everyone will stick to it, but it's amazing how many of the kids were extremely excited at the recruitment concerts, and really attached themselves to one instrument or another."

Students began classes in September, meeting twice a week to learn the fundamental physical skills of string teaching as well as elementary music theory and ear-training. Once a month, the small classes are combined into one large ensemble; the young students' first orchestra experiences. Through the Detroit Symphony Orchestra partnership, children hear special "Inspiration Day" performances featuring DSO musicians. For regular exposure to a working ensemble, they also have the opportunities to see their teachers perform together, setting the tone for the interns as role models that are part of a music community with the students.

The combination of curriculum and the communal environment is important to Roelofs, who believes it will encourage the young students to stay engaged and reach their potential, even as they discover the hard work and dedication needed for learning a musical instrument. "I would like them to get an idea that they can do more than they ever thought they could, especially because very high standards will be set for them as young music students, in terms of their attendance, their preparedness and doing things the right way from the beginning," she said. "My hope is that they're going to have a lot of self-esteem when they finish from realizing they have done something that's hard and have done it well."

About Dr. Laura Roelofs: Dr. Roelofs received an Mus. B. from Boston University's School of Fine Arts and an M.M. and D.M.A. from the Catholic University of America in violin performance. She performed for fourteen seasons as assistant concertmaster of the Richmond Symphony Orchestra, and as a member of the Oberon String Quartet, artists-in-residence at St. Catherine's and St. Christopher's Schools in Richmond. She has appeared as a soloist with a number of orchestras including the Baltimore Symphony and the Richmond Symphony. She is assistant concertmaster of the Michigan Opera Theatre and assistant professor of violin and viola at Wayne State University. She joined WSU in 2004.

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Degree of Distraction

What cell phones do to a driver's brain

by Amy Oprean

In today's fast paced, technology-saturated world, cell phones have changed daily life in a multitude of ways – and not always for the better. A major concern surrounding mobile phones is the hazard of conversation-engrossed drivers losing focus on the road, potentially contributing to crashes. But while anecdotes of cell phone-distracted drivers aren't hard to find, an actual scientific measure of how dangerous cell phones are – both hand-held and hands-free – is still a highly controversial topic among researchers, lawmakers and drivers.

Li Hsieh, Ph.D., associate professor in the Department of Communication Sciences and Disorders in the College of Liberal Arts and Sciences, is one such researcher working to assess the mechanisms underlying how cell phone conversations affect driver performance, with a specific focus on visual event detection.

"Humans were built for multitasking, that's why you see people doing all kinds of things in their cars without crashing; drinking a cup of coffee, playing with the radio, mothers driving with two or three kids fighting in the back," she said. "But there is a limit to this multitasking and finding that limit is key to my research."

While cell phones have exploded in popularity over the past decade, there hasn't been a corresponding rise in crashes on the highways, a finding that has led Hsieh to believe that some researchers may be drawing exaggerated conclusions from experiments assessing the danger of cell phones. Some of the most widely publicized studies, in fact, use methods that do not distinguish the conversation from other aspects of cell phones – such as dialing and looking for the phone – or even other manual tasks occurring at the time of a collision.

"If you look at a lot of these cell phone studies that have been conducted, they're investigating cell phones along with a lot of other simultaneous activities, such as talking to passengers, changing the radio, and handling the cell phone," she said. "More studies are needed to determine which of these tasks are actually causing the biggest distraction."

Keeping this in mind, Hsieh has designed her study to isolate the conversation element – the cognitive act of conversing in a hands-free cellular call – with the goal of gauging the effects of the conversation alone. Knowing what aspect of cell phone conversations causes the biggest distraction, Hsieh said, could lead to determining appropriate countermeasures that improve driving safety. Her experiment considered not only the behavioral effects of cell phone conversations on a driver's accuracy and reaction time, but also the neurological underpinnings – the areas of the brain that are active when a person is talking on a cell phone while driving.

"We're trying to see what things make people the most distracted, and the neural mechanisms behind that type of distraction," she said.

Hsieh is leading an interdisciplinary and multi-institutional research collaboration on the effect of cell phone conversations on driving performance, funded with a $1.24 million grant from the Michigan Economic Development Corporation from the State of Michigan. Conducted at Wayne State University, Henry Ford Hospital and the University of Michigan Transportation Research Institute, Hsieh recruited participants to partake in a computer-based driving simulation and on-road driving tests while engaging in a hands-free cellular conversation.

During the computerized driving simulations, participants use a steering wheel to keep a cursor centered on the vehicle's lane, while a self-propelled driving simulation steered through real video footage of metro-Detroit area roads. Throughout the simulations, participants were asked to press down on a foot pedal whenever they saw a "visual event" – a red light representing any sort of visual cue for which drivers should react by braking, such as a stop sign, red light, or pedestrian crossing the street. Participants taking the on-road tests performed the same event detection tasks while driving a real vehicle on open roads.

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Degree of Distraction continued

After this baseline trial, Hsieh ran several different phases of the experiment during which participants answered the questions of an automated caller. In one, the caller had a neutral voice tone; in another, the caller had an aggressive, emotionally charged tone; and another, the caller asked questions that were complex in nature. Reaction time – the time taken to respond to the visual events – and number of visual events missed were recorded for these trials as well. Depending on the test phase, Electroencephalogram (EEG), Magnetoencephalography (MEG), and functional Magnetic Resonance Imaging (fMRI) scans were done during the driving simulation. EEG recordings of the driver's brain activity were taken during the on-road tests.

Conversations slow driver reaction time

In both lab simulations and on-road tests, neutral conversations caused a delay in participants' reaction times by 60 to 120 milliseconds, but missing a visual event was rare. Reaction times during the alternate "emotionally charged" conversation were actually shorter than those during neutral conversations, but were still longer than the baseline, no-conversation trial. Dr. Hsieh said reaction times may have been faster during conversations with an aggressive caller because being irritated may have caused people to be more alert.

The brain's balancing act

Preliminary results of the brain imaging studies revealed the regions of the human brain that are activated as it juggles attention between the primary task of driving and the secondary task of holding a conversation. The frontal lobe, which controls the allocation of brain resources, showed an increase in activation during conversations taking place while participants performed the simulated driving and event detection scenarios. Other areas of heightened activity included Broca's area, a region that controls language production, and Wernicke's area, a region associated with language comprehension.

The brain appears to adjust and readjust how its resources are divided while multiple tasks are being carried out; an important job that Hsieh's results suggest is performed by several key regions, namely the frontal and parietal lobes. Because the brain does not have unlimited resources, however, some regions see a decline in event-related activation when this multitasking is taking place. This decrease in event-related activation – which Hsieh and her colleagues observed in the parietal lobe and secondary visual cortex – may provide a possible neural mechanism for the increase in visual reaction times while a conversation is taking place.

"The MEG and MRI imaging data show that when a person's reaction time gets longer, it is during times of reduced event-related activity in the parietal lobe as well as the visual cortex," she said. "But even though participants' reaction times were affected, their accuracy was still good. It's actually pretty hard to make someone completely miss a visual event in those we have tested so far."

Looking to the future

Hsieh's study intends to set a scientific foundation rather than determine a verdict on whether cell phones are safe enough to use while driving, the latter of which would require collecting real-world naturalistic data on actual behavior of drivers when using cell phones on the road. Although subjects did not miss significantly more visual events while conversing in her studies, adding different types of conversations at different intensities could change that, she said. In the meantime, the knowledge gained has provided new insight into how the brain multitasks, and will catalyze studies in several important areas of driver performance research, some of which Hsieh herself plans to pursue.

One area of research Hsieh plans to investigate is the possibility that cell phones negatively affect certain groups more so than others in the larger driving population. She and her collaborators hope to study teenagers, elderly and drowsy drivers to determine if cell phone conversations have a more profound effect on these groups. The results of these studies could be applied to future car or cell phone designs aimed to compensate for driver weaknesses as well as improve rehabilitation and prevention programs for safer driving.

Another area of interest Hsieh plans to investigate is attention blindness while driving. Also known as

Dr. L. Hsieh, associate professor of communications sciences and disorders

the "looked-but-didn't-see" phenomenon, attention blindness is said to occur when a driver's gaze is on a visual event, yet they fail to react and do not report seeing it. Hsieh said one of the main reasons for her research is to uncover whether certain types of hands-free cell phone conversations in certain groups of people might produce the degree of attention blindness capable of contributing to crashes.

"Rear end crashes are quite common; that means the object is right in front of you, and you still crash into it," said Dr. Hsieh, who also records the gaze of people while they participate in her driving simulations and on-road studies. "That's why we're doing these studies – to investigate the effect of cell phone conversations not just in ways that can be measured behaviorally, but in ways that allow us to find the neurological causes of those behaviors as well. That's when improvements in driver safety can be made more precisely and efficiently."

About Dr. Li Hsieh: Dr. Hsieh received a B.S. in English literature at Soochow University in Taiwan, Republic of China, and an M.A. in linguistics at Fu Jen Catholic University in Taiwan, Republic of China. She received an M.A. in speech-language pathology from Northwestern University and a Ph.D. in speech-language pathology from Purdue University. She did her post-doctoral work in the Department of Cognitive Science at Johns Hopkins University. She joined Wayne State University in 2001.

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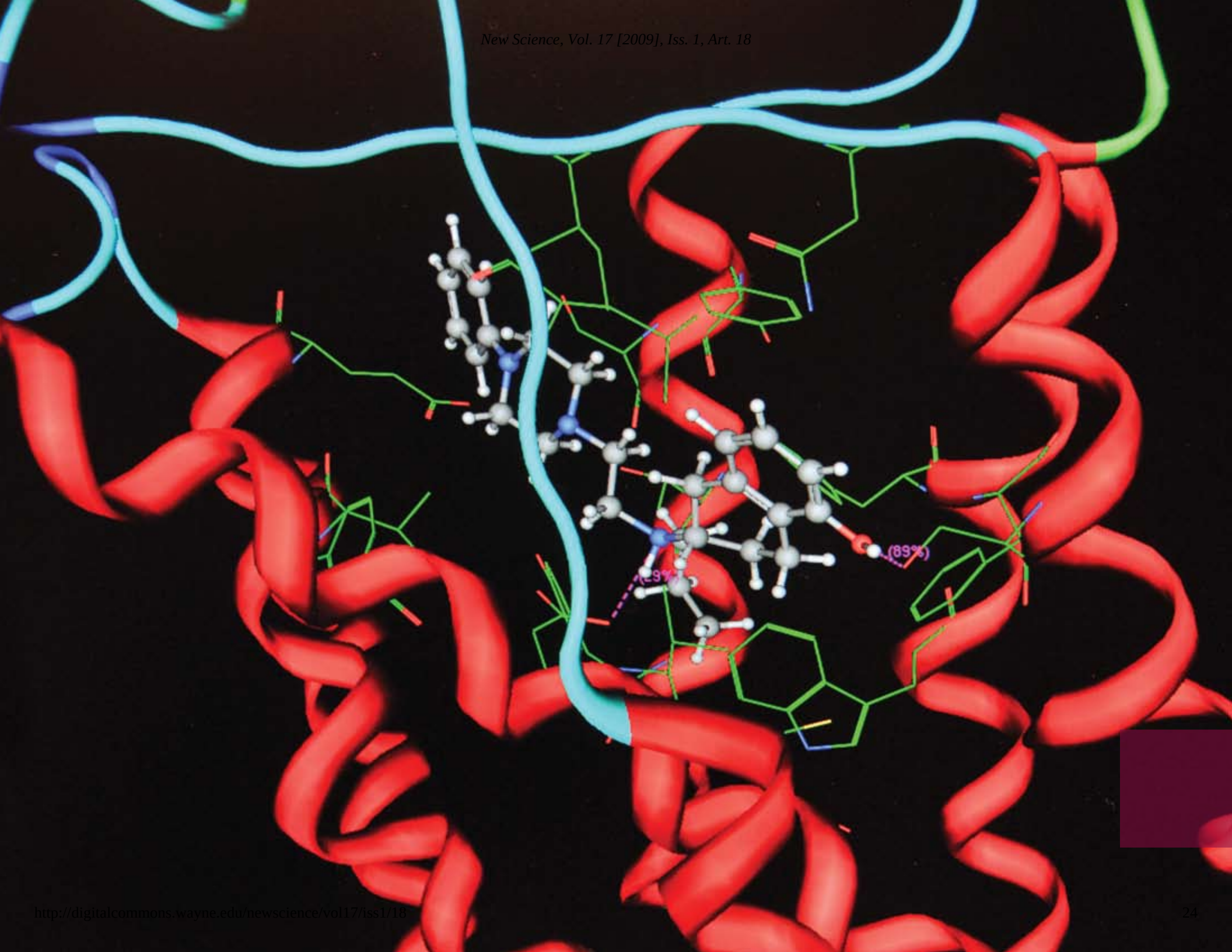
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Giving Hope Through Research

A search for novel treatments for Parkinson's disease, depression and drug abuse

by Julie O'Connor

Parkinson's disease affects approximately one percent of people older than 65 years of age. Nearly one million people in the United States have been diagnosed with Parkinson's disease, a chronic and progressively debilitating disorder. This motor system disorder which causes trembling in hands, arms, legs, jaw and face; stiffness of the limbs and trunk; slowness of movement; and impaired balance and coordination, is the result of the loss of dopamine-producing brain cells.

While there is great hope in Parkinson's disease research, there is no cure. A variety of medications provide relief from the symptoms, including levodopa, also known as L-dopa, that converts into dopamine as it reaches nerve cells in the brain. Levodopa therapy often results in the emergence of motor complications and eventually patients may not respond to the drug. Multiple years of L-dopa

Dr. Aloke Dutta, professor of pharmaceutical sciences and Dr. Prashant Khardar post-doctoral fellow, pharmaceutical sciences

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Giving Hope Through Research continued

treatment can cause severe side effects and possible neurotoxicity leading to the withdrawal of use of the drug.

But an answer to why Parkinson's disease develops in some patients and a cure for it remains a mystery. "No ideal therapies are available for slowing the progression of the degeneration process and at the same time relieving symptomatic abnormalities associated with the disease," said Aloke Dutta, Ph.D., professor of pharmaceutical sciences and medicinal chemistry in the Eugene Applebaum College of Pharmacy and Health Sciences at Wayne State University.

Dr. Dutta aims to change this by developing a neuroprotective therapy that may slow down the degeneration process. By developing new drugs that focus on relieving motor dysfunction while at the same time introducing other properties that will reduce oxidative stress in the brain, Dr. Dutta hopes to promote survival of more dopamine neurons and at the same time provide symptomatic relief of the disease.

Still early in their NIH-supported research, Dr. Dutta and his research team have developed some initial lead molecules with multifunctional activities which appear to exhibit some of the desired properties required for neuroprotection effects along with the property to alleviate motor dysfunction. Dr. Dutta and his interdisciplinary research team are collaborating with researchers at New York University School of Medicine and Baylor College of Medicine. Together they are combining drug discovery and computational chemistry along with in vitro and in vivo pharmacology, which ultimately will intensify development of such agents in the near future.

Promising new antidepressant technology

Dr. Dutta is also addressing drawbacks in current antidepressant treatments. Major depression is a disorder posing significant health problems. After cardiovascular disease, depression is considered the second most debilitating disease in the world. "Drug therapies currently on the market for treatment of depression have many problems and shortcomings," said Dr. Dutta. "A number of the therapies don't work for a significant number of patients, and some treatments work at first, but later are ineffective."

According to Dr. Dutta, these treatments don't address the dopamine component needed to interact with the relevant targets in the brain. Dr. Dutta and his research team along with collaborators from the New York University School of Medicine have discovered that by combining three monoamine transporters blocking activities into a single molecule, a new generation of antidepressants could be developed. One such lead polyfunctional molecule discovered in Dr. Dutta's laboratory interacts with norepinephrine, serotonin and dopamine systems in the brain, and exhibited remarkable activity in preclinical in vivo antidepressant tests, indicating that it might possess a potent antidepressant activity.

> "We believe a suitable treatment for such a devastating addiction will not only help people with overcoming such addictions, but also reduce a heavy economic burden of our society."
>
> **— Dr. Aloke Dutta**

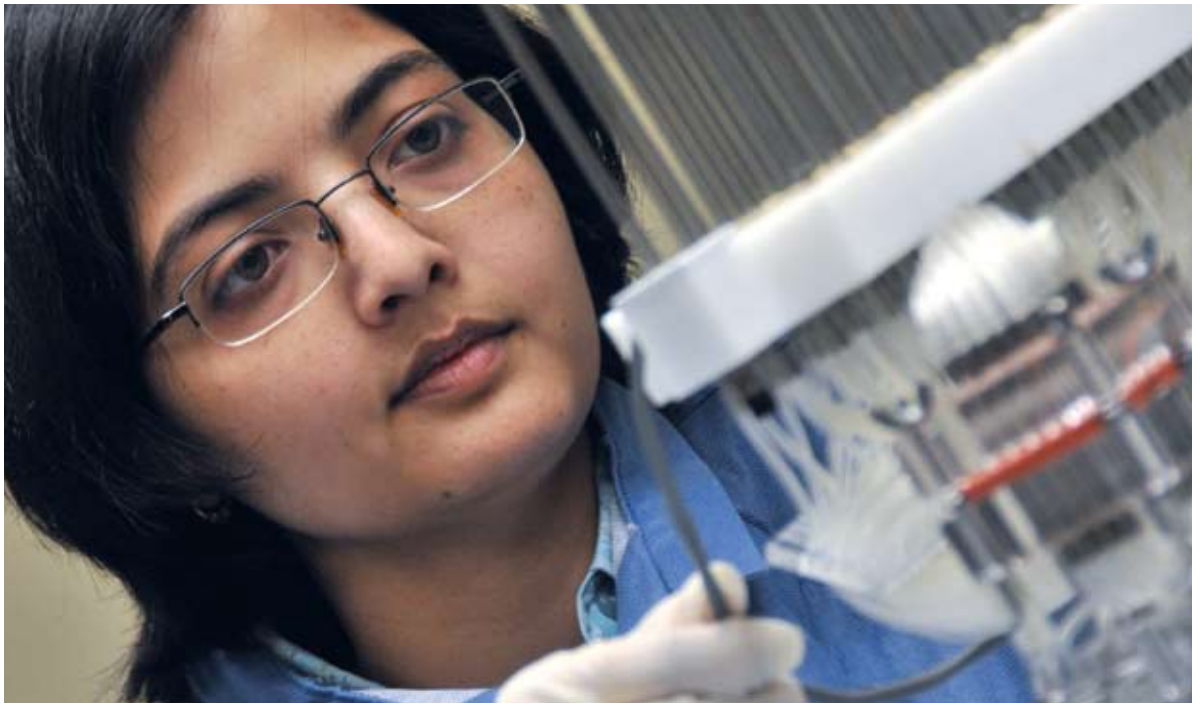
"One of our goals will be to study whether such novel triple uptake inhibitor molecules can produce more desirable therapeutic profiles as antidepressant agents compared to the current existing drugs and whether their chronic exposure might lead to the production of neurotrophic factors in the central nervous system via gene expression," said Dr. Dutta. "This study has the potential to lead to other possible applications, such as treatment of obesity and neuropathic pain. This patent pending technology has great promise to make a difference in the lives of many," he added.

Finding a treatment for cocaine dependency

According to the 2003 National Survey of Drug Use and Health, over 2.1 million U.S. adults reported using cocaine within 30 days prior to the survey. Currently no medication is approved for clinics to treat this addiction.

"The evidence from preclinical studies suggests that the reinforcing effect of cocaine that promotes its abuse is mostly mediated by blockade of the presynaptic dopamine transporter resulting in modulation of dopaminergic activity in the mesolimbic or meso-accumbens dopamine reward system of the brain," said Dr. Dutta. With repeated use, cocaine can cause long-term changes in the brain, leading to addiction. Tolerance to the cocaine high often develops, causing users to increase the amount they use to intensify and prolong the euphoria, which often leads to an increased risk of adverse psychological or physiological effects.

Dr. Dutta's research in the field of drug abuse has been supported by NIH for a number of years. "Our effort to combat cocaine addiction is directed toward rational development of small molecules targeting the sites of interaction of cocaine in the brain that are responsible for its strong reinforcing effect," said Dr. Dutta. Dr. Dutta's research team, which includes collaborators from New York University School of Medicine and Virginia Commonwealth University, employs in vitro and in vivo behavioral pharmacology and molecular biology studies to understand the potential of new drugs as treatment agents. His team recently identified a promising lead compound, D-84, which interacts specifically with the dopamine transporter. Currently, this compound is undergoing extensive preclinical in vivo evaluation to explore its potential to treat cocaine and methamphetamine abuse. Several other molecules are also being investigated.



"We believe a suitable treatment for such a devastating addiction will not only help people with overcoming such addictions, but also reduce a heavy economic burden of our society," commented Dr. Dutta.

About Dr. Aloke Dutta: Dr. Dutta received his B.S. in Chemistry and M.S. in Organic Chemistry from Calcutta University, Calcutta, India and his Ph.D. in Organic Chemistry from Ohio University. He joined Wayne State University in 1998.

Dr. Christine Chow, professor of chemistry

Counter Attack

Developing new weapons in the battle against antibiotic resistance

by Amy Oprean

In the course of human medicine, few discoveries have been as far-reaching and successful as the development of antibiotics in the 20th century. Introduced to mainstream medicine in the 1940s, these drugs have been utilized to vanquish a vast array of bacterial infections, relieving the suffering and saving the lives of millions of people. But antibiotics aren't the surefire defense they used to be. A drop in research over the past several decades in developing new antibiotics, coupled with bacteria's evolutionary drive to develop resistance, has caused the number of effective antibiotics to diminish, and with increasing speed.

Christine Chow, Ph.D., professor of Chemistry in Wayne State's College of Liberal Arts and Sciences, is leading a research team in developing a novel strategy to get an edge over bacteria's relentlessly evolving defense mechanisms. "Resistance is a huge problem," Dr. Chow said. "There are now strains of bacteria that are completely resistant to every known drug. We want to create something new that isn't as easy for bacteria to resist."

The key to Dr. Chow's research lies in ribonucleic acid, or RNA, a nucleic acid that consists of a long chain of nucleotide units, chemically similar to DNA, but consisting of one chain of nucleotides instead of DNA's double helix. RNA has a diverse set of functions, but one of the basic and most well-known is its job of containing the genetic "recipe" for synthesizing proteins. RNA's role has been highly conserved throughout evolution – organisms from bacteria all the way to humans depend on its functions.

Being such an important aspect of all life also makes RNA an incredibly useful target for antibiotics. The RNA of bacteria is one of the two most common targets for antibiotics – the other being enzymes that synthesize bacteria's cell walls – for several reasons, Dr. Chow explained. First, RNA is more chemically and structurally diverse than other possible target areas, such as DNA, meaning RNA has an abundance of unique structures for an antibiotic to "latch on to." It's also more accessible than DNA, and doesn't have the defense enzymes that protect DNA. Lastly, RNA comprises the physical structure of the ribosome, RNA-protein complexes that are found in all living organisms. Ribosomes perform the essential function of synthesizing all the proteins in an organism. Like RNA itself, these protein-making machines can be found from bacteria all the way up to humans, and are important to maintaining all life. Because of this importance, ribosomes are already one of the most common targets of antibiotics – one of simplest ways to eliminate unwanted bacteria is to shut down its ribosomes.

Chow's strategy for battling antibiotic resistance takes the tried and true method of targeting a bacteria cell's ribosomes and aims to improve it, by targeting sites that are particularly vulnerable and attacking with a compound the bacteria has never seen before. "If your antibiotics are derived from natural compounds, there has already been time for the bacteria to evolve resistance mechanisms, and that's why we have this big problem with antibiotic resistance," she said. "So we want to find compounds that don't look like anything from nature. That way, resistance mechanisms will hopefully take longer to develop."

Selecting a target

Just like DNA, RNA's "genetic code" is subject to modifications – changes in either its chemical make-up or structure that enable it to carry out vital functions. With her lab, Chow has selected regions of RNA with six different natural modifications as potential antibiotic targets. Chosen for their importance to ribosome function, Chow's lab is synthesizing these modified portions of RNA, using miniaturized versions of the full scale RNAs so that individual nucleotides can be monitored more closely. All six modified portions of RNA are located at different places on the physical structure of the ribosome, and are believed to control such vital processes as the maintenance of protein assembly and control of turning protein synthesis on and off. "We wanted to target areas that are very essential for the survival of cells," she said.

Finding the weapon

With the targets of the "protein machine" chosen, Chow's task at hand is finding a chemical "monkey wrench" that will bind to a ribosome and shut down its protein production. The process will involve several steps, beginning with finding a compound that has an affinity for one of the modified sites, and will bind to it. "If there is a strong interaction, that means the compound has potential to be a drug," Dr. Chow said. "The next step is to look and see if it affects the ribosome function. In other words, does it stop protein synthesis? If that does happen, that's great, but there is still another question, which is, can this compound get into cells? If the drug never gets into the cells, then it can't kill them."

To find additional information on the nature of bacterial RNA, Chow is also performing these trials on the corresponding modified RNA sites in human ribosomes, looking for any functional or structural differences that will further her understanding of bacterial RNA at these modified sites. "We want to know if the function of these modifications is the same in both organisms" she said. "We believe that even though the modifications occur in both, they might have slightly different roles or effects on the RNA. And what we really want to do is determine the differences so that we can take advantage of them for drug targeting."

Even with the advantage of brand new chemical compounds, however, Chow knows that bacteria may still develop resistance to the antibiotics she develops. She is collaborating with Phil Cunningham, Ph.D., associate professor of biology in WSU's College of Liberal Arts and Sciences, to utilize the genetic system Cunningham developed that predicts "functional mutants" – the potential mutations bacterial RNAs are likely to take on. "We're trying to do a screening to find compounds that bind to functional mutants, so once the bacteria develops a mutation to an antibiotic, we'll already have a drug ready," she said.

In the meantime, Chow is hard at work looking for a drug that will be a new challenge for bacteria to defend against. "Our hope is to find a lead compound, something that could potentially lead to an antibiotic," she said. "If not, we'll at least learn a lot about the rules for how compounds bind and that would help other people to design new drugs."

About Dr. Christine Chow: Dr. Chow received an A.B. in environmental studies and chemistry from Bowdoin College and an M.A. in organic chemistry from Columbia University. She studied inorganic chemistry with a focus on the interactions of transition metal complexes with RNA at the California Institute of Technology, where she earned a Ph.D. She then became a National Institutes of Health postdoctoral fellow at the Massachusetts Institute of Technology, studying the interactions of proteins with DNA modified by the anticancer drug Cisplatin. She joined Wayne State University in 1994.

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Aging Out

by Sarah James

At a time in the United States when a record number of parents are financially and emotionally supporting their children well into adulthood, one group of adolescents and probably the most ill prepared, is forced to fend for themselves at age eighteen. Each year, approximately 20,000 American adolescents "age out" of the foster care system, often without the resources needed to live successfully on their own for the first time. Usually without a family support system, savings or training for independent living, odds are doubly against these youth already at increased risk for negative economic and social outcomes. Children in the foster care system typically come from poor communities, receive inadequate education, undergo frequent school changes and have suffered abuse and neglect as children, which prompted their placement in foster care.

Wayne State University's Research Group on Homelessness and Poverty and the group's founder, Professor Paul Toro, have been studying the issue of homelessness from a variety of angles since the 1980s. "I never get bored with studying this issue because homelessness is such a complicated problem," says Dr. Toro. "We are probably the only scholars in the world who have studied most aspects of homelessness, from public opinion to prevalence to intervention to prevention research."

Their research findings led them to the foster care population. "We became interested in the population of kids who have aged out of foster care because there have been a whole series of studies, including some of ours, in which homeless adults have been asked about their history, and an amazingly high number indicate that they have been in foster care," explains Dr. Toro. He estimates that less than 2 percent of the overall population in the United States has been in the foster care system. However, among homeless adults, that number rises to as high as 35 percent in some studies. With a rate of homelessness over 15 times that of the general population, foster care youth are at significant risk of becoming homeless as young adults.

> "We're interested in the population of kids who have aged out of foster care because there have been a whole series of studies, including some of ours, in which homeless adults have been asked about their history, and an amazingly high number indicate that they have been in foster care."
>
> **— Dr. Paul Toro**

Through a grant from the National Institute on Alcohol Abuse and Alcoholism, the Research Group on Homelessness and Poverty has been tracking the welfare of 400 at-risk youth into adulthood over a seven-year period. This project, termed Housing, Adolescence, and Life Outcomes (HALO), examines the housing situation, educational and income status, substance use, conduct problems, psychological health, experience of community and

Dr. Paul Toro, professor of psychology

domestic violence, sexual behavior, recent stressful events, and physical health symptoms of its participants. Measures from the HALO study were modified and applied to a follow-up study targeting youth who have aged out of the foster care system and have been on their own for an average of 3.5 years. Michigan's Department of Human Services provided names and contact information on the 816 young adults in the Detroit tri-county area foster care system that turned 18 (the age in which youth are released from the foster care system) in 2002-2003. Since data was more than three years old, Dr. Toro was pleased that his research assistants were able to track down one third of the youth and nearly all who were contacted agreed to be interviewed.

Despite the obvious need, Dr. Toro says that many foster children have reported receiving no preparation for life skills before leaving the foster care system and nearly half have not received training in how to obtain housing services. And this shows in the interview results. "If you look at the group prospectively," shares Dr. Toro, "you see lots of problems. For example, 17 percent, within this 3.5-year period, have spent some time literally homeless, on the streets, in a shelter, in an abandoned building, this kind of situation. And even more, 49 percent, if you want to include a broader definition of homelessness, what I might call precarious housing – living with somebody but knowing they could kick you out at anytime, or staying with friends for a few days and not knowing

Aging Out continued

where you'll go next. That's just one outcome. If you look at other things, like education, only 41 percent finished high school, another 16 percent got a GED, but we're still talking more than 40 percent who don't have a high school education or GED. The employment situation shows that the kids were working, on average, only about half of the time during the 3.5 year follow-up period and that the average income, when they were working, was only $598 per month. The most common workplace was fast food. So, these kids are not doing well in terms of jobs or educational attainment. Almost half, 48 percent, have received some kind of public assistance, such as food stamps or welfare."

The next step is intervention research. Data from the telephone surveys will be used to design a comprehensive intervention program that will provide a continuum of educational, psychosocial, medical and practical support before and during the transition into adulthood. Dr. Toro and his research team expect to begin with a small-scale intervention pilot study in which they will interview 100-200 adolescents who are close to aging out of the foster care system. They will collect data on how these teenagers are doing at the beginning of the study and provide a random half of the group with intervention. Afterward, they will assess what worked and what didn't, in order to demonstrate a model that can help prevent homelessness and other negative outcomes in the foster care population. They would then like to apply this model on a larger, national, and possibly international, scale.

About Dr. Paul Toro: Dr. Paul Toro earned his bachelor's degree in psychology from the State University of New York at New Paltz and his doctoral degree in clinical/community psychology from the University of Rochester. He joined Wayne State in 1992. You can learn more about his research at http://sun.science.wayne.edu/~ptoro/.

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Turning Down Tinnitus

Giving veterans their peace and quiet

by Amy Oprean

For many people, it's a temporary annoyance – the high-pitched ringing in the ears that comes after working with a power saw, a leaf blower or perhaps most commonly, the unwanted souvenir from a concert. But while tinnitus may be a transient hassle for many, there is another group of people for which it's a permanent and debilitating phenomenon. Military personnel stationed in the warzones of Iraq and Afghanistan experience the "phantom sound" of tinnitus much like civilians do, but for troops, the perpetual exposure to roadside bombs, gunfire, and rocket-propelled grenades exacerbates the condition to the point of no return.

Wayne State researchers Anthony Cacace, Ph.D., and Jinsheng Zhang, Ph.D., are working to change that with two potential treatments for chronic tinnitus. Different by design but united with a common goal of suppression, these potential treatments pose the possibility of curing an injury that stays with soldiers long after other battle wounds have healed.

"Imagine you have this ringing in your ears. It disrupts your sleep, it disrupts your concentration; it's really loud and it never goes away," said Dr. Cacace, professor of otolaryngology in WSU's School of Medicine, and communication sciences and disorders in the College of Liberal Arts and Sciences. "Some people can deal with it and it doesn't bother them, but then there's a segment of people who have a very difficult time dealing with it, and these are the ones we are trying to help."

Dr. Jinsheng Zhang, associate professor of otolaryngology

Dr. Anthony Cacace, professor of otolaryngology and communications sciences and disorders

Tinnitus, which is believed to result from hyper neural activity in the ear or brain, is most commonly produced by repeated exposure to noise levels above the 80 to 85 decibel threshold, the level of average traffic. In soldiers exposed to noise levels exceeding 200 decibels on a daily basis, about 50 percent will develop tinnitus, hearing loss, or both. According to the Department of Veterans Affairs, nearly 70,000 of the more than 1.3 million troops who have served in the two war zones are collecting disability compensation for tinnitus, and 58,000 are on disability for hearing loss. Together, that amounts to $500 million spent each year – an amount expected to increase 18 percent a year,

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Turning Down Tinnitus continued

Dr. Avril Genene Holt, assistant professor of anatomy and cell biology and project collaborator, demonstates repetitive transcranial magnetic simulation

according to an analysis of VA data by the American Tinnitus Association.

"One of the things that we're trying to do now is develop a model of blast-induced tinnitus analogous to what the soldiers are going through in Iraq or Afghanistan, so that we can potentially try to diagnose it, treat it, and most importantly, try to prevent it," Dr. Cacace said.

With a grant from the Tinnitus Research Consortium, Dr. Cacace is studying a potential method of tinnitus suppression called repetitive transcranial magnetic stimulation, or rTMS. The noninvasive procedure consists of placing a magnet coil on the side of a patient's head and delivering a low frequency magnetic pulse through the skull, potentially suppressing tinnitus. To test the effectiveness of the procedure, Dr. Cacace is administering a "sham-controlled crossover design" to tinnitus patients, wherein patients are given both a sham rTMS regimen and the real treatment over the course of two weeks. The crossover trials will allow him to assess for any placebo effect in patients. He is also using magnetic resonance spectroscopy to assess changes in the brain chemistry following treatment, and will evaluate any changes in brain chemistry using another MRI analysis tool called voxel-based morphometry. He is collaborating with Jiani Hu, Ph.D., an MR physicist in the Department of Radiology in the School of Medicine and noted expert in magnetic resonance spectroscopy.

Dr. Zhang, associate professor and assistant research director of otolaryngology and the director of the Laboratory of Auditory Prostheses Research in the Department of Communication Sciences and Disorders, is studying a significantly different approach to tinnitus suppression. He is testing the direct electrical stimulation of the auditory cortex – the region of the brain associated with hearing. Clinically, it has been shown that direct electrical stimulation of the auditory cortex can actually suppress the "phantom sound" caused by damage

> "We believe that with help from advancing engineering technology, it is possible to develop miniaturized and less invasive implantable devices to suppress tinnitus."
>
> **— Dr. Jinsheng Zhang**

to the peripheral and central auditory system. The effectiveness of the treatment, however, varies greatly from patient to patient. Zhang's ultimate goal is to develop a permanent prosthesis that, when implanted in the auditory cortex, will rid the brain of tinnitus by continuous electrical impulses. In addition, Dr. Zhang has recently been awarded a grant from the Tinnitus Research Initiative to study the potential of tinnitus suppression by electrically stimulating certain acupoints in the human body.

Dr. Zhang is developing an animal model for tinnitus suppression using electrical stimulation of the auditory cortex. From this novel method, which combines electrical stimulation, electrophysiology and behavioral testing, he will test whether animals develop tinnitus following noise exposure, and determine whether tinnitus-positive animals experience suppression following electrical stimulation of the auditory cortex. Working with collaborators from Henry Ford Hospital, Dr. Zhang will then test his new stimulation targets in the brain and new stimulation strategies.

Although the technique is invasive, other implants have progressed to safe and effective clinical use, Dr. Zhang said, one of the most notable being the cochlear implant for hearing loss. Implants to the cochlea – the spiral shaped cavity of the inner ear – take on the job of damaged hair cells by converting acoustic sound into electrical signals. "Three decades ago, the cochlear implant was developed, and at the time, everyone thought it was crazy," he said. "And now it's considered the most successful bionic implant used today. Similarly, we believe that with help from advancing engineering technology, it is possible to develop miniaturized and less invasive implantable devices to suppress tinnitus."

Using another grant from the Tinnitus Research Initiative, Dr. Cacace is also utilizing several MRI methods to comparatively examine numerous aspects of brains with noise-induced hearing loss with and without tinnitus. Methods like magnetic resonance spectroscopy are of high interest to Cacace and Zhang, since having a chemical model of tinnitus would open the door for researchers to develop medication that counters these chemical changes.

Whether Dr. Cacace's noninvasive rTMS method of tinnitus suppression, Dr. Zhang's electrical stimulation, or a pharmaceutical will provide the most effective treatment is yet to be determined, and could actually vary from person to person, Dr. Cacace said.

"What we do know is that some people respond to medicines, some don't, some respond to rTMS, or direct electrical stimulation, and others don't – and we don't know exactly know why this is," he said. "But we hope to make all these methods more effective, so that returning vets and anyone else with this chronic problem can finally get some permanent relief."

About Dr. Anthony Cacace: Dr. Cacace received a B.S. in speech pathology and audiology from the State University of New York at New Paltz. He received an M.S. in audiology and a Ph.D. in communication sciences and disorders (audiology) and neuroscience from Syracuse University. He obtained his postdoctoral fellowship training in neurophysiology at the Wadsworth Laboratories of the New York State Health Department. He spent 20 years in the ear, nose, otolaryngology and neurology departments at the Neuroscience Institute and Advanced Imaging Research Center of Albany Medical College. He joined Wayne State University in August 2007.

About Dr. Jinsheng Zhang: Dr. Zhang received a B.S. in biology and an M.S. in physiology from Hebei Normal University in China, and a Ph.D. in auditory neurophysiology at University of Fribourg in Switzerland. He serves on the board of the Lions Hearing Institute of Michigan. Dr. Zhang joined Wayne State University in 1997.

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Translating Science to Improve Urban Health

An international linkage of geospatial information with environmentally induced asthma models

by Julie O'Connor

Wayne State University has a long-standing commitment to bringing change to urban health, particularly through research on disparate outcomes in disease, prevention and cure experienced among different ethnic, cultural and socio-economic groups.

Through WSU's *Research Enhancement Program to Support Clinical Translational Science in Urban Health*, the university is joining together researchers from multiple institutions. These teams bring together expertise from their respective disciplines to analyze problems from many perspectives, with the goal of resolving them across a variety of domains such as biological, psychological and environmental.

By fostering multidisciplinary clinical and translational research at WSU, its affiliates and collaborating institutions, WSU hopes to be a true academic home for research that will impact healthcare throughout the United States and beyond. One such project funded through this initiative has great potential in aiding the control and management of community, family and school-based interventions of asthma and potentially other diseases in children and adults in the cities of Detroit and Windsor.

The study, *Linking Geospatial Information with Public Health Outcomes: Modeling Asthma Morbidity Across an Urban International Border*, is potentially one of the first international studies that is comparing and contrasting environmental indicators with specific health outcomes in cities with shared pollution sources, yet very different healthcare systems.

In collaboration with the University of Windsor, University of Toronto, Henry Ford Health System, Air Health Science Division of Health Canada and the Canadian Institute for Health Information, Linda Weglicki, Ph.D., R.N., assistant professor of adult health in WSU's College of Nursing is leading this study that is building upon the University of Windsor's research that developed land use regression and air dispersion models to map key environmental indicators and their relationship to health conditions in Detroit and Windsor.

"Through the North American Public Health Institute, a joint effort between Wayne State University and the University of Windsor, a mapping and health promotion group formed about two years ago," said Dr. Weglicki. "While the group met fairly often during those first two years, the focus for this research didn't come together until the RFP for the Research Enhancement Program was announced. While developing the proposal, we not only added additional researchers who had expertise in specific areas, we also felt that it was important to identify an advisory board that reviewed and advised us on key sections of our proposal which is a study to develop spatial-temporal models using GIS to identify and predict environmentally induced health conditions in adults and children in and across our international border." The research team, known as the Geospatial Determinants of

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> "This project was an exciting introduction to research for a large group of undergraduate students,"
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> **— Dr. Larry Lemke**

from left: Dr. Phil Granerio, University of Windsor; Alice Grgicak-Mannion, Great Lakes Institute of Environmental Research; Dr. D. Martin Raymond III, Eastern Michigan University; Dr. Linda Weglicki; WSU College of Nursing; Dr. Larry Lemke, WSU Department of Geology; Shanti Menon, Project Director (WSU); Dr. Lois Lamerato, Henry Ford Health System, and Jason Booza, Demographer, Department of Family Medicine and Public Health Sciences, WSU.

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Translating Science continued

Health Outcomes Consortium, or GeoDHOC, is subdivided into three expert teams to accomplish the project aims.

Team I, led by Dr. Iris Xiaohong Xu, associate professor of civil and environmental engineering at the University of Windsor, is primarily focused on gathering spatially distributed air quality data from Detroit and Windsor and testing the applicability of static land use regression and air dispersion models. Team I is also responsible for deployment of air samplers for both sampling periods in Detroit and Windsor. Larry Lemke, Ph.D., assistant professor of geology at WSU and Phil Graniero, Ph.D., associate professor of earth and environmental sciences at the University of Windsor are key members of Team I.

Team II, led by Dr. Weglicki, is focused on health outcomes and health outcome data. As such, they are responsible for identifying and collecting comparable and compatible measures of asthma morbidity from Detroit and Windsor health systems. This team comprises Lois Lamereto, Ph.D., health services epidemiologist and Richard Krajenta, programmer/analyst at Henry Ford Health System; Helen Krouse, Ph.D., R.N., professor of adult health in the College of Nursing at WSU; Delbert Raymond, Ph.D., R.N., assistant professor of nursing at Eastern Michigan University; Paul Villeneuve, Ph.D., professor of public health sciences at the University of Toronto and research scientist at Health Canada; and John Reiners, Ph.D., professor in WSU's Institute of Environmental Health Sciences.

Team III, led by Jason Booza, research assistant and demographer in WSU's Department of Family Medicine in the School of Medicine, is focused on geospatial information systems (GIS) and data integration. This includes geospatial modeling for deciding the best locations for sampling sites based on land use, traffic patterns, meteorological conditions, and population differentials. They will also integrate the air quality data, spatial attributes, and health outcomes into a final GIS framework. Alice Grgicak-Mannion, GIS manager for the Great Lakes Institute for Environmental Research (GLIER) at the University of Windsor and Richard Krajenta, Henry Ford Health System, are key members of the GIS and data integration team. Teams of 20 undergraduate students and two graduate students from Wayne State University and the University of Windsor's departments of geology, environmental science, and civil and environmental engineering were recruited to support this project. They received extensive training on the science and technology of the various air samplers, and were integral in the handling, set up and removal of air samplers for the first round of air sampling. "The air samplers will be deployed on two separate occasions at 100 locations throughout Windsor and Detroit," commented Dr. Lemke. "Sampler locations are chosen to cover a consistent geographic distribution throughout both cities, and prioritized locally based on land use, population density, and security for air sampling equipment."

"This project was an exciting introduction to research for a large group of undergraduate students," said Dr. Lemke. "Hands-on experience is often a much more effective way of learning, and this project gave our students an opportunity to learn more than a traditional textbook or classroom experience could provide. It has also motivated many of them to think seriously about the possibility of furthering their studies in graduate school," he added.

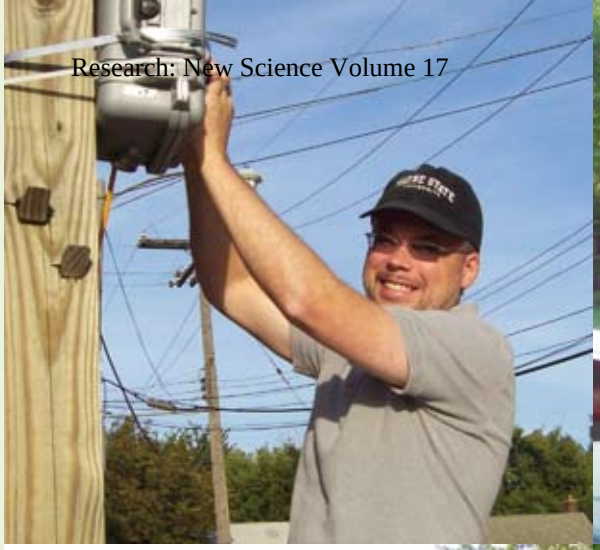
In addition to GeoDHOC team members and student researchers, myriad other university staff and administrators, outside consultants, city employees, customs brokers and numerous others were needed to help navigate through many unexpected challenges that were faced with this international project. "We were confronted with unforeseen situations such as obtaining special university permission to pull city permits to deploy air samplers; transferring equipment and air samplers across the border without being opened and contaminated by customs agents; deploying air samplers in secure places such as city fire stations; and dealing with numerous other financial situations brought on by this international project," said Dr. Weglicki. Many employees throughout Wayne State University and the University of Windsor faced unusual challenges in their jobs to help get this project under way and within the

proposed timeline. “We are within our projected timeline but would not be here without the help and expertise of so many throughout our colleges and administrative departments – it truly has been a learning experience for all and we are appreciative of the time and assistance of so many people,” she added.

Translating research; finding disease interventions

This project will aid in the development of communities and school-based interventions to control and manage asthma in children and adults throughout Detroit and Windsor. It will establish the foundation for translational research that can be applied to other diseases and health outcomes by merging disparate data frameworks that are not normally integrated, offering a new pathway for expanding research into other health outcomes.

“The broader, long-term goal for the group is to be able to apply similar geospatial models to investigate other diseases such as cardiovascular diseases, cancer, diabetes and more, and to inform targeted policies to improve the health of urban residents,” said Dr. Weglicki. “Once we have data from the second deployment of air samplers in May 2009, we will be able to begin making comparisons for our current study. Incorporating other health conditions in to the research project is a major goal of this team.”



Moving Beyond the

By Amy Oprean

Wayne State University's commitment to improving human conditions is far reaching, and the School of Social Work has taken this on as a serious challenge. In 2008, the school launched a new center that merges research and practice – with the goal of improving both.

The culmination of strong leadership, hard work and years of planning, the Center for Social Work Practice and Policy Research is a state-of-the-art hub that will assist WSU faculty in their research, engage in partnerships with Detroit community service providers and communicate social work policy and practice information to the public.

"We're trying to generate and disseminate knowledge that improves the lives of the disadvantaged through research, consultation and dissemination," said Joanne Sobeck, Ph.D., associate professor and director of research in the School of Social Work, and the center's inaugural director.

Since its induction, the center has served as a dynamic resource to Wayne State faculty members for support in their research, outside community organizations for technical support and collaboration opportunities, and the public for developments in social work research and policy.

One of the main goals of the center is connecting faculty members with community organizations with similar interests. These mutually beneficial partnerships bridge the gap between researchers and practitioners through a number of valuable exchanges, including idea mapping, research summits, and community research exchange networks – scaled down seminars for researchers and practitioners of a specific expertise to discuss issues in their field.

To help facilitate these dialogues, Sobeck and her collaborators teamed up with some of the

Top left to right: Dr. Joanne Sobeck, associate professor and director of research; Dr. Debra Hernandez Jozefowicz-Simbeni, assistant professor; Dr. Cheryl Waites, associate dean; [illegible]

Campus to the Community

area's largest and oldest community organizations. These six "strategic partners" are Matrix Human Services, the Children's Center of Detroit, Oakland Family Services, Black Family Development, Inc., Spaulding for Children and Detroit-Wayne County Community Mental Health Agency.

Reaching out

Debra Hernandez Jozefowicz-Simbeni, Ph.D, assistant professor of social work, is involved in one such partnership. She and her colleague, Dr. Bart Miles, assistant professor of social work, will be collaborating with Matrix Human Services on a study of homeless youth and youth in care in Detroit. They will be collecting data from youth residing in homeless shelters and residential programs, focusing specifically on their adjustment, service needs and program experiences. In return, Matrix Human Services will be able to use the research to improve their facilities and services, as well as engage in study groups where improvements can be discussed.

The center will not only facilitate real change in social work practice, but will accelerate the speed at which research can progress from an idea in a researcher's notebook to a working study.

"When you do community-based research, there's so much that goes into developing relationships and maintaining them, that it can at times become very onerous for the faculty member as well as the agency," Jozefowicz-Simbeni said. "So I think the center is creating an infrastructure for facilitating research collaborations that are meaningful and mutually beneficial to both academic research and community stakeholders."

This aspect of the center will be particularly useful to Cheryl Waites, Ed.D., associate dean in the School of Social Work, who uses a community-based, participatory method of research that relies heavily on interaction with local organizations. In beginning her research on "healthy aging," – an investigation assessing changes in senior centers and assisted living needed to accommodate older adults and baby boomers as they enter the later stages of life – the center assisted in locating community agencies focused on aging. Waites, who is new to the Detroit area, said the assistance saved her the time and energy of doing the legwork herself, and allowed her to focus on getting her research started.

For Shawna J. Lee, Ph.D., assistant professor in the School of Social Work and faculty associate of the Merrill Palmer Skillman Institute at Wayne State, the center will be a valuable mechanism for disseminating the findings of several studies examining paternal child abuse. Using data from a large sample of urban families, Lee's research assesses risk factors related to fathers' physical and psychological aggression toward their children. The center will connect Lee with agencies that provide intervention efforts focusing on fathers and with the community through "research dialogue" sessions that engage community members and practitioners with relevant and timely research intended to advance child abuse prevention efforts.

Improving the future

Reflecting on its first year, Sobeck said the center is off to a promising start in achieving its long-term goals of obtaining research funding, as well as heightening Wayne State's visibility as a source for expertise in ongoing social work research.

"Internationally, if someone in Germany is doing research on urban populations or policy issues, we hope that they will consider the expertise of our faculty here," Sobeck said. "If someone in L.A. is seeking partners for domestic violence research, we want them to see our center as a viable resource with researchers that address that issue. Locally, we'd like the center to be a go-to place for consultation and technical assistance as well as recent updates and integration of research and practice."

"I'll know I have done my job if we become known and accessed for what we do."

About Dr. Joanne Sobeck: Dr. Sobeck received a bachelor of social work degree from Northern Michigan University and a master of social work from Western Michigan University, where she studied policy, planning and administration. She received her Ph.D. in political science from Wayne State University. She joined Wayne State University in 1983 as a member of the staff at the Addiction Research Institute. She is the co-chair of the Community Practice Concentration and directs the Center for Social Work Practice and Policy Research.

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The A to Zzzz's of Exercise

Treating sleep disruptions with exercise prescriptions for post-menopausal women

by Amy Oprean

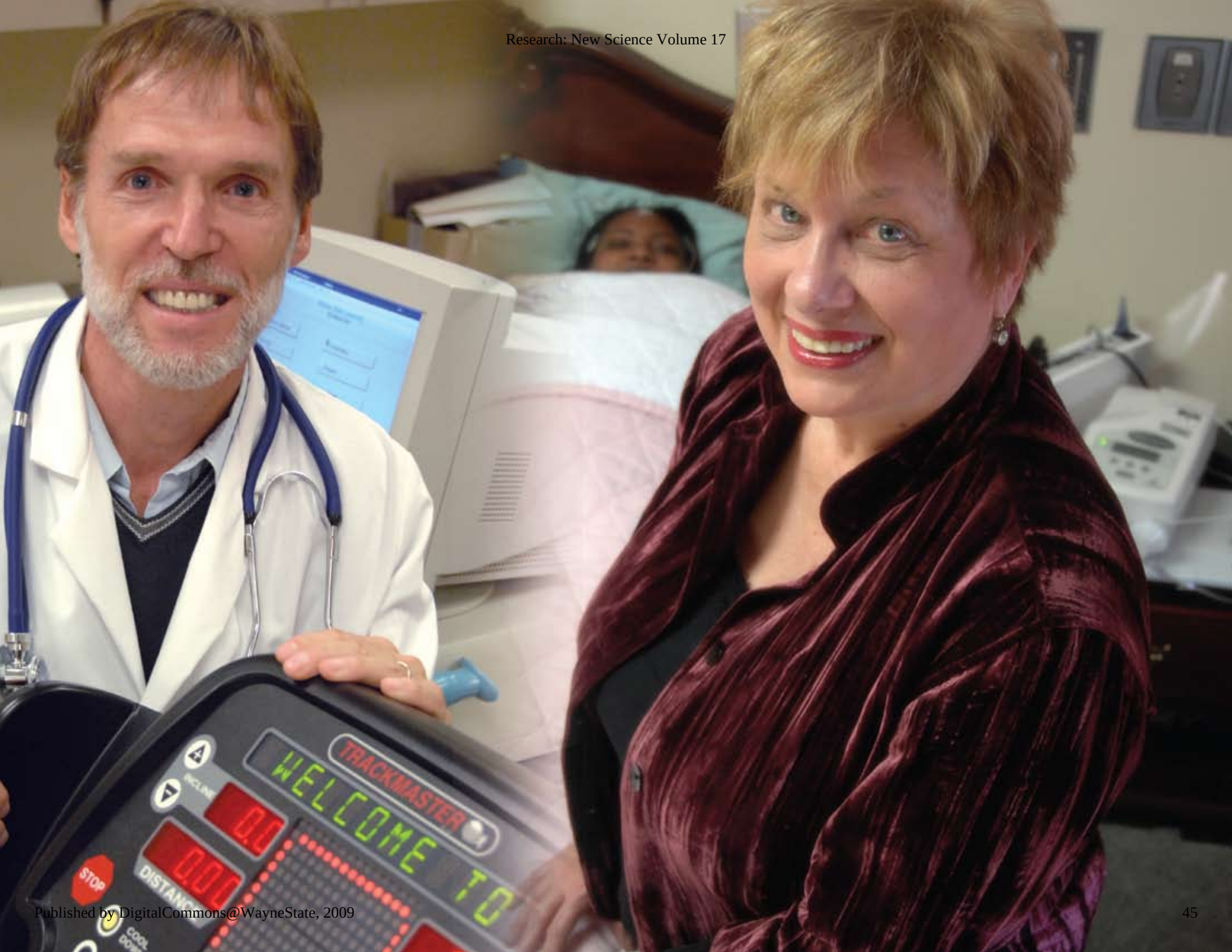
When it comes to improving overall health, few activities are cited as frequently as exercising regularly and getting enough sleep. These activities are not only important in their own right, but now appear to be connected. Research in recent years has uncovered exercise's ability to help people fall asleep faster and stay in deeper stages of sleep longer, revealing that a better night's sleep could be attainable without the prescription sleep aids that some people need. Specific exercise regimens may be the answer for those who have trouble sleeping.

Jean Davis, Ph.D., associate professor and assistant dean for adult health in WSU's College of Nursing, and Hermann-Josef Engels, Ph.D., professor of exercise physiology in WSU's College of Education have been working to find a solution to getting a better night's sleep. Funded by the National Institute of Nursing Research, their interdisciplinary team conducted a study to determine whether a personalized exercise program could serve as a non-pharmacological treatment for sleep problems. They focused specifically on post-menopausal women, a group for which disrupted sleep – difficulty falling asleep, difficulty staying asleep, or both – is one of the most common complaints.

"We're interested in intervening, actually offering someone a prescription for improving their sleep that doesn't involve drugs, which is what makes this study unique," Dr. Davis said.

While working as a faculty member at the University of Florida, Davis became interested in the topic after learning of the negative side effects

Dr. Herman-Josef Engels, professor of exercise physiology and Dr. Jean Davis, associate professor and associate dean for adult health


TRACKMASTER
WELCOME TO
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The A to Zzzz's of Exercise continued

of prescription sleep medications. Though exercise is often suggested by health care professionals as a sleep aid alternative, literature review revealed a lack of objective scientific studies on the topic. "In advanced practice, we frequently advise patients to exercise to sleep better," Dr. Davis commented. "And women would often tell us that their sleep was better, but we had no objective laboratory data that showed this is something that legitimately works."

Of the previous exercise studies that were conducted, many focused on athletes and people who weren't currently suffering with sleep problems. Wanting to assess the potential benefits of exercise on disrupted sleep specifically in post-menopausal women, she approached Engels upon joining Wayne State in 2003. Eager to pioneer research on the understudied topic, Engels agreed to join forces.

"There hadn't been much research looking at exercise as a treatment for sleep disturbances," Dr. Engels said. "We're both very genuinely interested in this, and thought we could really make a vital contribution to help answer some lingering questions in this area."

In order to keep as many confounding factors out of their study group as possible, Davis and Engels disqualified subjects with health problems that included sleep apnea, hypertension, obesity and heart disease, cutting the group of approximately 600 women interested in the study to less than 40. At the beginning of the study, subjects underwent a maximal oxygen uptake (or VO2max) test in the WSU Exercise Physiology Laboratory to assess their physical work capacity, and based on that measurement, were given an individualized exercise prescription. The workout program consisted of a 16-week, home-based walking program conducted five times per week for 30 minutes per session at a moderate level of intensity.

The VO2max tests were given again at the end of the study to verify the subjects' physical fitness improvements and their correlation with improvements in sleep. A control group underwent the same assessments without an exercise program, to further analyze the effects of the exercise program on sleep. Other controls included monitoring subjects' day-to-day exposure to light and not allowing subjects to exercise within two hours of going to bed – both factors that have been suggested to affect sleep patterns.

> "I think that the quality of the research is much better when you have experts from different disciplines making a contribution."
>
> **— Dr. Herman-Josef Engels**

The same rigor was applied to measuring subjects' sleep patterns throughout the study. Conducted in the Sleep Disorders Center at Hutzel Hospital in Detroit, Davis and Engels continuously measured subjects' brain waves, eye movements and chin muscle tension as they slept. These three measures were used to score the subjects' sleep and determine the amount of time subjects were spending in the different stages of sleep (NREM and REM sleep), as well as instances of arousal or awakening. "We were very meticulous," Dr. Engels said. "In order to be able to look at the potential of exercise to improve sleep, we employed widely accepted 'gold standard' procedures for both the exercise and sleep components of the study."

The team also measured core body temperature, a strong indicator of an individuals' circadian rhythm – the 24-hour physiological cycle that influences the 24-hour sleep/wake pattern. The body's daily physiological "cue" to fall asleep is a drop in body temperature. As people age, the rise and fall of their daily core temperature becomes less stable, possibly causing fragmented sleep. Davis and Engels are for the first time characterizing the 24-hour temperature curve specifically of post-menopausal women, looking for clues as to why this group in particular reports sleep problems so frequently.

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Restoring the cycle

If post-menopausal women experience a shift in their circadian rhythm, the question remains as to why. One theory suggests it may be due to a decrease in estrogen levels around the suprachiasmatic nucleus – the body's inner clock, Dr. Davis said. "There is some evidence that the area around the suprachiasmatic nucleus is rich with estrogen receptor sites. Postmenopausal women who are estrogen deficient may have fewer estrogen receptor sites. The loss of estrogen in the area of the suprachiasmatic nucleus could make for a less stable temperature cycle, and therefore, women aren't going to sleep as well."

If improvements in physical fitness improve sleep quality in post-menopausal women, it may also be attributed to a slight increase in estrogen released into the bloodstream as stored fat is mobilized, Dr. Davis said. A second possible explanation is that habitual exercise could improve sleeping patterns by providing a new daily "cue" that restores stability to women's circadian rhythm, she added. "We don't know for sure if one of these explanations is the reason exercise improves sleep, but that's also part of the study. The clinical trial sought to answer not only if exercise has this positive effect, but if it does, why?"

With their study complete, Davis and Engels are in the process of analyzing the extensive amount of data collected. Though the results will heavily influence the direction of subsequent research, their interests include the therapeutic aspects of passive and active body warming on sleep patterns and exercise "intervention" therapies for post-menopausal women suffering from hypertension or other chronic ailments.

Whichever direction their results will lead, however, Engels and Davis plan to continue studies that combine their expertise.

"It's been a challenging and enjoyable experience to work with people outside my department," Dr. Engels said. "I think that the quality of the research is much better when you have experts from different disciplines making a contribution."

"There is an incredible environment at Wayne State University for collaborating," Dr. Davis added. If there is a research problem you want to study, people from across the campus will help you make it happen."

> "The loss of estrogen in the area of the suprachiasmatic nucleus could make for a less stable temperature cycle, and therefore, women aren't going to sleep as well."
>
> **— Dr. Jean Davis**

About Dr. Jean Davis: Dr. Davis earned a B.S. in nursing from Michigan State University and an M.S. in nursing from Hunter College, the City University of New York. She completed her Ph.D. in nursing research and physiology with a specialty in neurophysiology at the University of Arizona. Dr. Davis has been on the faculty at UCLA and the University of Florida, and joined Wayne State University in 2003.

About Dr. Hermann-Josef Engels: Dr. Engels received a B.S. and M.S. from the Florida International University in Miami, Fla. He completed his doctoral training in exercise physiology at Florida State University in Tallahassee. Dr. Engels is a fellow of the American College of Sports Medicine and of the Research Consortium of the American Alliance for Health, Physical Education, Recreation and Dance. He joined Wayne State University in 1989.

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Finding the Missing Puzzle Piece of Autism

By Julie O'Connor

Photo by Donna Terek

Autism, one of the greatest mysteries of medicine – and the most pervasive development disorder that is characterized by the impairment of social interactions and communication, severely restricted interest levels and highly repetitive behavior – is prevalent in one to two per 1,000 people. Autism affects many parts of the brain, but how it happens is not clearly understood. Signs of autism become noticeable in the first three years of a child's life, and early intervention can help children gain important social, communication and self-care skills they would otherwise lack. There is no single known cause of autism and there is no cure for the disease that requires a lifetime of support.

Dr. Diane Chugani, professor of pediatrics and radiology at Wayne State University's School of Medicine and director of the Translational Imaging Laboratory at Children's Hospital of Michigan, is doing research to find the origins and a possible treatment for autism.

Dr. Diane Chugani, professor of pediatrics and radiology

Unlocking the hidden mind

Dr. Chugani received a $5.79 million grant from the National Institute of Neurological Disorders and Stroke of the National Institutes of Health for a study that may open doors to finding a treatment for improving those afflicted with autism. This Autism Center of Excellence Network Grant, *"Early Pharmacotherapy Guided by Biomarkers in Autism,"* will continue earlier research which showed that the brain serotonergic system is abnormal during critical periods of brain development in children with autism.

Dr. Chugani and her team demonstrated that their positron emission tomography (PET) studies on the serotonin synthesis capacity in children younger than six years was significantly altered when compared to non-autistic children. Serotonin, an important factor involved in postnatal synaptogenesis – or specialized junctions through which neurons signal to each other and other non-neuronal cells to form interconnected circuits within the central nervous system that are crucial to the biological processes that underlie perception and thought – is thought to be one potential target to treatment of autism. Through use of the 5HT1A serotonin agonist, buspirone, in children younger than six, Chugani hopes to uncover a new and safe treatment in groups or subgroups of autistic children.

Chugani's research brings new hope to those with autism who have difficulty with social skills, communication and repetitive motor actions. Her previous studies that treated children with a drug similar to serotonin improved many of the participant's social interactions and reduced the repetitive behaviors, and this study will further test this novel treatment.

"Dr. Chugani is one of the leading scientists in the field of autism," commented Dr. Joseph Dunbar, associate vice president for Research at Wayne State University. "Her previous work utilizing PET imaging studies has led to the discovery of potential mechanisms involved in the pathogenesis of autism that may someday lead to new treatments for the growing number of children diagnosed with this complex disability," he added.

About Dr. Diane Chugani: Dr. Chugani is a member of the scientific advisory boards of Autism Speaks and the Tuberous Sclerosis Alliance. She was a founding board member of the International Society for Autism Research. She received her Ph.D.. in pharmacology from the University of California, Los Angeles and her B.A. (Cum Laude) in psychology from the University of Maryland, College Park. She joined Wayne State University in 1993.

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When the Eyes Fail

By Julie O'Connor

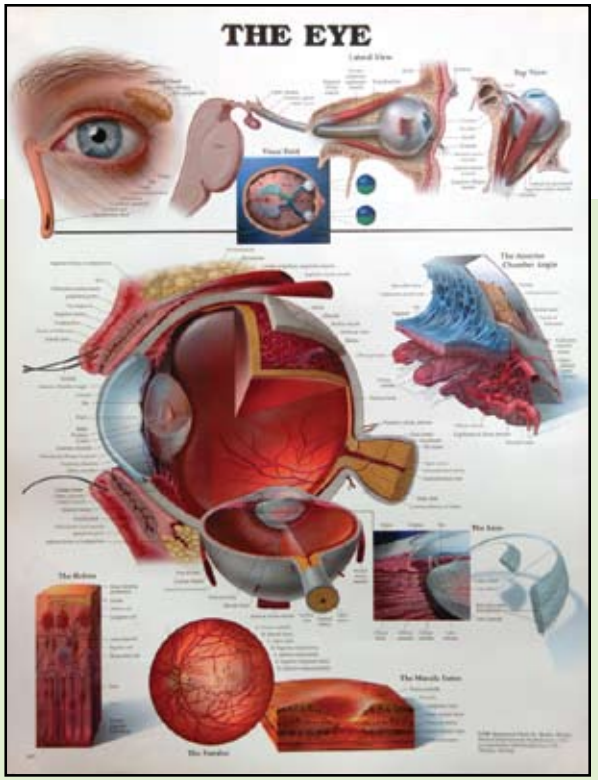
"I'm so sorry, Mrs. Smith. Your son's loss of night vision and decreased peripheral vision is caused by an inherited genetic eye disease that affects the retina called retinitis pigmentosa or RP. RP causes the degeneration of photoreceptor cells in the retina. It is programmed into his cells, and is not caused by injury or infection. Genetic mutations essentially send faulty messages to the retinal cells which lead to their progressive degeneration. Eventually this leads to vision loss and most diagnosed with RP are legally blind by age 40. Some studies suggest that treatment with Vitamin A may slow the progression of this disease, and current research shows some promising strides for future treatments, but currently there is no effective treatment for recovery of visual loss from RP as of today."

Wayne State University researchers and colleagues, led by Zhuo-Hua Pan, Ph.D., professor of anatomy and cell biology in the School of Medicine, have reported a novel strategy for treatment of blinding retinal degenerative disease such as retinitis pigmentosa (RP). This National Eye Institute of the National Institutes of Health supported research was published in *Neuron*, a highly regarded journal which publishes reports of novel results in any area of the neurosciences.

A search for a cure for retinitis pigmentosa

Vision normally begins when rods and cones, also called photoreceptors, respond to light and send signals through other retinal neurons, inner retinal neurons or interneurons, and the optic nerve to the visual cortex of the brain where visual images are formed. The severe loss of photoreceptor cells caused by congenital retinal degenerative diseases results in partial or total blindness. These disease conditions affect one in 3,000 people worldwide. At present, no treatment is available for restoring vision once rods and cones, the normally light-sensitive cells in the retina, have been lost.

Dr. Pan and his colleagues took a novel strategy for developing a potential treatment of blindness caused by retinal degenerative diseases by genetically converting light-insensitive inner retinal neurons into photosensitive cells – thus restoring light-sensitivity to retinas that lack photoreceptors. Using a harmless virus, they introduced a gene encoding a light-sensitive protein from green algae, called channelrhodopsin-2 (ChR2), into surviving inner retinal neurons in mice that were genetically bred to lose rods and cones, a condition similar to



the blinding disease, retinitis pigmentosa, in humans. They found that the introduced ChR2 protein made the inner retinal neurons become light sensitive. What's more, they found the ChR2 protein persisted for long periods in these neurons, and the neurons generated signals that were transmitted to the visual cortex of the animals' brains.

"Our study demonstrates the feasibility of restoring visual responses in mice after they lose the light-sensitive photoreceptor cells," said Dr. Pan. "It raises the possibility that this approach may be a potential strategy for the treatment of blindness caused by rod and cone degeneration in humans."

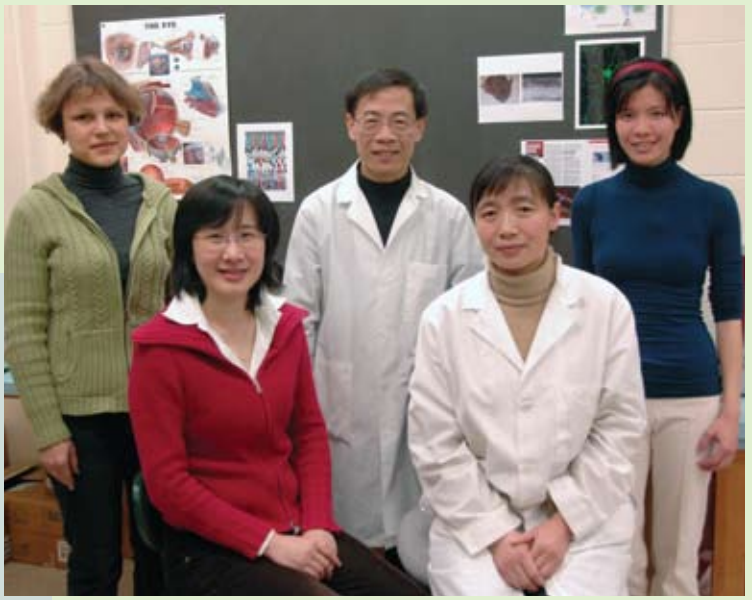
"With this strategy, the investigators have made a paradigm shift in the field and opened the possibility of genetically modifying the surviving retinal interneurons to function as a replacement light-sensing receptor," wrote John Flannery and Kenneth Greenberg of University of California, Berkeley, in a preview of the paper in the same issue of *Neuron*. "This publication is clearly a significant first step into this new field of re-engineering retinal interneurons as genetically modified 'prosthetic' cells," they wrote.

"This innovative gene-transfer approach is certainly compelling," said Paul A. Sieving, M.D., Ph.D., director of vision research at the National Institutes of Health. "This is a clever approach that offers the possibility of some extent of vision restoration at some time in the future."

Dr. Pan and his colleagues are working to determine whether the light signals reaching the visual cortex can be perceived by the brain as useful vision. They are also making a number of technical improvements to better fit the need for vision restoration, for example, by selectively targeting ChR2 in certain populations of inner retinal neurons and using other similar light sensitive proteins to increase light sensitivity and restore both ON and OFF pathways in the diseased retina.

This research is providing many people with hope that one day there will be a treatment for restoring vision to those afflicted with RP.

About Dr. Zhuo-Hua Pan: Dr. Pan received his B.S. degree from the University of Science & Technology of China, his M.S. from the Institute of Biophysics at the Chinese Academy of Science, and his Ph.D. from the State University of New York at Buffalo. He joined Wayne State University in 1999.



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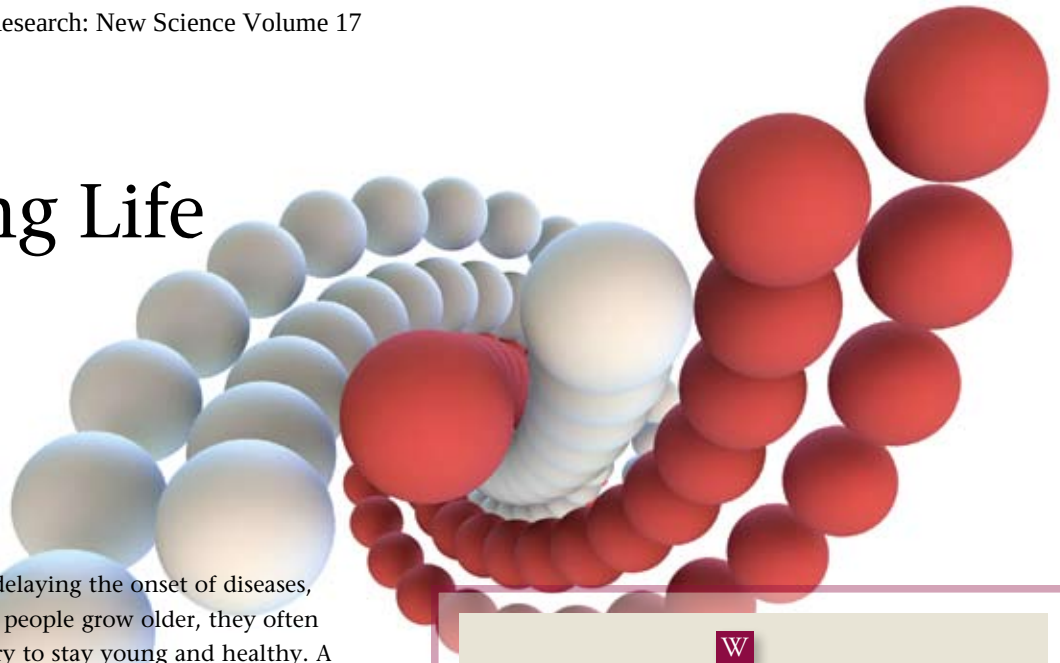
EXTending Life

by Julie O'Connor



Slowing the aging process, delaying the onset of diseases, extending cellular life… as people grow older, they often seek products or therapies to try to stay young and healthy. A researcher in the School of Medicine at Wayne State University may have discovered the proverbial "fountain of youth" that may one day help us all to live better and happier lives.

Stanley R. Terlecky, Ph.D., associate professor of pharmacology in the School of Medicine has identified a novel technology that can reduce or even eliminate accumulation of free radicals or oxidants in cells long associated with the aging process. His research focuses on peroxisomes, essential subcellular structures whose critical roles in metabolism, aging, and disease have only recently come to light.

The technology

As we age, our cells undergo an irreversible physiological decline caused by a variety of factors including shortening of chromosome ends, DNA damage and the accumulation of harmful oxygen species. Peroxisomes are at the center of this process to an extent never before appreciated. They not only carry out critical cellular functions but also produce potentially toxic metabolites as the "spent fuel" from these reactions. Hydrogen peroxide is one of these harmful byproducts generated by peroxisomes that can be deadly to cells.

> "We are currently examining whether or not our biologic can be aerolized in a form which permits delivery to the lung as a potential treatment for this devastating class of pulmonary disease."
>
> **— Dr. Stanley Terlecky**

To neutralize its toxic effects, peroxisomes pull the antioxidant enzyme catalase from the cytosol of the cell – the "soup" within which all the other cell organelles reside. A healthy peroxisome will then use the imported catalase to convert potentially dangerous hydrogen peroxide to harmless water and oxygen. This process can be thrown off kilter however, as cells age or are affected by disease or mutation. The result is that catalase

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EXTending Life continued

Mr. John Tesija, vice president and head of operations, EXT Life Sciences, Inc

is not properly utilized by peroxisomes, with dire consequences to the cell and the entire organism.

"By doing focused research on the peroxisome, we discovered it is a viable, druggable target," said Dr. Terlecky. "Unlike mitochondria, to which you can't deliver a protein directly, peroxisomes are mechanistically much different." Dr. Terlecky and fellow expert in cellular trafficking pathways, Paul A. Walton, Ph.D., from the University of Western Ontario, created a novel protein therapeutic that can be delivered into a human cell and then sent to the peroxisome to neutralize harmful oxidants. This proprietary technology is called CATSKL™.

> "Through all of this, I have learned that it takes time to develop a marketable compound."
>
> **— Dr. Stanley Terlecky**

"The compound has great potential for treating serious health problems including ischemia-reperfusion injury associated with heart attack or stroke, inflammation and related arthritic conditions, and type 2 diabetes, among others," Terlecky commented. In addition, idiopathic pulmonary fibrosis kills 40,000 people per year and there are no cures or effective treatments. There is evidence the pathology is associated with excessive production of reactive oxygen species (i.e. oxidants). "We are currently examining whether or not our biologic can be aerolized in a form which permits delivery to the lung as a potential treatment for this devastating class of pulmonary disease," added Dr. Terlecky.

Dr. Terlecky and a team of researchers also are looking at other potential uses for their technology including treatment of a number of skin diseases such as psoriasis and dermatitis, as well as treating and protecting surrounding skin tissue exposed or damaged by radiation or photodynamic therapies. "We are also looking at CATSKL™ as a preservation solution," Dr. Terlecky said. In heart, lung, liver, and kidney transplants, the cessation and subsequent commencement of blood flow causes reperfusion injury that result in inflammation and oxidative damage to the organ. "CATSKL™ may be able to thwart this from occurring in the transplant process," he said.

In addition to the many pharmaceutical uses, CATSKL™ has tremendous potential as an "active" component of so-called cosmeceutical products. It can be formulated with a number of other ingredients as an effective antioxidant in various skincare products.

Bringing CATSKL™ to life – *EXT Life Sciences, Inc.*

In 2004, Dr. Terlecky and his friend, John Tesija, were having a discussion about this discovery. What was meant to be a casual conversation turned into a partnership that brought EXT Life Sciences, Inc.,

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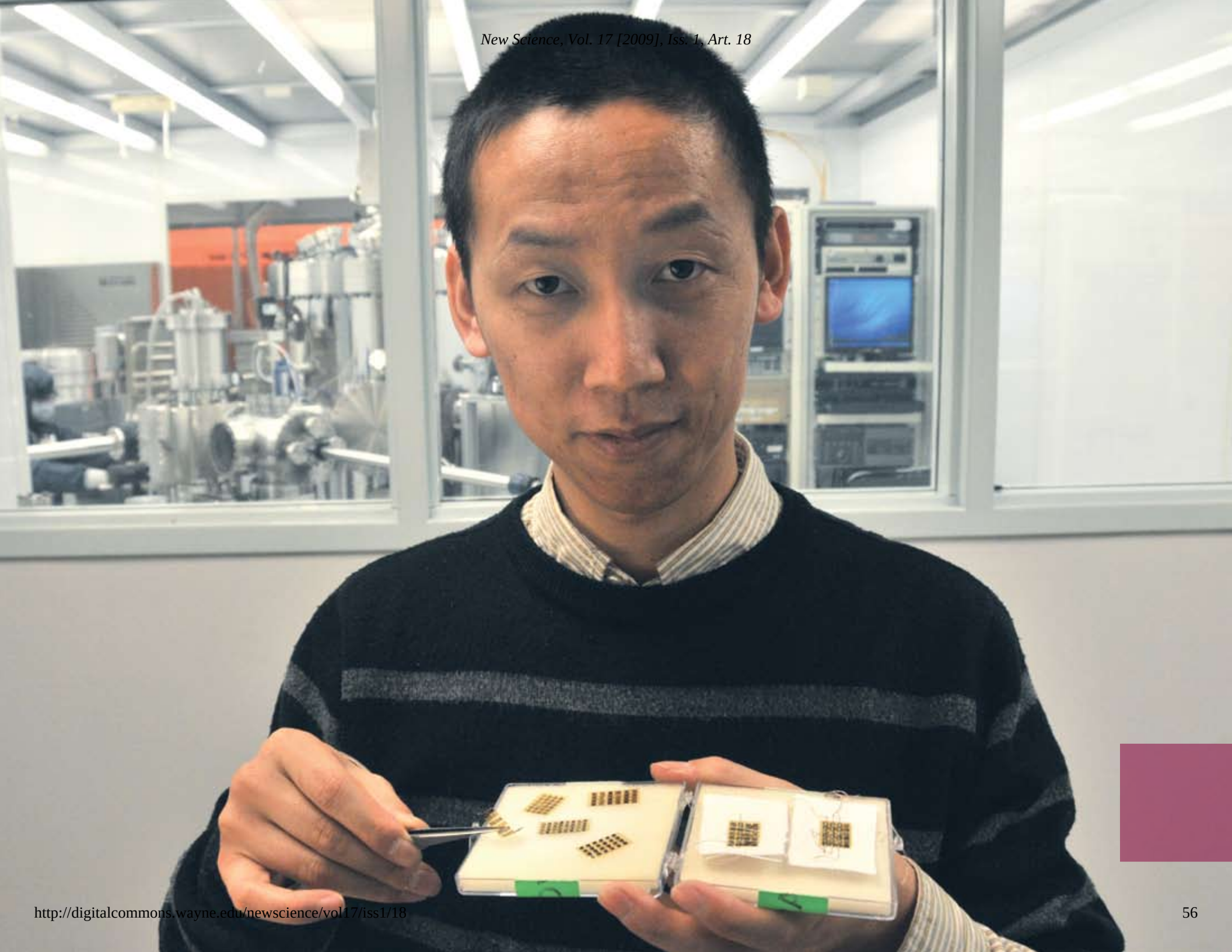
Dr. Stanley Terlecky, associate professor of Pharmacology and co-founder, EXT Life Sciences, Inc.

to fruition. With Terlecky's scientific expertise and Tesija's legal and business savvy, the two became partners, along with Gary Novara. Tesija and Novara are the principle partners of Southfield's Novara and Tesija, P.L.L.C., a law firm with expertise in pension and corporate law. Today, EXT Life Sciences, Inc. is working with development partners to bring their first product to market.

"We are currently partnering with carefully selected companies to develop the product, with the goal of bringing an over-the-counter skin care product to market in 2009," said Dr. Terlecky. The product will be marketed as a novel targeted antioxidant in a formulation specifically designed to prevent collagen breakdown and reduce skin aging.

"Through all of this, I have learned that it takes time to develop a marketable compound," said Dr. Terlecky. He welcomes the process adding, "Our research truly bridges the translational gap – having been developed in the laboratory but ultimately being of benefit in the clinic." Through his important research, Dr. Terlecky may one day find potential treatments or cures for numerous skin and systemic pathologies, ultimately helping many in their fight against disease.

About Dr. Stanley Terlecky: Dr. Terlecky received his B.A. in the history of art from New York University and his Ph.D. in cellular and molecular physiology from Tufts University. He joined Wayne State University in 1998 after completing an NIH-sponsored postdoctoral fellowship in the Department of Biology at the University of California, San Diego.



Small in Scale, Big in Possibilities

Wayne State researcher develops nano- and micro-scale devices for improved medical practices

by Amy Oprean

The stethoscope is a longstanding symbol of the medical profession, having been used by doctors for more than two centuries to obtain basic vital signs through listening to the heart and respiratory noises. Although it is a fundamental part of almost every medical exam and surgical procedure, stethoscopes have several major disadvantages. Among these is the inability to give continuous readings and a bulky size that prevents their use in some situations.

Yong Xu, Ph.D., associate professor of electrical and computer engineering in the College of Engineering, received a National Science Foundation CAREER award, a prestigious award given to promising faculty early in their career, to develop a stethoscope alternative that has the potential to change the paradigm for respiratory sound monitoring. Using a micro-scale cantilever design and intelligent textile technology, Xu is developing a micro-sensor that is sensitive and compact; capable of picking up the weak vibrations given off by breathing, yet small enough to be worn comfortably throughout the day for continuous monitoring.

> "This polymer skin can be stitched into fabric or made into a bandage, allowing the sensor to be applied to the patient very conveniently."
>
> — Dr. Yong Xu

One of the major disadvantages of stethoscopes is that they cannot be used for continuous respiratory sound monitoring. For example, during surgery, readings are taken only intermittently. And because of their size, stethoscopes cannot be applied to obstructed locations, such as the side of the body a person is lying on during surgery.

An accelerometer, an electromechanical device that measures acceleration forces, could be a feasible alternative sound monitoring device, Xu said, as long as it is designed with both sensitivity and comfort in mind. He has proposed two novel approaches to address these requirements, the first being an air-spaced cantilever design for the accelerometer. Easily observed in two inch by three-quarter inch metal macro version, Xu's cantilever design consists of a flat rectangular metal base with a rectangle-shaped depression in the middle. A flat, thinner piece of piezoelectric material sits on top of the base, creating a bridge over the depression from which a vibration will be made. Though other accelerometers have been designed with respiratory noise monitoring in mind, the geometry of Xu's design has been optimized for maximum sensitivity.

Xu is now working to micro-fabricate the macro version of this device, the end result being a two millimeter by two millimeter silicon sensor. Using intelligent textile technology, Xu will fashion these micro sensors on a flexible polymer skin, allowing the device to bend with a patient's movement. "This polymer skin can be stitched into fabric or made into a bandage, allowing the sensor to be applied to the patient very conveniently," he said. "The key is to keep it very small and lightweight, because patients would have problems wearing a heavy device for 20-plus hours a day."

Dr. Yong Xu, associate professor of electrical and computer engineering

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Small in Scale, Big in Possibilities continued

The need for this type of continuous respiratory sound monitoring is apparent in several areas of medicine, and could result in an improved paradigm in monitoring respiration of patients under anesthesia, asthma management, patient monitoring in intensive care units, nursing facilities, emergency medical services and sleep studies. There is also the potential application for non-invasive vital sign monitoring for pilots and other military personnel, for which there is no method of continuous respiratory sound tracking.

Xu is collaborating with Hong Wang, M.D., Ph.D., associate professor of anesthesiology in WSU's School of Medicine, on the medical aspects of the research, and Le Yi Wang, Ph.D., professor of electrical and computer engineering in WSU's College of Engineering, to develop signal processing for the device. Once completed, the sensor will be tested using a human simulator at Harper Hospital in Detroit, as well as on humans. "Ultimately, it will be tested on humans to see if we can detect a useful signal," he said. "We'll do that by testing it against a state-of-the-art stethoscope, to see how the components of this device compare with the stethoscope."

Xu is also working on another type of cantilever with a completely different application. Funded by WSU's Presidential Research Enhancement Program, he has spent two years developing a piezoresistive cantilever for biochemical sensing.

Biochemical sensors allow scientists to perform tasks such as reading DNA sequences, an essential part of disease diagnoses. They also play crucial roles in drug discovery, national security, environmental monitoring and food safety.

Scientists measure biochemicals by immersing nanoscale cantilevers in the substance of interest and measuring the biomolecules that move over their surfaces. The most popular technique used is the optical lever method, in which the change in a cantilever's surface stress is measured by reflecting a laser off its surface and measuring the displacement with photo sensors. However, the method has several disadvantages in that it's bulky, expensive, not easily portable and difficult to use when monitoring a large number of cantilevers.

"The problem with this is that you need a laser and a photo sensor, which is expensive," Xu said. "Also, it cannot be miniaturized, and it's difficult to monitor a large number of cantilevers simultaneously. If you have one cantilever, it's no problem, but for ten cantilevers, you would need ten lasers. That's not easy to do."

The piezoresistive method, by contrast, uses electricity to measure changes in the cantilever's resistance. However, because of their relatively low sensitivity, piezoresistive cantilevers are still inferior to optical cantilevers. Xu is working to develop a more sensitive piezoresistive cantilever using two novel approaches. The first is to use parylene, a family of thermoplastic polymers as the cantilever material. The second innovation is to increase the surface area of the cantilever using nanoparticles.

A cantilever of this size would be an ideal solution for producing a high volume, low cost portable device that can be rapidly deployed. The improved piezoresistive cantilever method will have a large number of diverse biochemical sensing applications such as detection of mercury vapors, explosives, hydrogen gases, volatile organic solvents, heavy metals, DNA hybridization, DNA-RNA binding, antigen-antibody binding and protein ligand binding. These applications will play significant roles in increasing protection in war zones, making the environment cleaner and lowering medical costs, ultimately impacting the lives of many.

About Dr. Yong Xu: Dr. Xu received a B.S. in electronic engineering from Tsinghua University in Beijing, China. He received an M.S. and a Ph.D. in electrical engineering from the California Institute of Technology. His research interests include smart skins based on micro-electro-mechanical system, intelligent textiles, microfluidics, biosensors, medical devices, neural interfaces, energy harvesting and nanotechnology. He joined Wayne State in 2002.

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