

In the Clinic

Dr. Pescovitz Comes to Michigan

ORA HIRSCH PESCOVITZ, M.D. —

the new U-M executive vice president for medical affairs and CEO of the U-M Health System — admits she was a bit intimidated on May 11 when she moved into the office formerly occupied by her long-time friend and professional colleague, Robert Kelch, M.D.

“I knew I had big shoes to fill,” Pescovitz says. “It’s remarkable what Dr. Kelch accomplished here in such a short period of time. A significant part of what attracted me to U-M was the extraordinary alignment he created between U-M Hospitals and Health Centers, the Medical School and the School of Nursing. This alignment is unique among academic medical centers and a tremendous source of strength for the institution.”

A nationally recognized pediatric endocrinologist, researcher and university administrator, Pescovitz came to the U-M from the Indiana University School of Medicine where she treated children with endocrine disorders and served as executive associate dean of research affairs. In 2004, she also became the first president and CEO for the Riley Hospital for Children in Indianapolis where she actively spearheaded both the development and planning efforts that led to a \$470-million addition to the hospital. In her most recent position as IU’s interim vice president for research administration, Pescovitz was responsible for the



Ora Hirsch Pescovitz

research infrastructure at all eight IU campuses.

Although still in the listening and learning phases of her new job, Pescovitz says she already has identified major areas of strength at the U-M — including an institutional culture of “partner or perish,” which encourages research collaboration, an outstanding faculty group practice and a genuinely warm and collegial working atmosphere.

“U-M is a top-tier research powerhouse with a down-to-earth perspective and Midwestern values,” she says. “These are exceptional qualities that bode well for the future.”

One of four children, Pescovitz grew up in Bethesda, Maryland, with her three younger brothers. In high school, she was torn between becoming a doctor or a concert pianist. Fortunately for the University of Michigan Health System

and countless patients, she chose medicine.

Pescovitz received her M.D. degree in 1979 from Northwestern University’s Feinberg School of Medicine. She began a residency in pediatrics at the University of Minnesota Medical Center and completed it at Children’s National Medical Center in Washington, D.C. Her husband, Mark Pescovitz, M.D., is a transplant surgeon and professor at the Indiana University School of Medicine. The couple has three grown children in college or graduate school.

Optimistic and excited about the move to Ann Arbor, Pescovitz has applied for a license to practice medicine in Michigan and says she is learning the words to “The Victors” in preparation for the September 5 kick-off of the U-M football season. —SALLY POBOJEWSKI

A Warning Sign for Diabetics

PEOPLE WITH DIABETES, AND PHYSICIANS WHO TREAT THEM, should pay close attention to the results of a common blood test for fats called triglycerides, according to a new study by scientists at the U-M Medical School and Wayne State University.

The researchers found that diabetics with elevated triglyceride levels were more likely to develop a serious complication called neuropathy. Nerve damage from neuropathy can cause disabling numbness, tingling and pain — most often in the hands, arms, legs and feet.

About 60 percent of the 23 million people in the United States with diabetes develop diabetic neuropathy and the U-M study identifies those at greatest risk. Most often, the condition is diagnosed after irreversible nerve damage has already occurred.

A predictive test for neuropathy could help doctors and patients take proactive steps when interventions can do some good, says Eva Feldman, M.D., Ph.D., the Russell N. DeJong Professor of Neurology, who also serves as director of the U-M's A. Alfred Taubman Medical Research Institute.

Feldman and her collaborators analyzed data collected over a 12-month period from 427 diabetes patients with mild-to-moderate neuropathy. The researchers found that study participants with elevated triglycerides were more likely to report during the study that their neuropathy symptoms were getting worse. Biopsies of peripheral nerves from study participants showed that diabetes patients with high triglycerides lost five times more nerve fibers over 12 months than patients with normal triglyceride levels.

The link between elevated triglycerides and lost nerve fibers was

more statistically significant than for any other variable in the study — including the patient's age, disease duration, cholesterol levels and blood glucose levels.

"Results from our study suggest that clinicians should address lowering lipid counts with their diabetes patients as vigilantly as they pursue glucose control," says Feldman. She adds that people can reduce blood triglyceride levels by avoiding fats and exercising regularly. —SP

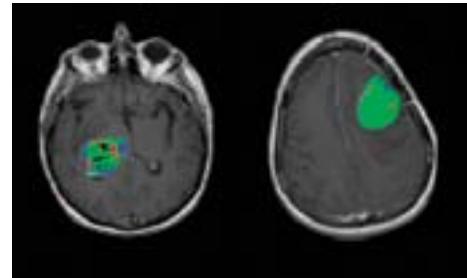
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Eva Feldman

LEFT: SCOTT GALVIN, U-M PHOTO SERVICES; RIGHT: COURTESY OF CRAIG GALBÁN

Mapping Survival



Images of brain tumors that did not (left) and did (right) respond to treatment. Colors within the tumors indicate areas where blood volume increases (red), decreases (blue) or remains unchanged (green).

U-M researchers have developed a way to analyze magnetic resonance imaging, or MRI, data to predict — as early as one week after the start of treatment — how long patients with brain tumors will survive. The method creates what the researchers call parametric response maps that make it possible to monitor changes over time in the amount of blood in the tumor within individual MRI data points.

"We see responses that can't be detected at all with existing technology and we see them as soon as one week into treatment, which is amazing for brain tumors," says Craig Galbán, Ph.D., assistant professor of radiology. Working with Brian Ross, Ph.D., professor of radiology, Galbán tested the technique in a clinical study of 44 people with high-grade glioma, a type of brain tumor.

"Parametric response mapping has the potential to become a generalized analytical approach to quantify treatment intervention in patients," says Ross, who adds that the method also might be useful with other imaging techniques like PET and CT scans. The U-M has filed a patent application on the technology. —SP

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In the Clinic

Child-Friendly Alternatives

COMPLEMENTARY AND ALTERNATIVE therapies — like yoga, acupuncture and herbal remedies — aren't just for grown-ups anymore. They are becoming popular with children and adolescents, as well. If used under a doctor's supervision, many of these treatments can be a safe, effective way for children

and adolescents to get and stay healthy, says Dolores Mendelow, M.D., a clinical assistant professor of pediatrics and communicable diseases.

Mendelow recommends alternative therapies for many of her young patients. She suggests yoga as a beneficial therapy for patients with asthma and to reduce stress in teenagers. Tai chi also helps reduce stress, depression and anxiety. Taking probiotics, either as supplements or in foods like yogurt, can help children with antibiotic-associated

diarrhea return to school or day care faster.

However, Mendelow warns that some alternative therapies can be harmful to children. These include a popular Chinese medicine called Ma Huang, a muscle-building supplement called creatine and chiropractic spinal manipulation.

What's safe for one child may not be safe for another, so Mendelow emphasizes that parents should check with their child's pediatrician before starting any new treatment. —SP

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Caregivers from Michigan Visiting Nurses celebrated the organization's 100th anniversary during National Nurses Week on May 11 by releasing 100 balloons into the sky. MVN, which has served the Ann Arbor community in various capacities during the last century, today provides home care services for patients being discharged from U-M hospitals.

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Want Strong Bones? Keep It Moving!

STAYING ACTIVE IS JUST AS IMPORTANT FOR HEALTHY BONES AS IT IS FOR A healthy cardiovascular system, says Ronald Zernicke, Ph.D., director of the U-M Bone and Joint Injury Prevention and Rehabilitation Center. Weight-bearing activities like running, walking, playing basketball and dancing are best for strengthening bone.

While exercise can increase bone mass density in all age groups, the benefits are greatest during childhood and adolescence, when new bone is added to the skeleton faster than old bone is removed. This means that adolescents have a window of opportunity to enhance bone mass and strength that will benefit them for the rest of their lives.

"Physical activity is absolutely beneficial for overall bone health," says Zernicke, a U-M professor of biomedical engineering, of kinesiology, and of orthopaedic surgery. "It is a modifiable factor under our control that develops and maintains healthy bone mass." —SP

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Health Briefs

A simple blood test could help diagnose an often-lethal tear, called an aortic dissection, in the body's largest blood vessel, according to a study led by Cardiovascular Center specialists. They found dramatically elevated levels of a substance called D-Dimer in the blood of patients experiencing an aortic dissection. Symptoms of aortic dissection are similar to those of an acute heart attack, but treatments for the two conditions are different, so a rapid and accurate diagnostic test could save lives.

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Doctors are reporting an increase in cases of children with kidney stones, a condition usually seen in middle-aged men. Common symptoms are back and abdominal pain that are often mistaken for appendicitis or gastritis. Gary Faerber, M.D., professor of urology, blames diet and lifestyle. He says sugary drinks, a fast-food diet, obesity, dehydration and lack of exercise add up to increased risk of kidney stones for children as well as adults. Faerber's prescription: Fewer sodas, more water.

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A national survey of pediatricians and family medicine physicians found that one out of seven did not recognize the symptoms of whooping cough in a standardized adolescent case patient. U-M researchers say the survey indicates a need for more physician education. —SP

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In the Lab

U-M's Cancer Dream Team Targeting better treatments for breast cancer

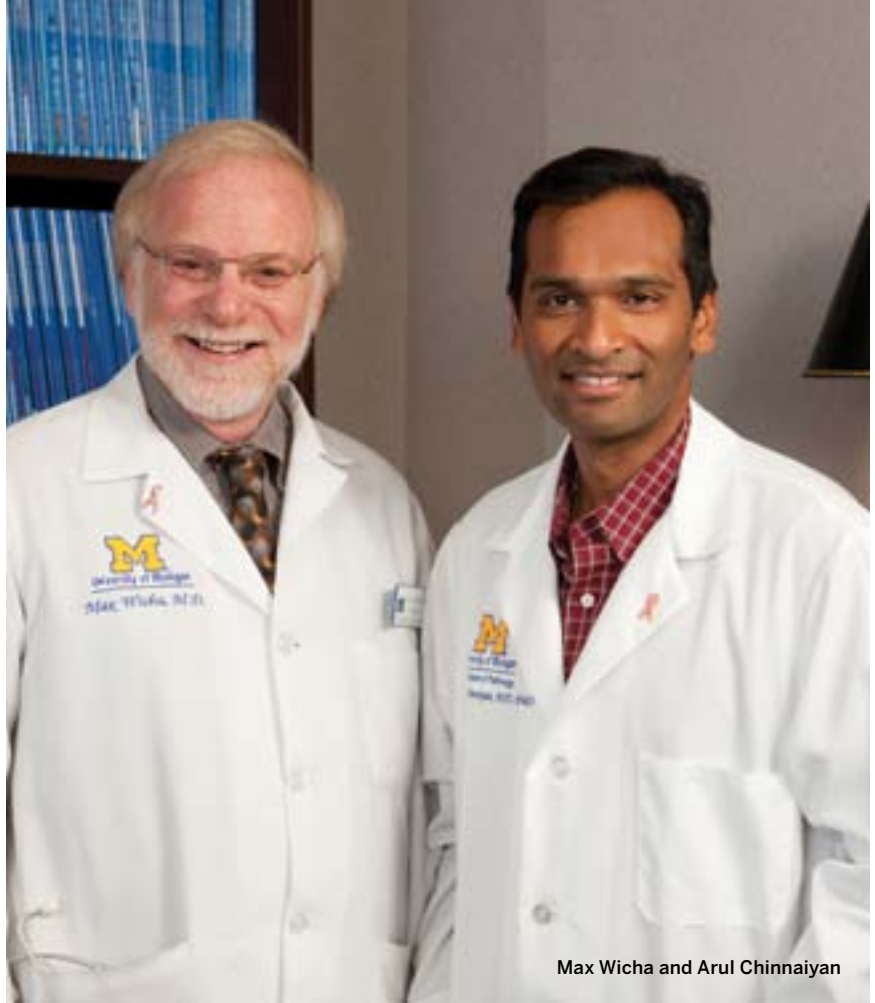
THERE ARE DREAM TEAMS IN

basketball and dream teams in business, but you don't hear much about them in the sedate world of academia. So, it was a surprise when Cancer Center researchers Max Wicha, M.D., and Arul Chinnaiyan, M.D., Ph.D., learned they were part of a national "dream team" of biomedical research scientists selected to receive an \$18 million grant from a charitable initiative called Stand Up To Cancer.

It was even more unusual to see the dream team awards announced May 27 in a national media blitz that featured prime-time coverage on ABC, CBS and NBC. But then, nearly everything about Stand Up to Cancer, or SU2C, is out of the ordinary.

The organization was started in 2007 by six women in the media and entertainment industries whose lives were affected by cancer. Most of the \$73.6 million in research funding awarded by SU2C to five teams of cancer researchers was donated on September 5, 2008, during a celebrity-studded fundraising event broadcast live by all three major TV networks.

SU2C's fund-raising methods may be unconventional, but the scientists being funded are among the best in the country. Wicha and Chinnaiyan



Max Wicha and Arul Chinnaiyan

will work with 11 other researchers from major U.S. medical schools and cancer centers. They will focus on finding molecular differences among the three major subtypes of breast cancer, especially those that help the cancer become resistant to treatment over time. The team's goal is to develop targeted therapies that will be less toxic and more effective, because they are designed to attack the specific genes or signaling pathways active in each type of breast cancer.

One fundamental mechanism the team will study is the role of cancer stem cells — small populations of cancer cells believed to be responsible for the growth and spread of breast tumors.

"The goal of current therapies has been to kill as many cancer cells as possible," says Wicha, Distinguished Professor of Oncology, director of the U-M Comprehensive Cancer Center and one of several U-M scientists who discovered cancer stem cells in breast tumors. "The current model may lead

to treatments that are limited in their effectiveness, because they are not targeted at cancer stem cells, which are resistant to existing therapies."

Chinnaiyan, the S.P. Hicks Endowed Professor of Pathology, professor of urology and director of the Michigan Center for Translational Pathology, will be responsible for another important component of the SU2C study — creating a Web-based database to integrate existing molecular information about breast cancer. Having all the relevant information available in one searchable database will help researchers select and evaluate new drug combinations and breast cancer targets for future clinical trials.

"We've made significant progress in our understanding of the molecular basis of cancer," adds Chinnaiyan. "Now, we need to bring this knowledge to clinicians, so we can move beyond a one-size-fits-all approach to cancer treatment." —SALLY POBOJEWSKI

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Toxic Trigger

TOO MUCH ACETAMINOPHEN CAN BE TOO MUCH OF A GOOD THING.

Acetaminophen overdose is the leading cause of acute liver failure in the U.S., but the amount required to damage the liver and trigger a dangerous inflammatory response varies widely. What makes some people more sensitive to the drug than others?

Researchers in the Comprehensive Cancer Center studied mice to find clues to the mechanism of the drug's toxicity. They discovered a signaling pathway that protected mice against the immune response triggered by acetaminophen-induced liver damage. If proteins in the pathway were missing, an overdose of the drug caused death within a few hours. Understanding how these cellular signals work could lead to new treatments for liver failure and other types of tissue damage. The notion has broad implications for host response to cancer, of which cellular damage of the same sort, necrosis, is a hallmark. —SP

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Rat Tales

WHEN PLACED IN A NEW ENVIRONMENT, HIGH-ANXIETY RATS TEND TO COWER

in the dark, while their low-anxiety companions explore bright, open spaces. Scientists at the Molecular and Behavioral Neuroscience Institute found that these behavioral differences were linked to a brain chemical called fibroblast growth factor 2. Rats that were genetically prone to high anxiety had lower levels of FGF2 and fewer new brain cells in the hippocampus than low-anxiety rats.

Providing enriched living quarters or direct FGF2 supplements increased production of FGF2 in high-anxiety rats, decreased their anxious behavior, and increased production of adult stem cells in the hippocampus. U-M scientists also found that FGF2 is decreased in the brains of depressed humans, so they believe FGF2 could be a promising target for drugs to treat human depression and anxiety disorders. —SP



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LEFT: MARIO BEAUREGARD/CORBIS; RIGHT: MARTIN VLOET, U-M PHOTO SERVICES

Stroke Aftermath



New research by David J. Pinsky, M.D., the J. Griswold Ruth, M.D., and Margery Hopkins Ruth Professor of Internal Medicine, and a team of Cardiovascular Center researchers indicates that an enzyme called CD39 could be the key to preventing permanent brain damage after a stroke.

In previous research, Pinsky, who also is a director of the Cardiovascular Center, discovered CD39 on the surface of cells that line the inside of arteries and blood vessels where clots form. Now, his research team has shown that CD39 also is produced on the surface of white blood cells.

By studying mice that lacked the ability to make CD39, scientists discovered that the enzyme's job is to mediate a delicate balancing act between signals that accelerate inflammation in damaged blood vessels and competing signals that suppress platelet activation and cool inflammation down. Pinsky says additional research to understand how CD39 works could someday lead to safer, more effective stroke treatments. —SP

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In the School

Early Exposure, Lasting Benefit

Medical students
get hands-on
clinical training

AN EXTERNSHIP PROGRAM IN

THE Department of Anesthesiology is providing some first- and second-year medical students with significant time and experience in the clinical setting, an aspect of medical education more typically reached by students in their third year during clinical rotations.

“We started this program in 2003 after we noticed that some of the strongest applicants to our anesthesiology residency were Iowa Medical School graduates who had completed an anesthesiology externship,” says Christopher Turner, M.D., Ph.D., an associate professor in the Department of Anesthesiology. “We decided that this type of exposure for beginning medical students would be worthwhile.”

Each fall, the externship recruits two or three new first-year students by sending an e-mail to all members of the new class explaining the benefits, responsibilities, and pay scale of the program. Turner normally receives 15-20 applications, and he and his team choose those who they feel will benefit most from the experience.

There are five externs in the program at one time; each works a five-hour shift one weekday evening. All begin as first-year students and continue through their second year.



Kevin Duan and Amy Li prepare anesthesia equipment and supplies in the operating room.

“The externs function as anesthesia technicians in the operating room,” explains Turner. Their duties include stocking carts, cleaning anesthesia machines, turning over rooms between cases, bringing drugs and equipment to anesthesiologists and assisting with the transport of critically ill patients.

As students gain experience, they can run intraoperative labs and provide some direct patient care, such as assisting with placement of central venous or pulmonary artery catheters or airway management duties — under close observation. “It starts with basic technician work,” Turner says, “but by the end of the second year, they’re providing patient care side by side with the anesthesia residents.”

Megan Krajewski, M.D., who graduated in May and will do her anesthesiology residency at Brigham and Women’s Hospital in Boston, Massachusetts, says that the externship was an integral part of her success. “The benefits were enormous,”

she says. “It enabled me to gradually develop my confidence. After being in the program, I felt very comfortable, not only interacting with the staff, but also being in clinical situations.”

Amy Li, who just completed her second year, values the experience. “I’ve watched all kinds of procedures, including neurosurgeries, laparoscopic surgeries, ENT, and orthopedics.” First-year student Kevin Duan feels the same way. “It’s allowing me to see the different specialties in a way that you don’t normally see until your third year. For me, it’s about exposure.”

“The externship wasn’t developed as a way to recruit students into anesthesiology,” Turner says. “We set the program up to give students an exposure to critical care medicine. If they go into emergency medicine, medical or surgical critical care, or any of the surgical specialties, including trauma and burn, these are skill sets that they will put to use every day.” —NICK CHARLES

CNN medical correspondent Sanjay Gupta (M.D. 1993, Residency 2000) addressed the Medical School Class of 2009 at the May 8 commencement ceremony in Hill Auditorium. To read more about his remarks, watch a podcast of the event and view photos from the ceremony, visit www.medicineatmichigan.org/magazine.

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Sanjay Gupta

LEFT: SCOTT SODERBERG; RIGHT, TOP: COURTESY OF THE MAYO CLINIC; RIGHT, CENTER & BOTTOM: D.C. GOINGS

Going Global



On June 1, Joseph C. Kolars, M.D. (Fellowship 1989), began a new appointment as the Medical School's first senior associate dean for education and global initiatives. An internationally recognized expert on physician education and global health, Kolars will lead efforts to adapt and enhance the full spectrum of training at the Medical School — from students to continuing physician education to biomedical research education — and integrate it with global impact. Before beginning his U-M appointment, Kolars, a professor of internal medicine, was a member of the Mayo Clinic faculty and also developed medical education initiatives for the Bill and Melinda Gates Foundation.



Jessica Schwartz, Ph.D., professor of molecular and integrative physiology, and Graciela Piwien-Pilipuk, an investigator at the Leloir Institute in Buenos Aires, Argentina, have received a Fogarty International Research Collaboration Award designed to encourage collaborative research on global health issues between scientists in the U.S. and those in developing countries. Schwartz and Piwien-Pilipuk will study genes and proteins that regulate fat cell differentiation. Graduate students from Argentina will complete part of their studies in Schwartz's U-M laboratory.



Medical student Matthew Simpson was one of several U-M students selected to participate in the Clinton Global Initiative University, held in February at The University of Texas in Austin. Working with students from the School of Dentistry, School of Information and the Gerald R. Ford School of Public Policy, the team presented a plan to make the Medical School's two-year pre-clinical curriculum available via the Web as an open educational resource for local health care professionals working in Africa. —SP