

## In the Lab

## Stem Cell Strides

### New lines will lead to disease-specific research

**U-M SCIENTISTS HAVE CREATED THE** state's first human embryonic stem cell line — a major step toward future development of new stem-cell-based therapies for many diseases. The cell line was derived from a cluster of about 30 cells removed from a 5-day-old human embryo, originally created for reproductive purposes in a fertility clinic and later donated for research.

"Our ability to derive new embryonic stem cell lines will allow us to take the next step: disease-specific research that could someday lead to new treatments," says Gary Smith, Ph.D., a professor of obstetrics and gynecology who led the project.

Smith adds that creation of human embryonic stem cell lines in Michigan

was not possible before November 2008, when state voters approved a constitutional amendment permitting scientists to derive cell lines from donated surplus embryos in fertility clinics.

Work to create the cell line took place at the U-M A. Alfred Taubman Medical Research Institute's Consortium for Stem Cell Therapies, established in March 2009. The consortium will distribute cell samples to its research collaborators at the U-M and statewide.

The project was supported with private gifts, including major support from Taubman, and internal resources. No federal funding was involved. All procedures and policies are in compliance with federal and state law, as well as new regulations established

by the National Institutes of Health. The project was approved by U-M's Human Pluripotent Stem Cell Research Oversight Committee and the Medical School's Institutional Review Board.

Consortium researchers also have developed techniques to convert adult skin cells into induced pluripotent stem cells, known as iPS cells. Earlier this year, the consortium created its first iPS cells, using skin samples donated by healthy individuals and by patients with diseases including amyotrophic lateral sclerosis (ALS) and several ataxias.

"There are few university programs in the U.S. deriving disease-affected stem cell lines," says Sue O'Shea, Ph.D., professor of cell and developmental biology and co-director, along with Smith, of the consortium. "Our special niche will be creating, studying and understanding normal and abnormal development of disease-affected stem cell lines — both embryonic and iPS."

In the future, consortium researchers plan to use genetically abnormal embryos to create cell lines that carry genes for diseases such as cystic fibrosis, Huntington's disease, spinal muscular atrophy and Tay-Sachs disease.

Smith and O'Shea announced the creation of the new cell line on October 3 at the World Stem Cell Summit in Detroit, an international symposium which this year was co-sponsored by the U-M. "Our efforts have finally started to bear fruit, so now the truly exciting and novel work can begin," says Smith.

In addition to Smith and O'Shea, 14 other U-M scientists made research presentations at the meeting. — JIM ERICKSON AND SALLY POBOJEWSKI

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Sue O'Shea and Gary Smith

## Targeting Asthma

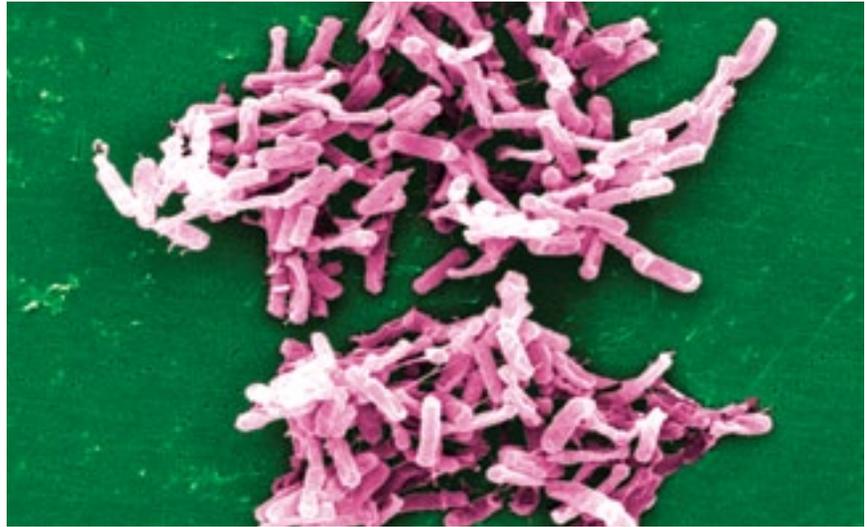
### WHY DOES CATCHING A COLD

cause asthma patients to develop coughing, chest tightness and wheezing, while people without asthma get by with just a runny nose and stuffy head? A new U-M study suggests it's because immune cells in the lungs of asthmatics are hyper-responsive to viral infection.

When U-M scientists infected mice sensitized to allergic airway disease with the human rhinovirus that causes the common cold, immune cells called macrophages produced a flood of pro-inflammatory molecules, including a protein called eotaxin. Control mice infected with rhinovirus did not produce these immune system triggers.

Results from the study could help researchers identify cellular and molecular targets for new drugs to treat viral-induced asthma, says Marc Hershenson, M.D., the Frederick G.L. Huetwell Professor of Pediatrics and Communicable Diseases, who directed the research. —SP

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## Dealing with *C. Diff*

### NEED ONE MORE REASON TO PRACTICE COMPULSIVE HAND-WASHING?

Consider *Clostridium difficile* — a nasty intestinal bug that infects nearly 500,000 Americans every year. The bacterium forms spores that can pass from person to person or be picked up from the environment, but not everyone who is infected shows symptoms. People who become ill usually start feeling sick during or immediately after taking antibiotics. Antibiotics kill off many of the normal bacteria living in the gut, making it easier for *C. difficile* to multiply and take over.

Infection with what doctors call “*C. diff*” can cause several days of watery diarrhea or a life-threatening colon inflammation. Researchers don't know why the bacterium causes mild symptoms in one person and severe symptoms in another, but believe it involves differences in individual immune responses and changes in the number and variety of microbes living in the gut.

Perhaps because they have a weakened immune response, people age 65 and older who have been hospitalized or live in a nursing home are especially vulnerable. This makes *C. difficile* infections a serious and growing problem for hospitals and extended care facilities. The number of infections has doubled in the last few years and cases of severe, recurrent infection and deaths are becoming more common.

U-M investigators have received a \$7.5 million research award from the National Institutes of Health to probe the many mysteries of *C. difficile*. The goal is to find more effective ways to prevent, treat and avoid the recurrence of infection — according to Vincent B. Young, M.D., Ph.D., associate professor of internal medicine and of microbiology and immunology, who will lead the study. —SP

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## In the School

# Partnering with China

## U-M, Peking University establish joint institute

### THE MEDICAL SCHOOL'S GLOBAL

initiative took another major step forward on October 12 when officials from the University of Michigan and the Peking University Health Science Center signed an unprecedented agreement to establish a joint institute for collaborative research in cardiovascular, pulmonary and liver diseases — areas of interest to both institutions.

In addition to research collaborations, the institute will feature exchanges of faculty, medical residents, fellows and other researchers, and completion of

large-scale clinical trials. More than simply sharing data, faculty at the U-M and Peking will collaborate actively on projects on an equal basis. A \$7 million commitment from each university will fund the initiative. An executive board comprised of leaders from both organizations will delineate the scope of the collaboration, establish priorities and oversee a strategic plan to ensure the success of the joint institute.

“This kind of partnership will give our Medical School ... exposure to new ideas, new ways of thinking, and the problems

facing our world,” says Ora Pescovitz, M.D., executive vice president for medical affairs and CEO of the Health System. “Without that, we can’t make the major discoveries that we strive for and that we are committed to achieve.”

Pescovitz will serve as a member of the joint institute’s executive board, as will Medical School Dean James O. Woollicroft, M.D. (Residency 1980); Senior Associate Dean for Education and Global Initiatives Joseph Kolars, M.D. (Fellowship 1989); Steve Forrest, Ph.D., U-M vice president for research; and Steve Kunkel, Ph.D., senior associate dean for research at the Medical School.

Kolars notes that there are 19 Medical School departments that already are collaborating with 31 Chinese universities, including a joint laboratory.

In the summer of 2009, a leadership team that included Kolars and Woollicroft traveled to China to visit four institutions. Peking University held the best match for research interests, and its similar governing structure made it a good fit for a formal collaborative effort.

With 6,688 beds in its health centers — compared to U-M’s 930 — Peking University offers tremendous potential for gathering patient data. Peking has 32,431 outpatient visits on a daily basis; U-M has 6,411. Emergency room visits are also much higher at Peking: 1,810 daily, compared to U-M’s 319.

Says Kolars: “This (joint institute) is evidence of the University of Michigan Medical School’s intention to have a global impact on the way physicians are trained, and to be leaders in research that can solve the medical problems of our world.” —MARY MASSON AND RICK KRUPINSKI

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Joseph Kolars; Executive Vice President of Peking University and its Health Science Center, Yang Ke, M.D.; James Woollicroft; Ora Pescovitz; and Vice President of the Peking University Health Science Center, Weigang Fang, M.D.

## Student Dies from Uganda Traffic Accident

### SUJAL PARIKH, A FOURTH-YEAR

U-M medical student, died October 12 from injuries sustained in a motorbike accident in Kampala, Uganda. Parikh was a 2010-11 Fogarty International Clinical Research Scholar at the Joint Clinical Research Centre in Kampala studying pediatric HIV/AIDS.

Known for his passion for social justice and human rights, Parikh was an active member of several groups addressing human rights and health care disparities across the globe, including the Student Advisory Board for Physicians for Human Rights, Student Advisory Committee for the Global Health Education Consortium, the American Medical Student Association's AIDS Advocacy Network Steering Committee, and Board of Trustees for the Uganda Village Project. He also was associate editor-in-chief of *Global Pulse*, the international health journal of the American Medical Student Association.

Born and raised in Dallas, Texas, Parikh earned his undergraduate degree in public health and neurobiology from the University of California, Berkeley. Elizabeth Petty, M.D., associate dean of medical student education,

called Parikh "a visionary young man who was incredibly humble and generous with his time. He will be deeply missed." —RK



LEFT: COURTESY OF THE U-M CENTER FOR GLOBAL HEALTH  
RIGHT: MARTIN VLOET, U-M PHOTO SERVICES

## Medicine at Michigan's Newest Recruits

### FORTY-NINE PERCENT SPEAK

more than one language; 37 percent speak three. Twenty-four percent have published research and 92 percent have been involved in research. More than half have tutored; others have served in the Peace Corps, AmeriCorps or the Red Cross. And about 99 percent had offers from other medical schools, but chose to come to Michigan.



The Medical School's 2010 entering class helps paint an early portrait of the future of health care and medical research in America and beyond. Service-oriented, academically gifted, active in sports and community, the 170 members of the class (chosen from nearly 5,200 applicants) represent a dynamic group of idealistic individuals determined to make a difference in the world. Other characteristics of the entering class are shown below. —RK

<b>Female</b>	<b>50%</b>	<b>COLLEGE FIELDS OF STUDY</b>	
<b>Male</b>	<b>50%</b>	<b>Biology/biomedical</b>	<b>46.5%</b>
<b>Average age</b>	<b>23.5</b>	<b>Science/mathematics</b>	<b>13.5%</b>
	<b>(range: 21-31)</b>	<b>Chemistry/biochemistry</b>	<b>10.0%</b>
<b>Underrepresented</b>		<b>Engineering</b>	<b>7.7%</b>
<b>Minority</b>	<b>12.9%</b>	<b>Psychology/psychology-biology</b>	<b>6.5%</b>
<b>Michigan residents</b>	<b>51.2%</b>	<b>Other science</b>	<b>4.7%</b>
<b>Non-residents</b>	<b>48.8%</b>	<b>Humanities</b>	<b>4.1%</b>
<b>U-M undergrads</b>	<b>29.4%</b>	<b>Other</b>	<b>4.1%</b>
<b>Average GPA</b>	<b>3.77</b>	<b>Business/economics</b>	<b>2.9%</b>
<b>Average MCAT</b>	<b>11.58</b>		

## HHMI Selects Three Fellows from U-M

### THREE UNIVERSITY OF MICHIGAN MEDICAL STUDENTS ARE TAKING TIME

off from their studies to spend a year doing hands-on research at the U-M, thanks to a Howard Hughes Medical Institute program to encourage students to pursue careers in scientific research. Alan Chu, Nicholas Dewyer and Erin Gillespie were selected from a pool of 274 students to be HHMI Medical Research Fellows for 2010-11. HHMI sponsors a range of programs to nurture the careers of researchers who bridge the gap between clinical medicine and basic science as part of its goal to foster the translation of basic research discoveries into improved diagnoses and treatments. —RK

## In the Clinic

Dueling  
GuidelinesRoutine mammogram  
screening still  
recommended

**FOR WOMEN WHO CONSIDER AN** annual mammogram to be insurance against breast cancer, it was confusing. Doctors and clinics all over the United States, including at the U-M Health System, were flooded with questions when the U.S. Preventive Services Task Force issued new mammography screening guidelines in November 2009.

“The reasons for the change weren’t clear to patients or even to their doctors,” says Mark Pearlman, M.D., the S. Jan Behrman Collegiate Professor of Reproductive Medicine, professor of obstetrics and gynecology and of surgery.

The task force, an advisory group for the U.S. Center for Medicare and Medicaid Services, issued its original guidelines on breast cancer screening in 2002. At that time, they recommended annual screening mammograms for women 40 years and older. The 2009 guidelines endorsed mammograms every two years for women age 50-74, but did not recommend them for women age 40-49 or for women over age 74.

As soon as the new guidelines were released, the American Cancer Society, the American Medical Association and the American College of Obstetricians and Gynecologists issued public announcements opposing the change. Clinicians at the U-M Comprehensive Cancer Center



Mark Pearlman

met the next day to discuss changing the policy on screening women in their 40s, but decided against it, says Pearlman.

“There was an immediate backlash from all sectors — including the U.S. Congress, cancer organizations and physician societies,” he says. “I’ve been in medicine for 28 years and I’ve never seen a reaction that dramatic.”

Based on the widespread negative reaction, the task force updated its recommendation on December 4, 2009, to state “the decision to start regular, biennial screening mammography before age 50 should be an individual one and take patient context into account.”

The task force based its new guidelines on a review of mortality outcomes from clinical trials involving women with breast cancer. They found that screening mammography reduced the risk of death from breast cancer in women of all ages, but the greatest risk reduction

was for women age 60-69 — the years when breast cancer is most common.

The additional benefit of routine screening for women age 40-49 was small, and the task force concluded it was outweighed by the potential harms — including anxiety, discomfort, radiation risk, the risk of unnecessary biopsies, and overtreatment for cancers that would never become life-threatening.

While careful not to suggest that younger women’s lives are more valuable than older women’s, Pearlman suggests that the implications are different, “because younger women are more likely to be mothers and to be managing the lives of others. This takes us out of the scientific arena and into socio-ethical areas,” he says, “but we need to be aware as a society of the implications of not screening a woman in her 40s.” —SALLY POBOJEWSKI **MORE ON THE WEB** ↗

## Brock Mealer's Victory

**BROCK MEALER WAS GREETED BY 113,090 CHEERING FANS AS HE WALKED** onto the field of the Big House and reached up to touch the "Go Blue" banner before the Wolverines' September 4 game against the U-Conn Huskies. The brother of U-M offensive lineman Elliott Mealer, Brock Mealer was injured in a December 2007 car accident that left him paralyzed from the waist down. Two years of intensive inpatient rehabilitation and outpatient therapy by U-M spinal cord injury treatment specialists and physical therapists, followed by eight months of strength training and conditioning by U-M Athletic Department staff, helped make it possible for Mealer to walk again. —SP



Brock Mealer (center) with his brother Elliot Mealer (right) and Athletic Department Assistant Strength and Conditioning Coach Parker Whiteman (left)

## Health Briefs

Few people who suffer cardiac arrest outside a hospital survive. A U-M study found that chest compressions before defibrillation in patients with sudden cardiac arrest were just as successful as immediate treatment with an electrical defibrillator. So if EMS providers are not immediately at hand, starting chest compressions right away could save a life.

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Doctors with a healthy lifestyle are more comfortable talking to patients about diet and exercise, according to results of a U-M survey. While few physicians felt confident about their ability to change patient behavior, doctors who exercised regularly, were not overweight and had received training in counseling techniques were most likely to encourage patients to improve their diet and start exercising.

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With \$5.7 million in funding from the National Institutes of Health, the U-M has established the Michigan Nutrition Obesity Research Center, one of 13 federally funded centers that will focus on studies related to diet and metabolism. The center is a cross-campus effort that includes faculty from the U-M Medical School, School of Public Health and School of Kinesiology. —SP

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## In the Clinic

# Statin Controversy

**CHOLESTEROL-LOWERING DRUGS CALLED STATINS ARE USED SO WIDELY** today, some people say it would be easier to just add them to the public drinking water supply. Statins are known to be effective at reducing levels of artery-clogging LDL cholesterol and lowering the risk of death in people diagnosed with coronary heart disease. But can statins reduce mortality in healthy individuals who have risk factors for future development of cardiovascular disease?

According to Lee A. Green (M.D. 1983, Residency 1986), professor of family medicine and associate chair for information management, the use of statin drugs for primary prevention has been a “long-simmering controversy” in the medical community. “The stakes in the debate are high,” says Green. “Three-quarters of patients who take statins are taking them for primary prevention, so enormous expenditures from the payors’ perspective, or revenues from industry’s perspective, are at stake.”



Lee Green

Now, based on a recent study, Green says physicians finally have a definitive answer. In a meta-analysis of 11 previously published studies, researchers found no evidence that statins were associated with a reduced risk of death among people with risk factors, but no history of cardiovascular disease. The meta-analysis included a total of 32,623 study participants assigned to take statins and 32,606 assigned to take placebo. Over an average of 3.7 years of follow-up, study investigators found no statistically significant reduction in the risk of dying associated with statin use.

“In the short term, for true primary prevention, the benefit of statins, if any, is very small,” says Green. “In the long term, we really must admit that we do not know.” —SP

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## HELPING HEARTS

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