SOMnews
University of Maryland School of Medicine
November 2009 Vol.11 No.3

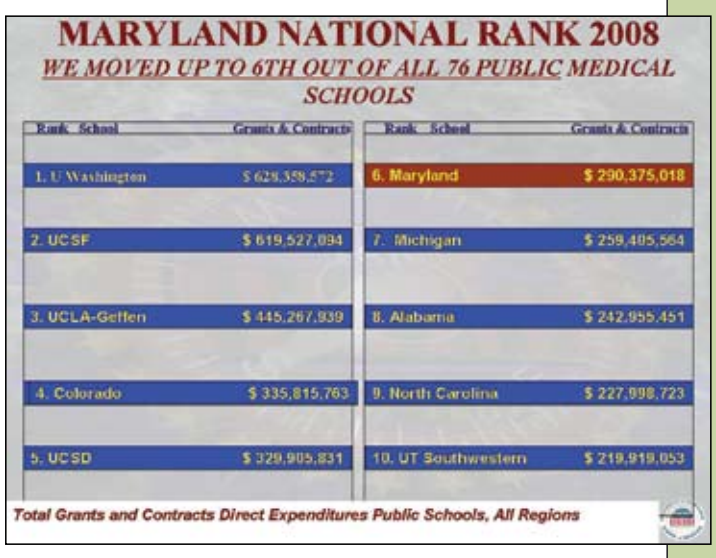
2009 STATE OF THE SCHOOL ADDRESS

"Navigating and Prevailing Through Challenging Times" was the theme for the 2009 State of the School Address, delivered by E. Albert Reece, MD, PhD, MBA, Vice President for Medical Affairs, University of Maryland and the John Z. and Akiko K. Bowers Distinguished Professor and Dean, University of Maryland School of Medicine. Speaking to a standing-room-only crowd in the MSTF auditorium, Dean Reece said the School of Medicine has thrived in the face of extraordinary challenges, including constraints in NIH funding, furloughs and hiring freezes, and space limits that threaten continued growth.

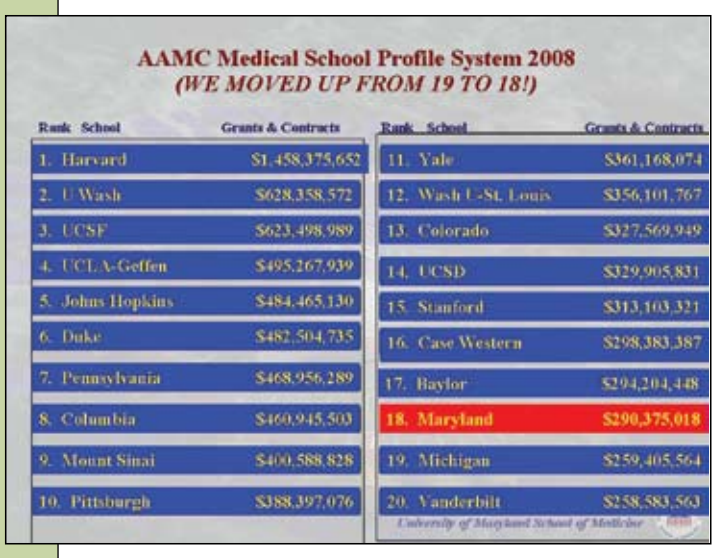
"We kept our eyes firmly on our goals to overcome the unexpected barriers," said Dean Reece. "Through the use of creative navigational means, we were able to create a successful path to those goals and have had an extraordinary year in many ways, thanks to the outstanding accomplishments of our faculty, staff and students."

At a time when NIH funding remained relatively flat (the impact of stimulus funding won't be seen until next year), researchers at the School of Medicine were awarded $425.8 million in grants and contracts in FY09, a 13 percent increase over FY08 *(Slide 1)*. "This is a huge deal," said Dean Reece. "The growth in research funding reflects the enormous quality, strength and high caliber of excellence of our research enterprise."

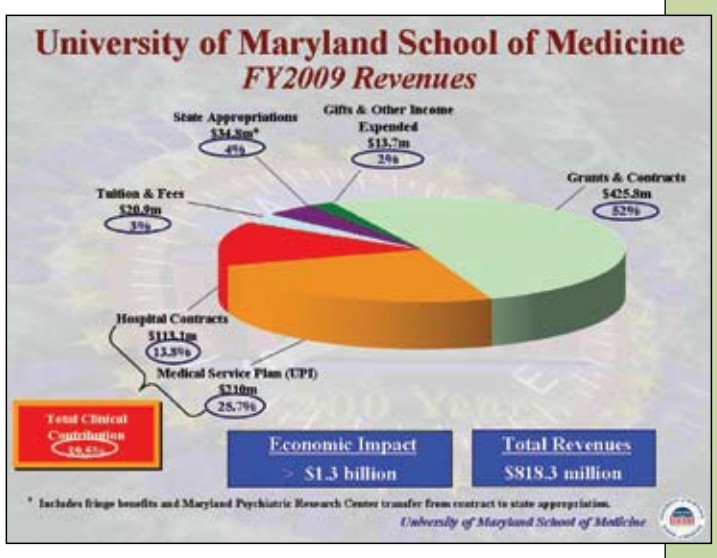
(Slide 1). Despite widespread economic woes, total grants and contracts experienced a 13 percent increase—to $425.8 million.



(Slide 2). Our School of Medicine jumped up to a rank of 6th out of all 76 public medical schools.



(Slide 3). According to the AAMC, the University of Maryland School of Medicine moved up from 19 to 18, amongst all 131 public and private schools, in total grants and contracts direct expenditures.



(Slide 4). The school's total revenue was $818.3 million in FY09.

The continued growth in research funding helped propel the School of Medicine to even higher rankings by the Association for American Medical Colleges (AAMC). **Among all 76 public US medical schools, the School of Medicine jumped from 7th to 6th place** *(Slide 2)*. **Among all 131 private and public medical schools, the School of Medicine now ranks 18th** in direct grants and contract expenditures—up from 19th place last year *(Slide 3)*.

The school's total revenue, which includes grants, tuition, state funding, faculty practice and philanthropic gifts, was $818.3 million. Fifty-two percent of total revenue comes from grants and contracts, while clinical revenue accounts for roughly 40 percent *(Slide 4)*. Patient care is obviously a very important part of the School of Medicine's mission. Clinical faculty treated over one million patients, a two percent increase over the previous year. This year the practice plan generated $210 million in revenues, an eight percent increase over the previous year *(Slide 5)*. "This is truly exceptional in the current fiscal environment," said Dean Reece. "Our clinical faculty deserve a great deal of credit for their outstanding performance." Dean Reece noted that the School of Medicine's partnership with the University of Maryland Medical System (UMMS) remains very strong. **Together, the School of Medicine and UMMS generate an economic impact of nearly $5 billion for the state of Maryland.**

Despite plummeting investment returns, **philanthropic funding for the school remained strong, thanks to generous private gifts, which increased 9.5 percent to $53.8 million** *(Slide 6)*. These included three gifts of more than $2 million each to fund endowed professorships in radiation oncology, transplant surgery and OB/GYN. Assessing the school's fundraising efforts, Dean Reece said, "In light of the difficult economic times, it was our best year ever."

Media coverage generated by faculty accomplishments was also extraordinary: The total number of story placements rose by 13 percent to nearly 26,300; national placements rose by 12 percent to nearly 24,000; television placements rose by 36 percent to 8,000; and internet placements rose by 76 percent. Dean Reece said, "This is an enormous amount of coverage, and is due to the hard work and tremendous discoveries of our faculty and staff. I am pleased they are recognized nationally and internationally for their efforts."

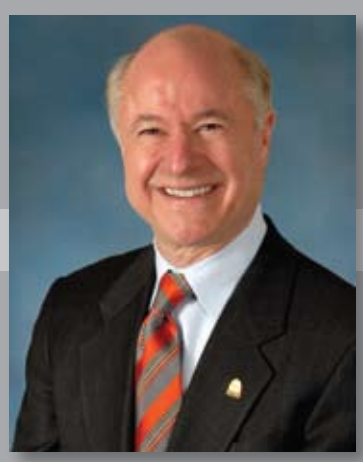
(Slide 5). Total clinical revenues grew to $210 million in FY09, an eight percent increase, due to excellent practice plan performance.

(Slide 6). Philanthropic funding remained strong, increasing 9.5 percent to $53.8 million.

Despite tough economic times, development of Health Sciences Facility III research building remains a high priority, along with continued growth in research funding, and finding ways to leverage federal stimulus funds. "We have been extremely grateful for all the successes the School of Medicine has experienced this past year," said Dean Reece. "We envision many challenges ahead, and since the national economic downturn continues, we have to be realistic about the future. We are optimistic that our momentum will continue, and we believe, despite the very real challenges that exist, we will prevail."

Q&A

with Curt Civin, MD—Stem Cell Pioneer



Curt Civin, MD

By Danielle Ulman *This interview appeared in* The Daily Record *on September 18, 2009. It is reprinted here with permission.*

Curt Civin, MD, a doctor nationally renowned for his research on cancer and stem cells, moved across town last year from the Johns Hopkins University School of Medicine to the University of Maryland School of Medicine to lead the newly founded Center for Stem Cell Biology and Regenerative Medicine

Dr. Civin, who co-chaired the fifth annual World Stem Cell Summit, which ran September 21–23 at the Baltimore Convention Center, sat down with *The Daily Record* to discuss how stem cell research changed in 2001 after President George W. Bush restricted federal funding of human embryonic stem cell lines—and what the future holds now that President Barack Obama has reversed the Bush order.

Q What was your research like before the Bush administration came in and changed the guidelines?

What President Bush did was unprecedented. To have this strange restriction…I've called it before a silly restriction on stem cell research. It was silly in that he said, "Well, you can use these"—he thought there were 70, when it turned out there were only 20-some—"lines that have already been made, because they were already out the barn door." It was a funny sort of logic that to many people appeared not to be based on a principle. If it was really based on a principle, you would shut that barn door. [It was] the shutting off of perhaps the most exciting research that you can do.

Q Tell me about what your lab was like before regulations changed and NIH couldn't fund all embryonic stem cell research.

One of the interesting problems was how to keep research projects separate. It sounds simple, but a laboratory environment is highly informal and highly interactive, so there's a lot of talk, there's a lot of interdisciplinary science and interpersonal collaboration involving more than one person that goes on.

So what if someone who was working with Maryland Stem Cell Research Fund support on a project involving human embryonic stem cell lines that were not authorized by the President Bush guidelines? What if somebody makes a new discovery?

Well, the natural thing in the lab on any other discovery would be for somebody else to say, "Oh, and my expertise could help you here. I have an idea." My natural impulse would, of course, be to encourage that. But what if those other people with ideas were funded by an NIH grant that said they couldn't do research involving anything but the federally approved stem cell lines?

Here was an unnatural clamp on the research. An unnatural fence that really prevented what we're trying to do, which is try to make discoveries that help people, and they couldn't work together because this person is 100 percent funded with federal money.

Q So the Obama administration came out with new rules through NIH. What did those new rules say?

I think I understand the rules now. The rules are really very, very good. Not perfect, but very, very good. There is going to be a greatly expanded list of human embryonic stem cell lines we can study. The spirit of the guidelines is that all of the stem cell lines that were obtained ethically are going to be allowed to be used.

Q With this regime change and with these rules and regulations changing, how has your lab changed? Or has it not made that transition yet?

The full transition, of course, is a potential transition. We just have the guidelines, we don't have the list of stem cells, so practically nothing has changed much, but trust that it will in the future. We're looking forward to those changes and starting to plan.

Q What kind of impact do you think the Stem Cell Summit will have on Baltimore?

I think it's got to catalyze stem cell research at both our large centers—Maryland and Hopkins—as well as across the state. I hope the impact is to encourage expansion of stem cell research funding from the state as well as interest from the young people here because that's really our future. At the University of Maryland we train many of the people who will be our doctors in the state, our nurses, our social workers, our lawyers, our pharmacists.

Many of these people are coming to the meeting. We need to generate enthusiasm among the public that this is nothing to be afraid of. Most of this is about cells growing in test tubes and finding out information that may be used to develop new medicines.

If there are two things that I'd like to communicate, one is that research is the business [in Maryland] and that this is our way out of the recession. The other thing is that stem cell research doesn't depend only on transplanting stem cells.

From my own discoveries in bone marrow stem cells, I'm really gratified that thousands of people have been transplanted with purified bone marrow stem cells; in fact, 50,000 transplants are done a year with this. That's wonderful, but these are very expensive, very toxic, often last-chance therapies that frequently fail and cost $1 million or more per patient.

I worked with blood-forming stem cells, teaming with colleagues who trained in my lab. We discovered receptors on the surfaces of these cells and then that a molecule which triggers these receptors helps to make stem cells grow. That discovery is used for other discoveries and for patient use today. Further, we found that this molecule and this pathway is mutated in leukemia—a colleague of mine developed a drug against this pathway, which is used now to treat leukemia. It doesn't cost millions of dollars per patient to use, isn't as toxic, in fact it's one of these new targeted therapies that has very, very low toxicity. This is the kind of therapy I'd prefer to get, if I got a cancer.

Stem cells is not just about the transplant and first world therapies, it's about discovering and understanding, and thereby inventing whole world therapies.

Fasano and Levine Win UMB Founders Week Awards

Research Lecturer of the Year

Alessio Fasano, MD

Alessio Fasano, MD, a professor in the Departments of Pediatrics, Medicine and Physiology, and director of the Center for Celiac Research and the Mucosal Biology Research Center (MBRC) at the School of Medicine is the 2009 Research Lecturer of the Year. Dr. Fasano was also awarded the first UMB Founders Week Entrepreneur of the Year Award in 2006.

When Dr. Fasano moved from Italy to the United States in 1993 to join the University of Maryland School of Medicine, celiac disease was considered extremely rare in North America. Today, his research has not only dispelled that notion, it has brought hope to the two million Americans affected by the disease.

"Dr. Fasano developed the first medical center in the United States to diagnose, treat and enhance the lives of people with celiac disease," said Elaine Monarch, executive director of the Celiac Disease Foundation. "Through his efforts, the Center for Celiac Research has become synonymous with scientific expertise and excellence of care."

In 2000, Dr. Fasano and his colleagues discovered the protein zonulin, which regulates the permeability of the intestine. In an upcoming article in *Proceedings of the National Academy of Sciences*, Dr. Fasano's group reports that when the zonulin system is turned on, it can trigger an autoimmune response, such as the unfavorable intestinal reaction that occurs in celiac patients. As outlined in his article in the August 2009 issue of *Scientific American*, Dr. Fasano's discoveries also could aid those with type 1 diabetes, multiple sclerosis, rheumatoid arthritis and inflammatory bowel disease.

Research at the Center for Celiac Research and the MBRC has led to more than 200 pending and issued patents worldwide and the foundation of Alba Therapeutics, a biopharmaceutical company spinoff of the University of Maryland with $40 million in capital funding. Founded in 2004, the MBRC is a collaborative hub for campus scientists engaged in translational research with innovative biotechnology and pharmaceutical companies.

"We want to get the fruits of our labor—whether newly developed novel drugs, new models of human diseases, new therapies or new drug delivery systems—to the patients who need them," Dr. Fasano said.

Entrepreneur of the Year

Myron Levine, MD, DTPH

Thirty-five years after founding the School of Medicine's Center for Vaccine Development (CVD), Myron "Mike" Levine, MD, DTPH, is known worldwide for his role in developing vaccines to prevent the spread of diseases such as cholera, typhoid fever and Shigella dysentery. The CVD currently is working on an H1N1 vaccine, and evaluating one for malaria. But to his colleagues, it's the industry as a whole that has benefited from his efforts.

"Myron Levine has been one of the most successful, passionate and resilient pushers of the vaccine field," said Rino Rappuoli, PhD, head of research for Novartis Vaccines. "He moved the field as a real entrepreneur by being a pioneer in building the infrastructure to perform clinical trials in developing countries and by building a new institute [CVD], which was the first center to allow phase I testing of new vaccines. These two activities cleared the way for many other vaccines developed by others that without him were not going to have the opportunity to be tested."

Under his careful guidance and extraordinary vision the CVD has gone on to become one of the flagship centers for both academic excellence and entrepreneurial collaborations. Dr. Levine, who is also the Department of Medicine's Simon and Bessie Grollman Distinguished Professor, has seen his work take him from advising prestigious universities, including Oxford and Harvard, to working in extremely remote locations in developing countries. Under his leadership, the CVD has successfully competed for grant and contract awards, averaging $65 million annually over the past five years.

"I take great pride in the emergence of the CVD as a large, multidisciplinary center committed to the development of vaccines and, in particular, vaccines to fight the infectious diseases that afflict impoverished populations in the developing world," said Dr. Levin.

Additionally, he is the principal investigator for a historic project, funded by a $29.4 million grant from the Bill & Melinda Gates Foundation, that is measuring the burden of severe diarrheal illness in infants and young children in sub-Saharan Africa and South Asia, and he heads the Middle Atlantic Regional Center of Excellence for Biodefense and Emerging Infectious Diseases.

Critical Molecule Pinpointed to Celiac Disease and Possibly Other Autoimmune Disorders

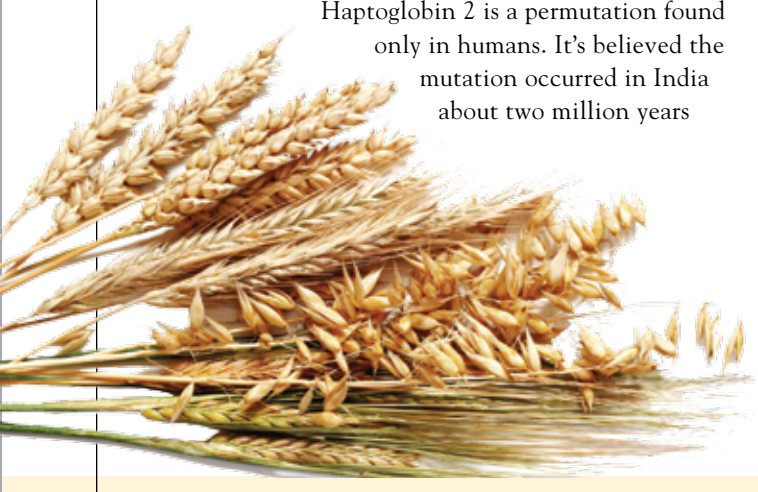

Alessio Fasano, MD

It was nine years ago that University of Maryland School of Medicine researchers discovered that a mysterious human protein called zonulin played a critical role in celiac disease and other autoimmune disorders, such as multiple sclerosis and diabetes. Now, scientists have solved the mystery of zonulin's identity, putting a face to the name, in a sense. Alessio Fasano, MD, and his team have identified zonulin as a molecule in the human body called haptoglobin 2 precursor.

Pinpointing the precise molecule that makes up the mysterious protein will enable a more detailed and thorough study of zonulin and its relationship to a series of inflammatory disorders. The discovery was reported in a new study by Dr. Fasano, which was published September 8, 2009, in the online version of the *Proceedings of the National Academy of Sciences*. Dr. Fasano is a professor in the Departments of Pediatrics, Medicine and Physiology and director of the Center for Celiac Research and the Mucosal Biology Research Center.

Haptoglobin is a molecule that has been known to scientists for many years. It was identified as a marker of inflammation in the body. Haptoglobin 1 is the original form of the haptoglobin molecule, and scientists believe it evolved 800 million years ago.

Haptoglobin 2 is a permutation found only in humans. It's believed the mutation occurred in India about two million years ago, spreading gradually among increasing numbers of people throughout the world.



Dr. Fasano's study revealed that zonulin is the precursor molecule for haptoglobin 2—that is, it is an immature molecule that matures into haptoglobin 2. It was previously believed that such precursor molecules served no purpose in the body other than to mature into the molecules they were destined to become. But Dr. Fasano's study identifies precursor haptoglobin 2 as the first precursor molecule that serves another function entirely—opening a gateway in the gut, or intestines, to let gluten in. People with celiac disease suffer from a sensitivity to gluten.

"While apes, monkeys and chimpanzees do not have haptoglobin 2, 80 percent of human beings have it," said Dr. Fasano. "Apes, monkeys and chimpanzees rarely develop autoimmune disorders. Human beings suffer from more than 70 different kinds of such conditions. We believe the presence of this pre-haptoglobin 2 is responsible for this difference between species."

> "This molecule could be a critical missing piece of the puzzle to lead to a treatment for celiac disease, other autoimmune disorders and allergies and even cancer . . ."

"This molecule could be a critical missing piece of the puzzle to lead to a treatment for celiac disease, other autoimmune disorders and allergies and even cancer, all of which are related to an exaggerated production of zonulin/pre-haptoglobin 2 and to the loss of the protective barrier of cells lining the gut and other areas of the body, like the blood brain barrier," said Dr. Fasano.

"The only current treatment for celiac disease is cutting gluten from the diet, but we have confidence Dr. Fasano's work will someday bring further relief to these patients. Zonulin, with its functions in health and disease as outlined in Dr. Fasano's paper, could be the molecule of the century," said Dean E. Albert Reece, MD, PhD, MBA.

People with celiac disease cannot tolerate gluten, a protein found in wheat, and suffer gastrointestinal distress and other serious symptoms when they eat it. In celiac patients, gluten generates an exaggerated release of zonulin that makes the gut more permeable to large molecules, including gluten. The permeable gut allows these molecules access to the rest of the body. This triggers an autoimmune response in which a celiac patient's immune system identifies gluten as an intruder and responds with an attack targeting the intestine instead of the intruder. An inappropriately high level of production of zonulin also seems responsible for the passage through the intestine of intruders other than zonulin, including those related to conditions such as diabetes, multiple sclerosis and even allergies. Recently, other groups have reported elevated production of zonulin affecting the permeability of the blood brain barrier of patients suffering from brain cancer.

"We hope pre-haptoglobin 2 will be a door to a better understanding of not just celiac disease, but of several other devastating conditions that continue to affect the quality of life of millions of individuals," emphasized Dr. Fasano. "This is quite a remarkable molecule that was just flying under the radar. We would have never have thought it would be the key. Now that we have identified this molecule, we are able to replicate it in the lab to use for research purposes. We hope to learn much more about it and its potential for treating and diagnosing celiac disease and other autoimmune conditions. This molecule has opened innumerable doors for our research."

Shock Trauma Center to Participate in Consortium to Study Extremity Injuries


Andrew N. Pollak, MD

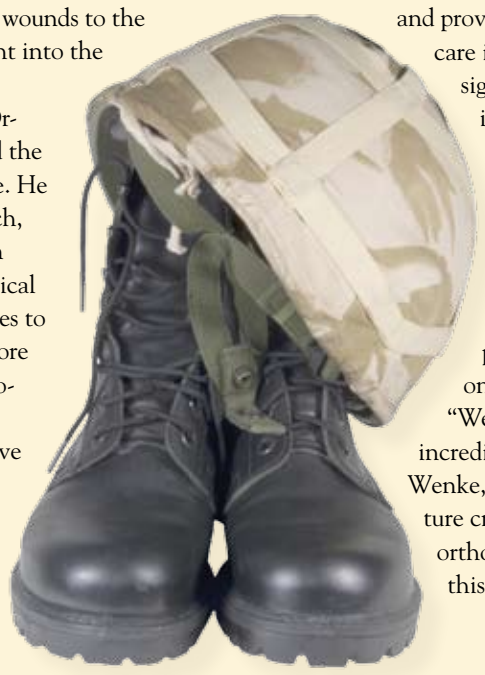
The University of Maryland R Adams Cowley Shock Trauma Center will serve as one of 12 core clinical centers in a newly established Extremity Trauma Clinical Research Consortium funded by the US Department of Defense.

The consortium will work closely with several major military treatment centers and the US Army Institute of Surgical Research (USAISR) at Fort Sam Houston, Texas, to conduct multi-center clinical research studies relevant to the treatment and outcomes of severe orthopaedic trauma sustained on the battlefield. These studies will help establish treatment guidelines and facilitate the translation of new and emerging technologies into clinical practice.

"This clinical research network offers us a unique opportunity to investigate treatments for a variety of injuries common in military and civilian patients," said Andrew N. Pollak, MD, co-chair of the consortium, and associate professor, Department of Orthopaedics and head, Division of Orthopaedic Traumatology at Shock Trauma. "We needed more funding to conduct definitive studies on severe wounds to the legs and arms. The results of this research will give us better insight into the best ways to treat severe, high-impact injuries to the limbs."

Dr. Pollak, who served as chair of the American Academy of Orthopaedic Surgeons' Extremity War Injury Project Team, will lead the orthopaedics studies at Shock Trauma as part of the new initiative. He has championed the need for increased funding for trauma research, citing the devastating extremity injuries suffered by US soldiers in Iraq and Afghanistan. "There is a profound need for targeted medical research to help military surgeons find new limb-sparing techniques to save injured extremities, avoid amputations and preserve and restore the function of injured extremities," he told the US Senate Appropriations Subcommittee in 2007.

The Johns Hopkins Bloomberg School of Public Health will serve as the coordinating center for the consortium. The Orthopaedic Extremity Trauma Research Program of the Department of Defense has awarded the Bloomberg School of Public Health $18.4 million over five years to establish the consortium. "The need for such a consortium is evident," says Ellen MacKenzie, PhD, principal investigator and the Fred and Julie Soper Professor and Chair of the Bloomberg School's Department of Health Policy and Management. "Eighty-two percent of all service members injured in Operation Iraqi Freedom and Operation Enduring Freedom sustain significant extremity trauma. Many sustain injuries to multiple limbs. The research to be conducted by the consortium will help us better understand what works and what doesn't in treating these injuries and ensure that our service members are provided with the best care possible."



Dean E. Albert Reece, MD, PhD, MBA, said, "The University of Maryland R Adams Cowley Shock Trauma Center is internationally recognized for its expertise in caring for the most critically injured patients and is a leader in trauma research. Our faculty members will play a very active role in this new consortium, working together with trauma specialists at other centers to develop innovative new therapies to treat traumatic limb injuries."

Initial funding of the consortium will help establish the research network and provide resources to address some of the critical needs in acute clinical care identified by the military. These include the reconstruction of significant bone defects and the management of musculoskeletal infections. Over time, the consortium will expand and leverage its expertise to address many other priority topics relevant to the long-term management of severe extremity trauma, including the prevention of osteomyelitis, chronic pain and disability.

An important feature of the consortium will be its ability to expand the number of clinical sites participating in any one study. More than 30 trauma centers across the country have pledged support for the consortium and are eager to participate in one or more of the studies.

"We are thrilled to be partnering with the consortium and the incredible team of investigators they have assembled," said Joseph Wenke, PhD, of the USAISR. "Together we will develop the infrastructure critically needed to address some of the most pressing issues in orthopaedic trauma care. Without a large, multi-center effort such as this, many of these issues would never be solved."

Thank You 2009 Mini-Med School Faculty!

Thank you to the following faculty members whose participation in and contributions to the 2009 session of Mini-Med School helped make it a great success! Over 200 members from the community attended to gain insight into the medical issues that may affect their health and to benefit from our faculty's expertise.

Welcome and Emcee—Claudia Baquet, MD
Topics in Medical Ethics—Henry Silverman, MD, and Leslie Meltzer Henry, JD, PhD(c) (School of Law)
Genomics & Personalized Medicine—Claire Fraser-Liggett, PhD
Stem Cells: Hype vs. Reality, or Political Science?—Curt Civin, MD
Male Reproductive Health—Andrew Kramer, MD, MBA
Prostate Issues & Cancer of the Male Reproductive System—Mike Naslund, MD, MBA
Death Investigation in Maryland—Mary Ripple, MD (SOM and Office of the Chief Medical Examiner)
Improving Outcomes for Children with Emergency Conditions—Richard Lichenstein, MD
Graduation—Dean E. Albert Reece, MD, PhD, MBA

Mini-Med students listen to Dean Reece speak before graduation.

Medical Student Profile: Nancy Lentz

Everyone needs a second chance. No one knows that better than Nancy Lentz, a third year student at the University of Maryland School of Medicine. When Nancy graduates, she will have had six years of medical school training. That's because this is Nancy's second time around as a medical student.

Nancy first enrolled in medical school right after earning her undergraduate degree. "I loved the material," she said, "but I wasn't ready for the personal changes and all the stress that comes along with it. The first two years are really tough." So Nancy took a detour, teaching high school physics, chemistry and biology for 10 years. She loved to teach, and it allowed her to pursue a lifelong love of science. But her dream of practicing medicine would not go away. "I kept thinking, 'What if?' So I decided to go for it," she said.

This time Nancy was accepted to the University of Maryland. "I loved it from day one, said the Wisconsin native. "I've been so incredibly impressed by the faculty here, and, having a teaching background, I know how hard it is. Especially when you consider the faculty are not only teaching, they are conducting research and treating patients. They are amazing people." Nancy attributes much of her success to the learning environment at the School of Medicine. "Everything about the student experience is warm and friendly. It's not competitive. You feel like you are in a family."

Nancy is beginning to apply what she's learned in her clinical rotations. "We've been sitting in lecture halls and discussing our cases on paper, and now we are spending time with patients and learning how medicine is really practiced," she said. Nancy is currently in the OB/GYN rotation, but she is leaning toward cardiology as her specialty. How does she know? "We had a patient who came in with a minor heart problem and I had to hold back my excitement about her possible cardiac issue because the main reason she came in was to have a baby!"

Medical Student Research Day

The Office of Student Research held its 32nd Annual Medical Student Research Day on September 24. Participating students presented posters and their research for judging during the day, which was followed by a celebratory dinner where keynote speaker Cynthia Bearer, MD, PhD, the Mary Gray Cobey Professor of Neonatology in the Department of Pediatrics, presented "The Role of Lipid Rafts in Developmental Toxicity." In the photo, Dr. Bearer and Jordan Warnick, PhD, assistant dean for Student Education and Research, (both top, far left) pose with some of the participating medical students.

SOMnews

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ecosmart Green Inks

Mark Your Calendars!

School of Medicine Council Meeting

November 18, 2009
3:00 to 4:00 pm
Taylor Lecture Hall, 1st Floor
Bressler Research Building
655 W. Baltimore Street

Monthly School of Medicine Council Meetings are open to all faculty, staff and students. Please come, and bring a colleague!