### UNIVERSITY of MARYLAND School of Medicine

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# DEAN'S MESSAGE: What's On My Mind

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UNIVERSITY of MARYLAND SCHOOL OF MEDICINE SHOCK, TRAUMA AND ANESTHESIOLOGY RESEARCH CENTER

Mark Your Calendars!

### JOIN US AS WE BEGIN A YEAR OF CELEBRATION

25 YEARS OF RESEARCH: Innovations in Injury Prevention Charles "McC." Mathias, Jr. National Study Center for Trauma and Emergency Medical Services

#### NOVEMBER 21, 2011

Seminar 2:00–4:00 pm

Reception 4:00–6:00 pm

University of Maryland Southern Management Corporation Campus Center

To register: http:/tinyurl.comNSC25AnniversaryRSVP For more information contact: Jackie Milani at *jmilani@som.maryland.edu* 



► BY SARAH PICK

hat's on my mind this month is the School of Medicine's newest research institute—the Clinical and Translation Science Institute (CTSI). The CTSI is a unique umbrella organization that creates an infrastructure to facilitate the translation of fundamental science to patient care and to the community. Through expanded collaboration across the University of Maryland and the University System of Maryland, the CTSI will transform the research and clinical enterprise at the University of Maryland, and allow us to make a quantum leap in our ability to conduct translational science. The CTSI will harvest the richness of our university centers, institutes, and hospitals to create a multidimensional, multidisciplinary research infrastructure that will traverse and integrate clinical and translational science. Under the CTSI, basic science research will develop rapidly into novel therapies that can prevent the

occurrence of common chronic diseases prevalent in our region, our country, and around the world. The institute is led by co-directors Alan R. Shuldiner, MD, and Stephen Davis, MBBS. Dr. Shuldiner is the John L. Whitehurst Professor of Medicine, and Associate Dean for Personalized and Genomic Medicine. Dr. Davis is the Dr. Theodore E. Woodward Professor and Chair in the Department of Medicine. Both are experienced clinical and translational investigators whose combined expertise spans from basic discovery at the level of DNA to clinical research and community engagement. Both have a long track-record of continuous NIH funding and extensive experience in the administration of large multidisciplinary research programs and infrastructure grants, and in the mentoring and training of young investigators.

Under the CTSI, our basic science and clinical researchers will focus on chronic preventable diseases and diseases with high morbidity, high mortality, and high disability—areas where we can make an impact and transform lives for the better. These signature research areas include cancer, heart disease, infectious and inflammatory diseases, diabetes, schizophrenia and head injury. These illnesses have disproportionately higher morbidity and mortality in urban and rural underserved populations, and affect people across the entire lifespan.

Our CTSI partners will come together in an unprecedented and transformative way. Participating institutions include the professional schools of the University of Maryland, the University System of Maryland, the University of Maryland Medical System, the Baltimore VA Medical Center, the University of Maryland Medical System, and others. We will also partner with key institutions to strengthen our existing capabilities.

The CTSI will align with the newly emerging NIH NCATS and CTSA network, which embraces a reengineering of the clinical research enterprise. The institute will promote team science among investigators by providing an infrastructure to serve and support multidisciplinary research teams across the full spectrum of clinical and translational research. Such an infrastructure brings about efficiency and economies of scale, enhances the quality of research execution, and makes monitoring and compliance more effective.

In addition to conducting translational research, the institute will help advance interdisciplinary education of students in medicine, dentistry, nursing, pharmacy, social work, law, public health, biomedical engineering, and graduate studies. The CTSI will provide improved forums for setting priorities and enhancing communications with state and local agencies, community organizations and healthcare practitioners outside academia to help further provide evidence based interventions designed to reduce healthcare disparities.

The CTSI will enhance our stature within the local community as well as our leadership in state and federal biomedical research and economic development arenas. It will give us a competitive edge in the pursuit of NIH funding, create jobs, promote technology transfer, and advance public health opportunities. In the months and years ahead, we will be providing you with more information on how you can participate and help contribute to the CTSI's mission to transform the research and clinical enterprise at the University of Maryland and across the nation.

In the relentless pursuit of excellence, I am Sincerely yours,

& albert bece

E. Albert Reece, MD, PhD, MBA Vice President for Medical Affairs, University of Maryland John Z. and Akiko K. Bowers Distinguished Professor and Dean, University of Maryland School of Medicine

# Institute for Genome Sciences Director Claire Fraser-Liggett ELECTED TO THE INSTITUTE OF MEDICINE

#### CLAIRE FRASER-LIGGETT, PHD, professor, Departments of Medicine and Microbiology & Immunology and

director, Institute for Genome Sciences, has been elected a member of the Institute of Medicine of the National Academies. Dr. Fraser-Liggett is one of 65 new members and five foreign associates named to its membership this year.

Election to the IOM is considered one of the highest honors in the fields of health and medicine and recognizes individuals who have demonstrated outstanding professional achievement and commitment to service. New members are elected by current active members through a highly selective process that recognizes individuals who have made major contributions to the advancement of the medical sciences, health care and public health.

Dr. Fraser-Liggett is a world-renowned scientist, who through her pioneering research, her extensive peer-reviewed scientific publications, and her leadership of several preeminent research institutions, has contributed significantly to the development of scientific progress of genomic medicine.

Over the past 16 years, Dr. Fraser-Liggett's research team has applied large-scale DNA sequencing and analysis to the study of the microbial world and how it impacts human health. With the groundbreaking 1995 publication of the first complete genome sequence of a free-living organism, the bacterium, *Haemophilus influenzae*, she and her team launched the field of microbial genomics, creating a paradigm

shift in the study of microorganisms, and laying the foundation for new approaches to personalized medicine. Today, she is one of the most highly cited investigators in the field of microbiology microbial genomics. The completion of more than 1,000 microbial genome sequences today is a direct result of her team's pioneering work in the developing new experimental and computational approaches to analyzing large quantities of genetic information.

"It is a great pleasure to welcome Dr. Fraser-Liggett to the Institute of Medicine," said Dean E. Albert Reece, MD, PhD, MBA. "This membership is recognition of Claire's impressive body of research and her overall contributions to science and biomedicine, which are many. It's also an affirmation of the growing recognition of the potential of genomics to improve human health. Since we launched the Institute for Genome Sciences here on our campus in 2007, it has had a positive impact on countless peoples' lives worldwide."

"It is a tremendous honor to be elected a member of The Institute of Medicine. I look forward to contributing to my new colleagues' efforts to aid those in government and in the private sector in dealing with our most pressing health care issues," said Dr. Fraser-Liggett. "IOM's inclusion of genomic scientists demonstrates how integral this new interdisciplinary and innovative field has become to making breakthroughs in medical treatments and to developing new approaches to address the important biomedical challenges facing our nation."

# Fiskum, Roth and Strome are Founders Week Award Winners

Three of the four University of Maryland 2011 Founders Week award winners are School of Medicine faculty or staff. The winners received their awards at the black-tie Founders Week Gala held on October 25.



### **Researcher of the Year** Gary Fiskum, PhD

Matjasko Professor for Research in Anesthesiology and Vice Chair for Research, Department of Anesthesiology

In his 13-plus years at the School of Medicine, Dr. Fiskum has distinguished himself as an exceptional research scientist and learned to master some complex issues. His work pertaining to mitochondrial dysfunction associated with traumatic brain injury and optimizing cerebral resuscitation, in particular, has made him a speaker very much in demand, nationally and internationally.

But to fully appreciate Dr. Fiskum, his colleagues say, one must look beyond the research. For instance, Margaret McCarthy, PhD, associate dean for graduate

studies and interim chair of the Department of Pharmacology & Experimental Therapeutics, points out that the task of Xeroxing, collating, and stapling isn't beneath Dr. Fiskum.

Told that his stature—which includes being principal investigator (PI) or co-PI on five grants supported by \$7 million in funding (from such organizations as the National Institutes of Health, Department of Defense and U.S. Air Force)—would preclude him from such menial chores, Dr. Fiskum replied simply, "No task is unimportant when working on very complicated projects."

David Hovda, PhD, director of the UCLA Brain Injury Research Center, added, "Dr. Fiskum displays the very best in character. He has always been a humble colleague who is enthusiastic about science; but, more importantly, he values friendships and ethical standards."

Dr. Fiskum also finds time to mentor young researchers and host monthly neuroprotection seminars and periodic meetings and lectures of the UM Mitochondrial Research Interest Group, which he is happily opening to Johns Hopkins researchers this year.

Says colleague and former University Researcher of the Year J. Marc Simard, MD, PhD, "what has been especially noteworthy has been the collaborative nature of his work and the tremendous efforts that he has put into the lecture series."

Despite performing research weighty enough to change American Heart Association guidelines, Dr. Fiskum has a simple answer when asked what is the nicest compliment you can get as a researcher. "Honesty," he said. "I also believe that being recognized as an effective mentor is very important and gratifying."

### Public Servant of the Year Jean Marie Roth

Academic Program Specialist, Office of Student Research

A University employee since 1973, Ms. Roth has volunteered countless hours of her time both inside and outside the workplace. Externally she volunteers at the Hippodrome Theatre, the city of Baltimore, and the Hereford Optimist Club, and she has chaired numerous fundraisers at her church, Our Lady of Grace Parish. Within the University, she chairs the Staff Senate Community Outreach Committee. On behalf of the less fortunate, she has led food and holiday drives, collecting coats and gloves, school supplies and toiletries, paper goods and food staples, to name a few, for the likes of



Our Daily Bread, the Ronald McDonald House, Cell Phones for Soldiers and United States military veterans.

She brushes off any praise, saying, "We should do as much as we are able to and then some."

University President Jay A. Perman, MD, recognized her work for the Virtual Food Drive and the Cell Phones for Soldiers initiative with a note that said, "I thank you for going above and beyond your charge and I applaud you for setting such a high standard of selflessness that others throughout the campus would be proud to follow."

Ms. Roth humbly says joining the Staff Senate and becoming involved with the Community Outreach Committee was just something she wanted to do. "I am thankful to the committee for working to inject that spirit of giving back to others on this campus," she said.

### Entrepreneur of the Year

**Scott Strome, MD, FACS** Professor and Chair, Department of Otorhinolaryngology-Head and Neck Surgery

Dr. Strome directs a large translational research program and is interested in all aspects of head and neck cancer patient care. The startup company, Gliknik, Inc., he formed in 2007 with CEO David Block, MD, MBA, is broadly recognized as one of Maryland's most promising early-stage biotech companies. In 2007, the *Daily Record* named Dr. Strome "Inventor of the Year," and in 2009 named Gliknik "Best Incubator Company of the Year." Based in the University of Maryland BioPark, Gliknik has raised more than \$10 million, licensed two patents



► BY KAREN WARMKESSEL

#### [please turn to back page]

# Young Women with Early-Stage Breast Cancer HAVE SIMILAR SURVIVAL WITH BREAST-CONSERVATION THERAPY AS MASTECTOMY

### New study by University of Maryland researchers analyzed data from nearly 15,000 patients



Young women with early-stage breast cancer have similar survival rates with a lumpectomy and radiation treatment, known as breast-conservation therapy, as with mastectomy, a new study conducted at the University of Maryland has found. The results of the analysis of nearly 15,000 patients listed in a nationwide cancer registry were presented at the 2011 Breast Cancer Symposium held in September in San Francisco. tween those who had breast-conservation therapy and those who had a mastectomy." Dr. Mahmood, a former resident in the Department of Radiation Oncology at the University of Maryland who is now at the University of Texas MD Anderson Cancer Center, will present the data at the Breast Cancer Symposium.

Steven J. Feigenberg, MD

Steven J. Feigenberg, MD, associate professor, Department of Radiation Oncology, says that mastectomies among young women have been on the rise, in part because of concerns regarding recurrence of their cancer. Dr. Feigenberg is also a radiation oncologist at the University of Maryland Marlene and Stewart Greenebaum Cancer Center.

"We believe these findings are very significant for young women with early-stage breast cancer who might choose to

have a mastectomy in the hope of improving their outcome. This study confirms that breast-conservation therapy is a safe, effective treatment option and will not have a detrimental effect on survival," Dr. Feigenberg, the study's senior author, said.

He says this is the largest study to date to compare survival in young women with early-stage breast cancer who had breast-conservation therapy vs. mastectomy. Women under 40 can have more aggressive tumors and are often at higher risk for having their cancer recur. Previous studies have suggested that young women have higher local recurrences of their cancer with breast-conservation therapy, but these studies did not demonstrate an effect on survival, Dr. Feigenberg stated.

Usama Mahmood, MD, the lead author, said, "We looked at data from nearly 15,000 women in our retrospective analysis and saw no difference in survival be-

Researchers analyzed data from the SEER (Surveillance, Epidemiology and End Results) registry, which is maintained by the National Cancer Institute. They identified 14,764 women, age 20 to 39, who were diagnosed with early-stage breast cancer between 1990 and 2007. Forty-five percent of the women had breast-conservation surgery, and 55 percent had a mastectomy. Patients who received breast-conservation therapy were older and had smaller, lower-grade tumors and less lymph-node involvement. The median follow-up was nearly six years, although some patients were followed for 10 years, 15 years and beyond. All of the breast cancers were earlystage. Sixty-four percent of the patients were white.

To confirm the results of the study, the researchers did a "matched pair analysis, using a smaller group of 4,644 patients who had undergone breast-conservation therapy and mastectomy. Patients were matched for such factors as year of their diagnosis, age, grade, tumor size, number of positive lymph nodes, the number of nodes removed and their particular type of breast cancer, and still there was no difference in overall survival or survival specific to breast cancer. Similarly, a separate analysis was performed on the youngest group of patients, under age 33, again seeing no difference in outcomes.

The overall survival for those who had breast conservation therapy was 92.5 percent after five years, 83.5 percent after 10 years, and 77 percent after 15 years. That compares with [continued]



# Whole-Parasite Malaria Vaccine Shows Promise Vaccine is First of Its Kind to Earn FDA Approval to Test in Humans

#### FOR THE FIRST TIME, A MALARIA VACCINE

that uses the entire malaria parasite has proven safe and shown promise to produce a strong immune response in a clinical trial, according to a new study co-authored by researchers at the Center for Vaccine Development. The vaccine is unique in that it employs the entire malaria parasite, while most experimental malaria vaccines consist of just one or at most a few proteins

found in the parasite.

Researchers found that the vaccine—the first whole parasite vaccine to be approved by the U.S. Food & Drug Administration for clinical trials—could provide unprecedented immune responses against malaria when administered intravenously. The study was published online in the journal Science in September.

"This is the first whole-organism malaria vaccine ever produced," said Kirsten Lyke, MD, associate professor, Department of Medicine, and a research scientist at the Center for Vaccine Development. Dr. Lyke was one of three lead authors and two senior authors on the study, along with colleagues from the U.S. Military Malaria Vaccine Program at the Naval Medical Research Center, the Vaccine Research Center at the National Institutes of Health (NIH), and the Rockville-based biotechnology firm Sanaria, Inc.,

which developed and manufactured the vaccine. "No vaccine has completely

protected against malaria in a challenge trial, in which vaccinated volunteers are subjected to the bite of an infected mosquito to measure their immunity," said Dr. Lyke. "This vaccine showed strong promise. We hope that with further study it could help revolutionize the field and prevent death and illness from malaria worldwide, and be used to eliminate malaria from certain areas."

Though malaria has been largely eliminated in much of the developed world, it is still a widespread threat in warm, tropical areas where infected mosquitoes thrive, such as Africa. Malaria, caused by a parasite transmitted through the bite of an infected

mosquito, kills nearly one million people and infects 300 million annually worldwide. The condition can be treated with anti-parasite drugs, but can have fatal consequences for vulnerable patients who have no immunity to the disease. Children under the age of five succumb at high rates to the neurological and cardiac effects of malaria, particularly in Africa.

Researchers found that the vaccine produced a partial protective response in the 80 volunteers who were immunized subcutaneously, or under the skin, by traditional needle and syringe in the trial at the Center for Vaccine Development in Baltimore. However, this response was significantly less than the 80 to 90 percent protective immunity the research team is intent on achieving. Researchers suspected that administering the vaccine more directly into the bloodstream, accelerating its path to the liver, might produce an even stronger response. Further study conducted by collaborating authors from the Vaccine Research Center at the NIH found that administering the vaccine intravenously produced a very high level of immune response in animal subjects.

infected blood. Using mosquitoes raised in aseptic conditions, Sanaria Inc. developed a unique large-scale production and cryopreservation process, allowing the parasite to be frozen, shipped to remote locations and safely thawed.

Dr. Lyke collaborated with fellow University of Maryland School of Medicine scientists including Matthew B. Laurens, MD, MPH, assistant professor, Departments of Pediatrics and Medicine, and Christopher Plowe, MD, professor, Departments of Medicine, Epidemiology & Public Health and Microbiology & Immunology, and leader of the Malaria Group at the School of Medicine. Robert Edelman, MD, clinical professor, Departments of Medicine and Pediatrics, also contributed to the paper. The group co-authored the study with colleagues from the Howard Hughes Medical Institute, the Walter Reed Army Institute of Research, the PATH Malaria Vaccine Initiative and the biotechnology firm Protein Potential LLC.

The parasite used in the vaccine is a sporozoite, an early life-cycle stage of the parasite Plasmodium falciparum, the most dangerous type of malaria parasite. The sporozoite is carried in the salivary glands of a mosquito, where it infects







a human through the mosquito's bite. The sporozoites used in the vaccine were rendered harmless

when Sanaria's manufacturing team administered radiation to the mosquitoes carrying the parasites. The radiation leaves the sporozoites incapable of reproducing and incapable of causing malaria once the human is bitten. Instead, the sporozoite is intended to stimulate the body's immune response, creating immunity to malaria.

Previous studies have shown that the bites of infected, irradiated mosquitoes have the ability to immunize humans against malaria. In fact, previous trials pioneered at the University of Maryland School of Medicine and the U.S. Navy almost 40 years ago showed that 90 percent of humans bitten by at least 1,000 irradiated malaria-carrying mosquitoes did not contract

malaria from the bites of ordinary malaria-infected mosquitoes. However, the bite of a mosquito—essentially using a mosquito as a syringe and needle—is not a practical method of administering a vaccine to large groups of people. Sanaria's large-scale production and cryopreservation process creates the potential for the vaccine to be administered globally.

The study included 98 adult volunteers, 18 of whom served as control volunteers. As a Phase I trial, the study's focus was to establish that the vaccine was safe and well tolerated. The results have guided the design of the next study, a Phase II clinical trial in which scientists will administer the vaccine intravenously to human volunteers and measure immunity to determine the effectiveness of Sanaria's vaccine. Scientists have traditionally regarded intravenous delivery as an impractical strategy for large-scale global immunization, but Dr. Lyke said the researchers will evaluate its potential in future studies. Other possibilities for administering the vaccine might include novel microneedle injection devices. If these studies continue to show promise, the next step would be to test the whole parasite vaccine's ability to prevent malaria in people naturally exposed to malaria. "We would love to test this vaccine in Mali," said Dr. Plowe, who has led several malaria vaccine trials in Mali, West Africa. There, his team found that highly variant malaria parasites are difficult to prevent with single-strain, single-protein vaccines. "That will be the real test-does this vaccine have enough immunological firepower to protect against all the different strains circulating in the field, not just the strain the vaccine is based upon? If the whole parasite doesn't work, I don't know what will-this is the best chance we've got."



EMPLOYS THE ENTIRE MALARIA PARASITE, WHILE MOST EXPERIMENTAL MALARIA VACCINES CONSIST OF JUST ONE OR AT MOST A FEW PROTEINS FOUND IN THE PARASITE.

2011

'Our hope is that we can optimize the delivery of this vaccine to prevent and eliminate malaria on a global level," said Dr. Lyke. She and her colleagues are already at work designing new studies to find the best way to administer the vaccine.

Scientists consider a whole-parasite vaccine to be the "holy grail" of malaria vaccine research. Such a vaccine is believed to be more capable of broadly protecting people against the scores of varying strains of malaria. Historically, vaccines are comprised of various proteins found in the virus or, in the case of malaria, the parasite. Recombinant vaccines-those comprised of various components of the parasite-often are narrowly protective against just certain strains. Whole-parasite vaccines have seemed unattainable because of the many challenges of large-scale production and preservation of whole parasites, which can only be produced by infecting mosquitoes with malaria-

91.9 percent, 83.6 percent and 79.1 percent, respectively, for those who had mastectomies. In addition, the breast cancer-specific survival rates were similar between the two groups.

The study's authors include members of the multidisciplinary breast cancer team at the University of Maryland Marlene and Stewart Greenebaum Cancer Center. In addition to Dr. Feigenberg, co-authors include Katherine Tkaczuk, MD, professor, Department of Medicine, and a medical oncologist who heads the Breast Evaluation and Treatment Program; Susan Kesmodel, MD,

assistant professor, Department of Surgery, and a surgical oncologist; and two medical oncologists, Saranya Chumsri, MD, assistant professor, Department of Medicine, and Ting Bao, MD, assistant professor, Department of Medicine.

The 2011 Breast Cancer Symposium is a three-day multidisciplinary symposium, sponsored by the American Society of Clinical Oncology, American Society of Breast Disease, the American Society of Breast Surgeons, the American Society for Radiation Oncology, the National Consortium of Breast Centers and the Society of Surgical Oncology.

### Founders Week [continued from page 2]

and applied for several more. Led by Dr. Strome, Gliknik is developing novel biotechnology drugs for patients with cancer and autoimmune/in-flammatory diseases.

Dr. Strome praises the state biotech tax credit and the Maryland Industrial Partnerships program in College Park for contributing to Gliknik's success. In addition, "Jim Hughes and the entire staff at the Office of Research and Development have really done a terrific job in guiding me through this process," he commented, "and the offices of President Perman and Dean Reece have been incredibly supportive."

Meeting the definition of a true entrepreneur, Dr. Strome sees this award as fuel for further translational discoveries. "It is my goal for our lab and our department to remain active in discovering new biologic pathways and in working collaboratively with industry to create new therapeutic interventions to help patients across a wide range of disorders," he said.

> **E. Albert Reece, MD, PhD, MBA** Vice President for Medical Affairs, University of Maryland John Z. and Akiko K. Bowers Distinguished Professor and Dean, University of Maryland School of Medicine Cordially invites you to the



### Saturday, February 4, 2012

RECEPTION 6:30 pm DINNER & PROGRAM 7:30 pm DESSERT 9:00 pm Marriott Inner Harbor at Camden Yards 110 South Eutaw Street, Baltimore, MD 21202 Complimentary self-parking at the Marriott garage

> FEATURING GUEST SPEAKER Vivian W. Pinn, MD Former Director, Office of Research on Women's Health National Institutes of Health

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Baltimore Inner Harbor, Beautiful Day Photo by: **Mike Busler**, Technical Services Supervisor, Information Technology Management Department, University of Maryland Faculty Physicians, Inc.

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