



DEAN'S MESSAGE: What's On My Mind



What's on my mind this month is this quote by Henry Ford, the founder of the Ford Motor Company who embodied the American Dream, "Coming together is a beginning; keeping together is progress; working together is success."

In the last few weeks, I've witnessed all three parts of Mr. Ford's quote in action across the School of Medicine, and I'd like to share these reflections.

"Coming together"

At the end of April and beginning of May, we saw two extremes of what can happen when people come together to enact change: rioting and rebuilding. In the end, those seeking reform using peaceful and constructive means won out. We recognize the School of Medicine has a key role in reducing the disparities plaguing the communities which surround us. Not only do we help our neighbors as individuals, but as a leading academic medical center, we provide care for the citizens of Baltimore City through the work of our hospital, community clinics and outreach programs.

Most importantly, we train the next generation of physicians, allied health professionals and research scientists who will devote their careers to improving the health and well-being of all people. On May 14th, we came together as teachers, leaders, family and friends to celebrate the graduation of the School of Medicine Class of 2015. Highlights from this year's commencement ceremonies appear in this issue of the newsletter.

"Keeping together"

I think the idea of "keeping together" is similar to persevering, even when faced with challenges, toward a greater goal. That kind of determination is what led Dean Emeritus Donald Wilson to staunchly advocate for greater diversity in medical training and biomedical research, and motivated him to become one of the founders of the Association for Academic Minority Physicians nearly three decades ago.

Perseverance is what led Dr. Myron "Mike" Levine to establish a School of Medicine Center, the Center for Vaccine Development, devoted to improving the health and well-being of some of the most vulnerable among us—those living in developing countries around the world.

Through their life's work, they inspired progress and new directions in how we heal, who we teach and how our

incredible innovations in medicine reach in the world.

"Working together"

The center spread of the June 2015 issue of SOMnews highlights the most recent accomplishments of the Institute for Genome Sciences (IGS), led by Claire Fraser, PhD. Since joining the faculty at the School of Medicine, the exceptional scientists at IGS have revolutionized genomic discoveries in medicine, agriculture, environmental science and biodefense. One of the keys to their success has been collaborating with other faculty members across the School of Medicine. Some of these partnerships have resulted in clinically-oriented projects, which help increase the breadth and depth of our translational medicine research. I strongly encourage you to read the IGS feature article to learn more.

This concept of working together is a major component of the University of Maryland Medicine's strategic vision plan, Vision 2020, and will help drive our future success. For example:

- The School of Medicine leaders have supported seed funding programs, such as the **Dean's Challenge Award** and the **UMB/UMBC Challenge and Innovation Awards**, to foster interdisciplinary research.
- We have launched major clinical initiatives, such as the **Program in Lung Healing**, because we recognized that taking care of high-risk patients requires a team of our leading experts.
- Our students have gained a greater appreciation for the scientific discoveries underlying the advances in medicine today by working together with research scientist and physician-scientist mentors through the **Foundations of Research and Critical Thinking** course.

These are only a few of the ways in which we are working together to advance the ambitious goals of our bold, strategic and innovative vision for the next four years at the School of Medicine.

In the relentless pursuit of excellence, I am

Sincerely yours,

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

Point of Pride

Graduating Class of 2015



This makes us proud!

Esteemed School of Medicine Leaders Honored

Donald E. Wilson, MD, MACP, AGAF, Dean Emeritus of the University of Maryland School of Medicine, and Myron M. Levine, MD, DTPH, Associate Dean for Global Health, Vaccinology and Infectious Diseases, were both honored on April 30 for their outstanding contributions to medicine. The American College of Physicians (ACP) presented Dr. Wilson with the 2015 W. Lester Henry Award for Diversity and Access to Care, which is given to an ACP member with outstanding accomplishments in advancing diversity in clinical medicine or research and/or access to care in relation to diverse populations. Dr. Levine received the ACP Award for Science for Outstanding Work in Science as Related to Medicine, which was established in 1958 to honor recipients who have made exceptional contributions to medicine.

Dr. Wilson became the nation's first African-American dean of a non-minority medical school in 1991. During his 15-year tenure Dean Wilson created one of the most diverse student bodies and faculties in the country, with the School of Medicine more than tripling the number of full-time underrepresented minority faculty. Dean Wilson's commitment to the education and training of minorities in medicine and research led him to become one of the founders of the Association for Academic Minority



Physicians in 1986. Dr. Wilson is past chairman of the Association of American Medical Colleges (AAMC) and the AAMC Council of Deans, the first African-American to hold each of these positions.

The W. Lester Henry Award for Diversity and Access to Care was established in 2008, and in 2012 was named in honor of Dr. W. Lester Henry, the first African-American Regent and Master of the College. "There is no one more deserving of this award than Don Wilson," said Dean E. Albert Reece, MD, PhD, MBA, who is also the vice president for Medical Affairs, University of Maryland, and the John Z. and Akiko K. Bowers Distinguished Professor. "He has done more to advance the cause of diversity in medicine more than anyone I know. We are fortunate to stand on his shoulders to continue his pioneering legacy.



At the School of Medicine, we join the ACP in extending our heartfelt congratulations for this important honor."

Dr. Levine, the Bessie & Simon Grollman Distinguished Professor in the Department of Medicine, founded the Center for Vaccine Development (CVD) at the school in 1974 and served as its director until December 2014. For the past 40 years, under Dr. Levine's leadership, the CVD has conducted a wide range of research relating to the development of vaccines for a variety of diseases, including cholera and malaria. The CVD also developed new delivery systems, as well as public health and vaccine policy. Most recently, Dr. Levine lead CVD's involvement in the World Health Organization's consortium to test an Ebola vaccine.

Dr. Levine also served as a World Health Organization consultant to the Smallpox Eradication Program in Bangladesh in 1975. From 2000 to 2002, he was a member of the first Working Group of the Global Alliance for Vaccines and Immunization (now called the GAVI Alliance), and was co-chair of its Task Force on Research and Development.

"Professor Levine richly deserves this important honor," said Dean Reece. "His decades of diligent work have yielded many innovations, which have saved many thousands of lives around the globe."

IGS Breaks New Ground

Unraveling Gut Bacteria, Battling Malaria, and Diagnosing Genetic Disease in Newborns

From understanding more about how certain commensal bacteria benefit humans, to developing new ways to combat deadly cattle disease in Africa, to unlocking the mysteries of human genomics, the Institute for Genome Sciences (IGS) is involved in a wide range of cutting-edge research in a variety of areas. IGS, which was founded in 2007, focuses on research involving the genome—the complete set of genetic material of a given organism—in everything from bacteria to humans. Over the past year, IGS faculty received several new grants that involve close collaboration with other researchers at the School of Medicine and the University of Maryland, Baltimore (UMB).

“This is an especially exciting time for us,” says **Claire M. Fraser, PhD**, the director of the IGS as well as a professor of Medicine and Microbiology & Immunology at the University of Maryland School of Medicine. “Our investigators have begun to move into translational studies that will likely have an impact on human and environmental health in the future.”

Among those doing innovative work is Fraser herself. Earlier this year, she published a paper showing a possible mechanism for how a common probiotic bacterium helps foster human gut health. The strain of bacteria, called *Lactobacillus rhamnosus* GG (LGG), is a component of many popular probiotic products. It has a reputation as a helpful microbe: researchers have found evidence that it can help with intestinal problems, respiratory infections and some skin disorders.

But it was unclear exactly how LGG produces these benefits. Fraser and her team found that LGG may act as a facilitator, modifying the activity of other gut bacteria. This is the first time this mechanism has been described; the discovery could eventually help scientists create more effective strategies to foster a healthy gut. The paper was published in the April issue of the journal *mBio*.

“This is a new idea, that some probiotics may work by affecting the activity of key commensal species in the gut,” says Fraser. “Previously we believed that LGG and other probiotics worked directly on the host.” She says it lends support to the idea that we need to look at the microbes in the gut as an interconnected ecosystem rather than a series of solitary bacteria.



IGS faculty were part of the East Coast Fever (ECF) Consortium, which met in Ethiopia in February to share their research.

Gut Microbes and Transplant Organs

Other IGS researchers are investigating the microbiome as well. **Emmanuel Mongodin, PhD**, Assistant Professor of Microbiology & Immunology at IGS, and **Jonathan Bromberg, MD, PhD**, Associate Professor of Surgery and Microbiology & Immunology, have been examining whether certain gut bacteria can reduce the body’s immune response to transplanted organs.

“The microbiome has a huge impact on immunity,” says Mongodin. Knowing this, he and Bromberg wondered whether adjusting the microbiome could affect transplant organ rejection. This is a significant problem among patients who have transplants. Even in those who take immunosuppressive drugs, the immune system does not accept the new organ; in a significant proportion of people, the transplanted organ becomes increasingly damaged from chronic immune response.

Mongodin and Bromberg transplanted hearts into a group of mice. Some were also implanted with microbes that dampened the activity of the immune system, while others were given microbes that activated immunity. A third group did not receive any new bacteria. After a month, the researchers examined the transplanted hearts. Those in the first group—with the microbes that decreased immune activity—had much less heart damage than those in the other two groups.

“The mice that had the anti-inflammatory microbiome did much, much better,” says Mongodin. “This is something that we need to pay a lot of attention to.” He and Bromberg now plan to look at gut bacteria in humans, to see if they can find signature differences between anti-inflammatory and pro-inflammatory gut microbial ecosystems.

Other IGS researchers are exploring how these microbes may influence diseases elsewhere in the body. **Jacques Ravel, PhD**, Professor of Microbiology & Immunology and Associate Director for Genomics at IGS, is now investigating how the urogenital microbiome affects the severity of two sexually transmitted infections, chlamydia and gonorrhea.

Both diseases pose major public health problems in this country. Chlamydia is the most common bacterial infection in America, with 2.8 million cases estimated annually. Gonorrhea causes around 820,000 infections in America each year. Together these bacteria cause most of the 750,000 cases of pelvic inflammatory disease diagnosed annu-



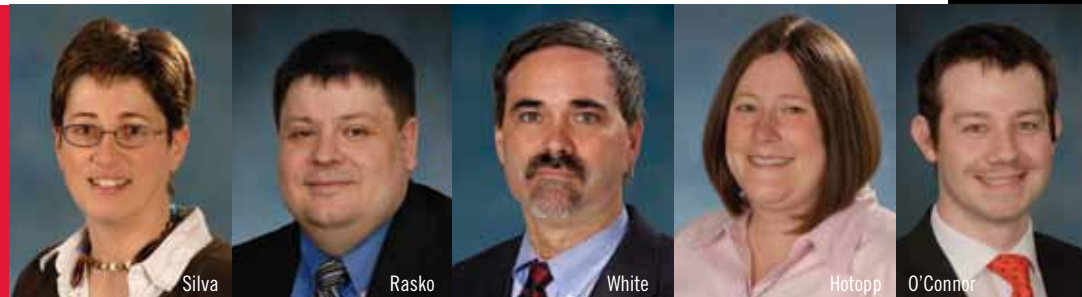
Mongodin

Bromberg

Ravel



As more clinical researchers apply genomics tools to their work, and as sequencing tools become faster and more affordable, genomics is allowing medical researchers ways to pose new questions about drugs, health, transplantation, cancers, longevity, and to be able to measure changes in more precise ways.



ally in in the United States. Pelvic inflammatory disease is a leading cause of female infertility and life-threatening conditions in women such as ectopic pregnancy.

Last year, Ravel was awarded a five-year, \$10.7 million grant from NIH to study these questions. The grant also involves researchers at UMB's School of Dentistry, as well as other outside institutions, including Duke University, who will look for patterns among microbes in the urogenital microbiome that might offer clues as to how and why some people become infected with chlamydia and gonorrhea while others are protected.

"This research is the first time that a comprehensive systems biology approach will be used in STDs," said Ravel, who is the co-principal investigator on the study. "By looking at how human genetics and the microbiome affect and influence infections in humans, we can better understand how to protect against these infections."

Gauging a Parasite's Vulnerability

IGS scientists are focusing on global public health issues, too, including malaria, a leading cause of disease and death throughout the world. Every year the disease infects over 200 million people and causes more than half a million deaths. In parts of sub-Saharan Africa and South Asia, the disease is common and causes enormous suffering and hardship.

"This is a key question—how likely are these parasite species to jump to humans?" says Silva. "And according to our results, 'host switching' by malaria-causing parasites is not at all a common event on an evolutionary time scale."

In recent years, public health experts have increasingly explored the idea of eliminating the most dangerous malaria-causing parasite. But they have questioned whether getting rid of this species, called *Plasmodium falciparum*, would allow other species of the parasite to jump in and start infecting humans with malaria.

A study by IGS indicates it is very unlikely that *Plasmodium* species that infect other animals—such as apes, birds and reptiles—would cross over easily to humans. Using sophisticated genetic analysis, **Joana C. Silva, PhD**, found evidence showing that five other common *Plasmodium* species have not changed which animals they infect for at least three million years.

The research was published earlier this year in the journal *Molecular Biology and Evolution*. Silva, Assistant Professor of Microbiology & Immunology at IGS, was the lead author.

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More than 200 *Plasmodium* species have been identified. *Plasmodium falciparum* is the most lethal of the five that are known to infect humans. Researchers are examining new approaches to reduce or eliminate *Plasmodium falciparum* by developing vaccines against it, for example, or spreading a bacterium that kills the mosquitoes that carry it. But some scientists have expressed concern that *Plasmodium falciparum*'s ecological niche might be quickly filled by other *Plasmodium* species.

Silva and her co-authors looked at hundreds of genes spread across five different species of *Plasmodium*. Their goal was to discover how closely related the genes were—in effect, how long ago they had diverged from each other. If they had separated recently, it was more likely that they could jump from infecting one species to another.

To get their results, Silva and her colleagues developed a new statistical approach to determine when *Plasmodium* species split off from one another. The new method uses molecular data from thousands of genes; current techniques, by contrast, use at most sequences from dozens. This new approach is not only more reliable, but also faster.



NIH Funds a New Center at IGS

Last year, IGS was awarded a five year, \$15.2 million grant from the National Institute of Allergy and Infectious Diseases (NIAID) to develop the Genome Center for Infectious Disease (GCID). The center will focus on three areas—(i) the interaction among human hosts, enteric pathogens, and the microbiome; (ii) the genomic analysis of fungal pathogenesis; and (iii) genomics-enabled studies of drug and vaccine resistance in parasitic tropical diseases. Fraser leads the project, along with two other IGS researchers: **David Rasko, PhD**, Associate Professor of Microbiology & Immunology at IGS, and **Owen White, PhD**, Professor of Epidemiology & Public Health and Associate Director of Informatics at IGS. "This kind of research wouldn't have been possible even five years ago," says Rasko. "But with new technological advancements, we can make new discoveries."

IGS scientists are also working on possible links between bacteria and human cancer. **Julie Hotopp, PhD**, Associate Professor of Microbiology & Immunology, is leading an innovative research program to investigate lateral gene transfer (LGT)—the transmission of genetic material between organisms in the absence of sexual reproduction. She has found evidence that bacteria may transfer genes to human cells. This material is more likely to become part of tumor cells than normal cells. This phenomenon might play a role in the



development of cancer and other diseases associated with DNA damage. "Our research may help us understand how cancers form and grow," says Hotopp. "We think this has a lot of potential." Others are also recognizing her work: last year, NIH honored her with its prestigious New Innovator Award for her gene transfer work.

IGS is also working in more patient-focused areas. **Timothy D. O'Connor, PhD**, Assistant Professor of Medicine at IGS, is collaborating with the multidisciplinary team in the Program for Personalized and Genomic Medicine (PPGM) at the School of Medicine to develop a sequencing-based approach to quickly search for a wide array of genetic abnormalities in infants. This method will allow the research team to quickly identify a genetic cause in some affected newborns. Previously, this process would take months; with this new approach, it takes days. This innovative project was initiated by **Alan Shuldiner, MD**, John C. Whitehurst Professor of Medicine and Director of PPGM. Dr. O'Connor and **Linda Jeng, MD, PhD**, Associate Professor of Medicine in PPGM and Laboratory Director of the Translational Genomics Laboratory are co-leading this study protocol to implementation in the UMMC NICU. "This is cutting edge technology," says Dr. O'Connor. "It's really exciting. You can see the impact of what you've discovered right away."

Recognition for Bioinformatics Innovation

IGS scientists have received an impressive number of awards for contributions in their respective fields. Earlier this year, White, who is also the co-director of the University of Maryland Center for Health-Related Informatics and Bioimaging (CHIB), received the Benjamin Franklin Award for Open Access in the Life Sciences from Bioinformatics.org.

White has been dedicated to open source/open access for years. As a principal investigator with the Human Microbiome Project Data Analysis and Coordination Center (HMP DACC), he led a complex multi-year, multi-institutional organization of data. White has also developed several web resources such as the Comprehensive Microbial Resource and Pathema, containing annotation from microbial genomes. He has also developed automated annotation systems for bacterial, eukaryotic and microbiome organisms as well as several bioinformatic training programs.

"The range of work we're doing at IGS amazes me every day," says Fraser. "With a relatively small research team and state-of-the-art core facilities for DNA sequencing and analysis, our influence in the genomics field has been great—both locally and internationally. This has been facilitated by the support of SOM since we arrived in 2007. As more clinical researchers apply genomics tools to their work, and as sequencing tools become faster and more affordable, genomics is allowing medical researchers ways to pose new questions about drugs, health, transplantation, cancers, longevity, and to be able to measure changes in more precise ways."

“Take a deep breath, and enjoy the journey.”



Serving patients well is not an easy task in these tumultuous times. “Great challenges await you,” **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, proclaimed to the students. “You are entering into this profession at a time of unparalleled convergence: a vastly changing health care environment, new and emerging life-saving technologies and a phenomenally growing need to improve human health. Never has the time to make your mark been greater than in the days and years ahead of you.”

In his keynote speech, Philip Needleman, PhD, former President of Research & Development at Searle and former Chief Science Officer at Monsanto, reflected upon the amazing progress medicine has made in the last 200 years, particularly since he earned his PhD in Pharmacology from the University of Maryland School of Medicine in 1964. Whole new areas of medicine have been created, including vaccinology, genomics, epidemiology and public health, and immunotherapy. Changes will continue to come at a faster and faster pace “when you graduates master new skills, experience new adventures, and take on the great challenges in our society, said Dr. Needleman. “Take a deep breath, and enjoy the journey. I wish I could be in your shoes.”



The Class of 2015 received their doctoral hoods in a special graduation ceremony at the Baltimore Convention Center on May 14. Hundreds of family, friends and faculty were there to cheer on the 157 graduates as they officially transitioned from students to doctors. “No longer will you be able to use your favorite excuse ‘I’m only the med student,’” joked **David Mallott, MD**, Associate Professor, Department of Psychiatry, and Associate Dean of Medical Education, who



also advised the new doctors that “being a physician is defined much more by what you think and say than by what you do. Our technical prowess is an extension of what we think and what we say. What you say, not only to

patients but in all aspects of life, now matters much, much more. Let your words ring with truth.”

The power of words was a recurring theme throughout the ceremony. “The Class of 2015 is the class with a voice,” declared class president **Greg Lassans** in his speech. “We have used our voices to express our support and dissent time and time again. We have published, we have written letters and petitions, we have given speeches, and we have sung songs. And, for the record, I doubt any other class has achieved the amount of You Tube fame that we have! (The class is infamous for their medical school parody videos.) In four years we have been many, many things. But we have seldom been quiet. Through our voices we have made our mark on this school. That doesn’t end this morning. If we are to be successful doctors to our patients, our country and our world, we must continue to get our messages across.”

Alexi Pappas, who was chosen to receive the Faculty Gold Medal for Outstanding Qualifications in the Practice of Medicine, believes that listening is as important as speaking.

“Being effective caregivers requires not only the application of our technical expertise, not only our intense focus on fixing particular presenting pathologies, but a real commitment to learning about patients’ experiences,” he said. “We need to understand the social and cultural factors that influence health and be engaged citizens and community members. We have so much left to learn to be good at what we do, to become effective doctors. Let’s remember to learn some of it from the people we serve.”



somnews

UNIVERSITY OF MARYLAND SCHOOL OF MEDICINE JUNE 2015 VOL.16 NO.10

SOMnews is produced by the University of Maryland School of Medicine, Office of Public Affairs
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 ▲ Submitting information to SOMnews: Please email your submission six weeks prior to the month you wish to see your submission included to Caelie Haines, Public Affairs Manager, at chaines@som.umaryland.edu.
 ▲ Printed using environmentally-responsible low VOC inks.