

IGS

INSTITUTE FOR GENOME SCIENCES

NEWSLETTER
Spring 2019

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Greetings Colleagues,

Much has happened at IGS in the past few months and we have much to celebrate. Congratulations to our outstanding faculty members who continue to successfully compete for extramural funds and who are publishing the results of their collaborative research in high-impact journals.

A few of the projects profiled in this issue include:

- NIAID's \$17.5 million award to IGS for GCID ([pg.11](#))
- Dr. David Serre's recent malaria paper ([pg.5](#))
- Robin Bromley and Dr. Julie Hotopp's innovative animated videos for scientific educational outreach ([pg.6](#))
- Dr. Jacques Ravel's recent preterm birth paper ([pg.8](#))

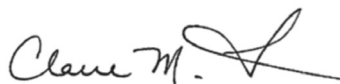
In early January, I received word that I had been named as the next President-Elect of the American Association for the Advancement of Science (AAAS) – the world's largest interdisciplinary scientific professional society with over 120,000 members. It is a tremendous honor to have been elected to this position by my peers, and I thank all of you who supported me with your vote and your congratulations. As I said in my candidacy statement, "One of the most important roles of the AAAS President is to serve as an ardent spokesperson for science and to promote application of the scientific method to the solution of our most pressing problems." At a time when science is under what seems like ever-increasing attack, it is essential that we find a strong collective voice to speak on the value of science – to our elected officials and to the general public whose tax dollars fund much of our research.

One of the issues that AAAS and other scientific professional societies that publish specialty journals is grappling with is the European Plan S that was launched in September 2018. Plan S will require that all research funded by public grants in Europe after January 2020 be published in compliant Open Access journals. The fact that funders – both public and private – want the scientific community and the public to have access to research results that they fund is both understandable and laudable. Plan S proposes to do away with any subscription-based business model for scientific publishing in today's digital age, and while at first glance this might seem like a good idea, this is a complicated issue. I will be involved in the discussions of Plan S at AAAS, and I would encourage you to become familiar with this issue, if you haven't been following the story. A good place to start is a recent opinion piece in the New England Journal of Medicine by Charlotte J. Haug, MD, PhD [NEJM (2019)380;12: 1181-1185].

I also remind you that the three cores embedded within IGS – the Genomics Resource Center, the Informatics Resource Center, and the Microbiome Service Laboratory – are eager to work with you to enhance your research programs.

Please don't hesitate to contact any of us at IGS to discuss your needs and concerns.

Happy Spring!



Claire M. Fraser, PhD

- Dean's Endowed Professor in the School of Medicine
- Professor of Medicine, Microbiology and Immunology
- Director, Institute for Genome Sciences University of Maryland School of Medicine

Dr. Owen White Receives Prestigious Microbiome Award

Using Big Data to Better Understand Human Bacterial Communities

Owen White, PhD, Professor, Epidemiology and Public Health, Associate Director for Informatics at the Institute for Genome Sciences, received the 2018 Microbiome Pioneer Award. The prestigious honor is given as part of the Bioinformatics for the Microbiome Symposium organized by Stanford University. The symposium is a gathering for global leaders in medical informatics.

"We bring together innovative researchers who catalog the human microbiome using modern genetic tools, and who are applying new computational technologies to solve complicated problems, particularly involving patients and disease," said Ami Bhatt, MD, Assistant Professor in the Departments of Medicine and Genetics, Divisions of Hematology and Blood and Marrow Transplantation at Stanford University, and one of the conference founders. "We selected Dr. White for our award this year because he has been a pioneer in informatics as the principal investigator for two NIH-funded data centers, which developed tools used by the community to evaluate the biological properties of the microbiome and its effect on the host."

Dr. White, an internationally recognized expert in bioinformatics, is a pioneer in this field, leading a team of experts at IGS.

"Our research illuminates how the microorganisms that make up the human microbiome interact with our species, and with each other," says Dr. White. "These organisms play a crucial



Owen White, PhD receiving award from Ami Bhatt, MD

role in many key aspects of our health. So far we have barely scratched the surface of what we will learn."

Dr. White's team is responsible for developing database systems and tools for analyzing genomes and other genomic information. He has led efforts to publicize and openly share numerous tools for genome analysis and visualization, so that scientists around the world can use them.

In 2017, he and several colleagues published a study that uncovered millions of previously unknown genes from microbial communities in the human gut, skin, mouth, and vaginal microbiomes, allowing for new insights into the role these microbes play in human health and disease. The work tripled the amount of data previously analyzed by any projects and was the

largest human microbiome study ever. The results were a significant jump in the amount of information available to scientists.

"Our research illuminates how the microorganisms that make up the human microbiome interact with our species, and with each other..."

– OWEN WHITE, PHD

For more information, see:

▶ <https://www.medschool.umaryland.edu/profiles/White-Owen/>

IGS Research Highlighted at UMSOM 2018 Festival of Science

In November 2018, the University of Maryland School of Medicine celebrated groundbreaking research at the 6th Annual Festival of Science, held in Leadership Hall, with over 600 attendees present. The goal of the Festival of Science is to help increase the pace and scope of basic, translational, and clinical sciences research, and to dramatically impact and improve human health and well-being. The theme of this past year's Festival of Science was OMICS Biology: Basic, Translational & Clinical Application.

Huntington Willard, PhD, Director of Geisinger National Precision Health, Associate Chief Scientific Officer, and Howard Hughes Medical Institute Professor was the featured keynote speaker.

IGS was well-represented among the roster of speakers. Dr. Claire Fraser, Director of IGS, presented an Overview of Genomics Research at the School of Medicine, followed by a presentation by one of the inaugural Dean's Challenge Award recipients, Joana Carneiro da Silva, PhD and her colleagues in the Center for Vaccine Development, Drs. Kristen Lyke and Shannon Takala Harrison. The title of their presentation was "Leveraging Parasite Population Genomics Data to Understand Malaria Vaccine Efficacy and Drug Resistance."

Other IGS faculty speakers included:

Vincent Bruno, PhD, Associate Professor, Microbiology & Immunology; "Genome-Guided Discovery of Novel Antifungal Therapies."



(Left) Claire Fraser, PhD, (Top to Bottom) Joana Carneiro da Silva, PhD, Jacques Ravel, PhD, Emmanuel Mongodin, PhD

Scott Devine, PhD, Professor, Medicine; "Discovering Sequence Variation in Human Genomes: Population Genetics, Human Diseases and Clinical Genomics."

Jacques Ravel, PhD, Professor, Microbiology & Immunology, Associate Director Genomics; "The Vaginal Microbiome in Health and Disease."

Emmanuel Mongodin, PhD. Associate Professor, Microbiology & Immunology, co-presented with his collaborator, Jonathan Bromberg, MD, PhD, Professor and Vice Chair for Research, Department of Surgery; "Gut Microbiota, Innate and Adaptive Inflammation, and Host Immunity: A Ménage à Trois That Determines Transplant Outcome."

For more information, see:

- ▶ <http://www.medschool.umaryland.edu/news/2018/UMSOMs-2018-Festival-of-Science-Explores-Intersection-of-Genomics-and-Medicine.html>
- ▶ <https://www.medschool.umaryland.edu/ACCEL-Med/SOM-Festival-of-Science-2018/>

IGS Scientists Develop Novel Approaches to Studying Widespread Form of Malaria

Analyses of Plasmodium vivax parasite gene expression in vivo help understand transmission and antimalarial treatment response

Scientists at IGS have developed a novel way to study and better understand the transmission of *Plasmodium vivax*, the most widespread form of malaria. *P. vivax* is a unicellular parasite transmitted by mosquitoes and is responsible for more than 8.5 million clinical malaria cases worldwide and threatens more than two billion people in 90 countries. Unlike *Plasmodium falciparum*, another species of malaria parasite, *P. vivax* cannot be cultured *in vitro* and remains poorly understood and resistant to elimination efforts.

IGS researchers teamed with researchers at the Institut Pasteur in Cambodia to analyze the parasite gene expression profiles from *P. vivax* malaria patients enrolled in a study to determine the effectiveness of chloroquine as a malaria treatment. Using a combination of genomic and bioinformatic approaches, they compared the parasite expressed genes from different patient infections and analyzed how the parasites responded to chloroquine, a common antimalarial drug. The study was published in *Nature Communications*.

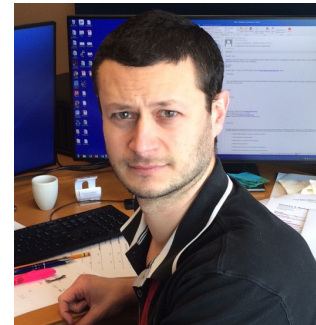
David Serre, PhD, Associate Professor, Microbiology and Immunology at IGS, analyzed the gene expression changes induced by chloroquine treatment and demonstrated that this antimalarial drug, while efficiently eliminating *P. vivax* parasites, acts differently than it does on *P. falciparum* parasites. "This emphasizes the biological differences between these two human malaria parasites and the importance to specifically study

this important pathogen if we hope to eventually eliminate malaria worldwide," he said.

"By analyzing the parasite expressed gene directly from infected patient blood samples, we were also able to observe that not all infections contained the same proportions of the male and female parasites that are required for infecting mosquitoes and propagating the disease. This observation suggests that parasite transmission is more complex than we previously thought and, perhaps, that the parasite is able to modify its development to ensure optimal survival," said Dr. Serre.

Genome sequencing studies have provided unique insights on this neglected human parasite but are limited to identifying biological differences encoded in the genome sequence. However, gene expression studies, which could provide information on the regulation of the parasite life cycle and its response to drugs, have been challenging to implement for this pathogen, due to the heterogeneous mixture of parasite stages present in every patient's infection.

"This important research will help us better understand how to treat, prevent and ultimately eliminate this species of malaria. This is particularly critical amid a growing concern of drug resistance to antimalarial treatments," said UMSOM Dean E. Albert Reece, MD, PhD, MBA,



David Serre, PhD
Associate Professor
Microbiology and Immunology

University Executive Vice President for Medical Affairs and the John Z. and Akiko K. Bowers Distinguished Professor.

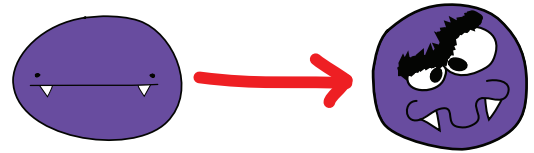
Dr. David Serre and Dr. Adam Kim at IGS, collaborated with Dr. Jean Popovici and Dr. Didier Menard at the Malaria Molecular Epidemiology Unit at the Institut Pasteur in Cambodia. This study was funded by a National Institutes of Health, (NIH) grant award to Dr. Serre (R01 AI103228).

For more information, see:

- ▶ <https://www.medschool.umaryland.edu/profiles/David-Serre/>
- ▶ <http://www.igs.umaryland.edu/labs/serre/>



Using Animated Software to Reach Wider Audiences about Complex Scientific Topics



Horizontal Gene Transfer Videos Go “Viral”

When applying for a National Science Foundation (NSF) grant six years ago, Julie Dunning Hotopp, PhD, Associate Professor, Microbiology & Immunology at IGS, was looking for a new and impactful way to fulfill the grant’s outreach requirement. At the same time, her findings on bacterial lateral gene transfer and human cancer, research funded by her [NIH New Innovator](#) and [NIH Transformative Research Awards](#), were picked up by popular science blogs. The response was massive. While many commenters appreciated the research, a great number of comments revealed a deep misunderstanding and distrust of the science.

For her NSF grant, Dr. Dunning Hotopp realized she needed to do more than train summer interns in molecular biology and bioinformatics. She needed to reach a global audience of students, scientists, and people with a passing interest but strong opinions about science. Intrigued by a whiteboard animation on a dengue virus project website, Dr. Dunning Hotopp saw the potential for how to explain her research to everyone.

Converting complex scientific research into animated videos for the general public proved to be a challenging process. It takes a deep understanding of the material to communicate it simply. It also helps to understand how people learn, and to be familiar with the educational process. Then, to create animated illustrative videos, one needs

artistic abilities, creativity, an ability to see things visually, and a knack for mastering animation software.

With a background in visual and performing arts as well as education and molecular biology, laboratory research supervisor, Robin Bromley, was up to the challenge. Dr. Dunning Hotopp and Ms. Bromley focused on breaking down the lateral gene transfer research into a series of simple stories. Ms. Bromley sketched out the animations and the basic video structure by storyboarding. She then drafted a scientifically accurate yet engaging script. Using Adobe Illustrator and Photoshop, Sparkol Videoscribe, and a basic podcast-quality mic from Yeti, Ms. Bromley set to work animating and narrating their first whiteboard video.

That first video, [Horizontal Gene Transfer](#), was produced in late 2014. Since then awareness of that video and others has gone global and viral. Online and traditional undergraduate and graduate classes have used the videos, including Towson University (TU), the City University of New York (CUNY), Dyersburg State Community College (DSCC) in Tennessee, the Universidad San Francisco de Quito in Ecuador, the University of Alaska, and Stanford University. Popular websites such as the Taiwanese news site, <https://hssszn.com>, the science blog www.MostlyMicrobes.com, and the blog and podcast Science for the People have also featured the videos. In fewer than five years, the viewership has grown to over 10,000 views with

18-34 year olds making up nearly 90% of the viewers. People on all seven continents have watched the videos on the [JDH Lab YouTube channel](#). The videos are closed-captioned with positive feedback from the deaf and hearing-impaired community.

“I hope our videos help people to better understand our group’s research,” said Ms. Bromley. “With our citations and supplemental information, the videos are robust learning tools that are easily understood, and we’ve been pleasantly surprised by the feedback we’ve received. Today’s classroom is really global and it’s humbling to know that our videos are being watched from so many places around the world.”

The Dunning Hotopp team plans to continue this visual communication process to share important science results with a wider, and often non-scientific, audience.



(From left) Robin Bromley, Julie Dunning Hotopp, PhD

For more information, see:

- ▶ <https://www.medschool.umaryland.edu/profiles/Dunning-Hotopp-Julie-C/>
- ▶ <http://www.igs.umaryland.edu/labs/hotopp/>

Microbial Genomics Trailblazer Claire M. Fraser Named AAAS President-Elect

Claire M. Fraser, PhD, Professor, Medicine and Director, Institute for Genome Sciences, a pioneer in the field of microbial genomics, has been chosen as president-elect of the [American Association for the Advancement of Science](#) (AAAS), a leading organization that aims at advancing science, engineering, and innovation throughout the world.

She began her term on February 18, 2019 after the AAAS Annual Meeting, and she will be serving for one year as president-elect, one year as president and one year as chair of the AAAS Board of Directors.

"One of the most important roles of the AAAS President is to serve as an ardent spokesperson for science and to promote application of the scientific method to the solution of our most pressing problems," said Fraser in her candidacy statement, citing such challenges as climate change, antimicrobial resistance and food, water and energy security.

"Our ability to respond to these challenges has been hampered to a considerable extent by a lack of adequate funding, a tendency to fund 'safer' research projects, and a relative lack of public trust in science," Dr. Fraser said, noting the increasing political attacks on science in the U.S. and abroad.

"During these challenging times, it is essential that we find a strong collective voice to speak on the value of science," she said.

"Dr. Fraser is one of the pre-eminent scientists of our time in a field that is re-defining how we investigate and treat complex diseases," said E. Albert Reece, MD, PhD, MBA, Executive Vice President for Medical Affairs, UM Baltimore, and the John Z. and Akiko K. Bowers Distinguished Professor, and Dean, University of Maryland School of Medicine. "In addition to her own groundbreaking discoveries in microbial genomics, she has mobilized a team of world-renowned investigators at IGS who are leading the nation in harnessing the power and potential of large-scale genomic research, and exploring new genomic applications in precision medicine, therapeutics, infectious diseases, virology and cancer research."

Dr. Fraser was honored by AAAS as an elected Fellow in 2004 for her pioneering work in sequencing and analyzing microbial genomes. Her prior involvement with AAAS also includes serving on the AAAS Committee on Nominations from 2006 to 2008, on the AAAS Board of Directors from 2013 to 2017 and on the AAAS Biological Sciences Section' Electorate Nominating Committee from 2014 to 2017.

AAAS is the world's largest multidisciplinary scientific society and a leading publisher of cutting-edge research through its Science family of journals.



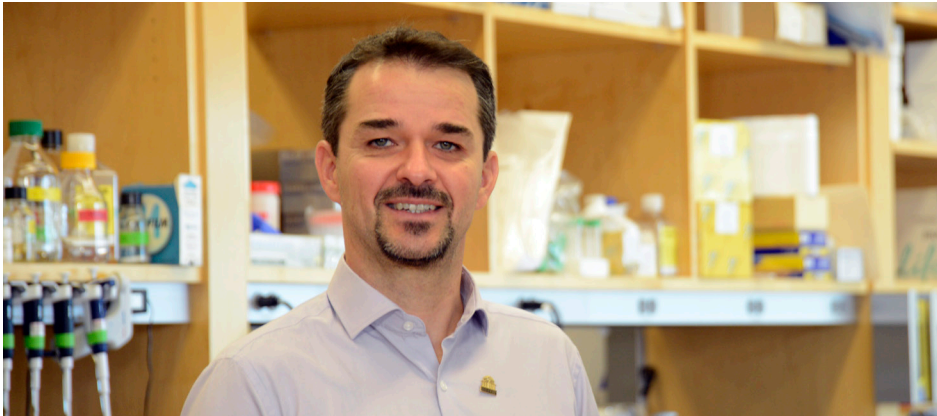
Claire M. Fraser, PhD

- *Dean's Endowed Professor in the School of Medicine*
- *Professor of Medicine, Microbiology and Immunology*
- *Director, Institute for Genome Sciences University of Maryland School of Medicine*

"During these challenging times, it is essential that we find a strong collective voice to speak on the value of science..."

– CLAIRE FRASER, PHD

Bacteria and Immunity in the Cervix May be Key to Predicting Premature Birth



Dr. Jacques Ravel, Professor, Associate Director, Genomics, Institute for Genome Sciences

Spontaneous preterm birth (sPTB), defined as birth before 37 weeks of gestation, and the related complications are the largest contributors to infant death in the United States and worldwide. Dr. Jacques Ravel, Professor, Microbiology & Immunology, and Associate Director, Genomics, Institute for Genome Sciences, and his team have discovered that bacteria and innate immune factors in a woman's vagina and cervix may increase the risk of spontaneous preterm birth or provide protection against such births.

Results of the study which was conducted in collaboration with Dr. Michal Elovitz, Professor in the Department of Obstetrics and Gynecology at the Perelman School of Medicine at the University of Pennsylvania, were published March 21, 2019 in *Nature Communications*. This research provides groundbreaking information that could help physicians better predict and prevent preterm births. The study sets the path for new research to develop rational strategy that would target "bad" bacteria or replenish "protective" bacteria.

The findings are key, as babies who survive an early birth often face serious, costly and lifelong health problems, including breathing problems, vision loss, cerebral palsy and intellectual delays. The economic burden of preterm birth is staggering, with an estimated cost of \$26 billion per year in the United States alone. A failure to predict and understand the causes of preterm birth have limited the development of effective interventions and therapeutics.

In this study, researchers examined cervicovaginal swabs taken at three distinct points in pregnancy from a sample of 2,000 pregnant women to determine the bacteria that made up their cervicovaginal microbiota. This is the largest cohort of pregnant women in whom the cervicovaginal microbiota was studied. Using innovative Bayesian modeling, seven bacteria were significantly associated with increased risk of sPTB, with a stronger effect in African American women. Interestingly, higher vaginal levels of the antimicrobial peptide β -defensin-2, a part of our innate immune system, lowered the risk of sPTB associated with cervicovaginal microbiota in an ethnicity-dependent manner.

"Previous studies, including ours, were limited by low sample size, and in establishing this large cohort, we aimed to identifying factors early in pregnancy that could be used to predict the risk to spontaneous preterm birth. Predicting prematurity has been a riddle that's troubled researchers and clinicians for years, but we are finally shedding light on a path toward offering treatment to women we can identify as being at risk," said Dr. Ravel. "These new findings are the result of a multidisciplinary team of experts in obstetrics and microbiology, who came together and took a new approach to address this major problem in the United States and the world."

These findings hold promise for diagnostics to accurately identify women at risk for sPTB early in pregnancy. Therapeutic strategies could include immune modulators and microbiome-based therapeutics to reduce this significant health burden.

This study was supported by the National Institute for Nursing Research of the National Institutes of Health under award number R01NR014784.

For more information, see:

- ▶ <https://www.medschool.umaryland.edu/profiles/Ravel-Jacques/>
- ▶ <http://ravel-lab.org/>

Dr. David Rasko Elected as Fellow to the American Academy of Microbiology

Dr. David Rasko Recognized for His Work in Infectious Diseases and Genomics

David A. Rasko, PhD, Professor, Microbiology & Immunology at IGS, has been elected to Fellowship in the American Academy of Microbiology. The academy is the honorific leadership group within the American Society for Microbiology (ASM).

Each year, Fellows are elected through a highly selective, peer-review process, based on their scientific achievement and original contributions that have advanced microbiology.

Dr. Rasko will be recognized at the Academy Fellows Luncheon and Meeting at the [ASM Microbe Meeting](#) in San Francisco on June 20-24, 2019.

Dr. Rasko has been very prolific for an investigator at this stage of his career, authoring 156 peer-reviewed papers, including first author publications in *Science*, *New England Journal of Medicine* and *PNAS*. His work has been cited over 10,000 times, and 27 of his articles have been cited more than 100 times. His highest profile papers have resulted in new paradigms in their research areas. In one, instead of killing bacteria with antibiotics, his approach serves to repress the virulence of the organisms until the host immune system can eliminate them. His 2011 *New England Journal of Medicine* paper describes the genomic analysis of the outbreak strains of *E. coli* in Europe, which was one of the first introductions of near real-time sequencing for the identification and comparison of ongoing bacterial outbreaks. Dr. Rasko and his group's recent work has expanded genomics methodologies to accelerate epidemiological investigation of infectious disease outbreaks and develop more rapid and precise diagnostics.

Dr. Rasko's laboratory is funded through several grants from the National Institutes of Health. Most notably, he has served as a PI in the multi-PI U19 on "Host, Pathogen, and the Microbiome: Determinants of Infectious Diseases Outcomes," and has been co-investigator on other collaborative grants at UMB.

He will be joining Drs. Fraser and Ravel in the American Academy of Microbiology.



David A. Rasko, PhD
Professor
Microbiology and Immunology

For more information, see:

- ▶ <https://www.medschool.umaryland.edu/profiles/Rasko-David/>
- ▶ <http://www.igs.umaryland.edu/labs/rasko/>
- ▶ <http://gcid.igs.umaryland.edu/>

University of Maryland School of Medicine Researchers Link Gut Bacteria to Heart Transplant Success or Failure



(from left) Emmanuel Mongodin, PhD, Jonathan S. Bromberg, MD, PhD

Researchers at the University of Maryland School of Medicine (UMSOM) have found that the gut microbiome appears to play a key role in how well the body tolerates a transplanted organ, such as the heart. The scientists found a causal relationship between the presence of certain microbes and transplant outcome.

The results have the potential to significantly change how researchers and doctors deal with the problem of chronic rejection and transplantation. This is the first study to identify specific bacterial species that can affect whether a heart transplant is rejected, and how quickly.

The new study was published in October 2018 in the *Journal of Clinical Investigation Insight*.

One of the study's two lead authors, Emmanuel Mongodin, PhD, an Associate Professor of Microbiology and Immunology at UMSOM, said the research had the potential to transform transplantation. "From our previous work we suspected that the microbiome – more specifically the gut microbiome – might have an effect on how

transplanted organs are accepted," said Dr. Mongodin. "This work clearly shows that there is a connection between these gut microbes and the body's response to the new organ. It's very exciting."

The link between the transplanted heart and the microbiome is the immune system. Many researchers have noted that the microbiome plays a key role in the immune system, either activating it or turning it down, depending on the bacterial species. Certain bacteria in the microbiome can trigger pro- or anti-inflammatory signals, and these signals can in turn affect how the immune system responds to the transplanted organ.

Organ rejection remains an urgent problem in transplantation. Despite intense research over the past 20 years, researchers and doctors have not been able to improve the long-term organ rejection rate – the rejection of organs that occurs after the first few years following transplantation.

The research began with Jonathan S. Bromberg, MD, PhD, a Professor of Surgery, Microbiology and Immunology at UMSOM. Dr. Bromberg, the study's other lead author, is a transplant surgeon,

and has transplanted hundreds of organs over the course of his career, so he is extremely familiar with the problem of rejection. Several years ago, he began wondering what other variables might help explain why long-term rejection occurred. He started looking at the microbiome.

"The more I looked, the more it seemed there might be something there," said Dr. Bromberg. "The immune system is deeply intertwined with our gut microbiome, and I wanted to explore this connection in more depth." Dr. Bromberg began collaborating with Dr. Mongodin, who spent much of his career studying the microbiome.

In an animal model, the two scientists showed that by adjusting the microbiome, they could improve the outcome of the heart transplant. They identified specific species that seem to have a beneficial or harmful effect on the transplant. They suspect that this process may be similar for other organs, such as kidneys. The next step will be to focus on the mechanisms behind this bacterial effect. With a better understanding of the molecular pathways, it may be possible to mimic the effect with drugs.

"This is a great example of translational research," said E. Albert Reece, MD, PhD, MBA, Executive Vice President for Medical Affairs at UM Baltimore, and the John Z. and Akiko K. Bowers Distinguished Professor and Dean, University of Maryland School of Medicine. "As we learn more about these microbes, we have the potential to truly change long-term rejection rates in heart transplants and perhaps in other organs as well."

UM School of Medicine's Institute for Genome Sciences Awarded \$17.5 Million Grant for Infectious Disease Research



(from left) Owen R. White, PhD, Claire M. Fraser, PhD, and David Rasko, PhD

The Institute for Genome Sciences (IGS) at the University of Maryland School of Medicine (UMSOM) was awarded \$17.5 million from the National Institute of Allergy and Infectious Diseases (NIAID) to fund the IGS Genome Center for Infectious Diseases (GCID) for another five years.

The Principal Investigator and Administrative Core Director for the grant, which is titled "A Genomics Based Investigation of the Determinants of Polymicrobial Infectious Disease Outcomes," is David Rasko, PhD, Professor of Microbiology and Immunology. Claire M. Fraser, PhD, the Dean's Endowed Professor of Medicine and Microbiology and Immunology, Director of the IGS, and Owen R. White, PhD, Professor of Epidemiology and Public Health, Director of Bioinformatics and Associate Director of IGS, will be team Principal Investigators.

The GCID uses large-scale genomics and bioinformatics approaches to investigate pathogen biology, virulence,

immune evasion, microbe-microbe as well as host-microbiome interactions. Scientific research projects focus on host/microbe interrelationships of diverse bacteria, fungi, and parasites. The interdisciplinary team will participate in the GCID research, including internationally recognized faculty from the IGS, the Department of Microbiology and Immunology and the Center for Vaccine Development and Global Health (CVD) at UMSOM and their long-standing collaborators.

"The GCID team has been in the forefront of applying genomic techniques to advance scientific understanding of infectious disease agents for the past 15 years, and this NIAID grant renewal will allow us to further deploy genomics approaches in the study of infectious diseases," said Dr. Fraser.

The NIAID grant will support research programs that focus on three areas. The first research area is the interactions of multiple bacteria with each other as well as the host and

associated microbiome, which is led by Dr. Rasko, Dr. Fraser, and Hervé S.G. Tettelin, PhD, Associate Professor of Microbiology and Immunology. The second area is research into the genomic and transcriptomic analysis of fungal pathogens interacting with the host, which will be led by Vincent M. Bruno, PhD, Associate Professor of Microbiology and Immunology. The third area of research is an integrated genomics research project in parasitic tropical diseases that will be led by Julie C. Dunning Hotopp, PhD, Associate Professor of Microbiology and Immunology, David Serre, PhD, Associate Professor of Microbiology and Immunology; and Joana Carneiro da Silva, PhD, Associate Professor of Microbiology and Immunology.

"This grant allows us to integrate the study of multiple pathogens in model systems and with human samples in a way that is more representative of natural infection processes, which will provide greater understanding and more in-depth insights into these interactions," said Dr. Rasko.

The center also supports a Technology Core, a Data Management Core and an Administrative Core. The projects include whole genome and targeted genome sequencing, transcriptome profiling by RNA-seq, rRNA community profiling, metagenomics and metatranscriptomic

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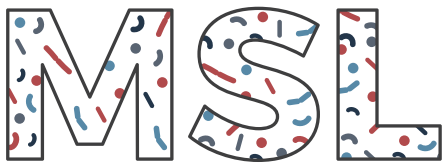
sequencing with a focus on interactions between microbes, the host and the resident microbiome. The sequencing will be performed using multiple platforms, including the Illumina MiSeq and HiSeq, Oxford Nanopore Technology and Pacific Biosciences systems.

"Integrating genomics with diagnostic and clinical medicine has advanced our biological understanding of diseases and health," says E. Albert Reece, MD, PhD, MBA, Vice President for Medical Affairs at the University of Maryland, and John Z. and Akiko K. Bowers Distinguished Professor and Dean of the University of Maryland School of Medicine. "This NIAID grant will foster new collaborations across disciplines within the clinical and research centers in the School of Medicine, as well as with international infectious disease communities."

In addition to the research projects, IGS will establish workshops and continue educational initiatives to expand the understanding of how to apply genomics to high priority research questions that impact global health.

IGS has previously received grants as a Genome Center for Infectious Diseases (GCID) an NIAID-funded five-year grant (2014-2019), a Genome Sequencing Center for Infectious Diseases (GSCID), an NIAID-funded five-year contract (2009-2014), and the lead investigators have also had Principal Investigator roles with the NIAID-funded Microbial Sequencing Center (MSC), a five-year contract (2004-2009). This U19 grant with number U19 AI110820 will run for five years until 2024, representing twenty years of cutting edge research in genomic sciences.

Microbiome Services Laboratory Update – Spring 2019



Microbiome Service Laboratory

The Microbiome Services Laboratory (MSL) has now established itself as a leader in providing microbiome services to the UMB and broader scientific community. The MSL continues to improve its services by further validating the assays it is offering. We have developed optimized protocols taking advantage of our new robotic platforms, including our new nanoliter-scale liquid dispenser, the Mosquito HTS. These investments will result in cheaper assays and cost savings for our customers.

The microbiome research community is very open, and publishing requires

the release of raw and processed sequence data to public databases. As such the MSL has been developing improved ways to deliver these large files to its customers. If your research requires these data, please make sure to contact us. We can now provide data files ready to be released to the NCBI Short Read Archive, for example.

The MSL is expanding! We have hired a new bioinformatic analyst, Jonathan Lim, who comes to us from the University of Glasgow. Jonathan has taken the major task to improve microbiome analysis reports and deliver encompassing information to MSL customers. MSL has queried its customers and we heard them loud and clear; they wanted more from us! These reports which will come online in the summer 2019, will provide additional

information such as runs and samples specific data, pre-processing statistics, data on positive and negative controls, and preliminary statistical analysis of the data.

MSL services include DNA/RNA extractions from biological or environmental samples, 16S rRNA gene amplicon sequencing, metagenomic and



(from left) Mike Humphrys, Jacques Ravel, PhD

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metatranscriptomic analyses, and associated bioinformatics analyses. All of the services can be ordered as complete study support or à la carte. We can analyze DNA that is already extracted or perform the complete analysis from samples to data. Microbiome analyses at the MSL are fully integrated with the other two cores at IGS – the [Genomic Resource Center \(GRC\)](#) and the [Informatics Resource Center \(IRC\)](#).

As with the GRC, we recommend people contact us early in the planning of their experiments. We have expertise not only in sample analyses but also sample collection. To that extent, we can provide you with optimized sample collection devices that would guarantee sample integrity and stability for complete microbiome analysis. [Please contact us for a free consultation.](#)

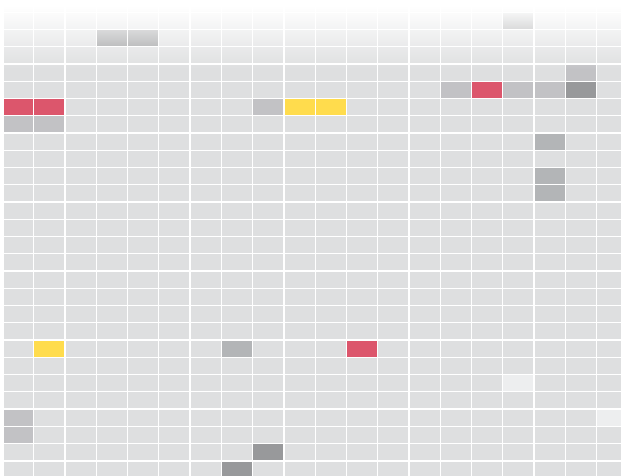
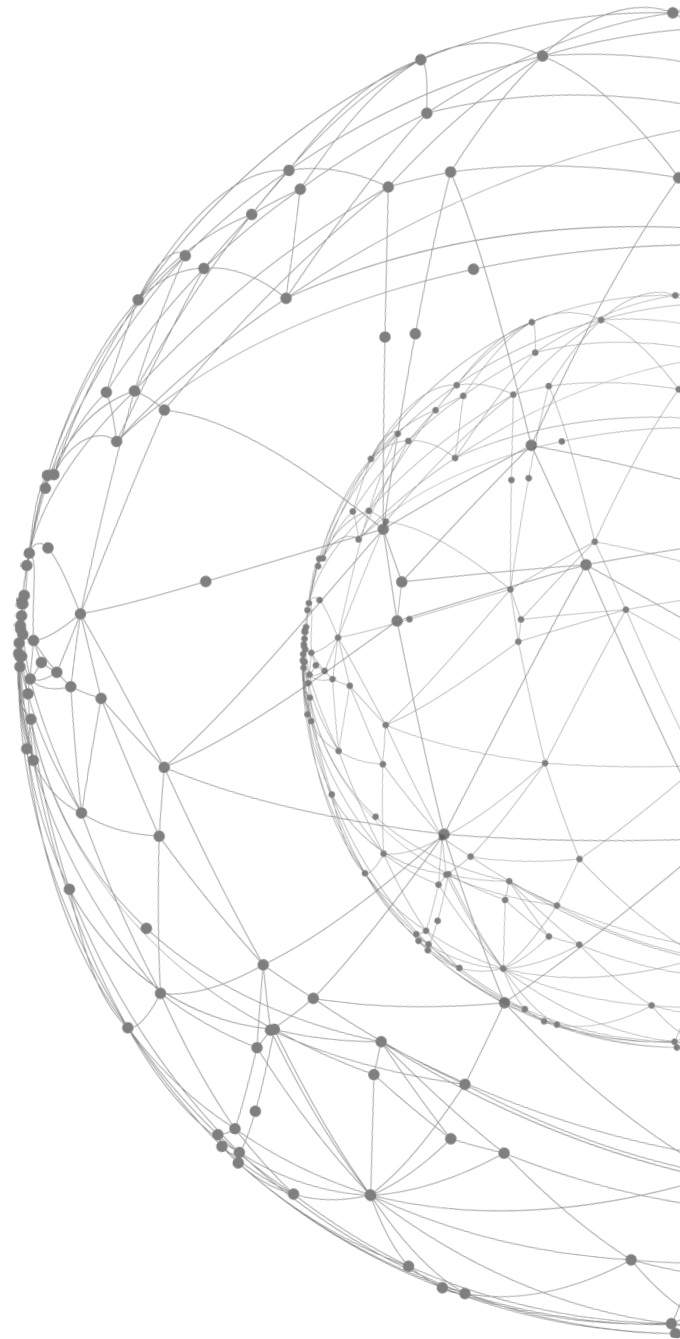
Q&A

Q: I want to do metatranscriptomics on my samples. How should I collect the samples?

To perform metatranscriptomics, generate a catalogue of the microbial genes expressed by a microbiota, one needs to preserve RNA in the collected samples. The MSL offers a range of sample collection devices and RNA preservative solutions that are compatible with our assays. Contact us and we could advise you on the best solution for your project and sample type.

Q: I need help with the analysis of my data. Can the MSL help me?

Yes! We have experts who could help you with both the bioinformatic as well as the statistical analyses. Also, remember that IGS offers a range of hands-on courses where you could learn how to perform microbiome analyses yourself. If the course is not what you are looking for, we are always there to help. [Please do not hesitate to contact us!](#)



GRC UPDATE

Update from the Genomics Resource Center (GRC)

Greetings from the Genomics Resource Center in the spring of 2019.

New genomic technologies and platforms are on the horizon. Since moving into our new laboratory in HSF III last year, we have rapidly expanded our capacity and capabilities. The 10x Genomics Chromium platform is now a widely used system for single-cell transcriptomics, immune profiling, linked-read variant phasing and de novo genome sequencing. We have also expanded our low-throughput single-cell offerings with new library preparation methods from Takara. So, whether you have a few cells or thousands, we have the technologies to sequence their genomes and transcriptomes!

As an extension of our long-term partnership as a PacBio Certified Service Provider, we have joined the Early Access Program for PacBio new Sequel II platform. This new instrument, utilizing an 8M ZMW SMRT Cell, promises significant increases in throughput compared to prior PacBio platforms and other long-read technologies. We have generated some exciting early data with this instrument, including ultra-long library runs exceeding 100Gbp and 10kb HiFi CCS runs exceeding 280Gbp, both of which represent >8x increases over current runs. This impressive throughput has the potential to change the landscape of non-model *de novo* genome sequencing, human structural variation analysis, and metagenome/



Lisa Sadzewicz, PhD, and Luke J. Tallon, co-directors, GRC

microbiome sequencing. We will begin offering sequencing services on the Sequel II in April 2019.

In addition to the new Sequel II platform and expanding single-cell offerings, we plan to dramatically increase our short-read sequencing capacity with the acquisition of an Illumina NovaSeq in the coming months. The newest Illumina flagship sequencer has a more flexible design with four different flowcells that span the spectrum from medium to ultra-high throughput. Not only will this platform increase our capacity and reduce sequencing costs, but it will provide for more flexible turn-around time for small and medium size projects.

Upcoming GRC events:

June 20-24: ASM Microbe meeting in San Francisco – come see us at booth #861

Q&A

Q: I'd like to try single-cell sequencing, how do I get started?

Contact us! Because single-cell sequencing is a delicate assay, we customize the project plan and coordinate logistics carefully with each investigator. An initial project consultation is crucial to a successful experiment and is free!

Q: What are the advantages of the new PacBio Sequel II platform?

Throughput and cost! The new 8M chip will enable project completion with fewer runs, higher multiplexing capability, and reduced project cost. If you'd like to take advantage of this new, cutting-edge long-read sequencer, [please contact us for a consultation!](#)

Please check out our [blog](#) or [email us!](#)

Grants & Contracts: 2019

Congratulations to our productive faculty on their recent grants and contracts!



Bing Ma, PhD, Research Associate, Microbiology & Immunology, received a three-year \$322,151 grant from The Gerber Foundation for "An accurate, non-invasive discriminatory screening test for rapid detection of elevated intestinal permeability in preterm infants at risk for necrotizing enterocolitis (NEC)."



Seth Ament, PhD, Assistant Professor, Psychiatry, received a one-year \$143,609 grant from Western Washington University (Prime: CHDI Foundation), A CHDI/WWU Joint Steering Committee.



David Serre, PhD, Associate Professor, Microbiology & Immunology, received a two-year \$441,275 grant from NIH for "Are all sporozoites equal? Analyses of transcriptomes from individual *Plasmodium* sporozoites using single cell RNA-seq."



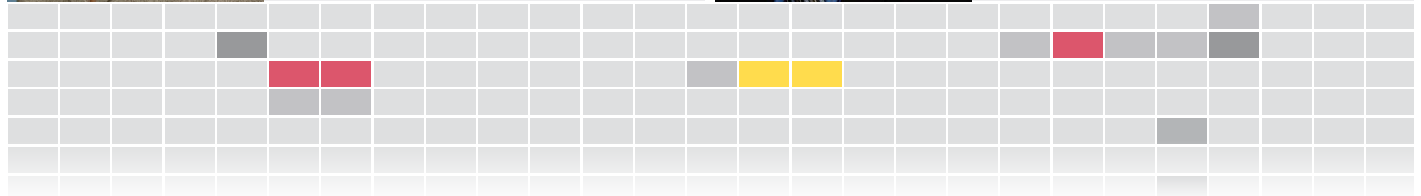
Joana Carneiro da Silva, PhD, Associate Professor, Microbiology & Immunology, received a five-year \$3,631,550 grant from NIH for "Genome-wide Sieve Analysis and Immunological Validation to Identify Targets of Protective Efficacy in Field Trials of a Whole-Organism Malaria Vaccine."



Claire Fraser, PhD, Professor, Medicine, and Microbiology & Immunology, Director IGS, received a three-year \$226,294 subcontract with Georgetown, from NIH for "Exploratory Pilot Studies to Demonstrate Mechanisms of Preventing Antibiotic-Associated Diarrhea and the Role for Probiotics."



David Rasko, PhD, Professor, Microbiology & Immunology, Claire Fraser, PhD, Professor, Medicine, and Microbiology & Immunology, Director IGS, Owen White, PhD, Professor, Epidemiology & Public Health, Associate Director, Informatics IGS, received a five-year \$17,552,940 grant from NIH/NIAID for "A Genomics Based Investigation of the Determinants of Polymicrobial Infectious Disease Outcomes."



IGS Newsletter is produced by the **Institute for Genome Sciences** at the **University of Maryland School of Medicine**.

Jacques Ravel, PhD
Sarah Pick
Lance Nickel
Riham Keryakos

Scientific Editor
Editor
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Contributor

Publication List

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