

IGS NEWSLETTER

FALL 2014

 UNIVERSITY of MARYLAND
SCHOOL OF MEDICINE
INSTITUTE FOR GENOME SCIENCES

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Greetings Colleagues,



Almost 20 years ago when our team was working in Rockville, we successfully competed for a Microbial Sequencing Center (MSC) grant award from the National Institute of Allergy and Infectious Diseases (NIAID) of the NIH. We were fortunate to be early “architects” in the process of applying powerful new technologies to sequence priority pathogens. In 2009 in the early days of IGS, we successfully competed for the next generation MSC, called the Genome Sequencing Center for Infectious Diseases (GSCID), which was again funded through NIAID. We are proud to announce that in June 2014, we were awarded the latest development of the NIAID grant, the Genome Center for Infectious Diseases or the GCID. The range of what we have been able to research and sequence has changed so much over the years that the evolution of the “MSC” to the “GSCID” to the “GCID” is a historic snapshot of how genomics research is being applied to microbiology, epidemiology and medicine.

In his recent interview in Bio-IT World, reporter Aaron Krol summarized the situation of 21st century genomics this way, *“for billions of people, infectious disease is still a daily reality, and emerging problems like antibiotic resistance threaten to reverse a century of gains even in the wealthiest countries. In this environment, pathogen researchers are still racing to catch up with data-hungry approaches, like population genetics, transcriptomics, and metagenomics, which are almost routine in other fields... The GCID will be the third NIAID-funded pathogen-sequencing center Fraser has overseen, through a decade when projects have evolved from creating single reference genomes, to using genetic markers to track complex interactions between hosts and pathogens over time.”*

Located on the campus of the University of Maryland, Baltimore surrounded by seven professional schools, we have been in an ideal environment to benefit from increasingly complex, interdisciplinary collaborations with experts in virology, epidemiology, infectious diseases, bio-imaging, and other fields. For the new GCID, we are producing genomic data in greater volumes to explore how pathogens survive, thrive and cause disease. We share highlights of the GCID on [page 2](#).

Another innovative grant that demonstrates our systems biology approach to genomics is the renewal of Dr. Jacques Ravel and Dr. Patrik Bavoil's NIH-funded Collaborative Research Center on Sexually Transmitted Infections (U19) (see [page 3](#)). Systems biology is an emerging discipline that focuses on the complex interactions between genes, proteins, metabolism and the 3D structural components of microbial and human cells. By applying “omics” technology, the study aims at identifying novel molecular “biomarkers” of susceptibility to sexually transmitted infections (STI's), and protection from STIs and STDs.

We are excited by the ever-increasing capabilities of what is possible in the field of genomics and infectious diseases, and by the complex and important work led by our faculty.

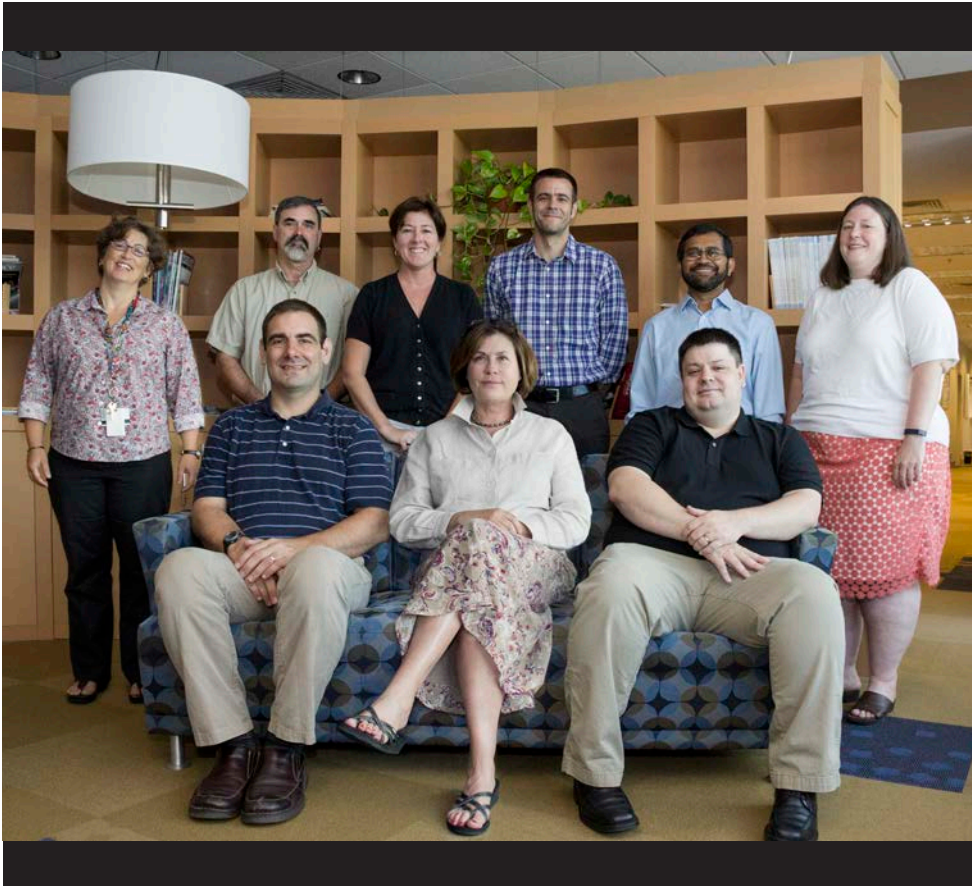
As always, I welcome your feedback,

Claire M. Fraser, PhD

*Professor of Medicine and Microbiology and Immunology
Director, Institute for Genome Sciences
University of Maryland School of Medicine*



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IGS Awarded \$15.2 M NIAID Grant on Infectious Disease Research

IGS has received a grant award of \$15.2M over five years from the National Institute of Allergy and Infectious Diseases (NIAID) of the NIH to create a research center to apply genomic techniques to the study of pathogens and their hosts, and to expand understanding of the ways that pathogens can cause harm.

The IGS Genome Center for Infectious Diseases (GCID) will use large-scale genomics and bioinformatics approaches to investigate pathogen biology, virulence, drug resistance, immune invasion, and host-microbiome interactions.

“This team has been in the forefront of applying genomic techniques to advance scientific understanding of infectious disease agents, and the NIAID grant will catalyze further development of genomics approaches within global infectious disease communities,” said Claire Fraser, PhD, Director of the Institute for Genome Sciences, and professor of Medicine and Microbiology and Immunology at the UMSOM.

“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. “The NIAID grant will foster new collaborations across disciplines within the clinical and research centers in the School of Medicine, as well as within international infectious disease communities.”

The grant, “Host, Pathogen, and the Microbiome: Determinants of Infectious Disease Outcome” will be led by **Claire Fraser, PhD**, as Principal Investigator and Administrative Core Director, and Drs. **David Rasko** and **Owen White**, will be team Principal Investigators.

The funding will support a technology core, a data management core, an immunology core, and an administrative core, as well as research programs that focus on three areas: host/ bacterial pathogens and the microbiome, led by David Rasko, PhD; the genomic analysis of fungal pathogenesis, led by **Vincent Bruno, PhD**; and integrated genomics research in parasitic tropical diseases led by **Joana C. Silva, PhD** and **Julie C. Dunning Hotopp, PhD**. The projects will include whole genome and targeted genome sequencing, transcriptome profiling by RNA-seq, rRNA community profiling, and metagenomics and metatranscriptomic sequencing. The sequencing will be performed using three platforms, including the Illumina MiSeq and HiSeq, and the Pacific Biosciences RS II system.

In addition to vital 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.

UNIVERSITY OF MARYLAND SCHOOLS OF DENTISTRY AND MEDICINE RECEIVE \$10.7M GRANT

for Systems Biology Research on Control and Prevention of Sexually Transmitted Infections

UM SOD and UM SOM have received a five-year \$10.7 million grant award from the National Institute of Allergy and Infectious Diseases (NIAID) of the NIH to study the causes, prevention and treatment of sexually-transmitted diseases (STD's). The research will study STD's as the outcome of complex interactions between the host genetics,

the microbiome and the pathogen's unique genetics. By applying modern "omics" technology, the study aims at identifying novel molecular "biomarkers" of susceptibility to sexually transmitted infections (STIs), ensuing disease severity, and protection from STIs and STDs.

"The grant is significant because it is the first time that a comprehensive systems biology, or 'multi-omics' approach will be utilized to conduct STD research with the ultimate goal of developing knowledge to prognose, diagnose, prevent and treat sexually transmitted infection and disease," said Jacques Ravel, PhD, Professor of Microbiology and Immunology and Associate Director for Genomics at IGS, who is the co-principal investigator on the study.

"We will be identifying human and microbial biomarkers that tell us who is most susceptible to infection, who is most susceptible to severe disease, even in the absence of symptoms," said Patrik Bavoil, PhD, Professor and Chair of the Department of Microbial Pathogenesis at the UM SOD, and the co-principal investigator.



MORE INFO

- Visit the [Ravel SOM page](#)
- View the [IGS page](#), with video
- Link to [Bavoil's page](#)



Ravel at Pasteur Institute

We wish Jacques Ravel a bon voyage as he begins his sabbatical at the Pasteur Institute in France in the Molecular Microbial Pathogenicity Unit led by US National Academy Member Philippe Sansonetti, M.D. The Pasteur Institute is one of the premier infectious diseases research centers in the world, and we congratulate Jacques on this prestigious opportunity. He will be travelling back and forth regularly, meeting with his colleagues here at UMB and active with his lab here at IGS. He will be investigating the bacterial and immune factors associated with colonization of the human body by the beneficial species of *Lactobacillus*. Understanding these factors will lead to the selection and development of probiotics with improved therapeutic capabilities.



UPDATE FROM THE

(GRC)

The Genomics Resource Center (GRC) has recently expanded its two year, \$1.6M contract with the U.S. Food and Drug Administration (FDA) to sequence, assemble, and annotate bacterial pathogens using two high-throughput sequencing (HTS) technologies in support of the development and expansion of a comprehensive, curated public reference database. Now targeting the completion of more than 600 bacterial genomes over the next two years, the GRC has completed the first batch of 96 isolates and is ramping up sequencing of the next batch of samples. Project progress and a discussion of microbial NGS standards will be presented at a workshop hosted by NIST in October.

The GRC recently hosted the Pacific Biosciences East Coast User Group Meeting on the UMB campus, which was attended by more than 100 users and developers of this rapidly expanding long-read sequencing technology. The meeting featured 12 presentations focused on a wide variety of uses and developments of the PacBio technology. The GRC Scientific Director, Luke Tallon, presented on the use of PacBio sequencing in support of the FDA contract.

The GRC continues to explore and develop new genomic technologies. Most recently, IGS investigators Dr. David Rasko and Dr. Timothy O'Connor have been selected as participants in the Oxford Nanopore MinION Early Access Programme. The GRC is leading our joint efforts to evaluate and develop this new single molecule sequencing platform and early results have been promising.

Q&A

WITH THE CO-DIRECTORS OF THE GRC

What sets the GRC apart?

Our team is made up of seasoned experts who have been working in this field since large-scale sequencing was first expanded in the early 1990's. We've been at the forefront of every generation of sequencing technology, and we understand exactly how to apply different approaches and techniques to deliver the most cost-effective and high-quality results for investigators. Together with our informatics team, we are a one-stop shop for genomics research.

You describe GRC as a "one stop shop" – what does that mean?

To us this means that investigators with any level of background or knowledge of genomics can approach us and we will help them map out a targeted, cost-effective research program that takes the project from the initial consultation through to publication, including sequencing, informatics, and interpretation."

You work on many large multi-year, multi-institutional projects. Are there projects that are too small for your center?

The GRC is committed to bringing its expertise and state-of-the-art genomic technologies to an ever-expanding field of investigators. We have projects that range from a single sample to thousands of genomes and we are dedicated to the success of each project and investigator.

The Implications of BIG DATA and the Future of Healthcare

In May 2014, a group of over 80 business and legislative leaders gathered at IGS for a half-day program hosted by IGS, Leadership Maryland, and UMB Center for Health-related Informatics and Bioimaging (CHIB) on "The Implications of Big Data and the Future of Healthcare." Welcoming remarks were given by 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, and the two presenters were Owen White, PhD, who spoke about "Large-Scale Data Collection and Healthcare Improvement" and Amitabh Varshney, PhD, who spoke about "Visualizing Big Data for Healthier Living." This program on bioinformatics and medicine was well received by attendees.

Dr. White is Professor Epidemiology and Preventive Medicine, and Associate Director, Institute for Genome Sciences at the University of Maryland School of Medicine. Dr. Varshney is Professor, Computer Science at the University of Maryland, College Park. Drs. White and Varshney are Co-Directors of CHIB. CHIB is a multidisciplinary collaborative center that aims to address grand challenges in genomic research, medical information management and precision medicine. It combines advanced computing resources at the University of Maryland, College Park (UMD) with clinical data and biomedical expertise at the University of Maryland, Baltimore (UMB). Our research faculty, clinicians and technical staff from these two institutions are committed to revolutionizing the efficiency and effectiveness of health care in the state of Maryland and beyond.



LINKS

[Owen White](#) faculty page

[CHIB](#) website

IGS Seminar Series

IGS has been hosting a scientific seminars series for several years, featuring our faculty, their collaborators and high profiles scientists in the field of genomics. In the past year, from September 2013 through June 2014, the program has expanded.

A faculty committee headed by Jacques Ravel, PhD and Vincent Bruno, PhD planned weekly speakers including external speakers invited from IGS faculty network of collaborators and leading scientists in the field of genomics. Riham Keryakos coordinated invitation and speakers' travel and local logistics. Featured speakers have included Dr. Julia Segre from NHGRI, who received the Samuel J. Heyman Service to America Medal for groundbreaking use of DNA sequencing techniques to end the **2011 outbreak** of a hospital-acquired "superbug" that killed seven patients and sickened many others at the National Institutes of Health's Clinical Center, this year. Dr. Martin Blaser from New York University, a leading scientist in the Human Microbiome field, was also our invited speaker for the 2nd Annual Frontiers in Genomics lecture. He spoke on the impact of antibiotic use on the microbiome, obesity and metabolic disorder. Dr. Wendy Garrett from Harvard School of Public Health, presented her fascinating research on the role of gut microbes in colorectal cancer. A complete list of speakers and the title of their presentation is available on the [IGS website](#). This program has helped IGS faculty, post-doctoral fellow, graduate students and staff continue to develop their scientific knowledge, as well as helped IGS expand collaborations with other investigators on campus and at other institutions.



Photo: Martin Blaser, M.D.

past post-doctoral fellows at IGS:

where are they now?

Post-doctoral researchers are an important part of the IGS community, and IGS faculty and leadership are dedicated to providing a nurturing learning environment. The post-doctoral program is a bridge between the graduate curriculum and possible career progression in the academic, industrial or nonprofit sectors. The post-doctoral fellows conduct research under the mentorship of a faculty member. Some of the specialized research that IGS post-docs have done include development of novel methodologies and software for the analysis of bacterial genomes and human microbiomes. IGS faculty have mentored post-doctoral fellows who have gone on to very prestigious appointments. A few of our previous post-doctoral fellows are listed below:

William Hsaio PhD, (2007-2011) from Dr. Claire Fraser's laboratory is currently a Clinical Assistant Professor at the British Columbia Centre for Disease Control in Vancouver, Canada. Emiley Eloie-Fadrosch, PhD (2011-2013) also from Dr. Fraser's lab has recently moved from the Gordon and Betty Moore Foundation to the Department of Energy Joint Genome Institute (JGI) in Walnut Creek, CA as a Senior Scientist studying metagenomics of the environment.

Jason Sahl PhD (2009-2011) and Susan Leonard PhD (2011-2012) from Dr. Rasko's laboratory were involved in the analysis of enteric pathogen genomes and transcriptomes with a focus on *Escherichia coli*. Both have continued the work they initiated at IGS in their new positions. Dr. Leonard is now an ORISE Fellow at the FDA in Laurel, Maryland and Dr. Sahl is a Senior Post Doctoral Fellow at Translational Genomics North (TGEN North).

Panos Ioannidis PhD (2011-2013), from Dr. Dunning Hotopp's laboratory is currently a Post-doctoral researcher at Université de Genève as part of the i5K initiative that aims at sequencing insect genomes in Europe.

CAROLYN MORRIS



DISSERTATION DEFENSE

In June 2014, Carolyn Morris successfully defended her doctoral dissertation, "Utilizing genomics and transcriptomics to identify and characterize mediators of pathogenesis in *Shigella*." Carolyn's advisors were Drs. Eileen, Barry Professor of Medicine in the Center for Vaccine Development and Department of Microbiology & Immunology and David Rasko, Associate Professor of Microbiology & Immunology, and one of IGS' lead investigators in enteric pathogenesis and infectious diseases. Carolyn's study represents a global view of *Shigella* transcriptional activity in the extracellular versus intracellular environment and identified novel species-specific regulatory factors. Her work provides a foundation for discovery of new regulatory pathways and novel vaccine targets. Carolyn is currently getting settled in Colorado with her family and will be pursuing a post-doctoral position in the near future. We wish all the best to Dr. Morris!

Guoyun Bai PhD (2008-2011) from Dr. Ravel's laboratory is a Senior Scientist at Pfizer in Groton, working on mass spectrometry based metabolomics. Joyce Sakamoto, PhD (2008-2011) who trained with both Drs. Jacques Ravel and Vish Nene is Research Assistant Professor at the University of Pennsylvania in the Department of Entomology.

Maximo Rivarola PhD (2008-2010) who trained with Dr. Pablo Rabinowicz is now a faculty member at the Instituto de Biotecnologia INTA studying plant genomics.

There are a number of trainees who have remained within IGS such as James Munro PhD (2010-2013) from Dr. Silva's Laboratory, and Yang Song PhD (2012-2014) from Drs. Fricke's and Fraser's laboratories who have moved into positions within the Informatics Resource Center at IGS. Others have joined the IGS faculty including Rebecca Brotman PhD, MPH (2007-2009), an Assistant Professor in the Department of Epidemiology & Public Health, and Bing Ma PhD, (2010-2013), an IGS Research Associate and the Department of Microbiology & Immunology. Both are studying aspects of the human vaginal microbiome and have trained with Dr. Ravel.

KUDOS ON PROMOTIONS

Bing MA, Ph.D., post-doctoral fellow, Ravel Laboratory, Department of Microbiology & Immunology and Institute for Genome Sciences, has been promoted, to Research Associate, effective May 1st, 2014.

Julie Dunning Hotopp, Ph.D., Assistant Professor, Department of Microbiology & Immunology and Institute for Genome Sciences, has been promoted, to Associate Professor, on tenure track, effective July 1st, 2014.

the microbiome and tobacco

IGS' part of
innovative UMD research
studying tobacco and
public health



Chemical and physical composition of tobacco products and their associated adverse health effects are well documented. However, there is a paucity of data regarding the microbial constituents of these products. As new and highly engineered formulations of cigarettes and smokeless tobacco products are becoming popular, there is a critical knowledge gap regarding the diversity of tobacco microbial constituents, and as a result, their health impacts are not yet well understood. The US Food and Drug Administration (FDA) has set up 14 centers nationwide to compile critical background information to comprehensively regulate new and manipulated tobacco products, and to apply new technologies to learn more about the impact of the tobacco bacterial constituents on human health. The University of Maryland Tobacco Center of Regulatory Science (UMD TCORS) in College Park has been designated one of those 14 centers, and Dr. Pamela Clark, director of the center, has assembled a team of experts in epidemiology, biostatistics, microbiology, toxicology, genomics and bioinformatics for this unique multi-disciplinary research.

Emmanuel Mongodin, PhD, Assistant Professor at IGS and in the Department of Microbiology and Immunology, and Claire Fraser, PhD, Director at IGS, are leading the genomic aspects of the research. This study may be the first to apply next-generation sequencing technologies to the study of new and manipulated smoked and smokeless tobacco products and cigarette smoke. Mongodin and Fraser are working with IGS' GRC, harnessing next-generation sequencing technologies to comprehensively characterize the microbial diversity of tobacco products and their subsequent public health effects.

Links

[FDA info](#)
[TCORS press release from Sept 2013](#)
[Mongodin faculty page](#)

IGS&NICU Collaboration

The Neonatal Intensive Care Unit (NICU) Babies Sequencing Project seeks to use rapid whole genome sequencing for very early diagnosis of severe illness. While this initiative is just beginning, the ultimate goal is to improve clinical outcomes and family satisfaction, as well as reduce hospital stays duration, by using whole genome and exome sequencing to inform clinicians. This project is a collaboration between IGS's Drs. Timothy O'Connor, Owen White, and Luke Tallon and the Program in Personalized Genomic Medicine (PPGM) led by Dr. Alan Shuldiner. Other lead team members are associated with five UMB-SOM departments, UMB-School of Law, School of Pharmacy, and University of Maryland College Park. This multidisciplinary project with translational potential is putting IGS's genomic expertise into the hands of the University of Maryland School of Medicine NICU clinicians.

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