IGS NEWSLETTER

FALL 2015

UNIVERSITY of MARYLAND
SCHOOL OF MEDICINE
INSTITUTE FOR GENOME SCIENCES

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DIRECTOR'S CORNER

Greetings Colleagues,

In July 1995, a team of investigators at The Institute for Genomic Research (TIGR) published the first genome sequence for a free-living organism, *Haemophilus influenzae*. The team included Owen White, PhD, IGS Associate Director for Bioinformatics and myself. Sequencing this free-living organism was an accomplishment that many in the scientific community didn't think possible – but one that launched the field of microbial genomics. The Human Genome Project was really just getting started at that time – with an estimated completion date of 2015. Very quickly the scientific community realized the power of random shotgun sequencing, and an explosion of fully sequenced genome sequences rapidly followed. The Department of Energy, with a strong interest in extremophiles – microbes that live in extreme environments (from a human perspective), was the first funding agency to jump on the microbial genomics bandwagon. Soon after this, the National Institutes of Health embraced this new approach as a means to study important human pathogens. And the Human Genome Project revised its strategy to include random shotgun sequencing, finishing well ahead of schedule.

As the final base pairs of the *H. influenzae* genome sequence were falling into place, we eagerly anticipated the first look at a complete parts list for a free-living organism. We believed that we would be able to identify the function of every gene in the *H. influenzae* genome sequence and reconstruct its metabolism from this information. One of the biggest surprises was the large number of predicted open reading frames that encoded proteins of unknown function. This would become a recurring theme in all subsequent genome-sequencing projects, and we quickly realized how much biology was still to be deciphered.

An important question that was discussed at the time was how many bacterial genome sequences would be "enough". At a meeting that we hosted in 1996, a small group of microbiology experts, along with Program Officers from NIH and DOE, tackled this question. This would be limited to some extent by cost – given that each genome sequence cost ~$750,000 to complete. But we were also limited by our understanding of the diversity of life on earth. It may come as a surprise today that the final recommendation from this planning meeting was to carefully select up to 20 additional representative bacterial species for whole genome analysis. Once that information was in hand, we believed that the scientific community would have nearly everything needed for downstream studies.

Multiple other 'omics approaches have come online since the completion of the first bacterial genome, and collectively these technologies have enabled advances in biomedical sciences not dreamed of 20 years ago. Today, more than 70,000 sequencing projects on bacteria, archaea and eukaryotes have been completed or are underway. We are at a point today where genome-enabled vaccines are now on the market, genome analysis of tumors allows for more precise chemotherapeutic strategies, and individual genome sequences may soon be included as part of our medical records.

It is impossible to predict where we will be 20 years from now, but I suspect that we will look back and realize how limited our understanding of organismal biology was in 2015. It has been a privilege to help launch a new field of research, and I am grateful to all of my colleagues who I've had the pleasure of working with. They have taught me so much about the complexities of life on Earth.

As always, I welcome your feedback,

UNIVERSITY of MARYLAND
SCHOOL OF MEDICINE
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Claire M. Fraser, PhD

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

Dr. Chamindi Seneviratne

Dr. Chamindi Seneviratne: Applying Genomics to Research on Alcoholism

In February 2014, the University of Maryland School of Medicine (UMSOM) established the Brain Science Research Consortium Unit (BSRCU) to bring together faculty from multiple disciplines to probe the inner workings of the brain and to develop new therapies offering hope to those with neurological disorders. The BSRCU is led by Bankole A. Johnson, DSc, MD, MBChB, MPhil, FRCPsych, DFAPA, Dip-ABAM, FACFEI, The Dr. Irving J. Taylor Professor and Chair of the Department of Psychiatry.

Dr. Chamindi Seneviratne worked with Professor Johnson at two other institutions before she came to UMSOM to join the Department of Psychiatry and newly formed BSRCU in 2014. Dr. Seneviratne had worked as a post-doctoral student on a five year research fellowship studying alcohol and other drug addictions at the University of Virginia mentored by Prof. Johnson and Dr. Ming Li.

Dr. Seneviratne is continuing her work on pharmacogenetics, specifically researching the development of personalized treatments for alcohol addiction. In addition to her collaborative projects, Dr. Seneviratne is currently conducting a phase trial at the UMSOM's Clinical Neurobehavioral Center (CNC) and General Clinical Research Center (GCRC) to validate novel biomarkers for prediction of recent heavy drinking in alcoholics.

To maximize the impact of her research, Dr. Seneviratne is part of both the BSRCU and the Institute for Genome Sciences (IGS). She works with the BSRCU research team through her work with Prof. Johnson and she also has her office and lab space on the sixth floor at the IGS. She hopes that her interactions at IGS will spark other interdisciplinary research. She presented a seminar at IGS in January 2015 on molecular mechanisms underlying alcohol addiction and is interested in continuing to apply genomic tools to analyze patient studies.

"When you are studying complex disorders, such as addiction, it's important to look at the entire system," explained Dr. Seneviratne. "At IGS, the focus on the microbiome provides an excellent opportunity for collaboration for many disciplines, such as psychiatry. Indeed, new research has shown that the activities of our gut microbial partners can influence the functioning of the brain in conditions such as depression and even schizophrenia."

Julie Dunning Hotopp, PhD
High Risk, High Reward

Julie Dunning Hotopp, PhD, Institute for Genome Sciences, Associate Professor, Microbiology & Immunology, UM School of Medicine, received a Transformative Research Award from the NIH Common Fund for a five year High-Risk, High-Reward (HR, HR) grant of over $3 Million. The award winners will attend a formal ceremony with NIH Director Francis S. Collins, MD, PhD, in December 2015.

"This program has consistently produced research that revolutionized scientific fields by giving investigators the freedom to take risks and explore potentially groundbreaking concepts," said Dr. Collins.

The Transformative Research Award, established in 2009, supports exceptionally innovative, unconventional, paradigm-shifting research projects that are untested. It promotes interdisciplinary approaches and is open to individuals and teams of investigators who propose research that could potentially create or challenge existing theories.

"This award allows me to continue our research on identifying bacterial DNA mutating the human genome and to examine whether these mutations may cause cancer, work that began a few years ago through the NIH New Innovator program," said Dr. Hotopp.

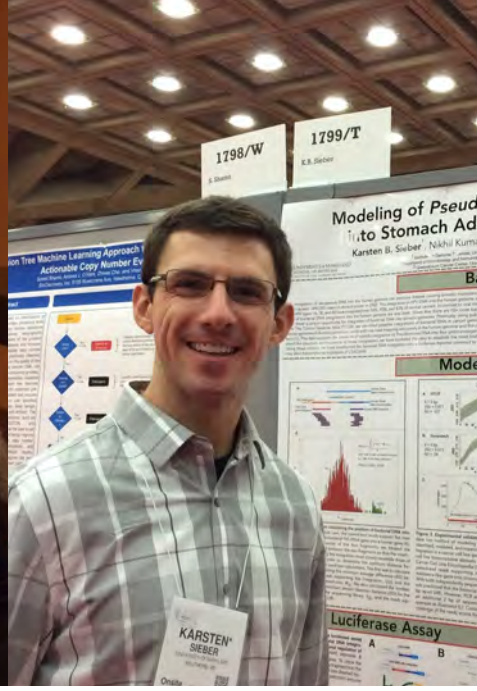
Rebecca Brotman, PhD, MPH
Best Paper of the Year Award
November 2015

Rebecca M. Brotman, PhD, MPH, Institute for Genome Sciences, Assistant Professor, Epidemiology & Public Health, UM School of Medicine was recognized by the North American Menopause Society (NAMS)/**Lippincott Williams & Wilkins for the Best Paper of the Year Award**. Dr. Brotman was recognized for her outstanding contributions to the field of women's health and menopause.

This award recognizes the best paper published in *Menopause* in 2014. The recipient is selected by the Editor-in-Chief of the journal. Dr. Brotman was presented with the award at the 26th NAMS Annual Meeting on October 2-3 in Las Vegas.

The title of her paper was "Association between the vaginal microbiota, menopause status, and signs of vulvovaginal atrophy" *Menopause*, Vol. 21, No. 5, 2014, pp. 450-458 and was co-authored with IGS and Johns Hopkins University collaborators.

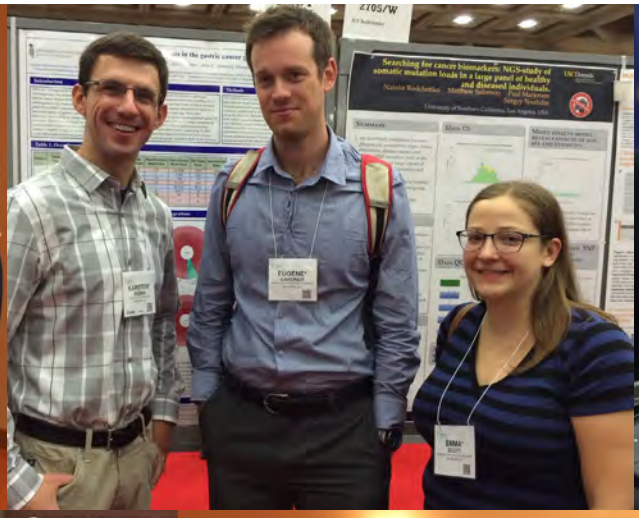
ASHG



IGS Exhibits & Presents at

American Society of Human Genetics

meeting in Baltimore, October 2015



Jacques Ravel, PhD Selected As a **PROMISE** Outstanding Faculty Mentor

Jacques Ravel, PhD, was chosen as one of the twelve University System of Maryland's PROMISE AGEP Outstanding Faculty Mentors, for 2015-2016 (AGEP is the Association for Graduate Education and the Professoriate).

Latéy Bradford is a PhD Candidate in the Medical Scientist Training Program (MD/PhD program) in the Ravel Lab who was recognized at a TED-style conference sponsored by the University System of Maryland PROMISE Alliance for Graduate Education for her talk on "The Dynamics in the Vaginal Ecosystem and Development of Vulvovaginal Candidiasis".

The **University System of Maryland's (USM) PROMISE AGEP** is sponsored by the National Science Foundation. The PROMISE Outstanding Faculty Mentors were chosen by underrepresented graduate students in STEM fields, and leaders of STEM diversity programs such as the NSF Louis Stokes Alliance for Minority Participation Bridge to the Doctorate Programs (LSAMP-BD) at UMBC and College Park, and the NIH Meyerhoff Biomedical Graduate Fellowship Program at UMBC and UMB.

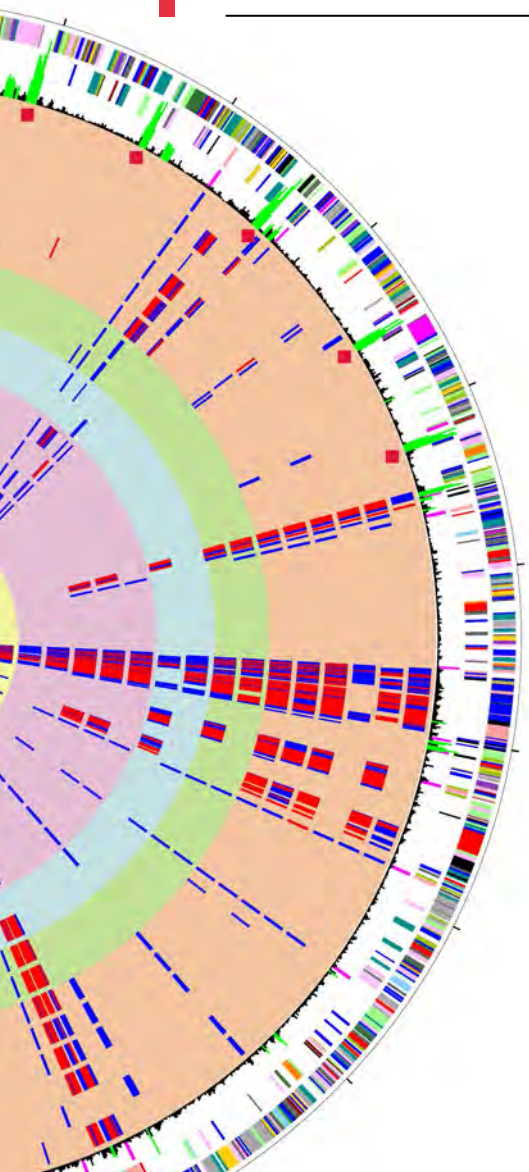
The nominees include a range of STEM faculty from assistant to full professors who are mentoring students and postdoctoral fellows at UMBC, UM College Park, and UMB. Mentors were selected for one or more of the following reasons: recommended and applauded by graduate students for diversity and inclusion efforts and actions, involvement in STEM diversity conversations, participation in PROMISE and Graduate Student Development activities (e.g., seminar panels, round table discussions), and/or a research agenda that broadens the participation of underrepresented STEM scholars.

"It is an honor to be recognized as one of the PROMISE AGEP Outstanding Faculty Mentors. My research goals in improving women's health disparity have contributed greatly to my mentoring of fantastic and highly motivated female students and postdoctoral fellows over the years. Their successes and accomplishments are very much the reason I received this honor," said Dr. Ravel.

NIH GRANT/ OSDF

UM Institute for Genome Sciences **Awarded NIH Grant** to Organize Cloud Distribution for "Big Data"

The National Institutes of Health (NIH)'s roadmap initiative, the Human Microbiome Project (HMP), generated a wealth of microbiome data that has become increasingly vital for clinical and public health research. While the data is now publicly accessible at the National Center for Biotechnology Information (NCBI), it is not yet available in uniform pipelines and more readily usable forms. NIH has awarded a supplemental grant worth more than $1,067,000 to IGS to organize and process the microbiome data using common sets of pipelines through Amazon S3 public databases repository, a cloud-based system.



With the grant, IGS bioinformatics experts will utilize the Open Science Data Framework (OSDF), to provide the architecture and software necessary for conducting bioinformatics analyses in a federated cloud-enabled data and computational environment. The OSDF will improve how the scientific community accesses, analyzes and visualizes genomic data sets. Since the publication of the HMP data, the data generated from related studies has doubled, and value-added datasets have been developed and will be made available at Amazon. The project is among four other pilot projects testing the utility of cloud-based systems for the NIH Big Data Initiative.

To ensure the utility and ease of these analysis pipelines, IGS will also host two pilot projects involving virtual meetings and workshops for beta testing these cloud-based data and analysis systems with the user communities.

Owen White, PhD, Professor of Epidemiology and Public Health and Associate Director of Informatics at the Institute for Genome Sciences (IGS) at the University of Maryland School of Medicine, will lead the OSDF project. Anup Mahurkar, Director of the Informatics Resource Center (IRC) and the Executive Director for Software Engineering and IT at IGS, will be the co-investigator and project manager on the grant.

Dr. White is a pioneer in open access informatics, and for the past five years, he has been the principal investigator on the NIH HMP Data and Analysis Coordination Center (DACC) project. "Datasets are now so huge that storage and access have become major challenges. Our team has been innovative in pioneering new cloud applications that have democratized data management for individual researchers and smaller research centers," said Dr. White.

IGS will be supporting the OSDF with web portals and community outreach workshops. All of the information will be stored in databases at the University of Maryland School of Medicine Institute for Genome Sciences.

Spot light on IGS Seminar Series

Recent speaker Keith Crandall, PhD

Since the Institute moved into the BioPark space in 2009, IGS faculty have organized seminars on various scientific topics. The purpose of the scientific seminar series is to provide a platform for IGS faculty and the UMB community to learn about new research in genomics and bioinformatics. The seminar programs are offered free of charge to attendees and the audience includes anyone interested in the topic, which has been faculty and staff from IGS, the UMB professional schools, the tenants in the BioPark, and other researchers in the vicinity.

For the past three years, Drs. Vincent Bruno and Jacques Ravel have co-chaired the seminar series and they have expanded the reach and frequency of the seminar schedule. The seminar schedule follows an academic calendar year, starting in September and continuing through June. The presentations are generally held on Thursday mornings in the Discover Auditorium at the UM BioPark. Speakers often attend a lunch 'question and answer' session with graduate students, post-doctoral fellows or IGS staff interested in their presentation.

"We look for speakers whose work is novel, exciting and we believe would be of interest to our IGS and campus colleagues," explained Dr. Bruno. "Often, someone at IGS wants to introduce one of their research collaborators who is expert on a certain subject. This allows IGS to familiarize campus colleagues with the capabilities of genomics and bioinformatics."

Because genomics changes so rapidly, this high caliber seminar series allows IGS faculty to keep themselves updated on many aspects of these complex fields. Periodically, an informal discussion about one of the seminar will spark new research direction at IGS.

Over the years, the scope of the presentations has expanded to include many out-of-town colleagues. IGS budget savvy planners often synchronize their invited speaker's visit here with their planned meetings in the Baltimore/Washington area. That has allowed IGS to bring in internationally accomplished scientists who are visiting the NIH or the FDA, which is a lucky side benefit for IGS' proximity to the federal agencies.

A recent speaker was Keith Crandall, PhD, the Director of the Computational Biology Institute at George Washington University. Dr. Crandall spoke about "*Computational Approaches to Biodiversity Informatics*." Dr. Crandall exemplified the high caliber research ongoing in the Washington/Baltimore area and the potential for developing local collaborations. IGS also invited Joanne Berghout, PhD, who is the Outreach Coordinator of Mouse Genome Informatics at The Jackson Laboratory in Bar Harbor, Maine. In her talk entitled "*Fundamentals of Mouse Genetics and the Mouse Genome Informatics Database (MGI)*," Dr. Berghout introduced the vast array of informatics approaches available at the Mouse Genome Informatics Database to study human diseases through mouse model genetics. This presentation was also highly relevant to IGS and UMB microbiome researchers who now rely on mouse models to explore the critical functions of the microbes that inhabit our bodies.

The series schedule is posted on the IGS website under **Events** or to join the email distribution list, contact Riham Keryakos at **rkeryakos@som.umaryland.edu.**

Save the Date

June 15th 2016

Our speaker for the 4th annual **Frontiers in Genomics** will be Atul Butte, MD, PhD, from the University of California, San Francisco.

Halloween in the BioPark

Featuring Dr. Vincent Bruno

Vincent Bruno, PhD

Institute for Genome Sciences

Assistant Professor

Microbiology & Immunology

UM School of Medicine

Fungal infections are a serious cause of disease with extremely limited treatment options. Designing effective drugs against fungi is very difficult because of the strong similarities between fungal and human cells. So many compounds that can clear a fungal infection are often also toxic to the patients. Since invasive fungal infections kill more than half of those infected, new therapies are desperately needed.

With the hopes of identifying new drug targets, Dr. Bruno's lab combines sequencing-based gene expression analyses (RNA-seq) and comparative genomics to understand at the molecular level, how human cells and fungal pathogens interact with one another. "Understanding the complex nature of the host-pathogen interaction is essential to developing needed therapies to treat fungal infections," explains Dr. Bruno. "RNA-seq enables a systems-level understanding of infection by facilitating comprehensive analysis of transcriptomes from multiple species simultaneously."

As a postdoctoral fellow, Dr. Bruno was trained in microbial pathogenesis and genomics by Drs. Jorge Galan and Michael Snyder, respectively. In his lab here at IGS, he combines these two disciplines to understand Candidiasis, Mucormycosis and Aspergillosis, which together represent ~90% of the invasive fungal infections reported in the US.

DNA is transcribed (copied) into mRNA molecules and are referred to as transcripts. A transcriptome is a collection of all the mRNA molecules present in a cell. Dr. Bruno has recently published two exciting papers:

"**New Signaling Pathways Govern the Host Response to C. albicans infection in various niches**"

"**Transcriptomic Analysis of Vulvovaginal Candidiasis Identifies a Role for the NLRP3 Inflammasome**"

"Our second paper is an exciting proof-of-principle that, with genomic analyses, we may be able to leverage drugs already approved by the FDA and re-purpose them to treat fungal infections."

Dr. Bruno is also the project lead of one of the **Genomic Center for Infectious Diseases (GCID)** research programs, focusing on the genomic analysis of fungal pathogenesis. The GCID is a five year NIAID-funded initiative to apply genomic techniques to the study of pathogens and their hosts.

View **Dr. Bruno's lab page**.

GRC UPDATE

with **Luke J. Tallon**, Scientific Director &
Dr. Lisa Sadzewicz, Administrative Director

Things in the Genomics Resource Center (GRC) sure have been busy! We are excited to announce a new contract to extend our collaboration with the U.S Food and Drug Administration (FDA). Following on the heels of our successful $1.2M contract with the FDA Center for Devices and Radiological Health (CDRH) to support the inception of the FDA dAtabase for Regulatory Grade micrObial Sequences (FDA-ARGOS), the new $2.7M contract will support the sequencing and analysis of almost 1,500 bacterial, viral, fungal, and parasite pathogen genomes. The combination of Illumina short-read and PacBio long-read data, as well as the assembled and annotated genome sequences will be publicly available via the NCBI **BioProject** page. Included in the new contract is a special emphasis on viral pathogens, including **Ebola**.

We are also excited to announce the winner of our recent SMRTest Microbe grant competition, Dr. Erin Price at the **Menzies School of Health Research** in Australia! The grant program, co-sponsored by PacBio and the GRC, was very competitive, with over 100 submitted proposals. Dr. Price will receive SMRT® Sequencing and analysis from the GRC — using up to 4 SMRTbell libraries and 8 SMRT Cells — to characterize the mechanisms behind the emergence of antibiotic resistance in *Burkholderia pseudomallei*, a highly pathogenic bacterium that causes the potentially deadly disease melioidosis. Dr. Price and colleagues have recently uncovered the development of meropenem resistance in local cases of *B. pseudomallei* infection, along with evidence that this resistance is linked to at least two mortalities in Australia, so far.

In early October, we attended the annual ASHG Annual Meeting here in Baltimore, where PacBio announced the long-awaited new Sequel System. Promising up to seven times the throughput of the existing RS II System, this new long-read sequencing platform has the potential to change the genome and metagenome sequencing landscapes. Stay tuned for more news on this new technology in early 2016.

Please check out our **blog** or **email us**!

Q&A

What types of samples do you sequence and analyze? Do I need to extract DNA/RNA?

If it's a nucleic acid, we'll take it! We sequence whole genomes, metagenomes, transcriptomes, targeted capture samples, amplicons, ChIP DNA, and other custom DNA and RNA samples and applications. Though we do not typically offer DNA or RNA extraction services, we will work with you to make sure your samples can be sequenced. For some projects, we will offer extraction services. For others, we may advise you on the extraction protocol or put you in touch with a sister UMB core lab that can extract nucleic acids from your samples.

What sequencing platform is best for my project?

It all depends on the goals and scope of your project. We strive to offer the full range of sequencing and analysis services. Prior to each project, we consult with you to learn more about the project and advise on approach and platform selection. Don't hesitate to **contact us**! No question is too small!

Q&A with Anup Mahurkar

Executive Director, Software Engineering & IT

What does a typical engagement with the IRC look like?

AM: We work closely with the Genomics Resource Center (GRC) to provide investigators with a "one-stop-shop" for sequencing and analysis. When an investigator reaches out to the IRC, we start the process by meeting with the investigator to learn about the project and identify goals and priorities, as well as providing advice on study design. When relevant, we will include the GRC or other IGS faculty in the planning discussion. Once data has been generated, we assign an analyst or engineer to serve as a liaison between the investigator and other members of the team. The liaison will chaperone the project through the different stages of analysis including data QC, primary and secondary analyses, and, as needed, help with tertiary analysis and manuscript generation.

How long do analyses typically take?

AM: Depending on the complexity of the project and the ability to utilize existing analysis pipelines, a project may take anywhere from one week for a simple microarray analysis to over twelve weeks for more complex transcriptome analyses. A typical analysis will take between 4 to 8 weeks from the time the data is delivered to the IRC.

Links

The Informatics Resource Center (IRC)

The IRC Projects and Software

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

Jacques Ravel, PhD	Scientific Editor
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