UNIVERSITY of MARYLAND
SCHOOL OF MEDICINE
INSTITUTE FOR GENOME SCIENCES

IGS NEWSLETTER

SUMMER 2017

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Greetings Colleagues,

This May marked a milestone for the Institute for Genome Sciences. In 2007, our new institute was created at the University of Maryland School of Medicine, recognizing the ever-growing power of genomics to address some of the biggest challenges in biology and medicine. Ten years later, we are poised to celebrate the anniversary of IGS as an integral member of the UMB campus community, a leader in genomic research, a nucleus for innovation and discovery, and home to some of the field's most promising and productive investigators.

To recognize our legacy of achievements this year we are planning a day-long **Frontiers in Genomics Symposium** on November 16, 2017 featuring a number of distinguished speakers who will cover a broad range of topics in the field. Our keynote speaker for this event will be Eric Green, MD, PhD, Director of the National Human Genome Research Institute at NIH. Dr. Green was a seminal contributor to the Human Genome Project, while also using comparative genomics approaches to understand genome structure, function and evolution.

Over the past ten years, IGS has grown from an organization with fewer than 50 faculty and staff to more than 120 employees. Through 11 targeted faculty recruitments, we have significantly expanded our research portfolio in both basic and clinical science. Our research is focused on all branches of the phylogenetic tree of life. Our awarded research funding over the past 10 years has totaled $160,273,877.

I hope that you can join us in November for the celebration of IGS' anniversary.

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

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Welcome to David Serre

Associate Professor Microbiology and Immunology

A big welcome to Dr. David Serre who joined IGS in October 2016!

Dr. Serre is interested in developing genomic approaches to better understand the biology of eukaryotic pathogens and their interactions with their hosts. **Dr. Serres' lab** primarily focuses on *Plasmodium vivax*, an important human parasite responsible for most malaria cases outside Africa. Since this parasite cannot be continuously propagated in cultures and need to be studied *in vitro*, Dr. Serre and his team are using a variety of genomic assays to characterize its response to antimalarial drugs and other environmental stresses using patient samples and animal models. Their studies also include genomic analyses of the host response to infection, and of the *Anopheles* mosquitoes that transmit the parasite.

Dr. Serre has ongoing collaborations with the Pasteur Institute in Cambodia for the patient studies and the Laboratory of Malaria and Vector Research at **NIAID** (NIH) for the animal studies. He is working with Dr. Christopher Plowe, the Founding Director of the **Institute for Global Health (IGH)**, and other members of the Division of Malaria Research to further extend the scope of his research. Dr. Serre graduated in Biology from the Max Planck Institute for Evolutionary Anthropology and completed his postdoctoral fellowship at the McGill and Genome Quebec Innovation Centre in Montreal. Prior to coming IGS, Dr. Serre was a faculty member at the Genome Medicine Institute at the Cleveland Clinic.

Dr. David Serre

SAVE THE DATE

Frontiers in Genomics Symposium

Thursday November 16th, 2017
8:30 am – 4:00 pm

University of Maryland Baltimore
School of Nursing Auditorium
655 W. Lombard St. Baltimore MD 21201

Please join us for a day of innovative discussion and scientific exchange, celebrating the 10th anniversary of our Institute. We will be hosting internationally recognized scientists who will share their latest discoveries in genomics and bioinformatics. Our keynote speaker will be Eric Green, MD, PhD, Director of the National Human Genome Research Institute at NIH.

For more information, please contact: Riham Keryakos

The Genomic Standards Consortium (GSC)

Enabling genomic data integration, discovery and comparison through international community-driven standards and making genomic data discoverable is the driving mission of the **Genomic Standards Consortium (GSC)**.

In 2005, the GSC was formed to address the pressing need to build and implement community-based standards for harmonizing the capture and exchange of genomic metadata across the wider genomics community. GSC members include biologists, computer scientists, those building genomic databases, building community-based standards and conducting large-scale comparative genomic analyses. The GSC is an open-membership organization, working actively with community members to develop additional metadata standards. Dr. Pelin Yilmaz, Max Planck Institute for Marine Microbiology, leads the GSC's metadata standards working group. The GSC's annual meeting **(GSC19)** was held in Brisbane, Australia (May 14-17, 2017) hosted by the Australian Centre for Ecogenomics and the University of Queensland. GSC19 focused on Extending Standards to Viruses and Microbial Eukaryotes.

Lynn M. Schriml, PhD, Associate Professor at IGS and the department of Epidemiology & Public Health, at UMSOM, joined the GSC in 2005 as a standards developer. Dr. Schriml has served on the GSC Board since 2009, as GSC Treasurer (2010-2015) and began her third year as GSC President in May 2017. Dr. Schriml's current research focuses on developing bioinformatic tools, metadata standards and ontologies to gain a broader understanding of the relationship between infectious pathogens, their genomic sequence and disease. Dr. Schriml leads a number of ontology and metadata standard development and implementation projects.

Lynn Schriml, PhD

Comprehensive Evaluation of Pluripotent Stem Cell Quality

The Progenitor Cell Biology Consortium (PCBC) published a 2016 study in **Stem Cell Reports** reporting the outcome of a comprehensive evaluation of the quality and stability of induced pluripotent stem cells (iPSCs) generated using a wide range of technologies and cell sources from multiple independent laboratories.

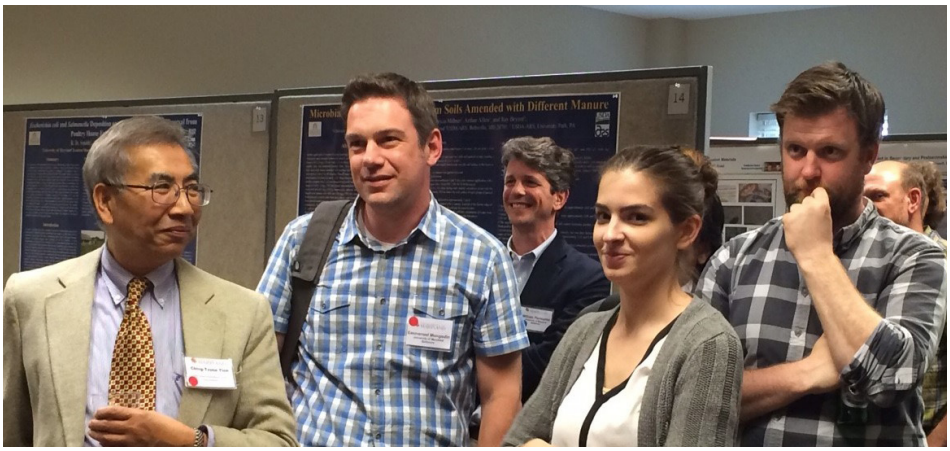
The study combined large-scale molecular testing and characterization in a laboratory setting with computational analyses to examine and generate large sets of data on the interplay between different methods of cell programming, gene regulation and the functional quality of iPSCs. The data revealed new and subtle telltale signs of iPSC lines that had already lost their ability to make all necessary adult cell lines. The study involved comprehensive experimental and genomic analyses of 58 iPSCs using a variety of reprogramming genes, vectors, and cells. Associated global molecular characterization studies identified functionally informative correlations in gene expression, DNA methylation, and/or copy-number variation among key developmental and oncogenic regulators as a result of donor, sex, line stability, reprogramming technology, and cell of origin.

Lynn M. Schriml, PhD, Associate Professor, Epidemiology & Public Health at UMSOM, as a member of the PCBC Bioinformatics Core, co-developed the project's metadata standard to capture the origin of each line, starting cell type, donor demographics, and reprogramming parameters (derivation method, vector type, reprogramming genes, culture conditions), to identify differences associated with major cell-line variables. The metadata standard and associated data are available through an **interactive data Synapse portal**.

UMD School of Public Health Receives $10M to Lead USDA Center of Excellence for Sustainable Water Reuse, Food & Health

As the planet experiences record heat and states like California suffer from historic droughts, the clean water that we need to safely and sustainably grow food crops is in short supply. In the face of climate change, finding alternative sources of water to grow food that is safe to eat has become an urgent national priority.

A multidisciplinary team, led by Dr. Amy R. Sapkota at the **University of Maryland School of Public Health**, is dedicating itself to developing innovative, safe and sustainable ways to irrigate food crops in variable climates. With a $10 million grant from the USDA National Institute of Food and Agriculture, awarded over a four-year period, the "CONSERVE" Center of Excellence links experts from the Mid-Atlantic and Southwest to identify the best nontraditional water sources and new water treatment technologies that farmers can safely use on food crops without compromising public health.



Emmanuel Mongodin, PhD (pictured second from left)

Emmanuel Mongodin, PhD (pictured far left)

Emmanuel Mongodin, PhD, Assistant Professor at IGS and the department of Microbiology and Immunology, is a key investigator in the "CONSERVE" Center of Excellence. One aspect of his work will be to characterize the microbial constituents from nontraditional water sources and new water treatment technologies, to understand what is required to make the water acceptable and safe for irrigation by farmers on food crops, without compromising public health.

MORE INFO

For more information about Emmanuel Mongodin's Lab, please visit http://www.medschool.umaryland.edu/profiles/Mongodin-Emmanuel/

For more information about UMD, please visit https://sph.umd.edu/laboratory-resources/conserve

Bioinformatics Workshops

As sequencing technologies improve and costs decline, learning how to handle large datasets has become essential for researchers in biology and medicine. Bioinformatics has exploded with increasingly complex tools and software which are being developed to manage analysis of sequence data.

Education has been a strong part of the IGS mission since our launch in 2007.

Michelle Gwinn Giglio, PhD, Associate Professor, Medicine at the University of Maryland School of Medicine and Associate Director, Analysis at IGS, has led the team developing curriculum for IGS workshops. Five different workshops are part of the program and are offered to anyone interested in learning about the topics. Past attendees have included not only researchers from the region, federal agency employees from the FDA and USDA, but also attendees from as far away as New Zealand and Africa.

IGS revises content in the workshops based on attendee feedback, so the workshops are continually adapted to current research needs. One of the most popular workshops is "Introduction to Genomics and Bioinformatics" focusing on the most frequently used informatics pipelines and tools. Another fundamental workshop is "Python, Databases, and R for Bioinformatics" which covers some basics of programming to give biologists the tools they need to operate in a Linux/Unix environment and to learn how to manipulate data files, analyze them, and effectively store and retrieve their data.

Michelle Giglio, PhD conducting a Bioinformatics workshop

The IGS workshops are taught by a team of informatics faculty and staff, whose expertise spans a continuum of the biology/programming spectrum. All workshops feature hands-on exercises in a small group setting. The goal is for attendees to return home and be able to apply the informatics tools and techniques that they've learned to their own work.

"Hands-on components to these workshops is absolutely key. Only through actually using a tool can attendees truly understand how to run it and interpret the results," said Dr. Giglio. "All of our workshops require no previous experience in bioinformatics or programming."

For Dr. Giglio, the best reaction that the team gets is when an attendee comes and tells them the class is exactly what they needed and what they were searching for. "When new students attend and tell us that they heard about the workshops from previous attendees who recommended the program, that's a great testimonial for us," said Dr. Giglio.

MORE INFO

For more information about the Bioinformatics Workshops schedule, please visit http://www.igs.umaryland.edu/education/workshops.php

IGS Leading the Way in Women's Health Research

Over the past ten years since it launched in 2007, IGS has developed a strong and recognized program in women's health. These efforts are led by IGS Associate Director for Genomics, Jacques Ravel, PhD, and Rebecca Brotman, PhD, MPH, Associate Professor. They have leveraged IGS technology platforms in genomics and their expertise in microbiology and epidemiology and built an inter-disciplinary collaborative local and global network. They and their collaborators address important questions about women's health with a focus on sexually transmitted infections, as well as gynecological and obstetric outcomes.

Jacques Ravel, PhD and Rebecca Brotman, PhD

In the early 2000s, Dr. Ravel was an Assistant Investigator at The Institute for Genomic Research (TIGR), the preeminent and pioneering genomics center where the first microbial genome was sequenced. The molecular characterization and study of microbial communities living in or on the human body (microbiome) and their impact on health or diseases was in its infancy. Traditional microbiology has relied on cultivated samples, such as in a petri dish, and because most microbes cannot be cultivated in the laboratory, the approach is biased and time-consuming. On the other hand, molecular methods, such as metagenomics approaches (sequencing the genomes of all members of a community at once) are less biased and more high-throughput, however, they increase data complexity resulting in a shift from a technical to a computational problem. The more complex the community, the more difficult it is to sequence. While it was technically possible to characterize complex microbial communities such as those inhabiting the human intestine, at that time, it was extremely costly and making sense of the sequence data remained the major challenge.

Because the vaginal microbiota is less complex than other human-associated microbiota, Dr. Ravel felt that it was the perfect microbiota to study considering the sequencing and computational limitations of the technologies that were available in the early 2000s. It had always been thought that the vaginal microbiota was the first line of defense against pathogens and that a "healthy" vaginal microbiota was important to gynecological and obstetrics health. However, little was known about the composition and dynamics of the vaginal microbiota in women across diverse socioeconomic and ethnic groups.

In 2005, he began a collaboration with Dr. Larry J. Forney, now University Distinguished Professor at the University of Idaho, and together, they started groundbreaking work on one of the first NIH grants to use metagenomics to characterize the composition and dynamics of the vaginal microbiota in women. The team's 2011 seminal paper, published in the Proceedings of the National Academy of Sciences demonstrated that women's vaginal microbiota belong to one of five types (called Community State Type or CST), four of which were dominated by a species of *Lactobacillus* while the fifth one lacked *Lactobacillus*, and was more complex and comprised of anaerobic bacteria. Interestingly, the latter was more prevalent in African American (40%) and Hispanic (39%) than Asian (19%) and Caucasian (10%)

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women. This finding was paradigm changing and opened the door for personalized women's health. After his move to the UMSOM and IGS, Dr. Ravel was awarded a grant under the NIH's Human Microbiome Project (HMP, with Co-PI Forney and Co-I Brotman), to continue exploring the role of the vaginal microbiome in disease, utilizing prospective longitudinal study design which is critical to establish causal disease pathways.

Reflecting on that period, Dr. Ravel says, "The HMP funding gave us an opportunity to go from studying individual samples from different women to longitudinally studying women over time. It was a huge breakthrough because if one wants to understand risk or establish causality, it is necessary to study a women's microbiome before, during and after they acquire a disease."

Critical to the success of the program, and early on after moving to UMSOM, Dr. Ravel brought Dr. Rebecca Brotman, a talented epidemiologist, to IGS, and together, they expanded many collaborations throughout UMB - with investigators at the SOM, the School of Nursing, and the School of Dentistry.

Dr. Brotman came to IGS as a Post-Doctoral Fellow, with a PhD in Epidemiology and Public Health from the Johns Hopkins University, and her research also focused on women's health. She rapidly moved up the ranks after being awarded a prestigious NIH K01 training grant and is now a R01-funded Associate Professor in the Department of Epidemiology and Public Health and IGS.

Leveraging samples that Dr. Brotman collected during her doctoral work, she and Dr. Ravel published the first description of the dynamics of the vaginal microbiota in reproductive age women. The **paper** published in **Science Translational Medicine** received a lot of attention and showed that some women had very stable *Lactobacillus*-dominated microbiota when sampled twice weekly for 16 weeks, while others had unstable microbiota that fluctuated from being dominated by *Lactobacillus* species to lacking *Lactobacillus*. They further demonstrated the critical role of lactic acid, produced by *Lactobacillus* species, in the defensive feature of the microbiota using for the first time, a metabolomics approach to characterize vaginal metabolites present in different types of microbial communities. As part of the HMP project, the team recruited 160 participants to a study that aimed to characterize the composition and function of the vaginal microbiota with high-resolution in daily collected vaginal samples over a 10-week period.

Studying women over time, with clinical samples and genomic analyses, was an innovative approach. The team also considered behavioral, clinical and environmental factors and applied their unique expertise, developing new ways of analyzing

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populations of women, with each study and new publication asking questions about increasingly complex conditions, such as how vaginal microbiota affect HPV infection and clearance or the effect of HIV microbicides on the vaginal microbiota.

Dr. Ravel also began studying the potential role of the vaginal microbiota in prematurity and pregnancy with Dr. Roberto Romero, Chief of the Perinatology Branch at NIH. This collaboration resulted in several publications about the composition of vaginal microbiota in pregnancy and an analysis of how the vaginal microbiota relates to the challenging problem of preterm birth. Dr. Ravel has expanded his work in this domain with collaboration with Dr. Mary Regan at the UM School of Nursing, studying how diet can affect a pregnant women's microbiome and prematurity outcomes. He also works with Dr. Michal Elovitz, Professor of Obstetrics and Gynecology and Director of the Prematurity Prevention Program at the University of Pennsylvania, on the role of vaginal microbiota and cervical remodeling that lead to preterm labor. These ongoing projects leverage Dr. Ravel's continuing technical and computational developments in studying aspects of the vaginal microbiota from a descriptive and functional point of view.

Over the past seven years, with co-PI Dr. Patrik Bavoil, Professor and Chair of Microbial Pathogenesis at the UM School of Dentistry, Dr. Ravel has led a large 10-year $20 million collaborative center funded by the National Institute for Allergy and Infectious Diseases (NIAID), Ecopathogenomics of Sexually Transmitted Infections (EPSTI). EPSTI aims to understand the interaction of human host genetic variation, pathogens genomics, and the vaginal microbiota in the acquisition of sexually transmitted infection such as chlamydia and gonorrhea. This multi-disciplinary system biology program leverages IGS/UMB genomic capabilities and that of co-Investigators at Duke University, University of Virginia and the Johns Hopkins University.

Dr. Brotman has become increasingly well-known and recognized in the women's health field for incorporating genomic analysis to her epidemiological research. Among the many awards she has received, in 2015, the North American Menopause Society recognized her work on the "Association between the vaginal microbiota, menopause status and signs of vulvovaginal atrophy" published in Menopause journal and which recieved the NAMS/ Lippincott Williams & Wilkins Best Paper of the Year award. Using innovative study designs, she continues to produce novel findings on how behaviors, including smoking, sexual activities, and

Chlamydia (top), ***Gonorrhea*** (bottom)

feminine hygiene, affect a women's microbial partners and determined to what extent the vaginal microbiota can protect against pathogenic infections. Her research is supported by two NIH R01 grants to study different aspects of behavior and medical practices on the composition and function of the vaginal microbiota, as well as on the acquisition of sexually transmitted pathogens. In addition, the Dean's Program in Health Disparities and Population Health recently awarded Dr. Brotman a grant to probe factors of ethnic disparities and the vaginal microbiota, a grant she now works on with Dr. Natalie Slopen from the UM School of

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Public Health at College Park. This research explores how socioeconomic factors, perceived stress, and the vaginal microbiota affect risk for acquisition of sexually transmitted infections.

Both Drs. Ravel and Brotman are now focusing on the translational aspects of their research and what interventions can be done to influence the microbiome to restore a protective vaginal microbiota. They are leveraging the knowledge they have accumulated over the years leading the field of microbiome and women's health and are exploring their entrepreneurial spirits.

"Our next goal is to formulate a personalized microbiome-based product that would be used to restore a healthy and protective vaginal microbiota. It is the future, and our science supports the design of such a product. I envision a time where before her annual exam, a woman would sample herself at home, her doctor would evaluate her vaginal microbiota profile and decide on an appropriate and personalized treatment to restore vaginal health - - - one we will develop!" says Dr. Ravel.

To facilitate these discoveries, they are about to launch a citizen scientist project called YourPrivateBiome where women (and men) can have their microbiota characterized for supporting the research financially. This project is an important step to understanding the vaginal microbiota in a large-scale population study and while it is limited to the United States at launch, they are seeking partnerships to open it to other countries.

Reflecting on his ten years of research at IGS, Dr. Ravel said, "We are in the process of revolutionizing the study of women's health. Applying systems biology approaches to understand health from a systems perspective will afford an increasingly complete picture of women's health. We are just starting, and our interdisciplinary collaborative and inclusive team is key to our success at UMSOM, UMB and globally."

Global research trends are slowly bridging the connections between clinical and genomic research and leading to more precise diagnostics and drugs. Drs. Ravel and Brotman are leading some of the most intriguing research on women's health, and because of their research and collaborations, IGS is becoming an increasingly significant part of global women's health research.

> **"We are in the process of revolutionizing the study of women's health. Applying systems biology approaches to understand health from a systems perspective will afford an increasingly complete picture of women's health."**
>
> -Dr. Jacques Ravel

MORE INFO

For more information on Dr. Ravel's lab, please visit http://ravel-lab.org/

For more information on Dr. Brotman's lab, please visit http://www.medschool.umaryland.edu/profiles/Brotman-Rebecca-M/

GRC UPDATE

Update from the Genomics Resource Center (GRC)

It's another exciting time for the Genomics Resource Center (GRC) and the application of genomic technologies to human health. New technologies and applications have been brought to the GRC and our collaborators. After many months of working with PacBio as a beta test site, the Sequel System and the new v2 chemistry are yielding impressive results. With per-run yields exceeding 5 Gbp and average read lengths >10kb, we are slowly increasing utilization of this new high-throughput, long-read platform in our *de novo genome* and transcriptome projects.

We have also recently acquired a Nanostring nCounter FLEX instrument. Nanostring technology is based on the hybridization of barcoded probes to nucleic acid samples. With up to 800 unique probes and millions of copies of each probe in each assay, the ability to digitally count molecules is ideal for gene expression, CNVs, community profiling, and other counting applications.

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

As announced in December, the winner of our 3rd annual SMRTest Microbe Grant is Jessica Sieber from the University of Minnesota Duluth, who impressed reviewers with her proposal, "Metagenomic analysis of the gut microbiota of the 13-lined ground squirrel, a model fat storing hibernator." Read more about this exciting project on our **blog**. We shared the results at the 2017 ASM General Meeting in New Orleans, LA June 1 – 5.

Please check out our blog or email us!

Q&A

What are the sample requirements for Nanostring digital gene expression?

Because of the simple hybridization based chemistry, the platform is particularly suited for working with limited or degraded material, including RNA extracted from FFPE samples. Sample requirements vary, but many applications require only 25ng of RNA.

When will I be able to submit projects for the PacBio Sequel System?

Now! We are emerging from the beta testing phase with this platform and beginning to take projects from external researchers. If you have a project that might benefit from the Sequel System, or any of our platforms, please **contact us!**

Graduations 2017

Congratulations to all graduates who have been part of the IGS team!

Dr. Kelly Robinson (right) with her mentor Mentor Dr. Julie Dunning Hotopp

Dissertation:

Microbiome Composition and Effects in Tumors, with a Focus on Gastric Carcinomas

What's Next?

Kelly will be an Assistant Scientist at Personal Genome Diagnostics in Baltimore

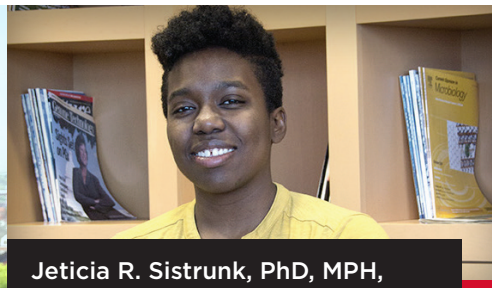
Dr. Steven Smith (right) with his mentor Dr. Jacques Ravel

Dissertation:

Identification and Characterization of Regulatory miRNAs and mRNAs in the Longitudinal Human Host Response to Vaginal Microbiota

What's Next?

Steven will be a Bioinformatics Scientist at Personal Genome Diagnostics in Baltimore



Jeticia R. Sistrunk, PhD, MPH, mentor Dr. David Rasko

Dissertation:

Characterization of Enterotoxigenic *Escherichia coli* Isolates of Varying Clinical Presentations using Comparative Genomics and Transcriptomics

What's Next?

Jeticia is currently a Postdoctoral Research Fellow at Emory University Rollins School of Public Health Department of Environmental Health

Dr. Eugene Gardner, mentor Dr. Scott Devine

Dissertation:

Mobile Element Discovery and Activity in Human Populations and Diseases

What's Next?

Eugene is now a Postdoctoral Fellow at the Wellcome Trust Sanger Institute in the UK

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Christina Stennett (left) with her mentor Dr. Rebecca Brotman

Dissertation:

Mode of Birth and Vaginal Microbiota in Reproductive-Age Women

What's Next?

Christina will be working on her doctorate in Epidemiology at the University of Maryland Baltimore

Dr. Karsten Siebel with his mentor Dr. Julie Dunning Hotopp

Dissertation:

Identification of Bacterial DNA Integration into the Human Cancer Genome

What's Next?

Karsten is now a scientist at GSK in Philadelphia

Dr. Kemi Ifeonu (left) with her mentor Dr. Joana Carneiro da Silva

Dissertation:

Genomic Resources for *Cryptosporidium* Species, Human Pathogens of Public Health Significance in Developing Countries

What's Next?

Kemi is a Bioinformatics Analyst at IGS

PUBLICATION LIST

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