IGS

INSTITUTE FOR GENOME SCIENCES

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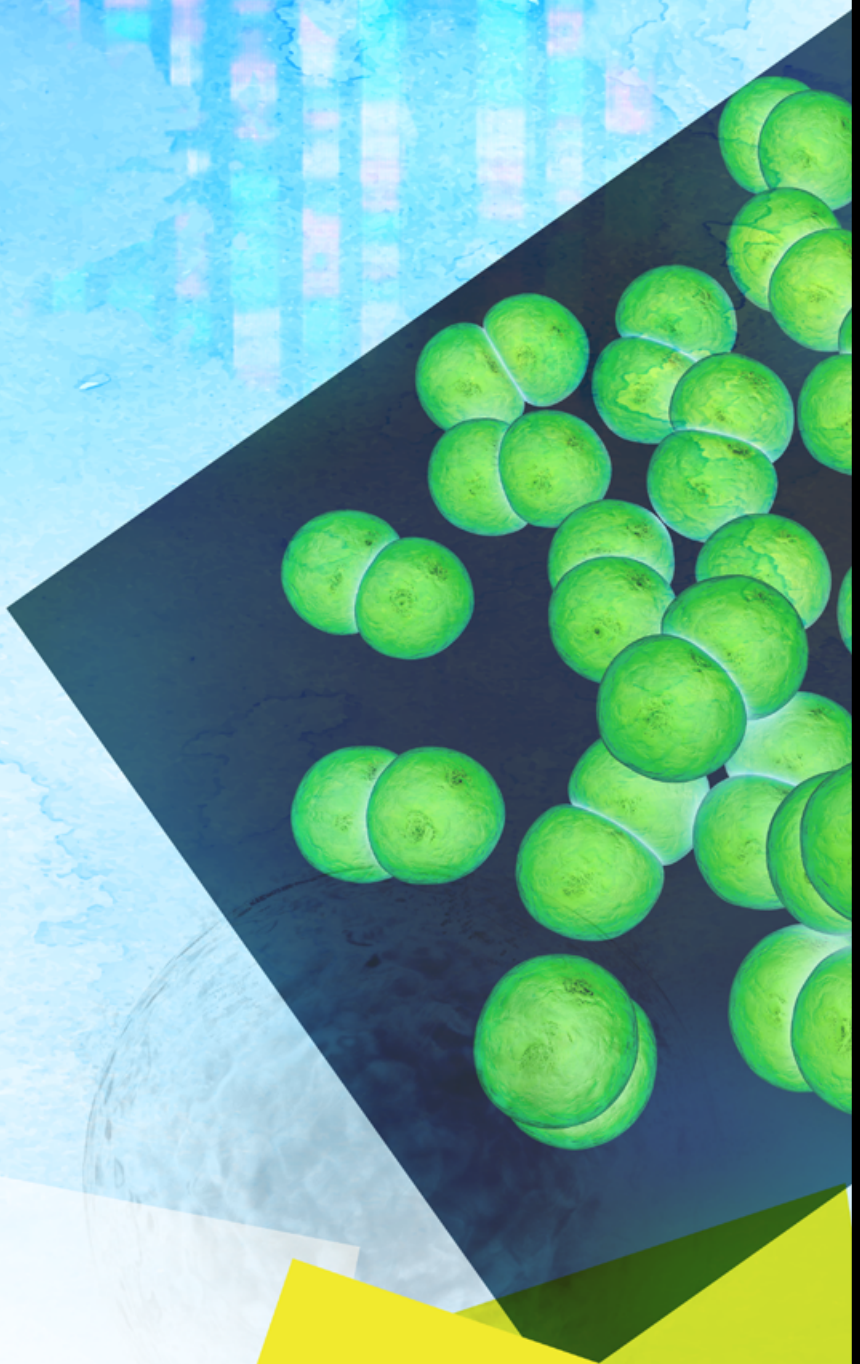

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Greeting Colleagues,

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

As hard as it is to believe, it has now been over a year that we've been working remotely. As we start our phased return back to campus in summer 2021, it is worth considering the many ways that the quarantine has profoundly changed us, and it is also a time to reflect on the long-term impact on all of us.

What have we learned, as we go back to on-site interactions?

Some have shared with me how much they appreciate the smaller things at work and within our personal lives. Face-to-face interactions with colleagues – impromptu discussions in a hallway or even shared laughs after a meeting - are some of the small things that have been missing from our virtual work lives. Others have shared that they have appreciated the respite from their long commutes in and out of Baltimore and the extra time that they have gained each day. We don't know yet what our "new normal" will be, but it is almost certain that it will be different from what we experienced before the pandemic.

Despite the challenges of the past year, I am both pleased and impressed that the collegial spirit that I consider a hallmark of IGS, has not been lost. Our faculty have used this time to apply for new grants and catch up on manuscript writing, and our staff have figured out ways to overcome the challenges of restricted research environments. Many of the IGS team members have been involved with COVID-19 testing and genomic surveillance efforts, and it has been most gratifying to be part of the state-wide effort to tackle the COVID-19 pandemic.

I am proud to share our news about many IGS accomplishments in this issue:

- The UMB campus recognition of the MSL team as "Champions of Excellence" for their extraordinary work leading COVID-19 testing **(pg.6)**
- We are at the two year milestone with our GCID grant from NIAID and we have three updates on research, tools and workshops that are part of that initiative: Julie Dunning Hotopp's FADU bioinformatic tool **(pg. 4)**, David Serre's single cell RNA sequencing work **(pg. 5)** and Michelle Giglio's online IGS workshops **(pg. 10)**
- Scott Devine's full human genomes sequencing paper **(pg. 15)**
- Tim O'Connor's paper on new increased genetic diversity in TopMed **(pg. 16)**
- Ronna Hertzano's paper on loud music and hearing loss at gyms **(pg. 7)**
- Chamindi Seneviratne and her UMB colleagues organized the 1st SIPS International meeting in the US, inviting multi-disciplinary experts on placebo research **(pg. 12)**
- We have also included highlights from my plenary session on "Understanding Dynamic Ecosystems" at the annual AAAS meeting in February. As we communicate to broad scientific communities, we have the opportunity to prioritize scientific challenges for consideration. I welcome your feedback about that session and any thoughts you might have on addressing those challenges **(pg. 13)**

I hope that you are as inspired by the stories in this issue as I am. In these challenging times, please stay safe, strong and continue your excellent work.

Sincerely,

MARYLAND COLLEGES' PROGRAM FOR COVID-19 TESTING

As Marylanders struggled with the impact of the COVID-19 health crisis during the spring 2020, leaders of educational institutions in our state were debating the safest ways to maintain a continuum of learning for students of all ages.

Early in the pandemic, Bruce E. Jarrell, MD, FACS, President, UMB, met regularly with other leaders of Maryland higher educational institutions. Dr. Jarrell realized that for a safer environment for students to return to their campuses, the colleges needed to add COVID-19 testing to maximize the likelihood for safer interactions. The planning for COVID-19 testing was one of many steps the universities had begun in the spring 2020 to help prepare a safer student environment. Other steps also included using Personal Protective Equipment (PPE), maintaining social distances for in-person interactions, limiting in-person classroom attendance, increasing virtual learning platforms, and of course, following mask requirements. Testing of students would be one of many factors that would help increase campus safety.

In April 2020, IGS had received State funding to organize and manage high-throughput COVID-19 testing to be handled at IGS through the Maryland Genomics laboratory. In June and July 2020, Lori McKay, Administrator IGS, joined Dr. Jarrell in the discussions with the leadership of Maryland colleges and universities to help the colleges link their campuses to the COVID-19 testing which IGS had begun launching that spring. In early summer 2020, accurate COVID-19 testing was not widely available everywhere, so knowing that samples could be tested within Maryland at a reputable scientific research center solved the back-end part of the challenge.

These university/college leaders quickly established the systems needed for the safest management of student sampling and the delivery of samples back to IGS. Early on, university leaders organized three specialized teams for each university: first, an Administrative group involving the President's offices/ staff to handle approvals, oversight and leadership; second, a Health Center, involving the nursing/ health staff to safely organize and collect the student samples, and third, an IT office/team for transferring large data back and forth between IGS and each university. By summer's end, sixteen Maryland colleges and universities became part of this initiative.

Anup Mahurkar, Michelle Giglio, PhD, Luke Tallon, Lisa Sadzewicz, PhD, Mike Humphrys

Lori McKay attributes the university's commitment, organizational skills and determination to the success of the program.

"When you look at the general population, positivity rates have been as high as 4-5 percent but for the university programs, positivity rates have been around one percent," McKay explains. "We've worked with such dedicated people who were resolved to have a successful testing program on their campus."

Each college has found ways to organize samples collection and delivery within their parameters.

"One factor in making this program successful is that each campus knew their student populations and knew what systems would or wouldn't work on their campus," McKay said. "They have moved quickly and efficiently to set up their own sample collection and delivery systems while maintaining the integrity of the tests."

The college testing program will continue for the future, until a greater number of students are vaccinated. Testing throughout the Maryland colleges/universities has been an extensive program, involving many people throughout all the sites, and because of the thoroughness and organization, has been a great success.

The team at IGS – involving dedicated staff from the Microbiome Service Laboratory (MSL), the Genomics Resource Center (GRC) and the Informatics Resource Center (IRC), which together make **Maryland Genomics**, as well as people at the University of Maryland Medical Center – have all worked hard for the success of this program.

FADU: NEW QUANTIFICATION TOOL FOR MEASURING BACTERIAL TRANSCRIPTOME DATA CREATED BY IGS RESEARCHERS

An important part of the NIAID **Genomic Centers for Infectious Diseases (GCID)** grant awarded to IGS in 2019 was the establishment of a Technology Core to facilitate collaborative solutions between biologists, computational informatics, and sequencing experts to improve the analysis of the infectious disease omics' data developed through the grant.

A research team led by **Julie C. Dunning Hotopp, PhD,** at IGS created a new informatics tool for analyzing bacterial transcriptomic sequence data, as part of her work applying genomics to look at the determinants of polymicrobial infectious disease outcomes.

An article describing the tool, **Feature Aggregate Depth Utility (FADU) was published in January 2021 in the journal mSystems**, an open access journal from the American Society for Microbiology (ASM).

Julie C. Dunning Hotopp, PhD, Professor, Microbiology & Immunology, UMSOM and IGS was last author, and Matthew Chung, PhD, now with NIAID Division of Intramural Research, and Shaun Adkins both from IGS, were the lead authors.

FADU was created not only to improve transcriptome analysis in GCID research projects, but to provide the larger infectious disease research community, with a data analysis tool designed specifically for prokaryotic transcriptomics research. Transcriptomic analysis is the study of the complete set of RNA transcripts (expressed genes) that are produced by the genome, using high-throughput methodologies.

As part of the GCID research projects, researchers are using large-scale genomics to investigate pathogen biology, virulence, immune evasion, microbe-microbe interactions, as well as host-microbe interactions, with a focus on improving our functional understanding of the mechanisms by which organisms exert their pathogenic potential using transcriptomics.

In their paper published in mSystems, the authors note that "most currently available quantification tools for transcriptomics analyses have been designed for human transcriptome sequence datasets, in which full-length transcript sequences, including the untranslated regions, are well annotated. In most prokaryotic systems, full-length transcript sequences have yet to be characterized, leading to prokaryotic transcriptomics analyses being performed based only on the coding sequences. In contrast to eukaryotes, prokaryotes contain polycistronic transcripts, and when genes are quantified based on coding sequences instead of transcript sequences, this leads to an increased abundance of improperly assigned ambiguous multigene fragments, specifically those mapping to multiple genes in operons." Because FADU was designed specifically to facilitate prokaryotic transcriptome analysis, it minimizes errors in the transcript quantification process, which can occur with other eukaryotic focused tools.

"One of the important aspects of the GCID Technology Core is the development and implementation of novel bioinformatics tools to take advantage of the enormous amount of sequence data that

Julie C. Dunning Hotopp, PhD

is being generated with today's high throughput sequencing technologies," says Dr. Rasko. David Rasko, PhD, Professor, Microbiology & Immunology UMSOM and IGS, is one of the Principal Investigators of the GCID grant, as well as the bacterial project leader and Administrative Core Director. He adds, "While this tool will be advantageous to the analysis of data within GCID research projects, it will have broader impact on the field as it is adopted by the infectious diseases research community."

"FADU was designed to provide 'best estimations' in systems where the structure of transcripts is unavailable, to assist in transcriptomics analysis for infectious diseases researchers," said Dr. Dunning Hotopp. "We are continuing to develop a suite of bacterially-focused tools for infectious disease bioinformatics."

GCID PARASITIC TROPICAL DISEASES: SERRE LAB & SINGLE CELL RNA-SEQ ANALYSIS

IGS was awarded the **Genomic Centers for Infectious Disease (GCID)** grant in spring 2019 from NIAID. The GCID comprises of several projects, one of which focused on integrated genomics in parasitic tropical diseases. This research involves three IGS faculty: Julie C. Dunning Hotopp, PhD, Professor of Microbiology and Immunology, Joana C. Silva, PhD, Professor of Microbiology and Immunology and David Serre, PhD, Associate Professor of Microbiology and Immunology.

Dr. Serre has been studying the life cycle of malaria parasites for many years, focusing on *Plasmodium vivax* and its response to drugs. In May 2020, his group published a paper in ***PLOS Biology*** that applied single cell genomics to study the regulation of *P. vivax* parasites.

One of the goals of GCID is to apply genomic technology to pathogen research to ultimately develop improved means of controlling these diseases in different parts of the world.

In the past, when the investigators sequenced parasite mRNA extracted from the blood of infected mammals, it was challenging to identify what was going on with what appeared to be complicated mixed samples. Were the parasites in different patients at different stages of development? Were the parasites genetically identical or did they represent different clonal populations? As part of the GCID, the Serre Lab is analyzing the gene expression of thousands of individual parasite cells present in one infected patient using single cell RNA-seq analysis. This approach affords a clear understanding of the regulation of these heterogeneous populations.

Analysis of single cell parasites allows the Serre Lab to study how individual parasites interact with each other and to examine if one parasite clone changes its regulation in the presence of another population of parasites (from the same or different species).

"We are investigating if there are 'cross-talks' between the two *Plasmodium* parasite species and if it affects the progression or severity of malaria," explains Dr. Serre. "A better understanding of the parasite populations and how they regulate their genes' expression will afford optimizing treatments to infected individuals."

David Serre, PhD

Under COVID-19 guidelines, which limit the number of researchers who can be in the laboratory at one time, it has been challenging for the Serre Lab to perform this research, especially since this work requires tight collaboration between researchers at the NIH and UMB.

https://www.medschool.umaryland.edu/profiles/David-Serre/
https://www.igs.umaryland.edu/labs/serre/

UMB CHAMPIONS OF EXCELLENCE
MICROBIOME SERVICE LABORATORY TEAM, INSTITUTE FOR GENOME SCIENCES, SCHOOL OF MEDICINE

Even before the COVID-19 pandemic unfolded in Maryland in March 2020, Mike Humphrys, MSc, and his Microbiome Service Laboratory (MSL) team got to work on addressing the novel coronavirus. The mission: Transform a genomics lab into a large-scale COVID-19 testing platform.

"We were discussing COVID-19 testing in late February and early March, and we bought the supplies we needed to develop the test and figured it out," said Humphrys, director of MSL, which is part of the Institute for Genome Sciences (IGS) at the University of Maryland School of Medicine (UMSOM).

"Once you have a swab sample in the lab, you have to extract nucleic acids — DNA and RNA —do a couple of purification steps, and then perform the actual test. We use programmable robots for that, so we took the robots and built an assembly line, then bought more robots with state funding and programmed all of them to run only COVID-19 tests."

Once the system was functional, the lab was capable of processing 1,000 samples a day, but it wasn't receiving that many because of the initial global struggles setting up COVID-19 test collection. After those front-end issues resolved and tests started pouring in, the lab could process 10,000 or more samples a day coming from various collection sites around Maryland and other nearby states.

"Our capabilities have progressed a lot since the start," Humphrys said. "During the Thanksgiving and Christmas surges, the system was able to adjust to about 1,000 to 1,200 samples an hour. It was pretty cool to see it in action."

"I think the most we've done recently is 11,000 samples in a 10-hour day," he added. "I don't think that at any time along the way we've really hit our capacity or have been totally overloaded."

Humphrys says the MSL team worked long hours, with some staff working on-site and some remotely. It was common for employees to work 12- to 18-hour days, six or seven days a week. Because of these yeoman efforts and the success of the testing initiative, the MSL team was named University of Maryland, Baltimore (UMB) 2020 Champions of Excellence.

IGS collaborated with University of Maryland Pathology Associates, UMB, the state of Maryland, and the city of Baltimore on the project, and IGS director Claire Fraser, PhD, also the Dean's Endowed Professor at UMSOM, called the MSL team's work "extraordinary."

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"The Microbiome Service Laboratory has overcome many technical and logistical challenges to make this testing program a success," Fraser said. "With Mike's calm and steady leadership and the staff's work ethic, ingenuity, and collaborative approach, the lab has inspired all of those involved in this effort across campus and across the state."

In normal times, MSL supports research studies designed to characterize the bacteria that compose the human microbiome, essentially anything on Earth that is inhabited by bacteria and microorganisms. And while most of the nearly 40-person team is still working on COVID-19 research — including the study of coronavirus variants in positive test samples — a few have shifted back to other research studies.

No matter the project, Humphrys says his team is up to the challenge, and he appreciates MSL's recognition as a UMB Champions of Excellence.

"Everybody has worked tirelessly and selflessly to get this done, and I'm proud of them all," he said. "Robotics and molecular biology are familiar to us, because we are all researchers. This clinical component was very new to us, but we basically shed our previous lives and switched over to combat this virus. And that's pretty remarkable."

— Lou Cortina

LOWERING MUSIC VOLUME AT GROUP SPIN CLASSES DOES NOT AFFECT INTENSITY OF WORKOUTS, UM SCHOOL OF MEDICINE RESEARCHERS FIND

Research Calls Attention to Dangerous Noise Levels in Gym to Protect Against Noise Induced Hearing Loss

Ronna Hertzano, MD, PhD

Fitness instructors often crank up the music in gyms – sometimes loud enough to cause hearing damage -- based on their assumption that people will work out harder when the music is louder. A new University of Maryland School of Medicine study, however, found that those who attend spinning classes do not lower the intensity of their workouts when the volume gets turned down to a safer decibel level. The findings were published in March 2021 in the journal *Noise & Health*.

"Our findings make a strong case for reducing music volumes in fitness classes to protect against hearing loss without sacrificing the intensity of the workout," said study senior author Ronna Hertzano, MD, PhD Associate Professor of Otorhinolaryngology-Head & Neck Surgery at UMSOM, with a joint appointment at the Institute for Genome Sciences (IGS). She was an avid gym goer before the COVID-19 pandemic. "In fact, our study participants reported that they preferred the reduced sound level during their workouts."

Previous research suggests that the average sound levels in group fitness classes frequently exceed 90 decibels (as loud as an approaching subway train) and often exceed 100 decibels (as loud as a power lawn mower). The National Institute of Occupational Safety and Health recommends that the noise exposure of one hour not exceed 94 decibels, whereas exposures to levels of 100 decibels not exceed 15 minutes to protect against permanent hearing loss.

In the new study, the researchers selected a gym in the local Baltimore area and conducted surveys on participants, age 31 on average, who signed up for one-hour spinning classes. Music volumes in the spinning classes during the study ranged from 93 to 101 decibels. In the classes that were 2 to 3 decibels lower than the loudest classes—

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which translates to about a 50 percent reduction in power and a 20 percent reduction in perceived loudness—participants reported no differences in their exercise intensity. Those in classes with the lowest volume experienced a slight reduction in exercise intensity, but only two of these participants reported below average exercise intensity.

Overall, more than 1 in 4 study participants reported experiencing auditory symptoms following their spinning class including ringing in their ears or muffled hearing. In those in classes with the highest sound levels, nearly one-third of participants reported that the sound level was too high, and nearly one-third reported that they would prefer a decrease of the music level. Only three of the participants reported using hearing protection, like ear plugs, during the study.

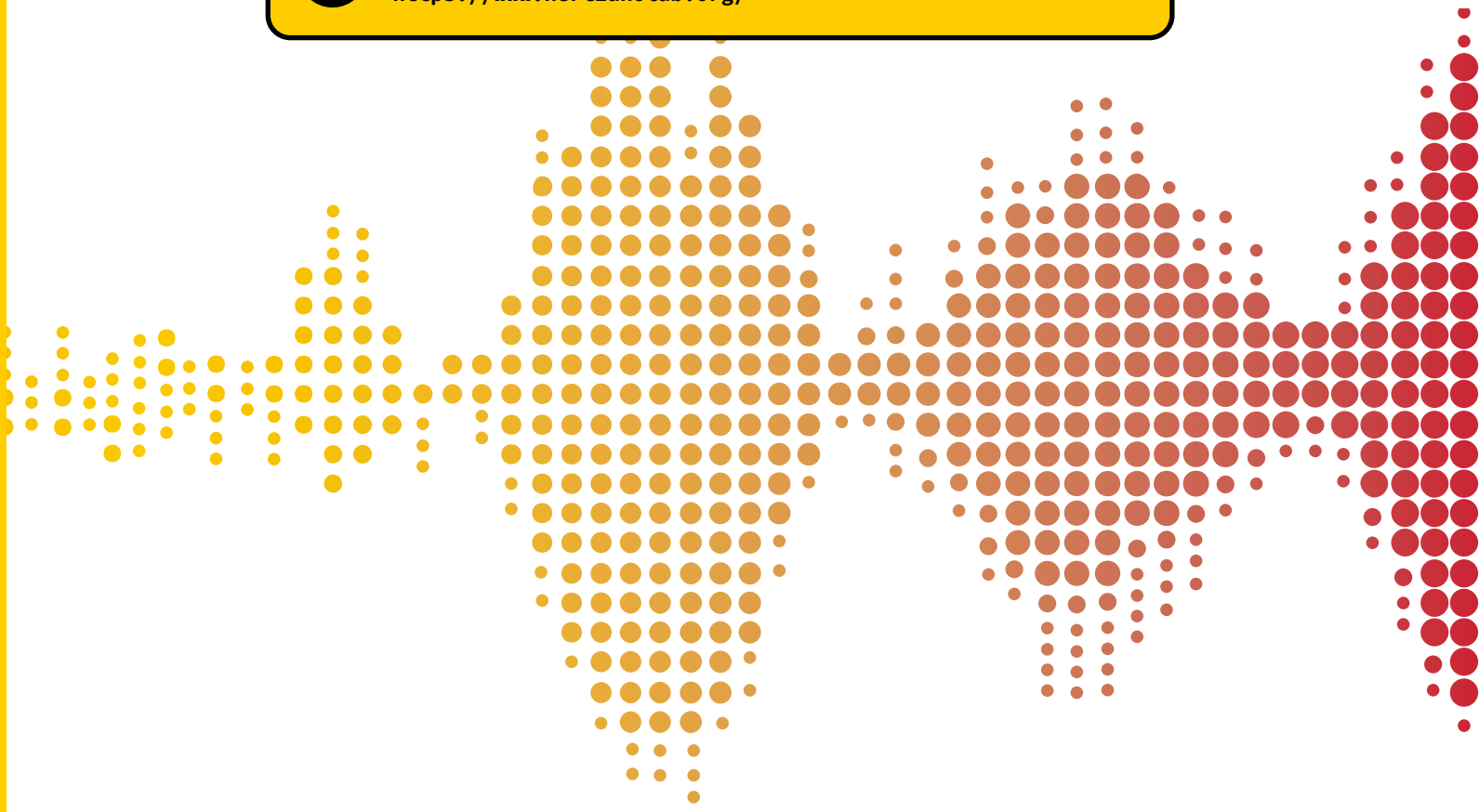
"We also found that participants were most likely to report that the music level was satisfactory in classes where sound levels were lowest," said Dr. Hertzano. "Importantly, the gym elected to maintain the music at the softer level after we made them aware of our study results."

Lawrance Lee, a 4th year medical student at UMSOM, Benjamin Shuster, a research fellow in the Department of Otorhinolaryngology-Head & Neck Surgery at UMSOM, and Yang Song, PhD, a postdoctoral fellow at IGS, all served as lead co-authors on the paper. Researchers from Massachusetts Eye and Ear in Boston and Otolith Labs in Washington, DC also participated in this study.

"This is an important new finding that calls attention to the dangers of sound levels in fitness classes and the subsequent hearing loss that can result from prolonged exposure," 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. "Fitness facilities should take note of the dangers highlighted in the new study finding and turn down the volume to protect against hearing damage."

https://www.medschool.umaryland.edu/profiles/Hertzano-Ronna/

https://www.hertzanolab.org/



INSTITUTE FOR GENOME SCIENCES WORKING WITH THE STATE OF MARYLAND TO SEQUENCE MORE THAN 10 PERCENT OF POSITIVE COVID TESTS

In an effort to monitor the spread of COVID-19 variants in the State of Maryland, **Maryland Genomics** at UMSOM is performing genome sequencing of variants in at least 10 percent of COVID-19 test samples, reaching an important benchmark set by the federal government to help control the spread of these variants.

The State has entered into separate agreements with UMSOM and Johns Hopkins Medicine in an effort to double the state's surveillance of coronavirus variants to more than 10 percent of COVID-19 cases, Governor Larry Hogan announced in March. This enabled Maryland to achieve the surveillance goal set by the Centers for Disease Control and Prevention to monitor the spread of variants.

The sequencing is being conducted at **Maryland Genomics**, a high-throughput sequencing and analysis center at IGS. The laboratory team, which has more than two decades of high-throughput sequencing expertise, is sequencing the viral genomes to identify variants in positive samples containing the SARS-CoV-2 virus which causes COVID-19.

"We are monitoring for any variants including those that were originally discovered in South Africa, the United Kingdom, Brazil, the US and India. Some of these, including the UK variants tend to be more contagious," said **Jacques Ravel, PhD**, Professor of Microbiology and Immunology at UMSOM and Associate Director of IGS.

"More importantly, viral genome sequencing can detect new variants that are circulating, and we do not yet know about."

Information from variant monitoring can be used in multiple ways. First and foremost, it provides valuable surveillance data to state health officials on the spread of variants through local cities and communities. This information is used along with contact tracing to determine whether certain variants are more contagious. It is also used to determine whether vaccinations are protecting against these variants.

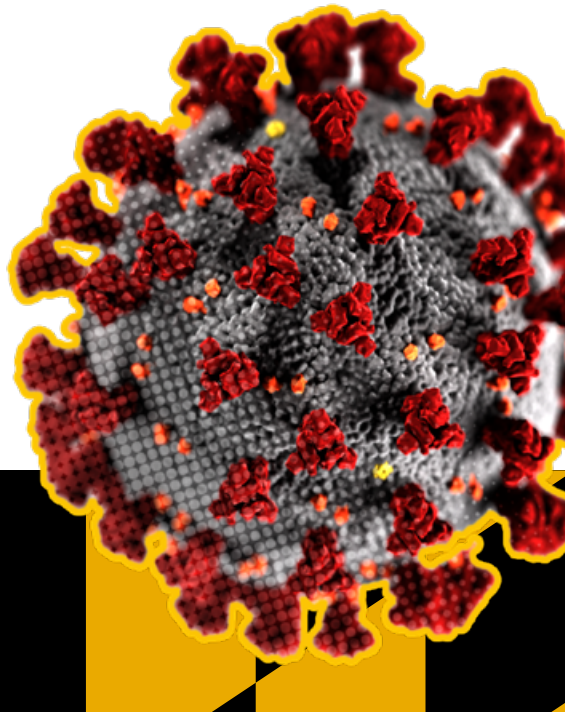
"If a previously vaccinated individual tests positive for SARS-CoV-2, genome sequencing will tell us whether they contracted a variant strain," said Luke Tallon of IGS, and Scientific Director of Maryland Genomics. "This information helps us to determine whether vaccines protect against variants."

Over the past year, Maryland Genomics, in collaboration with the University of Maryland Pathology Associates (UMPA) and with support from the State, has performed close to 1 million COVID-19 tests supporting universities, nursing home facilities, urgent care locations, correctional facilities and community testing sites throughout the State. The new sequencing effort involves using positive test samples identified by the testing lab and from all hospitals in the University of Maryland System.

"Since we refocused much of our high-throughput laboratory infrastructure to COVID-19 testing almost a year ago, we have achieved many impressive milestones that have enabled us to become an important partner with the State of Maryland in helping to provide rapid and accurate testing to Maryland residents," said **Claire Fraser, PhD**, the Dean's Endowed Professor and Director of IGS.

> **"Our new mission to perform genome sequencing of variants is a natural progression of this effort, and we are proud to partner with the State once again on this important public health mission."**
>
> **— Claire Fraser, PhD**

Over the past two decades, the Maryland Genomics/IGS team have contributed to large-scale genome sequencing and analysis of prior viral outbreaks, including influenza, rhinovirus (common cold), Zika, Ebola, and others.



IGS WORKSHOPS – PIVOTING TO VIRTUAL PLATFORMS

Offering workshops to help a broader community learn the essentials of bioinformatics is an integral part of IGS' mission.

Pre-Covid Workshops

When the pandemic shutdown began in mid-March of 2020, the first workshop of the year, Microbiome Analysis, was just about to begin. **The Microbiome Analysis Workshop** is one of IGS' most popular workshops and attracts a broad and international audience of faculty members, post-doctoral fellows, and graduate students. The first step was to immediately postpone the March 2020 workshop to November 2020 with the logic at that time that the quarantine would only last a few weeks or months. However, as it became clear that the pandemic would be long-lasting, the IGS educational team pivoted to figure out ways to offer the workshop online.

Transitioning an in-person learning program to a virtual platform involves complex logistics. Typically for IGS bioinformatics workshops, the informatics/IT department spend considerable advance time to prepare datasets, tools, and computational workspaces for the participants so that exercises can be smoothly executed, the appropriate data is ready, and that attendees can complete their work. All of this continued for the virtual workshops as well, but with the added challenge that everything would need to work outside of the IGS environment and be easy for attendees located anywhere to access and use. Michelle Giglio, PhD, IGS Outreach Coordinator, Heather Creasy, Microbiome Workshop Content Coordinator, IT staff Erik Anderson and David Shoemaker, and workshop instructors planned the content for the online experience. The team prepared tools and resources that registrants had to download to their own laptops or use on an Amazon Cloud environment.

For in-person workshops, organizers always prepare backup laptops for attendees to use, in case there are problems using their own laptops. In this case, use of IGS laptops was not an option so everything needed to be clear and easy for attendees to do remotely. "During the training, when inevitable technical difficulties arose, things that would have been easy to address in person were more challenging to resolve remotely," explained Dr. Giglio, "but ultimately, we were able to use the online conference platform and breakout rooms to get things sorted out for all of the attendees."

Interestingly, one challenge for hosting these virtual workshops for an international registrant group is scheduling the hours to be conducive for global time zones. To accommodate the people on the North American West Coast as well as European attendees, the best "sweet spot" for timing was late morning EST until late afternoon – a slightly shorter workday than the class usually involved. However, even those hours were a bit late for attendees in Europe and future virtual workshops will have shorter hours each day with added days to make up the lost time.

There is much interest in the microbiome and for learning more about host/microbe interactions so the Microbiome Analysis workshop continues to be one of IGS' most popular classes. The fall 2020 workshop was completely full, with a waitlist of more than 20 people.

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Dr. Giglio and other workshop organizers are planning out the workshop schedule for the rest of 2021 and will likely continue offering workshops virtually only. Other workshops that may be offered virtually in 2021 are the Introduction to Python workshop and the Introduction to 'Omics workshop. As the IGS Informatics and Educational groups look to 2022, it is anticipated that there will be a mix of in-person and virtual workshops. Dr. Giglio comments, "One thing we've discovered through our experience in 2020 is that workshop content can be very effectively communicated online, and many people are able to attend virtually who would otherwise find the cost and time commitment of a trip to our campus prohibitive. Thus, we expect virtual workshop offerings to be part of our ongoing program moving forward."

Dr. Giglio is Associate Professor, Medicine (Endocrinology) at the UM School of Medicine and lead Educational Coordinator at IGS. Heather Creasy is a Lead Bioinformatics Analyst at IGS.

Michelle Giglio, PhD

https://www.medschool.umaryland.edu/profiles/Giglio-Michelle/
https://www.igs.umaryland.edu/education/outreach.php

FIRST TIME SOCIETY FOR INTERDISCIPLINARY PLACEBO STUDIES (SIPS) HOSTED IN US

IGS Researcher and Three UMB Colleagues Hosted International Conference

The University of Maryland, Baltimore (UMB) hosted the third International Conference of the Society for Interdisciplinary Placebo Studies (SIPS) virtually May 26-28, 2021. The conference was titled "Harnessing Placebo Mechanisms for Optimal Pain Management and Treatment of Alcohol and Other Drug Use Disorders."

Chamindi Seneviratne, MD

This was the first time the conference was hosted by an institution outside of Europe. The event was a collaboration among the UM schools of Medicine (UMSOM), Nursing (UMSON), and Pharmacy (UMSOP).

The planning committee consisted of Luana Colloca, MD, PhD, MS, Associate Professor, UMSON; Chamindi Seneviratne, MD, Assistant Professor, UMSOM; Jason Noel, PharmD, Associate Professor, UMSOP; and Patricia Franklin, PhD, RN, adjunct Assistant Professor, UMSON.

SIPS

SIPS is an international association of scholars who share the goal of understanding the placebo effect in medical treatment, psychotherapy, and complementary and alternative treatment.

Expert faculty from UMSOM, UMSON, and UMSOP collaborated with SIPS to design an interdisciplinary and international conference to advance the science of placebo research and mind-body mechanisms, and to apply this knowledge to alcohol use and pain disorders.

The audience included scientists, clinicians, researchers, students and any people interested in placebo effects in pain, alcohol and substances.

"There is a global interest in placebo effects, and many of the top researchers in this field presented at the conference," said Dr. Seneviratne. "Placebo effects are well studied in pain research, but not as thoroughly researched yet in alcohol and other substance use disorders. We had a great exchange of ideas because of the interdisciplinary mix of attendees."

Chamindi Seneviratne, MD, is Assistant Professor with joint appointments in SOM, Psychiatry and IGS. She has been studying placebo effects in alcohol use dependency (AUD) and applying genomic tools to study genetic predictors for certain behaviors. In 2018, she was awarded a five-year RO1 grant through the **National Institute of Alcohol Abuse and Alcoholism (NIAAA)**, part of the NIH. Her primary focus is in developing genomic biomarkers to improve treatment and diagnosis of alcohol use disorders.

Registrants had access to live presentations and networking events on a virtual platform. Attendees also received continuing education credits for the conference. To learn more, go to **https://sips-conference.com/home.**

https://www.medschool.umaryland.edu/profiles/Seneviratne-Chamindi/

Claire M. Fraser, PhD

IGS DIRECTOR CLAIRE M. FRASER, PHD, DELIVERS PLENARY LECTURE AT AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE (AAAS) ANNUAL MEETING

Dr. Fraser, Pioneer in Genomic Medicine, Delivered Remarks as Capstone to Her Presidency of AAAS During the Past Year

Claire M. Fraser, PhD, Director of IGS, recently concluded her illustrious year as President of the **American Association for the Advancement of Science (AAAS)** with a stirring lecture at the group's annual meeting. She called for forceful changes that will leave the U.S. and world better prepared for the next global pandemic. Such changes, she said, include the need to address the systemic racism and health disparities that led to higher COVID-19 hospitalization rates and death rates in Black communities. They also include a reframing of climate change policies to help the public understand the immediate and long-term health benefits of lower carbon emissions including cleaner air and potential protection against future epidemics.

With much of her tenure focusing on the COVID-19 pandemic and the worldwide upheaval it caused, Dr. Fraser decided to focus her lecture on "Lessons from the COVID-19 pandemic in an interconnected world". She delivered the **Plenary Lecture** on February 8th at the 2021 Annual Meeting, which she chaired.

This year's meeting was virtual with online lectures and sessions to discuss the latest research. With 120,000 members from more than 91 countries, AAAS is the world's largest multidisciplinary scientific society and the publisher of the well-respected Science family of journals.

Dr. Fraser opened her remarks by explaining the theme of the annual meeting, "Understanding Dynamic Ecosystems," which she chose before COVID-19, to focus on the complex networks that we study, and those in which we live and work.

"To me, one of the most fascinating attributes of ecosystems is that of emergent properties – a term that has been used in science, systems theory, philosophy, urban studies and even art," Dr. Fraser said in her opening remarks. "When we talk about emergent properties, we refer to those properties that are entirely unexpected based on our understanding of the individual components of any given ecosystem – the properties that arise from the collaborative functions across scales."

Evolution of Fraser's 25 Years of Research

Dr. Fraser went on to highlight the evolution of her own research over the past twenty-five years to embrace – indeed, to require, an ecosystems perspective. In 1995, she and her colleagues were the first to apply the tools of the genomics revolution to sequence the first complete genome of a free-living organism, *Haemophilus influenzae*, a bacterium responsible for meningitis, ear infections and other respiratory ailments, primarily in children. This achievement took place at The Institute for Genomic Research (TIGR), where Dr. Fraser served as Director from 1998 until 2007.

This first genome sequencing project forever changed microbiology and launched a new field of study—microbial genomics.

"As our understanding of the human microbiome increases, it's requiring us to think very differently about health and disease – not just from the perspective of individual organ systems, but instead from an appreciation that we as humans, are a complex ecosystem embedded in a larger planetary ecosystem," said Dr. Fraser during her lecture.

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"Only a tiny fraction of the viruses that surround us pose any threat to humans, but given the staggering numbers of viruses, it should then come as no surprise that SARS-CoV-2 emerged with pandemic potential. To many who study viral diversity and evolution, it was just a matter of time."

In an editorial entitled **"A genome to celebrate"** published in the February 5, 2021 issue of *Science*, Dr. Fraser noted that one of the enduring legacies of these early genome efforts is the research ecosystem that was created for tackling complex, technology- driven, data-intensive multidisciplinary projects that has effectively been leveraged for other large-scale efforts that include the 1000 Genomes Project, the Cancer Genome Atlas, the Human Microbiome Project, and the Human Brain Project.

During her time at TIGR, Dr. Fraser and her team also sequenced the bacteria behind syphilis and Lyme disease, and eventually the first plant genome and the first human-pathogenic parasite. She and her colleagues also helped identify the potential source of a deadly 2001 anthrax attack in one of the biggest investigations conducted by U.S. law enforcement. In 2007, Dr. Fraser launched the Institute for Genome Sciences (IGS) at the University of Maryland.

Link Between Climate Change and Global Pandemics

Dr. Fraser also highlighted in her lecture the importance of climate change as part of the continually evolving COVID-19 pandemic. "History has shown us that disasters can often be the time of biggest change," she said. "A first we hopefully have learned from the past year is that when necessary, we can mobilize on a global scale to get things done."

She suggested experts strategize on how to make new climate policies more appealing to the public. Rather than focusing on the specifics of emissions reductions, they should instead focus on the economic, social, and health benefits of new climate policies.

"Each of us must play a more active role in engaging with the public in meaningful ways - getting out into our respective communities to work with civic leaders, and local and state policy makers to address a range of issues that they deem to be relevant to them."

— Dr. Fraser

She pointed out that just as the COVID pandemic has disproportionately burdened the economically disadvantaged, climate change and its mitigation policies will also disproportionately affect the poor. The burden of increasing temperatures and the loss of jobs in the fossil fuel industry will take a greater toll on them.

"Climate change poses an existential threat to our natural world and the fabric of society – and we must remember that this is not an 'us vs them' situation. We must showcase successful bipartisan action, whenever possible, to reduce polarization," she said.

Need to Reverse Systemic Racism

Dr. Fraser underscored the need to address the systemic racism that exists in the sciences quoting a *Science* editorial written last year that pointed to racial biases and structural racism embedded in academic institutions. "We will pay a substantial price if we don't tackle systemic racism now," she said.

In closing, she focused on the critical role science has to play in setting policies to help combat future globally disruptive threats. "As we saw with COVID-19, data may be contradictory at times, and diverse views may emerge, and these will need to be refined and discussed as more data accumulate," she said.

Dr. Fraser emphasized that if any lesson can be learned from the COVID-19 pandemic, it is that we need to fully embrace "a science of preparedness" and understand that our actions have consequences and that our world holds the capacity for transformative action.

"Listening to Dr. Fraser's presidential address, I am spurred to champion the causes that she highlighted so passionately," said Kaye Husbands Fealing, PhD, Dean of Ivan Allen College of Liberal Arts and Ivan Allen Jr. Chair at the Georgia Institute of Technology. "We need to ensure that diverse communities are engaged in the scientific enterprise. It is an honor to serve on the AAAS Executive Board with such an impactful leader who believes that science should be in the service of humanity."

IGS RESEARCHERS PARTICIPATE IN LANDMARK STUDY DETAILING SEQUENCING OF FULL HUMAN GENOMES TO BETTER CAPTURE GENETIC DIVERSITY

64 Human Genomes Sequenced Will Serve as A New Reference for Genetic Variation and Predisposition to Human Diseases

Researchers at IGS at UMSOM co-authored a study, published **February 25 in the journal *Science***, that details the sequencing of 64 full human genomes. This reference data includes individuals from around the world and better captures the genetic diversity of the human species. Among other applications, the work will enable population-specific studies on genetic predispositions to human diseases, as well as the discovery of more complex forms of genetic variation.

Twenty years ago in February 2001, the International Human Genome Sequencing Consortium announced the first draft of the human genome reference sequence. The Human Genome Project, as it was called, required 11 years of work and involved more than 1000 scientists from 40 countries. This reference, however, did not represent a single individual, but instead was a composite of humans that could not accurately capture the complexity of human genetic variation.

Building on this, scientists have conducted several sequencing projects over the last 20 years to identify and catalog genetic differences between an individual and the reference genome. Those differences usually focused on small single base changes and missed larger genetic alterations. Current technologies now are beginning to detect and characterize larger differences – called structural variants – such as insertions of new genetic material. Structural variants are more likely than smaller genetic differences to interfere with gene function.

The new finding in *Science* announced a significantly more comprehensive reference dataset that was obtained using a combination of advanced sequencing and mapping technologies. The new reference dataset reflects 64 assembled human genomes, representing 25 different international human populations. Importantly, each of the genomes was assembled without guidance from the first human genome composite. As a result, the new dataset better captures genetic differences from different human populations.

"We've entered a new era in genomics where whole human genomes can be sequenced with exciting new technologies that provide more substantial and accurate reads of the DNA bases," said study co-author **Scott Devine, PhD**, Associate Professor of Medicine, UMSOM and IGS. "This is allowing researchers to study areas of the genome that previously were not accessible but are relevant to human traits and diseases."

Institute for Genome Sciences (IGS)' Genome Resource Center (GRC) was one of three sequencing centers that generated the data using a new sequencing technology that was developed recently by Pacific Biosciences. The other two centers were Jackson Labs and the University of Washington. The GRC is one of only five early access centers that was asked to test the new platform.

Scott Devine, PhD

Dr. Devine helped to lead the sequencing efforts for this study and also led the sub-group of authors who discovered the presence of "mobile elements" (i.e., pieces of DNA that can move around and get inserted into other areas of the genome). Other members of the IGS at the University of Maryland School of Medicine are among the 65 co-authors. Luke Tallon, Scientific Director of the GRC, worked with Dr. Devine to generate one of the first human genome sequences on the Pacific Biosciences platform that contributed to this study. Nelson Chuang, a graduate student in Dr. Devine's lab also contributed to the project.

DATA DEMONSTRATES NEW INCREASED DIVERSITY IN GENETIC STUDIES AND PROVIDES NEW INSIGHTS INTO POPULATION-SPECIFIC DISEASES

Timothy O'Connor, PhD

Researchers at the UMSOM and IGS and their colleagues published a new analysis on February 10, in the journal ***Nature*** from genetic sequencing data of more than 53,000 individuals, primarily from minority populations. The early analysis, part of a large-scale program funded by the **National Heart, Lung, and Blood Institute (NHLBI)**, examines one of the largest and most diverse data sets of high-quality whole genome sequencing, which makes up a person's DNA. It provides new genetic insights into heart, lung, blood, and sleep disorders, and how these conditions impact people with diverse racial and ethnic backgrounds, who are often underrepresented in genetic studies.

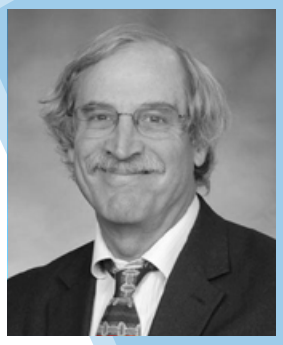
The program, called **Trans-Omics for Precision Medicine (TOPMed)**, seeks to understand the genetic variations that occur among individuals both in nuclear families and in populations from diverse ethnicities residing on different continents. The project's ultimate goal is to improve the diagnosis, treatment, and prevention of the most common conditions that lead to disability or death.

"We have already identified some surprising new insights," said study corresponding author Timothy O'Connor, PhD, Associate Professor of Medicine & Endocrinology UMSOM and IGS. For example, the team identified more than 400 million genetic variations, but 97 percent of them are extremely rare, occurring in less than one percent of the population. Gene variations or variants can occur by random chance when genes get recombined or mutate.

"Most of the time, these variants mean nothing," said Dr. O'Connor, "but they can provide a new understanding of mutational processes and recent human evolutionary history."

The TOPMed team includes more than 180 researchers from leading institutions in genomics worldwide, who have been compiling huge datasets in systematic and defined ways to increase knowledge about diversity in genetic studies. Since its launch in 2014, the TOPMed investigators have begun adding whole genome sequencing and "omics" analyses (which includes a study of genetic and molecular profiles like proteins) to research studies in order to better understand how variations affect different organ systems giving rise to disease in, for example, the heart and lungs.

In the new *Nature* paper, the researchers pointed out that the program "aims to identify causal genetic variants and how they interact with the environment, to characterize disease and its molecular subtypes, to understand differences in disease across diverse ancestries, and to establish a foundation for personalized disease prediction, prevention, diagnosis, and treatment." **Braxton Mitchell, PhD**, Professor of Medicine at UMSOM, and **Jeffrey O'Connell, PhD**, Associate Professor of Medicine at UMSOM, were co-authors on this paper.



Braxton Mitchell, PhD

Jeffrey O'Connell, PhD

TOPMed is the largest sequencing project to date and has identified over 400 million gene variants with an overarching mission of understanding global genetic diversity. Since joining the TOPMed program in 2016, UMSOM researchers have

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published valuable new insights on genetic diversity, including sequencing data from the initial flagship paper on the first 53,831 TOPMed samples.

The increasing diversity of the population samples will help investigators learn more about how specific diseases impact different ethnic populations around the world. In addition, the group has established uniform standards for sequencing performed on a massive scale. The standards maximize the integrity of the data as the large group of international researchers use uniform methods as they continue to add other "omics" methods for analysis such as the study of metabolic differences.

In addition to enabling detailed analysis of the combined genomic and health data for sequenced samples, TOPMed has enhanced the analyses of genotyped samples through a new reference panel that now includes over 97,000 individuals. The TOPMed imputation reference panel is publicly available for review and input of new genetic data by researchers.

The first stage of the data release in the *Nature* study demonstrated a greater inclusion of a diversity of samples, which will be invaluable to the international group in learning more about the diseases impacting these populations. Because of the vast sample sizes and the longitudinal scope of many of the population samples, the investigators were able to demonstrate that the rare variants represent recent and potentially deleterious changes that can impact protein function, gene expression, or other biologically important elements.

"This is a major effort to rectify the underrepresentation of minority participants in genomic studies and tracks with a broader mission within the School of Medicine to increase diversity in clinical trials," said **E. Albert Reece, MD, PhD, MBA**, Executive Vice President for Medical Affairs, UM Baltimore, the John Z. and Akiko K. Bowers Distinguished Professor and Dean, University of Maryland School of Medicine.

Cashell Jaquish, Ph.D., an NHLBI program officer for TOPMed and a corresponding author on the Nature paper, agrees. "The NHLBI's TOPMed program is a huge resource for the scientific community. We didn't really know what genomic variation looked like in diverse groups until now. This new study represents truly historic findings, and we look forward to continued research studies in this area as we move toward personalized medicine."

WELCOME DARIA GAYKALOVA – NEW IGS FACULTY

Daria Gaykalova, PhD joined the IGS faculty in September 2020, in the midst of the global COVID quarantine and campus remote teleworking. She is an Associate Professor with joint appointments in the Department of Otorhinolaryngology - Head and Neck Surgery, at the **Marlene and Stewart Greenebaum Comprehensive Cancer Center (UMGCCC)**, and with IGS.

Daria Gaykalova, PhD

As a cancer biologist with a background in pharmacology, Dr. Gaykalova is focused on developing novel cancer therapies, particularly for tumor types that lack effective disease-specific treatment options, such as head and neck squamous cell carcinoma (HNSCC). She heads the Cancer Epigenetics laboratory, which defines the functional role of epigenetics in the regulation of expression of canonical and alternatively spliced transcripts. Her team has recently characterized the landscape of the cancer-specific alternative splicing events (ASE) in HNSCC and defined their potential role in cancer formation. Moreover, the recent data from her group suggest that chromatin, and in particular, enhancers, have a regulatory role in the expression of cancer-specific ASE isoforms. Dr. Gaykalova is interested in exploring if both processes (splicing and

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chromatin remodeling) can be therapeutically controlled. Such potential therapeutic strategy can form the basis for the development of effective disease-specific therapeutics for this disease, as well as other solid tumors.

Her campus collaborations include the Department of Otorhinolaryngology, the School of Dentistry, Medical Oncology, and many researchers within the UMGCCC, with Pathology Biorepository Shared Service (PBSS), with the Translational Laboratory Shared Service (TLSS), the Genomics Shared Service (GSS), the Biostatistics Shared Service (BSS), and primarily IGS Maryland Genomics (GRC and IRC).

On the first day at work, Dr. Gaykalova met the entire team of IGS faculty over Zoom, recognizing many of the faculty from her interview meetings. She also met some of IGS faculty and staff on-site.

CORE VALUES AWARDS

Riham Keryakos

Riham Keryakos' Help with Core Values Committee

The University of Maryland, Baltimore (UMB) Core Values Awards recognize faculty, staff and students who exemplify UMB's core values of accountability, civility, collaboration, diversity, excellence, knowledge and leadership.

These values are central to UMB's mission and are bestowed by the UMB president to recognize members of the University community, who, through their actions, work to foster and strengthen UMB's value-driven culture. The Awards are given to individuals and/or teams who demonstrate outstanding contributions to the UMB community. A nomination may be for an action, a special project or initiative, exemplary service or an achievement that occurred during the calendar year.

The deadline for award submissions was in February and the Core Values Award winners were announced in early April.

We are fortunate at IGS that Riham Keryakos, Office Manager, Ravel Laboratory, has been active for the past two years in the President's Core Values Awards selection committee. This year, Riham is serving on the selecting committee for two of the Core Values Awards, in the category of Diversity and Collaboration Teams.

Asked about her experience helping select the individuals or units who best exemplify the Diversity and Collaboration Teams, Riham encourages everyone to get involved in services to the UMB community. "UMB is a large campus and when involved in organizations like the Staff Senate and various committees, you learn more about our work environment, and you are part of initiatives to improve it. You appreciate the opportunities UMB is giving to its employees and students, and you build strong collaborations across campus. You can also find out about the exemplary people who are nominated for the Core Values Awards," said Riham.

Riham has also served as a Member-at-Large, and Vice President, for Staff Senate Executive Committee. Additionally, she previously chaired Staff Senate Communications and Board of Regents Staff Awards' committees, where in 2020, UMB has three staff employees winning USM Staff Awards.

She is passionate about representing IGS at different UMB committees, as well as advocating for School of Medicine Staff, helping communicate various work issues to the President's Office, through Staff Senate. (Note: the Faculty Senate is a different entity that represents faculty interests). Started in 1994, the Staff Senate serves as an advisor and a channel of communication to the UMB President and the President's cabinet in the areas of policy and procedures.

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