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INSTITUTE FOR GENOME SCIENCES

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UNIVERSITY of MARYLAND
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Greetings Colleagues,

It certainly feels good to be back on campus, and to re-engage with colleagues in person after many months away. COVID-19 is not yet fully in the rear-view mirror, and our testing operations will continue, at least through the end of this academic year, as we provide ongoing support to some of the State's colleges, universities, and nursing homes in their COVID-19 surveillance efforts. I again want to acknowledge the heroic efforts of the COVID-19 team that kept normal IGS operations going, while also running the high-throughput testing laboratory for the past 20 months. Their willingness to step up during this time of great challenge has been truly inspirational.

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

- A new $7.5M U19 award to Jacques Ravel to develop a model of female reproductive tract to study infections **(pg.3)**
- IGS promotions **(pg.15)**
- Tale of Two Parasitic Diseases **(pg .8)**
- Probiotic Yogurt and Microbiome Changes **(pg. 10)**
- Johanna Holm's KO1 grant **(pg.5)**
- The Sokolove mentoring award to Jacques Ravel **(pg.11)**
- The GPILS PhD Scholar award to Maddy Alizadeh **(pg.15)**
- The Researcher of the Year Award to Ronna Hertzano **(pg.12)**
- The BICCN papers **(pg.14)**

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

Finally, I want to take this opportunity to tell you about some upcoming IGS transitions. Beginning in February 2022, I will be taking a sabbatical to spend some time exploring pressing issues that I was involved with during my time as President of AAAS – in particular, the challenge of implementing science-based policy against a backdrop of tremendous skepticism and distrust on the part of the general public. During my time away, Dr. Jacques Ravel will serve as Interim Director of IGS. We will also be saying good-bye to two long-term IGS employees in the next few months. Sarah Pick, our Director of Marketing & Public Relations, will be retiring December 31, 2021, and Lori McKay, our Senior Administrator, will be retiring January 31, 2022. Sarah and Lori have been instrumental in our success of over the past 14 years, and they have been outstanding IGS ambassadors here on campus and beyond. In particular, I want to acknowledge Lori's extraordinary effort in coordinating all the COVID-19 testing operation for 21 Maryland colleges and universities. We wish them both much happiness as they start a new chapter in their lives.

Stay tuned for updates early next year on our 15th anniversary events.

I wish you all a safe and healthy holiday season!

Sincerely,

INSTITUTE FOR GENOME SCIENCES RECEIVES $7.5 MILLION GRANT TO CREATE COMPLEX MODEL OF FEMALE REPRODUCTIVE TRACT TO STUDY INFECTIONS

Research Will Help Identify Mechanisms by Which the Microbiome Affects the Susceptibility to Sexually Transmitted Infections

Researchers at the Institute for Genome Sciences (IGS) at the University of Maryland School of Medicine have received a $7.5 million federal grant to create a complex model of the female reproductive system to study sexually transmitted infections (STIs). They plan to create a realistic three-dimensional (3D) model that integrates vaginal and cervical epithelial cells, feeder endothelial cells and the complex bacterial communities that colonize the lower reproductive tract, i.e., the vaginal microbiome. They aim to use this model to identify factors that play a role in chlamydial and gonococcal infections experienced by an ever-growing number of young women in the U.S. and worldwide.

The grant was awarded to principal investigator **Jacques Ravel, PhD**, Professor of Microbiology and Immunology at UMSOM and Associate Director of UMSOM's IGS. His co-principal investigators will be long-time collaborator and chlamydia expert, **Patrik Bavoil, PhD,** Professor of Microbial Pathogenesis at the University of Maryland School of Dentistry, and **Jason Gleghorn, PhD**, Associate Professor of Biomedical Engineering at the University of Delaware. Over the course of the 5-year grant, the research team that also includes **Vonetta Edwards, PhD**, Laboratory Research Lead Specialist, IGS, will simultaneously develop the reproductive tract 3D model in a stepwise fashion while integrating studies of polymicrobial, endocrine and immune factors that determine the disease outcome post exposure to the sexually transmitted pathogens, *Chlamydia trachomatis* and *Neisseria gonorrhoeae*, causative agents of chlamydia and gonorrhoea, respectively.

Constructing this "organ-on-a-chip" 3D model will require state-of-the-art biomedical engineering. Experimental "tours de force" will include growing all cell types from vaginal and cervical tissue biopsy samples collected from research volunteers, coaxing the cervical cells to produce the critical protective mucus layer, and producing reconstituted cervicovaginal microbiomes to mimic the polymicrobial diversity existing at both of these anatomical sites. Dr. Ravel is a world-renowned expert on the role of the genital microbiome in female reproductive health.

"We are trying to mimic as much as possible what occurs naturally in the female reproductive tract," said Dr. Ravel. *"We cannot look at fixed tissue on a slide under a microscope to determine how infections take hold and persist in the body."*

Chlamydia is the most frequently reported sexually transmitted infectious disease in the United States, according to the **Centers for Disease Control and Prevention**. Many women experience repeated or persistent infections, which can ultimately lead to pelvic inflammatory disease, ectopic pregnancy and infertility. Gonorrhea can present similar complications if infections persist.

"We have so many unanswered questions when it comes to understanding why some patients can clear these infections naturally or with a course of antibiotics,

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Patrik Bavoil, PhD, Vonetta Edwards, PhD, Jacques Ravel, PhD

while others cannot," Dr. Ravel said. *"We would like to map out how healthy cells in the reproductive tract interact with the microbiome and how that interaction prevents or facilitates the infection, which has not been done before."*

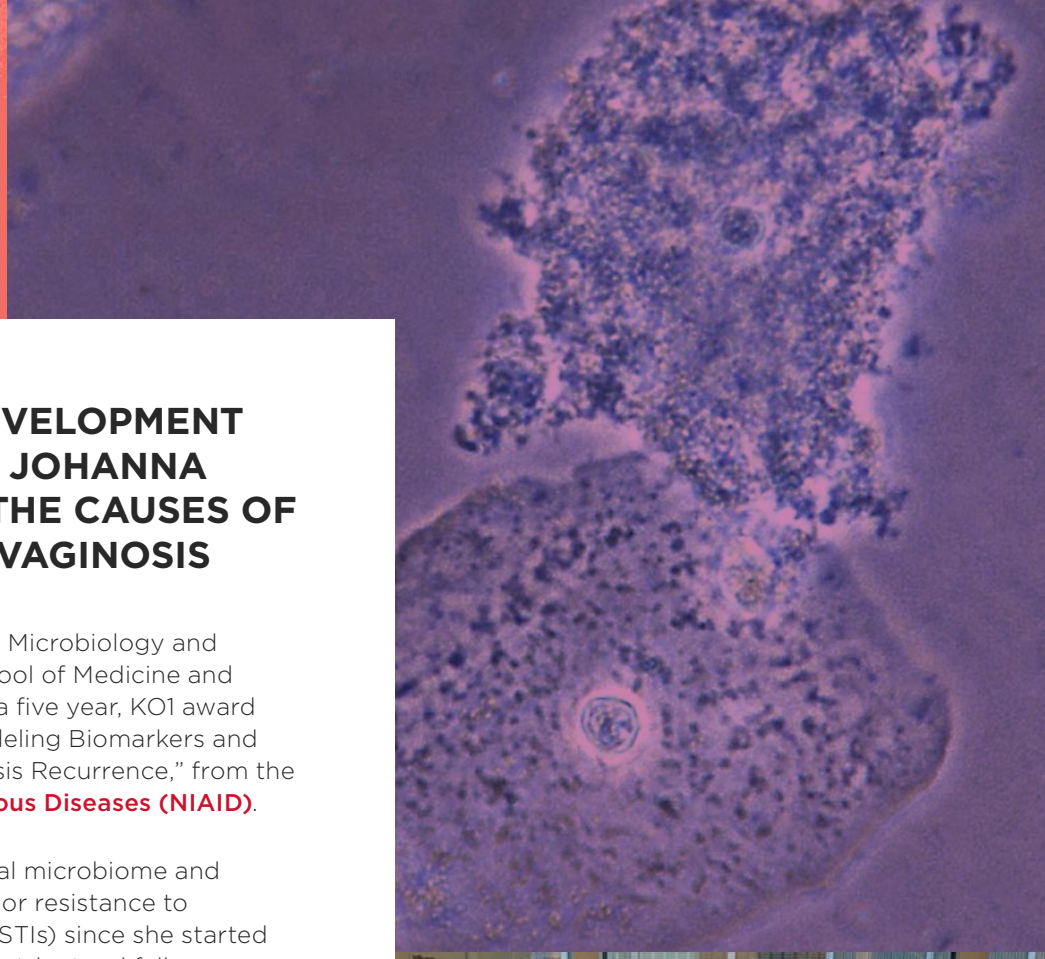
Current 3D models of the genital tract do not integrate the presence of the microbiome. *"It is logical to hypothesize that the interaction between cells and these colonizing bacteria plays a critical role in infection outcomes,"* Dr. Ravel said, *"but we do not know for certain until we test this theory in our new model, as we cannot do that in humans. This is a major innovation in this project."*

The research ultimately aims to improve our understanding of STI pathogenesis, the cause(s) of treatment failure, and susceptibility to repeat infections. Over time, such findings may lead to improved approaches to manage STIs, including testing new probiotic treatments. These preclinical studies are often required by the Food and Drug Administration before experimental treatments can be tested in patients. *"The model could replace the inadequate animal models currently used,"* Dr. Ravel said. *"None of these reproduce the unique microbial ecosystem found in a female genital tract."*

"We plan to use genomics and bioinformatics platforms developed at IGS and apply system biology approaches in order to gain a fuller understanding of the interactions between cells of the reproductive tract, the microbiome, and invading pathogens," Dr. Ravel said.

The large project grant is funded by the National Institutes of Health (U19AI158930) and includes collaborations with the University of Virginia School of Medicine.

"Our leading genomics researchers at IGS aim to improve our understanding of the mechanisms by which the microbiome affect human reproductive health, and translate this knowledge into novel therapeutics measures to modulate the microbiome and optimize women's health in the US and worldwide," 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. *"As IGS investigators apply the tools of genomic analysis to medical challenges, the impact of this research is far-reaching and could potentially help millions of women who suffer from not only serious sequelae from sexually transmitted infections but also poor reproductive health outcomes such as preterm birth."*



RESEARCH SCIENTIST DEVELOPMENT NIH AWARD (K01) TO DR. JOHANNA HOLM TO UNDERSTAND THE CAUSES OF RECURRENT BACTERIAL VAGINOSIS

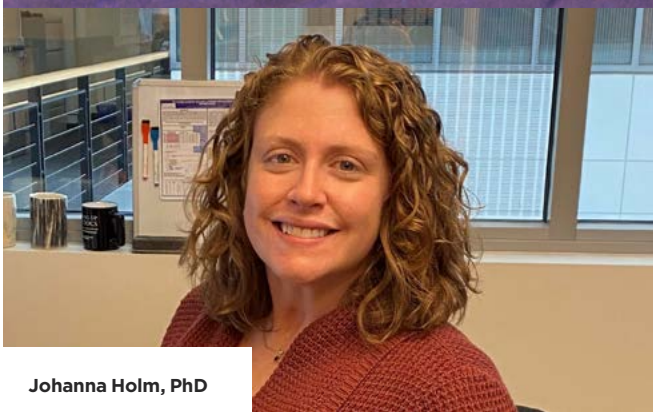
Johanna Holm, PhD, Assistant Professor, Microbiology and Immunology, University of Maryland School of Medicine and Institute for Genome Sciences, received a five year, KO1 award titled, "Integrating Multi-omics data: Modeling Biomarkers and Mechanisms to Reduce Bacterial Vaginosis Recurrence," from the **National Institute of Allergy and Infectious Diseases (NIAID)**.

Dr. Holm has been researching the vaginal microbiome and determining biomarkers of susceptibility or resistance to incident sexually transmitted infections (STIs) since she started as a postdoctoral fellow in the Ravel and Brotman Laboratories in 2016.

Bacterial vaginosis (BV) is a condition that affects nearly 30% of reproductive-age North American women and closer to 50% of sub-Saharan African women.

Bacterial vaginosis (BV) is often symptomatic and in many women is recurrent, dramatically affecting quality of life. Having BV is associated with serious adverse health outcomes, such as increased risk for sexually transmitted infections, including HIV, and preterm birth. BV is characterized by a vaginal microbiota with a low abundance of protective lactobacilli and higher abundances of anaerobic bacteria. Thus, the vaginal microbiota is believed to play a key role in the development and resolution of BV. An ideal BV treatment would modulate the vaginal microbiota and favor the establishment of lactobacilli that are resistant to disturbances such as douching, menstruation and sexual activities, thus reducing the risk of recurrence.

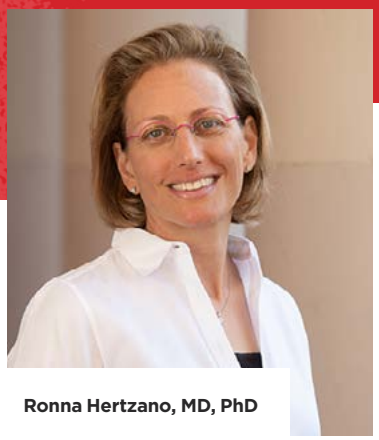
Dr. Holm aims to functionally characterize the vaginal microenvironment (the microbiome, the metabolome and the immune response) and integrate the data to develop a prognostic indicator of recurrent BV and identify candidate biomarkers and causal mechanisms which reduce recurrence. The research could lead to the development of novel approaches to modulate the vaginal microenvironment to prevent BV reccurence.



Johanna Holm, PhD

MORE INFORMATION

- https://www.medschool.umaryland.edu/profiles/Holm-Johanna/



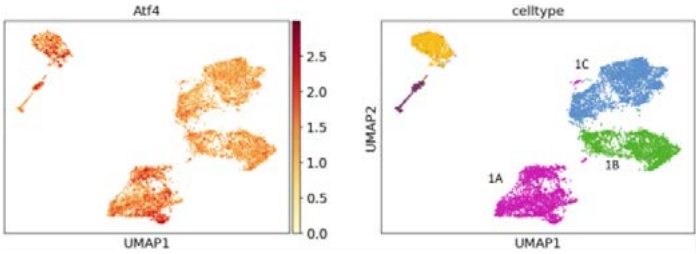
Ronna Hertzano, MD, PhD

UNDERSTANDING HEARING LOSS FROM NOISE DAMAGE THROUGH GENE EXPRESSION CHANGES

Findings suggest several FDA-approved drugs, such as a common diabetes medication and anesthetics, could protect from noise-related hearing loss

A growing number of people are suffering from hearing loss due to exposure to loud noises from heavy machinery, concerts, or explosions. As a result, scientists have been working to understand the mechanism behind how the damage to hearing actually occurs.

A team led by **Dr. Ronna Hertzano**, Professor, Department of Otorhinolaryngology-Head & Neck Surgery and Affiliate Member of Institute for Genome Sciences, has published an online interactive atlas representing the changes in the levels of RNA made in the different cell types of ears of mice, after damage due to loud noise. These changes in RNA levels are known as changes in "gene expression."



An example of gene expression changes (left, shade of orange) in different cells types (right, yellow, blue, green, purple) of the ear. Source: gEAR.org

Once they determined the larger trends in gene expression following the damage, the UMSOM scientists then searched a database of FDA-approved drugs to find those that are known to produce opposite patterns of those caused by the noise. From this analysis, the research teams identified a handful of drug candidates that may be able to prevent or treat the damage, and ultimately preserve hearing. Their analysis was published online in *Cell Reports* on September 28.

"As an otolaryngologist surgeon-scientist, I see patients with hearing loss due to age or noise damage, and I want to be able to help prevent or even reverse the damage to their hearing," said study leader **Ronna Hertzano, MD, PhD**. "Our extended analysis gives us very specific avenues to follow up on in future studies, as well as provides an encyclopedia that other researchers can use as a resource to study hearing loss."

The team added their newest data on noise-induced hearing loss to **gEAR – Gene Expression Analysis Resource** — a tool developed by her laboratory in collaboration with IGS scientists that allows researchers not trained in informatics to browse gene expression data (**published earlier this summer**).

Dr. Hertzano explained that the inner ear resembles the shell of a snail, with separate fluid compartments and sensory cells along its entire length. The ear functions like a battery with a gradient of ions between the fluid compartments that is generated by the side wall of the shell by adding in potassium. The sensory cells detect sound and then communicate with the neurons that interact with the brain to interpret the signal. The sensory cells are surrounded by support cells. The inner ear also has resident immune cells to protect it from infection.

Research Supervisor Beatrice Milon, PhD, in Dr. Hertzano's laboratory initially did an analysis on the sensory cells and the support cells of the ear in mice. She collected data on the changes in gene expression from before and after noise damage. After making their study known to other researchers in their field, the team heard from scientists at

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Decibel Therapeutics (led by Joe Burns, PhD) and the **Karolinska Institute** (led by Barbara Canlon, PhD), who had the gene expression data from the inner ear's neurons, side wall and immune cells from before and after noise damage. The teams then combined the datasets and performed their analysis.

The bioinformatic analyses were led by Eldad Shulman, MA, MS, from the lab of Ran Elkon, PhD, **Tel Aviv University**, a bioinformatics expert that has been working collaboratively with Dr. Hertzano now for over two decades. Together, they leverage advanced computational techniques and combine them with biological insights to analyze and interpret data, providing impactful insights to the hearing research field.

Dr. Hertzano says it was so important that they looked at a cell specific level, rather than looking at the entire ear because they found that most of the gene expression changes were specific to only one or two cell types.

"We expected the subset of neurons typically sensitive to noise and aging, to have "bad" changes in genes, so that we could counter them with drugs, but there was no such thing," said Dr. Hertzano. "On the contrary, we found that the subset of neurons that are resistant to noise trauma, turn on a program that protects them while the very sensitive neurons had little change in gene expression. We are currently looking into approaches to induce the protective changes in the noise-sensitive neurons to prevent their loss from noise and aging."

In another example, the researchers found that only one out of the four types of immune cells detected showed major differences in gene expression.

Additionally, immune-related genes were turned up in all cell types of the inner ear after noise damage with many of them controlled by two key regulators.

The research team took the overall gene expression trends and plugged them into DrugCentral, a database of known molecular responses to FDA-approved drugs, specifically searching for changes that would be opposite of those happening in the noise-damaged cells. They identified the diabetes drug metformin as a potential candidate, as well as some inhaled anesthetic medications used in surgeries and other medications.

"Hearing aids and cochlear implants are used to alleviate hearing loss, however, there are no therapies available to prevent or treat hearing loss," 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, UMSOM. "The studies that follow up on these findings may eventually lead to medications to prevent occupational noise-induced hearing loss, for example in factory workers, and to changes in standardizing anesthesia protocols for ear surgery, particularly in hearing preservation procedures."

This work was funded by the Eunice Kennedy Shriver National Institute of Child Health and Human Development (R01DC013817, R01DC03544), the Department of Defense Congressionally Directed Medical Research Program (MR130240, RH200052), the Carolyn Frenkil Foundation, the Hearing Restoration Project of the Hearing Health Foundation, the Swedish Medical Research Council and Hörselforskningsfonden, the Karolinska Institutet, Tysta Skolan and Office of the Assistant Secretary of Defense for Health Affairs through the Neurosensory and Rehabilitation (W81XWH-16-1-0032), the European Union's Horizon 2020 research and innovation programme (722046, 848261), the United States - Israel Binational Science Foundation (2017218), the Edmond J. Safra Center for Bioinformatics at Tel Aviv University, Teva Pharmaceutical Industries Ltd, and the Israeli National Forum for BioInnovators.

MORE INFORMATION

- **https://www.medschool.umaryland.edu/profiles/Hertzano-Ronna/**
- **https://www.hertzanolab.org/**
- **https://umgear.org/**

A TALE OF TWO PARASITIC DISEASES:

RESEARCH PARALLELS IN MALARIA AND EAST COAST FEVER

Milk from the village's livestock is part of the healthy nutrition of Maasai children in Kenya.

Malaria is the leading cause of mortality from parasitic infectious diseases in humans, with over 400,000 deaths each year. The burden from malaria is most acutely felt by children under 5 years of age, who represent >60% of all deaths. Despite a vaccine search that has lasted for over 100 years, the first malaria vaccine, Mosquirix™, was only just approved by the World Health Organization (WHO) in October of this year. However, the efficacy of Mosquirix™, made by GlaxoSmithKline, is far from ideal, as it reduces the probability of severe malaria by only 30%. And so, the search continues. One of the most promising alternatives is PfSPZ Vaccine™, a malaria vaccine developed by a Maryland-based biotech company, Sanaria, Inc. While Mosquirix™ is based on a single parasite protein, PfSPZ Vaccine™ uses a whole malaria parasite strain in its formulation.

The rationale for the design of PfSPZ Vaccine™ largely rests with a highly effective vaccine against a livestock disease, East coast fever (or ECF), which kills hundreds of thousands of livestock each year in sub-Saharan Africa. In the affected smallholder communities, livestock is key to survival, as the source of nourishment, rawhides, animal traction in agriculture and more. The ECF vaccine contains a cocktail of three strains of ECF-causing parasite, *Theileria parva*.

Joana C. Silva, PhD

This is where **Joana C. Silva, PhD**, Professor, Microbiology & Immunology, University of Maryland School of Medicine, Institute for Genome Sciences, comes into this tale. In a bid to help interpret the high efficacy of the vaccine against ECF, in 2015, her team published the genome sequence of the three strains in that vaccine, having discovered that two of those strains are nearly identical, while the third one differs from those by as much as any two strains in *T. parva* can (over 1% genome-wide). Her team has since published a string of papers to facilitate translational research on this parasite, including a **complete revision of the entire parasite protein set**, the discovery of a potential mechanism by which the **parasite takes over the replication machinery in bovine immune system cells**, and more recently, a novel genomics-based assay that allows the genotyping of the complete genome of new *T. parva* strains, published in **PLOS Neglected Tropical Diseases in 2020**. This work is contributing to our understanding of the immune system response to the parasite, as she shows with new work just published in the ***Journal of Immunology***, and is expected to facilitate the development of new vaccines against the parasite.

With knowledge of Dr. Silva and her team's contributions to the field of East coast fever vaccinology, the leadership team at Sanaria reached out to her for feedback on their malaria vaccine development program, based on PfSPZ Vaccine and related products. In collaboration with Sanaria, Dr. Silva's team has **now published the genome of the parasite strain in PfSPZ Vaccine**, the NF54 strain of the parasite *Plasmodium falciparum*, as well as the genomes of other *P. falciparum* strains used to challenge vaccinees and hence assess vaccine efficacy in the laboratory. Now, working with teams of clinicians, researchers and staff conducting clinical trials in malaria-endemic areas, Dr. Silva's team is working to uncover the gaps in the protection imparted by PfSPZ Vaccine, so that more effective vaccines can be designed. Her first results in this field was presented

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Indigenous African cattle breed

virtually this past November at the annual meeting of the American Society for Hygiene and Tropical Medicine and at the annual meeting of the **Vaccine Development Center of San Antonio**, where she was a keynote speaker. This fruitful cross talk between research in parasites of livestock and of humans has been central to Dr. Silva's research program for close to two decades.

Her team is contributing further to efforts to combat malaria with the development of several additional assays. In collaboration with a team at the Laboratory of Malaria and Vector Research, at the National Institutes of Health, her team contributed to the development of a simple genotyping assay, described in a Sept 30th paper in ***Communications Biology***, to determine the geographic source of malaria infections, and monitor malaria importation. This assay is based on the *P. falciparum* Pfs47 gene, which has a strong geographic population structure, because only those parasites with Pfs47 genotype compatible with the local mosquito vector species are efficiently transmitted. As countries work towards malaria elimination, it is important to monitor imported cases to prevent reestablishment of local transmission.

Finally, as part of her close collaborations with the Malaria Research Program (MRP) of the **UMSOM Center for Vaccine Development and Global Health**, she guided, together with a counterpart at MRP, **the development of a novel transcriptomics assay** to characterize the expression of parasite genes that determine the binding of malaria parasites to human cells and contribute to malaria disease.

Joana C. Silva, PhD and colleagues share morning coffee ahead of an annual meeting of the East Coast Fever Consortium in Addis Ababa, Ethiopia.

Understanding how the interactions between the human host and the parasites are effected by the proteins that these genes encode is key to the rational development of next-generation vaccines and drugs to combat infectious diseases.

MORE INFORMATION

- **https://www.medschool.umaryland.edu/profiles/Carneiro-da-Silva-Joana/**

PROBIOTIC-CONTAINING YOGURT PROTECTS AGAINST MICROBIOME CHANGES THAT LEAD TO ANTIBIOTIC-INDUCED DIARRHEA

About one in five people who are prescribed antibiotics develop antibiotic-associated diarrhea because their healthy gut microbiota has been perturbed. As a result, some patients stop taking their antibiotics early after developing diarrhea, a decision that could cause their original infection to persist, or that could lead to the emergence of antibiotic-resistant bacteria. A small percentage of patients who take antibiotics may develop a life-threatening infection with the bacteria *Clostridioides difficile*, which can reside in the gut but is usually kept in check by good bacteria in the gut microbiome.

In a study published in the journal ***Nutrients***, a randomized clinical trial led by **Dr. Claire M. Fraser** at the University of Maryland School of Maryland (UMSOM), Dr. Maureen Kane at the University of Maryland School of Pharmacy (UMSOP), and Dr. Daniel Merenstein at Georgetown University Medical Center, revealed that yogurt containing a particular strain of a well-studied probiotic was found to protect against changes in the gut microbiome that are associated with antibiotic administration. The study found that yogurt containing the probiotic, *Bifidobacterium lactis* BB-12, worked better than a placebo at maintaining the community of bacteria in the colon following antibiotic therapy. The findings were so positive that the NIH funded an additional follow-up study.

In the study, 42 healthy volunteers were randomly assigned to consume a daily serving-size container of yogurt containing BB-12 along with a standard week-long regimen of the antibiotic amoxicillin clavulanate. They continued to consume the yogurt every day for a week after finishing the antibiotic. An additional 20 participants served as the control group and were randomly assigned to consume a daily yogurt without the probiotic for two weeks while also taking the same antibiotic regimen.

The researchers found that levels of the short chain fatty acid acetate, a beneficial metabolite produced by the microbiota, were reduced in all subjects after taking the antibiotic; however, the reduction in acetate was significantly greater in subjects receiving the placebo yogurt as compared with BB-12 supplemented yogurt. Acetate levels in subjects who received BB-12 also returned to baseline levels by 30 days, while they remained below baseline in subjects receiving the placebo. Consumption of BB-12 was also associated with significantly less disruption of the gut microbiota.

"This finding provides important new insights into the mechanisms by which the probiotic, BB-12, may protect against antibiotic-associated diarrhea," said study co-leader **Claire Fraser, PhD**, Professor of Medicine and Dean's Endowed Professor, UMSOM and Director of the Institute for Genome Sciences. *"The new insights that we obtained regarding BB-12 reflect the multi-omics approach that we used in our study. This was possible only because of the different expertise that each of the principal investigators brought to this collaboration."*

"An important reason why our study may have demonstrated positive results may be the timing of the probiotic administration on the day antibiotics were initiated by the study volunteers," said study co-leader Daniel Merenstein, MD, Professor of Family Medicine and Director of Research Programs for the Department

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of Family Medicine at Georgetown University School of Medicine. *"Starting the probiotic as early as possible, before the antibiotic symptoms have progressed, may result in a greater opportunity for the probiotic mechanisms to be expressed and may ultimately lead to more beneficial clinical outcomes."*

The researchers are planning a follow-up study to further explore this question and assess when is the best time to consume a probiotic.

Funding research was supported by the National Center for Complementary and Integrative Health of the National Institutes of Health under Award Number R61AT009622. Additional support was provided by the University of Maryland School of Pharmacy Mass Spectrometry Center (SOP1841-IQB2014).

"Our researchers seek to advance treatments for patients by truly understanding the mechanisms behind those treatments using sophisticated technologies. We are delighted to be able to collaborate with the School of Pharmacy and its distinguished faculty on this very important project," 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. *"The multi-disciplinary approach to understanding how probiotics work to maintain a healthy microbiome is crucial for advancing this field and ultimately helping patients avoid debilitating side effects from antibiotics."*

JACQUES RAVEL RECEIVES SOKOLOVE MENTOR AWARD

Jacques Ravel, PhD, Professor, Microbiology & Immunology, University of Maryland School of Medicine, Associate Director, Genomics, IGS was awarded the 2021 Dr. Patricia Sokolove Outstanding Mentor Award. This award honors those who expend great effort in aiding and mentoring graduate students and is given by the UMB Graduate Student Association.

Madeline Alizadeh, MD/PhD student, summarized Dr. Ravel as a mentor, *"There's no one reason that Dr. Ravel has been an incredible mentor. He is supportive while still encouraging independence and autonomy, he is flexible and understanding while still pushing us to do our best, and he offers constructive feedback without judgement."*

Bern Monari, a graduate student who has also worked with Dr. Ravel, said *"Dr. Ravel has been an incredibly supportive mentor, allowing me to pursue research that was both personally and professionally important to me."*

Jacques Ravel, PhD and Madeline Alizadeh, MD/PhD graduate student

RONNA P. HERTZANO, MD, PHD
RESEARCHER OF THE YEAR: FOUNDERS WEEK

Ronna P. Hertzano, MD, PhD, once wanted to become an orthopedic surgeon, but "Mom and chance," as she puts it, led her down a different path.

"My mom is an audiologist and taught in the school of speech and languages in Israel, where I grew up," says Dr. Hertzano, Professor, Department of Otorhinolaryngology-Head and Neck Surgery and Affiliate Member of the Institute for Genome Sciences. *"Her office was in the school for the deaf, across from my high school. I grew up among audiologists, deaf children, and consultants to families with hearing loss."*

In her second year at the Sackler School of Medicine at Tel Aviv University, Hertzano happened to attend a lecture by American-Israeli professor Karen Avraham, PhD, about the genetics of hearing loss and how mouse models contribute to the understanding of the disorder. A few months later, they crossed paths again, and Avraham offered Hertzano a summer genetics research position in her lab.

"By the end of the summer, I was hooked," Hertzano said. *"The research in the laboratory was fascinating. The ability to visualize the sensory cells and see how each genetic mutation changes structure and function was mind-blowing. And the thought of being able to develop treatments by using these very tools was inspiring."*

She switched to an MD/PhD track and reveled in meeting surgeon-scientists who could combine their passion for research on hearing loss with the treatment of patients who have hearing and balance disorders. *"From that point on, I knew I wanted to be an otolaryngologist and surgeon-scientist. It's a dream I was so fortunate to realize,"* Hertzano said.

Dr. Hertzano is a highly respected otolaryngologist, researcher, and educator who holds a secondary appointment in UMSOM's Department of Anatomy and Neurobiology and is an affiliate faculty member of the Institute for Genome Sciences (IGS). She is being recognized as the University of Maryland, Baltimore's (UMB) 2021 Researcher of the Year.

With significant grants from the National Institutes of Health and other sources, Hertzano's research is focused on developing therapeutics to prevent and treat genetic and acquired hearing loss. Her lab has three main focus areas: cell-type specific molecular pathways in inner ear development; sex differences in hearing and the molecular basis of acquired hearing loss; and tools for sharing, visualizing, and analyzing multi-omics data. ("Omics" refers to a field of study in biology that ends with "omics," such as genomics, transcriptomics, proteomics, or metabolomics.)

As a clinician, she focuses on the diagnosis and treatment

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of diseases of the ear, with an emphasis on hearing restoration. Hertzano also has a strong interest in mentorship, and her research team includes undergraduates, graduate students, medical students, residents, audiologists, and postdoctoral fellows.

UMSOM colleague Martin Flajnik, PhD, professor, Department of Microbiology and Immunology, supported her UMB award nomination, recalling his thoughts after first meeting Hertzano in 2006, when she was beginning her residency at the school.

"I immediately saw in her a scientist with a drive and earnestness rarely found together," Flajnik said. *"When she became an assistant professor, I offered advice on grant writing, how to make connections with other departments, and suggested collaborators. While this advice helped to kick-start her independent career, within a few years she started offering me advice — the mentee became the mentor — and her rise as a physician-scientist has been meteoric."*

"Her sincere interest in science combined with the compassion shown in her clinical work is unrivaled at the School of Medicine. Add to that her extraordinary productivity in procuring grants and publishing in the most prestigious journals, her clinical aptitude in otorhinolaryngology, her teaching skills, her organizing workshops and classes in mouse genetics and bioinformatics, and her mentorship skills, and I can't think of a more deserving recipient of Researcher of the Year."

Hertzano also has deep entrepreneurial roots. Seventy years ago, her grandfather, Ephraim Hertzano, invented Rummikub, a popular worldwide family game and one that her father still manufactures today. Hertzano grew up working in the family business, taking an active role in the organization of the Rummikub world championships.

Pulling from all those skill sets, Hertzano and her IGS colleagues have developed a research portal called **gEAR (gene Expression Analysis Resource)**, an online tool that could more quickly advance medical discoveries designed to reverse progressive hearing loss. The tool provides easy access to genetic and other molecular data from hundreds of technical research studies involving hearing function and the ear, allows researchers to rapidly access data, and provides easily interpreted visualizations of datasets.

"The gEAR portal is an exciting addition to UMB's research portfolio," said Curt Civin, MD, professor, Departments of Pediatrics and Physiology, and associate dean for research, UMSOM. *"With her elegant and dedicated combination of deep science and collegiality, Dr. Hertzano is helping many others incorporate omics into their own research."*

After completing her residency at UMSOM in 2011, Hertzano joined the school as an instructor. She was promoted to assistant professor in 2012, associate professor in 2016, and professor in 2021. Reflecting on her 15 years in Baltimore, she finds great satisfaction in working with medical and graduate students, postdoctoral fellows, and colleagues at UMSOM, other UMB schools, and around the world.

"As a mentor, I have the immense responsibility to support the education of highly talented individuals who offer me the opportunity to meaningfully shape their learning experience as budding scientists or clinician-scientists," she said. *"There are very few things more gratifying than seeing your students succeed, present in meetings, make new discoveries, and go from crawling to walking to running in the world of research."*

"Our lab forms a unit with a shared identity, values, and knowledge base. We are all driven by the hope of making meaningful contributions that will alleviate or prevent the suffering from hearing loss."

Asked about her reaction to winning the UMB award, Hertzano said she was *"surprised and deeply moved by this recognition,"* thanking UMSOM for its backing.

"The School of Medicine has always been extremely supportive, from providing me the necessary protected time for research, philanthropic and seed funds, collaborations, opportunities for training and growth, and, most recently, the relocation of our laboratory to the fantastic Health Sciences Research Facility III, which certainly catalyzed discovery by working in the same space with our collaborators and friends."

"We all work extremely hard to be the best clinicians and scientists we can possibly be. I lead a wonderful team that is highly collaborative. This award, therefore, is a recognition of the team for its efforts and culture, as well as the many researchers who choose to work with us, with the sole purpose of advancing the care of hearing health," said Hertzano.

by Lou Cortina

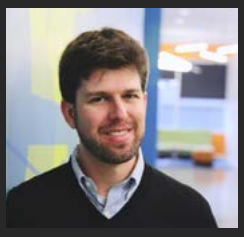
IGS SCIENTISTS CONTRIBUTE TO MAJOR BRAIN RESEARCH FEATURED IN NATURE MAGAZINE

New neurotechnologies have dramatically revolutionized brain research to the point that the entire October 5th issue of *Nature* was dedicated to neuroscience updates. Four years ago, the NIH' Brain Research through Advancing Innovative Neurotechnologies **(BRAIN) Initiative Cell Census Network** (BICCN) was launched, with the aim of identifying and cataloguing the diverse cell types in human, monkey and mouse brain. This Nature magazine issue featured papers from the BICCN collaborative network, including investigators from IGS. The **flagship paper** of this BICCN project, aims to establish a unified atlas of cell types in the primary motor cortex, the brain region that controls movement. The consortium's experiments and analyses describe the organization of the primary motor cortex, including its molecular wiring and functional components at a level of detail never previously achieved for any brain region. Additionally, the flagship paper serves to validate the BICCN's systematic strategy of defining cell types, opening up future directions for the application of a similar collaborative and comprehensive approach to generate a brain-wide cell census and atlas of the mouse brain.

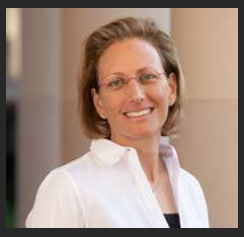
Owen White, PhD, Professor, Epidemiology & Public Health, University of Maryland School of Medicine, Associate Director, Informatics, IGS; **Ronna Hertzano, PhD**, Professor, Otolaryngology—Head and Neck Surgery, University of Maryland School of Medicine and Affiliate Faculty Member, IGS; and **Seth Ament, PhD**, Associate Professor, Psychiatry, University of Maryland School of Medicine, and IGS, have leadership roles in the BICCN. Many IGS researchers contributed to the publications featured in this issue, including Shaun Adkins, Alex Casella, Carlo Colantuoni, Jonathan Crabtree, Heather Creasy, Victor Felix, Peter Gandt, Michelle Giglio, Brian Herb, Anup Mahurkar, Carrie McCracken, Dustin Olley, and Joshua Orvis.

These collaborations have produced a variety of different large-scale data sets to better define brain cell types. IGS researchers have been involved with the **Neuroscience Multi-Omic** (NEMO) archive which contains over 1 million BICCN files with molecular data deposited for public consumption. These files require 282 TB of storage and vary depending on the type of assay considered. Users have downloaded over half a petabyte of information from the archive, demonstrating its broad use by the community. Many of the BICCN datasets can be visualized and analyzed in **NeMO Analytics**, a web-based, biologist-friendly platform that researchers at IGS have built for the consortium.

Owen White, PhD
Director of Bioinformatics,
UM School of Medicine



Seth A. Ament, PhD
Assistant Professor
Psychiatry



Ronna Hertzano, MD, PhD
Professor
Otorhinolaryngology-Head &
Neck Surgery

MADELINE ALIZADEH AWARDED THE 2021 GRADUATE PROGRAM IN LIFE SCIENCE PHD SCHOLAR AWARD

The Graduate Program in Life Sciences (GPILS) PhD Scholars Award recognizes a student who is within his/her first three years of study and research. The student should have an outstanding academic performance record and show great potential as a scientist.

Madeline Alizadeh

Madeline (Maddy) Alizadeh started her second year as a MD/PhD student in the Molecular Medicine/Genome Biology track in Jacques Ravel's laboratory. Madeline's interests in gastroenterology and her extensive knowledge of biostatistical modeling and analyses have been a great addition to the Ravel Lab.

She is working on several projects examining the role of the gut microbiome in extra-intestinal manifestation of IBD. Maddy has demonstrated an outstanding ability to work independently. She has an amazing amount of energy that is fueled by her passion for her work. She has conceived, designed and implemented two clinical studies, which she is running as study coordinator, even performing the necessary clinical procedures (collecting intestinal biospies and performing Fribroscans). These studies are integral parts of Maddy's thesis work, which aims to explore the role of the gut microbiome and metabolome in extra-intestinal manifestations of IBD. In executing these studies, she works closely with Dr. Erik von Rosenvinge, Associate Professor, Department of Medicine, UMSOM, and Chief of Gastroenterology, VA Maryland Health Care System, who is also her co-mentor, and Dr. Raymond Cross, Professor of Medicine, UMSOM and Director of the Inflammatory Bowel Disease Program, and Dr. Uni Wong, Assistant Professor of Medicine, and Gastroenterology Fellowship Associate Program Director. Maddy has been submitting abstracts and manuscripts while exploring possible grants from foundations and the NIH. She has been an outstanding doctoral student, impressing her mentors and collaborators with her passion and her knowledge. She is driven to make an impact in medicine and patient care. ***Congratulations, Madeline Alizadeh on this recognition!***

Congratulations!

IGS PROMOTIONS

The success of IGS is the sum total of the work of many dedicated investigators who are propelled to keep exploring scientific challenges in innovative ways.

Congratulations to the following individuals for their **well-deserved promotions:**

- **Seth Ament, PhD**, on his promotion to Associate Professor in the Department of Psychiatry
- **Timothy O'Connor, PhD**, Associate Professor in Medicine (Endocrinology) for receiving tenure.
- **Ronna Hertzano, MD, PhD**, on her promotion to Professor in the Department of Otorhinolaryngology.
- **W. Florian Fricke, PhD**, Professor, University of Hohenheim, Stuttgart, Germany who joined the Institute for Genome Sciences as an Affiliate Faculty Member.
- **Tracy Hazen, PhD, Bing Ma, PhD,** and **Johanna Holm, PhD** on their promotions to Assistant Professors, in the Department of Microbiology and Immunology.

PUBLICATIONS

1. Andrade Pessoa Morales, J, C Marconi, M El-Zein, J Ravel, GV da Silva Pinto, R Silveira, MD de Lima, NS de Carvalho, RR Figueiredo Alves, CMG de Lima Parada, SH Morais Leite, LL Villa, EL Franco and M Guimaraes da Silva (2021). **Vaginal microbiome components as correlates of cervical human papillomavirus infection.** *J Infect Dis*.

2. Badros, AZ, M Meddeb, D Weikel, S Philip, T Milliron, R Lapidus, L Hester, O Goloubeva, TF Meiller and EF Mongodin (2021). **Prospective Observational Study of Bisphosphonate-Related Osteonecrosis of the Jaw in Multiple Myeloma: Microbiota Profiling and Cytokine Expression**. *Front Oncol 11*: 704722.

3. Blevins, D, C Seneviratne, XQ Wang, BA Johnson and N Ait-Daoud (2021). **A randomized, double-blind, placebo-controlled trial of ondansetron for the treatment of cocaine use disorder with post hoc pharmacogenetic analysis**. *Drug Alcohol Depend* 228: 109074.

4. Bakken, TE, NL Jorstad, Q Hu, BB Lake, W Tian, BE Kalmbach, M Crow, RD Hodge, FM Krienen, SA Sorensen, J Eggermont, Z Yao, BD Aevermann, AI Aldridge, A Bartlett, D Bertagnolli, T Casper, RG Castanon, K Crichton, TL Daigle, R Dalley, N Dee, N Dembrow, D Diep, SL Ding, W Dong, R Fang, S Fischer, M Goldman, J Goldy, LT Graybuck, BR Herb, X Hou, J Kancherla, M Kroll, K Lathia, B van Lew, YE Li, CS Liu, H Liu, JD Lucero, A Mahurkar, D McMillen, JA Miller, M Moussa, JR Nery, PR Nicovich, SY Niu, J Orvis, JK Osteen, S Owen, CR Palmer, T Pham, N Plongthongkum, O Poirion, NM Reed, C Rimorin, A Rivkin, WJ Romanow, AE Sedeno-Cortes, K Siletti, S Somasundaram, J Sulc, M Tieu, A Torkelson, H Tung, X Wang, F Xie, AM Yanny, R Zhang, SA Ament, MM Behrens, HC Bravo, J Chun, A Dobin, J Gillis, R Hertzano, PR Hof, T Hollt, GD Horwitz, CD Keene, PV Kharchenko, AL Ko, BP Lelieveldt, C Luo, EA Mukamel, A Pinto-Duarte, S Preissl, A Regev, B Ren, RH Scheuermann, K Smith, WJ Spain, OR White, C Koch, M Hawrylycz, B Tasic, EZ Macosko, SA McCarroll, JT Ting, H Zeng, K Zhang, G Feng, JR Ecker, S Linnarsson and ES Lein (2021). **Comparative cellular analysis of motor cortex in human, marmoset and mouse**. *Nature 598*(7879): 111-119.

5. Break, TJ, V Oikonomou, N Dutzan, JV Desai, M Swidergall, T Freiwald, D Chauss, OJ Harrison, J Alejo, DW Williams, S Pittaluga, CR Lee, N Bouladoux, M Swamydas, KW Hoffman, T Greenwell-Wild, VM Bruno, LB Rosen, W Lwin, A Renteria, SM Pontejo, JP Shannon, IA Myles, P Olbrich, EMN Ferre, M Schmitt, D Martin, Genomics, C Computational Biology, DL Barber, NV Solis, LD Notarangelo, DV Serreze, M Matsumoto, HD Hickman, PM Murphy, MS Anderson, JK Lim, SM Holland, SG Filler, B Afzali, Y Belkaid, NM Moutsopoulos and MS Lionakis (2021). **Response to Comments on "Aberrant type 1 immunity drives susceptibility to mucosal fungal infections"**. *Science* 373(6561): eabi8835.

6. Brown, SE, CK Robinson, MD Shardell, JB Holm, J Ravel, KG Ghanem and RM Brotman (2021). **Assessing the Concordance Between Urogenital and Vaginal Microbiota: Can Urine Specimens Be Used as a Proxy for Vaginal Samples?** *Front Cell Infect Microbiol* 11: 671413.

7. Cannon, MV, HN Bogale, D Bhalerao, K Keita, D Camara, Y Barry, M Keita, D Coulibaly, AK Kone, OK Doumbo, MA Thera, CV Plowe, MA Travassos, SR Irish, J Yeroshefsky, J Dorothy, B Prendergast, B St Laurent, ML Fritz and D Serre (2021). **High-throughput detection of eukaryotic parasites and arboviruses in mosquitoes.** *Biol Open* 10(7).

8. Cavaletti, G, P Marmiroli, CL Renn, SG Dorsey, MP Serra, M Quartu and C Meregalli (2021). **Cannabinoids: an Effective Treatment for Chemotherapy-Induced Peripheral Neurotoxicity?** *Neurotherapeutics*.

9. Chen, X, AF Neuwald, L Hilakivi-Clarke, R Clarke and J Xuan (2021). **ChIP-GSM: Inferring active transcription factor modules to predict functional regulatory elements**. *PLoS Comput Biol* 17(7): e1009203.

10. El Hage, J, P Gravitt, J Ravel, N Lahrichi and E Gralla (2021). **Supporting scale-up of COVID-19 RT-PCR testing processes with discrete event simulation**. *PLoS One* 16(7): e0255214.

11. Feder, KA, A Patel, VR Vepachedu, C Dominguez, EN Keller, L Klein, C Kim, T Blood, J Hyun, TW Williams, KA Feldman, HH Mostafa, CP Morris, J Ravel, M Duwell, D Blythe and R Myers (2021). **Association of E484K spike protein mutation with SARS-CoV-2 infection in vaccinated persons---Maryland, January - May 2021**. *Clin Infect Dis*.

12. Garofano, K, CS Park, C Alarcon, J Avitia, A Barbour, D Diemert, CM Fraser, PN Friedman, A Horvath, K Rashid, M Shaazuddin, A Sidahmed, TJ O'Brien, MA Perera and NH Lee (2021). **Differences in the Platelet mRNA Landscape Portend Racial Disparities in Platelet Function and Suggest Novel Therapeutic Targets**. *Clin Pharmacol Ther* 110(3): 702-713.

13. Danko, D, D Bezdan, EE Afshin, S Ahsanuddin, C Bhattacharya, DJ Butler, KR Chng, D Donnellan, J Hecht, K Jackson, K Kuchin, M Karasikov, A Lyons, L Mak, D Meleshko, H Mustafa, B Mutai, RY Neches, A Ng, O Nikolayeva, T Nikolayeva, E Png, KA Ryon, JL Sanchez, H Shaaban, MA Sierra, D Thomas, B Young, OO Abudayyeh, J Alicea, M Bhattacharyya, R Blekhman, E Castro-Nallar, AM Canas, AD Chatziefthimiou, RW Crawford, F De Filippis, Y Deng, C Desnues, E Dias-Neto, M Dybwad, E Elhaik, D Ercolini, A Frolova, D Gankin, JS Gootenberg, AB Graf, DC Green, I Hajirasouliha, JJA Hastings, M Hernandez, G Iraola, S Jang, A Kahles, FJ Kelly, K Knights, NC Kyrpides, PP Labaj, PKH Lee, MHY Leung, PO Ljungdahl, G Mason-Buck, K McGrath, C Meydan, EF Mongodin, MO Moraes, N Nagarajan, M Nieto-Caballero, H Noushmehr, M Oliveira, S Ossowski, OO Osuolale, O Ozcan, D Paez-Espino, N Rascovan, H Richard, G Ratsch, LM Schriml, T Semmler, OU Sezerman, L Shi, T Shi, R Siam, LH Song, H Suzuki, DS Court, SW Tighe, X Tong, KI Udekwu, JA Ugalde, B Valentine, DI Vassilev, EM Vayndorf, TP Velavan, J Wu, MM Zambrano, J Zhu, S Zhu, CE Mason and SUBC International Meta (2021). **A global metagenomic map of urban microbiomes and antimicrobial resistance**. *Cell* 184(13): 3376-3393 e3317.

14. Gogate, N, D Lyman, A Bell, E Cauley, KA Crandall, A Joseph, R Kahsay, DA Natale, LM Schriml, S Sen and R Mazumder (2021). **COVID-19 biomarkers and their overlap with comorbidities in a disease biomarker data model**. *Brief Bioinform* 22(6).

15. Guimaraes Alves, AC, NM Sukow, G Adelman Cipolla, M Mendes, TP Leal, ML Petzl-Erler, R Lehtonen Rodrigues Souza, I Rainha de Souza, C Sanchez, M Santolalla, D Loesch, M Dean, M Machado, JY Moon, R Kaplan, KE North, S Weiss, ML Barreto, MF Lima-Costa, H Guio, O Caceres, C Padilla, E Tarazona-Santos, IF Mata, E Dieguez, V Raggio, A Lescano, V Tumas, V Borges, HB Ferraz, CR Rieder, A Schumacher-Schuh, BL Santos-Lobato, P Chana-Cuevas, W Fernandez, G Arboleda, H Arboleda, CE Arboleda-Bustos, TD O'Connor, MH Beltrame and V Borda (2021). **Tracing the Distribution of European Lactase Persistence Genotypes Along the Americas**. *Front Genet* 12: 671079.

16. Hamosh, A, JS Amberger, CA Bocchini, J Bodurtha, CJ Bult, CG Chute, GR Cutting, HC Dietz, HV Firth, RA Gibbs, WW Grody, MA Haendel, JR Lupski, JE Posey, PN Robinson, LM Schriml, AF Scott, NL Sobreira, D Valle, N Wu and SA Rasmussen (2021). **Response to Biesecker et al**. *Am J Hum Genet* 108(9): 1807-1808.

17. Hayward, RJ, MS Humphrys, WM Huston and GSA Myers (2021). **Dual RNA-seq analysis of *in vitro* infection multiplicity and RNA depletion methods in *Chlamydia*-infected epithelial cells**. *Sci Rep* 11(1): 10399.

18. Im, H, KL Kruckow, A D'Mello, F Ganaie, E Martinez, JN Luck, KH Cichos, AN Riegler, X Song, E Ghanem, JS Saad, MH Nahm, H Tettelin and CJ Orihuela (2021). **Anatomical site-specific carbohydrate availability impacts *Streptococcus pneumoniae* virulence and fitness during colonization and disease**. *Infect Immun*: IAI0045121.

19. Jackson, R, N Matentzoglu, JA Overton, R Vita, JP Balhoff, PL Buttigieg, S Carbon, M Courtot, AD Diehl, DM Dooley, WD Duncan, NL Harris, MA Haendel, SE Lewis, DA Natale, D Osumi-Sutherland, A Ruttenberg, LM Schriml, B Smith, CJ Stoeckert, Jr., NA Vasilevsky, RL Walls, J Zheng, CJ Mungall and B Peters (2021). **OBO Foundry in 2021: operationalizing open data principles to evaluate ontologies**. *Database (Oxford)* 2021.

20. Jasarevic, E, EM Hill, PJ Kane, L Rutt, T Gyles, L Folts, KD Rock, CD Howard, KE Morrison, J Ravel and TL Bale (2021). **The composition of human vaginal microbiota transferred at birth affects offspring health in a mouse model**. *Nat Commun* 12(1): 6289.

21. Kirk, JM, J Magaziner, MD Shardell, AS Ryan, AL Gruber-Baldini, D Orwig, MC Hochberg and AM Rathbun (2021). **Depressive symptom heterogeneity among older adults after hip fracture**. *Age Ageing* 50(6): 1943-1951.

22. Lewis, A, TP McKeon, AJ De Roos, J Ravel, MA Elovitz and HH Burris (2021). **Associations of public water system trihalomethane exposure during pregnancy with spontaneous preterm birth and the cervicovaginal microbial-immune state**. *Environ Res* 199: 111288.

23. Li, Z, VM Bruno and KS Kim (2021). **Central Nervous System-Infecting Pathogens *Escherichia coli* and *Cryptococcus neoformans* Exploit the Host Pdlim2 for Intracellular Traversal and Exocytosis in the Blood-Brain Barrier**. *Infect Immun* 89(10): e0012821.

24. Lin, J, X Yang, W Kosters, T Xu, Y Jia, S Wang, Q Zhu, M Ryan, L Guo, C Zhang, C Lee, SE Devine, EE Eichler, K Ye and C Human Genome Structural Variation (2021). **Mako: A Graph-based Pattern Growth Approach to Detect Complex Structural Variants**. *Genomics Proteomics Bioinformatics*.

25. Loesch, DP, A Horimoto, K Heilbron, EI Sarihan, M Inca-Martinez, E Mason, M Cornejo-Olivas, L Torres, P Mazzetti, C Cosentino, E Sarapura-Castro, A Rivera-Valdivia, AC Medina, E Dieguez, V Raggio, A Lescano, V Tumas, V Borges, HB Ferraz, CR Rieder, A Schumacher-Schuh, BL Santos-Lobato, C Velez-Pardo, M Jimenez-Del-Rio, F Lopera, S Moreno, P Chana-Cuevas, W Fernandez, G Arboleda, H Arboleda, CE Arboleda-Bustos, D Yearout, CP Zabetian, T andMe Research, P Cannon, TA Thornton, TD O'Connor, IF Mata and D Latin American Research Consortium on the Genetics of Parkinson's (2021). **Characterizing the Genetic Architecture of Parkinson's Disease in Latinos**. *Ann Neurol* 90(3): 353-365.

26. Malaiya, S, M Cortes-Gutierrez, BR Herb, SR Coffey, SRW Legg, JP Cantle, C Colantuoni, JB Carroll and SA Ament (2021). **Single-Nucleus RNA-Seq Reveals Dysregulation of Striatal Cell Identity Due to Huntington's Disease Mutations**. *J Neurosci* 41(25): 5534-5552.

27. Malayil, L, S Chattopadhyay, EF Mongodin and AR Sapkota (2021). **Coupled DNA-labeling and sequencing approach enables the detection of viable-but-non-culturable Vibrio spp. in irrigation water sources in the Chesapeake Bay watershed**. *Environ Microbiome* 16(1): 13.

28. Martin, OA, S Grant-Beurmann, ER Orellana, A Hajnal and CM Fraser (2021). **Changes in the Gut Microbiota Following Bariatric Surgery Are Associated with Increased Alcohol Intake in a Female Rat Model**. *Alcohol Alcohol* 56(5): 605-613.

29. Mattick, J, S Libro, R Bromley, W Chaicumpa, M Chung, D Cook, MB Khan, N Kumar, YL Lau, S Misra-Bhattacharya, R Rao, L Sadzewicz, A Saeung, M Shahab, BC Sparklin, A Steven, JD Turner, LJ Tallon, MJ Taylor, AR Moorhead, M Michalski, JM Foster and JC Dunning Hotopp (2021). **X-treme loss of sequence diversity linked to neo-X chromosomes in filarial nematodes**. *PLoS Negl Trop Dis* 15(10): e0009838.

30. Milon, B, ED Shulman, KS So, CR Cederroth, EL Lipford, M Sperber, JB Sellon, H Sarlus, G Pregernig, B Shuster, Y Song, S Mitra, J Orvis, Z Margulies, Y Ogawa, C Shults, DA Depireux, AT Palermo, B Canlon, J Burns, R Elkon and R Hertzano (2021). **A cell-type-specific atlas of the inner ear transcriptional response to acoustic trauma**. *Cell Rep* 36(13): 109758.

31. Molina-Cruz, A, N Raytselis, R Withers, A Dwivedi, PD Crompton, B Traore, G Carpi, JC Silva and C Barillas-Mury (2021). **A genotyping assay to determine geographic origin and transmission potential of *Plasmodium falciparum* malaria cases**. *Commun Biol* 4(1): 1145.

32. Mongodin, EF, V Saxena, J Iyyathurai, R Lakhan, B Ma, E Silverman, ZL Lee and JS Bromberg (2021). **Chronic rejection as a persisting phantom menace in organ transplantation: a new hope in the microbiota?** *Curr Opin Organ Transplant* 26(6): 567-581.

33. Morrison, WI, A Aguado, TA Sheldrake, NC Palmateer, OO Ifeonu, K Tretina, K Parsons, E Fenoy, T Connelley, M Nielsen and JC Silva (2021). **CD4 T Cell Responses to *Theileria parva* in Immune Cattle Recognize a Diverse Set of Parasite Antigens Presented on the Surface of Infected Lymphoblasts**. *J Immunol* 207(8): 1965-1977.

34. Mtshali, A, JE San, F Osman, N Garrett, C Balle, J Giandhari, H Onywera, K Mngomezulu, G Mzobe, T de Oliveira, A Rompalo, A Mindel, SS Abdool Karim, J Ravel, JS Passmore, Q Abdool Karim, HB Jaspan, LJP Liebenberg and S Ngcapu (2021). **Temporal Changes in Vaginal Microbiota and Genital Tract Cytokines Among South African Women Treated for Bacterial Vaginosis**. *Front Immunol* 12: 730986.

35. Novak, J, J Ravel, B Ma, CST Ferreira, ADR Tristao, MG Silva and C Marconi (2021). **Characteristics associated with *Lactobacillus iners*-dominated vaginal microbiota**. *Sex Transm Infect*.

36. Oberstaller, J, L Zoungrana, CD Bannerman, S Jahangiri, A Dwivedi, JC Silva, JH Adams and S Takala-Harrison (2021). **Integration of population and functional genomics to understand mechanisms of artemisinin resistance in *Plasmodium falciparum***. *Int J Parasitol Drugs Drug Resist* 16: 119-128.

37. Resnick, B, E Galik, A Kolanowski, K VanHaitsma, M Boltz, S Zhu, J Ellis, L Behrens, K Eshraghi, C Renn and SG Dorsey (2021). **The Relationship Between Pain, Function, Behavioral, and Psychological Symptoms of Dementia and Quality of Life**. *Pain Manag Nurs*.

38. Roghmann, MC, AD Lydecker, M Shardell, RT DeBoy, JK Johnson, L Zhao, LL Hittle and EF Mongodin (2021). **Effect of mupirocin for *Staphylococcus aureus* decolonization on the microbiome of the nose and throat in community and nursing home dwelling adults**. *PLoS One* 16(6): e0252004.

39. Salerno-Goncalves, R, T Rezwan, D Luo, H Tettelin and MB Sztein (2021). **B Cells Control Mucosal-Associated Invariant T Cell Responses to *Salmonella enterica* Serovar Typhi Infection Through the CD85j HLA-G Receptor**. *Front Immunol* 12: 728685.

40. Saul-McBeth, J, J Dillon, A Lee, D Launder, JM Kratch, E Abutaha, AA Williamson, AG Schroering, G Michalski, P Biswas, SR Conti, 3rd, AC Shetty, C McCracken, VM Bruno, EI Parsai and HR Conti (2021). **Tissue Damage in Radiation-Induced Oral Mucositis Is Mitigated by IL-17 Receptor Signaling**. *Front Immunol* 12: 687627.

41. Schriml, LM, JB Munro, M Schor, D Olley, C McCracken, V Felix, JA Baron, R Jackson, SM Bello, C Bearer, R Lichenstein, K Bisordi, NC Dialo, M Giglio and C Greene (2021). **The Human Disease Ontology 2022 update**. *Nucleic Acids Res*.

42. Seplyarskiy, VB, RA Soldatov, E Koch, RJ McGinty, JM Goldmann, RD Hernandez, K Barnes, A Correa, EG Burchard, PT Ellinor, ST McGarvey, BD Mitchell, RS Vasan, S Redline, E Silverman, ST Weiss, DK Arnett, J Blangero, E Boerwinkle, J He, C Montgomery, DC Rao, JI Rotter, KD Taylor, JA Brody, YI Chen, L de Las Fuentes, CM Hwu, SS Rich, AW Manichaikul, JC Mychaleckyj, ND Palmer, JA Smith, SLR Kardia, PA Peyser, LF Bielak, TD O'Connor, LS Emery, NT-OfPM Consortium, TOPGW Group, C Gilissen, WSW Wong, PV Kharchenko and S Sunyaev (2021). **Population sequencing data reveal a compendium of mutational processes in the human germ line**. *Science* 373(6558): 1030-1035.

43. Shah, Z, MT Naung, KA Moser, M Adams, AG Buchwald, A Dwivedi, A Ouattara, KB Seydel, DP Mathanga, AE Barry, D Serre, MK Laufer, JC Silva and S Takala-Harrison (2021). **Whole-genome analysis of Malawian *Plasmodium falciparum* isolates identifies possible targets of allele-specific immunity to clinical malaria**. *PLoS Genet* 17(5): e1009576.

44. Shi, X, X Wang, AF Neuwald, L Halakivi-Clarke, R Clarke and J Xuan (2021). **A Bayesian approach for accurate *de novo* transcriptome assembly**. *Sci Rep* 11(1): 17663.

45. Sikorski, MJ, TH Hazen, G Vyas, JM Michalski and DA Rasko (2021). **Draft Genome Sequences of Two Enteroinvasive *Escherichia coli* Strains Representative of Major Enteroinvasive E. coli Clades**. *Microbiol Resour Announc* 10(23): e0031921.

46. Tebben, K, K Bradwell and D Serre (2021). **Variation in selective constraints along the *Plasmodium* life cycle**. *Infect Genet Evol* 92: 104908.

47. Thapa, E, J Aluvathingal, S Nadendla, A Mehta, H Tettelin and NJ Weyand (2021). **Complete Genome Sequence of *Neisseria musculi* Using Illumina and PacBio Sequencing**. *Microbiol Resour Announc* 10(23): e0045221.

48. Trent, M, J Perin, J Rowell, M Shah, J Anders, P Matson, RM Brotman, J Ravel, P Sharps, R Rothman, HE Yusuf and CA Gaydos (2021). **Using Innovation to Address Adolescent and Young Adult Health Disparities in Pelvic Inflammatory Disease: Design of the Technology Enhanced Community Health Precision Nursing (TECH-PN) Trial**. *J Infect Dis* 224(Supplement_2): S145-S151.

49. Tuddenham, S, CA Stennett, RA Cone, J Ravel, AN Macintyre, KG Ghanem, X He and RM Brotman (2021). **Vaginal cytokine profile and microbiota before and after lubricant use compared with condomless vaginal sex: a preliminary observational study**. *BMC Infect Dis* 21(1): 973.

50. Turpin, R, N Slopen, JC Borgogna, CJ Yeoman, X He, RS Miller, MA Klebanoff, J Ravel and RM Brotman (2021). **Perceived Stress and Molecular Bacterial Vaginosis in the National Institutes of Health Longitudinal Study of Vaginal Flora**. *Am J Epidemiol* 190(11): 2374-2383.

51. Turpin, R, S Tuddenham, X He, MA Klebanoff, KG Ghanem and RM Brotman (2021). **Bacterial Vaginosis and Behavioral Factors Associated With Incident Pelvic Inflammatory Disease in the Longitudinal Study of Vaginal Flora**. *J Infect Dis* 224(Supplement_2): S137-S144.

52. Tvedte, ES, J Michalski, S Cheng, RS Patkus, LJ Tallon, L Sadzewicz, VM Bruno, JC Silva, DA Rasko and JC Dunning Hotopp (2021). **Evaluation of a high-throughput, cost-effective Illumina library preparation kit**. *Sci Rep* 11(1): 15925.

53. Udagawa, T, PJ Atkinson, B Milon, JM Abitbol, Y Song, M Sperber, E Huarcaya Najarro, M Scheibinger, R Elkon, R Hertzano and AG Cheng (2021). **Lineage-tracing and translatomic analysis of damage-inducible mitotic cochlear progenitors identifies candidate genes regulating regeneration**. *PLoS Biol* 19(11): e3001445.

54. Vita, R, J Zheng, R Jackson, D Dooley, JA Overton, MA Miller, DC Berrios, RH Scheuermann, Y He, HK McGinty, M Brochhausen, AY Lin, SB Jain, MC Chibucos, J Judkins, MG Giglio, IY Feng, G Burns, MH Brush, B Peters and CJ Stoeckert, Jr. (2021). **Standardization of assay representation in the Ontology for Biomedical Investigations**. *Database (Oxford)* 2021.

55. Wang, Y, E Chan, SG Dorsey, CM Campbell and L Colloca (2021). **Who are the placebo responders? A cross-sectional cohort study for psychological determinants**. *Pain*.

56. Wu, J, D Danko, E Afshinnekoo, D Bezdan, M Bhattacharyya, E Castro-Nallar, A Chmielarczyk, NH Hazrin-Chong, Y Deng, E Dias-Neto, A Frolova, G Mason-Buck, G Iraola, S Jang, P Labaj, PKH Lee, M Nieto-Caballero, OO Osuolale, CA Ouzounis, MH Perlin, B Prithiviraj, N Rascovan, A Rozanska, LM Schriml, T Semmler, H Suzuki, JA Ugalde, B Young, J Werner, MM Zambrano, Y Zhao, C Mason, T Shi and SUBC Meta (2021). **Annotating unknown species of urban microorganisms on a global scale unveils novel functional diversity and local environment association**. *Environ Res*: 112183.

57. Yang, C, B Hallmark, JC Chai, TD O'Connor, LM Reynolds, AC Wood, M Seeds, YI Chen, LM Steffen, MY Tsai, RC Kaplan, ML Daviglus, LJ Mandarino, AM Fretts, RN Lemaitre, DK Coletta, SA Blomquist, LM Johnstone, C Tontsch, Q Qi, I Ruczinski, SS Rich, RA Mathias, FH Chilton and A Manichaikul (2021). **Impact of Amerind ancestry and FADS genetic variation on omega-3 deficiency and cardiometabolic traits in Hispanic populations**. *Commun Biol* 4(1): 918.

58. Yao, Z, H Liu, F Xie, S Fischer, RS Adkins, AI Aldridge, SA Ament, A Bartlett, MM Behrens, K Van den Berge, D Bertagnolli, HR de Bezieux, T Biancalani, AS Booeshaghi, HC Bravo, T Casper, C Colantuoni, J Crabtree, H Creasy, K Crichton, M Crow, N Dee, EL Dougherty, WI Doyle, S Dudoit, R Fang, V Felix, O Fong, M Giglio, J Goldy, M Hawrylycz, BR Herb, R Hertzano, X Hou, Q Hu, J Kancherla, M Kroll, K Lathia, YE Li, JD Lucero, C Luo, A Mahurkar, D McMillen, NM Nadaf, JR Nery, TN Nguyen, SY Niu, V Ntranos, J Orvis, JK Osteen, T Pham, A Pinto-Duarte, O Poirion, S Preissl, E Purdom, C Rimorin, D Risso, AC Rivkin, K Smith, K Street, J Sulc, V Svensson, M Tieu, A Torkelson, H Tung, ED Vaishnav, CR Vanderburg, C van Velthoven, X Wang, OR White, ZJ Huang, PV Kharchenko, L Pachter, J Ngai, A Regev, B Tasic, JD Welch, J Gillis, EZ Macosko, B Ren, JR Ecker, H Zeng and EA Mukamel (2021). **A transcriptomic and epigenomic cell atlas of the mouse primary motor cortex**. *Nature* 598(7879): 103-110.

59. Zhao, N, DF Khamash, H Koh, A Voskertchian, E Egbert, EF Mongodin, JR White, L Hittle, E Colantuoni and AM Milstone (2021). **Low Diversity in Nasal Microbiome Associated With *Staphylococcus aureus* Colonization and Bloodstream Infections in Hospitalized Neonates**. *Open Forum Infect Dis* 8(10): ofab475.

60. Ziffra, RS, CN Kim, JM Ross, A Wilfert, TN Turner, M Haeussler, AM Casella, PF Przytycki, KC Keough, D Shin, D Bogdanoff, A Kreimer, KS Pollard, SA Ament, EE Eichler, N Ahituv and TJ Nowakowski (2021). **Single-cell epigenomics reveals mechanisms of human cortical development**. *Nature* 598(7879): 205-213.

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