

The Pathogen and Microbiome Institute presents

PMI Quarterly

Summer 2019



DR. EMILY COPE

ASSISTANT DIRECTOR,
ASSISTANT PROFESSOR
OF
BIOLOGICAL SCIENCES



Director's Corner

Welcome to the summer edition of PMI Quarterly! This summer, the Museum Fire burned almost 2000 acres north of town. Thanks to a quick response by a team of firefighters, it is now fully contained. Our summer was also marked by the loss of our friend and colleague, Dr. Nate Nieto. His legacy will live on at NAU and PMI through his important research on tick-borne disease. As the beautiful (if dry!) summer weather starts to change, I'd like to reflect on the exciting work done at PMI.

Summer 2019 was filled with several research developments and student accomplishments that we'd like to share with you. This issue highlights two publications, one by Dr. Crystal Hepp and one from Dr. Greg Caporaso and his team. Dr. Hepp discusses her research on translational epidemiology. You can also learn about QIIME 2, a microbiome bioinformatics platform developed by Dr. Caporaso and his team. Keep reading to learn about a new collaboration between PMI researchers, Drs. Patricia Mongoni and Bridget Barker, who are studying a potential link between Valley Fever and B-CLL, the most common leukemia affecting adults. Our PMI students have also had an exceptional year! Read about their many awards and exciting travels to Ecuador and Norway in this edition. Finally, peek inside to learn about the inaugural Southwest One Health Symposium, held this summer at the Museum of Northern Arizona.

We hope you enjoy this edition of PMI Quarterly,

Emily

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NAU NORTHERN ARIZONA UNIVERSITY

QIIME 2™: NAU team reengineers bioinformatics software for next generation of microbiome science

Heather Tate — NAU News - July 24th, 2019

Over the last 20 years, rapid advances in DNA sequencing and bioinformatics technologies have significantly improved scientists' understanding of the microbial world. Examples include increased knowledge about the vast diversity of microorganisms; how microbiota and microbiomes impact disease and medical treatment; how microorganisms impact the health of our planet; and the potential for applications of microbiome biotechnology in the medical, forensic, environmental and agricultural fields.

In 2009, Associate Professor, Greg Caporaso of the Center for Applied Microbiome Science at NAU's Pathogen and Microbiome Institute—who was at that time working as a Postdoctoral Scholar in Rob Knight's laboratory, then at the University of Colorado at Boulder—led the development of the first open-source QIIME™ (Quantitative Insights Into Microbial Ecology) bioinformatics software platform under Knight's guidance. An announcement of the software launch was published in *Nature Methods* in 2010. The software enables scientists to perform microbiome analysis from increasingly large amounts of DNA sequencing data, and was designed to take users from raw sequencing data through publication-quality graphics and statistics.

Since its initial release, QIIME (pronounced "chime") has supported many microbiome studies and gained a broad user and developer community. In fact, QIIME has been cited in more than 15,000 academic papers, making it one of the most often-cited scholarly works by an NAU author.

Beginning in 2016, Caporaso and his team completely reengineered the platform to facilitate reproducible and modular analysis of microbiome data. The project to redesign and disseminate QIIME 2 was funded by a National Science Foundation grant awarded to Caporaso and Knight, and is described in a recently published paper in *Nature Biotechnology*.

"As we interacted with QIIME users in our online support forum, in our workshops and through direct collaborations, we realized there was potential for better serving the growing community of microbiome researchers in academia, government and industry," Caporaso said. "QIIME 2 retains the features that made QIIME a powerful and widely-used analysis pipeline, while providing new features that will drive the next generation of microbiome research," Caporaso said, "including interactive spatial and temporal analysis and visualization tools; support for metabolomics and shotgun metagenomics analysis; and automated data provenance tracking to ensure reproducible, transparent microbiome data science."

"A core goal of QIIME 2 is to cultivate a diverse and inclusive community of scientists, software engineers, statisticians, educators, students and other microbiome stakeholders who are openly sharing methods, data and knowledge to advance microbiome research."

QIIME 2 A GLOBAL COMMUNITY EFFORT

According to Caporaso, QIIME 2 is a community effort that his team is leading. Collaborators on the project represent 77 research institutions from 9 countries

all over the world: Canada, China, Denmark, Germany, Italy, South Korea, the Netherlands, Australia and the United Kingdom.

NAU Research Software Engineers, Evan Bolyen, Matthew Dillon, and Jai Ram Rideout performed the primary development of QIIME 2, along with Postdoctoral Scholar, Nicholas Bokulich. Additional NAU collaborators include faculty researchers, Paul Keim, Emily Cope and Tal Pearson; research staff, Jorden Kreps and Charles H.D. Williamson; and students, John Chase, Kestrel Gorlick, Chris Keefe, Ahmad Turan Naimey, and Arron Shiffer.

"Advances in microbiome research promise to improve many aspects of our health and our world, and QIIME 2 will help drive those advances by enabling accessible, community-driven microbiome data science," Caporaso said.

Caporaso and others on the team have already led 25 workshops for QIIME 2 users all over the world, including two workshops at the National Institutes for Health—each one attracting 75 participants—as well as a workshop for 40 students in Copenhagen, Denmark, conducted in June 2019.

To learn more about QIIME 2, visit <https://qiime2.org>.

Right: Dr. Greg Caporaso



B-cell chronic lymphocytic leukemia (B-CLL) and the Valley Fever fungus (*Coccidioides*)

Dr. Patricia Mongini — PMI



Dr. Patricia Mongini

B-CLL, the most common leukemia in adults, typically surfaces after the age of 60, making it highly relevant to a major group of Arizonans. While leukemic lymphocytes in blood are small and quiescent, a fraction of those infiltrating lymph nodes and spleen cycle rapidly and accrue further mutations, leading to B-CLL progression in patients.

A major advance in understanding why B-CLL progresses relatively rapidly in some cases and slowly in others is the recognition that the malignant B cell's receptor for antigen (BCR) plays an important role.

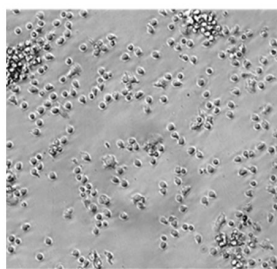
Patients whose malignant B-CLL clones express BCR able to engage many diverse microbial antigens (as well as body apoptotic cells) have significantly reduced survival. In contrast, patients with malignant clones expressing more selective BCR have better prognosis.

This and epidemiological findings lead those in the field to believe that microbial exposure may have a role in the development of B-CLL.

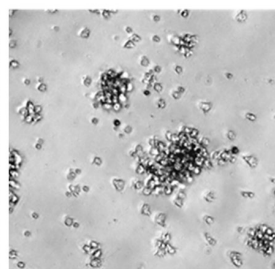
Patricia Mongini (B.S. from NAU in 1972; Ph.D. from Stanford University in 1976) is an Adjunct Professor at PMI, whose east-coast research career focused on discovering

Phase microscopy of human B-CLL cell cultures (day 6):

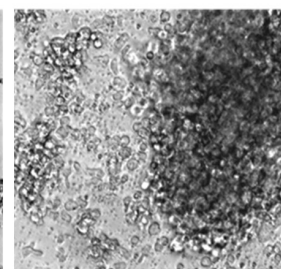
Culture: IL-15 alone



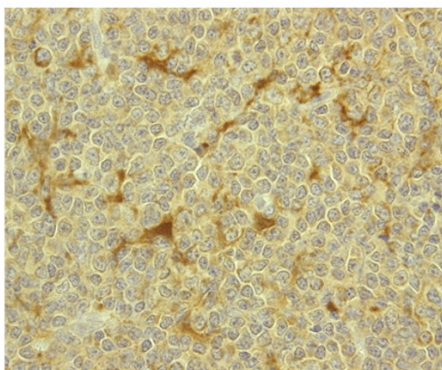
CpG DNA



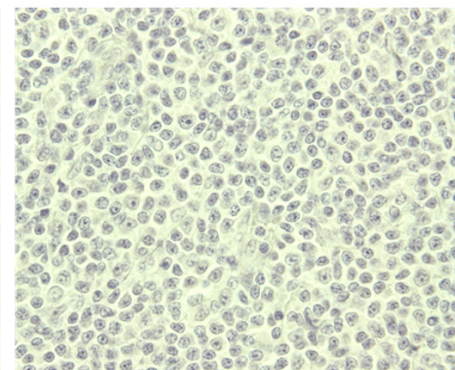
CpG DNA + IL-15



Immunohistochemical evidence of IL-15-producing stromal cells within B-CLL-infiltrated lymph node



Goat anti-human IL-15



Normal Goat IgG

how normal and malignant B cells growth is initiated and controlled. Most recently, she led a study culminating in several Journal of Immunology papers that illuminated stimuli/mechanisms for human B-CLL growth within in vitro cultures. The fact that sources of such stimuli were found proximal to foci of proliferating B-CLL cells in patient lymphoid tissues enhanced their relevance.

In 2018-2019, the papers were recognized as ranking in the top 10% of those published by the journal. It is notable that the identified synergistic stimuli, CpG DNA which is abundant in microbes and engages toll-like receptor 9 (TLR-9) and the

cytokine IL-15, are elevated during microbial infections.

Since moving back to her home state of Arizona, Dr. Mongini has begun collaborating with Dr. Bridget Barker of PMI (an expert in *Coccidioides* fungus – the agent of Valley Fever) to investigate whether chronic lung exposure to *Coccidioides* may accelerate B-CLL development and/or growth. The study is being conducted with a novel transgenic mouse strain (Eμ-TCL-1), developed and contributed by Dr. Carlo Croce, which is prone to B-CLL development upon aging.

IN THE SPOTLIGHT

2018-2019 is the Year of record breaking student achievement

Dr. Dawn Birdsell, Associate Director — PMI



Dr. Dawn Birdsell

This 2018-2019 academic year, we had a record number of students receiving competitive awards and scholarships. Among the ~32 students enrolled, 21 (>62% of PMI students) of them were recipients – with numerous individuals receiving multiple awards and scholarships. In previous years about ~30% of PMI students were recipients. This 2018-2019 upward jump in student awardees reflects the solidification of PMI's mission that an important part of professional training is the pursuit of competitive awards and scholarships.

PMI mentors systematically expose students to various award opportunities and provide significant support in this effort. This upward jump also reflects the composition of our student population in respect to their level of motivation and caliber. As a consequence, 2018-2019 has been a record breaking year in the number of student awardees. This type of achievement increases a student's professional value and future opportunities.

Among the awards competitively won was the prestigious Goldwater scholarship (GW), which went to Chris Keefe from Dr. Greg Caporaso's lab. This is on the heels of last year's win where two PMI students (Shelby Hutton and Austin Dikeman) were 2018 GW recipients. This repeated record is in part the fruition of a PMI work environment that intersects dedicated mentors, high caliber students, and exciting research. PMI's very first GW Scholar was Dr. Amy Vogler (awarded in 1998) followed by Cedar Mitchell (awarded in 2014).

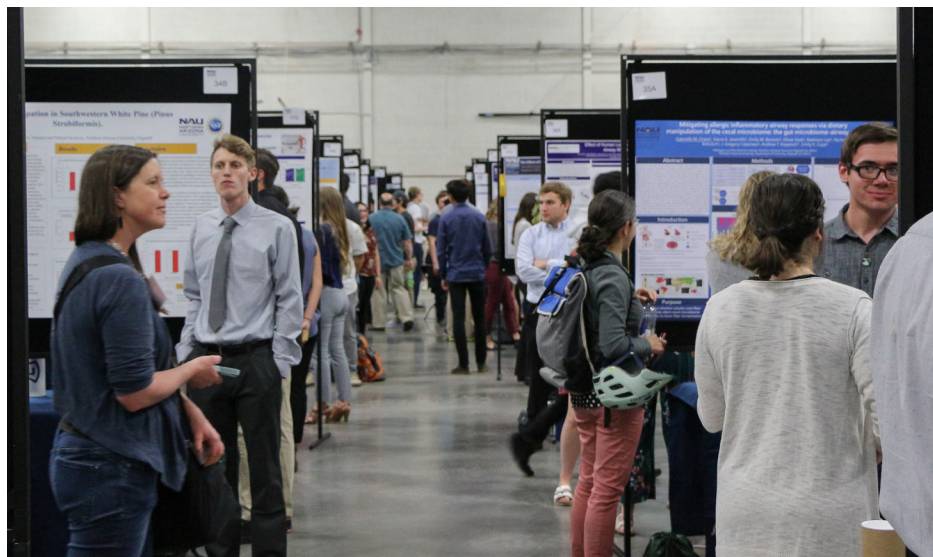
Our record breaking trend of student achievement spilled over into the 2018-

2019 conference arena as well (locally, nationally, and internationally). PMI students swept up awards at two local conferences, NAU Undergraduate Research Symposium (UGRADS) and the 58th Branch American Society for Microbiology (ASM). At UGRADS, PMI students placed 1st, 2nd, and 3rd for poster prize (1st = Madison Martz, 2nd = Allen Clarke, 3rd = Nicole Bratsch) and at the Branch ASM meeting, several PMI students were placed as winners for poster and oral presentations. Jordyn Upton traveled to Australia for a conference and won best poster prize. Several of our students traveled to national conferences to present their research.

The visibility and prestige of our undergrad program has allowed us to recruit higher caliber students. The many lab tours put on by our undergrads enabled us to showcase the exciting research done by our PMI students to the greater community and to other existing organizations. This in turn has enabled us to successfully recruit high caliber students from organizations such as the NAU honors program, AZ Flinn scholarship program (two Flinn scholars have joined our ranks - Nicole Bratsch 2016 and Kailee Savage 2019), and any ambitious NAU student motivated enough to join an exciting prestigious research program.

The high caliber nature of the students in our program should not come as a surprise. The application and interview process is not a walk in the park. The training program is rigorous and the level of research involvement expected of PMI students require focused commitment. The result is a fantastic program that enables high caliber students to perform quality research and professionally achieve more than they thought possible as evidenced by the accounts of students' achievement recited in this article.

2019 Undergraduate Research Symposium



PMI Undergraduate in Ecuador

Kaitlyn Parra, Undergraduate Research Assistant — PMI



Left: Undergraduate Student, Kaitlyn Parra / Right: A cow from a home where Kaitlyn and the team collected soil

My name is Kaitlyn Parra. I am an undergraduate student working under Dr. Bridget Barker at PMI. This summer, I conducted research at the Universidad de San Francisco de Quito in Quito (USFQ), Ecuador through the Minority Health and Health Disparities Research Program (MHIRT), an NIH funded program that allows minority students at Northern Arizona University to do an eight-week summer research internship abroad.

The principal investigators for this project were Dr. Talima Pearson of PMI and Dr. Verónica Barragan of USFQ. Besides the PIs, the people involved were Dr. Catherine Propper and Kristi Mascarenas who were in charge of the program. I did also have a marvelous research partner, Christina Anaya.

The project was focused on the presence of pathogenic *Leptospira* spp., the causative

agent for the world's most common zoonosis, *Leptospirosis*, in rural coastal Ecuador. The goal was to study the prevalence of the bacteria in the soil from homesteads where pigs previously tested positive for the pathogen in Rocafuerte, Ecuador. Christina and I were under the guidance of Dr. Barragan's doctoral student, Ligia Luna. The most rewarding part of the lab work was being able to conduct research in Spanish. As a bilingual person this was a personal triumph!



From left to right: Ligia Luna, Christina Anaya, Patricia Zambrano, Kaitlyn Parra, and Dr. Talima Pearson.

Though the lab work was a phenomenal experience, my favorite part of the trip was just being in Ecuador. The best part wasn't seeing the rich history of Quito, or even the Amazon, rather the people of Ecuador, especially my host family. Everyone who I met made my trip even better. This summer was truly unforgettable and has reinforced my love for infectious disease!



Translational Epidemiology

Dr. Crystal Hepp, Assistant Professor in the School of Informatics, Computing, and Cyber Systems, published a perspective piece in a special issue of *mSystems*, a publication of the American Society for Microbiology. In "[Towards Translational Epidemiology: Next-Generation Sequencing and Phylogeography as Epidemiological Mainstays](#)," Hepp details research projects that her group collaborates on with county and state public health agencies where the objective is to identify pathogen source locations with the longer-term goal of implementing proactive interventions.

THE BAT CAVE

News from NAU's Bat Ecology and Genetics Lab (B EGL)

Bat team travels to Norway for the 8th International Barcode of Life Conference

Daniel Sanchez, Graduate Research Assistant (PhD Program) — July 30th, 2019

DNA barcodes are short genetic fragments used for taxonomic identification and species discovery. At the Pathogen and Microbiome Institute, we use the 16S rRNA barcode for microbiome studies to address topics of human, veterinary, and environmental health. Barcodes other than 16S allow the same types of studies for Eukaryotic organisms. I am part of PMI's Bat Team. Led by Dr. Faith Walker, we use DNA barcodes to reveal taxonomic mixtures from complex substrate (e.g., feces, water, ancient bat and bison bones) using a method called metabarcoding. Given an appropriate combination of PCR primers and computational tools, metabarcoding is a Swiss-army knife that allows us to conduct bat roost surveys, study animal diet, probe foodwebs, or profile ancient communities. It is no surprise that the application and promise of DNA barcoding has become a global phenomenon.

Every other year, the International Barcode of Life (iBOL) consortium holds a major conference dedicated to a wide range of topics in DNA barcoding. I am happy to have represented the Bat Team and PMI at the 8th conference in the series this last June. The conference was held in the Norwegian city of Trondheim, a gorgeous city bordered by an enormous fjord and fairytale forests of spruce and birch. Founded by Vikings over a thousand years ago, Trondheim is now the country's technological capital. With an attendance of 450 participants from 61 nations, I gave a talk on the diet of the endangered New Mexico jumping mouse and presented a poster on our expedition to Zambia to capture the diet of large African mammals with MinION sequencing. Lucky for me, there were plenty of diet researchers to bounce ideas off of. But other fascinating topics involved the use of DNA barcodes for dating Antarctic ice sheet

collapse, understanding and monitoring biogeochemical cycling, barcoding the entire country of Costa Rica's species (project Bioalpha), and even barcoding the world's species and their interactions (project BIOSCAN). As an early career scientist, I am highly appreciative of the experience because the international setting provided the ultimate snapshot of the field's state. Attending iBOL allowed me to network and discuss ideas with a good sample of the international community. It also validated where our team's work fits in this field and where it can go. Afterwards, I took some time to do a road trip through the country. There was no shortage of breathtaking landscape, sites of folk heritage, and awesome Viking stuff. My travel and participation was supported by the ARCS Templin/Lauber endowment scholarship.

Below: Barcode of Life 2019 Conference Group Photo



2019 Southwest One Health Symposium

Alyssa Barrett, Administrative Associate — PMI — August 15th, 2019



Southwest One Health Collaborative



The inaugural Southwest One Health Symposium was hosted in Flagstaff, AZ on August 6th and 7th, 2019. The symposium is designed to bring together diverse disciplines, resources, and strengths to establish a comprehensive view of One Health research and action in the American Southwest.

The symposium was highly interactive and included state-of-the-art science talks, micro-presentations, One Health collaborative activities, and even a grant competition! The symposium was hosted by the Translational Genomics Research Institute's One Health Collaborative and sponsored by The NARBHA Institute.

At this symposium, two of PMI's researchers were awarded for their excellent micro-presentations. These micro-presentations were challenging to present as there were strict rules stating that only 4 or 5 slides total could be used and the presentation had to be under 4 or 5 minutes depending on the session you were in.



AMALEE NUNNALLY, RESEARCH TECHNICIAN

For her talk titled "A One Health Approach to *Clostridioides difficile*," Amalee received first place and a \$100 cash prize.

Amalee was one of four speakers to present their micro-presentations on August 6th. Amalee was restricted to giving a 4-minute presentation with a max of 4 slides.

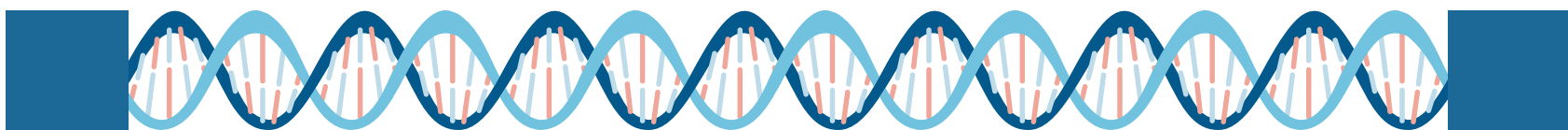
SIERRA JARAMILLO, GRADUATE RESEARCH ASSISTANT (MASTER'S PROGRAM)

For her talk titled "The Gut Microbiome, Prebiotic Fiber, and Asthma," Sierra won first place in her August 7th session. She was one of four other speakers, and Sierra won a \$100 cash prize.

Sierra was restricted to giving a 5-minute presentation with a max of 5 slides.



Left: Sierra Jaramillo / Right: Amalee Nunnally



The Keim Award for Excellence in Undergraduate Research

"Science is more than just learning facts and principles;
it is a process and it needs to be experienced.

The research experience changes a student's development and
ultimately they will approach problem solving and life differently."

- Dr. Paul Keim

Established by Paul & Jenny Keim, The Keim Award for Excellence in Undergraduate Research is designed to reward outstanding student research effort and to encourage the participation of students in research endeavors.

The Keim Award will be awarded annually in the spring semester by a committee organized by the NAU Vice President of Research.

Your contributions to this award will make you a part of a community that supports NAU students. Even a small gift makes you a formal part of this network and we will keep you informed as we announce this award each spring.

To make a gift to the Keim Award for Excellence in Undergraduate Research visit nau.edu/NAUKeimAward or mail your gift to:

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