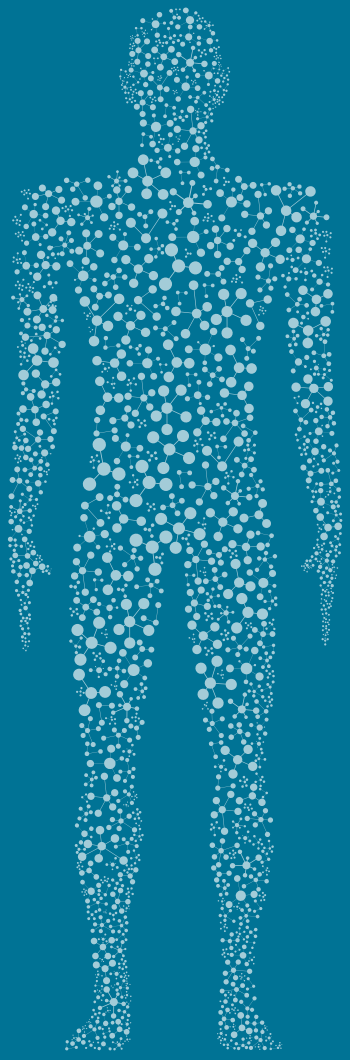
THE UNIVERSITY OF CHICAGO

The Duchossois Family Institute

2023 Impact Report

DFI CREDO

The DFI will optimize wellness and thriving longevity through groundbreaking science on the human immune system, genetics, the microbiome, and their shared systems.



By developing new knowledge about the optimal relationships between the human body and the microbiome, the DFI will identify, develop, and disseminate practices and treatment methods that break new ground in improving health around the world.

Written by Daniel Story | Designed by Alyssa Cieslak and Jaimie Lake

Essential steps to optimizing health and thriving longevity:

Demonstrate impact of the microbiome in causing disease

Engage clinicians who will commit time to study specific patient populations

Show how changes in the microbiome and metabolome are associated with disease states

Correct microbiome and metabolome defects associated with adverse outcomes

The Duchossois Family Institute:
Harnessing the Microbiome and Immunity for Human Health

There is palpable excitement among the researchers at the Duchossois Family Institute: 2023 was both a banner year and a stepping stone to even bigger advances. "It is an amazing place with amazing infrastructure," says DFI scientist Laurie Comstock, PhD. "Faculty want to come here and graduate students want to work in one of our labs."

The opening of the current Good Manufacturing Practices (GMP) facility and the start of the DFI's first clinical trial will further distinguish the institute from its peers. The addition of dedicated clinical faculty members will maximally leverage its resources to accelerate laboratory research toward clinical application and impact for patients. "While there are lots of microbiome centers, the DFI uniquely brings together microbiome-focused laboratories and core facilities with embedded clinicians to move things from experimentation to treatment in humans," says DFI Director Eric Pamer, MD.

Many of the significant advances made last year at the DFI deal with the chemicals resulting from cellular metabolism, called metabolites—similar to the carbon dioxide expelled during human breathing. The residents of the gut microbiome produce a wide range of metabolites, which can have profound effects on the microbial community and on our bodies.

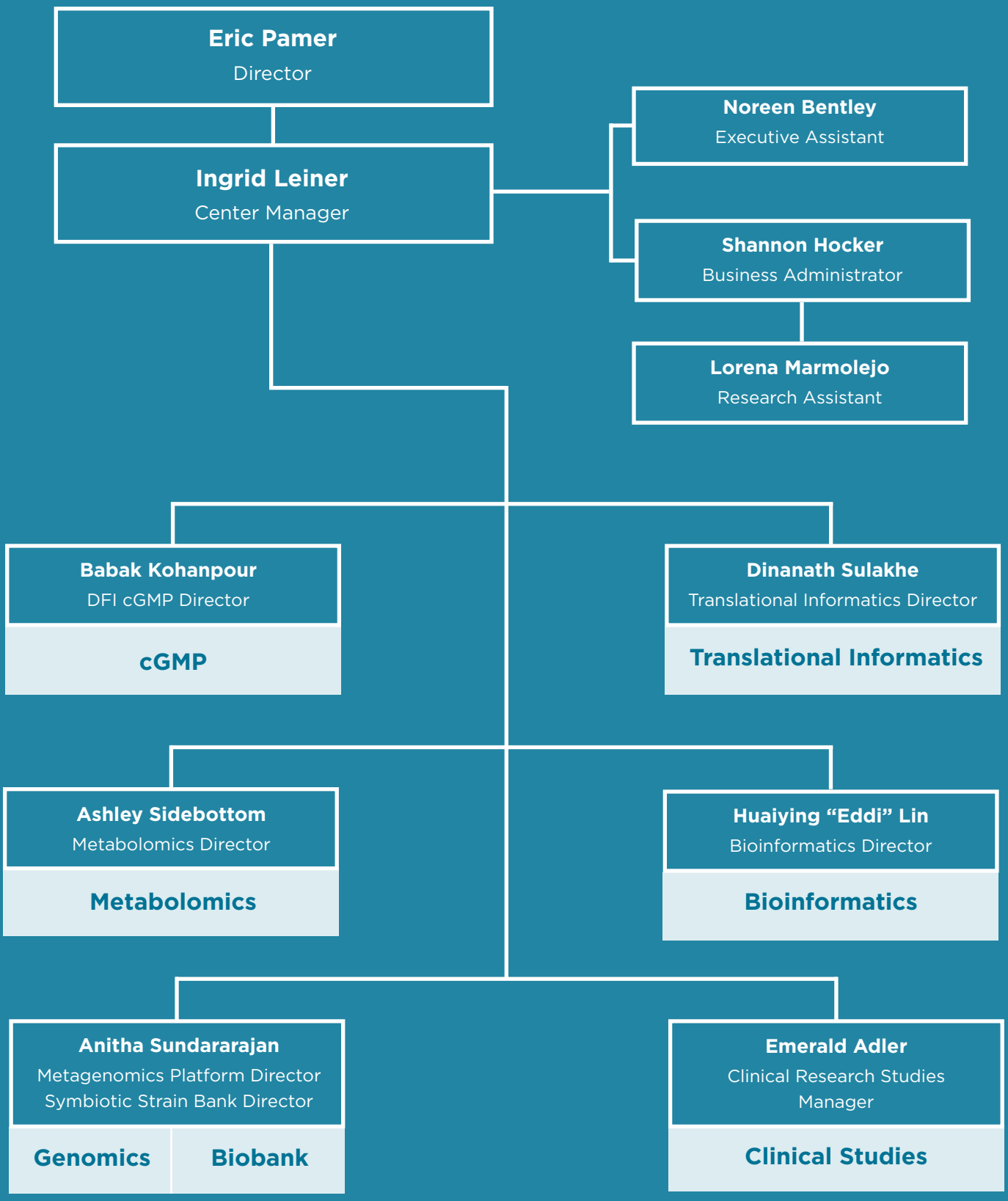
Metabolites can be "drug-like," says Samuel Light, PhD, Neubauer Family Assistant Professor of Microbiology. "They enter the bloodstream and travel throughout our body, and interact with our cells and organs much in the same way that drugs can."

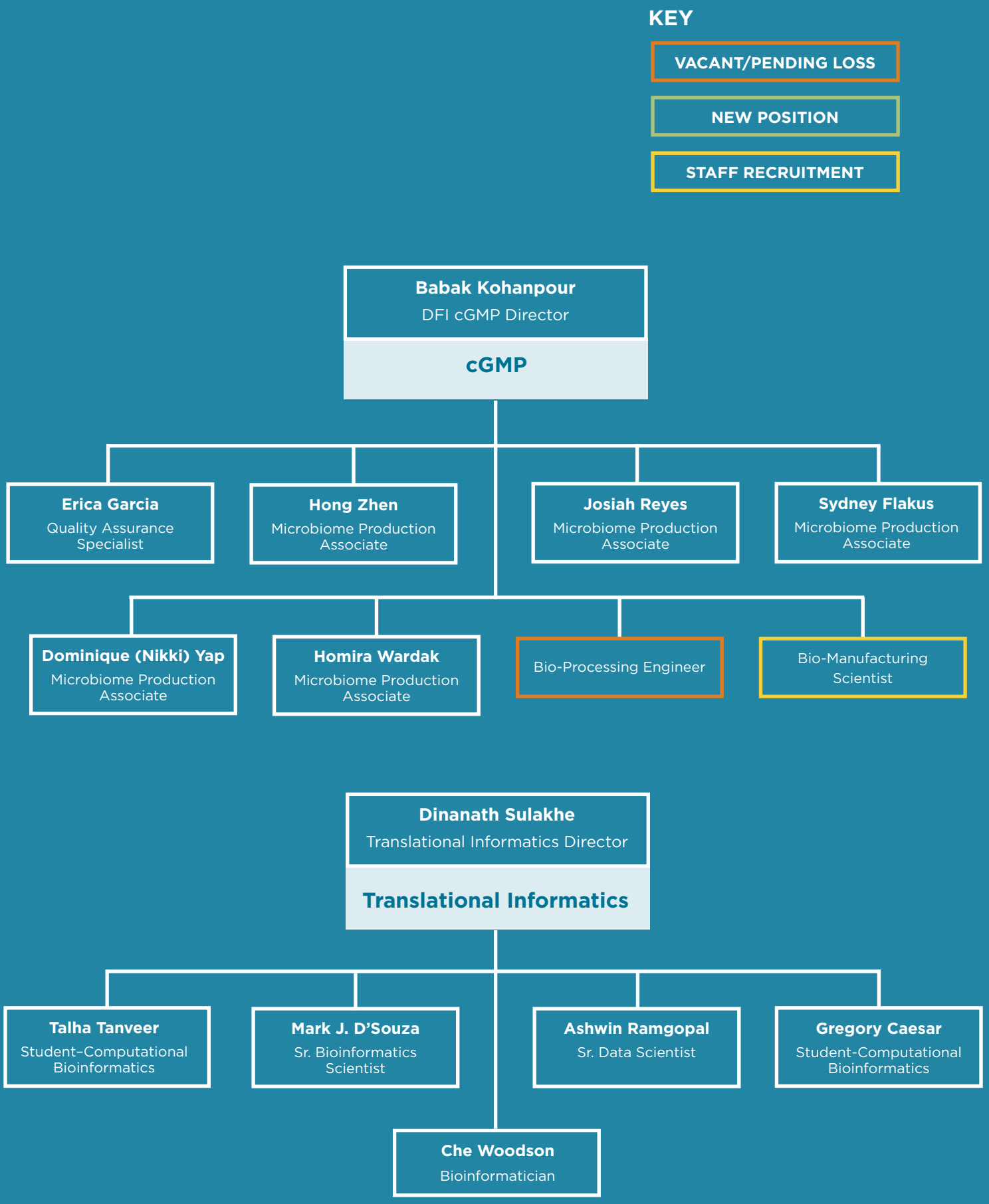
In harmonious states, we give our gut microbes what they need and they release metabolites that support our health. This is comparable to our relationship with houseplants, where the carbon dioxide we exhale is essential for their life, while the oxygen they give off is essential to ours. Conversely, metabolites can cause harm: imidazole propionate, a metabolite found in elevated levels in patients with type 2 diabetes, interferes with the body's use of insulin.

Metabolites represent a critical focus area for research and a key tool for clinical application: they are so important that a core facility, the Host-Microbe Metabolomics Facility (HMMF), is dedicated to them. Understanding how bacterial metabolism works, what metabolites microbes produce under what circumstances, and how metabolites affect our bodies is essential for using the microbiome to improve human health.

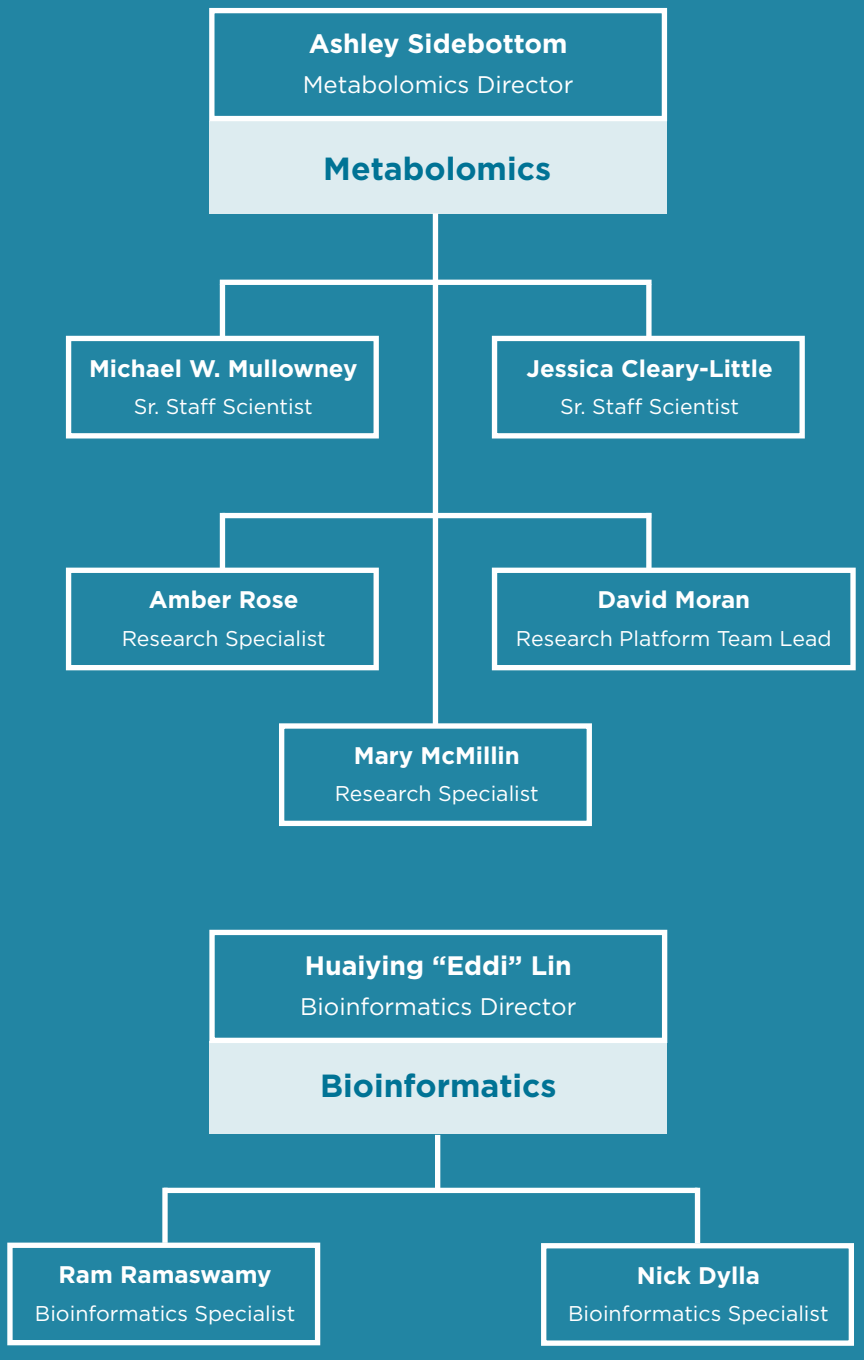
Philanthropy brought this energetic research ecosystem to life, and continues to accelerate its progress. This report highlights some of the advances made at the DFI in 2023.

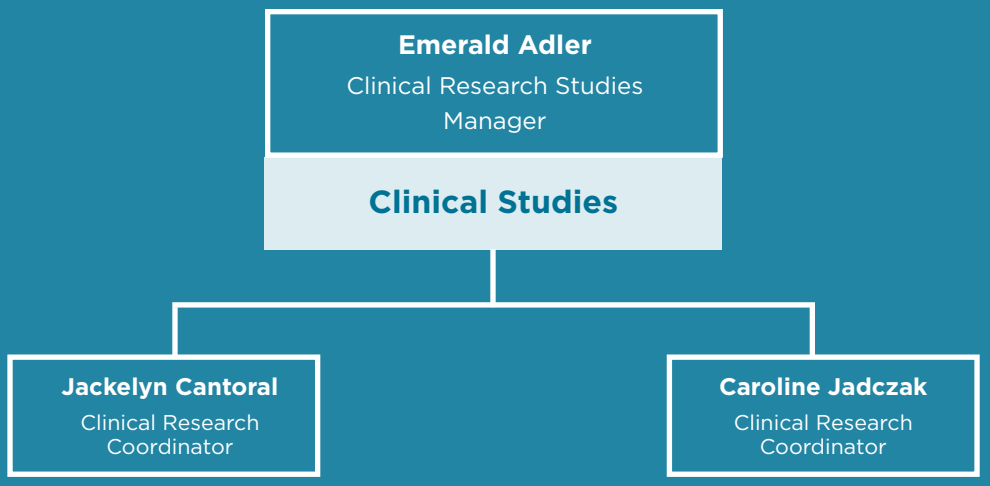
DFI Organization Chart

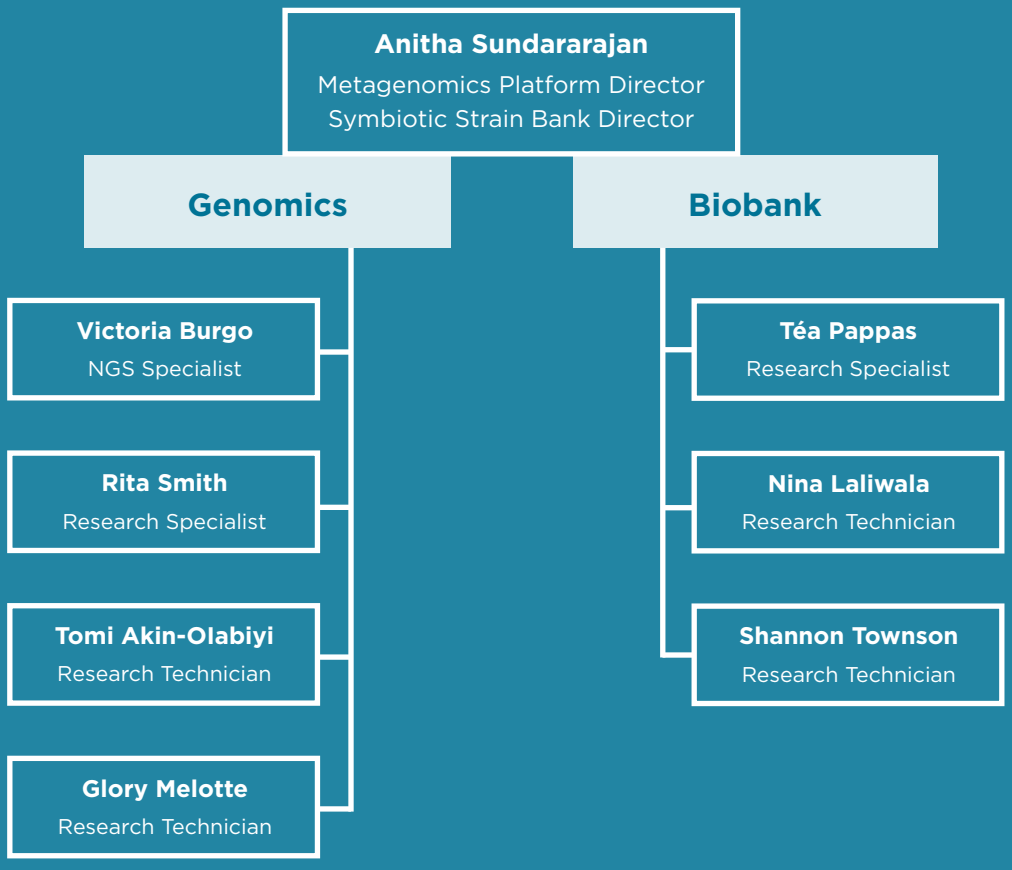



KEY
VACANT/PENDING LOSS
NEW POSITION
STAFF RECRUITMENT
Babak Kohanpour
DFI cGMP Director
cGMP
Erica Garcia
Quality Assurance Specialist
Hong Zhen
Microbiome Production Associate
Josiah Reyes
Microbiome Production Associate
Sydney Flakus
Microbiome Production Associate
Dominique (Nikki) Yap
Microbiome Production Associate
Homira Wardak
Microbiome Production Associate
Bio-Processing Engineer
Bio-Manufacturing Scientist
Dinanath Sulakhe
Translational Informatics Director
Translational Informatics
Talha Tanveer
Student-Computational Bioinformatics
Mark J. D'Souza
Sr. Bioinformatics Scientist
Ashwin Ramgopal
Sr. Data Scientist
Gregory Caesar
Student-Computational Bioinformatics
Che Woodson
Bioinformatician

DFI Organization Chart




Emerald Adler
Clinical Research Studies Manager
Clinical Studies
Jackelyn Cantoral
Clinical Research Coordinator
Caroline Jadczak
Clinical Research Coordinator


Anitha Sundararajan
Metagenomics Platform Director
Symbiotic Strain Bank Director
Genomics
Biobank
Victoria Burgo
NGS Specialist
Rita Smith
Research Specialist
Tomi Akin-Olabiyi
Research Technician
Glory Melotte
Research Technician
Téa Pappas
Research Specialist
Nina Laliwala
Research Technician
Shannon Townson
Research Technician

The DFI Good Manufacturing Practice (GMP) Facility

The DFI's Good Manufacturing Practice (GMP) facility was completed in 2023 and is now undertaking the final steps to enable FDA-adherent production of drugs for clinical trials of microbiome augmentation. Once full approval is received, DFI faculty will be able to produce novel bacterial treatments based on UChicago research for use in patients.

The GMP facility completes the full pathway from inquiry to impact: a new laboratory discovery can be translated into a new therapy and applied in clinical trials, all without leaving campus. This capability sets the DFI apart from other microbiome-focused academic research institutes—and marks a new stage in microbiome research generally. "We are moving into an area that is unique in the US," says Dr. Pamer.

The faculty are eager to begin. “People here at the DFI are lining up to use it,” says Dr. Comstock.

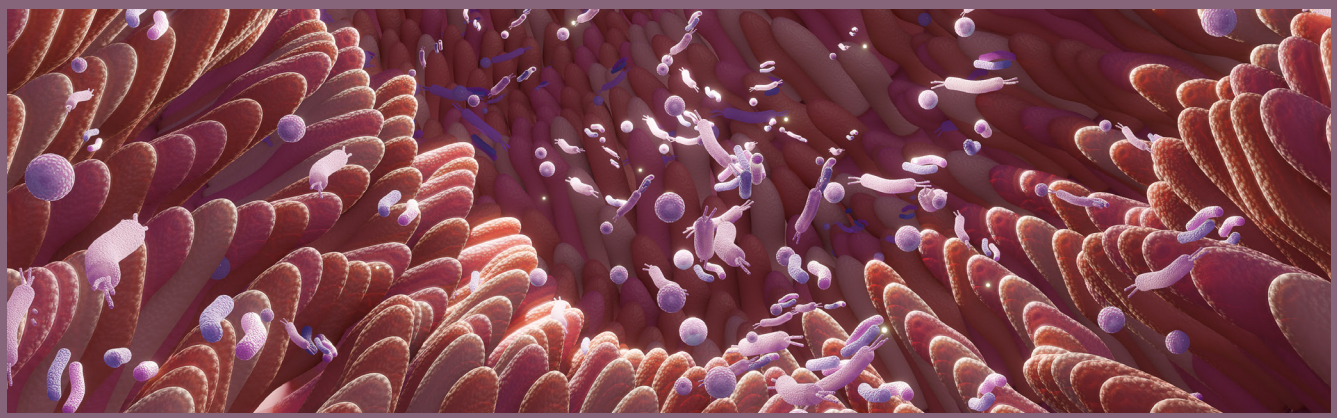
The GMP facility joins other established resources in the DFI, including the HMMF, Microbiome Metagenomics Facility (MMF), the Symbiotic Bacterial Strain Bank (SBSB), and the bioinformatics and translational informatics teams. These groups collaborate to an unusual degree among core facilities: faculty investigations often use all of them. “It’s kind of like a family,” says Dr. Comstock. “What Eric has set up here is unlike anywhere else.”

Clinical Research

To best leverage the GMP facility and accelerate the pace of translation from discovery to delivery, the DFI added two clinical faculty members in 2023: **Christopher Lehmann, MD**, and **Matthew Odenwald, PhD'15, MD'17**. Through shared appointments with the Department of Medicine—a hallmark UChicago structure that encourages inter-unit collaboration—they will bridge the lab to the clinic.

Led by **Drs. Lehmann** and **Odenwald**, the DFI's first trial will test a novel treatment to reestablish healthy microbiomes in patients with liver disease. The broad-spectrum antibiotics these patients receive all but destroy their microbiomes, putting them at risk for a wide range of potential problems—especially the development of life-threatening infections caused by antibiotic-resistant bacteria. By reconstituting their microbiomes with a community of healthy bacteria, the team aims to prevent such infections and improve patients' health.

This clinical trial represents a complete in-house effort: DFI clinicians delivering a DFI-designed and -produced treatment to patients screened with a DFI-designed diagnostic, all based on DFI laboratory research. Progress in key areas over the past year set the stage for this exciting venture to proceed.



A Picture of Health

To help patients build healthy microbiomes from scratch, the team needs to know what a healthy microbiome looks like in the context of liver disease. **Dr. Odenwald** led an observational study, published last November in *Nature Microbiology*, to answer two key questions: what bacterial populations appear in patients with better outcomes, and what are those bacteria doing that helps?

Encompassing more than 250 patients with liver disease at UChicago Medicine, the study examined hundreds of fecal samples to identify which bacteria were present and what metabolites those bacteria produce. They then correlated those data points with clinical information including medications and patient outcomes.

The result was one of the most comprehensive pictures ever assembled of microbiome health in patients with liver disease. Patients showed vastly reduced microbiome diversity—which was expected following antibiotic treatment—and decreased levels of metabolites known to support immune function and tissue health. Their investigation especially highlighted that a specific group of beneficial bacteria, *Bifidobacterium*, is associated with prolonged survival and reduced risk of antibiotic-resistant infection.

> **"(The study) gives us a strong rationale to start an interventional trial where we aim to modify the gut microbiome."**

The study "gives us a strong rationale to start an interventional trial where we aim to modify the gut microbiome," says Dr. Odenwald.

Research like this could only be done at the DFI—because of the DFI's own unique resources and its connections with other University units. The DFI's MMF and HMMF examined the samples; the University's Center for Research Informatics powered high-level data collection and analysis; and clinical partnerships provided access to patients at UChicago Medicine.

New Diagnostics for New Treatments

The new treatment will be among the first of its kind—so how will doctors know when to prescribe it?

DFI research led by **Christopher Lehmann, MD**—along with scientific advances from Ashley Sidebottom, PhD, and the team in the HMMF—provides an answer. The study, published in *Cell Host & Microbe*, identified connections between gut microbiome composition, metabolite levels in fecal samples, and clinical outcomes in patients undergoing liver transplantation.

Crucially, they demonstrated that metabolite profiling on its own could reliably predict risk of post-operative infection: they didn't need to know the exact composition of a patient's microbiome, just the metabolites it was putting out.

This discovery means that metabolite profiling could be used as a diagnostic tool to identify which patients have dysregulated microbiomes and could benefit most from a microbiome-based therapy. No such diagnostic tool currently exists. "Right now, if you're a doctor and you want to know if your patient's microbiome is messed up in real time, you can't do it, it's impossible," says Dr. Lehmann.

The most complete method for getting a snapshot of a patient's microbiome is metagenomic profiling, but those procedures take too long for clinical use on patients with severe conditions. "Even with the best facility—like we've got—it can still take weeks for that information to come back," says Dr. Odenwald. "That's not really quick enough for us to know who may benefit from microbiome therapy or who to approach for a clinical trial."

A metabolomic profile, by contrast, can be done much more quickly. While it doesn't give the full picture of a patient's microbial communities, the study proved that it gives doctors what they need to make an accurate prescription in the moment. Dr. Sidebottom and her team developed a novel assay that can measure clinically relevant metabolites in a single day. "Stool in the morning, answer in the afternoon," says Dr. Lehmann.

The HMMF team is patenting their discovery, and plans to use the new test in the forthcoming clinical trial—and it has potential for broad use in supporting patient care. "It will allow the clinician to know if their patient's microbiome is really bad or if it's okay," says Dr. Lehmann. "They can use that information to give them a probiotic, to recommend they eat certain foods, to isolate them from patients who have infections, or to decide what type of antibiotic they might need if they do get an infection."

Final Preparations

In addition to these studies, Drs. Lehmann and Odenwald have been engaged in a broad range of collaborative efforts to support the clinical trial launch, including preparing for submission of an Investigational New Drug (IND) application to the FDA in early 2024. Dr. Odenwald has been developing the clinical trial design for this application, including setting criteria for which patients to include, and devising of a protocol for recruiting such patients and monitoring them throughout the trial.

Dr. Lehmann's expertise in infectious diseases and clinical care have been essential. To demonstrate that the bacteria used in the treatment are safe, he searched their genetic codes for DNA signatures that might indicate toxin production or antibiotic resistance. He also tested a wide variety of antibiotics against them to show that they could be killed if they did somehow cause an infection. This novel work—antibiotic research has historically focused on dangerous rather than helpful bacteria—has the side benefit of identifying antibiotics that spare "good" bacteria and thus do less damage to healthy microbiomes.

He is also partnered with GMP technicians to design the treatment in a patient-friendly way, which increases the chances that patients complete the full treatment course appropriately. "I talk to patients all the time so I have a good feel for what people can and can't do at home," he says.

Together with the rest of their DFI colleagues, Drs. Odenwald and Lehmann are excited to begin. "It's a really unique and exciting environment," says Dr. Odenwald. "We're the only academic center that has a team and facility like this. You have to be here to do this."

Basic & Translational Research

Clinical research through the GMP facility feeds and is fed by basic and translational work to better understand the highly complex human microbiome. With the combined resources your philanthropy has made available to them, DFI researchers led innovative, high-impact investigations in 2023.

Samuel Light, PhD

Dr. Light led a landmark study, published in *Nature Microbiology*, into the unusual metabolic strategies employed by bacteria in our digestive tracts. Where most bacteria have genes to encode just a handful of respiratory enzymes—which means they must live on a very limited diet of specific molecules—Dr. Light found bacteria whose genes encoded dozens of enzymes, indicating they could gather the energy they need from a wide range of different foods. These microbes engage in diverse metabolism so we don't have to. "There's so much chemical complexity within the food that we eat that we couldn't possibly encode enough digestive enzymes to break everything down," says Dr. Light. "Evolution outsourced that job to the gut microbiome."

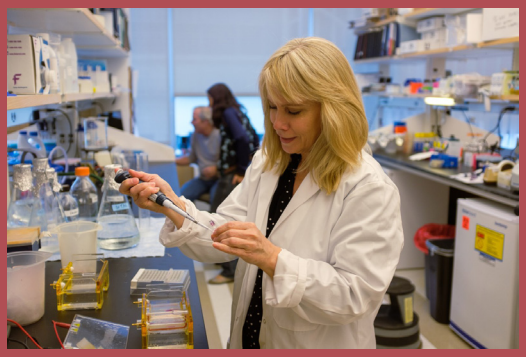
Because the gut is hypoxic—low on oxygen—microbes there tend to make energy through fermentation, a chemical process that we are familiar with from yeast. Most respiration (including ours) requires oxygen, but other molecules can do the job if a cell is set up for it. However, no research had previously identified bacteria, in any environment, with such a wide range of respiratory capabilities. Furthermore, the team identified three distinct groups of such bacteria, which were only distantly related: their respiratory diversity evolved separately.

This discovery also provides clues to what the inside of our gut is actually like as an environment, in the same way that the shape of a bird's beak can give information about the local plant life. The fact that these abilities evolved separately indicates that they provide a meaningful survival advantage—which might suggest, for example, that their environment changes rapidly and unpredictably.

"If you have a really stable environment, that favors more streamlined, specialized microbes," says Dr. Light. "If you have a changing environment that favors microbes that are capable of doing all these different things to survive."

Beyond its value in the field of microbiology, this research and other studies like it is essential for designing effective microbiome-based treatments, which depend heavily on specific microbes making specific metabolites. It's like using sheep dogs to care for your flock: you need to know what the dogs eat, how they like to live, and what conditions they work best in to get the results you're looking for in the sheep.

"Once we have a better picture of that ecosystem and the role of individual microbes in it, we'll be able to better interpret what it means when we see changes between healthy and disease states," says Dr. Light. "That will also help us to go in and fix things that are off."



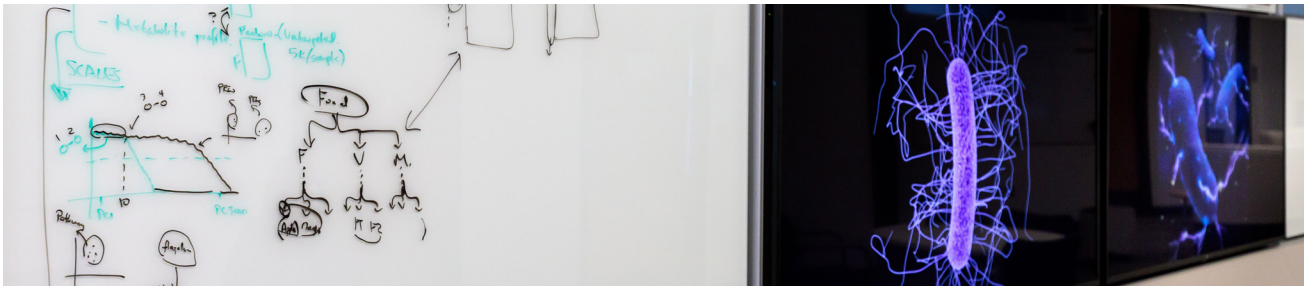
Laurie Comstock, PhD

In 2023, Dr. Comstock made major steps in translating her earlier laboratory discoveries into new treatments for patients.

Dr. Comstock assembled an international team to develop a new treatment for bacterial vaginosis (BV) from an antimicrobial molecule discovered in her laboratory. BV is extremely common—affecting approximately 30 percent of women between 14 and 49—and is associated with adverse health outcomes including sexually transmitted infections, infertility, and life-threatening pregnancy-related complications. The antibiotics currently used to treat BV offer initial symptomatic improvements, but the disease recurs in 45 percent of patients. The team is working toward validating their proposed treatment in animal models. Dr. Comstock is in discussions with a biotech company to support the treatment's future development, and will seek NIH support for the work in 2024.

In a separate project, she applied for a patent on her earlier discovery of a genetic modification to *Bacteroidales* bacteria—the most abundant order of bacteria in the human gut—to improve their chances of surviving in a new host.

Many microbiome-based treatments, including the one to be tested in the DFI's first clinical trial, consist of communities of bacteria custom tailored to achieve a specific effect in the body. Their success as treatments relies on those beneficial bacteria establishing a stable presence—or "engrafting"—in their new environment. To do so, they must outcompete other bacteria who live in the same space or need the same resources: just like macro-scale animals, these cellular lifeforms will readily attack competitors to survive. "Bacteria make toxins to kill each other," says Dr. Comstock.



"The protective factors we have identified will allow them to withstand other microbes' toxins so they can get a foothold in the ecosystem and persist to deliver health-promoting molecules to the host. Most live biotherapeutic microbial consortia will include multiple species of *Bacteroidales*," says Dr. Comstock. "If you engineer them in this particular manner, they should be more resilient." As microbiome medicine grows, such advances will make a greater and greater impact.

If not at the DFI, Dr. Comstock would not have the resources at hand—from core facilities to the Polsky Center for Entrepreneurship and Innovation—to push these projects forward herself.

Arjun Raman, AB'08, MD, PhD

"A big push in our lab over the last year and a half has been trying to understand how to design microbiomes for our uses," says Dr. Raman. Beyond studying individual microbes to learn their structures and functions, or studying individual conditions to create a microbiome-based treatment for them, Dr. Raman's lab is creating a platform that could generate healthy, functional bacterial communities for any biologically possible function.

Because these bacterial communities are complex and interactive—greater than the sum of their parts—Dr. Raman is approaching the problem by studying whole groups rather than individuals.

Using statistically driven machine-learning approaches, he simulates hundreds or thousands of microbial communities to identify the hidden, critical factors that govern group function and identify successful compositions.

> For their first test case, Dr. Raman's lab is applying this method to Klebsiella pneumoniae: a multi-drug-resistant pathogen that kills nearly 200,000 people annually, often through hospital-acquired infections.

His platform designed a 15-member bacterial community that kills *Klebsiella pneumoniae* in laboratory conditions, and outperforms whole-stool transplant from a healthy donor—the current most effective treatment—in mouse models. In partnership with Dr. Lehmann and the GMP facility, Dr. Raman aims to bring this bacterial community to clinical trial as a new treatment within a year. "It's a position of luxury to have everything in one house," he says, "so you can immediately go talk to the person you need to talk to in order to get things done."

The whole point of his platform, however, is the ability to do something similar for any condition that could be modulated by the gut microbiome—such as preeclampsia, a life-threatening autoimmune dysfunction in which the immune system targets the placenta or fetus during pregnancy. Last year, Dr. Raman received a $1.5 million grant from the Bill and Melinda Gates Foundation to apply his platform to that problem, with the goal of developing a microbial community that will dampen the immune response and prevent preeclampsia.

Dr. Raman ultimately aims to commercialize this platform, so that the resources of the pharmaceutical industry could dramatically accelerate the pace at which it is applied to new conditions and the resulting treatments come to market. But for the time being, the DFI has engineering and manufacturing capabilities to rival the best in each category—all under one roof—making it the best place for this research to proceed at maximum speed. "Eric has really built up a full-stack operation," he says. "I can't stress enough how unique that opportunity is."

Multidisciplinary Grants

DFI multidisciplinary grants draw researchers from around the University to apply their abilities, perspectives, and efforts to urgent questions in microbiome research. They are a powerful mechanism through which the DFI can take best advantage of its place within a world-class research university and academic medical center, with access to leading experts in nearly every field.

With the GMP facility fully operational, Dr. Pamer intends to use future DFI grants to support research projects focused on microbiome modification: investigations that could not be done anywhere else. He anticipates putting out a call for proposals in summer of 2024.

Research supported by previous DFI grants continues to advance both in the laboratory and in the clinic.

CHRISTINA CIACCIO, MD

CATHRYN NAGLER, PHD

The Effect of Fiber Supplementation on Oral Immunotherapy Outcomes in Children with Peanut Allergy

Funded by a DFI multidisciplinary grant in 2021, **Drs. Ciaccio** and **Nagler** are leading a clinical trial of a new combination therapy for pediatric peanut allergies. Currently, children with severe peanut allergies are treated by desensitization: starting with miniscule amounts, they are exposed to peanuts in increasing doses over a long period of time in hopes their bodies will acclimate. Desensitization causes significant side-effects and doesn't succeed for every patient; even if it is effective, patients require daily maintenance therapy—eating a single peanut—to sustain its benefits. "We want something that looks more like a cure," says Dr. Ciaccio.

For the trial, patients receive potato starch as a prebiotic before beginning desensitization. Research has shown that this prebiotic fiber can affect the composition of patients' microbiomes and the metabolites their microbiomes produce—especially butyrate, which has been shown to calm immune responses.

So far, they have recruited 23 patients for their phase I, placebo-controlled trial. Most have not yet completed the full course of treatment, but preliminary data is extremely promising with some able to tolerate unusually high doses of peanuts. The team aims to complete the study, publish the results, and move the treatment into a phase II trial.

DARIA ESTERHÁZY, PHD

MARIA LUCIA MADARIAGA, MD

Human Mucosal Lymph Node Compartments as Local Responders to the Microbiome

With a grant awarded in 2022, **Drs. Esterházy** and **Madariaga** are studying the lymph nodes surrounding the gut and lungs, to identify structural and functional differences between locations.

The human body has hundreds of lymph nodes—more than 150 connected to the gut alone—which play central roles in the adaptive immune system: the cells and processes that "learn," through infection or vaccination, how to fight specific invaders. "All the big intestinal diseases, such as inflammatory bowel diseases, food allergies, celiac disease, colon cancer, all involve this adaptive branch," says Dr. Esterházy.

Through RNA sequencing—a method for measuring which genes cells are using, and thus what shapes they take and what activities they perform—the team has identified significant structural differences in lymph nodes depending on their placement along the digestive tract. Using mice, they further found out that these architectural differences are conferred by access to microbes and Vitamin A in the small bowel. This architectural variance suggests variance in local immune activity, which is especially relevant along the gut: different parts of the digestive tract perform different functions, house different microbes, and fall victim to different diseases.

This project represents early-stage, exploratory research—no one has previously catalogued the differences in these lymph nodes in humans, and little is known about how lymph node structure affects immune response—and, because of the role lymph nodes play in adaptive immunity, it has broad implications. For example, vaccines may be more effective if administered in certain parts of the body to engage specific lymph networks. The team aims to publish their results next year.

Dissemination, Commercialization, & Sustainability

Ken Onishi, PhD, the DFI's dedicated manager for business development and licensing at the Polsky Center for Entrepreneurship and Innovation, advances commercialization efforts for both individual faculty and the DFI broadly. In addition to supporting faculty and identifying protectable assets, Dr. Onishi also helps build industry-specific relationships for the DFI.

There continues to be broad commercial interest in the DFI's Symbiotic Bacterial Strain Bank (SBSB), as well as its stores of data collected from both microbes and clinical samples.

In the past year, there are two major relationships to report on: **Archer-Daniels-Midland Company (ADM)** and **Seres Therapeutics**.

ADM is a multinational food processing and commodities trading corporation headquartered in Chicago. With a market cap of $49 billion, ADM has a diverse portfolio spanning sectors intertwined with the human and environmental microbiome. Representatives from ADM have been meeting with Drs. Pamer and Onishi to discuss licensing isolates from the SBSB to use in probiotic products. Negotiations are underway toward a material transfer agreement, through which microbes from the SBSB are sent to ADM for their own research and development. A separate, royalty-bearing license agreement will be negotiated for the subset of those microbes they choose for use in future products.

Seres Therapeutics, a late-clinical-stage biotechnology company, is a pioneer in live biotherapeutics to modulate the human microbiome. Seres was the first company to gain approval for a live microbiome biotherapeutic in 2023 with a product treating recurrent *Clostridioides difficile* infections, which typically occur after use of antibiotics. Overlapping interests between Seres and the DFI include consortia design and reverse translational clinical studies to understand which bacteria confer protective and therapeutic effects in patients. Seres is especially interested in using the DFI's rich clinical datasets to develop future therapies.

New technologies in 2023

The DFI's originating vision as a research institute that makes an impact on human health continues to drive entrepreneurial activity. DFI researchers patent their discoveries at a rate unusual among their peers, with the institute accounting for more than one application per month in 2023.

Items in the following list are arranged by date of submission. The lead inventor is indicated in **bold**.

Limosilactobacillus reuteri *normalizes blood-brain barrier dysfunction and neurodevelopment deficits resulting from maternal immune activation*

Provisional Patent | January 29, 2023

Inventors: Erika Claud, Jing Lu, Lei Lu

When administered while mothers are nursing, *Limosilactobacillus reuteri* alleviates neurodevelopmental disorders observed in mouse offspring subject to maternal immune insult.

Directing Lachnospiraceae biosynthesis with novel genetic tools

Provisional Patent | May 20, 2023

Inventors: Mark Mimee, Jack Arnold

This patent involves a set of genetic tools and strategies to engineer bacterial species from the Lachnospiraceae family which natively produce compounds thought to benefit human health. These tools consist of different molecular "parts" which can change the capacity of these bacteria to produce compounds of interest, including but not limited to therapeutic molecules.

A clinical isolated avirulent strain protects against wildtype virulent Clostridioides difficile *infection*

Non-Provisional Patent | May 31, 2023

Inventors: Eric Pamer, Qiwen Dong

Co-administration of this avirulent strain of *Clostridioides difficile* with an antibiotic can provide long-term protection against future virulent *Clostridioides difficile* infections. The team is in discussions with VIC Technology Venture Development regarding this asset.

Microbiota Augmentation to Reestablish Commensal Organisms (MARCO)

Provisional Patent | June 13, 2023

Inventor: Eric Pamer

This patent covers the compositions and methods of using bacterial consortia to alleviate infections in patients with liver disease based on metabolomic profiles, including the combination of microbes to be used in the DFI's forthcoming clinical trial.

Induction of Bacteroidales *protective responses to increase and enable gut colonization*

Non-Provisional Patent | July 19, 2023

Inventor: Laurie Comstock

These genetic modifications to bacteria from the gram-negative *Bacteriodales* order, which constitutes about 50 percent of bacteria in the human gut, promote better engraftment.

Use of bacteriophage as antimicrobial agents against Klebsiella pneumoniae

Non-Provisional Patent | August 1, 2023

Inventors: Mark Mimee, Ella Rotman

This patent contains a phage library obtained from a Chicago sewage system and a combination of phages that modifies *Klebsiella pneumoniae* so the body's own immune system can destroy it.

Stool metabolic profile to predict hospital-acquired infection

Non-Provisional Patent | August 21, 2023

Inventors: Eric Pamer, Nicholas Dylla, Christopher Lehmann

This screening tool predicts hospital acquired infections and liver transplant-associated infections, based on fecal microbiota and fecal metabolite profiles.

Spectral Correlation Analysis of Layered Evolutionary Signals (SCALES)

Nationalized in the USA & awaiting response from USPTO | September 15, 2023

Inventors: Arjun Raman, Mark Zaydman

SCALES can characterize gene function of unannotated parts of bacterial genome inferred by using a library of evolutionarily conserved genomes of other bacteria.

A process to statistically relate structure with function of biological systems

Provisional Patent | September 25, 2023

Inventors: Arjun Raman, Benjamin Doran

The statistical model relates protein sequences with the function of biological systems, potentially leading to efficient screening of proteins for therapeutic uses.

Bifidobacteria *expansion and associated metabolite production correlates with reduced incidence of infections in advanced liver disease,* and *Lactulose-mediated gut* Bifidobacteria *expansion is associated with improved survival*

Provisional Patent | September 25, 2023

Inventors: Eric Pamer, Huaiying Lin, Matthew Odenwald

Administration of lactulose reduces the rate of Vancomycin-resistant *Enterococcus* (VRE) by increasing *Bifidobacteria* populations in the gut.

Microbiome metabolite profile

Non-Provisional Patent | October 11, 2023

Inventors: Eric Pamer, Nicholas Dylla, Matthew Stutz

This screening tool utilizes fecal metabolite levels to predict COVID-19 respiratory failure.

A process mirroring evolution to design synthetic consortia that perform a function

Provisional Patent | October 12, 2023

Inventors: Arjun Raman, Seppe Kuehn, Rita Oliveira

This computational tool selects specific microbes to combine to achieve a therapeutic effect.

A microbial consortia that depresses Klebsiella pneumoniae

Provisional Patent | October 12, 2023

Inventors: Arjun Raman, Seppe Kuehn, Rita Oliveira

This bacterial consortia reduces the rates of *Klebsiella pneumoniae*, and preliminary data suggests it is generalizable to other pathogens, including VRE.

A novel statistical framework for spatial transcriptomic analysis

Provisional Patent | November 8, 2023

Inventor: Arjun Raman, Vivek Behera, Benjamin Doran, Hannah Giba

This is a computational model that analyzes spatial transcriptomic data to find new therapeutic targets, as well as stratify patients for clinical trials in oncology.

Bacteroides *lysogenic bacteriophage for in situ delivery of genetic payloads to bacteria in a gastrointestinal tract*

Provisional Patent | December 8, 2023

Inventor: Mark Mimee, Jay Fuerte-Stone

Lysogenic bacteriophage isolated from *Bacteroides* bacteria have been engineered to deliver genetic payloads to susceptible bacterial hosts in the gastrointestinal tract. These bacteriophage can be used to specifically increase or decrease abundance of the target bacteria via natural selectivity of the bacterial phage.

Combinatorial therapy using saponins and defined human-derived bacterial consortia for Klebsiella pneumoniae *suppression*

Provisional Patent | October 26, 2023

Inventor: Eric Pamer, Jessica Little, Rita Oliveira

DFI bacteria can modify saponins—a compound produced in many plants—to help fight *Klebsiella pneumoniae* infection.

Duchossois Family Institute Fellows

Philanthropy creates opportunities for excellent young scientists to work at the forefront of microbiome research and train with the field's leading minds. This year, two researchers joined the DFI: their experiences here will prepare them for long careers of innovative, multidisciplinary work.

Bum-Joon Jung, PhD

Dr. Jung completed his PhD in nanoscience and technology from the Korea Advanced Institute of Science and Technology. His University of Chicago co-mentors are Anindita Basu, PhD, in the Department of Medicine and Supratik Guha, PhD, in the Pritzker School of Molecular Engineering. He will be leveraging his experience in designing microfluidic devices to develop the first fast and high-throughput cell lysis platform that can break apart any kind of microbial cell without destroying the contents, thus enabling single-cell genomics of the microbiome.

Natalia Cortés-Delgado, PhD

Dr. Cortés-Delgado holds a PhD in ecology and evolution from the University of Illinois at Chicago, where she investigated the role of the Andes as a driver of genetic differentiation in bat populations. Under the mentorship of Cara Brook, PhD, assistant professor of ecology and evolution, she is investigating how bat gut microbiomes respond, and confer resistance, to viral infection. This work could lead to exciting applications, such as the development of microbiota-based prophylaxes to prevent illness in other species, including humans.

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