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**CHICAGO**  
UChicago Medicine

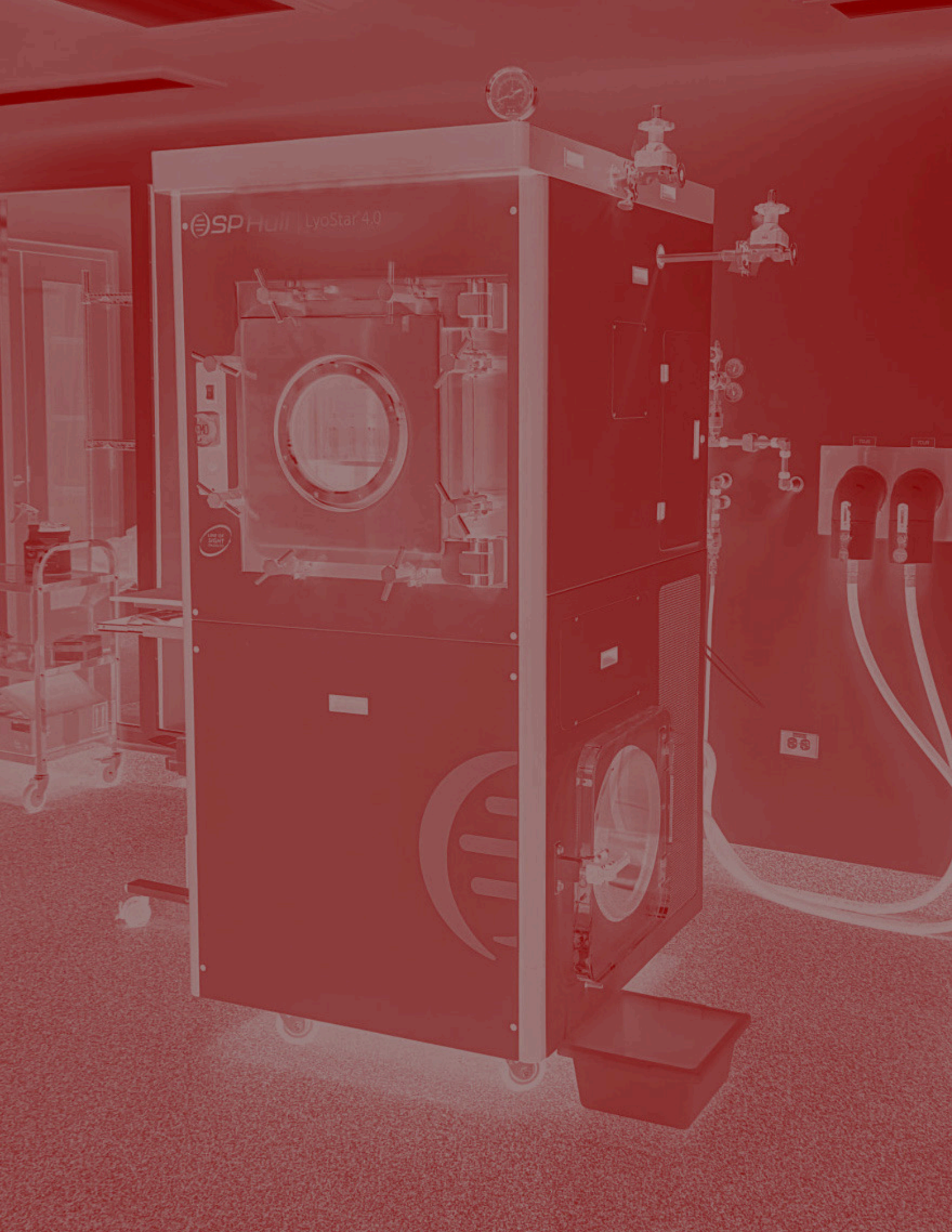
**Duchossois  
Family  
Institute**

# **HARNESSING THE MICROBIOME AND IMMUNITY FOR HUMAN HEALTH**



2024

[www.dfi.uchicago.edu](http://www.dfi.uchicago.edu)



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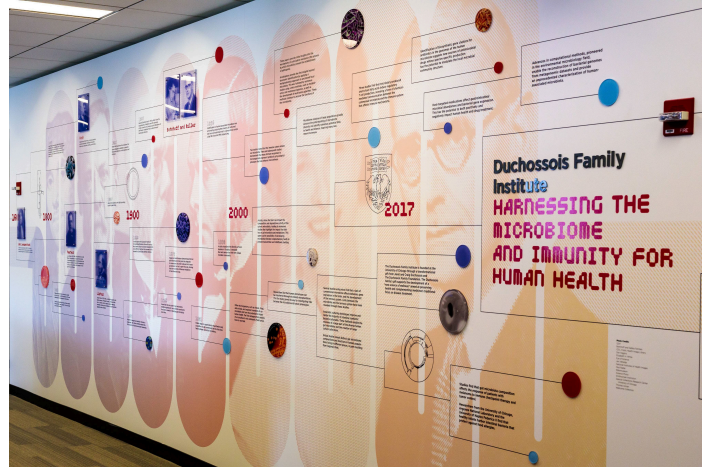


# A Note from the Director



## Eric G. Pamer, MD

Director, Duchossois Family Institute  
Donald F. Steiner Professor, Department of Medicine



The Duchossois Family Institute was established in 2017 with the goal of enhancing human health by investigating the microbiome and its impact on the immune system. The microbiome is composed of a vast array of microorganisms, and our understanding of these complex microbial populations and their impact on health and disease has, until recently, been limited. Technical, bioinformatic, and computational advances, however, have enabled us to precisely identify and characterize the microbes colonizing humans and other mammals. Clinical studies have correlated microbiome compositions with a wide range of human diseases, including autoimmunity, inflammatory bowel disease, metabolic syndrome, atherosclerosis, cancer and infectious diseases.

While much remains to be discovered about the interactions between colonizing microbes and their human hosts, there is increasing evidence that the microbiome can be optimized to improve health by enhancing disease resistance. Translating laboratory and experimental discoveries into clinical therapies that enhance the health of individuals and human populations, however, remains a major challenge. The DFI is working with laboratory investigators and clinicians to correlate microbiome compositions with disease susceptibility or resistance, with the goal of identifying targetable mechanisms to prevent or ameliorate disease. To accelerate the development of microbiome-targeting therapeutics, the DFI has established core facilities, assembled teams of investigators, and developed manufacturing capacity to conduct clinical trials to enhance health by optimizing microbiome compositions and functions. The DFI has built a current Good Manufacturing Practices (cGMP) facility to manufacture live biotherapeutic products for clinical trials of microbiome optimization at the University of Chicago Medical Center. The DFI's cGMP facility will enable University of Chicago investigators to translate laboratory discoveries into novel clinical therapies.

The microbiome's impact on human health is widely recognized and well-established. The DFI and investigators at the University of Chicago are excited to be leading the way into a new era of enhancing health by microbiome optimization.

## Laurie Comstock, PhD

Professor, Department of Microbiology



The Comstock lab studies bacteria of the order Bacteroidales, which are abundant members of the human gut microbiota. Studies in the lab focus on understanding how these bacteria interact with each other both cooperatively and antagonistically to form health-promoting microbial communities. The lab uses basic microbiological, genetic, biochemical, and gnotobiotic mouse analyses, combined with genomic, metagenomic, and computational analyses to understand these complex interactions. They have discovered several classes of new antimicrobial proteins that these bacteria use to compete in their ecosystem, and are studying their mechanisms of action, ecological properties, and how those molecules can be translated for human health benefits. Another focus of the Comstock lab is the evolution of microbes in the human gut: how genetic elements horizontally transferred between bacterial species personalize each individual's gut microbiota, and confer community benefits and phenotypes.

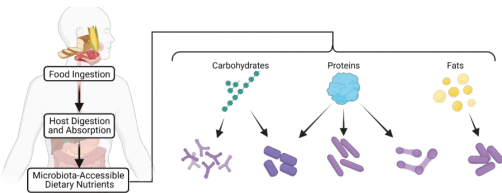


## Sam Light, PhD

Neubauer Family Assistant Professor, Department of Microbiology



We are currently limited in our understanding of the ecological strategies by which diverse microbes colonize the gut microbiome. With the goal of establishing context to inform the interpretation and manipulation of microbiome states, the lab's research is focused on defining the microbes and/or genes that enable colonization of distinct ecological niches within the gut. Current projects primarily focus on elucidating the basis of metabolic specialization within the gut microbiome and take three separate approaches: 1) As part of an unbiased discovery approach, the lab is performing high-throughput microbial enrichments to elucidate novel modes of metabolic specialization. 2) As part of a bioinformatically driven approach, they are applying genome mining-based analyses to evaluate the distribution of broad enzyme classes and to generate testable hypotheses about the microbes responsible for particular types of metabolic specialization. 3) As a final metabolite-inspired approach, the lab is working backwards from biomedically relevant metabolites to identify the microbes and energy metabolisms that produce them.



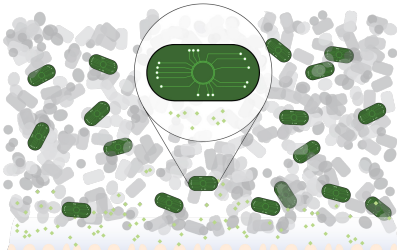


## Mark Mimee, PhD

Assistant Professor, Department of Microbiology



The Mimee Lab leverages synthetic biology to engineer the microbiome, exploring strategies to modify commensal bacteria and bacteriophage for diagnostic and therapeutic applications. By genetically manipulating commensal microbes, they seek to create living devices that can serve as biosensors to probe the structure and function of the microbiome and as cell-based therapeutics for infectious and inflammatory disease. Additionally, they develop approaches to augment the natural properties of bacteriophage—viruses that infect bacteria—to create novel therapies for antibiotic-resistant bacterial infections. Mimee's long-term vision is to implement these synthetic biology technologies to chart new basic and translational studies to exploit the microbiota for human health.



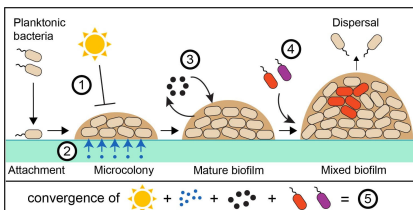
## Sampriti Mukherjee, PhD

Assistant Professor, Department of Molecular Genetics & Cell Biology



Bacterial responses to self-generated and environmental stimuli influence their survival, persistence in particular niches, and lifestyle transitions between individual and collective behaviors. How the information encoded in multiple sensory inputs is extracted and integrated to control collective behaviors is largely mysterious. To address this knowledge gap, the Mukherjee lab focuses on two research areas:

- 1) Photo sensory signal transduction. Although light is a ubiquitous environmental stimulus and photoreceptors have been well-studied in the context of photosynthetic organisms, the function of photosystems in non-photosynthetic bacteria are mostly unknown. They have identified an entire photo-sensing cascade in the human pathogen *Pseudomonas aeruginosa* — enabling crucial insight into light-driven control of bacterial behaviors relevant to human disease. The lab is characterizing the photo-sensing signaling system, defining the physiological role of light, and exploring the possibility of using light as an antibacterial therapeutic.
- 2) Convergence of sensory signaling pathways. It is imperative that bacteria integrate varied sensory cues to make key behavioral transitions; however, the mechanisms by which they do so are poorly understood. Mukherjee's goal is to identify the molecular mechanisms by which information from different sensory signaling pathways are combined in the control of bacterial behaviors. She and her lab are currently studying how photo-sensing, quorum-sensing, and nutrient-sensing cues are integrated into the regulation of collective behaviors.

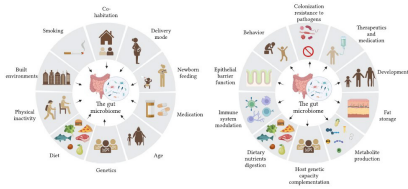


# Eric Pamer, MD

Donald F. Steiner Professor, Department of Medicine



The Pamer laboratory studies interactions between pathogenic and beneficial bacteria and their mammalian hosts. His laboratory's research focuses on a wide range of commensal bacteria that have been characterized at the genomic, proteomic, and metabolomic levels and they are using gnotobiotic mice to test assembled commensal consortia for their ability to enhance resistance against pathogenic bacteria. Using these platforms, they have identified mechanisms of antimicrobial resistance that can be exploited to reduce the risk of infection by highly antibiotic-resistant pathogens.



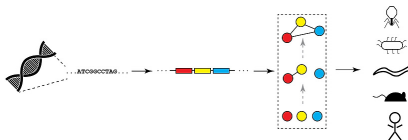
# Arjun Raman, MD, PhD

Assistant Professor, Department of Pathology



Understanding engineered systems composed of many parts is predicated on robust physics-based theories. Understanding natural systems is challenging because such systems have come from a completely different design process: iterative variation and selection. Thus, we do not have access to a 'wiring diagram' of biological systems. The Raman laboratory is focused on two questions: 1) What is a strategy for inferring the architecture of interactions for evolved systems? 2) Why is the architecture the way it is? Using bacteria as a model, the lab has shown that hierarchical patterns of protein interactions, i.e. the emergence of pathways from individual proteins, can be derived purely from the statistics of evolutionary variation.

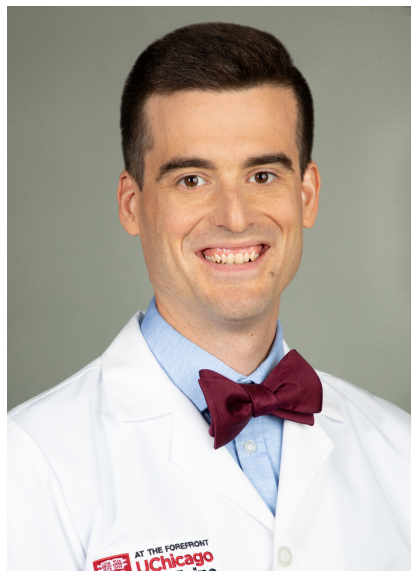
Ongoing work in the laboratory moves in three directions. First, how general is their strategy? With ever-increasing high content biological data, the generality of their statistical approach across different systems can be tested. Second, what influences the pattern of interactions defining an evolved system? As evolved systems interact with the environment, they are testing whether environmental structure may drive system structure. Finally, can statistical variance enable the creation of synthetic systems? Raman's lab is using statistical potentials derived from their approach to create complex consortia of bacteria designed to perform specific functions.





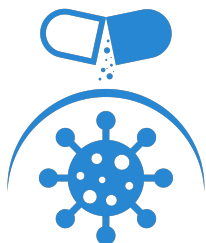
# Christopher Lehmann, MD

Assistant Professor, Department of Medicine - Section of Infectious Diseases



Before humans learned to use antibiotics, the healthy bacteria living within our microbiome were in a constant state of competition and cooperation. In this state, healthy bacteria competed against harmful ones and prevented infection. When antibiotics are introduced, the healthy bacteria are killed, drug-resistant harmful bacteria bloom, and deadly infections ensue.

The solution to this problem is to restore the microbiome back to health by bringing back the balance of beneficial bacteria. Microbiological, genetic, metabolic, and mouse studies have demonstrated which bacteria are most likely to be beneficial and how those benefits work, but these studies have yet to be proven in humans. Because of this, options for restoring the microbiome in humans is relegated to inelegant fecal transplant or unreliable probiotics. Guided by our ever-growing understanding of the microbiome, Dr. Lehmann is working to restore the microbiome in patients to prevent drug-resistant infections. This offers the opportunity to undo the damages caused by antibiotics, augment our current strategies to fight antibiotic-resistant infections, and preserve the effectiveness of life-saving antibiotics for future generations.

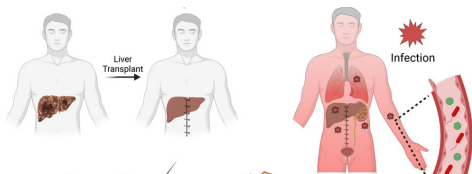


# Matthew Odenwald, MD, PhD

Assistant Professor, Department of Medicine - Section of Gastroenterology



Chronic liver disease and cirrhosis are usually clinically silent until an initial decompensating event occurs, after which treatment does not significantly alter the course of disease. Dr. Odenwald's work focuses on understanding how the gut microbiome contributes to the progression of liver disease and the development of complications of cirrhosis. To this end, we have performed a large study of patients hospitalized with complications of liver disease where we observed a wide range of gut microbiome compositions, including low alpha-diversity and increased burden of potentially pathogenic taxa (e.g. Enterobacteriaceae and Enterococcus) that encode antibiotic resistance genes. These changes are accompanied by low concentrations of beneficial, microbially derived metabolites like short-chain fatty acids (e.g. butyrate) and secondary bile acids (e.g. deoxycholic acid). Microbiome compositional and metabolomic changes associate with both an increased risk of infection and shortened survival in our cohort. This suggests that reconstituting the gut microbiome with commensal organisms that generate beneficial metabolites may mitigate some of the most devastating complications of cirrhosis. We will test this hypothesis with commensal consortia that were designed and manufactured in the DFI cGMP facility, and our Phase 1b clinical trial will begin in 2024.

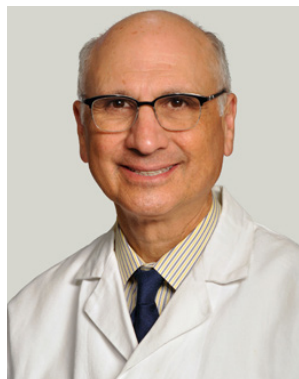


# Associated Faculty

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**Maria-Luisa Alegre, MD, PhD**  
Professor  
Department of Medicine



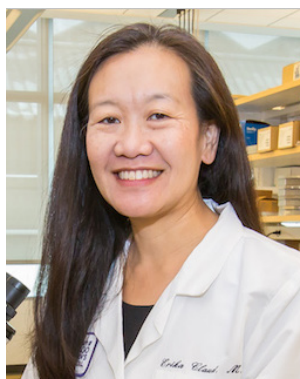
**John Alverdy, MD**  
Professor  
Department of Surgery



**Eugene Chang, MD**  
Professor  
Department of Medicine



**Alexander Chervovsky, MD, PhD**  
Professor  
Department of Pathology



**Erika Claud, MD**  
Professor  
Department of Pediatrics



**Daria Esterhazy, PhD**  
Assistant Professor  
Department of Pathology



**Thomas Gajewski, MD, PhD**  
Professor  
Department of Pathology



**Tatyana Golovkina, PhD**  
Professor  
Department of Microbiology



**Bana Jabri, MD, PhD**  
Professor  
Department of Medicine



**Cathryn Nagler, PhD**  
Professor  
Department of Pathology



**Samantha Riesenfeld, PhD**  
Assistant Professor  
Pritzker School of Molecular Engineering



# Clinical Research Support Team (CRST)

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**Emerald Adler**  
Manager

The CRST supports clinical studies by assisting in the development and design of projects, facilitating assembly of IRB documents and protocols, enrolling patients in clinical studies, ensuring adherence to clinical protocols and timing of sample collection, delivering samples to laboratories for analysis, and collecting and keeping track of clinical outcomes. The CRST is currently led by the clinical studies manager who supervises two clinical research coordinators. The CRST works very closely with clinical investigators, the bioinformatics team, and the DFI core facilities.



**Jackelyn Cantoral**  
Coordinator



**Caroline Jadzak**  
Coordinator



# Host-Microbiome Metabolomics Facility (HMMF)

Metabolites are essential for every cell to function and are often dispersed into the environment to help organisms adapt and persist. Often, bacteria and fungi produce metabolites because they do not have human sensory organs such as eyes, ears, and skin. Instead, they adapt by altering the surrounding metabolite profile. Since the discovery of penicillin, many new metabolites targeting bacteria, viruses, cancer, and fungi were discovered. As these drug discoveries grew, so did the field of metabolomics, i.e., the study of all metabolites in a sample. With advanced instrumentation and bioinformatic strategies, the high-quality measurement of thousands of metabolites from a single specimen are applied to study human well-being. In humans, measuring the types and amounts of metabolites from the gastrointestinal (GI) tract is particularly important because trillions of organisms live there, producing thousands of metabolites that directly impact the GI tract, brain, and other organs. The HMMF measures the metabolites in the GI tract, blood, tissue, urine, and those from laboratory experiments. We measure metabolites known to be involved in states of disease or maintenance of health. Additionally, we measure metabolites that have not been previously explored. Together, our work aims to uncover new biological roles for metabolites and to determine if metabolite types and amounts reflect a patient's previous, current, or future state of health.



**Ashley Sidebottom, PhD**  
Director



**David Moran**  
Research Platform Team Lead



**Jessica Little, PhD**  
Senior Staff Scientist



**Michael Mallowney, PhD**  
Senior Staff Scientist



**Mary McMillan**  
Research Specialist



**Amber Rose**  
Research Specialist



# Microbiome Metagenomics Facility (MMF)



**Anitha Sundararajan, PhD**  
Director

The millions of genes encoded by the gut microbiome profoundly influence their host's fitness, phenotype, and health. At the Microbiome Metagenomics Facility, we offer end-to-end services to reveal the diversity and functional ability of human gut microbes by using next generation sequencing (NGS) technology. Enabling seamless, accurate, and reproducible laboratory workflows, our state-of-the-art equipment includes high-throughput quality control instruments and top-notch liquid handling systems. We support numerous University studies, helping our clients accomplish their research goals where NGS approaches are needed. Using cutting-edge sequencing methods and other integrated approaches, we identify microbes that can potentially reverse dysbiosis in the human gut, which resonates well with the DFI's overarching goal of harnessing the microbiome for human health.



**Victoria Burgo**  
NGS Specialist



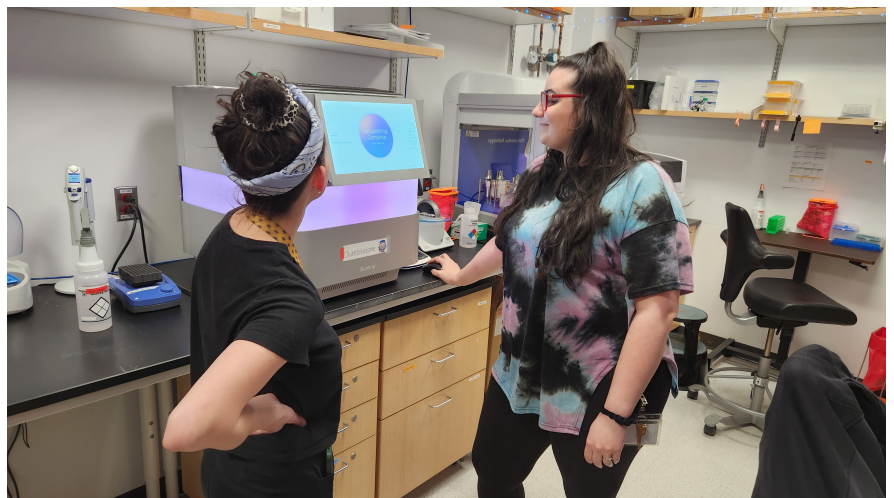
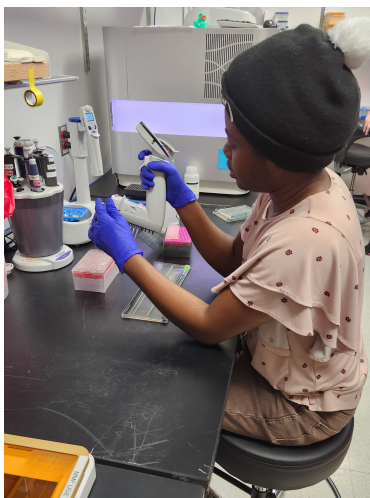
**Rita Smith**  
Research Specialist



**Glory Mellotte**  
Research Technician



**Tomi Akin-Olabiyi**  
Research Technician



# Symbiotic Bacterial Strain Bank (SBSB)

Our symbiotic bacterial strain bank consists of a collection of approximately 2000 bacterial strains, all isolated from healthy human fecal donors. It is a broad collection of isolates representing the gut microbiome that have been anaerobically cultured and characterized phenotypically and genotypically. In addition to banking strains and serving as an invaluable resource to the UChicago microbiome community, the SBSB team conducts experiments to identify optimum growth conditions for these isolates to maximize their metabolic potential. Those experiments in turn enable the team to screen candidate strains and select the ones capable of restoring gut function through their ability to produce beneficial metabolites.



**Anitha Sundararajan, PhD**  
Director



**Téa Pappas**  
Research Specialist



**Nina Laliwala**  
Research Technician



**Shannon Townson**  
Research Technician





# Informatics

## Bioinformatics



**Huaiying Lin**  
Director



**Nicholas Dylla**  
Bioinformatics Specialist



**Ramanujam Ramaswamy**  
Bioinformatics Specialist

The Bioinformatics team provides bioinformatic and statistical support for clinical and laboratory investigators by analyzing metagenomic sequencing data and metabolomic data. The Bioinformatics team uses the most up-to-date analysis platforms to determine microbiome compositions, and correlates the presence/absence of specific microbes with clinical outcomes and/or the presence/absence of specific metabolites. The team has played a central role in the DFI's investigation of associations between microbiome-derived metabolites and outcomes following COVID-19 infection, the incidence of rejection following heart transplantation, the development of infections in patients with severe liver disease, and the occurrence of peri-transplant complications following liver transplantation.

## Translational Informatics



**Dinanath Sulakhe**  
Director



**Mark D'Souza, PhD**  
Senior Bioinformatics Scientist



**Che Woodson**  
Senior Bioinformatician



**Ashwin Ramgopal**  
Senior Data Scientist

Data generated by HMMF, MMF, and SBSB during the course of clinical investigation is complex, but needs to be accessible to laboratory and clinical investigators. The Translational Informatics team is developing platforms that enable investigators to query vast databases to establish correlations between, for example, clinical interventions, microbiome compositions, and the concentration of metabolites in blood or fecal samples. This work requires precise curation of each database followed by the design of an intuitive website that investigators can use to test hypotheses and identify potentially important, clinically relevant associations.



# Good Manufacturing Practices Facility



In 2023, the DFI completed construction of and equipment installation in a two-suite cGMP facility to manufacture capsules containing individual symbiotic bacterial strains from the DFI cGMP Master Cell Bank. Small-scale production for phase 1B clinical trials will be executed within this facility. The facility consists of two fully isolated and equipped cleanroom suites. Within each cleanroom suite, temperature, humidity, differential pressure, and airflow are monitored and controlled. Equipment used for manufacturing processes, including fermentation, buffer exchange, lyophilization, and capsule generation is maintained, validated, and calibrated at specified intervals for safe, effective, and consistent operation. A team of dedicated operators, engineers, and scientists have been trained for their respective functions in areas of safety, aseptic standards, manufacturing processes, and unit operation performance within the cGMP facility.



**Babak Kohanpour, MSEE**  
Director



**Erica Garcia**  
Quality Assurance Specialist



**Sydney Flakus**  
Microbiome Production Associate



**Josiah Reyes**  
Microbiome Production Associate



**Homira Wardak**  
Microbiome Production Associate



**Nikki Yap**  
Microbiome Production Associate



**Hong Zhen**  
Microbiome Production Associate

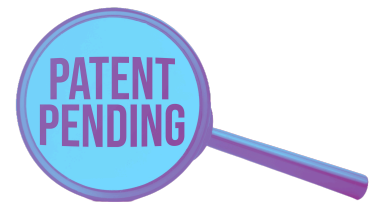
# Commercialization and Support

## Commercialization



**Kenneth Onishi, PhD**  
Manager, Polsky Center  
Business Development and  
Licensing - Microbiome

Ken Onishi, PhD, serves as manager for business development and licensing at the University of Chicago's Polsky Center for Entrepreneurship and Innovation. Ken works with faculty in the Duchossois Family Institute to build partnerships with companies working in the microbiome field and helps researchers recognize when their ideas and discoveries are patentable, facilitates licensing agreements, and guides the development of startups. Ken is dedicated to commercializing microbiome-related technologies to improve health outcomes via therapeutics and diagnostics.



## Administration and Support



**Ingrid Leiner**  
DFI Manager



**Noreen Bentley**  
Administrative Assistant to  
Eric Pamer



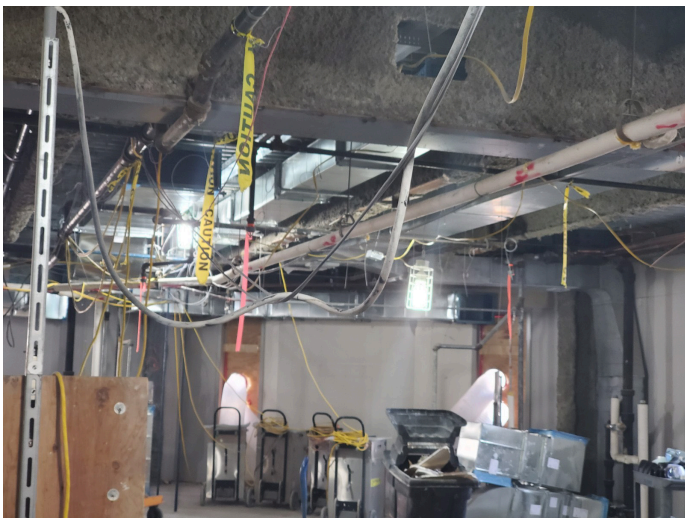
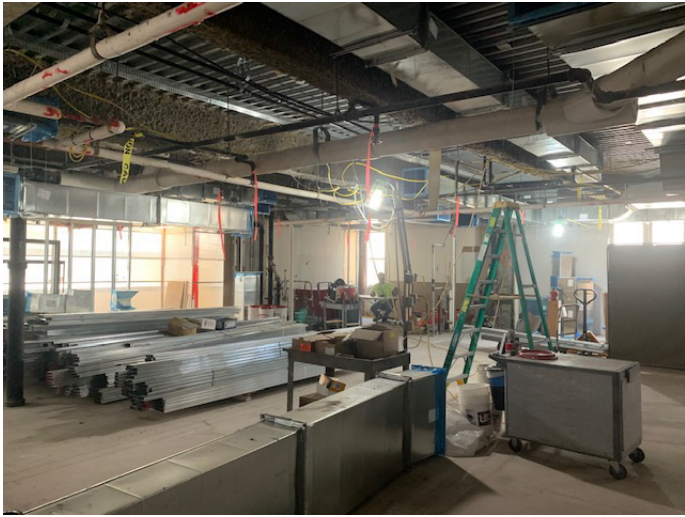
**Shannon Hocker**  
Business Administrator



**Lorena Marmolejo**  
Technical Research Support



# Construction of the GMP Facility





# Construction of the GMP Facility





# Advisory Boards

## Internal Advisory Board



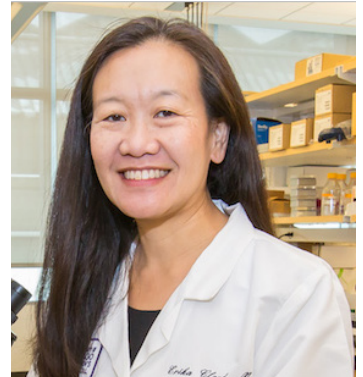
**Eric Pamer, MD**  
Director



**John Alverdy, MD**  
Department of Surgery



**Eugene Chang, MD**  
Department of Medicine



**Erika Claud, MD**  
Department of Pediatrics



**Thomas Gajewski, MD, PhD**  
Department of Pathology



**T. Conrad Gilliam, PhD**  
Dean for Basic Science

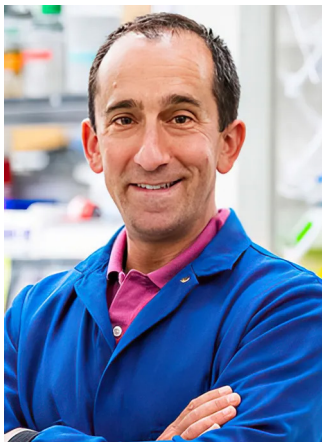


**Tatyana Golovkina, PhD**  
Department of Microbiology



**Bana Jabri, MD, PhD**  
Department of Medicine

## External Advisory Board



**Michael Fischbach PhD**  
Professor  
Stanford University

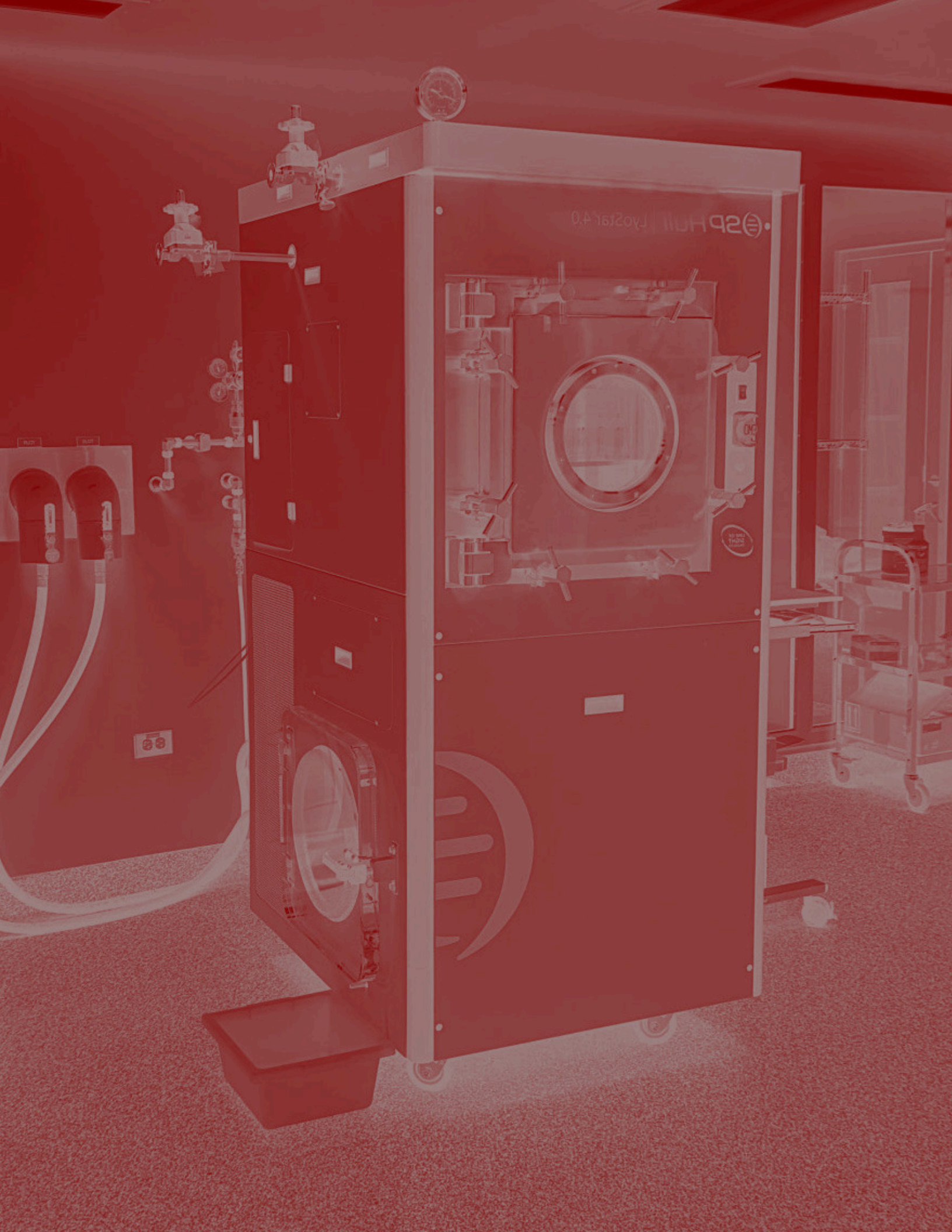


**Julie Segre, PhD**  
NIH Distinguished Investigator  
National Institutes of Health



**Jeffrey Gordon, MD**  
Professor  
Washington University in St. Louis









2024