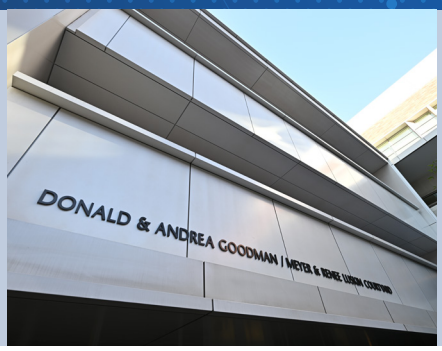
UCLA GOODMAN-LUSKIN MICROBIOME CENTER

2023 ANNUAL UPDATE

UCLA Health | David Geffen School of Medicine

UCLA is grateful to Andrea and Donald Goodman, and Renee and Meyer Luskin for establishing the UCLA Goodman-Luskin Microbiome Center, and thankful to Chip Rosenbloom and the Rosenbloom family for their long-standing support of pioneering research at UCLA. Under the administration of Eric Esrailian, M.D., M.P.H., Chief, UCLA Vatche and Tamar Manoukian Division of Digestive Diseases, and The Lincy Foundation Chair in Clinical Gastroenterology, the center leads scientific and patient-centered investigations to advance understanding of one of the most complex and promising of human biological systems, the brain-gut microbiome. Research at the center examines the role of brain-gut interactions and their effects on the gut microbiome, and the implications on human health, development, and well-being.



In September, the David Geffen School of Medicine hosted a naming ceremony for the ground floor courtyard of Geffen Hall. It is now the Donald & Andrea Goodman / Meyer & Renee Luskin Courtyard. The courtyard is the figurative and literal foundation of the school and a place for students and faculty to gather for academic collaboration, as well as for events to honor the medical school's many achievements. The courtyard naming celebrates and recognizes the impact of the new Goodman-Luskin Microbiome Center and the transformative avenues of scientific inquiry it will bring to the UCLA campus and its patients.

In the short time the microbiome center has been in existence, it has already bred groundbreaking research and dynamic and fruitful cross-core collaborations.

The microbiome center team meets every other week, alternating operations meetings and sessions where scientists share their research and grant applications. Researchers appreciate learning of their fellow microbiome center members' studies and discovering ways in which their work may complement others', along with gaining valuable input on grant applications.

The center's seven research cores — Biorepository, Clinical Studies and Database, Gnotobiotics, Human Probiotic, Integrative Biostatistics and Bioinformatics, Microbiome, and Neuroimaging — and administrative core streamline operations and centralize resources for cost-effectiveness. These methods also create efficiency in studying the role of the brain-gut microbiome system in common conditions such as inflammatory bowel disease (IBD), obesity, diabetes, liver disease, irritable bowel syndrome (IBS), substance use disorder, and dementia. This understanding will translate into novel therapies to combat these conditions.

One of many such fruitful collaborations resulted in a group of researchers from the Goodman-Luskin Microbiome Center receiving a UCLA Innovation Fund biomedical competition award from the UCLA Technology Development Group in the therapeutics track. Arpana Gupta, Ph.D., Adjunct Assistant Professor, Manoukian Division of Digestive Diseases; Tien Dong, M.D., Ph.D., Assistant Clinical Professor of Medicine; Jonathan Jacobs, M.D., Ph.D., Assistant Professor-in-Residence, Manoukian Division of Digestive Diseases; and Emeran Mayer, M.D., Founding Director, Goodman-Luskin Microbiome Center and Professor of Medicine, Physiology, and Psychiatry, were awarded funding for their treatment fighting obesity and food addiction by harnessing the brain-gut axis.

On the following pages are profiles of the founding members of the Goodman-Luskin Microbiome Center and a sampling of their achievements during the past year.

ELAINE HSIAO, Ph.D.

Director, UCLA Goodman-Luskin Microbiome Center
De Logi Chair in Biological Sciences
Associate Professor of Integrative Biology & Physiology
Director, Administrative Core; Director, Gnotobiotics Core
Program Lead, Neurodevelopmental and Neurodegenerative Diseases program

Dr. Hsiao's research program aims to uncover how the gut microbiota interacts with the nervous system, and how such interactions impact health and disease. In the past year, her lab has advanced projects in four main areas: dissecting communication pathways for microbial regulation of sensory neuronal activity, examining the functional effects of neurochemicals and related drugs on bacterial fitness, uncovering the effects of the microbiome during early immune and neural development, and examining the microbiome at the interface of gene-environment interactions in neurological disease.

One study now in review at the journal *Neuron*, "Vagal interoception of microbial metabolites from the small intestinal lumen," reveals new mechanisms by which specific metabolites from the gut microbiome signal neurons that extend from the gut to the brain. The Hsiao lab's research paper, "Sex-dependent interactions between prodromal intestinal inflammation and LRRK2 G2019S in mice promote symptoms of Parkinson's disease," in revision at *Nature Communications*, finds that early gut dysfunction expedites and exacerbates the risk for Parkinson's disease. "Ketogenic diet therapy for pediatric epilepsy is associated with alterations in the human gut microbiome that confer seizure resistance in mice" observes that the ketogenic diet modifies the gut microbiome in kids with pediatric epilepsy in ways that matter for the antiseizure effects of the diet. Therefore, specific microbial functions are associated with seizure protection. "The maternal microbiome promotes placental development in mice" is in press at *Science Advances*. This study discovered that the maternal gut microbiome modifies the development of the placenta during pregnancy and that specific microbial metabolites can be used to treat symptoms of IUGR (intrauterine growth restriction). "Gut microbiota Turicibacter strains differentially modify bile acids and host lipids," published in *Nature Communications*, concluded that a specific member of the gut microbiome transforms bile acids in ways that impact fat metabolism. Engineering the enzymes in bacteria that are involved can be used to lower triglycerides and cholesterol, the researchers found.

Dr. Hsiao recently received three new collaborative grants. A National Institutes of Health/Eunice Kennedy Shriver National Institute of Child Health and Human Development (NIH/NICHD) R01 grant is a collaboration with Nelson Freimer, M.D., Maggie G. Gilbert Endowed Chair in Bipolar Disorders, Professor of Psychiatry, UCLA Depression Grand Challenge, and Misty Richards, M.D., M.S., UCLA Maternal Outpatient Mental health Services Clinic, to study how the gut microbiome can be used to promote the efficacy of antidepressant drugs in perinatal depression. Dr. Hsiao received a UCLA Clinical and Translational Science Institute Core Voucher, a seed grant for collaborative research, with Nandita Garud, Ph.D., UCLA Department of Ecology and Evolutionary Biology, to study how microbial genomes evolve and adapt in aging disorders, such as Alzheimer's disease. A United States Department of Defense Congressionally Directed Medical Research Program Investigator-Initiated Research Award funds a collaborative project with J. Philip Karl, Ph.D., R.D., of the U.S. Army Research Institute of Environmental Medicine to study how diet and the microbiome can be used to protect against hypoxia-induced cognitive impairment.

The Hsiao lab has a strong educational mission, and lab members include five postdoctoral researchers, five Ph.D. students, two master's students, and nine undergraduates; while three Ph.D. students have graduated and one postdoctoral member has moved on.

In the past year, Dr. Hsiao was a Falling Walls Science Breakthrough of the Year Finalist, a BIOS Top 23 Women in Academic Entrepreneurship of 2023, and made the Clarivate Highly Cited Researchers list (top 1 percent worldwide). She has also been invited to share her research across the U.S. and Canada.

"It is a huge honor and blessing to work at a center dedicated to microbiome research," says Dr. Hsiao. "For one, building community and collaboration among the scientific talent at UCLA is hugely inspiring and synergizing. Secondly, launching numerous core facilities to help others bring microbiome research to their research programs gives a strong sense of purpose to advance the microbiome field together. Lastly, providing educational support and resources to amazing trainees who will carry forward a spirit of research excellence and public service roots makes our collective effort especially meaningful."

JONATHAN JACOBS, M.D., Ph.D.
Co-director, Goodman-Luskin Microbiome Center
Assistant Professor-in-Residence, Digestive Diseases
David Geffen School of Medicine at UCLA
Director, Microbiome Core
Program Lead, Inflammatory Bowel Diseases program

The inauguration of the Goodman-Luskin Microbiome Center fulfills a goal for Dr. Jacobs that was nearly a decade in the making.

"It has been a dream of mine since I joined the UCLA faculty in 2015 to establish an official center dedicated to microbiome research," Dr. Jacobs says. "The support of the Goodman-Luskin Microbiome Center has allowed me to implement plans that I have been formulating in recent years to expand the microbiome core to support innovative research that would put UCLA at the forefront of the microbiome field."

Dr. Jacobs, who completed both his undergraduate work and medical degree at Harvard University before earning his Ph.D. degree in cellular and molecular pathology at the David Geffen School of Medicine at UCLA, focuses his research on characterizing host-microbiome interactions in patients with gastrointestinal, metabolic, and inflammatory disorders. As co-director of the Goodman-Luskin Microbiome Center, Dr. Jacobs has been intimately involved in the ramp-up process for the center.

"I have recruited and trained two talented young scientists to perform the core's essential functions and offer new microbiome research-related services to Goodman-Luskin Microbiome Center members," Dr. Jacobs says.

This task has been particularly challenging because it involved finishing research left behind by former lab members. By posting a range of job titles and carefully screening applicants to find those with outstanding potential, Dr. Jacobs has been able to guard against unfinished work by guaranteeing that at least two members of his lab will be involved on every project moving forward, ensuring continuity of research.

The Jacobs lab has continued to be productive in the past year with many published papers and new collaborative projects with UCLA colleagues. Dr. Jacobs and his team recently authored a paper published in a journal covering exciting new research demonstrating that IBD patients with high-stress reactivity can be identified by gut bacteria and their byproducts in both the bloodstream and digestive tract. These microbiome biomarkers predicted risk of clinical flare and indicated pathways that can be investigated to understand how gut bacteria can promote stress-induced disease flares. Dr. Jacobs and his team are currently using scientific models colonized with gut bacteria from IBD patients to understand how these bacteria can increase stress reactivity and promote stress-induced clinical flares, a crucial key to better understanding this complex mind-gut relationship.

In addition to his research responsibilities, Dr. Jacobs mentored a total of five fellows, graduate students, and medical students in the past year. One mentee has completed her training and recently accepted a job at Takeda Pharmaceuticals; three others will be completing their training in the coming months.

ARPANA GUPTA, Ph.D.
Co-director, Goodman-Luskin Microbiome Center
Associate Professor, Vatche and Tamar Manoukian Division of Digestive Diseases
Member, UCLA Brain Research Institute
Director, Neuroimaging Core
Program Lead, Obesity, Metabolic Disorders, and Eating Behavior program

Dr. Gupta's broad research focus is on brain-gut interactions in obesity. In particular, she focuses on the links between obesity and living in disadvantaged neighborhoods and experiencing discrimination.

Her work has produced 12 recent articles published in scientific, peer-reviewed journals, some still in press, as well as generated abundant interest in popular media outlets, including *Forbes*, *CNBC*, *The Washington Post*, and the *TODAY* show.

For Dr. Gupta, the advantages of working at the Goodman-Luskin Microbiome Center are threefold:

"There is more opportunity to collaborate with established and world-renowned experts with varying areas of expertise; to establish and provide state-of-the-art neuroimaging expertise and services and, accordingly, to be able to hire the appropriate personnel to conduct leading-edge research, attracting them partly with salaries standard in the field; and to conduct high-risk/high-reward projects that would not otherwise be funded."

Some of Dr. Gupta's projects that have proven viable have received outside funding, such as a grant from the Alzheimer's Association to investigate brain-gut microbiome interactions related to aging in Middle Eastern and North African elderly in Los Angeles, in collaboration with the University of Southern California.

Dr. Gupta's team has won numerous other awards. Cardiology fellow Daniel Wang, M.D., was awarded a Goodman-Luskin Microbiome Center Seed Fellowship Award to investigate "Racial/ethnic disparities in cardiovascular risk amidst discrimination: A lipidomics, gut microbiome, and neuroimaging analysis." Yamaha Motor Corporation awarded the group a grant to investigate brain-gut microbiome interactions after using a YEX experience room to reduce stress and improve mood and cognition. YEX, or "you expanded," is a new division at the company intended to focus on technological developments in the health and mindfulness arenas.

The team also received a UCLA Technology Development Group grant to investigate the positive effects of a probiotic blend to impact food addiction and cravings in obesity. Dr. Gupta was presented with the 2022-23 Faculty Award for Research Diversity by the UCLA Academic Senate and has been accepted into the Justice, Equity, Diversity, and Inclusion Academic Mentorship program.

A dedicated educator, Dr. Gupta works with eight undergraduate students, two graduate students, two postdoctoral fellows, two medical students, three fellows, and three junior faculty members. She serves as preceptor to Roch Nianogo, M.D., Ph.D., M.P.H., an assistant professor in public health, who researches brain-gut interactions in obesity; Desiree Delgadillo-Chase, Ph.D., who investigates brain-gut microbiome interactions related to positive affect and resilience; and Rosario Jamie-Lara, Ph.D., F.N.P., R.N., on a diversity supplement grant to investigate brain-gut interactions in obese Mexican women.

Based on her work in the Goodman-Luskin Microbiome Center, Dr. Gupta has one patent application in process for a gut microbial signature/blend associated with resilience, and three patent applications completed for Compositions and Methods for Treating Metabolic Disease, Compositions and Methods for Diagnosing and Treating Patients with a History of Early Life Adversity, and Methods and Compositions for Improved Psychological and Resilience Measures. The team plans to conduct clinical trials with these probiotic blends, as well as seek additional funding to investigate brain-gut microbiome interactions related to diet, cravings, and obesity.

EMERAN MAYER, M.D., Ph.D.

Founding Director and Director Emeritus, Goodman-Luskin Microbiome Center
Director, UCLA G. Oppenheimer Center for Neurobiology of Stress and Resilience
Distinguished Research Professor of Psychology, Medicine, and Physiology
David Geffen School of Medicine at UCLA

"The Brain-Gut Connection with Dr. Emeran Mayer," a health special documentary series, recently launched on PBS. In the program, Dr. Mayer explains how changes in the gut microbiome can result in common chronic diseases, such as diabetes, heart disease, Alzheimer's, Parkinson's, and certain cancers and infectious diseases. He also makes recommendations on easy lifestyle changes to rebalance the brain-gut bond for a stronger immune system, weight loss maintenance, disease prevention, and an improved mental outlook.

Dr. Mayer notes that during the past 75 years, diet, lifestyle, and interactions with the world have resulted in an imbalance in the gut microbes, resulting in compromised immune systems. This imbalance between the brain and gut can lead to physical ailments and disease. In addition, now there is evidence that disruptions in the gut can also affect a person mentally.

In late 2023, Dr. Mayer's book was published, *The Mind-Gut-Immune Connection: Understanding How Food Impacts Our Mind, Our Microbiome, and Our Immunity*. Previously, he wrote *The Mind-Gut Connection: How the Hidden Conversation Within Our Bodies Impacts Our Mood, Our Choices, and Our Overall Health*. He is currently curating a gut-healthy, Mediterranean-inspired cookbook, *Interconnected Plates*. He has also authored 421 published scientific papers and co-edited three scientific books.

On January 4, 2024, a MasterClass.com session on the microbiome will be released, with Dr. Mayer as one of three experts included. On his "Mind Gut Conversation Podcast," Dr. Mayer talks to experts in various health and science fields.

Dr. Mayer has received numerous awards, including the American Gastroenterological Association's Distinguished Mentor Award, the American Psychosomatic Society Paul D. MacLean Award for Outstanding Neuroscience Research in Psychosomatic Medicine, and the German Society of Gastroenterology and Metabolic Diseases' Ismar Boas Medal.

LIN CHANG, M.D.

Vice Chief, Vatche and Tamar Manoukian Division of Digestive Diseases
Program Director, UCLA GI Fellowship Program
Co-director, UCLA G. Oppenheimer Center for Neurobiology of Stress and Resilience
Professor of Medicine, David Geffen School of Medicine at UCLA
Director, Clinical Studies and Database Core
Program Lead, Disorders of Gut Brain Interaction (SCORE) program

Dr. Chang's clinical expertise revolves around disorders of gut-brain interactions, focusing on conditions such as IBS, chronic constipation, and functional dyspepsia. Her research delves into the intricate pathophysiology of IBS, exploring stress, sex differences, genetic and epigenetic factors, neuroendocrine alterations, and gut microbiome, as well as the treatment of IBS.

In the past year, Dr. Chang has authored numerous papers with her colleagues at the Goodman-Luskin Microbiome Center. These have included "A multi-omic brain gut microbiome signature differs between IBS subjects with different bowel habits," published in *Neuropharmacology*; "Sex-specific brain microstructural reorganization in irritable bowel syndrome," published in the journal *PAIN*; "The Association Between a Mediterranean Diet and Symptoms of Irritable Bowel Syndrome" in *Clinical Gastroenterology and Hepatology*, and "Maximizing Training and Mentorship in Sex as a Biological Variable Research Across Different Brain-Body Disorders" in the *Journal of Women's Health*.

Dr. Chang was also senior author of "Colonic mucosal microbiota is associated with bowel habit subtype and abdominal pain in patients with irritable bowel syndrome," published in the *American Journal of Physiology*. She was also first author of "American Gastroenterological Association-American College of Gastroenterology Clinical Practice Guideline: Pharmacological Management of Chronic Idiopathic Constipation," a clinical practice guideline meant to inform clinicians and patients of evidence-based practice recommendations for the pharmacological treatment of chronic idiopathic constipation in adults, published in *Gastroenterology*.

Dr. Chang has benefited via her affiliation with the microbiome center through new research collaborations, grants, and areas of research. Her near-term future plans include submitting a grant

for microbiome-based treatments for visceral pain in IBS; submitting an application to the NIH as co-investigator on a multicenter Human Virome Program grant, where she will collect colonic mucosal tissue and other biological specimens in healthy controls; exploring sex differences in gut microbiome mechanisms in IBS as the focus of a SCORE grant renewal; and exploring clinical studies with novel probiotics. Currently, five residents and gastroenterology fellows work in the Chang lab.

Dr. Chang serves on the board of directors for the Rome Foundation, an independent, not-for-profit organization dedicated to supporting the creation of scientific data and educational information that can assist in diagnosing and treating disorders of the brain-gut interaction. She is an associate editor of the prestigious journal *Gastroenterology*. Dr. Chang previously served as a clinical research councillor of the American Gastroenterological Association (AGA) Governing Board, and president of the American Neurogastroenterology and Motility Society. She is a fellow of the AGA and the American College of Gastroenterology. Past awards have included the Janssen Award in Gastroenterology for Basic or Clinical Research, the AGA Distinguished Clinician Award, and the AGA Distinguished Educator Award.

BRIDGET CALLAGHAN, Ph.D.
Assistant Professor, Department of Psychology
Division of Life Sciences, UCLA College of Letters and Science
Director, Brain and Body Lab at UCLA
Program Lead, Mental Illness and Pain program

As a psychologist, Dr. Callaghan usually feels isolated in her interests, with few people in her department conducting research on the microbiome, the gastrointestinal system, or on mind-body interactions. "Being affiliated with the Goodman-Luskin Microbiome Center has made all the difference for me in terms of feeling like I am part of a community," says Dr. Callaghan.

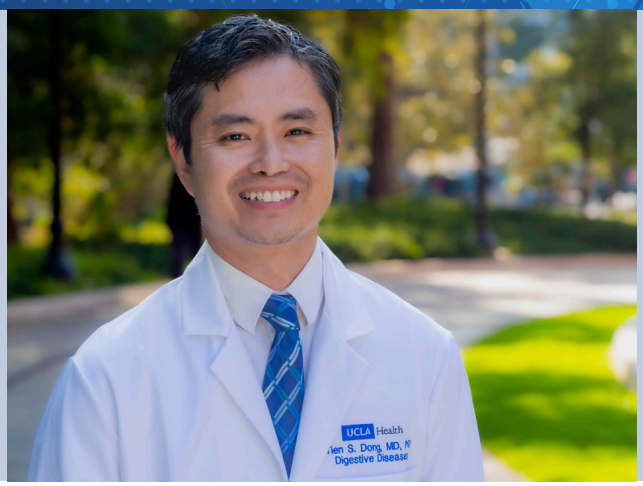
That sense of community has led to a high-profile paper in the *Proceedings of the National Academy of Sciences of the United States of America* journal on the impacts of adversity, both personal and intergenerational, on the gastrointestinal microbiome in humans. The paper received mainstream coverage in *The Washington Post*.

One National Institutes of Health Research Project Grant (R01) application Dr. Callaghan's research team has under review is for a project that will examine more mechanistic pathways for brain-gut communication by focusing on dopaminergic pathways. Another R01 being prepared will examine microbiome-immune interactions in the context of upward mobility and dementia risk. A third will examine interoception, or the subconscious and conscious collection of senses providing an organism information about its internal status, in pregnant women.

Additional papers recently published include "'It's Time to Rebrand 'Mommy Brain'" in *JAMA Neurology* and covered by ABC News; "Associations between the human immune system and gut microbiome with neurodevelopment in the first 5 years of life: A systematic scoping review" in *Developmental Psychobiology*; and "The Added Value of Crosstalk Between Developmental Circuit Neuroscience and Clinical Practice to Inform the Treatment of Adolescent Anxiety" in *Biological Psychiatry: Global Open Science*.

In the past year, Dr. Callaghan received a grant from the UCLA Norman Cousins Center for Psychoneuroimmunology at UCLA to serve as principal investigator on the enquiry, "The Effects of Economic Striving on Obesity, Inflammation, and Neural Response to Reward." She will serve as co-principal investigator on "Does positive parenting improve emotion regulation in at-risk youth across the transition to adolescence?" funded by the Mental Research Institute.

Graduate students in Dr. Callaghan's lab have benefited from the Goodman-Luskin Microbiome Center's facilities. Francesca Querdasi finished her first-year project on the microbiome in relation to early adversity, while Naomi Gancz completed her first-year project on the oral microbiome. The two were awarded a Goodman-Luskin Microbiome Center Seed Fellowship Award for their proposal, "Early Adversity and Internalizing in Middle Childhood to Adolescence: Gut Microbiome and Inflammatory Mechanisms," to be mentored by Dr. Callaghan.



TIEN DONG, M.D., Ph.D.

Assistant Professor, David Geffen School of Medicine at UCLA
Director, Biorepository Core; Director, Human Probiotic Core
Program Lead, Liver Disease program

Dr. Dong brings a distinct technological skillset to the team. As the lead bioinformatician for the microbiome center, Dr. Dong has successfully created a pipeline that incorporates machine learning with multidimensional datasets in order to understand the effects of the gut microbiome on the systems biology level. The creation of the center has already provided him the resources necessary to undertake projects at this juncture of medicine and technology.

"It has made the utmost difference," Dr. Dong says. "I have always been interested in microbiome research, and now as part of this center, I have the resources and collaborations needed to delve into new areas of research. It has also significantly increased my productivity in terms of grant and paper submissions."

Dr. Dong, who specializes in the study of the gut-liver axis, particularly as it relates to nonalcoholic fatty liver disease and metabolic syndrome, completed his undergraduate work at Stanford University and his medical degree and residency at The University of Chicago. He joined the David Geffen School of Medicine in 2016, completing both a fellowship in gastroenterology/hepatology and his Ph.D. degree in molecular, cellular, and integrative physiology in 2020.

Dr. Dong and his team have been busy since the center formally launched, working on a number of separate projects. The team has initiated a clinical trial studying a new novel probiotic and its effect on ingestive behavior and obesity. They have authored several published articles on this study and submitted grants to secure additional funding for this research. Dr. Dong, along with Dr. Arpana Gupta, discovered that social discrimination can alter the gut-brain microbiome system, which has important implications for public health. Their research was published in the August 2023 edition of the journal *Biological Psychiatry*, and they also shared their findings in an interview with MSNBC. In addition, Dr. Dong has discovered that a certain bacterium, Akkermansia, is related to glucagon-like peptide (GLP) expression and obesity, and may be responsible for some of the weight loss that patients experience after bariatric surgery.

In addition to his research efforts, Dr. Dong trains undergraduates, Ph.D. candidates, and postdoctoral fellows in microbiome research and data analysis. Over the past year, he mentored and collaborated with Dr. Delgadillo-Chase, who was awarded the University of California President's Postdoctoral Fellowship in June 2023.

SWAPNA JOSHI, Ph.D.
Adjunct Assistant Professor, Bioinformatics/Epigenetics
David Geffen School of Medicine at UCLA
Co-director, Integrative Biostatistics and Bioinformatics Core

At the Goodman-Luskin Microbiome Center, Dr. Joshi has trained UCLA students in biostatistic and bioinformatic analysis, co-mentored and collaborated with fellows, submitted grants as a co-investigator, initiated collaboration and a service contract with an investigator studying associations between microbiome and liver disease in scleroderma patients, and initiated new collaborations to study brain-gut-microbiome interactions and their association with stress.

Access to the center has nurtured this activity. "As a researcher studying irritable bowel syndrome (IBS) as a model for brain-gut-microbiome axis for several years, microbes' role in processing pain signals is becoming increasingly evident," Dr. Joshi says. "Additionally, the ability to target microbes and their metabolites makes it an important therapeutic target. Our studies on colon-adherent microbes suggested that changes in the abundance of specific microbes was associated with increased severity of IBS symptoms, in turn suggesting that changes in microbiome-host interactions may contribute to IBS symptoms. Similarly, collaborative projects on diet-microbiome associations and brain-metabolite-microbiome associations have provided insights into the role of microbes in disease pathogenesis."

Dr. Joshi's new projects under the microbiome center's Integrative Biostatistics and Bioinformatics Core are expected to result in innovative findings in areas previously uninvestigated. In addition, ongoing collaborative projects involving integrative analysis of microbiome and metabolite signatures to study pain mechanisms in conditions such as IBS are expected to provide novel therapeutic targets.
One of the primary activities of the Integrative Biostatistics and Bioinformatics Core is to develop pipelines

to analyze and integrate data from various sources or platforms that will help the principal investigators generate hypotheses that can then be tested in a laboratory. Dr. Joshi and her team plan to continue building these channels for different platforms and provide services to analyze data, and formulate and test hypotheses. Setting up these processes is challenging and requires extensive training in data science. In addition to providing services for already established avenues, Dr. Joshi is training the staff and students in the area of data processing and integration. She also plans to develop new, independent, and collaborative projects to investigate the role of the microbiome in health and disease.

In the past year, Dr. Joshi authored "The Association Between a Mediterranean Diet and Symptoms of Irritable Bowel Syndrome" and "Randomized controlled pilot study assessing fructose tolerance during fructose reintroduction in non-constipated irritable bowel syndrome patients successfully treated with a low FODMAP diet," which were published in highly regarded peer-reviewed journals. Both of these projects were done in conjunction with fellow researchers at the Goodman-Luskin Microbiome Center. She also wrote the published work, "Integrated DNA Methylation/RNA Profiling in Middle Temporal Gyrus of Alzheimer's Disease," as well as numerous abstracts.

JENNIFER LABUS, Ph.D.

Director, UCLA G. Oppenheimer Center for Neurobiology of Stress and Resilience
Adjunct Professor of Medicine, Vatche and Tamar Manoukian Division of Digestive Diseases
David Geffen School of Medicine at UCLA
Director, Integrative Biostatistics and Bioinformatics Core

This past year, Dr. Labus has continued her successful collaboration with the NIH-funded U19 Alzheimer's Gut Microbiome Project and the Alzheimer's Disease Metabolomics Consortium, which brings together international experts in the brain-gut microbiome and computational statistics and system biology methods for metabolomics and microbiome data. As part of this collaboration, Dr. Labus is examining brain-gut microbiome interactions associated with the MIND (Mediterranean-DASH Intervention for Neurodegenerative Delay) diet. She is also investigating links between the brain-gut microbiome dietary intake based on metabolomics-derived dietary output. This novel approach to deriving dietary intake,

known as "foodomics," is expected to be the future for assessing diet, as self-report measures of diet often do not accurately represent food intake. Further, Dr. Labus and her colleagues continue to find evidence for the brain-gut-liver connection in Alzheimer's disease and have linked the presence of gut microbial species involved in bile acid production to brain atrophy in regions preferentially targeted in Alzheimer's.

In collaboration with Dr. Emeran Mayer and Lisa Aziz-Zadeh, Ph.D., at the University of Southern California, Dr. Labus is performing integrative analysis between metagenomics, metabolism, and brain-imaging-derived phenotypes in youth with autism spectrum disorder.

"The center provides increased opportunities to network with UCLA experts on campus and engage in fruitful collaborations to push forward research on, and knowledge of, the brain-gut microbiome," Dr. Labus says.

She is also very involved with developing the next generation of researchers. Dr. Labus is hosting a rotation for a graduate bioscience student interested in biostatistics and bioinformatics for brain-gut microbiome data, and also mentored and trained several undergraduate, graduate, medical, and postdoctoral students in brain-gut microbiome biostatistics and bioinformatics.

Dr. Labus has successfully applied for several grants to study the brain-gut microbiome, along with colleagues at the Goodman-Luskin Microbiome Center. In the future, she plans to continue to break ground in examining brain-gut microbiome interactions in health and disease using state-of-the-art analytical tools.

Recent published papers include "Reproducible Microstructural Changes in the Brain Associated with the Presence and Severity of Urologic Chronic Pelvic Pain Syndrome (UCPPS): A 3-Year Longitudinal Diffusion Tensor Imaging Study from the MAPP Network," as well as eight additional papers based on research with other Goodman-Luskin Microbiome Center faculty.

JENNY SAUK, M.D.

Director, Clinical Care, UCLA Center for Inflammatory Bowel Diseases
Health Sciences Associate Clinical Professor of Medicine
Vatche and Tamar Manoukian Division of Digestive Diseases
David Geffen School of Medicine at UCLA
Program Lead, Inflammatory Bowel Diseases program

Dr. Sauk has been collaborating with Drs. Jacobs and Mayer in the Goodman-Luskin Microbiome Center to understand the microbiome alterations predictive of stress-associated symptom flares in subjects with ulcerative colitis. This work has been supported by the Crohn's & Colitis Foundation. The researchers found that in 91 subjects with quiescent ulcerative colitis, high-stress reactivity was characterized by alterations in fecal microbes, mainly the Ruminococcaceae and Lachnospiraceae families. There were also alterations in fecal metabolites, including decreased monoacylglycerols and bile acids, and increased 4-ethyl phenyl sulfate, 1-arachidonoylglycerol, and sphingomyelin. The results showed that high-stress reactivity in ulcerative colitis patients was associated with microbial signatures that could predict clinical flare and, therefore, the microbiome could contribute to stress-associated symptom flares in ulcerative colitis.

As a next step, the researchers are recruiting patients with active ulcerative colitis to evaluate stress reactivity and correlate with fecal microbial/metabolomic and brain magnetic resonance imaging signatures.

The research resulted in the papers "High Perceived Stress is Associated with Increased Risk of Ulcerative Colitis Clinical Flares," published this past March in *Clinical Gastroenterology and Hepatology*, and "Microbial and Metabolite Signatures of Stress Reactivity in Ulcerative Colitis Patients in Clinical Remission Predicts Clinical Flare Risk," published in *Inflammatory Bowel Diseases* this past August.

Dr. Sauk is also co-investigator on a project, "Hyperbaric Oxygen Therapy for Ulcerative Colitis Patients Hospitalized for Moderate to Severe Flares: A Multi-Center Randomized, Double-Blind, Sham-Controlled Trial," under a grant from the NIH/National Institute of Diabetes and Digestive and Kidney Diseases.

"It is wonderful to have microbiome research prioritized at our center," Dr. Sauk says. "It encourages more brainstorming of ideas and encourages execution of projects that may have never occurred without the support of the center."

ELIZABETH VIDELOCK, M.D., Ph.D.

Health Sciences Assistant Clinical Professor of Medicine
Vatche and Tamar Manoukian Division of Digestive Diseases
David Geffen School of Medicine at UCLA
Program Lead, Neurodevelopmental and Neurodegenerative Diseases program

Dr. Videlock's laboratory, housed in the UCLA Center for Inflammatory Bowel Diseases, focuses on the gut-brain axis in Parkinson's disease. She first became interested in researching the brain-gut axis during medical school under the mentorship of Dr. Lin Chang. After medical school, Dr. Videlock returned to UCLA to complete a gastroenterology fellowship in the Specialty Training and Advanced Research (STAR) program, and then completed her Ph.D., also as part of the STAR program, under the co-mentorship of Dr. Chang and Charalobos (Harry) Pothoulakis, M.D., Ph.D.

Research in humans and scientific models demonstrates that Parkinson's disease may begin in the gut. In the past year, Dr. Videlock was first author of "Experimental models of gut-first Parkinson's disease: A systematic review," published in *Neurogastroenterology & Motility*, which reviewed the two most frequently used experimental models of gut-first Parkinson's to construct a framework and useful reference for neuroscientists, gastroenterologists, and neurologists interested in applying their expertise to advancing understanding of gut-first Parkinson's.

She was first author of "Distinct Patterns of Gene Expression Changes in the Colon and Striatum of Young Mice Overexpressing Alpha-Synuclein Support Parkinson's Disease as a Multi-System Process" in the *Journal of Parkinson's Disease*. This study used RNA sequencing to analyze brain and gut tissue in preclinical models. The researchers' conclusions supported the emerging view of Parkinson's as a multisystem disease. "I have learned so much from the supergroup meetings," Dr. Videlock says. "It was extremely helpful to be able to get feedback on my research from the group."

Based on one of the group meetings, Dr. Videlock's lab will be looking at whether the microbial metabolite IPA is therapeutic in gut-first Parkinson's. This project represents a new direction for the lab.

This past year, Dr. Videlock was awarded the UCLA Clinical and Translational Science Institute (CTSI) KL2 Translational Science Award for "Intestinal Mitochondrial Dysfunction and the Gut-Brain-Immune Axis in Models of Parkinson's Disease."

Dr. Videlock is a member of the editorial board of *Gastroenterology*. In the past, she has served as chair of the UCLA Gastroenterology Fellowship Seed Grant Committee and on the Abstract Selection Subcommittee (Irritable Bowel Syndrome Pathophysiology) of the American Gastroenterological Association.

"I am grateful to have a larger team to be a part of," says Dr. Videlock. "More brains make better science and make it more rewarding and enjoyable."

JENNIFER FULCHER, M.D., Ph.D.
Assistant Professor, Division of Infectious Diseases
David Geffen School of Medicine at UCLA
Infectious Diseases Section, VA Greater Los Angeles Healthcare System
Program Lead, Substance Use Disorder program

Dr. Fulcher studies HIV and immunology; in particular, how gut bacteria may contribute to HIV infection susceptibility and how drug use can affect the microbiome to contribute to HIV susceptibility. She notes that substance use is highly comorbid in people with HIV. Methamphetamine use portends a particular risk for acquiring and the quick progression of HIV, as well as a lower ability to suppress the virus with treatments.

Dr. Fulcher served as principal investigator for a recent study that found that certain gut bacteria differ between people who later acquire HIV infection, and those who do not. Compared to the men who did not acquire HIV, those who did had decreased levels of Bacteroides species, a type of bacteria prevalent in the lower intestinal tract that have important metabolic functions in maintaining a healthy gut environment. They also had increased levels of Megasphaera elsdenii, another bacterium whose role in the gut is as yet unknown, as well as elevated inflammatory cytokines and bioactive lipids, both associated with systemic inflammation, which is also associated with a higher risk of HIV.

The implication is that gut microbiome could contribute to one's risk for HIV infection. A better understanding of if and how these bacteria affect HIV transmission could lead to a microbiome-based therapy that could help prevent HIV infection.

The research was published in the peer-reviewed journal *eBioMedicine*, as well as on HealthDay.com, and was funded by the National Institute of Allergy and Infectious Diseases, the National Institute on Drug Abuse, the National Institute of Mental Health, the UCLA AIDS Institute, the UCLA Center for Clinical AIDS Research and Education, and the UCLA Pediatric AIDS Coalition.

Dr. Fulcher recently received a grant from the National Institute of Allergy and Infectious Diseases. She will serve as the principal investigator on a study of increased HIV acquisition risk due to substance use, resulting from pro-inflammatory alterations of the intestinal microbiome and/or direct effects on the inflammatory state of the mucosa.

ALDONS "JAKE" LUSIS, Ph.D.
Professor, Microbiology, Human Genetics, and Medicine
David Geffen School of Medicine at UCLA
Program Lead, Cardiovascular Disease and Lipid Metabolism program

Research projects in Dr. Lusis's lab currently cover atherosclerosis, heart failure, fatty liver disease, and obesity. The team studies naturally occurring genetic variations in preclinical models and humans to help understand interactions underlying complex cardiovascular and metabolic disorders. A major focus has been to integrate clinical traits with "intermediate" phenotypes obtained through high-throughput technologies, or systems genetics, such as RNA sequencing, metabolomics, or proteomics. Dr. Lusis and his team have developed a reference resource to facilitate this approach that can be used to analyze genetic interactions and carry out whole-genome association mapping.

In the past year, Dr. Lusis authored "A ketogenic diet can mitigate SARS-CoV-2 induced systemic reprogramming and inflammation," published in *Communications Biology*, an open-source, peer-reviewed journal. The research explored the benefits of the ketogenic diet (KD) in modulating the immune response

and promoting a systemic anti-inflammatory state. In particular, the team investigated the effects of the KD on systemic toxicity in preclinical models following SARS-CoV-2 infection. The results indicated that with a KD, there was a reduction in weight loss, with overall improved survival. Muted multi-organ transcriptional reprogramming and metabolism rewiring suggested that a KD initiates and mitigates systemic changes caused by SARS-CoV-2. Data also suggested that a KD can alter transcriptional and metabolic responses following SARS-CoV-2 infection, resulting in improved health; reduced inflammation; and restored amino acid, nucleotide, lipid, and energy currency metabolism.

Dr. Lusis is currently researching a metabolite made by bacteria, indole propionic acid, that has an impact on heart failure in conjunction with the center's Dr. Hsiao.

The lab serves as an educational setting, as two graduate and two postdoctoral students are working on research projects there.

BRUCE NALIBOFF, Ph.D.

Project Scientist
Director, Pain Research Program
UCLA G. Oppenheimer Center for Neurobiology of Stress and Resilience
Vatche and Tamar Manoukian Division of Digestive Diseases
David Geffen School of Medicine at UCLA
Career Scientist, VA Greater Los Angeles Healthcare System (retired)
Co-director, Clinical Studies and Database Core
Program Lead, Mental Illness and Pain program

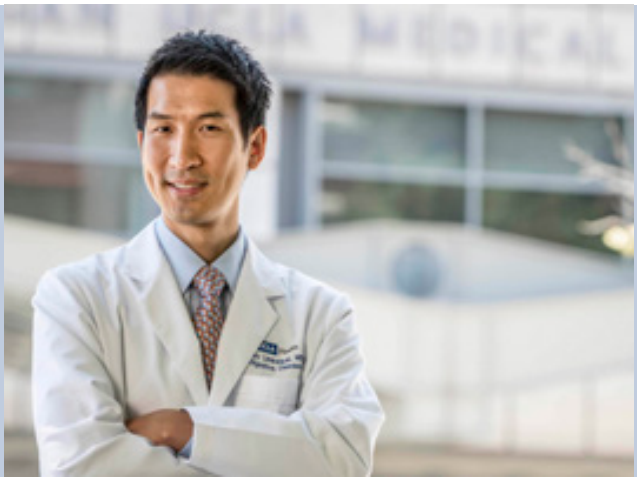
Dr. Naliboff has led vital studies into the perceptual and cognitive aspects of chronic pain states, including the role of negative and positive emotions in modulating pain symptoms and impact. He is also a leader in developing and evaluating nonpharmacological therapies for visceral and somatic pain, and has studied the clinical use of opioid medications.

As part of the Clinical Studies and Database Core of the Goodman-Luskin Microbiome Center, Dr. Naliboff helps support the integration, synergy, and productivity of the programs at the microbiome center by

creating and maintaining a multimodal database that includes clinical and biological information from center studies. This database is the foundation for the cross-modality and cross-project studies crucial to the center's overall goals.

Some recently published research Dr. Naliboff has been part of includes "Hypothetical model ignores many important pathophysiologic mechanisms in fibromyalgia" in *Nature Reviews Rheumatology*; "Clinically Important Differences for Pain and Urinary Symptoms in Urological Chronic Pelvic Pain Syndrome: A MAPP Network Study" in the *Journal of Urology*; and "Mediators of the association between childhood trauma and pain sensitivity in adulthood: a Multidisciplinary Approach to the Study of Chronic Pelvic Pain Research Network Analysis" in *PAIN*.

Dr. Naliboff has participated in numerous research studies with colleagues across other microbiome center cores. He has had continuous funding from the NIH and the VA, and has served as a consulting editor for numerous publications in psychology and medicine. Dr. Naliboff has participated on national and international committees as a grant reviewer and program consultant.



BERKELEY LIMKETKAI, M.D., Ph.D.
Director, Clinical Research
UCLA Health Center for Inflammatory Bowel Diseases
Health Sciences Associate Clinical Professor of Medicine
Vatche and Tamar Manoukian Division of Digestive Diseases
David Geffen School of Medicine at UCLA
Program Lead, Inflammatory Bowel Diseases program

As director of clinical research in the UCLA Health Center for Inflammatory Bowel Diseases, Dr. Limketkai strongly believes in harnessing the synergy between clinical care and investigations. He is keenly interested in studying the relationship between malnutrition and IBD, identifying novel treatment approaches for IBD, developing evidence-based frameworks for precision nutrition, and applying technology (e.g., digital health, artificial intelligence) for nutrition and gastroenterology. Dr. Limketkai serves as a research mentor to many medical students, residents, and gastroenterology fellows.

Dr. Limketkai and his collaborators are finding that diet and other environmental triggers are believed to play an important role in both the development of IBD and disease severity, along with factors such as genetic predisposition, the microbiome, and the sensitivity of the immune system. "A complex interplay of factors are involved," he explains. "As one of the components, nutrition is probably important for everybody, although it is more so for some than others. What we do know is that nutrition is something patients have control over, which is why many are eager to try to alter their diet in an effort to reduce symptoms and inflammation — and there is evidence that in some patients, this can be effective. We want to support patients by offering them the best evidence-based practice for nutritional care of IBD."

Dr. Limketkai's other research involves data analyses of clinical outcomes and health services utilization to better understand the factors that drive favorable or unfavorable outcomes in IBD. In his paper, "Longitudinal Trends in Pregnancy Outcomes Among Women With Inflammatory Bowel Disease in the Era of Biologics: A 20-Year Nationwide Analysis," published in *Inflammatory Bowel Diseases*, the study found that between 1998 and 2018, live deliveries in IBD patients steadily increased. Despite advances in treatment, IBD patients who are pregnant remain at risk for adverse pregnancy outcomes and further work is needed to address factors affecting disease control at the time of pregnancy, and to understand other factors beyond disease control that may affect pregnancy outcomes.

Clostridioides difficile infections (CDIs) are common among patients with IBD and can mimic and exacerbate IBD flares, thus warranting appropriate testing during flares. Dr. Limketkai's paper, "Recent trends and risk factors associated with Clostridiodes difficile infections in hospitalized patients with inflammatory bowel disease," published in *Alimentary Pharmacology & Therapeutics*, found that rates of CDI among hospitalized patients with IBD initially increased, but have declined since 2015. Increased comorbidity, large hospital size, public insurance, and urban teaching hospitals were associated with higher rates of CDI. These infections were also associated with increased mortality in hospitalized patients with IBD. Continued vigilance, infection control, and treatment of CDI can help continue the trend of declining infection rates.

ANDREA SHIN, M.D., MSCR

Health Sciences Associate Professor of Medicine
Vatche and Tamar Manoukian Division of Digestive Diseases
David Geffen School of Medicine at UCLA
Co-director, Clinical Studies and Database Core
Disorders of the Gut-Brain Interactions program

Leveraging her extensive clinical expertise, Dr. Shin focuses her research endeavors on pioneering diagnostic and therapeutic strategies for disorders of gut-brain interaction and gastrointestinal motility, including irritable bowel syndrome (IBS), functional diarrhea, functional constipation, and anorectal disorders.

Dr. Shin has vast experience conducting clinical trials with patients living with IBS, functional constipation, and gastroparesis. Results from studies led to the use of fecal bile acids, a group of crucial microbial metabolites, as actionable diagnostic biomarkers in patients with bowel dysfunction. She has also led prospective studies examining microbiome composition, short chain fatty acid profiles, bile acid profiles, intestinal transit, and bowel functions in IBS. Findings demonstrated changes in microbial metabolites, microbial composition, and microbial function in people with IBS and now inform the key themes of Dr. Shin's current research, which focuses on developing innovative microbiome-based tools that will enhance the delivery of precision care in IBS.

Since joining UCLA in August 2023, Dr. Shin has continued her microbiome-focused projects, while also contributing to other areas of research. Recently, she explored the possible expansion of the biopsychosocial model of disorders of gut-brain interaction to other important gastrointestinal diseases, such as IBD, in an editorial published in *The Lancet Gastroenterology & Hepatology*. In this editorial, she discussed the implications of a recent systematic review and meta-analysis performed by a group of investigators who examined the effects of psychological therapy on people with IBD. Through a discussion of their findings, Dr. Shin emphasized the importance of incorporating quality of life as a primary endpoint in future IBD trials, the potential effectiveness of third-wave psychological therapies, and that promising advancements in psychological treatments for IBD and IBS-IBD overlap are underway.

Dr. Shin's recent paper, "A systematic review and meta-analysis of diet and nutrient intake in adults with irritable bowel syndrome," featured in *Neurogastroenterology & Motility*, revealed that individuals with IBS tend to have suboptimal fiber and vitamin D intake, but overall dietary intake of other macro- and micronutrients is not compromised. Notably, reduced fiber intake in those with IBS was observed, emphasizing the need for further exploration into the causes and consequences of this deficiency. Specifically, this research provides insights into particular nutritional inadequacies that warrant attention in IBS and will also be important for advancing scientific progress in unraveling diet-microbiome interactions in IBS.

She completed her medical degree and gastroenterology fellowship at the Indiana University School of Medicine. In addition to her research, Dr. Shin actively participates in multiple professional committees, including the American Gastroenterological Association Research Awards Panel, and contributes to initiatives related to functional bowel disorders and patient education.

NEXT STEPS

Although researchers at the UCLA Goodman-Luskin Microbiome Center have already accomplished so much, their plans for the future are even more ambitious. The team completed a large outreach effort to the rest of the campus and have onboarded 30-plus additional faculty members. The new members have been recruited from all departments and divisions pertaining to microbiome research, including chemistry, ecology, and engineering. Adding this mix of interests to the digestive diseases center that already exists will leverage diverse expertise and breed ever more innovative research alliances. This larger community will initiate meetings in January 2024 to share research, socialize, and network to promote collaboration.

Goodman-Luskin Microbiome Center faculty have also forged relationships with other organizations on campus to augment their resources. They are working with the UCLA Depression Grand Challenge and the Institute for Precision Health, which collects human genomic data but which, to date, had not collected information related to the microbiome. The two organizations are merging their two complementary data sets to better explore how the human genome interfaces with microbial genomes.

The Goodman-Luskin Microbiome Center has launched Seed Fellowship Awards benefiting trainees, such as graduate students, postdoctoral fellows, or early-career faculty, who will conduct projects involving at least one core facility to form a stronger foundation of interaction among cores. More programs offering financial incentivization to collaborate will be launched in the coming year. An annual postdoctoral fellowship will honor excellence in microbiome research led by microbiome center fellows. These programs are meant to nurture the next generation of microbiome researchers and involve them in the center. In addition, the Goodman-Luskin Microbiome Center will offer a Pilot and Feasibility Program to support innovative microbiome research by center members that will fund faculty rather than trainees.

The center also plans to institute an annual symposium, providing a broad view of all microbiome research occurring across campus through research talks, presentations, posters, and more.

WITH GRATITUDE

The visionary investments of Andrea and Donald Goodman and Renee and Meyer Luskin, and continued support of Chip Rosenbloom and the Rosenbloom family, have generated groundbreaking research that has provided insights into diseases and will translate into improved patient treatments. Within a short period of time, the establishment of the UCLA Goodman-Luskin Microbiome Center Endowed Fund has changed the face of gut-mind interaction investigations, encouraging cross-discipline collaborations through relationships that might not have existed were it not for the center it funded.

UCLA's leadership and faculty of the Goodman-Luskin Microbiome Center appreciate the commitment demonstrated by the Goodman, Luskin, and Rosenbloom families to health sciences and pioneering research.

THANK YOU.