

# Beyond the Scope

A REPORT OF THE VATCHE AND TAMAR MANOUKIAN DIVISION OF DIGESTIVE DISEASES

California Institute for Immunology and Immunotherapy  
Forging a New Era of Discovery and Innovation  
at the UCLA Research Park



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## Going *Beyond the Scope*

The more we learn about the immune system, the more we understand about its central role in virtually every type of disease. This clarity is certainly the case in the field of digestive diseases, where the inextricable link between immunology and the gastrointestinal tract plays out in conditions such as inflammatory bowel diseases. We have also seen, from the dramatic results with certain cancers, the vast potential of immunotherapy — engineering the immune system to fight diseases.

This issue of *Beyond the Scope* highlights exciting developments on this front for our Vatche and Tamar Manoukian Division of Digestive Diseases. In January, UCLA announced that the California Institute for Immunology and Immunotherapy at UCLA (CIII) would serve as an anchor tenant at the new UCLA Research Park, a 700,000-square-foot property two miles south of the UCLA campus at the site of the former Westside Pavilion shopping mall ([see page 1](#)). This nonprofit public-private partnership leverages UCLA's considerable breadth of expertise as a premier research university while also bringing in top scientists and industry leaders from other institutions in California and beyond, all toward the goal of establishing an ecosystem for multidisciplinary research and entrepreneurship in which promising discoveries are rapidly translated to new therapies. My decision to become one of CIII's founders, alongside my visionary partners, was based on my certainty that this institute will foster untold opportunities for our division to contribute to transformational progress.

Among our programs that will benefit from CIII is the Center for Inflammatory Bowel Diseases, which has undergone a major expansion of its own under the leadership of Dr. Jenny Sauk. As the articles beginning on [page 4](#) detail, the center has brought in new IBD physicians and established subspecialty clinics where dedicated providers bring their expertise to IBD patients at every life stage. The center will now continue to expand with basic and translational science faculty.

Another major beneficiary, the UCLA Goodman-Luskin Microbiome Center, has taken great strides since its establishment early last year. As the article on [page 12](#) describes, this center — which galvanizes researchers across the UCLA campus to study the human microbiome and translate findings into new treatment strategies for a range of conditions — has launched core services for shared resources and expertise, as well as starting a seed funding program to help promising new investigators get their start. The center, under the direction of Dr. Elaine Y. Hsiao, has also kicked off a monthly seminar series. Microbiome research represents a new frontier with endless possibilities, and the center's investigators are at the forefront of that work, as studies by Dr. Hsiao's group ([page 14](#)) and a team led by Dr. Arpana "Annie" Gupta ([page 15](#)) illustrate.

Within the Goodman-Luskin Microbiome Center, we have one of the nation's few designated centers of excellence in disorders of gut-brain interaction (DGBI) — disorders such as irritable bowel syndrome, chronic constipation, abdominal pain, and others that are extremely common and can be highly debilitating. Our division has been a national leader in the research and treatment of DGBI for several decades, and that group has been greatly bolstered by the recent recruitment of Dr. Andrea S. Shin ([page 10](#)).

The articles in this issue reflect just a few of the many reasons I am thrilled with the direction of our division, department, medical school, health system, and university. I hope you enjoy reading about our faculty and fellows, and I look forward to sharing even more good news in the years to come.

# California Institute for Immunology and Immunotherapy Will Forge New Era of Discovery and Innovation at the UCLA Research Park



L-R (Founding Donors): Dr. Gary Michelson, Meyer Luskin, Dr. Eric Esrailian, Dr. Arie S. Belldegrun, Michael Milken

A nonprofit public-private partnership in California promises to usher in a new era of biomedical breakthroughs in the fast-growing fields of immunology and immunotherapy — and UCLA’s Vatche and Tamar Manoukian Division of Digestive Diseases will play an active role in the unprecedented effort.

The California Institute for Immunology and Immunotherapy at UCLA (CIII), which capitalizes on UCLA’s strengths in clinical and biomedical research across a range of disciplines, will serve as an anchor tenant at the new UCLA Research Park, located on the site of the former Westside Pavilion shopping mall — the iconic 700,000-square-foot property two miles south of UCLA’s Westwood campus. In that setting, CIII will bring together scholars and industry experts from around the world to create a nexus for discovery and innovation that will benefit Southern California and beyond. Top scientists from UCLA and elsewhere will pursue new tools, treatments, and vaccines for some of the most pressing

health challenges, in digestive diseases as well as other areas of medicine.

The acquisition of the UCLA Research Park site was made possible by an intended \$500 million investment, with \$200 million already allocated, from the State of California to fund the immunology and immunotherapy institute. The CIII is also supported by a group of founding donors from the biotechnology, academic, entrepreneurship, and philanthropic communities led by Meyer Luskin, Dr. Gary Michelson, Dr. Arie S. Belldegrun, Sean Parker, Michael Milken, and Dr. Eric Esrailian, chief of the Vatche and Tamar Manoukian Division of Digestive Diseases.

In addition to creating a thriving interdisciplinary environment for biomedical discovery, CIII will support the development of startups while attracting top immunology and immunotherapy scientists and helping to build the future workforce in these fields through training. The goal is to foster “the immunology equivalent of Silicon Valley in Los Angeles,” according to Dr. John Mazziotta, vice chancellor for health sciences and CEO of UCLA Health.

“Immunology plays a central role in the GI tract in both health and disease,” Dr. Esrailian says. “It is an honor for me to help create an opportunity for our division’s faculty, fellows, and students to be a part of this historic project for many years to come. It will be transformational for the field of digestive diseases as well as other disease areas by leveraging UCLA’s unique strengths and establishing an ecosystem for entrepreneurship that will ensure discoveries are translated to therapies and technology that benefit patients.”

“A deeper understanding of the science of immunology can transform biomedical sciences,” says Dr. Owen N. Witte, UCLA professor of microbiology, immunology, and molecular genetics and President’s Chair in Developmental Immunology. “I can’t think of a single disorder that wouldn’t be better treated if we had a greater insight into the immune system.”

Dr. Witte points out that among human organ systems, only the nervous system, vascular system, and immune system are distributed throughout the body. “Each of those systems influences all of the other systems in the body, and when

they don’t work correctly and synergistically, you get human disease,” Dr. Witte says. “There really isn’t a group of diseases that doesn’t have some immune interaction.”

A greater understanding of immunology has fueled the field of immunotherapy, which involves engineering the immune system to fight diseases. “Over the last 20 years, advances in immunotherapy for cancer alone have been breathtaking — the greatest new classes of drugs, like checkpoint inhibitors and cellular therapies, have been incredibly exciting,” says Dr. Witte, whose own group has played a pivotal role in cellular therapies with its contributions to the understanding of human leukemias, immune disorders, and epithelial cancers. “We are now seeing expansion of those types of therapies for lots of other diseases — including autoimmune diseases, which will be the next frontier. This is a revolution in medical treatment, and UCLA is going to be able to play an enormous role in it, in synergy with this new institute.”

Dr. Belldegrun, one of CIII’s founding donors and the founding director of the UCLA Institute of Urologic Oncology, has devoted much of his career to developing immunotherapy treatments for cancer. In 2009, based on research that started at UCLA, he founded Santa Monica-based Kite Pharma, a biopharmaceutical company that has led the way in developing cancer cell therapies and has treated more patients with CAR T-cell therapy than any company. Since then, Dr. Belldegrun has launched several other companies that have generated significant progress in the field of immunotherapy.

Genetic engineering paved the way for immunotherapy treatments, notes Dr. Belldegrun, who began his career at



L-R: Dr. Owen N. Witte, Dr. Michael V. Drake, Governor Gavin Newsom

## “A deeper understanding of the science of immunology can transform biomedical sciences,” says Dr. Owen N. Witte.

the National Cancer Institute under the mentorship of Dr. Steven Rosenberg, considered one of the field’s pioneers. “The fact that we could study the genes involved in the immune system led to the ability to correct a defective gene and use the immune system to keep patients alive and well for years,” he says. “This is now a \$100 billion industry in cancer, and we have moved to autoimmune disease, neurology, and other areas. There’s no other field like it, and this institute will put UCLA on the world map as a powerhouse for immune-mediated diseases of all types.”

As an independent institute, CIII will draw on the expertise not only of UCLA faculty members, but also of scholars affiliated with other universities in Southern California, along with leading scientists and practitioners outside of academia in fields such as human genetics, genomics, computer science, engineering, and information science. Dr. Esrailian notes that this structure, modeled after independent research institutes with strong university partnerships, such as the Broad Institute of MIT and Harvard, is advantageous. It allows for casting a wide net when it comes to bringing in leading experts, but it also provides an ability to promote rapid translation of findings to intellectual property, the launching of new biotech companies, and the development of effective new treatments. CIII is its own nonprofit organization with governance by a board of directors that includes UCLA and state administrators, but also leading business people and philanthropists. “That entrepreneurial spirit is embedded in the founding and mission of the institute,” Dr. Esrailian says. “With UCLA having premier schools and expertise in areas such as management, engineering, law, physical sciences, life sciences, medicine, as well as a world-class health system and hospital, all in close proximity — the opportunities for these types of partnerships are enormous.

Dr. Belldegrun notes that the institute will become an important source of support for scientists through these entrepreneurial activities. “This is a stand-alone institute that will hold the IP in order to generate multiple companies around UCLA, then return some of the equity from those companies back to the institute to continue the evergreen funding,” he explains. Already, Dr. Belldegrun says, the institute’s leadership has engaged in discussions with major biotech companies about future collaborations within the UCLA Research Park ecosystem.

The acquisition of the empty former mall represents the latest in a series of major land acquisitions as part of an expansion designed to broadly extend UCLA’s top-flight resources and

institutional expertise. In June 2023, UCLA bridged the gap between Westwood and Downtown Los Angeles with the purchase of UCLA Downtown, a 334,000-square-foot building in downtown’s Historic Core. And in September 2022, the university acquired its UCLA South Bay campus, including the 24.5 acres of the former Marymount California University campus in Rancho Palos Verdes and an 11-acre residential site in San Pedro.

But more than just a necessity, the new space is expected to create a synergy of scientists working in close proximity across disciplinary lines. Beyond the multidisciplinary California Institute for Immunology and Immunotherapy at UCLA, the research park will house the multidisciplinary UCLA Center for Quantum Science and Engineering, which conducts research in the emerging field of quantum science and technology — including quantum computing, communication, and sensing — as well as programs across the disciplines.

“It’s a lesson that’s reinforced over and over again — solving a big problem requires people with different expertise and a common purpose,” Dr. Witte says. “The people involved in this institute will come from disciplines such as physical sciences and chemistry, bioengineering and electrical engineering, computational biology, and all of the medical specialties. It will include experts in every imaginable class of disease that we have at UCLA, the associated hospitals, and the broader Southern California region. The idea is to have this cauldron to put all this energy together and achieve great outcomes faster.”

UCLA Research Park is scheduled to be completed in May 2027, but Dr. Esrailian notes that researchers will begin moving into the facility in phases, well before the completion of the entire complex. Goodman-Luskin Microbiome Center, the Center for Inflammatory Bowel Diseases, and many other division programs, and their scientists, will benefit from this acquisition and launch. CIII and the new UCLA Research Park are also expected to be a boon for recruiting given the massive potential in many domains.

“I’m incredibly grateful for my fellow co-founders and partners on this venture,” Dr. Esrailian says. “We have had tremendous support from the university and the state. Every person who has been a part of this project has rallied and come through despite many challenges, and it is all for the benefit of humanity — both now and in the future.”

# IBD Center Opens Subspecialty Clinics as Part of Comprehensive, Integrative Program

The [Center for Inflammatory Bowel Diseases](#) has expanded its offerings as it continues to build out its vision of a comprehensive, integrative, and collaborative family program for the Los Angeles IBD community.



Jenny Sauk, MD





“This is an exciting time for our center,” says Jenny Sauk, MD, the center’s director of clinical care and health sciences associate clinical professor of medicine in the division. “With the addition of our new IBD physicians, we have a team of experts highly committed to delivering the best-quality care for IBD patients as well as expanding access to specialty care. Working together in the same space, our priority is to serve patients at every life stage and provide an IBD home for patients — a place where all of their IBD care needs can be addressed.”

Given the complexity of IBD care, the center has established clinics where dedicated providers with expertise in subspecialty areas are able to offer more nuanced treatment, Dr. Sauk explains. This includes:

- A Pediatric-to-Adult Transition Clinic, under the leadership of Hassan Hamandi, MD, director of the Pediatric Inflammatory Bowel Disease Program and one of two recent additions to the center’s faculty;
- A Preconception, Pregnancy, and Postpartum Clinic, under the leadership of Nirupama N. Bonthala, MD, director of Women’s Health in IBD and the second recent faculty addition;
- An IBD Nutrition Clinic, under the leadership of Berkeley Limketkai, MD, PhD, the center’s director of clinical research; and
- A Medical-Surgery Clinic to address patients’ peri-surgical needs and postsurgical management, under the leadership of Mary R. Kwaan, MD, MPH, health sciences clinical professor of surgery, specializing in colon and rectal surgery.

Dr. Sauk notes that the center’s IBD clinicians are highly collaborative — both

within the team and with the community. In addition to the core team members, the center has dedicated IBD physicians in community practices throughout Southern California who participate in biweekly conferences to consult on difficult cases and potentially refer for subspecialty care.

The center is also attuned to the specific needs of the LGBTQIA+ population — including those who are receiving hormones for gender-affirming care, which can potentially interact with certain IBD medications. “Many of these patients have experienced poor access to care because of their discomfort or negative experiences with the healthcare system, and we want to make sure to provide a welcoming environment as well as high-quality, individualized care in partnership with their primary care provider,” Dr. Bonthala says. For all patients, a GI psychologist and integrative care nurse practitioner help to optimize wellness.

By conducting cutting-edge research, the center continually improves the care it can offer to patients. This includes an increasing number of translational research practices, led by Dr. Limketkai, as well as a growing array of clinical trials in IBD.

“It’s important for IBD patients to receive longitudinal care, and that’s something UCLA is particularly well suited to deliver,” Dr. Sauk says. “Patients can utilize local community practices and care centers around the Los Angeles area while still having access to our subspecialty IBD clinics in Westwood. We pride ourselves in this team approach that offers both convenience and access to subspecialty care as needs develop throughout the patient’s life course.”

# Transition Clinic Empowers Young Adults to Take Ownership of Their Ongoing Care Needs

Approximately one-third of patients with inflammatory bowel disease are diagnosed in childhood or early adolescence. As these individuals enter adulthood, a smooth transition out of the pediatric setting is especially important — both to ensure effective continuity of care as they begin to see new providers, and to empower them to take ownership of their ongoing healthcare needs. “Too often, there is not enough focus on making sure young adults with IBD are able to adjust to an environment in which there is a lot more onus to make their appointments, ensure they’re receiving their medications, and follow up with their doctors,” says Hassan Hamandi, MD, director of the Pediatric Inflammatory Bowel Disease Program and health sciences clinical associate professor in the Division of Pediatric Gastroenterology, Hepatology, and Nutrition and the Vatche and Tamar Manoukian Division of Digestive Diseases.

With that in mind, the Center for Inflammatory Bowel Diseases has launched a Pediatric-to-Adult Transition Clinic, focusing on IBD patients roughly in the age range of 18 to 26. As a pediatric gastroenterologist who also has young-adult patients, Dr. Hamandi will help to make the transition easier by overseeing the clinic while patients begin to interact with adult ancillary staff and experience other components of an adult health care setting. The transition clinic includes a focus on issues specific to the population, such as sexual health, while teaching patients to better understand their medical record and allowing parents to pull back from their child’s care.

For patients with a chronic condition such as IBD that requires ongoing care, the transition from pediatric to adult care can be fraught, Dr. Hamandi notes. Young people are often not used to making follow-up appointments on their own. If they are in college and away from home for the first time, they might not know what resources are available and, after relying on their parents to schedule their care, might not take the initiative. The transition clinic is designed to build that autonomy.

“In many ways, this transition clinic is as much for parents as it is for the young adults,” says Berkeley Limketkai, MD, PhD, health sciences associate clinical professor of medicine in the Vatche and Tamar Manoukian Division of Digestive

Diseases and director of clinical research for the Center for Inflammatory Bowel Diseases, who sees patients at the clinic. “Going straight from a pediatric to an adult setting can be jarring. It’s a completely new environment, and it often occurs when these patients are away in college. Parents not only have to worry about their child’s academics, but how they’re doing physically and emotionally. A big part of this clinic is helping to ease those concerns.”

Traditionally, there has been a divide between adult and pediatric GI — with little collaboration or interaction — but studies have suggested that helping IBD patients with the transition improves the quality of care. “In some institutions, a pediatrician might write a summary of the patient’s history and that’s all that patient goes into adult medicine with — and sometimes there are no records at all,” Dr. Hamandi says. “My goal is to be that bridge, so that providers are on the same page and patients have a period of time where they’re learning to take control of their care.”

**“For patients with a chronic condition such as IBD that requires ongoing care, the transition from pediatric to adult care can be fraught, Dr. Hamandi notes.”**



Hassan Hamandi, MD



# Preconception, Pregnancy, and Postpartum Clinic Helps Women Optimize Reproductive Outcomes

Women with inflammatory bowel disease who are either contemplating pregnancy or have already become pregnant face many uncertainties, as well as known risks. They are more susceptible to adverse outcomes such as preterm birth. If their inflammation is uncontrolled, they are at increased risk of flares during pregnancy, which can lead to newborns who are small for gestational age, intrauterine growth restriction, preterm birth, and miscarriage. And, although many medications that are used to treat IBD are safe, providers and patients are often reluctant to continue with them during the pregnancy for fear of harming the fetus.

To address these concerns, the Center for Inflammatory Bowel Diseases has established a multidisciplinary Preconception, Pregnancy, and Postpartum Clinic — one of only a handful in the world — in which a team that includes an IBD physician specializing in women’s health as well as a high-risk OBGYN collaborates with patients through preconception planning, pregnancy, and the postpartum period to alleviate fears, dispel misconceptions, and maximize outcomes.

“This is a coordinated effort to make sure mom and baby do as well as they possibly can,” says Nirupama N. Bonthala, MD, health sciences associate clinical professor of medicine and director of Women’s Health in Inflammatory Bowel Disease for the Vatche and Tamar Manoukian Division of Digestive Diseases, who directs the clinic. “In addition to working closely with our patients, we are committed to educating their referring GI and OB providers so that everyone is on the same page.”

At the clinic, women receive personalized guidance to ensure their IBD is well controlled prior to and during pregnancy, along with high-quality obstetrics care that includes close maternal-fetal medicine monitoring. Before becoming pregnant, patients can make an initial visit to discuss preconception concerns with Dr. Bonthala and her team, which includes a high-risk obstetrician, offering guidance to both the patient and her referring GI and OB providers on care during an upcoming pregnancy. Patients visit the multidisciplinary expert team at least once each trimester during the pregnancy, as well coming in for one postpartum visit. In addition to making a delivery plan and addressing any issues that come up during and after the pregnancy,

the clinic offers support that includes personalized dietary guidance, mental health care, and lactation support.

When women with IBD are considering becoming pregnant, inevitably they want to know whether their IBD medications will be safe through the pregnancy and during breastfeeding. “It’s natural to have some doubt about whether staying on a medication is keeping the baby safe, and in some cases a well-intentioned healthcare provider who doesn’t have experience in this area might recommend not taking it, just because of that doubt,” Dr. Bonthala says. “As a result, I have had patients who are flaring terribly by the time they come to see me.” Many women with IBD also assume they will need to deliver by C-section when that is generally not the case, Dr. Bonthala adds. Some patients worry that their IBD will impact their ability to become pregnant. “Women’s health in general has been under-researched and under-evaluated, and unfortunately IBD is no exception,” Dr. Bonthala says. “Our goal is to dispel any misinformation and apply the best evidence to maximize outcomes for mom and baby.”

**“In addition to working closely with our patients, we are committed to educating their referring GI and OB providers so that everyone is on the same page.”**



Nirupama N. Bonthala, MD

# Nutrition Clinic Recommends Evidence-Based Diet Strategies Personalized to Patient Needs

Nutrition has become an increasing focus in the management of inflammatory bowel disease. For some patients, altering the diet can help to reduce inflammation and improve symptoms. IBD patients are at risk for avoidant restrictive food intake disorder (ARFID), a form of overly selective eating that can lead to malnutrition. And importantly, the issue of nutrition is at the top of minds for patients with IBD. “A question from almost every IBD patient is, ‘What can I eat?’” says Berkeley Limketkai, MD, PhD, director of clinical research for the Center for Inflammatory Bowel Diseases and a health sciences associate clinical professor of medicine in the Vatche and Tamar Manoukian Division of Digestive Diseases.

The Center for Inflammatory Bowel Diseases’ newly established multidisciplinary IBD Nutrition Clinic incorporates the latest evidence in making dietary recommendations personalized to each patient’s needs. The clinic, directed by Dr. Limketkai and including a team of specially trained IBD registered dietitians, also assists with perioperative nutrition planning to optimize surgical outcomes.

Dr. Limketkai points out that dietary recommendations for IBD patients are not one-size-fits-all. His team takes each patient’s clinical profile — including their nutritional status, current and previous diets, and any known tolerances or intolerances. “We consider the person’s medical, social, and cultural history,” Dr. Limketkai says. “For example, you can’t just say ‘follow a Mediterranean diet,’ because that means very different things to individuals from different backgrounds.”

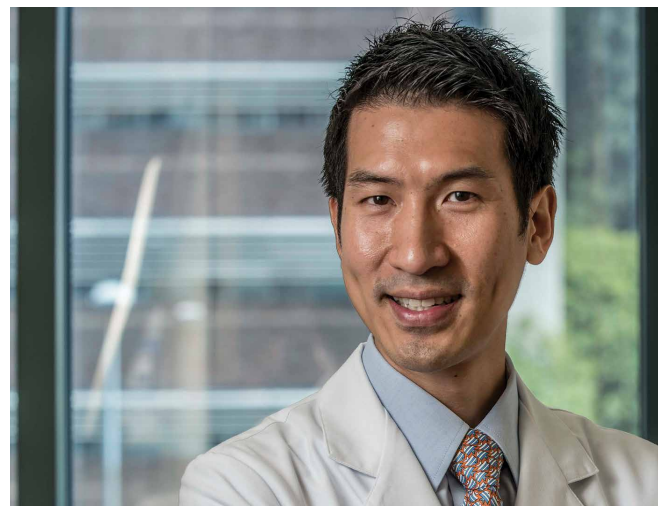
The recommended interventions include diets published in the research literature as well as those developed and studied at UCLA. To help identify optimal dietary strategies, the team utilizes a clinical decision-support tool based on dietary and outcomes data collected on previous patients — approximately 700 patients are currently in the database. “What we learn from each patient helps to inform the recommendations we make to future patients,” Dr. Limketkai explains.

The research conducted by the clinic is important because of the need for a better understanding of the role of nutrition

in IBD, and which patients are most likely to benefit from which approaches. “This is a relatively immature field in the sense that we have only begun to develop robust research data in humans in the last several years,” Dr. Limketkai says. “We are now seeing an acceleration of those studies, and by developing that knowledge base we can continue improving the care we provide.”

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, Dr. Limketkai says. “A complex interplay of factors are involved,” he explains. “As one of the components, nutrition is probably important for everybody, though more for some than for others. But 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 points out that dietary recommendations for IBD patients are not one-size-fits-all.”**



Berkeley Limketkai, MD, PhD

# Medical-Surgery Clinic Offers Single Setting for Addressing IBD Patients' Surgical Needs

When surgery becomes a potential option for patients with inflammatory bowel disease (IBD), many questions arise. If it's not clear whether surgery is the best path forward, a thorough discussion of the pros and cons becomes paramount. And when the need for surgery is clear, patients with IBD, their medical providers, and the surgical team must work in tandem to address issues such as medical and nutritional optimization prior to the surgery, surgical planning, and post-surgical management.

The combined Medical-Surgery Clinic at the Center for Inflammatory Bowel Diseases provides a single setting where patients with IBD can address all surgery-related needs with a team that includes their IBD physician, surgeon and dietitian. Patients start with a consultation to understand what the surgery will entail and why it is being considered. If they proceed with the surgery, they continue to visit the clinic both before and after the surgery to ensure optimal outcomes. The clinic is headed by Mary R. Kwaan, MD, MPH, a health sciences clinical professor of surgery who specializes in colon and rectal surgery, and Jenny Sauk, MD, director of clinical care for the Center for Inflammatory Bowel Diseases and a health sciences associate clinical professor of medicine.

Dr. Sauk points out that there are a number of circumstances in which IBD patients benefit from combined medical and surgical management. "In Crohn's disease, for example, perianal fistulas can be complex, and having a surgeon and IBD physician reviewing the data together with the patient allows that patient to best understand the sequence of events that need to occur for healing," she says. Patients with Crohn's disease may experience symptoms, such as abdominal pain, bloating, and nausea, due to stricturing disease, Dr. Sauk notes, and can benefit greatly from a joint consultation to determine whether continued medical treatment or a surgical intervention is the best approach. Dr. Sauk adds that patients who have had ulcerative colitis for many years may be at higher risk of developing dysplasia in the colon, raising difficult decisions about whether to consider colonic resection or consider further endoscopic surveillance. Joint discussions between the patient, surgeon and IBD specialist are important to determine optimal

strategies for management and ensure that there is clear communication with the patient about management.

Often, patients visiting the Medical-Surgery Clinic haven't decided whether surgery is the right option for them. "By meeting with both the surgeon and their IBD clinician in the same visit, patients can learn about the pros and cons so that they are more comfortable with the idea of surgery when they need it," Dr. Sauk says. Once the surgery is scheduled, the team works cooperatively with the patient on nutritional optimization and the management of medications, as well as in anticipating potential complications following the procedure. The team works jointly with the patient after the surgery to address issues such as when to resume IBD medications and how to manage any symptoms they experience during their recovery.

Seeing their IBD clinician and surgeon together at the same visit is something patients greatly appreciate, Dr. Sauk says. "We have many people who come from far away, and this allows them to have all of their IBD needs taken care of at the same time their peri-surgical needs are being addressed," she says. "It's also much more efficient for the patient, IBD provider and surgeon to meet together and come to decisions rather than going back and forth. By the time the patient comes in, we have reviewed the data and are ready for that discussion."



Mary R. Kwaan, MD, MPH

A stylized graphic of a human silhouette in black, set against a background of concentric, wavy red lines. The brain and stomach areas are highlighted in a bright pink color. The brain is depicted as a simple, rounded shape at the top of the head. The stomach is a larger, teardrop-shaped area at the bottom, filled with a pattern of small, repeating text characters. A vertical pink line connects the brain to the stomach, representing the esophagus.

# Building an Infrastructure Specifically Focused on DGBI Research and Care

Disorders of gut-brain interaction (DGBI), previously known as functional gastrointestinal disorders, encompass a wide range of conditions characterized by increased visceral sensitivity and alterations in gut motility, immune and mucosal function, and central nervous system processing of visceral information.

The changing terminology for these disorders — which include irritable bowel syndrome (IBS), chronic constipation, chronic abdominal pain, functional diarrhea, functional dyspepsia, and cyclic vomiting syndrome — reflects a greater understanding of their underlying causes. But, although a substantial body of evidence now supports the pathophysiology that the conditions involve alterations in brain-gut interactions, that pathophysiology is multifactorial, and not well understood. As a result, DGBI is challenging to diagnose and treat, notes Andrea S. Shin, MD, MSCR, who recently joined the Vatche and Tamar Manoukian Division of Digestive Diseases faculty as a health sciences associate clinical professor of medicine.

These conditions can be highly debilitating and are extremely prevalent: Collectively, according to epidemiological research, DGBI affects as much as 40% of the world's population and nearly half of all women. Dr. Shin explains that DGBI are symptom-based disorders, and reliable diagnostic tests are largely lacking. “The decision-making on treatment is



Andrea S. Shin, MD, MSCR

not always straightforward,” she says. “What’s most important is to both educate and listen to patients in order to clearly understand their symptoms, how their lives are affected, and the treatment approaches that most interest them.”

For decades, UCLA’s Vatche and Tamar Manoukian Division of Digestive Diseases has been a national leader in treating DGBI. Now part of the new Goodman-Luskin Microbiome Center, the program is a designated Center of Excellence — one of the few in the nation. Most recently, that tradition has been bolstered by the recruitment of Dr. Shin, who focuses on treating patients who suffer from DGBI, as well as running an active clinical research program. “Because these disorders aren’t fully understood, there is a lot of opportunity to investigate everything from pathophysiology and patients’ experiences to new tools and therapies aimed at improving diagnosis and treatment,” Dr. Shin says.

Dr. Shin’s clinical research homes in on the pathophysiology of IBS to provide a foundation for understanding of which treatments are likely to benefit which patients. She has a particular

interest in examining the interaction of diet and the microbiome, and how that relates to IBS symptoms. Her group is investigating how the human microbiome may reveal mechanistic information about individuals with IBS that could be used as a treatment target. Dr. Shin also studies what drives IBS symptoms, as well as patient-reported outcomes and experiences with the health care system.

After spending nearly a decade on the faculty at the Indiana University School of Medicine, Dr. Shin was drawn to UCLA by the opportunity to work with a wide-ranging group of DGBI experts. [UCLA’s DGBI program](#) has increasingly emphasized integrative care — an interdisciplinary approach in which the gastroenterologist works closely with GI dietitians, GI psychologists, and an integrative health nurse practitioner, all of whom collaborate closely while offering the full spectrum of care approaches. “There aren’t many institutions that build an infrastructure specifically focused on treating these disorders,” Dr. Shin says. “If you want to go ‘all in’ on improving the lives of DGBI patients, this is the place to be.”

# New UCLA Goodman-Luskin Microbiome Center Hits the Ground Running

## Barely more than a year after it was launched in early 2023, the [UCLA Goodman-Luskin Microbiome Center](#), based in the Vatche and Tamar Manoukian Division of Digestive Diseases, has hit the ground running.

The center facilitates multidisciplinary collaborations among the wide-ranging experts across the UCLA campus, all designed to investigate the role of the human microbiome in health and disease and to translate those findings into new strategies for health promotion, disease prevention, and treatment. The groundbreaking, interdisciplinary work is supported by seven research cores and one administrative core, which provide shared resources for specialized services that increase the efficiency and cost-effectiveness of the scientific endeavors. The research cores, now operational, include the Biorepository Core, the Clinical Studies and Database Core, the Gnotobiotics Core, the Human Probiotic Core, the Integrative Biostatistics and Bioinformatics Core, the Microbiome Core, and the Neuroimaging Core.

To help jump-start the promising, early-stage microbiome research programs of investigators just entering the field, the Goodman-Luskin Microbiome Center's Seed Funding Program has been established. The program already awarded its first five seed grants, and will soon expand these efforts to include a postdoctoral research fellowship and pilot and feasibility study awards, as well as educational programs in which leaders in the field share their latest insights. All of these activities are aimed at encouraging graduate students, postdoctoral fellows, and early-career faculty to enter the field, engage with the center's core facilities, and work with Goodman-Luskin Microbiome Center mentors.

Given the rapid developments in the field of microbiome and brain-gut microbiome research, opportunities for clinicians and researchers to share information and build relationships

that will facilitate further advances are especially valuable. In 2024, the center inaugurated a monthly seminar series where invited guest speakers, Goodman-Luskin Microbiome Center faculty, and UCLA trainees can present their latest work and discuss evolving areas of interest.

Established by a \$20 million gift from Andrea and Donald Goodman and Renee and Meyer Luskin, the Goodman-Luskin Microbiome Center aims to accelerate progress in the promising area of the human microbiome and the role played by the trillions of microorganisms that reside in the human gut in health and disease. Through this multidisciplinary effort, the center has greatly expanded the breadth of UCLA scientists and clinicians who are taking on the most important challenges in this new frontier of scientific inquiry. The center's research promises to identify new approaches to disease prevention and new treatments for a range of conditions, including inflammatory bowel disease; obesity and eating disorders; neurodevelopmental and neurodegenerative diseases, such as autism, Alzheimer's, and Parkinson's disease; irritable bowel syndrome; and substance use and psychiatric disorders.

The center is directed by Dr. Elaine Y. Hsiao, a leader in the field who was recently named among the world's most influential researchers by the analytics firm Clarivate, based on having authored studies ranking among the top 1% worldwide in scholarly citations. In addition to the important scholarly publications of the center's researchers, their work has recently been highlighted in major news outlets ranging from *NBC News* and *The Today Show* to *Forbes* and *The Washington Post*.

**“The groundbreaking, interdisciplinary work is supported by seven research cores and one administrative core, which provide shared resources for specialized services that increase the efficiency and cost-effectiveness of the scientific endeavors.”**

# High-Fat, Low-Carb Ketogenic Diet Produces Gut Microbiome Changes That May Prevent Seizures



Elaine Y. Hsiao, PhD

The high-fat, low-carbohydrate ketogenic diet is more than just a trendy weight-loss tactic. It has also been known to help control seizures in children with epilepsy, particularly those who don't respond to first-line, anti-seizure medications.

Now, a study by researchers in the laboratory of Elaine Y. Hsiao, PhD, De Logi Associate Professor of Biological Sciences and director of the Goodman-Luskin Microbiome Center, which is based in the Vatche and Tamar Manoukian Division of Digestive Diseases, provides an explanation. The study, published in the journal *Cell Reports*, demonstrates that the changes the keto diet causes in the human gut microbiome can confer protection against seizures in mice.

This understanding of how the function of the microbiome is altered by the diet could aid in the development of new therapeutic approaches that incorporate these beneficial changes while avoiding certain drawbacks of the diet, says Gregory Lum, PhD, the study's lead author and a postdoctoral researcher in Dr. Hsiao's lab.

The ketogenic diet is not recommended as a primary anti-seizure option because patients are often averse to drastic changes in their food intake. Many have trouble adhering to the diet's strict requirements, or tolerating side effects that can include, nausea, constipation, and fatigue.

In the hope of finding new ways to more effectively treat seizures in the approximately one-third of people with

refractory epilepsy who don't respond to existing anti-seizure medications, Dr. Hsiao's group sought to understand the underlying molecular mechanisms behind the diet's alteration of the human gut microbiome.

Previous research conducted by Dr. Hsiao's lab had found that in a mouse model bred to mimic epilepsy, mice fed a ketogenic diet had significantly fewer seizures than mice fed a standard diet. Dr. Lum took that research a step further, studying how the gut microbiome is beneficially altered in children with epilepsy who start ketogenic diet therapy. To that end, he transplanted fecal samples from pediatric epilepsy patients who were on the diet into mice to gauge whether the diet-associated gut microbiota would protect the mice against seizures.

The fecal samples were collected in collaboration with UCLA's Ketogenic Diet Therapy Program from 10 pediatric epilepsy patients who did not respond to anti-seizure medication and were subsequently treated with the ketogenic diet. The samples were taken both before they started the diet and after one month on the diet.

The study found that the mice that received fecal transplants from patients collected after a month on the diet were more resistant to seizures than mice that received pre-ketogenic diet fecal transplants. Importantly, the study also found that in the pediatric patients, the ketogenic diet altered key gut microbiome functions related to fatty acid oxidation and amino acid metabolism — and that these changes were preserved when the fecal matter was transplanted into the mice.

Dr. Lum notes that more research on these changes is needed, but believes the study holds promise as a step toward finding new microbiome-based therapies for pediatric epilepsy patients who do not respond to standard anti-seizure medications. "Narrowing down the functions of the microbes that are beneficial toward seizure protection can potentially lead to new ways to enhance the efficacy of the ketogenic diet or to mimic its beneficial effects," he explains.

**"The high-fat, low-carbohydrate ketogenic diet is more than just a trendy weight-loss tactic."**



# Experiencing Discrimination May Cause Biological Changes That Promote Unhealthy Eating Behaviors, Study Finds



Arpana Gupta, PhD

Experiencing racial or ethnic discrimination can increase a person's risk of obesity through a stress response that disrupts brain-gut communication — changing biological processes in how they process food cues and thereby promoting unhealthy eating behaviors, according to a study led by a member of the Vatche and Tamar Manoukian Division of Digestive Diseases faculty.

These changes appear to increase activation in regions of the brain associated with reward and self-indulgence, which could make individuals exposed to high levels of discrimination more likely to be drawn to “comfort foods” high in sugar and fat, according to the UCLA research team, which was led by Arpana “Annie” Gupta, PhD, co-director of the Goodman-Luskin Microbiome Center and a member of the G. Oppenheimer Center for Neurobiology of Stress and Resilience. The study, published in *Nature Mental Health*, also found that these individuals showed decreased activity in brain areas involved in decision-making and self-control. The findings are based on results of functional MRI brain scans, sophisticated statistical modeling techniques, and analyses of metabolites of the glutamate pathway in the digestive tract.

Racial and ethnic groups that face significant levels of discrimination in the U.S. have higher rates of obesity and the health conditions associated with it, but the factors contributing to these disparities haven't been clear. While previous research has examined issues including genetics, diet, and exercise, few studies have addressed the potential role of discrimination, and this is believed to be the first study providing direct evidence of a possible link between brain-gut interactions and obesity-promoting eating behaviors.

“We examined complex relationships between self-reported discrimination exposure and poor food choices, and we can see these processes lead to increased cravings for unhealthy foods, especially sweet foods, but also manifest as alterations in the bidirectional communication between the brain and the gut microbiome,” says Dr. Gupta, the study's senior author. “Our results show that a person's brain-gut crosstalk may change in response to ongoing experiences of discrimination — affecting food choices, cravings, and brain function, and contributing to alterations in gut chemistry that have been implicated in stress and inflammation.”

The UCLA team analyzed the brain activity and gut compounds of 107 participants from diverse racial and ethnic backgrounds who completed a validated and widely used questionnaire measuring chronic experiences of unfair treatment. Based on their scores, participants were divided into “high discrimination exposure” and “low discrimination exposure” groups. MRI scans were used to evaluate brain responses to pictures of high-calorie sugary and fatty foods, as well as healthier, low-sugar and low-fat foods.

For participants in the high-discrimination exposure group, unhealthy food cues caused greater activation in regions of the brain associated with reward processing, motivation, cravings, and appetite responses. The study found that stress from discrimination experiences altered brain responses in regions involved with self-regulation in response to food cues for unhealthy foods, but not for healthy foods.

Fecal samples were also provided to allow the researchers to study participants' gut microbiome — specifically, changes in 12 glutamate metabolites. Participants in the high-discrimination group showed elevated levels of two glutamate metabolites that have been implicated in inflammatory processes, oxidative stress, and increased risk for developing obesity.

“It appears that in response to stressful discrimination experiences, we seek comfort in food, and increased desire for highly palatable foods such as high-calorie foods and, especially, sweet foods,” Dr. Gupta says of the study findings. “These alterations may ultimately cause people exposed to discrimination to be more vulnerable to obesity and obesity-related disorders.” The study's findings have the potential to assist researchers in developing treatments that target the brain or gut — either by modulating brain changes associated with stress and discrimination exposure, or by targeting the glutamatergic pathways.

# New Clinical Faculty Members

The Vatche and Tamar Manoukian Division of Digestive Diseases at UCLA is a national leader in gastrointestinal care and research with nearly 100 faculty clinicians and scientists in and across UCLA Health locations throughout the greater Los Angeles area.

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## **Ellie Y. Chen, MD | Health Sciences Clinical Instructor of Medicine**



Dr. Chen earned her undergraduate degree in biology with concentration in human nutrition at Cornell University before returning home to complete medical school at University of Wisconsin School of Medicine and Public Health. During medical school, she received the NIH T35 Ruth L. Kirschstein National Research Service Award and studied outcomes of bariatric surgery. She completed her residency in internal medicine at Baylor College of Medicine in Houston, Texas.

Dr. Chen specializes in general gastroenterology with clinical expertise in disorders of the gut-brain interaction (IBS, functional dyspepsia, chronic constipation), motility disorders, esophageal and gastric disorders, celiac disease, colon cancer screening, inflammatory bowel disease, hepatology, colonoscopy, and endoscopy. During her fellowship, Dr. Chen received additional training in motility and disorders of the gut-brain interaction with the American Neurogastroenterology and Motility Society clinical training program.

Dr. Chen is a member of the American College of Gastroenterology, American Gastroenterological Association, and American Neurogastroenterology and Motility Society. She is board certified in gastroenterology and internal medicine.

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## **Vivy T. Cusumano, MD | Health Sciences Clinical Instructor of Medicine**



Dr. Cusumano graduated with honors from University of California, Los Angeles with a bachelor's degree in biology. She earned her medical degree at Albert Einstein College of Medicine, and then completed her internal medicine residency and gastroenterology fellowship at UCLA. She served as chief gastroenterology fellow at UCLA and was awarded the Compassionate Care Award, which honors the graduating fellow who demonstrates exceptional humanistic qualities in caring for their patients. Dr. Cusumano's primary research interests include inflammatory bowel disease and colon cancer screening.

Dr. Cusumano specializes in general gastroenterology with clinical interests that include inflammatory bowel disease, functional bowel disorders/disorders of brain-gut interaction, esophageal and gastric disorders, gastroesophageal reflux, colorectal disorders, and colonoscopy and endoscopy. She is a member of the American Gastroenterology Association, American Society of Gastrointestinal Endoscopy, and the American College of Gastroenterology. Dr. Cusumano is board certified in gastroenterology and internal medicine.

### **Shida Haghighat, MD, MPH | Health Sciences Clinical Instructor of Medicine**

Dr. Haghighat earned her undergraduate degree in biology and international studies with provost honors at University of California, San Diego. She simultaneously obtained her master's degree in public health and her medical degree at University of Miami, where she had the honor of being selected by her classmates as the medical school commencement speaker. She returned home to Los Angeles to complete her internal medicine residency at University of Southern California. Back at the University of Miami, she completed her gastroenterology and hepatology fellowship and received a National Institutes of Health T32 training grant, and conducted research in gastrointestinal cancer disparities.

Dr. Haghighat specializes in general gastroenterology with clinical expertise in gastrointestinal cancer screening and prevention, irritable bowel syndrome and other disorders of brain-gut interaction; inflammatory bowel disease; esophageal and gastric disorders; as well as EGD and colonoscopy.

Dr. Haghighat is an active member of the American Gastroenterology Association and American College of Gastroenterology. She is board certified in gastroenterology and internal medicine.

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### **Niharika Mallepally, MD, MPH | Health Sciences Clinical Instructor of Medicine**

Dr. Mallepally completed her undergraduate and master's degrees in economics at Texas A&M University. She attended medical school at Emory University. Dr. Mallepally then earned a master's in public health at the Harvard T.H. Chan School of Public Health, specializing in health management. She returned to Texas for internal medicine residency at Baylor College of Medicine, and then went on to complete a gastroenterology fellowship at the University of Southern California.

In her practice, Dr. Mallepally focuses on general gastroenterology with clinical expertise in colon cancer screening, esophageal and gastric disorders, irritable bowel syndrome, hepatology, and inflammatory bowel disease, as well as various types of endoscopy including EGD, pH studies, and colonoscopy.

Dr. Mallepally is an active member of the American Gastroenterological Association, American College of Gastroenterology, and the Southern California Society of Gastroenterology. She is board certified in gastroenterology and internal medicine.

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### **Demetrios Stavrakis, MD | Health Sciences Clinical Instructor of Medicine**

Dr. Stavrakis earned his undergraduate degree in molecular, cell and developmental biology at UCLA, graduating magna cum laude with departmental honors. He received his MD from the UC Irvine School of Medicine. During his medical school years, he was active in researching obesity, Crohn's disease and ulcerative colitis. He completed his internal medicine and gastroenterology training at the University of Arizona, where he was the recipient of many house-staff awards and was appointed chief fellow before returning to join the faculty at UCLA.

Dr. Stavrakis' clinical interests include gastrointestinal endoscopy, reflux disease, peptic ulcer disease, celiac disease, motility disorders, functional bowel disorders, inflammatory bowel disease and colorectal cancer screening. He is a member of the American College of Gastroenterology and American Gastroenterological Association and is board certified in gastroenterology and internal medicine.

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## 12th Annual UCLA-Mellinkoff Gastroenterology and Hepatology Symposium

March 15-16

UCLA Meyer and Renee Luskin Conference Center

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This program designed to offer healthcare professionals evidence-based and integrative approaches to treat common GI disorders that can easily be implemented into practice and have significant impact on patient outcomes. An endoscopy forum with video and live cases will also show complex cases and new technology. New to the program is an in-person workshop with visual and interactive methods to teach the process of patient-centered care to improve communication skills, patient-provider relationship, and patient satisfaction. Interactive, case-based presentations and panel discussions by experts in their field will engage attendees and enhance this learning experience.

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