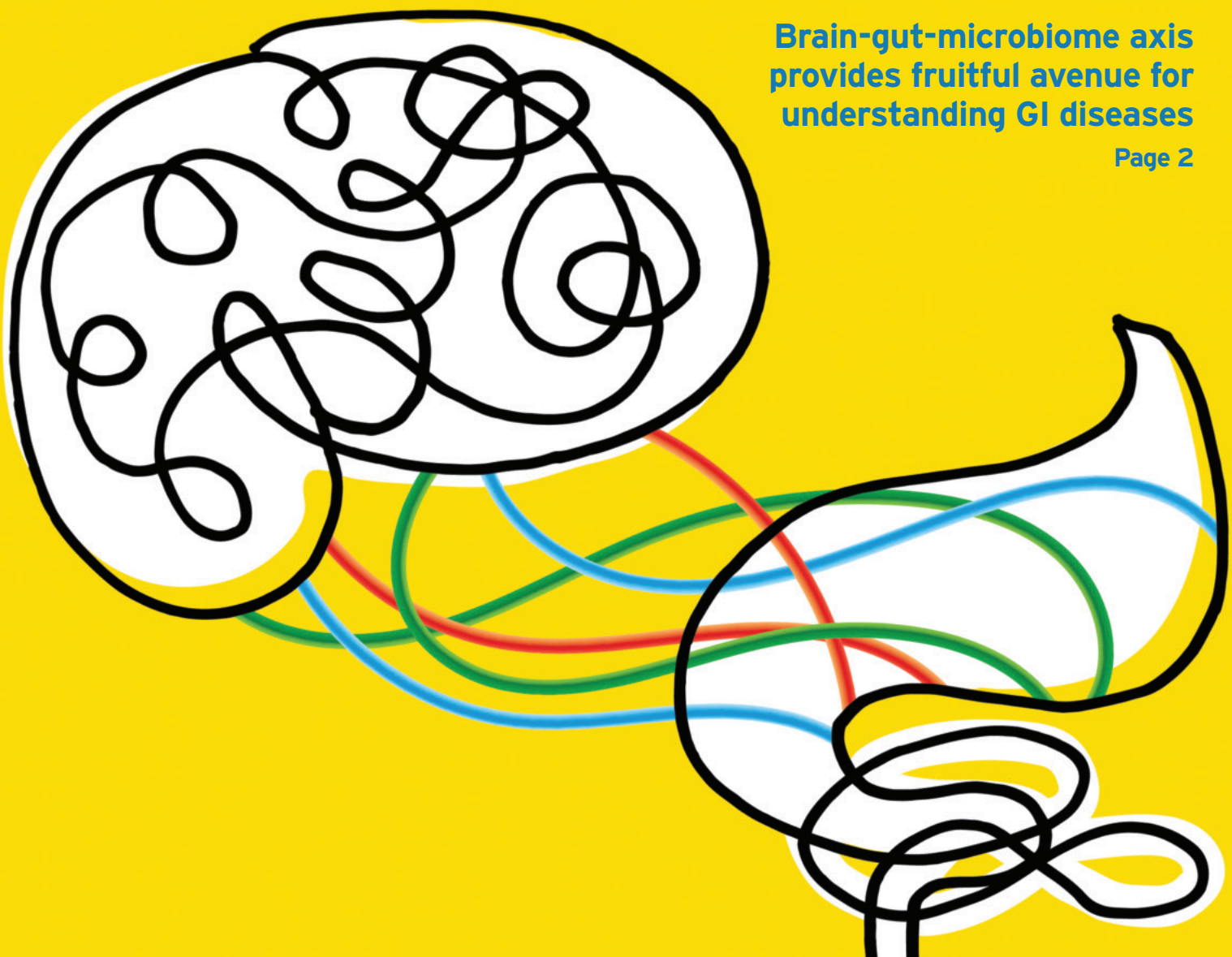


# Beyond the Scope

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



**Brain-gut-microbiome axis provides fruitful avenue for understanding GI diseases**

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**Eric Esrailian, MD, MPH**

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## Going *Beyond the Scope*

We know this issue of *Beyond the Scope* arrives during an unprecedented and difficult time for the world. The COVID-19 pandemic has been devastating on many levels, but we are looking forward to the potential of better days ahead for all of you. We are honored the UCLA Vatche and Tamar Manoukian Division of Digestive Diseases has again been recognized by *U.S. News & World Report* as being among the top five gastroenterology and GI surgery programs in the nation in the publication's 2020-21 "Best Hospitals" survey. However, as the article on the next page makes clear, our unique mission as part of a public university – the #1-ranked public university in the nation, also according to *U.S. News* – is what sets us apart. Our division faculty, fellows, and staff proudly participate in the larger UCLA mission to serve the public, advance knowledge, prepare leaders, and address issues of access and equity, to name a few of the ways this special university contributes to a better society.

This issue of *Beyond the Scope* highlights some of the many ways this mission drives state-of-the-art research, patient care, and training of the next generation of leaders in the field of digestive diseases. The exciting work featured includes our faculty research at the forefront of understanding the brain-gut-microbiome axis and its implications for GI and other conditions (page 2); the rapid progress of our investigators in pinpointing the roles played by stress and diet in inflammatory bowel disease as we move closer to precision-medicine treatment approaches (page 6); and the ambitious UCLA-led effort to provide the first-ever detailed structural and functional map of the colonic nervous system, which is expected to pave the way for entirely new therapies (page 8). At a new UCLA Health clinic for treating the GI symptoms of patients with Parkinson's disease (page 4), two of our physician-scientists are improving patients' quality of life while studying important clues about the origins of the disorder. This issue also features one of the cornerstones of our training program, the T32 grant from the National Institutes of Health (page 12); and introduces the newest members of our faculty (beginning on page 14), including graduates of our training program. You will also find coverage of the prestigious awards bestowed on two of our faculty by the American Gastroenterology Association for education and mentorship (page 11) – shining examples of the way in which expertise is shared and passed down from one generation to the next in our division.

All of this dynamic work is possible not only because of the talented and dedicated individuals who make up our division, but also as a result of their participation in a much broader effort on behalf of the nation's top public university. Working closely with UCLA Health physicians and scientists helps us to deliver the highest-quality care, whether it is in Westwood, Santa Monica, or one of our many affiliated hospitals and clinics throughout Southern California. Partnerships with the VA and L.A. County hospitals and clinics allow our faculty and fellows the privilege of caring for underserved populations. By collaborating on projects with world-renowned experts and schools from across the UCLA campus, in disciplines ranging from public health to engineering to law, we are striving to expand our impact beyond the traditional boundaries of a subspecialty of medicine. We hope you enjoy learning about these efforts, and we look forward to working with you in the years to come.

# UCLA chosen top public university in U.S.

## A testament to key role of division, UCLA Health in promoting public good

### For the fourth consecutive year, UCLA stands atop

the list of the nation's most outstanding public universities in *U.S. News & World Report's* annual "Best Colleges" survey – a recognition, as noted by Chancellor Gene Block, of the preeminence of the university's societal contributions through its mission of education, research, and service, and UCLA's commitment to advancing access, opportunity, and diversity. The prestigious designation also sets UCLA Health and the Vatche and Tamar Manoukian Division of Digestive Diseases apart as *U.S. News'* highest-ranked gastroenterology and GI surgery program for a public university.

"A top public research university such as UCLA has a special obligation to serve the larger population in ways that include educating the public, conducting important research and disseminating knowledge, driving innovation, and addressing societal issues," says Eric Esrailian, MD, MPH, chief of the division. "That role affects the day-to-day activities of all of us within UCLA Health,

and our division in particular, and we take our responsibility to contribute to the fulfillment of UCLA's mission very seriously."

UCLA fulfills its obligations as a public research university in ways that range from its commitment to making higher education accessible and affordable for families from all backgrounds to its civic engagement and partnerships that create jobs, inform public policy, and nurture new generations of private- and public-sector leaders, Dr. Esrailian notes. UCLA boasts 15 Nobel Laureates among its faculty and alumni – from Ralph Bunche, the first African American awarded the Nobel Peace Prize in 1950, to Andrea Ghez, who shared the Nobel Prize in Physics in 2020 as only the fourth woman to win physics' top honor. The campus has played a vital role in the civil rights movement for decades, and is the alma mater of countless icons of the athletic, entertainment, business, tech, and political worlds.

As a fundamental part of the university and a major source of support towards its mission, UCLA Health bears similar responsibilities for serving the public good, Dr. Esrailian explains. Like all

UCLA Health units, the Vatche and Tamar Manoukian Division of Digestive Diseases is committed to supporting vulnerable patient populations and promoting health equity in areas such as colorectal cancer screening, where there are significant disparities. Trainees complete rotations at affiliated institutions with diverse and vulnerable patient populations, from the Greater Los Angeles VA Medical Center to county-run hospitals and clinics. Division faculty are instrumental contributors to the UCLA Value-Based Care Consortium, a multidisciplinary research effort to inform strategies for improving the quality and outcomes of care while reducing cost; and, most recently, to UCLA Health's leadership roles in everything from fighting the COVID-19 pandemic to studying health equity.

"UCLA's continuing designation as the nation's top public university is a testament to the legacy of countless students, faculty, and dedicated staff who have earned that distinction through their hard work and excellence," Dr. Esrailian says. "Our division is proud to be part of that legacy, and we embrace our role in UCLA's contributions to a better society."



## Brain-gut-microbiome axis provides fruitful avenue for understanding GI diseases

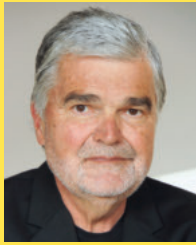
It's arguably the hottest area of investigation in biomedical science. Thanks to the power of modern research and computational tools, it has become apparent in recent years that the microbiome – the approximately 100 trillion microbes residing within the body – figures prominently in human health and disease.

Emeran A. Mayer, MD, a distinguished research professor of medicine, physiology, and psychology and director of the G. Oppenheimer Center for Neurobiology of Stress and Resilience (CNSR) in the Vatche and Tamar Manoukian Division of Digestive Diseases at UCLA, has referred to the microbiome as “a hidden organ, larger than any other in the body in terms of cell numbers.” One of the reasons the study of this hidden organ is so intriguing is the notion that the microbiome can adapt and be modified much more easily than human genes to dietary and environmental perturbations. “We’re still just scratching at the surface, but the field is moving extremely fast,” says Dr. Mayer, a world leader in this field.

Of particular interest to Dr. Mayer and his colleagues at the CNSR is the brain-gut-microbiome axis – the back-and-forth signaling between cells in the brain and gut, and how they're modulated by the microbiota, with implications for a host of GI, neurological, and psychiatric conditions. Dr. Mayer's team has developed a large database of patients with irritable bowel syndrome (IBS), inflammatory bowel diseases (IBD) and other chronic conditions, as well as healthy subjects; the database includes brain-imaging, microbiome, and behavioral data, and is using a “multi-omics” approach to integrate the data from the gut, microbiome, sympathetic nervous system, and brain in order to better understand how they interact, and what that means clinically. “We have learned that these are bi-directional interactions from the brain to the microbiome and back,” Dr. Mayer explains. “It's a holistic view that requires systems biology and bioinformatics approaches.”

In May 2020, the CNSR began a third five-year renewal of its Specialized Center of Research Excellence (SCORE) National Institutes of Health grant to study “Sex-Related Differences in Brain-Gut Microbiome Interactions in Irritable Bowel Syndrome.” Led by Dr. Mayer and Lin Chang, MD, co-director of the CNSR and professor and vice chief of the UCLA Vatche and Tamar Manoukian Division of Digestive Diseases, the SCORE grant focuses on the role of sex hormones in the modulation of brain-gut-microbiome interactions in IBS and chronic constipation. “IBS occurs more commonly in women than in men, and women's symptoms tend to fluctuate with changes in their estrogen levels,” Dr. Chang notes. “We think that sex hormone levels play an important role in the female disposition to IBS and chronic constipation, as well as to changes in their symptoms.”

Dr. Chang and Arpana “Annie” Gupta, PhD, co-lead one of the SCORE grant projects, which is studying the brain-gut microbiome interactions that mediate IBS in women, with a focus on how the processes change during the menstrual cycle and post-menopause – particularly at times when women's estrogen levels decline, and IBS



Emeran A. Mayer, MD



Lin Chang, MD



Arpana Gupta, PhD



Jennifer Labus, PhD



Jonathan P. Jacobs, MD, PhD



Jenny Sauk, MD

symptoms tend to become more severe. A separate SCORE project, co-led by Jennifer Labus, PhD, an associate professor and CNSR investigator, is examining sex differences by comparing brain networks made up of cortical, subcortical and brain-stem regions of men and women with IBS, as well as of healthy men and women.

A third SCORE grant project follows up on exciting results from a recently concluded study by Dr. Mayer, Dr. Gupta, and Jonathan P. Jacobs, MD, PhD, an assistant professor in the division, in conjunction with Jeffrey Lackner, PsyD, and colleagues at the University of Buffalo. In a small clinical trial, they found that certain microbiome features were predictive of a positive response to cognitive behavioral therapy (CBT) for IBS patients who had been refractory to other therapeutic approaches; moreover, the patients who responded positively to CBT also experienced changes in their microbiome and brain as a result of the therapy. "This suggests that signals from gut bacteria to the brain can influence whether an IBS patient benefits from CBT, and that when CBT works, the resulting changes in the brain affect the gut enough to change the microbiome," Dr. Jacobs says. Now, as part of the SCORE grant, Dr. Mayer is heading a larger study examining the role of sex-related differences in these CBT outcomes.

Dr. Jacobs is also studying brain-gut-microbiome interactions in inflammatory bowel disease. Research he has conducted with Dr. Mayer and Jenny Sauk, MD, clinical director of the UCLA

Center for Inflammatory Bowel Diseases, is following a group of ulcerative colitis patients who are in clinical remission. The researchers have performed detailed assessments of the brain-gut-microbiome axis in these patients through brain imaging, sequencing of their gut microbiome, measurements of bacterial metabolites in their stool and blood, and assessments of stress reactivity, using psychological questionnaires and laboratory tests.

"Through these multiple modalities, we are able to dissect out specific aspects of the brain-gut-microbiome axis to determine how they're related to disease activity in these patients over time," Dr. Jacobs explains of the study, which has been awarded to Drs. Mayer and Sauk by the Crohn's and Colitis Foundation for the last three years, and is likely to be renewed for another cycle. The study has found that patients with greater stress reactivity, are more likely to experience flares over time, and Dr. Jacobs' lab has identified a specific microbial signature that appears to be predictive of these patients' likelihood of flaring. (For more on the study, see page 6.)

Excitement over the potential to modify the microbiome for therapeutic purposes is what makes the obesity-related research of Dr. Gupta of special interest. Dr. Gupta, assistant professor in the division and director of the Neuroimaging Core at CNSR, is applying systems biology research methods in an effort to gain a comprehensive understanding of the pathophysiology underlying human obesity and metabolic syndrome. She is interested in how

brain-gut communications are affected by early adversity – including physical, emotional, sexual, and general trauma – and by psychological stresses in adulthood, as well as the potential role of protective factors such as resilience and exercise. Using advanced automated and mathematical analytic techniques, her group is integrating information from multiple neuroimaging sources, genetic profiles, microbiome markers, and both behavioral and adverse environmental factors to identify key obesity-related biomarkers. Dr. Gupta's goal is to develop a comprehensive model that would use these biomarkers to identify individuals at increased risk of obesity as a result of bio-psychosocial factors, which could lay the groundwork for more effective, targeted, and personalized obesity therapies. For example, her lab has identified race- and sex-related differences in eating patterns that are not only dependent on specific brain-gut-microbiome signatures, but are shaped by environmental influences such as discrimination, childhood adversity or stress.

"Obesity offers a perfect model to study brain-gut microbiome interactions because it's easily modifiable – for instance, through easy-to-implement changes in diet, we can see how the microbiome shifts to signal the brain and influence behavior and clinical symptoms," Dr. Gupta says. "We suspect that by using obesity as a model to better understand what makes for a healthy or unhealthy microbiome, we will gain insights that may apply to other diseases as well."

# New clinic treats gastrointestinal manifestations of Parkinson's disease while obtaining clues about the disease's pathogenesis



At a newly opened clinic within the integrated UCLA Health system for treating the GI symptoms of patients with Parkinson's disease, two clinician-scientist members of the UCLA Vatche & Tamar Manoukian Division of Digestive Diseases faculty are gleaning important clues about the early manifestations of the neurodegenerative disease at the same time that they are applying their expertise as gastroenterologists to improve patients' quality of life.

It is well established that gastrointestinal motor function can be negatively altered by Parkinson's disease, and an emerging body of research indicates that the disease may start in the gastrointestinal tract before later spreading to the brain. But the GI tract's role in the pathogenesis of Parkinson's disease, and the mechanisms by which Parkinson's disease alters gastrointestinal motor function, are not yet fully described.

Wael El-Nachef, MD, PhD, and Elizabeth Videlock, MD, PhD, assistant clinical professors in the division, note that most patients with Parkinson's disease experience GI symptoms such as constipation and bloating, and that in many cases these symptoms precede

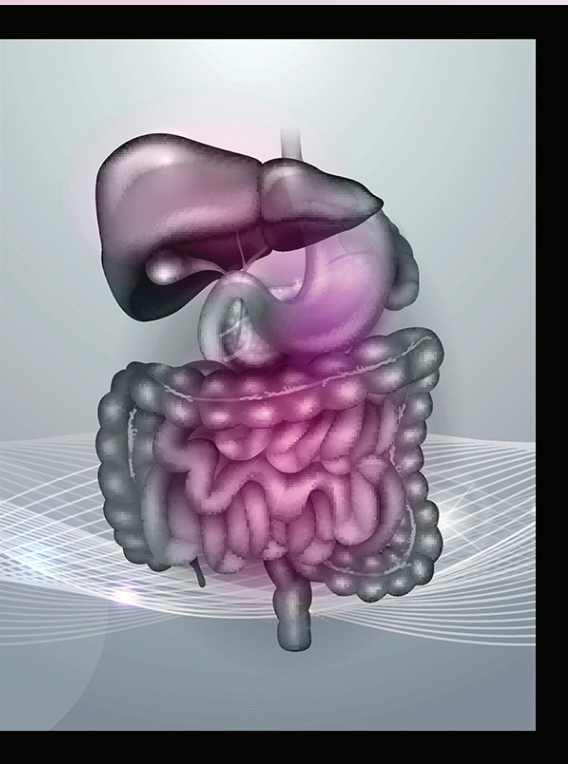
the diagnosis of Parkinson's by several years. "This has long been known, yet the reasons weren't well understood," Dr. El-Nachef says. "But there is growing evidence to suggest that the same process involved in the central nervous system is also involved in the enteric nervous system, through the aggregation of the alpha synuclein protein to form Lewy bodies. And some studies indicate that the enteric nervous system is involved first."

There is considerable interest in examining this potential pathogenesis for multiple reasons, Drs. El-Nachef and Videlock explain. The greater accessibility of the intestine vs. the brain could facilitate obtaining biopsy samples in patients at risk for Parkinson's disease, enabling earlier identification of the disease and potentially leading to the development of drugs to prevent its progression to the brain.

"Parkinson's disease progresses slowly, and by the time symptoms occur, it's usually at the end of the pathologic process," Dr. Videlock says. "Currently we can diagnose patients only once the neurons have died, but if we could identify patients earlier, we might

be able to prevent the neurons from dying and the symptoms we think of as Parkinson's disease from developing. We also know from population studies that constipation is a risk factor, and from talking to Parkinson's disease patients, many notice that those symptoms started as long as 10 years prior to their diagnosis. If we can identify that early process, it could lead to more effective therapy."

In the new clinic for Parkinson's patients with GI issues, Drs. Videlock and El-Nachef, along with Jeffrey L. Conklin, MD, a professor in the division and medical director of the UCLA Robert G. Kardashian Center for Esophageal Health and UCLA GI Motility Program, see patients with symptoms that include bloating and difficulty swallowing, as well as nutritional deficiencies. But the vast majority are experiencing unresolved constipation. "Symptoms such as constipation are difficult to treat in this population," Dr. Videlock says. "Our expertise as gastroenterologists is particularly important because we have more familiarity with the different constipation treatments, and we're also learning what works best in this population."



Adds Dr. El-Nachef: “Many of these patients don’t fit the textbook description of the symptom they’re experiencing, and so you really have to think outside the box. That’s where our focus on neuro-gastroenterology can be quite helpful.” The physicians at the Parkinson’s GI clinic work in close consultation with leading neurologists at UCLA, including Jeff Bronstein, MD, PhD, director of the UCLA Movement Disorders Program, in ensuring that the medications they prescribe for GI symptoms are optimal in the context of the patient’s disease and the other drugs they are taking.

Dr. Videlock notes that improving patients’ gut function is important not just for the quality-of-life benefits that come from alleviating their GI symptoms. “We know that addressing gut symptoms improves the efficacy of the Parkinson’s medications,” she says. “If you have slow gut motor function, with delays in the emptying of your stomach, you don’t get the full effect of the medicine. Studies have shown that the bacterial overgrowth that can occur if the gut moves too slowly can metabolize the medication. So by

improving GI symptoms, we can also improve Parkinson’s symptoms.”

In the lab, Dr. El-Nachef is working with Dr. Bronstein to study the involvement of the intestinal nervous system in a zebrafish model of Parkinson’s disease. “One of our goals in this research is to assess whether we see a loss of neurons in the intestine, what the timing of that is, and how it tracks with the development of motor symptoms in this model,” Dr. El-Nachef says.

Dr. Videlock’s laboratory research, in collaboration with Ming Guo, MD, PhD, a professor of neurology and molecular & medical pharmacology at UCLA, examines the role of intestinal inflammation in the development of Parkinson’s disease in mouse and human cellular models. “At UCLA we have research covering all of the integrated components of the gut in Parkinson’s disease, including the nerves, the gut microbiome and, in my case, the lining of the gut and the integrity of the barrier,” Dr. Videlock notes. “Parkinson’s patients have increased levels of cytokines, which are a sign of inflammation. And in some animal studies, gut inflammation can be a trigger for genetic forms of the disease.”

In the clinic, Drs. Videlock and El-Nachef are obtaining important insights about the history of their

patients’ symptoms that is helping to inform their research. “We would like to know more about the characteristics of constipation onset that might point to the possibility that a patient is at risk for developing Parkinson’s disease,” Dr. Videlock says. “What are the clues that this might be different from the normal variant of constipation? Does it usually happen suddenly or gradually? Is there a symptom cluster that might be indicative?”

At the same time, they are using systematic diagnostic and therapeutic approaches to improve patients’ quality of life. The clinic’s providers work closely with Dr. Bronstein to explore relationships between the neurological and gastrointestinal aspects of the disease. Dedicated GI dietitians work to improve the patients’ nutritional state, and UCLA speech pathologists diagnose the swallowing problems associated with Parkinson’s disease.

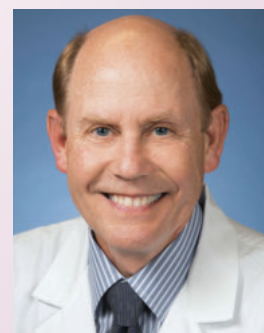
“We’re able to bring a different perspective to these patients and the treatment of their GI manifestations,” Dr. El-Nachef says. “And we believe that having this cohort of patients in our clinic will facilitate new clinical and translational research projects that will help bring the work we are doing in the laboratory to fruition.”



Wael El-Nachef, MD, PhD



Elizabeth Videlock, MD, PhD



Jeffrey L. Conklin, MD



## IBD research probes the role of stress and diet, moves toward precision-medicine approaches

For many years, the field of inflammatory bowel disease (IBD) research has been almost entirely focused on genetic and immune-system studies. But that has begun to shift. The Crohn's and Colitis Foundation (CCF), a nonprofit organization dedicated to finding cures for Crohn's disease and ulcerative colitis and an important IBD research funder, has initiated a process of supporting more investigations into environmental triggers. "The insights we have gained on the role of genetics and the immune system in IBD over the last decade have been significant, but are not enough to explain why someone with genetic vulnerability gets the disease, why it's more severe in some people, and why some experience flares while others stay in long-term remission," says Emeran A. Mayer, MD, research professor of distinction of medicine, physiology, and psychology and director of the G. Oppenheimer Center for Neurobiology of Stress and Resilience (CNSR) in the Vatche and Tamar Manoukian Division of Digestive Diseases at UCLA. "As a result, through a process of meetings among experts in the field, the foundation has identified diet and psychological stress as priority areas of study."

The CNSR was the first beneficiary of a grant under this newly established priority for "Brain-Gut-Microbiome Signatures of Stress-Related Inflammatory Bowel Disease Symptom Flares in Ulcerative Colitis Patients." The three-year longitudinal study, which is nearing its conclusion, is co-led by Dr. Mayer along with Jenny Sauk, MD, clinical director of the UCLA Center for Inflammatory Bowel Diseases; and Jonathan P. Jacobs, MD, PhD, assistant professor in the division. It has followed 112 patients with ulcerative colitis in clinical remission who provide quarterly blood and stool samples, fill out questionnaires on their behavioral assessments and disease activity, and undergo autonomic nervous system testing and brain imaging. The goal is to determine the impact of psychological stress on symptom flares, and to identify brain and microbiome changes associated with these flares.

Although the study is not yet completed, an interim analysis suggests that patients with higher stress reactivity report significantly more symptom flares than those with lower stress perception – and that members of the stress-hyperreactive group show

brain and microbiome features that distinguish them from the other study participants. "We know that other studies have found this association between higher perceived stress and symptom flares," Dr. Sauk says. "Now, we're trying to understand if there are objective biomarkers that would enable us to detect patients with higher stress reactivity, who might be more amenable to mind-body types of interventions or brain-targeted therapies to decrease symptom flares and improve their quality of life."

Drs. Mayer and Sauk note that many IBD patients are interested in mind-body approaches such as cognitive behavioral therapy. "In interviewing study participants, I was amazed at the stories they told about the role of psychological stressors in either the initial onset of the disease or their flares, but for many years this wasn't a topic of interest to IBD clinicians and scientists," says Dr. Mayer, a pioneer in research into the pathophysiology of how stress affects GI function. "Studies such as ours are leading to a paradigm shift, so that in the future if a patient is having symptom flares despite being on traditional treatment, rather than automatically





increasing the medication dose we might decide that if this is a stress-hyperreactive patient, we add a non-medical therapy to the regimen.” The CCF has already asked the UCLA team to submit a request for an additional three years of funding to delve further into the mechanisms underlying how the brain and sympathetic nervous system affect disease activity.

The CCF has also awarded funding to Berkeley Limketkai, MD, PhD, associate clinical professor of medicine and director of clinical research for the UCLA Center for Inflammatory Bowel Diseases, to study how nutrition influences IBD activity. A recently launched clinical trial will test a UCLA-designed diet for Crohn’s disease to determine its impact on symptoms, inflammation, the immune system, gut bacteria, and metabolites. “We are interested in understanding how specific food components influence those profiles,” Dr. Limketkai explains. “This knowledge would help us work

toward the goal of ‘precision nutrition.’ Not all diets work equally for everyone, so we still need to tease apart the clinical and genetic characteristics that drive one’s response to different food components in the context of IBD.”

Dr. Limketkai has also begun a study of the impact of COVID-19 on IBD patients’ risk perceptions. “Patients with IBD are often on immunosuppressive therapies. As such, during the current pandemic, they may be more fearful and anxious, which can affect their medical decision-making – such as whether they undergo tests, initiate certain medications, or even continue with their current immunosuppressants,” Dr. Limketkai explains. “We want to gain insights into how large of a problem this is, what fears our IBD patients might have, and how their decision-making is altered in a way that could influence their overall care, so that we can better address these issues.”

The ability to individualize treatment for IBD patients is becoming more possible thanks to research that is shedding light on the pathophysiology of the disease. Charalabos “Harry” Pothoulakis, MD, director of basic research for the UCLA Center for Inflammatory Bowel Diseases, has led an effort that has resulted in more than 160 published manuscripts since he was recruited to UCLA in 2007. Dr. Pothoulakis is also director of the Center for Systems Biomedicine, established in 2012 as a multidisciplinary effort to bring robotics and high-throughput systems to the study of complex disease processes. The center’s powerful research capabilities have been put to use by UCLA’s COVID-19 task force since the beginning of the pandemic,

with Dr. Pothoulakis’ group using its techniques to dramatically expand UCLA’s COVID-19 PCR and antibody testing capacity.

The IBD research of Dr. Pothoulakis and his colleagues has focused on identifying the role of neuropeptides involved in the inflammatory response; more recently, they have turned their attention to mechanisms involved in neuropeptide-associated epigenetic modulation of IBD. Dr. Pothoulakis’ group has published pivotal studies describing the role of microRNAs (small RNA molecules capable of regulating the function of multiple genes) in IBD, while developing strategies to translate those observations to the clinic.

“Our overarching goal is not only to conduct basic research to understand the disease process, but also to translate this research in a way that can be used directly to benefit patients with IBD,” Dr. Pothoulakis explains. “One of the ways we’re doing that is to develop novel biomarkers that can be used for clinical research by our IBD center to monitor activity following IBD therapy.”

Dr. Sauk notes that such efforts are paving the way for a precision-medicine approach to IBD diagnosis and treatment. “IBD is quite heterogeneous – it is really an umbrella for many disease processes – and as a result, we often have a difficult time knowing the right course of therapy for an individual patient,” she says. “Through the many translational research efforts at UCLA, we are moving toward a better understanding of each patient’s disease and how it can most effectively be treated.”



Emeran A. Mayer, MD



Jenny Sauk, MD



Jonathan P. Jacobs, MD, PhD



Berkeley Limketkai, MD, PhD



Harry Pothoulakis, MD



# UCLA-led team receives new SPARC funding for structural and functional mapping of the colonic nervous system

**A multidisciplinary, multi-institutional UCLA-led effort to provide the first detailed structural and functional mapping of the intrinsic and extrinsic innervation of the colon in humans and a porcine model has received funding for the second phase of its ambitious undertaking. The additional funding for SPARC (Stimulating Peripheral Activity to Relieve Conditions): Comprehensive Structural and Functional Mapping of the Mammalian Colonic Nervous System will allow the team led by Yvette Taché, PhD, distinguished research professor in the Vatche and Tamar Manoukian Division of Digestive Diseases at UCLA, to begin exploring important questions of clinical relevance as it builds on the groundwork it has laid since the research began in 2017.**

“When we have finished, we will have a comprehensive understanding of the innervation of the colon, and by working with three species – a rodent model as well as a porcine model and humans – we will be able to learn a great deal about the neuroanatomy that applies to human gastrointestinal pathophysiology and human colonic tissues,” Dr. Taché says. “As we build our understanding of colon innervation, learning about the similarities and differences between mouse and pig innervation as compared with the human colon will guide us in establishing experimental models that will have translational value for neuromodulation approaches.”

The UCLA-led SPARC consortium includes experts from three UCLA departments, as well as investigators from four other American, Australian and European universities. It is part of a larger program in which the NIH is funding multiple consortiums to map the body’s electrical wiring and develop approaches that will allow for the therapeutic stimulation of peripheral nerves. In the case of the colon, knowledge of the nerve circuitries and activities could facilitate targeted electroceutical treatments for intractable GI conditions. Dr. Taché notes that in recent years, the power of the brain-gut connection – including the role of the nervous system in regulating colonic function – has become increasingly clear, but previously the data on the structure and function of the colonic nervous system could be obtained mainly in small-animal studies. That has changed with the advent of cutting-edge research tools such as three-dimensional mapping, viral tracing, and advanced neuroimaging.

The additional funding supports the UCLA-led SPARC program’s continuing research on the neuroanatomical and functional mapping of porcine and human colons, both under healthy conditions and in subjects with irritable bowel syndrome (IBS) and opioid-induced chronic constipation. “Both IBS and chronic constipation are major problems affecting a large number of people in this country,” says Million Mulugeta, DVM, PhD, a professor in the division and co-director of the SPARC grant. “And we believe that down the road, this work will have implications for a number of other intractable diseases involving the gut.”

He explains that the SPARC’s contribution to advancing the science in these areas is threefold: providing a wealth of foundational data on the autonomic neurocircuitry of the peripheral organs, such as the colon; contributing to the refining of existing technologies; and developing new bioelectronic technologies that can be used by future translational researchers. “We are contributing to a data repository so that, moving forward, there can be predictive output on what happens when certain nerves or cells are electroceutically modulated,” Dr. Mulugeta says. (Story continued on page 10)

(Cont'd from page 9) Dr. Mulugeta, an expert in gut motility, also leads a team with a project in the new phase of SPARC that is using the porcine model to better understand which nerves and what types of stimulation modulate colon motility in an effort to find new ways to treat constipation induced by opioids. The motility team has experts including Muriel Larauche, PhD, associate professor in the division; Wentai Lui, PhD, distinguished professor in the UCLA Department of Bioengineering; and James Dunn, MD, PhD, professor in the Department of Surgery at Stanford University. "For the last three years we have been studying these questions under conditions of anesthesia, but we are now moving closer to human conditions with a model of high translational value, an awake porcine model, to tease out effective neuromodulation modalities for the treatment of refractory chronic constipation," Dr. Mulugeta says.

A team headed by Catia Sternini, MD, a professor in the division and the Department of Neurobiology and director of the Imaging Core of the UCLA Digestive Diseases Research Center, has conducted research during the previous SPARC phase using state-of-the-art high resolution imaging with multiple labeling immunohistochemistry that has found the porcine to be an effective model for studying neuronal innervation in humans, based on similar physiology and comparable morphology of the enteric neurons innervating the colon. For the second phase of SPARC, Dr. Sternini leads a study focusing on the neuronal circuitry of patients with opioid-induced constipation in collaboration with Roberto De Giorgio, MD, PhD, a professor of medicine and gastroenterology from the University of Ferrara, Italy. "We know that opioids are important for pain control, but in the gut these drugs act on molecules found in neurons and immune cells and chronic use induces constipation," Dr. Sternini notes. "To get an analgesic effect requires increased doses of the drug, and those increased doses make the condition in the gut more severe. Unlike in the brain, these neurons in the gut don't become more tolerant, so the more the drugs are used, the more the neurons in the gut block motility and secretion, increasing the constipation."

Not all patients experience the same level of constipation from opioid use, Dr. Sternini points out. Her team is investigating how specific neuronal receptors change in patients with opioid-induced constipation and what explains the differences in outcomes – findings that could point the way toward either

targeted neuromodulation therapies or the development of approaches that could be used to treat these patients in a new, more effective way.

For the new SPARC grant, the UCLA team has added a clinically focused researcher, Lin Chang, MD, professor and vice chief of the division and co-director of the G. Oppenheimer Center for Neurobiology of Stress and Resilience. Dr. Chang heads a project focusing on patients with IBS. One of the most common GI disorders, IBS is characterized by abdominal pain and diarrhea and/or constipation, despite the bowel looking normal. Dr. Chang's study will take advantage of a breakthrough technique known as CLARITY developed by Pu-Qing Yuan, PhD, a researcher and a SPARC co-investigator in Dr. Taché's lab. He led a team that traced the nerve fibers using CLARITY/3D imaging and computationally quantitated their densities in 3D contours of the human colon, findings recently published in *Neurogastroenterology and Motility*. This is opening up a new avenue for assessing the structure-function relationships and pathological alterations in colonic diseases.

"Past studies in which we and other groups have taken biopsies of the mucosa of the colon have suggested that there are alterations in neuronal signaling and immune function in many IBS patients, but there has been limited value in using the information from these biopsies as a biomarker to diagnose IBS or predict treatment response," Dr. Chang says. "With the CLARITY technique, we can look at spatial relationships between nerves and immune cells." Dr. Chang's group will use CLARITY to compare biopsies of the colon in IBS patients and healthy controls – broken down by gender and IBS subtype – to better understand the role neuromodulation can play and potentially identify novel biomarkers.

CLARITY is one example of new state-of-the art technologies and deeper perspectives that are emerging out of the SPARC's. "Besides the specific scientific questions we are pursuing, this is expanding our future research capacity through the development of new technologies and training of new investigators, and it is leading to many new research collaborations beyond the SPARC," Dr. Taché says. "It's very exciting to be part of a team that is involved with big science as well as with clinicians, all working together as we push forward in this new frontier."



Yvette Taché, PhD



Million Mulugeta, DVM, PhD



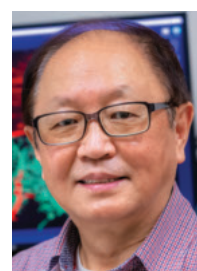
Muriel Larauche, PhD



Catia Sternini, MD



Lin Chang, MD



Pu-Qing Yuan, PhD

# AWARDS AND ACHIEVEMENTS

Three of the UCLA Vatche and Tamar Manoukian Division of Digestive Diseases' most distinguished faculty members were recently recognized for their contributions in mentorship and education.

## Dr. Lin Chang

### 2021 AGA Distinguished Educator Award

Lin Chang, MD, professor and vice-chief of the division, earned the American Gastroenterology Association (AGA) 2021 Distinguished Educator Award – an honor for which



Dr. Chang, program director of the UCLA GI Fellowship, was nominated by Dr. Eric Esrailian, chief of the division, and past and current fellows who have trained under her leadership, calling her “a prime example of what a distinguished educator should aspire to.”

As director of UCLA's GI fellowship program, one of the nation's largest, for the last eight years, Dr. Chang has fostered a culture that has celebrated each fellow's individual strengths while empowering them to pursue their own academic interests and goals. She has also contributed to education on a national and international level, including developing curriculum for gastroenterologists as a former director of the AGA postgraduate course; organizing multiple regional and national conferences; and delivering more than 500 lectures locally, nationally, and internationally as a leading expert in the field of IBS and other common brain-gut disorders.

“Education and training are among the most important responsibilities I have had in my career,” says Dr. Chang, a previous recipient of the AGA Distinguished Clinician Award. “I specialize in common GI conditions, such as IBS, that are not well understood and can be challenging to manage, so if I can educate providers in ways that allow them to help their patients, it means that education can reach many more people than the ones we are directly educating and that is gratifying. To be nominated by people I've trained who feel that I have had a positive impact on their career development is very rewarding.”

## Dr. Vay Liang W. (Bill) Go

### 2021 AGA Distinguished Mentor Award

Over the course of a career spanning five decades in research, education, administration, and public service in gastroenterology at the Mayo Clinic Rochester, National



Institutes of Health, and UCLA, Vay Liang W. (Bill) Go, MD, has trained and mentored more than 90 fellows, MDs, and PhDs in the fields of gastroenterology and pancreatology. The fact that so many of these mentees went on to prestigious leadership roles throughout the U.S. and abroad – in many cases becoming prolific mentors in their own right – has led colleagues to call Dr. Go the “mentor of mentors.”

In January 2021, Dr. Go, a distinguished professor in the UCLA Vatche and Tamar Manoukian Division of Digestive Diseases and former executive chair of the Department of Medicine at the David Geffen School of Medicine at UCLA, received the 2021 Distinguished Mentor Award from the American Gastroenterology Association (AGA), a year after winning the AGA Pancreas Section Research Mentor Award.

“It is an honor to be able to teach, guide, and develop careers to the fullest extent, and to see so many of these individuals become national leaders,” says Dr. Go, who is currently the co-director of the UCLA Agi Hirschberg Center for Pancreatic Diseases and co-founder of the UCLA Center for Human Nutrition. “This award is really the accomplishment of those mentees. It is their work that I am getting recognized for.”

Dr. Go says he has given all of his mentees two simple pieces of advice – the same advice that he took away from his own mentors: “Be yourself, and focus on what you can accomplish.”

## Dr. Yvette Taché

### ANMS Distinguished Scientist Award for Women in Neurogastroenterology

Yvette Taché, PhD, distinguished research professor in the UCLA Vatche and Tamar Manoukian Division of Digestive Diseases, will receive the American Neurogastroenterology and Motility Society (ANMS)



Distinguished Scientist Award for Women in Neurogastroenterology at the society's annual meeting in August. The award is given in recognition of Dr. Taché's landmark discoveries and pioneering work on brain-gut interactions and the role of specific peptides in the underlying mechanisms of stress-related gut dysfunction and vagal regulation of upper gut function.

The latest of Dr. Taché's many career awards carries particular meaning. In 1982, the year Dr. Taché joined the division's faculty, neurogastroenterology wasn't even a descriptor she was able to use when submitting her abstract for the American Gastroenterology Association's annual meeting. But Dr. Taché and her UCLA colleagues helped to change that with groundbreaking research establishing the importance of corticotropin-releasing factor (CRF) in stress-related gut function alterations, leading to a growing interest in CRF receptor antagonists as potential therapeutic agents for functional diseases such as irritable bowel syndrome.

The ANMS was known as the American Motility Society until 2007, when Dr. Taché and other members of the society's council spearheaded a successful effort to change the name to reflect the central place of neurogastroenterology. “To be recognized by the society in a field that I have devoted my career to is very rewarding,” Dr. Taché says. “I am especially appreciative of all of the outstanding fellows and faculty members at UCLA who have been instrumental in our work.”

# Long-held institutional training grant prepares GI fellows for successful research careers

For more than four decades, a continuously funded institutional training grant from the National Institutes of Health (NIH) has catapulted scores of post-doctoral fellows at UCLA to successful careers as academicians, physician-scientists, and other leadership roles in the GI field.

The NIH GI T32 training grant prepares the next generation of academicians and physician-scientists through career development and mentored GI-related research at UCLA, the UCLA/CURE: Digestive Diseases Research Core Center (DDRCC), and the VA West Los Angeles Medical Center. UCLA's competing continuation application recently received an outstanding score and is almost certain to be fully funded for another five-year period when the NIH budget is announced this spring, according to Dennis Jensen, MD, a professor in the UCLA Vatche and Tamar Manoukian Division of Digestive Diseases and associate director of UCLA/CURE: DDRCC, who has been principal investigator of the T32 grant for more than 20 years.

"The NIH GI T32 training grant has been a principal source of career development to support GI fellows and other future physician- and surgical-scientists at UCLA, CURE, and the VA," Dr. Jensen says. "It serves as a classroom for mentoring and GI research across the spectrum – from basic science in the

laboratory through clinical research, health services research, outcomes research, and translational research. Through this grant, we create new knowledge and use discovery and cutting-edge methods to prepare these trainees for future academic and leadership careers."

The T32 grant currently supports six trainees each year. In addition, the NIH offers supplemental funding for a seventh position to qualified minority

candidates, including one current T32 trainee. Most of the trainees remain on the grant for two years. In recent years, the grant has become a key source of funding for GI fellows who are part of the UCLA Specialty Training and Advanced Research (STAR) program, which prepares physician-scientists through a combined clinical fellowship training along with advanced research training. (For more on Drs. Jihane N. Benhammou and Tien S. Dong, two recent STAR



Dennis Jensen, MD

graduates who had T32 support and are now members of the division's faculty, see pages 14-15.)

"For many of our T32 trainees, such as the STAR fellows, part of the mentorship they receive is aimed at helping them develop an independent research career – teaching skills ranging from how to submit successful grant applications and present at meetings to writing abstracts and scientific papers," Dr. Jensen says. "In many cases, this sets them up to receive an NIH or VA career development award."

Dr. Jensen notes that the T32 grant, which brings approximately \$500,000 a year in funding, is a critical contributor to UCLA's reputation as a leader in training digestive disease researchers. "Mentored research is a very special enterprise," he says. "And without this grant, mentored GI research would be challenging to sustain because it has become increasingly difficult to fund." Beyond the T32 funding, the grant has an important multiplier effect by setting up trainees to receive funding from other sources both during and after their T32 support ends, Dr. Jensen notes.

The T32 grant is led by physician-scientists and basic scientists who have played leadership roles at UCLA, CURE, and the VA. Each of them has substantial experience and success in career development and GI research mentorship. In addition to Dr. Jensen, who is an endoscopic, clinical, and outcomes investigator, the team includes three co-directors: Yvette Taché, PhD, a neuroscientist and distinguished professor in the division; Joseph Pisegna, MD, a translational-science researcher who is a professor of medicine at UCLA and chief of the Division of Gastroenterology and Hepatology at the VA; and Martín Martín, MD, the newest addition to the leadership team, a clinician-scientist

*"Through this grant, we create new knowledge and use discovery and cutting-edge methods to prepare these trainees for future academic and leadership careers."*

– Dennis Jensen, MD

who serves as professor and associate vice chair for translational research in UCLA's Department of Pediatrics and co-director of the UCLA Center for Pediatric Diarrheal Diseases. Support from the leadership of the Vatche and Tamar Manoukian Division of Digestive Diseases, the Department of Medicine at UCLA, the VA, and CURE has been integral to the long-term success of the program, Dr. Jensen says

An executive committee consisting of approximately 10 senior investigators reviews the T32 applications as part of the process to determine which trainees are funded. The prospective trainees can choose from a pool of more than 35 NIH-approved mentors from UCLA, CURE,

and the VA, spanning the gamut of GI and other research areas. "The faculty mentors and their areas of interest have changed markedly in recent years," Dr. Jensen says. "It used to be that most of the mentors were basic scientists, but now we cover the entire spectrum from basic science through clinical research, health services, and translational research. We have applicants in GI surgery, pediatric GI, and nutrition and other related fields, as well as adult GI fellows. And we currently don't have any PhDs who are not MDs on the grant, which is another huge change." In addition to the increasing diversity brought by the supplemental funded slot for underrepresented minority candidates, more than half of the trainees funded in recent years have been women – another remarkable shift, Dr. Jensen notes.

Several factors have contributed to NIH's continuing support for UCLA's GI T32 training program, Dr. Jensen says. He and the grant's co-directors have maintained close relationships with the program director for the T32 program at NIH's National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), the institute that administers the T32 program, ensuring that UCLA's is responsive to the NIH's program priorities. "These are expensive programs, and the NIH wants to see the bang for their buck," Dr. Jensen says. "For that, you need a large institution capable of training a breadth of people who are going to stay in academics. We continue to be funded because we have evolved to meet the changing mandates and we have a very successful track record – our trainees are working with mentors on cutting-edge science, almost all of them publish two or more papers, and many go on to receive career development awards and their own NIH or VA funding, and have successful research careers."

# Dr. Tien S. Dong mines the gut microbiome for precision health approaches to treating NAFLD

**Approximately one in four U.S. adults have nonalcoholic fatty liver disease (NAFLD) – an umbrella term for a cluster of liver conditions unrelated to alcohol consumption, which are characterized by a buildup of fat in the liver. NAFLD is the most common cause of chronic liver disease, and is closely associated with obesity. “This is a growing problem that will soon become the leading reason for patients needing a liver transplant,” says Tien S. Dong, MD, PhD, an assistant professor in the Vatche and Tamar Manoukian Division of Digestive Diseases at UCLA.**

When he’s not seeing liver disease patients at the Veterans Affairs Greater Los Angeles Healthcare System, Dr. Dong seeks to contribute to solutions to this problem through his research into the complex interplay between the gut microbiome, the gut itself, and the

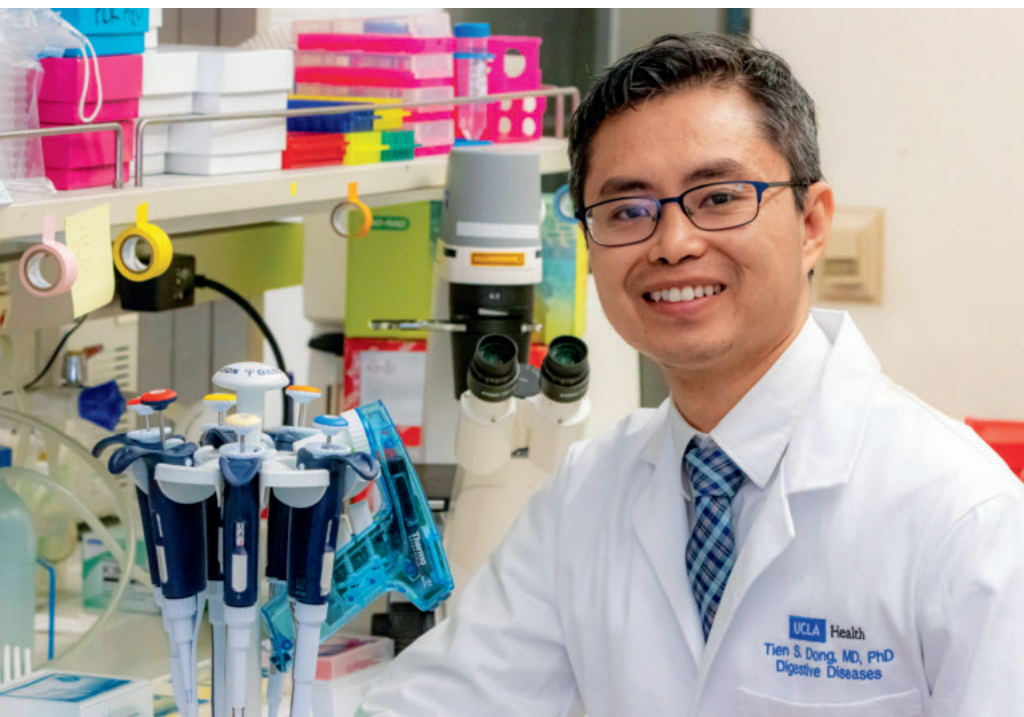
liver in the pathogenesis of obesity and NAFLD. Specifically, he is looking into how alterations to the gut-liver axis lead to NAFLD and obesity, as well as the impact of these alterations on the development of liver fibrosis and liver cancer. Through these insights, the translational studies of Dr. Dong’s multidisciplinary team could pave the way for more targeted, precision health-oriented management of fatty liver disease.

Dr. Dong’s current research trajectory was established during his training at the University of Chicago, where he completed his internal medicine residency and stayed on for an additional year as a liver hospitalist. While there, he was mentored by Eugene Chang, MD, an early pioneer in studying the role of the gut microbiome in inflammatory bowel disease and other GI conditions. “He was doing

groundbreaking work when microbiome research was in its infancy, and it really attracted me to the field,” Dr. Dong says. “I was already interested clinically in hepatology, and very few people were looking at the role of the microbiome and the gut-liver axis in liver disease.”

In 2016, Dr. Dong came to UCLA as a gastroenterology fellow and continued his research training through the Specialty Training and Advanced Research (STAR) program. He has already begun to report intriguing findings. Dr. Dong recently presented on research in which his group found in a mouse model that the microbiome plays a protective role against fatty liver disease and obesity after bariatric surgery. Using human data, Dr. Dong and his colleagues recently published a paper showing that the presence of a specific bacteria in the gut microbiome is highly predictive of which NAFLD patients go on to develop advanced liver fibrosis; they are now following up on that finding in a mouse model to determine whether the association is causative. Dr. Dong is also interested in applying artificial intelligence and machine learning to the huge data sets of bacteria in the microbiome as a way to develop predictive models for GI diseases.

For Dr. Dong, moving toward precision health approaches to treating NAFLD has a personal component – he has seen multiple family members suffer from liver disease. “The research over the last 5-10 years has shown that the microbiome is closely related to obesity and metabolic syndrome, and that alterations can lead to some novel targets and therapeutics for fatty liver and other diseases,” he says. “By finding these associations and proving causation, we can contribute to ways to treat these diseases that are more tailored to the individual patient.”



Tien S. Dong, MD, PhD



# Who among NAFLD population will develop liver cancer?

## Dr. Jihane N. Benhammou aims to find screening strategies

In her early clinical experiences as a hepatologist, Jihane N. Benhammou, MD, PhD, was struck by the large number of patients with nonalcoholic fatty liver disease (NAFLD) – and the reality that a significant percentage of these patients would go on to develop cancer without a chronic liver disease diagnosis.

It's estimated that one-fourth of U.S. adults have NAFLD, a condition characterized by excess fat in liver cells not caused by alcohol. Given the epidemic of obesity and type 2 diabetes – two leading risk factors – the prevalence is likely to continue to rise. But, despite the increased risk of liver cancer, most people with NAFLD don't know they have it. "What too often happens is that patients will come to the hospital vomiting blood from end-stage liver disease, after never having been diagnosed with a problem," notes Dr. Benhammou, an assistant professor in the Vatche and Tamar Manoukian Division of Digestive Diseases at UCLA.

There are no current guidelines for identifying which patients are at risk. "We have no blood test to screen for NAFLD; the current gold standard for diagnosis is a biopsy, which would be too expensive and invasive to use as a population-wide screening tool," Dr. Benhammou explains. "We screen for cancer if the patient has chronic liver disease or cirrhosis. Otherwise, we generally see these patients only after a mass is discovered incidentally on an imaging study. The problem is that by the time that mass is detected, it's often too late."

The 'holy grail' would be to determine, in a cost-effective manner, who among the large population with NAFLD and no chronic liver disease will go on to develop complications, so that physicians could intervene – both by counseling those individuals on the



Jihane N. Benhammou, MD, PhD

importance of reducing NAFLD risk factors, and by closely monitoring them for signs of early cancer.

Dr. Benhammou, a clinician-scientist who, in addition to her internal medicine and gastroenterology training at UCLA, earned her PhD through the UCLA Specialty Training and Advanced Research (STAR) program, heads a laboratory that is seeking to better understand the predictors, pathogenesis, and clinical outcomes of NAFLD and fatty liver-associated hepatocellular carcinoma in different ethnic populations. The ultimate goal is to identify screening tools to determine which patients with NAFLD are most likely to develop cancer and other complications of the disease.

In multidisciplinary research at UCLA and the Veterans Affairs Greater Los Angeles Healthcare System, Dr. Benhammou's group is examining patient clinical charts in an effort to make associations between risk factors

and outcomes; collecting blood and tissue samples from patient volunteers to glean insights on which lipid profiles predict poor outcomes; and bringing these observations back to the lab to better understand the mechanisms underlying the development of complications in these patients. Dr. Benhammou is particularly interested in learning more about the risk factors specific to the Hispanic population, which has higher rates of NAFLD than the general population.

She notes that her research continues to be driven by her experiences treating patients in the liver clinics at UCLA and the VA. "I am able to see the full spectrum, from patients whose NAFLD doesn't progress to those who do progress to cancer, and what I learn from those patients influences the questions I ask in the lab," Dr. Benhammou says. "With so much obesity and metabolic syndrome in our society, this is an urgent problem that needs to be addressed."

## Dr. Arpan A. Patel aims to improve palliative care for patients with cirrhosis through better communication



Arpan A. Patel, MD, PhD

Cirrhosis of the liver is one of the leading causes of death in individuals between the ages of 45 and 65, and cirrhosis-related deaths have increased by 60 percent over the last decade. As the disease progresses, liver function can be lost – a condition known as decompensated cirrhosis. At that point, the only cure is liver transplantation. “The problem is that while many more people are dying of decompensated cirrhosis, we don’t have enough organs for them,” says Arpan A. Patel, MD, PhD, an assistant professor in the UCLA Vatche and Tamar Manoukian Division of Digestive Diseases.

During his gastroenterology training, Dr. Patel noted that for all of the advances in hepatology care over the last several decades, patients with decompensated cirrhosis were still dying, and that health care providers were often more focused

on conversations about transplant instead of how to support their quality of life.

Through his training, Dr. Patel has been dedicated to documenting and addressing this shortcoming, both in his own clinical practice as part of a team of liver specialists at the VA Greater Los Angeles Healthcare System and in his research, which began during his PhD work as a UCLA Specialty Training and Advanced Research (STAR) and National Research Service Award (NRSA) fellow.

Dr. Patel is particularly interested in how to integrate palliative care in the management of patients with end-stage liver disease. “For patients with decompensated cirrhosis who are unlikely to receive a liver transplant, there’s not going to be a cure – we can only manage the complications of their disease,” he

says. “But we can also improve the time they have left. A lot of people think of palliative care as just involving the last moments of life, but it’s actually what we provide through the trajectory of patients’ illness that supports their quality of life.”

Unlike most clinician-researchers, Dr. Patel’s research is mostly qualitative – recording and then analyzing conversations with patients and providers to better understand their experiences. Doing so has revealed a culture of doctors not talking to their patients or their patients’ families about issues pertaining to dying, their preferences regarding care, and their mental health concerns such as depression and anxiety.

“When these patients first get sick, providers, patients, and their family members should engage in conversations about what to expect, but too often that doesn’t occur,” Dr. Patel says. “The burdens of the caregivers are rarely discussed, and we don’t do a great job of being holistic in managing patients’ mental health and symptom issues.”

None of these shortcomings had been described when Dr. Patel started his research in 2015. “We found that there is poor communication, and that most patients with end-stage liver disease die in the hospital after getting a lot of aggressive treatments, but don’t receive palliative care,” he says. Now, his research focus has shifted to identifying ways to promote better communication between health care providers and their patients and patients’ families. “As these patients become sicker, their care becomes more complex, and they need a lot more support,” Dr. Patel explains. “Improving communication is essential if we are going to properly deliver that support.”



Wael El-Nachef, MD, PhD

## By studying the enteric nervous system, Dr. Wael El-Nachef seeks ways to intervene early in Parkinson's disease

When he began an internal medicine residency at Harbor-UCLA Medical Center, Wael El-Nachef, MD, PhD, had no inkling he would end up becoming a physician-scientist – much less one who would devote the majority of his time to conducting research in a basic-science laboratory on fundamental biological questions related to the enteric nervous system.

But as he progressed through his residency, Dr. El-Nachef became frustrated with how little doctors understood about some of their patients. “We would get a flurry of admissions from the emergency room, and all of the residents wanted to take the ICU cases over patients with gastroparesis, because even though they were complex, at least we knew how to treat those patients – whereas with gastroparesis, the arsenal is much more limited,” recalls Dr. El-Nachef, now an assistant professor in the UCLA Vatche and Tamar Manoukian Division of Digestive Diseases. “That encouraged me to consider research.”

After receiving his introduction to basic research in a tissue-engineering laboratory at Children's Hospital Los Angeles, Dr. El-Nachef applied for and received a training grant from the California Institute for Regenerative Medicine and spent two years exploring tissue-engineering approaches to treating enteric neuropathies. Convinced he needed more formalized scientific training, he enrolled in UCLA's Specialty Training and Advanced Research (STAR) program, allowing him to take time during his gastroenterology clinical fellowship to work toward his PhD.

During his time in the STAR program, Dr. El-Nachef began working in the laboratory of a neural crest biologist, Marianne E. Bronner, PhD, at Caltech, with which UCLA has an established affiliation. Using the zebrafish model, Dr. El-Nachef studied enteric nervous system homeostasis, degeneration, and regeneration – an area of research with important implications

for intestinal disorders. Dr. El-Nachef has remained in that lab since receiving his PhD in 2019; most recently, he earned an NIH Career Development Award to continue his research under the mentorship of Dr. Bronner and Dr. Harry Pothoulakis, the Eli and Edythe Broad Chair in Medicine and director of basic research for the UCLA Center for Inflammatory Bowel Diseases.

As he transitions to running his own laboratory at UCLA, Dr. El-Nachef plans to develop a more disease-focused research program. His main interest is Parkinson's disease. “It's poorly understood at both the basic science and clinical levels,” he says. “I would like to learn why enteric nervous system homeostasis fails and regeneration doesn't occur in this disease.” Dr. El-Nachef has also been working with Jeff Bronstein, MD, PhD, a neurologist who heads the UCLA Movement Disorders program, on research into the role of the intestinal nervous system in a zebrafish model of Parkinson's disease.

This interest in learning more about Parkinson's disease in the laboratory is fueled by Dr. El-Nachef's clinical work, in which he sees Parkinson's patients who are experiencing gastrointestinal symptoms. “The majority of patients we see at the Parkinson's GI clinic tell us that GI issues are affecting their quality of life more than their motor symptoms,” Dr. El-Nachef says. “We can make a big difference by addressing those concerns.”

Beyond treating these patients' immediate symptoms, Dr. El-Nachef uses what he learns in his clinical work to inform his research. “We need to find biomarkers that can enable early diagnosis,” he says. “The turning point for Parkinson's disease will be when we have the ability to identify patients with the disease before they develop any motor symptoms, and then give them preventative treatments.”

# New clinical faculty members

The Vatche and Tamar Manoukian Division of Digestive Diseases at UCLA includes approximately 60 clinical faculty – individuals with expertise in the prevention, diagnosis and treatment of GI conditions. Below are the most recent additions to a team that is part of the division’s continuing expansion beyond UCLA Health’s main Westwood and Santa Monica campuses to meet the needs of patients through community practices.



## **Elliott Birnstein, MD | Health Sciences Clinical Instructor of Medicine**

Dr. Birnstein received his undergraduate degree from the University of California, Berkeley and his medical degree from the Keck School of Medicine of USC. He completed his internship and residency in internal medicine at the Los Angeles County-USC Medical Center, where he served as chief resident. Dr. Birnstein completed his gastroenterology fellowship at Memorial Sloan Kettering Cancer Center in New York City, where he received specialized training in gastrointestinal complications of cancers and cancer treatments.

Dr. Birnstein is a general gastroenterologist practicing in downtown Los Angeles. Apart from his clinical duties, Dr. Birnstein enjoys teaching medical students, residents, and fellows. He is board certified in gastroenterology and internal medicine.



## **Janet Kwok, MD | Health Sciences Clinical Instructor of Medicine**

Dr. Kwok received her undergraduate degree from the University of California, San Diego, graduating cum laude in physiology and neuroscience with a minor in cognitive science. She earned her medical degree from Stony Brook Medicine in New York, where she was elected to the Gold Humanism Honor Society. She returned to California to complete her internship and residency in internal medicine at the University of Southern California, and stayed at USC for her fellowship training in gastroenterology.

Dr. Kwok is a general gastroenterologist practicing in downtown Los Angeles. She is board certified in internal medicine and gastroenterology.



### **Benjamin Nulsen, MD | Health Sciences Clinical Instructor of Medicine**

Dr. Nulsen earned his bachelor's degree from Georgetown University in Washington, DC. He earned his medical degree from the Icahn School of Medicine at Mount Sinai in New York City, and continued there for his residency in internal medicine, serving as chief resident. He completed his gastroenterology fellowship training at UCLA, where he was chief fellow.

During training, Dr. Nulsen researched novel approaches to gastrointestinal bleeding and patterns of medication use in irritable bowel syndrome. He also worked with the American Gastroenterological Association to develop the Gastro Cards educational app.

Dr. Nulsen practices general gastroenterology in Santa Monica. He is a member of the American College of Gastroenterology and American Gastroenterological Association. He is board certified in internal medicine and gastroenterology.

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### **Ronald H. Omino, MD | Health Sciences Clinical Instructor of Medicine**

Dr. Omino completed his medical school training at Wayne State University School of Medicine in Detroit. He completed residency in internal medicine at Baylor College of Medicine. He then completed his fellowship training in gastroenterology at the University of Illinois at Chicago.

Dr. Omino practices general gastroenterology in Simi Valley. He is a member of the American College of Gastroenterology and the American Gastroenterological Association. He is board certified in internal medicine and gastroenterology. Dr. Omino speaks both English and Japanese.

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### **Kavya M. Reddy, MD | Health Sciences Clinical Instructor of Medicine**

Dr. Reddy earned her undergraduate degree in biology with a minor in psychology from Saint Louis University. She continued at Saint Louis University for medical school as part of the combined BS/MD Medical Scholars Program. She then came to Los Angeles where she completed her internal medicine residency at Kaiser Permanente Los Angeles Medical Center, where she served as a chief resident. After residency, Dr. Reddy joined the staff at Kaiser as an associate physician in internal medicine with outpatient and inpatient responsibilities. During this time, she was active in resident and student education and acted as the UCLA Primary Care Rotation site coordinator for medical students. Dr. Reddy then returned to Saint Louis University to pursue a fellowship in gastroenterology and hepatology. During her fellowship, she directed quality improvement projects and continued to demonstrate her passion for teaching by serving as an instructor for the medical school gastroenterology module. Dr. Reddy also participated in clinical research and authored and co-authored multiple peer-reviewed journal articles and book chapters.

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

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# Ninth Annual UCLA-Mellinkoff Gastroenterology and Hepatology Symposium

Case-Based Learning to  
Treat Common GI Disorders

March 6-7  
2021

**VIRTUAL**

**Due to public health and safety issues, the course is being offered as a live, virtual program.**

The 9th Annual UCLA-Mellinkoff Gastroenterology and Hepatology Symposium, a live, virtual CME activity, is designed to offer healthcare professionals novel and integrative approaches to treat common GI disorders that can easily be implemented into practice and have significant impact on patient outcomes. Interactive, lively case-based presentations by experts in their field will engage attendees and enhance this learning experience.

#### Accreditation

The Office of Continuing Medical Education, David Geffen School of Medicine at UCLA is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

The Office of Continuing Medical Education, David Geffen School of Medicine at UCLA designates this live activity for a maximum of **9.5 AMA PRA Category 1 Credits™**. Physicians should claim only the credit commensurate with the extent of their participation in this activity.

Successful completion of this CME activity, which includes participation in the evaluation component, enables the participant to earn up to **9.5 Medical Knowledge and Practice Assessment MOC points** in the American Board of Internal Medicine's (ABIM) Maintenance of Certification (MOC) program. Participants will earn MOC points equivalent to the amount of CME credits claimed for this activity. It is the CME activity provider's responsibility to submit participant completion information to ACCME for the purpose of granting ABIM MOC credit.

#### Registration and course information

- \$250 – Physicians
- \$200 – Past UCLA GI fellows, physician assistants, nurse practitioners, nurses, retired physicians and other non-physician healthcare professionals
- Complimentary – Fellows, residents and trainees (registration is required)

Visit: [www.cme.ucla.edu/courses/Mellinkoff2021](http://www.cme.ucla.edu/courses/Mellinkoff2021)

Questions? Contact [trishajames@mednet.ucla.edu](mailto:trishajames@mednet.ucla.edu)

#### Disclosure statement / Declaration

The FDA has issued a concept paper which classified commercial support of scientific and educational programs as promotional unless it can be affirmed that the program is "truly independent" and free of commercial influence. In addition to independence, the FDA requires that non-promotional, commercially supported education be objective, balanced, and scientifically rigorous. The policy further states that all potential conflicts of interest of the CME staff and faculty be disclosed to the program's participants. In addition, Accreditation Council for Continuing Medical Education policy mandates that the sponsor adequately manage all identified potential conflicts of interest prior to the program. We, at UCLA, fully endorse the letter and spirit of these concepts.



## Course directors



#### Director

V. Raman Muthusamy, MD, MAS  
Medical Director of Endoscopy,  
UCLA Health  
Professor of Clinical Medicine  
Vatche and Tamar Manoukian  
Division of Digestive Diseases



#### Co-Director

Eric Esraillian, MD, MPH  
Chief, Vatche and Tamar Manoukian  
Division of Digestive Diseases  
Lincy Foundation Chair in  
Clinical Gastroenterology  
Health Sciences Clinical Professor  
of Medicine

## Invited faculty



Marla Dubinsky, MD  
Chief, Pediatric Gastroenterology  
and Nutrition  
Co-Director, Susan and Leonard  
Feinstein IBD Clinical Center  
Icahn School of Medicine,  
Mount Sinai, New York



Rachel Issaka, MD, MAS  
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# Agenda

## Saturday, March 6

7:00 am	<b>Non-CME – Virtual Exhibit Hall*</b>
7:50 am	<b>Welcoming Remarks</b> Eric Esrailian, MD, MPH, UCLA
7:55 am	Course Overview V. Raman Muthusamy, MD, MAS, UCLA
	CME – Management of Crohn's Disease and Ulcerative Colitis Moderator: Jenny Sauk, MD, UCLA
8:00 am	2020-2021 Crohn's Disease Update Marla Dubinsky, MD, Icahn School of Medicine, Mount Sinai
8:25 am	2020-2021 Ulcerative Colitis Update William J. Sandborn, MD, UC San Diego
8:50 am	Rapid Fire Case-Based Discussions <ul style="list-style-type: none"> <li>• How do you use therapeutic drug monitoring in your practice?</li> <li>• When do you consider medical vs. surgical management?</li> <li>• What factors are you considering when determining therapeutic regimen?</li> </ul> <p>Panel Members: Marla Dubinsky, MD, Icahn School of Medicine, Mount Sinai, Berkeley Limketkai, MD, PhD, UCLA, Jenny Sauk, MD, UCLA, William J. Sandborn, MD, UC San Diego</p>
9:45 am	Q & A
10:00 am	<b>Non-CME – Break, Virtual Exhibit Hall*</b>
	CME – Updates in Colorectal Cancer Screening Moderator: Folasade P. May, MD, PhD, MPhil, UCLA
10:15 am	Welcome and Introductions Folasade P. May, MD, PhD, MPhil, UCLA
10:20 am	Early Onset Colorectal Cancer Rachel Issaka, MD, MAS, Fred Hutchinson Cancer Research Center
10:30 am	New Colorectal Cancer Screening Guidelines Carl Nordstrom, MD, UCLA
10:40 am	Racial and Ethnic Disparities in Colorectal Cancer Rachel Issaka, MD, MAS, Fred Hutchinson Cancer Research Center
10:50 am	Optimizing Quality of Screening Colonoscopy Priyam V. Tripathi, MD, MPH, UCLA
11:00 am	Q & A
11:45 am	<b>Non-CME – Lunch, Industry Theatre, Virtual Exhibit Hall*</b>
	CME – Interventional Endoscopy Moderator: Stephen Kim, MD, UCLA
12:30 pm	Transoral Incisionless Fundoplication (TIF) – Do We Finally Have an Effective Endoscopic Anti-Reflux Procedure? V. Raman Muthusamy, MD, MAS, UCLA
12:45 pm	Introduction to Endo-Hepatology: Closer Than Ever Adarsh M. Thaker, MD, UCLA
1:00 pm	Endoscopic Innovations for Weight Loss – Current and Emerging Techniques Danny Issa, MD, UCLA
1:15 pm	ESD and Novel Advanced Endoscopic Resection Techniques Alireza Sedarat, MD, UCLA
1:30 pm	Q & A
1:45 pm	<b>Non-CME – Break, Virtual Exhibit Hall*</b>
	CME – When the GI Motor Backfires Moderator: Jeffrey L. Conklin, MD, UCLA
2:00 pm	Welcome and Introductions Jeffrey L. Conklin, MD, UCLA
2:05 pm	Case Study: Haiku for the Pylorus Alireza Sedarat, MD, UCLA
2:25 pm	Case Study: When Scleroderma Gets Hard to Stomach Lisa D. Lin, MD, MS, UCLA
2:45 pm	Case Study: Shaking Palsy of the Gut? Wael El-Nachef, MD, PhD, UCLA
3:05 pm	Case Study: Eosinophilic Esophagitis (EoE) Kevin Ghassemi, MD, UCLA, and Nancee Jaffe, MS, RDN, UCLA
3:30 pm	Adjourn

## Sunday, March 7

7:00 am	<b>Non-CME – Industry Theatre, Virtual Exhibit Hall*</b>
7:55 am	<b>Welcoming Remarks</b> V. Raman Muthusamy, MD, MAS, UCLA
	CME – IBS and Other Disorders of the Gut-Brain Interaction Moderator: Lin Chang, MD, UCLA
	Panel Members: Christina T. Gentile, PsyD, MA, ABPP, UCLA, Emeran A. Mayer, MD, UCLA, Natalie Maniatus, MPH, RDN, UCLA, Suzanne Smith, MSN, NP, CMT-P, UCLA, Kirsten Tillisch, MD, UCLA
8:00 am	Introduction Lin Chang, MD, UCLA
8:00 am	Case Study: Patient with Chronic Nausea and Dyspepsia: Diagnosis and Treatment <ul style="list-style-type: none"> <li>• How do you diagnose functional dyspepsia with delayed gastric emptying vs gastroparesis?</li> <li>• What approaches do you find are effective in these patients?</li> </ul>
8:20 am	Lecture: FODMAP and Beyond Natalie Maniatus, MPH, RDN, UCLA
	Case Study: IBS Patient Who Seeks Dietary Treatment <ul style="list-style-type: none"> <li>• What is the approach to managing symptoms in a patient who eliminates multiple foods without good evidence of a consistent food trigger?</li> <li>• How should we manage patients who have been on a low FODMAP for an extended period of time and have symptom recurrence with reintroduction?</li> </ul>
8:40 am	Lecture: Microbiome and Gut Health Emeran A. Mayer, MD, UCLA
	Panel: <ul style="list-style-type: none"> <li>• What is the value of stool microbiome testing in IBS?</li> <li>• What are the microbiome targeted treatments you use for IBS or other DGBI?</li> <li>• How do you explain that a restrictive diet and/or multiple antibiotic courses for SIBO is not healthy for the gut microbiome and digestive health?</li> </ul>
9:10 am	Lectures: An Integrated GI Management Approach Christina T. Gentile, PsyD, MA, ABPP, UCLA, Suzanne Smith, MSN, NP, CMT-P, UCLA, Kirsten Tillisch, MD, UCLA
	Case Study: Patient with Chronic Abdominal Pain with Comorbidities <ul style="list-style-type: none"> <li>• How does your treatment change in a patient with GI symptoms and significant comorbidities?</li> <li>• How do you respond to a patient who believes symptoms are due to a structural cause?</li> <li>• How do you help patient understand realistic expectations and accept their chronic illness?</li> </ul>
10:00 am	<b>Non-CME – Break, Virtual Exhibit Hall*</b>
	CME – Liver Disorders Moderator: Sammy Saab, MD, MPH, UCLA
	Panel Members: Jihane M. Benhammou, MD, PhD, UCLA, Gina Choi, MD, UCLA, Mohamed El-Kabany, MD, UCLA, Steven-Huy Han, MD, UCLA, Beshoy T. Yann, MD, UCLA
10:15 am	Introduction Sammy Saab, MD, MPH, UCLA
10:30 am	Case Study: Treatment of Acute HBV and HCV Steven-Huy Han, MD, UCLA
11:00 am	Case Study: Suspected Autoimmune Hepatitis Gina Choi, MD, UCLA
11:30 am	Case Study: Diagnosis and Current Management of NASH Jihane N. Benhammou, MD, PhD, UCLA
12:00 pm	Case Study: Management of Acute Alcoholic Hepatitis Sammy Saab, MD, MPH, UCLA
12:30 pm	Conclusion Mohamed El Kabany, MD, UCLA

### ‡ Non-CME Virtual Exhibit Hall and Industry Theatres

Attendees will have the opportunity to visit virtual commercial exhibits and industry supported educational sessions prior to the start of the CME program and during breaks. This portion of the program is not accredited for CME credit.

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UCLA Gastroenterology and GI Surgery ranked #5 in the nation by *U.S. News & World Report* in its survey. UCLA Health hospitals in Westwood and Santa Monica also ranked #4 in the nation.



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