 Leading an International Effort of Structural and Functional Mapping of the Nervous System of the Colon

Page 2
Going *Beyond the Scope*

We are proud to lead a division populated with some of the world’s most outstanding clinicians and scientists in the field of gastroenterology. However, our ability to make a difference through our four core missions — research, patient care, education, and community engagement — stems not just from the expertise in our division. This ability also comes from our position within a world-class academic medical center, a premier research university, and as part of the broader Los Angeles community.

More than ever before, multidisciplinary collaboration is essential to our ability to tackle major challenges in biomedical research and healthcare, as well as in the training and education of the next generation of young scientists and health professionals. At the UCLA Vatche and Tamar Manoukian Division of Digestive Diseases, we not only recognize this imperative but we embrace the vast wealth of talent and expertise that surrounds us to forge partnerships across traditional boundaries.

Amid the revolutions in fields such as genetic studies, data science, and information technology, we recognize that the way to make breakthroughs in digestive diseases is by joining with experts in fields we never considered working with back when many of us were in medical school. At UCLA, we are in the rare position of having a leading academic medical center and medical school on the same physical campus as a top university, placing experts across diverse fields within a short walk from one another. This close proximity, along with a prevailing spirit of partnership, is leading to exciting new initiatives — some of which are featured in this issue of *Beyond the Scope*.

For example, our division is playing a central role in working with leaders across the UCLA campus and health enterprise on the new Institute for Precision Health at UCLA (page 6), which is leveraging the new technologies to pave the way for more individualized treatment and prevention strategies. Through a large Stimulating Peripheral Activity to Relieve Conditions (SPARC) grant from the National Institutes of Health, we are working with other UCLA departments as well as experts at institutions around the world in an ambitious effort to provide the first structural and functional map of the colonic nervous system in humans, which would allow for more targeted treatments of many GI disorders (page 2). Through our participation in the UCLA Value-Based Care Consortium — a multidisciplinary effort involving physicians, biomedical scientists and biostatisticians — we are participating in research aiming to inform strategies for improving the quality and outcomes of care while reducing cost (page 4).

We hope that these and the other articles featured in this *Beyond the Scope* provide a glimpse of the exciting activity in and outside of our division. We are proud to be part of the team of experts at UCLA and beyond that is taking advantage of the unprecedented tools we now have to make a difference in the health of our community and the world.
We are at the dawn of an exciting era in biomedical science – one that my colleagues and I would have been hard-pressed to envision in 1982, the year I joined the UCLA Vatche and Tamar Manoukian Division of Digestive Diseases faculty. Spectacular advances in molecular biology, genetics/genomics, and related fields, coupled with exponential leaps in imaging and information technologies, have brought us to the point where we can ask fundamental questions about human health and disease, using the answers to develop treatments and prevention strategies that are more precise – and, thus, potentially more effective – than ever before.

But tackling these critical matters is not something that any single research lab, or even any single scientific discipline, can undertake alone. We now understand, for example, that problems of the gut require more than just expertise in gastroenterology, but also endocrinology, immunology, microbiology and neuro-biology, among other fields. Because of this interconnectedness, what’s needed in many cases are large groups of experts coming together from divergent fields, working with requisite infrastructure and core facilities. This means breaking down disciplinary and even institutional silos. In recent years the National Institutes of Health has fueled this important trend by introducing the multi-principal investigator model “to maximize the potential of team science efforts in order to be responsive to the challenges and opportunities of the 21st century.”

This issue of Beyond the Scope showcases some of the ways our division is front and center in this movement – from the multi-department, multi-campus work of my SPARC (Stimulating Peripheral Activity to Relieve Conditions) team in providing the first comprehensive and detailed structural and functional mapping of the nervous system of the colon in humans and pigs, to the unprecedented multidisciplinary effort now underway by the new Institute for Precision Health at UCLA, of which our division is playing a central role. This issue also highlights how our division is working with other disciplines on campus to reduce so-called low-value care and to engage students from high school to graduate school in the sciences through mentorship.

This is an exciting time for those of us who have devoted our careers to unraveling the mysteries behind gastrointestinal conditions. With the tools we now have at our disposal, we are poised to make substantial progress toward new discoveries that can lead to new strategies to benefit patients with digestive diseases, as well as helping to ensure that people never experience these illnesses. By partnering with other experts within our division, across the UCLA Health system and campus, and at institutions across the nation and around the world, our division is ideally situated to play a leadership role in advancing the health of populations both at UCLA and worldwide.
SPARC team maps the colonic nervous system

The ability to modulate the electrical signals transmitted by peripheral nerves – the sympathetic and parasympathetic nerves that connect the brain to the rest of the body, controlling the function of each organ – could provide the key to a powerful new class of treatments for many intractable diseases and conditions, including GI disorders. The UCLA Vatche and Tamar Manoukian Division of Digestive Diseases is currently part of an unprecedented international effort to do just that.

A National Institutes of Health (NIH)-funded consortium headed by Yvette Taché, PhD, distinguished professor in the division, has completed the first year of a three-year, $7.5 million OT2 grant whose objective is to provide the first comprehensive and detailed structural and functional mapping of the nervous system of the colon in humans and the pig – a large animal model with structural and physiological similarities to humans. The grant is part of NIH’s Stimulating Peripheral Activity to Relieve Conditions (SPARC) program, which is expected to provide approximately $238 million in funding over a five-year period in an effort to map the body’s electrical wiring and develop devices that will allow for the therapeutic stimulation of those nerves.

More than two-dozen multidisciplinary teams are being funded through SPARC, including groups studying other organs such as the heart, lung and spleen, to gain new insights into how peripheral nerves control internal organ function through local circuitries. Such an understanding could ultimately lead to advances in neuromodulation that would allow for more precise treatment of diseases and conditions for which conventional therapies are inadequate.

Dr. Taché points out that the colon is involved in a multitude of disorders – including chronic constipation, diarrhea, diverticulitis, irritable bowel syndrome, inflammatory bowel diseases, *Clostridium difficile*, colitis, cancer, Parkinson’s-associated dysmotility, and age-related pelvic dysfunction – that are leading causes of morbidity and mortality, at an annual cost to the U.S. healthcare system of an estimated $21 billion.

“As we have learned more about the significance of the nervous system in regulating colonic function – the brain-gut connection – and its importance in issues relating to motility and inflammation, researchers have focused on understanding the neurochemical and electrophysiological properties, cell
Beyond the Scope

physiology, and functional roles of colonic enteric neurons and their interaction with the parasympathetic, sympathetic and sensory systems,” Dr. Taché explains. “But until recently, we have been able to obtain this data only through small-animal studies. Now, cutting-edge approaches such as 3-D mapping, innovative viral tracing tools, and neuroimaging make it possible to obtain detailed information on neural circuits and related functions in large animals and human tissues, which is what we need as a foundation for neuromodulation therapies.”

To undertake the complex task, Dr. Taché has assembled a multidisciplinary team of top investigators that includes individuals who have developed state-of-the-art neuroanatomical, molecular, electrophysiological and functional approaches, as well as those who are expert in the state-of-the-art methodologies and on the stimulation of nerves in the colon in humans. The team includes researchers both from UCLA – where four departments are represented – and from seven outside universities, including institutions as far away as Germany and Australia. In addition to the collaborations within the consortium, Dr. Taché’s group meets regularly with other SPARC consortium groups to exchange ideas and share data.

Dr. Taché’s group has benefited greatly from the groundwork established by a UCLA-led SPARC consortium that is mapping the heart’s nervous system. In many ways, that $8.6 million grant, awarded in 2016 to Kalyanam Shivkumar, MD, PhD, helped to establish a template that for Dr. Taché’s team as it lays the foundation for new ways to treat cardiovascular disease by modulating electrical signals in the heart’s autonomic nervous system. “Understanding the nervous system’s control of the heart is such a complex problem that it requires a collaborative approach, and we’re pleased that so many experts are coming together for this initiative,” says Dr. Shivkumar, the SPARC cardiovascular consortium’s lead investigator and director of the UCLA Cardiac Arrhythmia Center and Electrophysiology Programs. “Our goal is to precisely map the heart’s anatomy and code the function of the nerves that control the heart from a very basic level all the way to clinical studies in humans.”

Dr. Taché’s SPARC team is using the same sophisticated technological and imaging approaches to map the nerves and functional circuitries in the colon, setting the foundation for the project’s second phase, in which researchers will run therapeutic assays under pathophysiological conditions in an effort to develop electroceutical interventions to treat colonic disorders.

“We aim to understand how the colon responds to direct and indirect electrical stimulation,” explains James Dunn, MD, a principal investigator on the team and a member of the Department of Surgery at Stanford University. “This will lead to the development of devices that can modulate colon function in a variety of diseases such as inflammatory bowel disease and motility disorders.”

“Modern pharmaceutical-based treatments are not always precise or targeted,” adds Wentai Liu, PhD, a distinguished professor in the UCLA Department of Bioengineering and member of Dr. Taché’s SPARC team. “Electrophysiological intervention provides a promising alternative strategy to exert direct control of the autonomic nerves that regulate selected organs of interest. The implementation of this strategy has been slowed due to limited understanding of autonomic nervous system function and control. SPARC is fostering the science and engineering collaborations that will facilitate the understanding of the fundamental science of, as well as the manipulation of, autonomic networks. As an engineering researcher, I’m very pleased to be part of this challenging and exciting initiative.”
Approximately $3 trillion is spent on healthcare in the United States, and various studies have estimated that between 10 and 30 percent of that spending is on tests, procedures and medications for which, on average, the expected benefits to patients in a particular clinical scenario don’t exceed the potential harm when considering the risk of side effects and complications.

So-called low-value care is a widespread national problem that touches every specialty, notes John N. Mafi, MD, MPH, an assistant professor in the Division of General Internal Medicine and Health Services Research at the David Geffen School of Medicine (DGSOM) at UCLA. Gastroenterology is no exception. “If you order a screening colonoscopy for a 39-year-old patient with no symptoms and no family history of colon cancer, that patient is more likely to be harmed by the procedure than to get any benefit from it;” Dr. Mafi says. “If a patient has one-time, mild stomach gas with no red flags and is prescribed a proton pump inhibitor medication, that patient is also more likely to be harmed than to benefit.”

A number of factors are likely contributing to the problem of low-value care. Among the most commonly cited are incentives to order tests and procedures under the fee-for-service payment system, though Dr. Mafi points out that under payment models that provide disincentives to order more services, low-value care is still found. Another likely contributing factor is the fear of being sued for malpractice, along with the mindset among many patients that some care is always better than no care – or the assumption among physicians that their patients want a service to be ordered for whatever concern they are experiencing. “Unfortunately, we have a long way to go before our general
American culture embraces the concept that oftentimes in medicine, less is more,” says Catherine Sarkisian, MD, MSPH, a professor and health services researcher in DGSOM’s Division of Geriatrics and the VA Greater Los Angeles Healthcare System’s Geriatrics Research Education Clinical Center and the director of the recently launched UCLA Value-Based Care Research Consortium.

But Dr. Sarkisian adds that reducing low-value care is becoming a national priority – and deservedly so. “Like most of my colleagues, I went into medicine because I wanted to help people, so it has been very distressing to learn that so much of what we actually do for patients has no chance of being helpful — and even worse, is often harmful,” she says. “The recent increased focus on value-based care has evolved naturally in response to out-of-control healthcare spending combined with front-line clinicians seeing wasteful and harmful care delivered every day. Focusing on value-based healthcare simply means working to make sure that the care we deliver is known to improve meaningful health outcomes.”

As they aim to tackle the issue of low-value care and improve quality through research, Drs. Mafi and Sarkisian have found a partner in the UCLA Vatche and Tamar Manoukian Division of Digestive Diseases, under the leadership of division co-chief Eric Esrailian, MD, MPH. “Dr. Esrailian has been very enthusiastic and forward-thinking about the issue of improving value at UCLA,” Dr. Mafi says. With financial support from the division, as well as from the UCLA Clinical and Translational Science Institute, the Robert Wood Johnson Foundation, and the MacColl Institute, Drs. Mafi, Sarkisian and Folasade P. May, MD, PhD, MPhil, an assistant professor and health services researcher in the division, have embarked on a series of studies to measure and then engage clinicians in reducing low-value care for certain GI services at UCLA, with studies involving other clinical units at UCLA to follow.

“Value in healthcare is something that both hospitals and patients care about,” says Dr. May, who directs the division’s quality improvement program. “In recent years we have seen the introduction of many medical technologies and therapies, but the issue of what constitutes appropriate use of these services has been understudied.”

The researchers started by looking at inappropriate overuse of colonoscopy as a colorectal cancer screening tool. Although the underuse of colonoscopy screening for patients who meet evidence-based national guidelines is a serious concern, a study within the VA system found that there is also a significant amount of low-value care related to colorectal cancer screening. “Colonoscopy can remove cancers and save people’s lives, but there is a small risk of complications,” Dr. May says. “That means if we are performing 1,000 unnecessary colonoscopies, we’re going to have one, two or three patients with negative outcomes from the inappropriate use of that test.”

Drs. Mafi, Sarkisian and May developed and tested a reliable algorithm for determining low-value colorectal cancer screening. “Given that UCLA, like many health systems, is fee for service, we expected to find a significant amount of low-value care for colonoscopy cancer screening, yet the rates were very low, which is great,” says Dr. Mafi, who adds that the finding will be published so that other systems can build on the measurement tool to identify any problem they might have.

The research team is also evaluating the extent to which upper endoscopy is used for low-value care of patients with uncomplicated heartburn or dyspepsia. “Acid reflux is one of the most common GI conditions, and we have specific research-based guidelines that we can follow in defining overuse,” Dr. May says. A third project is studying the use of proton pump inhibitors — medications that have been widely prescribed for upper-GI symptoms, but have been linked in some studies to negative outcomes such as kidney damage and increased dementia risk. If the UCLA team finds high rates of overuse of these drugs, it will design an intervention aiming to influence UCLA Health physicians to prescribe them in a more evidence-based way, Dr. Mafi says.

Beyond sharing the results of their research across the UCLA Health system in an attempt to educate and engage frontline clinicians in the effort to reduce low-value care, the UCLA researchers hope that by publishing their findings they will help to catalyze a broader national movement. “There is a lot of interest in this work, and physicians recognize its importance,” Dr. May says. “In many cases we now have enough data to say when a service is appropriate and when it is not, and no one wants to perform an inappropriate service. Our first oath as physicians is to do no harm.”
Inflammatory bowel disease (IBD) is generally divided into two subtypes: ulcerative colitis and Crohn’s disease. But David Padua, MD, PhD, an assistant professor in the UCLA Vatche and Tamar Manoukian Division of Digestive Diseases and member of the research faculty at the UCLA Center for Inflammatory Bowel Diseases, is among a growing number of experts who suspect that IBD actually consists of many different subtypes—which may explain why it can be so hard to predict how an individual IBD patient will respond to a particular therapy.

“IBD can involve many different interactions in the body—diet and environmental exposures interface with genetics at the epithelial cell level as well as at the immune cell level, and if any of those go awry, that can lead to IBD,” Dr. Padua explains. “We have many pathways we can currently target to manage the inflammatory process with our current armamentarium of drugs, and many new drugs are in the pipeline looking at other strategies. But because IBD is so complex and there appear to be so many subtypes, the question is always which one to start with, and which one to move on to if the first medication doesn’t work. Currently, it’s a wait-and-see approach, but every clinician would love the ability to know in advance what therapy will work and what won’t for a given patient.”

“While this is an exciting time for IBD, it can be a confusing landscape for patients and providers, as novel therapies with various mechanisms of action become available,” adds Jenny Sauk, MD, the UCLA IBD center’s director of clinical care and an assistant clinical professor in the division. “With all of these promising therapies, it would be great to have sub-diagnosics to help guide our treatment decisions, and to better understand which patients are going to be at the highest risk of progression and complications. That’s the promise of applying precision health to IBD.”

The revolutions in genomic and information technologies are paving the way for the fulfillment of a long-held dream among clinicians—healthcare that takes into account individual characteristics to optimize diagnosis, treatment and prevention strategies. Seizing on the unprecedented opportunities, UCLA in 2017 launched the Institute for Precision Health to, among other things,
facilitate large-scale initiatives in genetic and genomic medicine and promote innovative discoveries that will help to usher in the new era.

“Advances in genetics and genomics are allowing us to have a complete picture of someone’s genetic makeup in a cost-effective manner, and to integrate that with other forms of genomic data,” says Daniel Geschwind, MD, PhD, senior associate dean and associate vice chancellor of precision health at UCLA. “This will help us to get a better grasp of which disorders individuals are at high risk for, or to better understand what is causing a current disorder and use that knowledge to optimize their treatment. At the same time, with the advances in computer science, machine learning and engineering, we can analyze the ‘big data’ we are collecting in ways that will present new patterns and generate totally new understandings of what is driving a particular disease.”

Clara Lajonchere, PhD, deputy director of the Institute for Precision Health at UCLA, believes the university is uniquely positioned to capitalize on these advances. “UCLA Health has established a substantial infrastructure, touching more than 4.7 million lives, with a robust electronic health record,” she says. “That, combined with the incredible diversity of Los Angeles, will allow us to capture genetic variability as we take a population health approach. And when you think about precision health, no single discipline can do this alone. UCLA not only has a world-class health system, but we have all of the medical school departments, engineering, computer science, bioinformatics, and all of the relevant social and physical sciences together on the same campus in a way that fosters the interdisciplinary collaboration that this undertaking requires.”

In bringing together these faculty, the institute is facilitating the development of platforms for big data integration, clinical diagnostics, and patient biobanking. The UCLA AtLAs California Health Initiative will create a biobank of nearly 150,000 blood samples from a representative cross-section of consenting UCLA patients, collected across many clinics at UCLA over a three-year period. This genotyping effort will likely include tens of thousand of patients with GI conditions, Dr. Geschwind says, providing a potential treasure trove of data for researchers. The institute will also apply technologies such as data-mining and machine-learning approaches.

The UCLA Vatche and Tamar Manoukian Division of Digestive Diseases is an active partner in the AtLAs Project and other institute initiatives. “We want to recruit as many of our patients to this effort as possible,” Dr. Sauk says. “As gastroenterologists we can provide not only blood samples for genetic analysis, but also tissue samples from colon biopsies, which we can then correlate with the genetic findings to learn more about how patients’ genetic makeup influences their response to therapy or their disease trajectory.”

“We are likely to discover over time that there are multiple subtypes of inflammatory bowel diseases, well beyond the current classifications,” Dr. Padua says. “The field of oncology is increasingly looking at the molecular mechanisms that are driving the tumor, and selecting therapies that address that specific aberration. We need to do that in IBD, and the only way to get there is through this precision health approach.”
Each summer, 5-8 high school students, undergraduates, medical students and medical residents spend three months as hepatology researchers in the UCLA Vatche and Tamar Manoukian Division of Digestive Diseases. Working part-time under the mentorship of the division’s hepatology faculty, and with their colleagues both in and out of the division, the participants take part in important clinical research and end up as co-authors on papers published in peer-reviewed scientific journals.

Between the clinical care and research he conducts as a hepatologist and professor in the division, Sammy Saab, MD, MPH, has a full plate of activities. But Dr. Saab decided to start the mentoring program, and continues to devote significant time during the summer to supervising the students and residents, to help shape the next generation of medical professionals.

“The idea is to expose participants to a world they might not otherwise see, in the hope that they will become excited about the possibilities and pursue a career in this area,” Dr. Saab explains. “A lot of people are interested in going into healthcare, but this introduces these individuals to another facet of medicine — research — that is critical to improving people’s quality of life and helping them live longer and better.”

In the six years since Dr. Saab established the program, every participant has been able to complete the work required to get on a publication as a co-author, Dr. Saab notes. “We design projects that allow these students and residents to be involved in the entire process — forming a hypothesis, conducting medical literature searches, developing methods, collecting and analyzing data, and contributing to the manuscript,” Dr. Saab says. Although the focus is on clinical research in hepatology, he notes that the skills learned by the program’s participants can easily be applied to basic research, and to other biomedical fields.

The work of the participants has been significant. Two high school students, for example, were part of a team that generated a hypothesis for the treatment of HIV-positive hepatitis C patients, after finding that the cure rate for mono-infected patients and co-infected patients was the same; their work led to a publication in the prestigious journal Hepatology. A UCLA undergraduate, working with Dr. Saab’s group as well as a radiologist who taught him how to read CT scans, contributed to a manuscript on the impact of muscle wasting on patients undergoing liver transplantation. A resident and an undergraduate collaborated on a study, accepted
Beyond the Scope, putting forth an argument for how hepatitis C could be eliminated in the United States.

It’s especially exciting and rewarding for the students to get to work as a team,” Dr. Saab says. “For example, the high school students are not only exposed to the work of attending physicians like me, but they also get to work with medical students and residents. It gives them the confidence to go forward.”

Mentorship that steers talented young people toward careers in liver-related medicine and research has public health benefits. “There’s a need for more hepatologists,” says Gina Choi, MD, an assistant professor in the division who specializes in transplant hepatology. Dr. Choi notes that antiviral medications now used to treat hepatitis C have made a huge difference, but fatty liver disease continues to be a major concern.

The UCLA Vatche and Tamar Manoukian Division of Digestive Diseases includes six full-time faculty members who are hepatologists — specially trained in both liver disease and transplant hepatology. “Many patients have abnormal liver tests which can be indicative of viral hepatitis, fatty liver and autoimmune liver disease,” Dr. Choi says. “We try to treat them, and if they develop liver failure, we can offer life-saving transplantation through one of the top programs in the country.”

As a group, the division’s hepatologists are internationally recognized for their clinical research. They are also heavily involved in educating medical students, residents, fellows, and the community. The Transplant Hepatology Fellowship Program, under the leadership of Steven-Huy Han, MD, a professor in the division, started in 2017, with one transplant fellow each year receiving advanced education in transplant hepatology. The annual UCLA Liver Diseases Symposium, held in Pasadena, is now in its 12th year, and the division will hold the 7th Annual UCLA-Mellinkoff Gastroenterology and Hepatology Symposium next spring.

While these efforts are providing hepatology education and training for health professionals who have already chosen their career path, the mentoring program continues to engage individuals during their formative years. Elizabeth Aby, MD, now a UCLA Health chief internal medicine resident, went through the summer program and has now been mentored by Dr. Saab for more than three years, during which she has worked with him in the hepatology clinic, shadowed him during liver transplant meetings, rounded with him on the inpatient hepatology service, and collaborated on four research papers that have been published, along with a review article currently in progress.

“It has been an incredible experience,” Dr. Aby says. “Not only is Dr. Saab a fantastic clinician educator and mentor, he has also helped me grow as a researcher. His mentorship has been instrumental to my career.” Dr. Aby is currently applying to a GI fellowship, with plans to become an academic hepatologist.

Matthew Ryan Viramontes was a first-generation college student at UCLA when he was drawn to the mentorship program, where he began to learn under the guidance of Drs. Saab, Aby and others. “I have been able to build lasting relationships and gain clinical and research experience that will help me in the future,” says Viramontes, who has begun applying to medical schools across the U.S. “This mentorship program has allowed me to see the life of GI and hepatology physicians and has steered me to aspiring to become a leader in the field.”
AWARDS AND ACHIEVEMENTS

Three of the UCLA Vatche and Tamar Manoukian Division of Digestive Diseases’ most distinguished faculty members — each a pioneer in his or her gastroenterology subspecialty — were recently recognized for their contributions in research and mentorship.

Emeran A. Mayer, MD
Ismar Boas Medal from the German Society for Gastroenterology, Digestive and Metabolic Diseases

Harry Pothoulakis, MD
2018 AGA Research Mentor Award

Yvette Taché, PhD
Andre Robert Prize
Emeran A. Mayer, MD
Ismar Boas Medal from the German Society for Gastroenterology, Digestive and Metabolic Diseases

Emeran A. Mayer, MD, director of the G. Oppenheimer Center for Neurobiology of Stress and Resilience and a professor in the UCLA Vatche and Tamar Manoukian Division of Digestive Diseases, received the Ismar Boas Medal from the German Society for Gastroenterology, Digestive and Metabolic Diseases. The award, named in honor of one of the leading historical figures in the field of gastroenterology, was presented at the society’s annual conference in September.

An internationally renowned leader in the clinical and research aspects of brain-body interactions, Dr. Mayer has made seminal contributions to the scientific understanding of the bidirectional communication between the brain and the gut in health and disease. He is a leading investigator in the study of brain-gut microbiome interactions in GI disorders, including functional and inflammatory bowel disorders and obesity. He has been continuously funded by the National Institutes of Health since 1989.

Dr. Mayer received his MD degree from the Ludwig Maximilian University in Munich, Germany, before completing his residency at the Vancouver General Hospital in Vancouver, Canada and then coming to Los Angeles for his GI fellowship at the UCLA/VA Wadsworth Training Program. In addition to being a member of the division’s faculty, he is a professor of physiology and psychiatry at UCLA.

Harry Pothoulakis, MD
2018 AGA Research Mentor Award

Harry Pothoulakis, MD, the Eli and Edythe Broad Chair in Medicine and director of basic research for the UCLA Center for Inflammatory Bowel Diseases in the UCLA Vatche and Tamar Manoukian Division of Digestive Diseases, received the 2018 Research Mentor Award from the American Gastroenterological Association (AGA) Cellular and Molecular Gastroenterology Section. The award, bestowed at Digestive Disease Week 2018 last April, recognizes AGA members for their achievements as outstanding mentors in a specific area of research.

Dr. Pothoulakis has been a primary mentor for approximately 50 MDs, PhDs, and postdoctoral fellows since becoming a faculty member more than three decades ago, helping them to launch their independent research programs before going on to successful careers in academia and industry. “It’s very nice to be recognized for work that I feel is so important to advancing the field of gastroenterology,” Dr. Pothoulakis says. “Mentoring the next generation is one of the most important responsibilities of any academic faculty member. We teach people not only how to develop a research program, but also how to move up the academic ladder. That’s the type of guidance that helped me to become an independent investigator.”

Dr. Pothoulakis trained at Boston University under the mentorship of Dr. J. Thomas Lamont. “Dr. Lamont is recognized as one of the best mentors of his generation in the GI field,” Dr. Pothoulakis says. “His door was always open, and I have tried to carry that tradition forward.”

Yvette Taché, PhD
Andre Robert Prize

Yvette Taché, PhD, a distinguished professor in the UCLA Vatche and Tamar Manoukian Division of Digestive Diseases, was awarded the prestigious Andre Robert Prize for her contributions to the field of GI pharmacology. The award, announced at the International Union of Basic and Clinical Pharmacology GI Section’s 10th International Symposium on Cell/Tissue Injury & Cytoprotection/Organoprotection (ISCTICO) series held in Kyoto, Japan in July, commemorates the work of the late André Robert, MD, PhD, originator of the concept of gastric cytoprotection.

The first ISCTICO symposium was held in Germany in 1986; over the years, it has continued to provide a forum for experts to present and integrate new findings regarding the mechanisms, manifestations, and consequences of cell and tissue injury as well as tissue repair/ulcer healing. Dr. Sandor Szabo, a professor of pathology and pharmacology at the UC Irvine School of Medicine and chair of the symposium standing committee, explains the series has evolved from focusing on the prevention of acute gastric mucosal injury to “gastroprotection,” including not only prevention, but also treatment of ulcerative and inflammatory acute and chronic lesions in the upper and lower GI tract.

In more than 35 years on the UCLA faculty, Dr. Taché has, with her colleagues, helped to shape the understanding of the complex brain-gut interactions. Her group was among the first to describe the role of peptides in brain to modulate gut function. In particular, her team established the dual actions of the vagus nerve to induce gastric cytoprotection or erosions as a function of the intensity of central vagal activation and delineated the underlying mechanisms in the brainstem and stomach. The role of corticotropin-releasing factor signaling in the brain and locally in the gut in mediating stress-related gut function alterations was of significant interest in using CRF receptor antagonists as potential therapeutic agents for functional stress-sensitive diseases such as irritable bowel diseases.
CURE Annual Research Meeting and Poster Session | March 22, 2019

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Agenda

7:45 am  Registration and Breakfast
8:30 am  Welcome Remarks ................................................................. Joseph R. Pisegna, MD, UCLA

Session I: Clinical / Translational
Moderators: Lin Chang, MD, UCLA and Dennis M. Jensen, MD, UCLA
8:35 am  Leveraging Signaling and Metabolic Vulnerabilities by Chronic Type I IFN in Pancreatic Cancer .......................................................... Timothy R. Donahue, MD, UCLA
9:05 am  Recent Advances in HIV Transmission Prevention and Treatment .................................................. Peter Anton, MD, UCLA
9:35 am  Break

Session II: Translational / Basic Science
Moderators: Joseph R. Pisegna, MD, UCLA and Harry Pothoulakis, MD, UCLA
9:50 am  Cholesterol and Phospholipid Metabolism in Intestinal Homeostasis ............................................................. Peter Tontonoz, MD, PhD, UCLA
10:20 am  DNA Methylation Analysis Reveals Differences in Aging Between Human Small Intestine and Colon ........................................................................... Leanne Jones, PhD, UCLA
10:50 am  Break
11:05 am  Remarks ......................................................................................... Eric Esrailian, MD, MPH, UCLA
11:10 am  State of CURE .................................................................................. Enrique Rozengurt, DVM, PhD, UCLA
11:25 am  John H. Walsh Memorial Lecture
Insights into Inflammatory Bowel Diseases Through the Lens of Human and Experimental Models ......................................................................................... Eugene Chang, MD, University of Chicago
12:30 pm  Lunch

Session III: Looking to the Future
Moderator: Catia Sternini, MD, UCLA
1:30 pm  Master Transcription Factors Form Inter-Connected Circuitry and Dysregulate Transcriptional Network in Esophageal Cancer ................................................................. Dechen Lin, PhD, Cedars Sinai Medical Center, Los Angeles
1:45 pm  Corticotropin-Releasing Hormone Mediated Enteric Gial Cell Function During Colitis .................................................. Jill Hoffman, PhD, UCLA
2:00 pm  Sex, Bugs and Drugs: Microbiome and Mucosal Interactions in HIV Pathogenesis ................................................................. Jennifer A. Fulcher, MD, PhD, UCLA
2:15 pm  Break

Poster Sessions
2:30 pm  Poster Session - Even Numbered Poster Session
3:00 pm  Poster Session - Odd Numbered Poster Session
4:30 pm  Adjourn
Amid the continuing national urgency to engage more young people in science, technology, engineering and math (STEM) education and careers, the UCLA Vatche and Tamar Manoukian Division of Digestive Diseases is providing underprivileged high school students with hands-on experiences and mentorship in STEM activities on the UCLA campus.

The program, called STEM at UCLA, enrolls approximately 35 students a year for a series of four full-day Saturday sessions in which they tour labs; interact with STEM students, faculty and other professionals at UCLA; participate in laboratory experiments and activities; and learn about STEM fields and career paths. At the end of the program, the students receive a certificate of completion and contact information for key staff to allow them to follow up.

The students are selected through a competitive application process from among the scholars of the Fulfillment Fund, the nonprofit college access organization founded by Dr. Gary Gitnick, co-chief of the division. “These students typically have had minimal exposure to STEM fields — they have expressed an interest in the subject matter, but they don’t know what to do with that interest,” explains program director Jill Hoffman, PhD, an adjunct assistant professor in the UCLA Center for Inflammatory Bowel Diseases, based in the division. “Our goal is to expose them to STEM activities and the opportunities that are out there for them.”

For their hands-on experiences in Dr. Hoffman’s laboratory, the students don protective gear and perform experiments. They hear from Dr. Hoffman and members of her lab, as well as other members of the division. The program also brings in partners from elsewhere on the UCLA campus, and outside of UCLA. “We want the students to have a breadth of experiences,” Dr. Hoffman says.

At the beginning of STEM at UCLA, the participants are surveyed about their interests. When members of this year’s group indicated an interest in aerospace engineering, the program partnered with the Rocket Project at UCLA, a student-run engineering outreach organization dedicated to inspiring youth and promoting STEM; this fall, students will learn about and participate in the launching of a rocket on the UCLA Intramural Field.

STEM at UCLA has also forged a partnership with CityLab, a science educational program run by UCLA undergraduate and graduate students to introduce high school students to biotechnology fields through hands-on experiences.

The STEM at UCLA participants also brainstorm about STEM careers. “From the first session to the last session it’s amazing to see how these students’ concept of what they can do in STEM expands based on the exposure we give them,” Dr. Hoffman says.

As he nears completion of this year’s program, Daniel Flores, a senior at New Designs Charter School in Los Angeles, is pondering a future as a bio-medical engineer. “Our world depends on STEM,” he says. “To be able to take this step as a teen, consulting with STEM professionals and engaging in hands-on tasks, has been inspiring.”
New Clinical Faculty Members

Scott A. Hahm, MD | Health Sciences Clinical Instructor of Medicine
Dr. Hahm received his undergraduate degree from the University of Wisconsin-Madison with a triple major in medical microbiology & immunology, biology, and zoology. After college, he spent two years at UCLA, on the Westwood campus, working in basic science research. Dr. Hahm then attended medical school at New York Medical College and returned to Los Angeles for his internship and residency in internal medicine at the University of Southern California. Dr. Hahm completed his fellowship training in gastroenterology and hepatology at Cook County Hospital in Chicago. He went on to pursue additional training at Northwestern University Hospital in Chicago to further specialize in gastrointestinal motility disorders. He is board-certified in internal medicine and gastroenterology.

Ara Kardashian, MD | Health Sciences Clinical Instructor of Medicine
Dr. Kardashian earned his undergraduate degree in biomedical and electrical engineering from Duke University. After earning his medical degree from New York Medical College, he completed internship and residency in internal medicine at Los Angeles County+USC Medical Center. He then went on to train in gastroenterology and hepatology at Scripps Clinic and Scripps Green Hospital in San Diego before joining UCLA. Dr. Kardashian is board-certified in internal medicine and gastroenterology. He is a member of the American College of Gastroenterology, the American Gastroenterological Association, and the American Society for Gastrointestinal Endoscopy.

Steven Kind, MD | Health Sciences Assistant Clinical Professor of Medicine
Dr. Kind earned his medical degree from Keck School of Medicine of the University of Southern California. He then completed his residency in internal medicine and fellowship in gastroenterology at Kaiser Sunset in Los Angeles, CA. After graduating, he returned to his hometown, Thousand Oaks, CA, where he was in private practice for more than 20 years. He is board-certified in gastroenterology.

Divya Mallam, MD | Health Sciences Clinical Instructor of Medicine
Dr. Mallam received her bachelor of science in neuroscience from UCLA. She then earned her medical degree from SUNY Downstate, and completed her internship and residency in internal medicine at Harbor-UCLA Medical Center. She subsequently pursued her fellowship training in gastroenterology at SUNY Downstate Medical Center. Additional training in gastrointestinal motility and functional disorders was completed at Cedars-Sinai Medical Center. Dr. Mallam is board-certified in internal medicine and gastroenterology.

Laura McEnerney, MD | Health Sciences Clinical Instructor of Medicine
Dr. McEnerney received her undergraduate degree in molecular and cellular biology from the University of Illinois. She then attended Southern Illinois University School of Medicine, where she received her MD degree. She completed her internal medicine residency and gastroenterology fellowship at the University of Southern California.

Dr. McEnerney is board-certified in internal medicine and gastroenterology and is a member of the American Gastroenterological Association and the American College of Gastroenterology. Dr. McEnerney is fluent in Spanish.
Gobind Sharma, MD | Health Sciences Clinical Instructor of Medicine

Dr. Sharma earned his undergraduate degree at Drexel University in Philadelphia, graduating summa cum laude with a degree in biological sciences. He remained in Philadelphia and received his medical degree from Drexel University College of Medicine. He completed his residency at Cedars-Sinai Medical Center and then returned to Drexel University to complete his fellowship in gastroenterology. Following his training, he returned to his hometown of Pittsburgh to practice as an assistant clinical professor with the University of Pittsburgh Medical Center (UPMC). Along with teaching responsibilities at UPMC, he worked closely with the division to create and establish a university-based GI practice at UPMC-Mercy Hospital.

Dr. Sharma is board-certified in gastroenterology and internal medicine. He is enthusiastic about medical education and mentoring, and enjoys working with trainees at all levels. He is a member of the American Gastroenterological Association and the American Society for Gastrointestinal Endoscopy.

Simi Singh, MD | Health Sciences Clinical Instructor of Medicine

Dr. Singh attended Drexel University where she completed a combined BS in biology/MD program. During her time in Philadelphia, she was actively involved in coordinating volunteer services for women’s community clinics. She completed her residency in internal medicine as well as her fellowship in gastroenterology at Mount Sinai Beth Israel in New York. During her training, she developed a particular interest in women’s gastrointestinal health and hepatology.

Dr. Singh is a member of the American Gastroenterology Association, the American College of Gastroenterology, and the American Society of Gastrointestinal Endoscopy. Dr. Singh is board-certified in internal medicine and gastroenterology.

Anna Skay, MD | Health Sciences Clinical Instructor of Medicine

Dr. Skay received her bachelor of science degree at UCLA in molecular, cell and developmental biology, graduating cum laude with highest departmental honors. She received her medical school training from Keck School of Medicine at University of Southern California. She completed her internship and residency in internal medicine, as well as gastroenterology and hepatology fellowship at Los Angeles County USC Medical Center.

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

Beshoy T. Yanny, MD | Program Leader, Hepatology, UCLA Medical Center, Santa Monica

Dr. Yanny specializes in general and transplant hepatology and focuses on treating patients with a wide spectrum of liver disorders. He is well versed in the treatment of hepatitis C with the new direct-acting antiviral agents. He cares for patients with liver cirrhosis and its spectrum of complications. He also cares for patients before and after liver transplantation. His research interests include non-alcoholic steatohepatitis, hepatocellular carcinoma and viral hepatitis B and C.

Dr. Yanny completed his internal medicine residency at Keck School of Medicine and county hospital of USC. Following his internal medicine training, he served as the inaugural transplant hepatology hospitalist at Kaiser Permanente, Los Angeles Medical Center for one year. He then completed his gastroenterology and hepatology fellowship at Kaiser Permanente, Los Angeles Medical Center. Dr. Yanny moved to UCLA as the inaugural transplant hepatology fellow, where he completed his training. He is board certified in internal medicine and gastroenterology and is board eligible for transplant hepatology. Dr. Yanny has presented research at multiple national and international societies including AASLD, EASL, GUILD, and DDW.
The 7th Annual UCLA-Mellinkoff Gastroenterology and Hepatology Symposium was designed to offer healthcare professionals practical and evidence-based approaches to diagnostic and treatment challenges that can have a significant impact on their daily practice. UCLA gastroenterology and hepatology experts and other renowned physicians will provide education to attendees through illustrative cases, lively panel discussions, formal lectures, Q & A and video sessions. Audience participation is highly encouraged to further enhance the learning experience.

Registration and Course Information

Go to www.cme.ucla.edu/courses

Hands-On Session*

The hands-on session will provide a valuable learning opportunity, though no accredited hours will be issued for this portion.

Overnight Accommodations

A limited block of rooms, at a special rate of $299 + tax (deluxe) has been reserved at The Beverly Hilton. To receive the special rate, you must make your reservation before the room block is filled and by the expiration date of February 5, 2019. To reserve a room, call 1-800-HILTONS and ask for the UCLA Digestive Diseases Mellinkoff Symposium or make a reservation online at https://aws.passkey.com/e/49710982.

For more information about the hotel, visit www.beverlyhilton.com

Course Director

V. Raman Muthusamy, MD, FACP, FASGE, AGAF
Director of Endoscopy, UCLA Health System
Professor of Clinical Medicine
Vatche and Tamar Manoukian Division of Digestive Diseases
David Geffen School of Medicine at UCLA

Course Co-Director

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Co-Chief, Vatche and Tamar Manoukian Division of Digestive Diseases
Director, Melvin and Bren Simon Digestive Diseases Center
Lincy Foundation Chair in Clinical Gastroenterology
Associate Clinical Professor of Medicine
David Geffen School of Medicine at UCLA

Accreditation

CME Credits

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 14.25 AMA PRA Category 1 Credits™. Physicians should claim only the credit commensurate with the extent of their participation in this activity.

ABIM MOC

Successful completion of this CME activity, which includes participation in the evaluation component, enables the participant to earn up to 14.25 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 the activity.

CE Contact Hours

Provider approved by the California Board of Registered Nursing, Provider Number 12511 for 8 contact hours for participation in day 1 and 9 contact hours for participation in day 2.

ABCGN

According to the criteria of the American Board of Certification for Gastroenterology Nurses (ABCGN), 11.01 hours earned in this activity are considered GI-specific for the purpose of recertification by contact hours through the ABCGN.
Mellinkoff Agenda

Friday, March 1

7:00 am Registration and Breakfast
7:50 am Welcoming Remarks ........................................ Eric Esrailian, MD, MPH
7:55 am Course Overview .............................................. V. Raman Muthusamy, MD

Hot Topics ................................................................. Moderator: V. Raman Muthusamy, MD

8:00 am The Microbiome and the Brain-Gut Connection:
What You Need to Know .............................................. Emeran A. Mayer, MD
8:20 am Precision Medicine: How is it Changing
the Management of GI Cancers? ............................... Zev Wainberg, MD
8:40 am State of the Art in Endoscope Reprocessing:
What You Should Be Doing Now ............................... Andrew Ross, MD
9:00 am Q & A ................................................................ Panel
9:20 am Break

Functional Bowel Disease ........................................ Moderator: Lisa D. Lin, MD, MS

9:40 am An Interactive Case-Based Discussion
• Role of Brain-Gut Interactions in IBS
• Insights into the Placebo Response in IBS Patients
• Pharmacotherapy for IBS: What Do We Have in Our Toolbox?
• Complementary and Alternative Medicines in IBS: Myths or Facts?
• Emerging Therapies for IBS
• Dietary Interventions for IBS Patients

Panel...J. Randall Hecht, MD, Stephen Kim, MD, Aasma Shaukat, MD, MPH
Emeran A. Mayer, MD, Kirsten Tillisch, MD

12:10 pm Lunch

Colorectal Cancer: Screening, Controversy and Management
Moderator: Folasade P. May, MD, PhD, MPhil

1:10 pm An Interactive Case-Based Discussion
• 80% by 2018: Where are We Now and Where are We Going?
• Improving Quality in Colonoscopy
• Endoscopic Mucosal Resection of Colon Polyps: Are You Doing It Right?
• An Update on CRC Treatment and Survival

Panel...J. Randall Hecht, MD, Stephen Kim, MD, Aasma Shaukat, MD, MPH

3:00 pm Break

Endoscopy Video Forum ............................................ Moderator: Bennett E. Roth, MD

3:20 pm From Common to Exotic: The Full Spectrum of GI Endoscopy
Panel...Dennis M. Jensen, MD, Stephen Kim, MD, V. Raman Muthusamy, MD, Andrew Ross, MD, Alireza Sedarat, MD, Adarsh M. Thaker, MD

4:20 pm Adjourn Didactic Session
5:30 pm Adjourn Hands-On Session*

*Hands-On Session Open to All Attendees / 4:30 pm*

This hour-long, hands-on session will provide a valuable learning opportunity, though no accredited hours will be issued for this portion of the program. It will feature up to seven stations demonstrating diverse endoscopic procedures, technologies and techniques using ex-vivo pig stomachs and/or other methods. The topics include the use of endoscopic mucosal resection, retrieval of difficult foreign bodies and food impactions, oncolytic endoscopy, treatment for Barrett’s esophagus, closure of perforations, dealing with fistulas, control of bleeding and more.

Faculty: Dennis M. Jensen, MD, Stephen Kim, MD, V. Raman Muthusamy, MD, Andrew Ross, MD, Bennett E. Roth, MD, Alireza Sedarat, MD, Adarsh M. Thaker, MD

Saturday, March 2

7:00 am Registration and Breakfast
7:55 am Welcoming Remarks ........................................ V. Raman Muthusamy, MD

Inflammatory Bowel Diseases .................................. Moderator: Jenny Sauk, MD

8:00 am An Interactive Case-Based Discussion

Management of Crohn’s Disease
• Surgery vs Medical Therapy in Crohn’s Disease
• Therapeutic Drug Monitoring
• Positioning of Therapies in Crohn’s Disease

Management of Ulcerative Colitis
• Positioning of Biologics and New Therapies in Ulcerative Colitis
• Recognizing and Managing Dysplasia in Ulcerative Colitis
• Medication Withdrawal and How to Manage Relapse

Panel...Stephen B. Hanauer, MD, Peter Higgins, MD, PhD, MSc, Mary Kwaan, MD, MPH, Hamed Nayeb-Hashemi, MD

10:30 am Break

Liver Disorders ......................................................... Moderator: Beshoy T. Yannry, MD

10:50 am Hepatitis B: An Update ...................................... Steven-Huy Han, MD
11:10 am The New Face of Hepatitis C .............................. Sammy Saab, MD, MPH
11:30 am Autoimmune Hepatitis and PBC ........................ Gina Choi, MD
11:50 am Epidemiology of NASH ................................. Simon W. Beaver, MD, PhD
12:10 pm Challenging Patient Cases and Q & A .......... Panel including Francisco Durazo, MD
12:30 pm Lunch

Pancreaticobiliary Disease ........................................ Moderator: Stephen Kim, MD

1:30 pm An Interactive Case-Based Discussion

Diagnosing and Managing Pancreatic Adenocarcinoma
• Diagnostic Tests to Detect Pancreas Cancer
• Role of Staging, Assessing Resectability and Surgical Outcomes: The UCLA Experience
• Chemoradiation Options to Treat Pancreas Cancer
• Endoscopic Palliation of Pancreas Cancer

Managing Complications of Acute and Chronic Pancreatitis
• Diagnosis, Etiology and Complications of Acute Pancreatitis
• Managing Pseudocysts and Walled-Off Necrosis: The Virginia Mason Approach
• Endoscopic Treatment for Chronic Pancreatitis: Worth the Effort?
• Pancreatic Fluid Collections and Chronic Pancreatitis: When to Call the Surgeon?

Panel...Timothy R. Donahue, MD, V. Raman Muthusamy, MD, Andrew Ross, MD, Alireza Sedarat, MD, Zev Wainberg, MD

3:10 pm Break

Upper GI Disorders .................................................. Moderator: Kevin Ghassemi, MD

3:30 pm An Evidence-Based Approach to PPI Use in 2019 .... Kevin Ghassemi, MD
3:50 pm Endoscopic Treatments for GERD: Finally Ready for Prime Time?...Alireza Sedarat, MD
4:10 pm Managing Motility Disorders of the Esophagus and Stomach...Jeffrey L. Conklin, MD
4:30 pm An Update on Celiac Disease ............................. Guy A. Weiss, MD
4:50 pm Challenging Patient Cases and Q & A ............... Panel
5:10 pm Course Summary and Final Announcements .... V. Raman Muthusamy, MD
5:15 pm Adjourn
UCLA Gastroenterology and GI Surgery ranked No. 7 in the nation by *U.S. News & World Report* in its survey. UCLA Health hospitals in Westwood and Santa Monica also ranked No. 7 in the nation.