

# Beyond the Scope

A REPORT OF THE UCLA DIVISION OF DIGESTIVE DISEASES

COVER STORY PAGE 4

## Social Medica

Using Social Media to Improve  
Health Care Quality



## Going **Beyond** the Scope

Delivering state-of-the-art, patient-centered care is paramount to our mission. But *Beyond the Scope* of our clinical work, we're educating students, trainees and practicing physicians or generating research findings that pave the way toward improved diagnosis and treatment.

In March 2013, we will hold the first UCLA-Mellinkoff Gastroenterology Symposium, a video and case-based CME program on current practice and future trends in GI and liver disorders (pg. 12). We are especially proud to name this program after our first division chief, Sherman M. Mellinkoff, MD, emeritus dean and emeritus professor of medicine at the David Geffen School of Medicine at UCLA. A passionate advocate for medical education and a highly respected clinician-teacher, Dr. Mellinkoff headed our division from 1953 to 1962, just before beginning a 24-year term as dean of the medical school. Please join us for this exciting symposium.

A special recognition goes out to Dean Jensen, MD, the 2012 recipient of the prestigious ASGE Rudolf V. Schindler Award (pg. 1). Dr. Jensen is the third UCLA faculty member to receive this award, making the UCLA division the most decorated with the honor. Past honorees include Melvin Schapiro, MD (1990) and Wilfred M. Weinstein, MD (2003).

We have recently recruited a group of talented investigators whose research initiatives and clinical programs have strengthened our division. Examples include Dimitrios Iliopoulos, PhD, who has brought his team from Harvard Medical School to establish the new Center for Gastrointestinal Systems Biology (pg. 2); Martijn van Oijen, PhD, who is exploring ways to use social media to improve the quality of healthcare (pg. 6); and Lynn S. Connolly, MD, MSCR, part of a team that is shedding new light on the role of brain pathways in obesity (pg. 10). We also highlight the cutting-edge research of Noriyuki Kasahara, MD, PhD, who has initiated a first-in-human clinical trial to test his novel gene therapy technology in brain cancer patients (pg. 8).

A strong research program is critical not only for the contributions it can make toward discoveries that improve digestive disease diagnosis and management, but for the environment it fosters within our practice community. By going *Beyond the Scope*, we ensure that patients receive the most advanced and compassionate care.

### *Gary Gitnick, MD*

Chief, Division of Digestive Diseases  
Fran and Ray Stark Foundation Chair  
Professor of Medicine  
David Geffen School of Medicine at UCLA

# Dennis (Dean) M. Jensen, MD, Earns Top Honor

American Society of Gastrointestinal Endoscopy (ASGE) honored Dean Jensen, MD, with the Rudolf V. Schindler Award at its annual award ceremony on May 20 in San Diego, California. The Schindler Award is the society's highest honor, recognizing the person whose accomplishments in endoscopic research, teaching or service to the society exemplifies the standards of Dr. Schindler, who founded the organization that was the forerunner of ASGE.

Dr. Jensen is associate director of UCLA's CURE: Digestive Diseases Research Center, where he directs the Human Studies Core. He also leads the CURE Hemostasis Research Group, which has conducted research in diagnosis and endoscopic hemostasis of gastrointestinal hemorrhage, primary and secondary prevention of GI bleeding, GI outcomes and health services and endoscopy technology assessment.

For more than three decades, Dr. Jensen has conducted research, taught and provided patient care at UCLA as well as at the Veterans Administration West Los Angeles Medical Center. His investigator-initiated research has been continuously funded for over 30 years by the NIH, VA, Department of Defense, GI Foundations and industry.

Calling the award a wonderful tribute Dr. Jensen says, "It gives important recognition to my colleagues, who for many years have worked side-by-side with me. My family, my fellows and my GI colleagues have given me the inspiration, support and encouragement to pursue my ideas."

Saying that few people showed interest in his area of research when he began work in his

field, "this award also offers encouragement to researchers who are now just getting their start to pursue their own areas of interest and to persevere."

Dr. Jensen's work has contributed to significant changes in the field of gastrointestinal hemostasis that have occurred over the span of his career. Diagnosing patients with ulcers and other GI bleeding has evolved from X-ray and angiography to visualization using endoscopy, including small bowel endoscopy, colonoscopy and capsule endoscopy. At the same time, treatment has moved from surgical intervention to medical therapies and endoscopic treatments.

"This field has changed markedly in patient care — whether for ulcers, varices, colon lesions or diverticular bleeding — and it's been driven by research and other technological advances," explains Dr. Jensen.

His current research interest is in the assessment and treatment of patients with small bowel and colonic bleeding. Conducting randomized control trials, cohort observational studies and technology assessment studies, Dr. Jensen hopes to document the most effective ways to care for these patients.



For over 12 years, Dr. Jensen has directed the NIH Institutional Research Training Grant (T32) for UCLA's Division of Digestive Diseases. In this role, he helps trainees in adult and pediatric gastroenterology, surgery and in some cases pathology determine research areas to study in digestive physiology and pathophysiology. "My role with the training grant extends my interest beyond my own work to the goal of moving the whole field of gastroenterology forward," states Dr. Jensen.

Colleagues praised Dr. Jensen as he accepted the Schindler Award. "In the world of gastrointestinal endoscopy, Dean Jensen stands out as an iconic character," declared Jonathan Cohen, MD, of NYU Langone Medical Center. "Dean has consistently championed the field of endoscopic investigation. He cared about outcomes research before it came in vogue."

Dr. Jensen plans to continue his research, mentoring, patient care and teaching at UCLA, CURE and the VA.

# UCLA Establishes the First Center for Gastrointestinal Systems Biology

**With the establishment of the new Center for Gastrointestinal Systems Biology (CGSB), UCLA has instituted a new paradigm for the rapid identification of new therapeutic agents to treat gastrointestinal diseases. This center will be the first GI-focused systems biology center in the world and will employ the latest highly automated technology to extract data from a large number of patient tissue samples in an effort to identify treatments from a large collection of potentially therapeutic compounds. The goal is to significantly reduce the time it now takes to develop new treatments by using high throughput technologies.**

Dimitrios Iliopoulos, PhD, Maria Hatzia Apostolou, PhD, and Christos Polyta rchou, PhD, recently joined UCLA from Harvard Medical School, where they began to develop this approach to GI research. Dr. Iliopoulos, currently an associate professor of medicine at UCLA, will be the director of this new center. Drs. Hatzia Apostolou and Polyta rchou currently are assistant professors at UCLA and will be program leaders.

“Systems biology is an approach that combines different specialties to contribute in many different ways to create an understanding of gastrointestinal disease pathogenesis and develop therapies based on that understanding,” explains Dr. Iliopoulos. The UCLA Center for Gastrointestinal Systems Biology will bring together a multidisciplinary group that includes gastroenterologists, medical oncologists, surgical oncologists, cancer biologists, computer scientists and biomedical engineers in an interactive and collaborative environment.

## Harnessing Technology and the Power of Scale

Technology will play a key role in the new center. Its large-scale approach to tissue analysis and therapeutic compound identification means that it will be processing hundreds of thousands of samples each year — multiple orders of magnitude more than that of a typical GI research laboratory. CGSB will rely on high-throughput, highly automated and robotic systems, including platforms for biobanking, generation of novel cellular systems, RNAi screening, drug discovery and bioinformatics.

To provide the volume of samples necessary to perform such large-scale analysis, the center will integrate with UCLA Center for Inflammatory Bowel Diseases and other UCLA existing gastrointestinal clinical practices, and is forming collaborations with other centers all over the world to share tissue samples, knowledge and technologies.

In the past, larger GI research studies have attempted to integrate the analyses performed at different centers to generate large collections of data from which they would attempt to draw inferences. But according to Dr. Iliopoulos, “You cannot integrate them because they have been processed, from the first step, in a different way. It is like trying to put together the pieces of a puzzle in order to see a large picture, but finding they don’t fit.”

From each sample of patient tissue, the researcher can extract different types of biological information. GI research labs usually extract one type of information — DNA, RNA or proteins — and perform their analyses. The center will perform all these analyses on each sample, yielding more data to help understand disease pathogenesis. To process the vast amount of data collected, the center includes software engineers and mathematicians who will develop specialized programs to meet the center’s data analysis needs.

## An Unbiased Approach to Discovery

The limited capacity traditionally available for gastrointestinal research has provided an incentive for investigators to take a biased approach in their choice of focus. Being aware of their limitation in analyzing the great number of biological factors that could yield a positive result, researchers have tended to show a bias toward selecting familiar areas of research or depending on unreliable indicators — such as large numeric differences in the expression levels of a given gene.

While biased selection can yield fortunate results, CGSB will increase chances for success by analyzing a large number of biological factors. Raw analytical power alone will greatly improve the center’s odds of identifying factors in disease pathogenesis and matching them to useful therapeutic compounds.

In addition, CGSB will narrow its field of selection by applying network analysis to understand how the factors that affect disease processes interrelate, with some factors functioning as central regulators of network blocks. By identifying and disabling the central regulators, researchers can sometimes neutralize the whole network block. Dr. Iliopoulos explains, “This kind of analysis applies to any type of network — even social networks — but has only recently started being applied to medicine.”

## Research Programs

When the new research center becomes operational in early 2013, inflammatory bowel diseases and GI cancers will be the first areas of research to benefit from this new scale of analysis. The program for inflammatory bowel diseases will be headed by Dr. Polyarchou and will focus on ulcerative colitis and Crohn’s disease. Beyond their health effects, these diseases can place a significant burden on patients’ quality of life and ability to work productively. The first aim of this research program would be to identify the alterations in the expression levels of all the coding and non-coding genes (transcriptome) and also of their chromatin regulators (epigenome) between healthy individuals and IBD patients. The differentially expressed genes could be potentially used as biomarkers and therapeutic targets.

Several research programs will be developed related to GI cancer research. The GI Cancer Biology Program will be headed by Dr. HatziaPOSTOLOU. This program will aim to develop new therapies for colon, liver and pancreas cancer, the latter two being very aggressive cancers for which there are currently few good pharmacologic treatments available. In addition, the Cancer Stem Cell Biology Program will be headed by Dr. Iliopoulos. This program will aim to characterize in the molecular level and identify novel drugs against cancer stem cell populations derived from GI human cancer tissues. Furthermore, the Tumor Microenvironment Program will be headed by Dr. Stavroula Baritaki and its aims is to identify the role and function of the different immune cell populations surrounding the epithelial compartment of a colon tumor. Identification of novel drugs targeting these immune cells could have therapeutic potential for colon cancer patients.

In addition to these programs, the Adipocyte Biology Program, headed by Dr. Iordanis Karagiannidis, will aim to identify the contribution of obesity in the development of IBD and GI cancers; the Neuropeptide Biology Program, headed by Dr. Harry Pothoulakis, aims to identify

the role and function of neuropeptides in the pathogenesis of IBD and GI cancers; and the Stem Cell Biology Program, headed by Dr. Daniel Hommes, will aim to develop novel technologies toward the purification, molecular characterization, ex vivo expansion and administration of stem cells in IBD patients.

## Educational Component

Because the center’s approach represents a significant new direction in gastrointestinal research, Dr. Iliopoulos stresses the benefit of educating others about its methods. “It’s very important that the new generation of gastroenterologists and clinicians be aware of these techniques that are now new to them,” he says. “When they understand how the system works, they’re better able to participate in the research.”

In addition to developing a course to teach fellows at UCLA about novel technologies and how they can be integrated into their own research and clinical practices, the new center plans to host seminars and lectures to share its methods with clinicians and scientists from around the world.



*Dimitrios Iliopoulos, PhD, Maria HatziaPOSTOLOU, PhD, and Christos Polyarchou, PhD*

# Social Medica



Twenty years ago, people who wanted to know more about symptoms they were experiencing or a diagnosis they had just received might consult a reference book – remember the encyclopedia? – or call a friend or family member. Today, a simple Google search can unearth more reading material on a health topic than anyone could hope to sift through. And in addition to friends and family members, patients can consult a vast community online, including peers who have experienced similar symptoms and diagnoses.

The recent explosion in popularity of social networking sites, along with the ubiquity of mobile devices that can access them, have only accelerated the information-sharing trend. On Twitter, for example, individuals with chronic illnesses “tweet,” in 140 characters or fewer, details about their daily symptoms, disease management and coping mechanisms for anyone to see. Patients whose paths would otherwise never cross exchange intimate details about living with their condition.

It goes without saying that the Internet has revolutionized the way patients learn about their illness and interact with their health care providers. But Martijn van Oijen, PhD, assistant professor in UCLA’s Division of Digestive Diseases, points out that these changes have also created important new opportunities for researchers and clinicians to glean information on how patients are experiencing their illness – and that these opportunities remain largely untapped. “In the past, we could never know what patients were talking about outside the clinic,” Dr. van Oijen notes. “Today, we can go online and see what they’re looking up, what information they have, their concerns and their needs. This can be used to improve the quality of care.”

The traditional way of learning about the unmet needs of patients with a chronic condition has been to rely on data from patient surveys, interviews and focus groups. Dr. van Oijen and colleagues have embarked on research to determine the extent to which Twitter and other social media can be employed to find and track patients, and to measure patient-reported outcomes. Dr. van Oijen has coined a new term, Social Medica, which he defines as the use of social media to improve health care quality; he and others have taken to using the #socialmedica hashtag on Twitter.



*Above: U.S. map; left inset photo: close-up of Los Angeles, California. Blue dots are locations of Twitter tweets, orange dots are locations of Flickr (for sharing photos), and white dots are locations that have been posted to both.*

His group recently completed a feasibility study to determine whether patients with Crohn’s disease could be easily identified on Twitter, and to explore how the social media site could be mined to better understand the impact of the condition. Crohn’s disease, an inflammatory disease of the GI tract associated with a significant quality of life burden, was chosen in part because, although currently available therapies are becoming increasingly effective, the patient population continues to have many unmet needs. Dr. van Oijen decided to focus initially on Twitter because unlike Facebook posts, most tweets can be seen by everyone, and subjects are easily searchable. As of January 1, 2012, more than 380 million Twitter user profiles had been created worldwide, including more than 107 million in the United States. The most active Twitter users tend to be young adults, providing a good match with the demographic of the Crohn’s disease population.



RONAL  
UCLA

*Martijn van Oijen, PhD*

For the feasibility study, his group analyzed all tweets in English or Dutch (Dr. van Oijen's native language) over a one-month period that included the word "Crohn," then classified them based on their content into five groups – patient, relative or friend, pharmaceutical company, health care professional, or foundation/non-profit organization. To Dr. van Oijen's surprise, of the 2,236 original Crohn-containing tweets, 44% originated from patients – a proportion that convinced the researchers that Crohn's disease patients could be easily identified through a Twitter search. "These were people who were tweeting about potentially valuable information, such as their diet, medication, and how they were handling their disease," says Dr. van Oijen.

As a next step, he and his colleagues have begun analyzing patient tweets (using software similar to that employed for patient interviews and focus groups) to create networks of information on what patients are discussing. By categorizing the information, the researchers can ultimately compare results with those from validated questionnaires that are used in the clinic. "We have created an online cohort of patients with Crohn's disease so we can see how many struggle with certain aspects of the disease," Dr. van Oijen explains. His group is preparing to study patients on Facebook as well as Twitter, and to expand to look at gastroesophageal reflux disease, irritable bowel syndrome and hepatitis in addition to Crohn's disease.

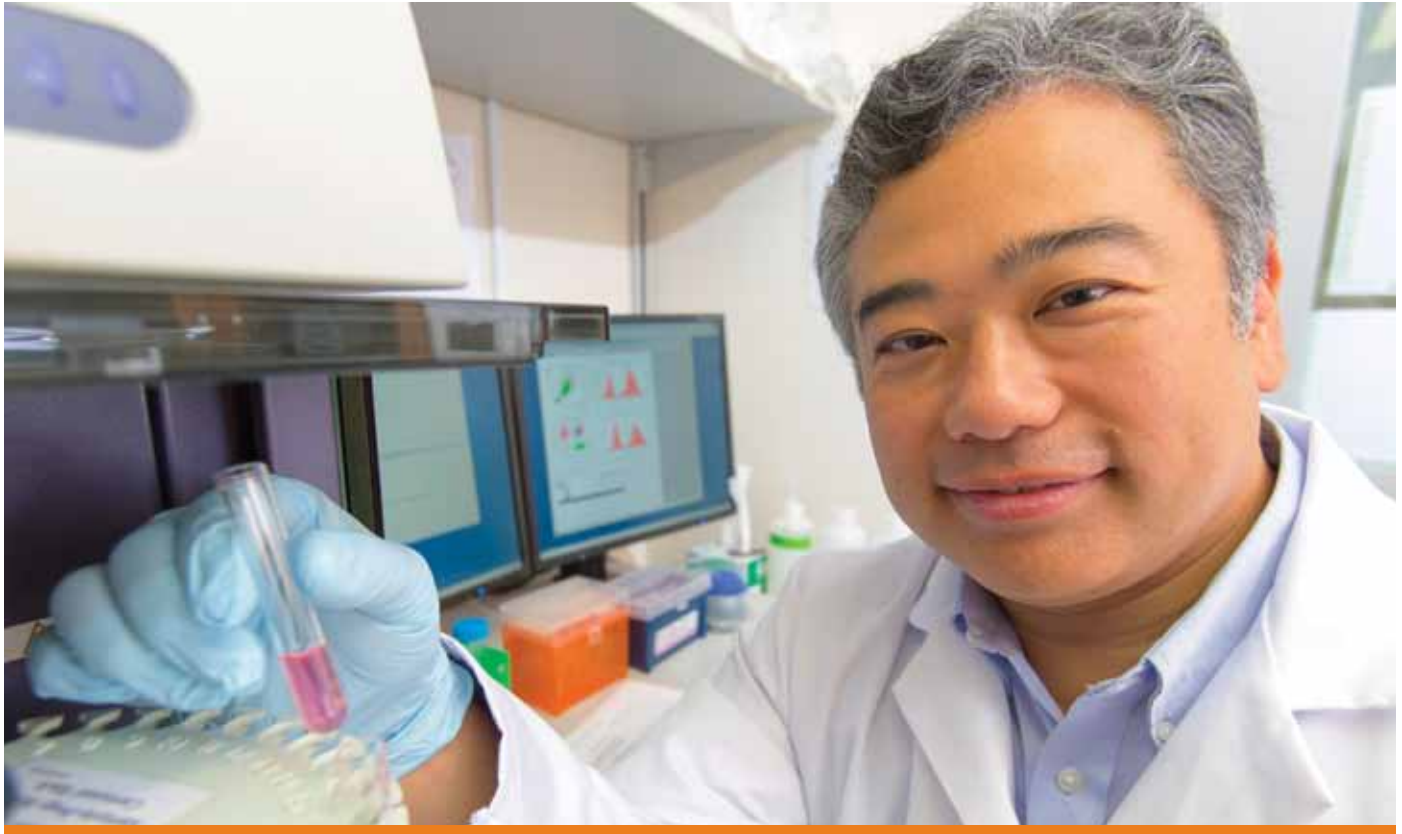
Dr. van Oijen believes monitoring social media sites at the population level could provide valuable input for large epidemiological studies.

Ultimately, though, he envisions going beyond passive monitoring to a phase he calls Social Medica 2.0. "The next step for us is to reach out to patients and follow them online over time," he says. "We want to see what their unmet needs are and how quality of care can be improved immediately." In addition to revealing insights that could be used for a patient's clinic visit, following patients online could pave the way for an intervention involving an online "coach" who would monitor social media updates and offer information or advice. Studying patients' online updates over time could also produce population-level data about behaviors or life events that trigger disease activity.

In the meantime, clinicians can use social media to gain insights about their patients with Crohn's disease and other chronic conditions. Patients within a disease community tend to share a common language that their health care provider should understand, Dr. van Oijen explains. In addition, online exchanges can provide lessons in what patients truly care about – which may be at odds with the focus of doctor-patient discussions. For example, he notes, a common discussion among patients online might center around whether they can go out for alcoholic drinks with friends – a topic unlikely to be broached in the clinic.

"Patients are the experts on their disease and their concerns," says Dr. van Oijen. "They have 100% of the data you would need as a provider. Our group's efforts are based on getting that information to physicians so that they are able to act on it to their patients' benefit."

# Reprogramming Cancer



*Nori Kasahara, MD, PhD*

Nothing as ambitious as developing an effective cancer gene therapy approach could be expected to come easily. Nori Kasahara, MD, PhD, started working in the gene therapy field as a graduate student in 1988. Then and now, one of the major obstacles to successful gene therapy has been finding an efficient method of delivering therapeutic genes to constantly proliferating cancer cells. But Dr. Kasahara, professor in UCLA's Division of Digestive Diseases and director of the Vector Core Facility for the CURE Digestive Disease Research Center, leads a team that has made steady progress for more than a decade. Now, the novel gene therapy technology developed and validated in his lab is being tested for the first time in human clinical trials.

Dr. Kasahara's lab focuses on the development of gene therapy as well as genetic engineering technologies for cell therapy, with applications not only in cancer but also in transplantation and regenerative medicine. The most advanced of these technologies is the one for cancer, which

Dr. Kasahara's group started on shortly before he was recruited to join the division's faculty in 2003. The strategy, if not the execution, is fairly simple: Genes are delivered to cancer cells, reprogramming them to make therapeutic proteins that kill the cells from within.

The nucleus of every human cell holds the genetic blueprints for dividing and differentiating to make other cells in the body. In cancer, cells run awry of normal programming and divide uncontrollably, replacing normal cells and taking over the body. "One of the main concepts driving gene therapy is that one way to attack this problem would be to go in at the blueprint level and reprogram the cell by delivering genes that will make them become quiescent, or cause them to self-destruct," Dr. Kasahara says.

Typically, researchers have used viruses as gene delivery vehicles, or vectors. "Viruses have evolved very efficient mechanisms to get their



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## Dr. Kasahara's group is now leading a consortium that has initiated a first-in-human clinical trial to test this novel gene therapy technology in brain cancer patients.

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genes into our cells," Dr. Kasahara explains. "With recombinant DNA technology, we can use them to replace harmful genes with the ones we want the cells to carry."

In order to efficiently reach all the cancer cells, viruses also offer the advantage of being able to replicate themselves, as they would in a natural infection. But to ensure safety in gene therapy studies, until recently the U.S. Food and Drug Administration required that virus-based gene delivery vectors be genetically modified so that they spread no further than the first cell they enter. Using these single-shot "crippled" viral vectors to deliver genes worked well enough in laboratory models, but this approach has been a failure in human clinical trials of cancer gene therapy. Dr. Kasahara's group was among the first to demonstrate that a tumor-selectively replicating virus could be used as a vector, greatly improving the efficiency of gene delivery to human cancers. "Cancer is a moving target – every cancer cell is dividing and making more copies of itself," Dr. Kasahara says. "When you 'un-cripple' the virus, you take advantage of its natural ability to spread from cell to cell, and it has the possibility of keeping up."

Specifically, Dr. Kasahara and colleagues used an un-crippled retrovirus vector and outfitted it with a "suicide gene." Once inside the cancer cell, the gene creates a protein that converts a non-toxic prodrug — an inactive form of a chemotherapy drug — into its active form, so the active chemotherapy drug is generated directly inside the cancer cell itself. "It's a two-step mechanism," Dr. Kasahara explains. "We infect the tumor with the virus, the virus spreads throughout the tumor mass, and as it spreads, it delivers the suicide gene blueprints that tell the cell how to activate the chemotherapy drug. Because the virus only infects cancer cells, the inactive prodrug, taken as an oral pill, is converted to the active form only inside the tumor cells, which then self-destruct."

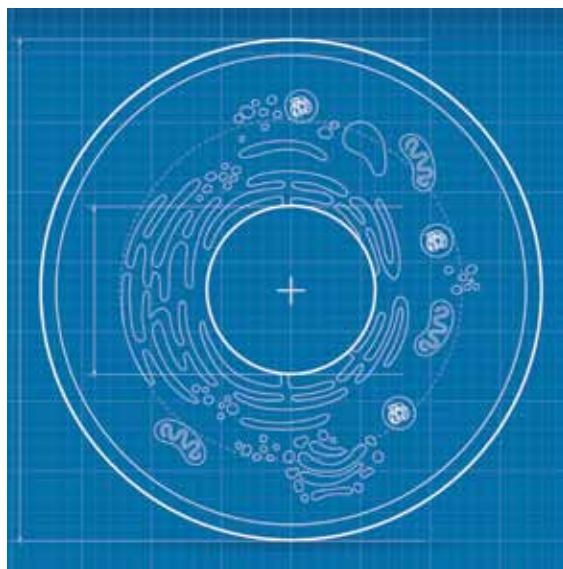
Other groups have also inserted other types of naturally replicating viruses into tumors through an approach known as oncolytic virus

therapy, which has met with mixed results. Oncolytic viruses are naturally destructive to their host cells, but this also triggers an immune response that prematurely eliminates the virus before the tumor is fully destroyed. Dr. Kasahara's group is the first to use a retrovirus, which permanently integrates itself into the cancer cell genome. "Unlike the other destructive viruses that have been used previously, retroviruses do not set off an immune response by directly damaging the cells," Dr. Kasahara explains. "Instead, the genetic blueprints encoded by the retrovirus become a permanent part of the cancer cell genome, so the cells can't get rid of them. It's like a stealth virus, which quietly takes up permanent residence in the community of cancer cells. Then, once

it infiltrates throughout the tumor, spreading its suicide gene blueprints, all the infected cancer cells are killed at once when you give the prodrug which is activated directly within the cells. And, because this happens only in the infected tumor cells, there are almost no side effects to normal tissues, such as those associated with chemotherapy."

After a decade spent developing and validating the approach in models of human colorectal cancer, prostate cancer and brain cancer, Dr. Kasahara's group is now leading a consortium that has initiated a first-in-human clinical trial to test this novel gene therapy technology in brain cancer

patients. Tocagen, a San Diego-based biotech company co-founded by Dr. Kasahara, licensed the technology from UCLA and received FDA approval to manufacture virus stocks for the multi-center clinical trial, now ongoing at UCLA, UC San Diego, UC San Francisco, Cleveland Clinic, Ohio State, and other major cancer centers around the country. This dose-escalation trial has already established the safety and tolerability of the virus, and Dr. Kasahara notes that, as the virus dose has been increased, they are seeing promising signs of therapeutic effectiveness. "One patient even decided to get married after her brain tumor went away with this treatment and has not shown any signs of recurring for more than six months now," he says.



# Hedonic Brain Response

## What Drives People to Eat?



*Lynn S. Connolly, MD, MSCR*

Obesity has reached epidemic proportions in most of the industrialized world – including the United States, where 34 percent of the population is obese and an additional 34 percent is overweight. In efforts to explain and address the problem, considerable attention has been paid to changes in the food environment and our more sedentary society. But Lynn S. Connolly, MD, MSCR, assistant professor in UCLA's Division of Digestive Diseases, argues that this focus is insufficient.

“The current paradigm is simply that if you're overweight, it's because you are eating too much and not exercising enough,” Dr. Connolly says.

“But that way of thinking is not working. We have a multibillion-dollar diet industry focusing on lower-calorie foods, and if anything, our society is only becoming more overweight.”

Her research has been within the Gail and Gerald Oppenheimer Family Center for Neurobiology of Stress, which directed by Emeran Mayer, MD. The research looks beyond the simple math of calories consumed/calories burned. Instead, Dr. Connolly and colleagues have been exploring the brain processes that drive people to eat, and how the drive might be different in people who are obese. Their findings provide intriguing evidence that, in a significant subset of women who struggle with obesity, the culprit could be a food addiction not unlike that experienced by drug-addicted individuals.

Dr. Connolly's research has focused on sex-related differences in the brain – particularly pertaining to women, who have higher obesity rates than men in the United States, with the differences most pronounced in minority populations. It's known that two distinct neural processes are involved when people are compelled to eat: the homeostatic drive and the hedonic drive. The homeostatic drive, dictated by signals in the primary interoceptive cortex of the brain, is guided by nutrient and caloric deficiency – eating to satisfy hunger; the hedonic drive, on the other hand, involves central reward pathways in the brain's insular cortex, operating without regard to nutrient or caloric need.

The research has been focused on the hypothesis that in certain obese people, the hedonic drive overpowers the homeostatic drive, resulting in overeating. “If you look at people who are addicted to heroin or tobacco, they know the drug is bad for them but they can't control that hedonic drive,” says Dr. Connolly. “Something similar may be happening in people struggling with food addiction.”

In a pilot study, Dr. Connolly and graduate student Kristen Coveleskie provided a group of 10 lean and 10 healthy obese women with blinded tastings of a 300-calorie sugary cranberry-juice beverage as well as a zero-calorie, artificially sweetened cranberry drink. After drinking one of the beverages, the women's brains were imaged while they were shown alternating pictures of either a food stimulus or a



neutral stimulus. Subjects were asked their opinions on the tastes of the two drinks, and about their hunger and satisfaction levels.

The researchers found that both groups of women were unable to distinguish between the two drinks, but the obese women rated the taste of the beverages significantly lower than the lean subjects. Both groups reported greater satiety after consumption of the beverages, but overall the obese women were less satisfied than the lean women. Most significantly, in the imaging studies, the obese women showed a greater hedonic brain response after drinking the beverages and being shown food images.

The finding that the obese women in the study rated the taste of the drinks lower and were less satisfied after consuming them than the lean women, yet still showed greater hedonic brain activity in response to images of food, is consistent with what is known about addiction. “For addicts, even as satisfaction is reduced with each fix, craving is amplified,” Dr. Connolly explains. In a separate study, Dr. Connolly with collaborators Dr. Lisa Kilpatrick and Kristen Coveleskie found a difference in the resting state of the brain between lean and obese women after ingestion of a sugary drink – providing additional support for the hypothesis that the balance between homeostatic and hedonic pathways is altered in obese individuals.

Among other things, the study findings suggest that in people with sugar addiction, artificially sweetened drinks – developed to reduce caloric intake without

sacrificing taste – promote the same addictive brain pathways as sugar, triggering greater craving and increased caloric ingestion, Dr. Connolly notes.

Moreover, if the food addiction hypothesis is confirmed, it could pave the way toward new approaches to treating obesity. These include novel drug targets and cognitive behavioral therapies. Dr. Connolly will collaborate with Dr. Claudia SanMiguel to conduct studies in obese patients who have undergone successful bariatric surgery in an effort to learn if and how the procedure changes the hedonistic and homeostatic pathways, in the hope that what they learn can be applied to a non-surgical treatment.

Bariatric surgery is currently the only successful obesity treatment, but given the morbidity associated with the surgery and the fact that only a small percentage of obese patients are eligible, there is a great need for new approaches.

“We have tried diet and exercise for many years, and for people who are obese, the long-term results are extremely poor,” says Dr. Connolly. “Similarly, focusing on peripheral targets has failed to make an impact on the problem. We need to start thinking about how the brain could be involved, and to come up with new ways to treat obese individuals. Some of the tools we have used for alcohol, tobacco and other addictions are likely to have a better chance of succeeding than simply telling patients to eat only half of their sandwich or to exercise another 20 minutes a day.”

The study findings suggest that in people with sugar addiction, artificially sweetened drinks — developed to reduce caloric intake without sacrificing taste — promote the same addictive brain pathways as sugar, triggering greater craving and increased caloric ingestion.

# Familial Mediterranean Fever

When properly diagnosed, Familial Mediterranean Fever (FMF) – a recessive genetic disorder characterized by sporadic bouts of severe fever, pain and inflammation of the body’s lining surfaces – is easily treatable. More than 90 percent of patients respond to colchicine, a drug long used to treat gout. But because FMF is extremely rare in much of the United States, diagnosis is often elusive. That’s where UCLA’s Familial Mediterranean Fever Clinic comes in as a national and international resource. The FMF Clinic at UCLA was established in the early 1960s by Arthur Schwabe, MD, professor and then chief of the division of gastroenterology. Over the last 50 years, more than 700 patients have been registered in our clinic.

“We receive calls and emails from physicians and patients all the time,” says Terri Getzug, MD, health sciences clinical professor in the UCLA Division of Digestive Diseases and director of the FMF Clinic, one of the nation’s only formal diagnostic and treatment programs. “Many of these patients have had nowhere to turn. It’s very gratifying to know that without a lot of technology, we can figure out what’s wrong with them and help them get better.”

FMF is most common among people of Middle Eastern descent, especially those of Armenian heritage, Sephardic and Ashkenazi Jews, Turks, and certain Arab populations. The carrier rate for Armenians is one in seven, though only about one in 500 expresses the disease clinically. In Iraqi Jews the carrier rate is one in four; in North African Jews, one in six. In the United States there are fewer than 10,000 people who have been diagnosed – likely due to both under diagnosis and environmental or genetic influences that may play a role in whether carriers develop FMF’s clinical manifestations.



*Terri Getzug, MD*

Los Angeles, however, has a large concentration of the most-affected populations: For example, according to the 2000 U.S. Census, 43 percent of the Armenian-American population lives in the Greater Los Angeles area. And anyone can be affected. “We’ve had patients who are Japanese, Chinese, and Latino, as well as patients who are Caucasian with backgrounds going back to England, Scotland or Ireland,” says Dr. Getzug. “You never know. Since the disease is based on a genetic mutation, it can affect anyone, so it always needs to be considered in the right clinical setting.”

The acute episodes of fever characteristic of FMF are often combined with inflammation that can manifest as peritonitis, pleuritis or arthritis; the associated severe abdominal or chest pain can



The consequences of not diagnosing and treating FMF can be serious. Dr. Getzug notes that some patients may develop amyloidosis, with protein deposition in the GI tract and kidneys leading to malabsorption and/or renal failure.

be either localized or diffuse. The bouts can be as infrequent as once a year or as frequent as every two weeks, but the fever tends to be transient, typically lasting only hours or up to one day, Dr. Getzug says. NSAIDs tend to provide little comfort. “When an attack occurs, patients can’t do anything except stay still in bed for three days, then it goes away and they are asymptomatic until the next episode,” Dr. Getzug explains. Once diagnosed, patients need to take colchicine every day for life to prevent future attacks – not just at the onset of an attack, as some mistakenly do.

The consequences of not diagnosing and treating FMF can be serious. Dr. Getzug notes that some patients may develop amyloidosis, with protein deposition in the GI tract and kidneys leading to malabsorption and/or renal failure. Others develop abdominal adhesions that may lead to bowel

obstructions or infertility. In addition, because the pain of FMF can mimic appendicitis or cholecystitis, some patients undergo unnecessary surgeries after being misdiagnosed. Others bounce around from doctor to doctor, enduring multiple diagnostic studies in a futile search for an answer. On top of these morbidities are the quality of life impacts. “For children, there is a lot of missed school, depression, as well as effects on growth and development because this is a chronic inflammatory condition,” Dr. Getzug says. “Adults may miss work, lose jobs, and even become addicted to the pain medicines prescribed by physicians who fail to make the proper diagnosis.”

When a physician knows about the disease, the diagnosis is not difficult to make, Dr. Getzug says. It is based on the clinical history in which a patient complains of acute attacks of pain with fever that are recurrent over a period of time (the frequency can vary), between which times the patient is otherwise healthy. “If the presentation is typical, there is really no other disease that FMF can be mistaken for,” says Dr. Getzug. “The problem is that the disease tends to cluster in certain areas where the high-carrier populations tend to live – mostly on the east and west coasts. In other parts of the country, where FMF isn’t often seen, and even in areas with higher disease prevalence such as Los Angeles, it can fall under the radar.” Thus, the FMF clinic at UCLA serves many purposes: to accurately diagnose, treat, and educate patients with FMF, to teach doctors in training about this condition so that they will be able to recognize and treat FMF when a patient presents in their office or emergency room, and to raise public awareness about this important condition.

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

IN RECOGNITION OF DR. SHERMAN M. MELLINKOFF'S COMMITMENT TO MEDICAL EDUCATION AND RESEARCH

# UCLA-Mellinkoff Gastroenterology Symposium

Current Practice / Future Trends  
Video and Case-Based Program

March 8-10, 2013

Montage | Beverly Hills | California

\$300 / \$175 / \$50 Registration / 19.25 *AMA PRA Category 1 Credits™*  
Continuing Education Hours Available for Nurses (19.8 are ABCGN GI-specific Contact Hours)

## Course Directors



### Eric Esrailian, MD, MPH

Vice Chief, Division  
of Digestive Diseases  
Lincy Foundation Chair  
in Clinical Gastroenterology  
Assistant Clinical Professor of Medicine



### V. Raman Muthusamy, MD

Director of Interventional Endoscopy  
Associate Director of Endoscopy  
Associate Clinical Professor of Medicine



### Bennett Roth, MD

Chief, Gastrointestinal Endoscopy  
Director, Medical Procedure Units  
Director, Post-Graduate  
Education Programs  
Medical Director, UCLA Center  
for Esophageal Disorders  
Professor of Clinical Medicine



The **UCLA-Mellinkoff GI Symposium** will provide updates on the diagnosis, management and palliation of various GI and liver disorders through video and case-based presentations, formal lectures, Q&A panel and audience participation activities. Video cases are highlighted to address important challenges and potential solutions in the endoscopic management of digestive and related disorders. This agenda has been specifically designed to offer practical approaches and solutions that healthcare professionals may readily integrate into their daily practice.

## Overnight Accommodations

A limited block of rooms, at a special rate of \$325 + tax per night, has been reserved at the Montage Beverly Hills. This special room block expires February 14, 2013. Call the reservation line at 888-860-0788 and ask for the "UCLA" block. For more information about the hotel, visit:

[www.montagebeverlyhills.com](http://www.montagebeverlyhills.com)



To learn more, scan  
the QR code or go to  
[www.cme.ucla.edu](http://www.cme.ucla.edu)



# Agenda

## Friday, March 8

### Registration and Breakfast

### Welcome and Introduction

Gary Gitnick, MD, UCLA

### Course Overview

V. Raman Muthusamy, MD & Bennett Roth, MD, UCLA

### Esophageal Disorders

Moderator: Bennett Roth, MD, UCLA

### Spectrum of GERD – PPI Failure, Esophageal Physiology Testing – Help or Hindrance?

Thomas Kovacs, MD, UCLA

### Barrett's Esophagus – Have We Found a Cure?

V. Raman Muthusamy, MD, UCLA

### Dysphagia – Stenosis, Dysmotility, and Eosinophilic Esophagitis

Kevin Ghassemi, MD, UCLA

### Q & A Panel

### Functional GI Disorders

Moderator: Daniel Cole, MD, MPH

### Chronic Constipation – When the Going Gets Tough

Kirsten Tillisch, MD, UCLA

### Chronic Nausea and Vomiting – Causes and Remedies

Lin Chang, MD, UCLA

### The Gut and the Brain – New Insights, Pathophysiology

Emeran Mayer, MD, UCLA

### Q & A Panel

### Break

### Liver Disorders I

Moderator: Myron Tong, MD, PhD, UCLA

### Hepatitis B – Treatment and Consequences

Steven-Huy Han, MD, UCLA

### Hepatitis C – New Therapeutic Paradigms

Sammy Saab, MD, MPH, UCLA

### Management of Difficult Problems Related to Portal Hypertension

Bruce A. Runyon, MD, UCLA

### Q & A Panel

### Lunch and Special Speaker

### Future of Endoscopic Practice in the New Era of Health Care Delivery

Thomas M. Deas, Jr., MD

President, American Society for Gastrointestinal Endoscopy (ASGE)

### Current and Future Issues in Endoscopy

Moderator: Daniel Cho, MD, UCLA

### Update on Endoscopy and GI Bleeding

Dennis M. Jensen, MD, UCLA

### Deep Enteroscopy – Which Technique is Right for Me?

Rome Jutabha, MD, UCLA

### Advances in Endoscopic Imaging – Help or Hype?

Sri Komanduri, MD, MS, Northwestern University

### Q & A Panel

### Break

### Quality Issues in Endoscopy

Moderator: V. Raman Muthusamy, MD, UCLA

### Controversies Before Performing Endoscopy – Antibiotics, Anti-Coagulants and Anesthesia

John Vargo, MD, MPH, Cleveland Clinic

### Colorectal Cancer Screening – Current and Future Practice – The Mandate for Quality

Brennan M.R. Spiegel, MD, MSHS, UCLA

### Q & A Panel

### Endoscopy Video Session I

Moderator: Bennett Roth, MD, UCLA

### Adjourn

## Saturday, March 9

### Registration and Breakfast

### Welcoming Remarks

Eric Esrailian, MD, MPH, UCLA

### Inflammatory Bowel Disease

Moderator: Daniel Hommes, MD, PhD, UCLA

### Inflammatory Bowel Disease – Three Things You Just Need to Know

Daniel Hommes, MD, PhD, UCLA

### Joint Problems in IBD – A Few Simple Take Home Messages

Bennett Roth, MD, UCLA

### IBD Medication – New Kids on the Block

Jennifer M. Choi, MD, UCLA

### Vaccinations in IBD Patients – Necessary? Hazardous?

Nimisha K. Parekh, MD, MPH, UC Irvine

### Challenging Cases – Panel Discussion

### Break

### Liver Disorders II

Moderator: Terri Getzug, MD, UCLA

### Non-Viral Hepatitis

Simon Beaven, MD, PhD, UCLA

### Liver Lesions – What to Do

Francisco Durazo, MD, UCLA

### Liver Transplantation 2013

Ronald W. Busuttil, MD, PhD, UCLA

### Q & A Panel

### Lunch

### Intestinal Disorders

Moderator: Mark Ovsowitz, MD, UCLA

### Celiac Disease – Current and Future Trends in Management

Gregory Harmon, MD, UCLA

### Clostridia Difficile – The Gift That Keeps on Giving

Daniel Hollander, MD, PhD, UCLA

### Microscopic Colitis

Eric Esrailian, MD, MPH, UCLA

### Chronic Diarrhea – When You're Running Out of Options

Wilfred Weinstein, MD, UCLA

### Q & A Panel

### Break

### Endoscopic Video Session II

Moderator: V. Raman Muthusamy, MD, UCLA

### Adjourn

## Sunday March 10

### Registration and Breakfast

### Welcoming Remarks

Bennett Roth, MD, UCLA

### New and Exciting Issues for the Gastroenterologist

Moderator: Lynn S. Connolly, MD, MSCR, UCLA

### Curing Diabetes with Bariatric Surgery

Erik Dutson, MD, UCLA

### The Role of the Gastroenterologist in Genetic Counseling

Erin O'Leary, Genetic Counselor, UCLA

### Value Based Health Care – You Get What You Pay For

Daniel Hommes, MD, PhD, UCLA

### Q & A Panel

### Break

### Issues of the Pancreas

Moderator: V. Raman Muthusamy, MD, UCLA

### Management of Recurrent Pancreatitis and Its Complications

Sri Komanduri, MD, MS, Northwestern University

### Evaluation of the Asymptomatic Cyst

Rabindra R. Watson, MD, UCLA

### Neuro-endocrine Tumors

Joseph Pisegna, MD, UCLA

### Pancreatic Cancer – The UCLA Surgical Experience

Timothy Donahue, MD, UCLA

### Chemotherapy for Pancreatic Cancer – Efficacy and Benefit

Zev Wainberg, MD, UCLA

### Q & A Panel

### Adjourn – Boxed Lunch



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U C L A

The UCLA Division of Digestive Diseases continues to be rated in the top ten among digestive diseases centers in the United States by *U.S. News & World Report* in its annual survey.

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### WEB

Learn more about UCLA Division of Digestive Diseases: [www.gastro.ucla.edu](http://www.gastro.ucla.edu)



I am proud to announce the UCLA Division of Digestive Diseases has once again been ranked in the top ten nationwide by *U.S. News & World Report*. We have maintained this ranking since 1990, when the ratings began. For information on our clinical services and research, visit [www.gastro.ucla.edu](http://www.gastro.ucla.edu) or email me at [eesrailian@mednet.ucla.edu](mailto:eesrailian@mednet.ucla.edu)

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