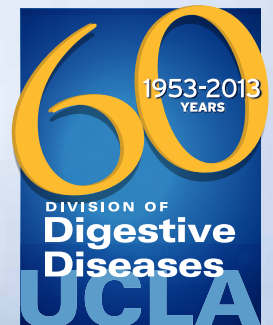


Beyond the Scope

A REPORT OF THE UCLA DIVISION OF DIGESTIVE DISEASES

**UCLA Division of
Digestive Diseases**

**Celebrating
60 Years**





Gary Gitnick, MD
Fran and Ray Stark
Foundation Chair
Professor of Medicine



Eric Esraillian, MD, MPH
Lincy Foundation Chair in
Clinical Gastroenterology
Assistant Clinical Professor
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60 Years of Achievement

With this issue of *Beyond the Scope*, we pause to reflect on the UCLA Division of Digestive Diseases' 60 years of research, teaching and patient care — our diamond jubilee. It's a time to acknowledge, as we do in our brief history of the Division (pg.2), the outstanding leaders who have helped make the Division of Digestive Diseases one of the jewels of the David Geffen School of Medicine at UCLA.

To continue its sparkling record of achievement, the Division depends on its excellent faculty. It has had great success over the years in recruiting some of the very best, and with this issue we welcome three new members to our team (pg. 3).

Among the things that add luster to our Division is its commitment to training future generations of clinicians, educators and researchers. One who exemplifies this value is Yvette Taché, PhD, who was recently honored by the American Gastroenterological Association Institute Council with the 2013 Neurogastroenterology & Motility Section Research Mentor Award (pg. 1). Dr. Taché has helped launch many successful careers, adding to the lasting impact of her own considerable research achievements.

Proudly featured in this issue of *Beyond the Scope*, Lin Chang, MD, discusses how diet affects bowel sensitivity and symptoms in digestive disorders and the important role of the dietitian at UCLA's Digestive Health and Nutrition Clinic (pg. 6). We look at how Dimitrios Iliopoulos, PhD, and his colleagues resourcefully apply existing drugs to new conditions to speed useful therapies from the lab to the clinic where they can benefit patients (pg. 4). And F. Charles Brunnicardi, MD, helps us all brace for impact as personalized medicine promises to transform healthcare (pg. 8).

Finally, we want to encourage you to visit us during Digestive Disease Week 2013. Many of our faculty will be sharing small gems from their research and clinical experience that will add new facets to your understanding (pg. 10). We look forward to seeing you there.

Yvette Taché, PhD, Honored with Mentor Award

When it comes to scientific impact, Yvette Taché, PhD, has amassed an impressive record: She was among the first to demonstrate the role of peptides in brain-gut interactions, and her group was the first to establish the importance of corticotropin-releasing factor (CRF) in stress-related gut function alterations and thyrotropin-releasing hormone in the brainstem to stimulate vagal outflow to the gut. Dr. Taché's findings laid the foundation for the current interest in using CRF-receptor antagonists as potential therapeutic agents for functional diseases such as irritable bowel syndrome.

But for Dr. Taché, professor in the Division of Digestive Diseases and co-director of the Gail and Gerald Oppenheimer Family Center for Neurobiology of Stress at UCLA, mentoring talented young scientists and watching their careers flourish after they leave is as gratifying as any paper she has published.

Her dedication and contributions to training dozens of outstanding researchers and clinicians in the field of neurogastroenterology over a three-decade career at UCLA was recently recognized when Dr. Taché was selected by the American Gastroenterological Association (AGA) Institute Council as the recipient of the 2013 AGA Institute Council Neurogastroenterology & Motility Section Research Mentor Award, presented in May during Digestive Disease Week in Orlando, Florida.

Dr. Taché has mentored more than 60 postdoctoral trainees and fellows from all over the world. Among them are current department heads, directors of hospitals and research centers, and professors at top universities across the United States, Canada, Europe and Japan, as well as leaders in the pharmaceutical industry.

"This award means a lot to me, because I consider training new generations of

scientists to be just as important as my own scientific contributions," Dr. Taché says.

"It's very fulfilling to see these motivated and talented young people, many of whom arrived with no experience in experimental research, bloom as scientists while they are here and then go on to be recruited to important positions and become successful in their own research. Publications tend to have an impact for a couple of years, but when you provide the seeds for another individual's successful career, that's more sustainable."

Dr. Taché's interest in the mechanisms by which stress contributes to gut dysfunction is rooted in her own training. After graduating from University Claude Bernard in her native Lyon, France, she earned a scholarship to pursue a PhD at the University of Montreal. There, she worked in an internationally renowned neuroendocrinology laboratory under the mentorship of Dr. Hans Selye, who coined the term stress and conducted pioneering research showing its consequences on the body, including the stomach. Thereafter, she spent two years at the Clayton Foundation Laboratories for Peptide Biology, The Salk Institute of Biological Studies, to work with the team



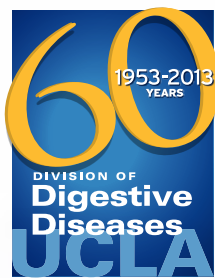
*Yvette Taché, PhD
Co-director, Gail and Gerald Oppenheimer
Family Center for Neurobiology of Stress
Professor of Medicine*

who pioneered the field of CRF signaling pathways by identifying CRF, related peptides and CRF receptors, and developed selective CRF antagonists.

Recruited to UCLA in 1982, Dr. Taché became a leading expert in unraveling the complex brain-gut interactions that occur when stress leads to gut dysfunction. Through collaborations with the division's clinicians, Dr. Taché hopes to translate this understanding into new drugs that could make a difference in the lives of patients with stress-sensitive GI disorders.

"Dr. Taché is an extremely dedicated mentor who makes sure mentees not only gain knowledge and skills, but also develop the curiosity to ask and reason well," says Million Mulugeta, DVM, PhD, presently a professor in the UCLA Division of Digestive Diseases who was trained by Dr. Taché and nominated her for the award. "Dr. Taché also has infectious energy for scientific discussions. She nurtures critical thinking and shows untiring interest in searching for approaches to solving problems."

Celebrating 60 Years



As the UCLA Division of Digestive Diseases celebrates its 60th year, we have much to be proud of. Today, we are one of the largest such divisions in the world. Our faculty train hundreds of gastroenterologists, treat thousands of patients annually, author papers and abstracts that change research

protocols and clinical practice, and improve the lives of millions through our global influence.

When Dr. Sherman Mellinkoff became Chief of the Division in 1953, there were no medical school or hospital facilities, and there were only 24 enrolled students.

While Dr. Mellinkoff worked to develop a laboratory in what had been an ice-skating rink, the first medical center opened in 1955. That year, Dr. Mellinkoff helped recruit Dr. Morton Grossman — one of the most important gastrointestinal physiologists in medical history — to become Chief of Gastroenterology at the VA Greater Los Angeles Healthcare System.

In 1962, Dr. Mellinkoff became Dean of the Medical School, and Dr. Arthur Schwabe succeeded him as Division Chief in 1967. Under Dr. Schwabe's guidance, the Division continued to grow, and he personally founded the largest — and finest — Familial Mediterranean Fever (FMF) clinic in the Western world.

Dr. Martin Pops joined the Division in 1966 to begin a long and influential career at the School of Medicine. After helping the Division establish itself in its early days, Dr. Pops served for 25 years in the Dean's Office, including as Dean of Students.

In 1970, Dr. Grossman recruited Dr. John Walsh to join the medical school. Together they set up a laboratory at the VA that would become a crucible of major medical advances. By 1973, the Division had four full-time faculty members:

Chief Schwabe, Dr. Gary Gitnick, Dr. Pops and Dr. Walsh. Two years later, Dr. Bennett Roth became the fifth.

In 1974, the Division took a stride forward through the development of the Center for Ulcer Research and Education (CURE). Advances there drove innovation in clinical and pedagogical practice as the number of the Division's patients and fellows continued to grow.

Upon Dr. Schwabe's retirement in 1988, Dr. Walsh became Chief. The Division flourished under his guidance, with the CURE: Digestive Diseases Research Center expanding in its scope and international reputation.

In 1993, Dr. Gitnick became Chief of the Division. Since then, we have established a structure that allows research units to proliferate and attracts even more of the world's best gastroenterologists. Our faculty, space and funding have quadrupled. In 2013, Dr. Eric Esrailian joined Dr. Gitnick as Chief. He is spearheading the growth and philanthropic efforts of our clinical enterprise.

The Division now consists of 10 clinical and 12 research programs, as well as a thriving fellowship program. We treat nearly 120 conditions and have more than 60 full-time faculty members. Our clinical section performs more than 13,000 diagnostic and therapeutic procedures annually.

Our research advancements are exemplary in their diversity, number and impact. To name just a few, we have made major advances in CT scan and endoscopy technologies, peptide biochemistry, brain-gut interactions, liver transplantation, gastric acid secretion and inhibition, the understanding of *H. pylori*, gastrointestinal motility, mucosal immunology and function, gene therapy, systems biomedicine, signal transduction and evidenced-based care.

As we move beyond our 60th year, we will continue working to build on our tradition of excellence and reach new heights through innovation.

UCLA Division of Digestive Diseases Recently Welcomed Three New Members to Its Faculty



Jeffrey L. Conklin, MD

*Director, Center for Esophageal Diseases and Gastrointestinal Motor Function Laboratory
Professor of Medicine*

Dr. Jeffrey L. Conklin recently joined the division as director of the Center for Esophageal Diseases and Gastrointestinal Motor Function Laboratory. Prior to coming to UCLA, he served as director of the Esophageal Center of Excellence at Cedars-Sinai Medical Center. Along with studies exploring esophageal and gastrointestinal motor function, he and his colleagues developed implantable electrical stimulation devices designed to treat obesity and gastroesophageal reflux disease. Dr. Conklin is now working on new devices for the treatment of these disorders. At the University of Iowa, where he earned his MD and stayed for his internal medicine and gastroenterology training, Dr. Conklin coauthored seminal papers exploring the physiological mechanisms controlling esophageal and colonic motor function. Following a postdoctoral fellowship at the University of Massachusetts Medical School, he returned to the University of Iowa, where he became professor of medicine and undertook groundbreaking studies demonstrating that nitric oxide is the neurotransmitter controlling relaxation of the lower esophageal sphincter and peristalsis in the smooth-muscle esophagus. After 15 years at the University of Iowa, Dr. Conklin joined the faculty at the Mayo Clinic in Rochester, MN, where he became director of the esophageal function lab.



Mary Farid, DO

Clinical Instructor of Medicine

Dr. Mary Farid practices general gastroenterology, with particular interest in inflammatory bowel disease, esophageal disorders, irritable bowel syndrome and colon cancer screening. She is committed to providing comprehensive care for men and women through a strong physician-patient partnership founded on compassion, dignity and respect. Dr. Farid completed her undergraduate work at UCLA, graduating Magna Cum Laude with a Bachelor of Science degree in Physiological Science, and earned her medical degree from the Western University of Health Sciences. She returned to UCLA to complete a residency in internal medicine at the UCLA-VA Greater Los Angeles Program, then went on to complete her fellowship in gastroenterology, also at UCLA. Dr. Farid is board-certified in both internal medicine and gastroenterology.



Rimma Shaposhnikov, MD

Clinical Instructor of Medicine

Dr. Rimma Shaposhnikov is helping to spearhead the effort to establish a northwest campus for UCLA in Westlake Village and Thousand Oaks. Dr. Shaposhnikov practices all aspects of gastroenterology, with particular interest in inflammatory bowel disease, esophageal disorders, irritable bowel syndrome and colon cancer screening. She completed her undergraduate work at Yale University, earning a Bachelor of Science in Molecular Biochemistry, before obtaining her medical degree from State University of New York at Buffalo. In medical school Dr. Shaposhnikov was one of six people selected by the Centers for Disease Control and Prevention to investigate an outbreak of Hepatitis B in Brazil. Her training in internal medicine and gastroenterology was done at USC, where her research focused on upper gastrointestinal bleeding, as well as molecular markers found in polyps. After completing her fellowship, Dr. Shaposhnikov joined a multi-specialty group in the San Fernando Valley. In addition to establishing a practice, she started an esophageal lab at Providence St. Joseph's Medical Center. Dr. Shaposhnikov is board-certified in both internal medicine and gastroenterology.

Metformin Trial Illustrates Value of Applying Existing Drugs to New Disease

Anti-diabetes Drug Shows Promise in Pancreatic Cancer



*Dimitrios Iliopoulos, PhD
Director, UCLA Center for
Systems Biomedicine
Associate Professor of Medicine*

An innovative research approach taken by a group led by Dimitrios Iliopoulos, PhD, director of the Center for Systems Biomedicine within UCLA's Division of Digestive Diseases, has resulted in a closely watched Phase II clinical trial testing the ability of metformin, a drug long used in the treatment of type 2 diabetes, to improve survival for patients with metastatic pancreatic cancer. But perhaps even more importantly, the success of Dr. Iliopoulos' group in quickly moving its research to the clinic underscores the value of identifying drugs used in one disease with the potential to benefit patients in another disease for which there is no effective treatment.

The trial, which began enrolling patients in February, tests the survival impact of combining the anti-diabetes drug metformin with standard chemotherapy in metastatic pancreatic cancer patients, a patient population with a median survival of only five to six months. Dr. Iliopoulos' group will perform the research analysis in this trial aiming to identify the downstream targets of metformin in these patients.

The trial is based on laboratory discoveries of the anti-cancer properties of metformin by Dr. Iliopoulos and his colleagues, Drs. Heather Hirsch and Kevin Struhl, in studies conducted at Harvard Medical School in 2009-2010. Unlike traditional approaches that identify targets and then develop novel drugs for testing, Dr. Iliopoulos' group sought drugs already known to be effective in other diseases that could confer therapeutic benefits for pancreatic cancer patients.

"When an effective new drug is identified through experiments in cells and animals, it can take at least eight to 10 years before it is brought to patients," Dr. Iliopoulos explains. "But we know that different human diseases can be caused by similar molecular mechanisms and defects. That means that a drug that is useful for one condition, such as heart disease or diabetes, has the potential, if the same pathway is involved, to be effective in cancer."

Following that hypothesis, Dr. Iliopoulos' group embarked on screening FDA-approved drugs for a variety of conditions – from diabetes and high cholesterol to cardiovascular disease and autoimmune diseases – to determine their applicability in cancer. In particular, the group focused on identifying established drugs with the potential to kill cancer stem cells – the aggressive population of cells that are believed to be involved in initiating tumors. Cancer stem cells tend to be highly resistant to chemotherapy and radiotherapy. "These are the 1 to 5 percent of cells that are typically left behind by the treatment," says Dr. Iliopoulos. "People will appear to be clear of cancer after their treatment, but then a few years later, these undetectable cells will potentially initiate a relapse or metastasis of the disease. That's why there is a great interest in identifying compounds that target these resistant cells."

Dr. Iliopoulos and colleagues found in animal models that metformin targets cancer stem cells not only in pancreatic cancers, but also in others such as breast and colon cancer. Based on

these findings, the current clinical trial was initiated. “No one expected that a drug being used in diabetes would be able to kill these chemotherapy-resistant cells,” Dr. Iliopoulos says. “But we found metformin to be highly effective.”

The realization that there could be many existing drugs with crossover benefits is relatively new. “We are learning that there are a lot of common molecular mechanisms among different diseases,” says Dr. Iliopoulos. “As genomic research gives us more information about the molecular basis of diseases, we are finding overlapping pathways.” Moreover, Dr. Iliopoulos notes, there are drugs that, while approved, are not well understood. “We know they are effective for a certain indication, but we don’t know exactly what they are doing,” he says. “In many cases, they may have properties that we haven’t identified.” With more than 1,000 FDA-approved drugs from which to choose, there may be many with previously undiscovered cancer-treating properties, Dr. Iliopoulos suggests.

The approach of Dr. Iliopoulos’ group has other advantages. The clinical trial started only three years after the studies by Dr. Iliopoulos and colleagues identifying metformin’s potential therapeutic benefits for pancreatic cancer patients. “We already have the safety profiles for existing drugs

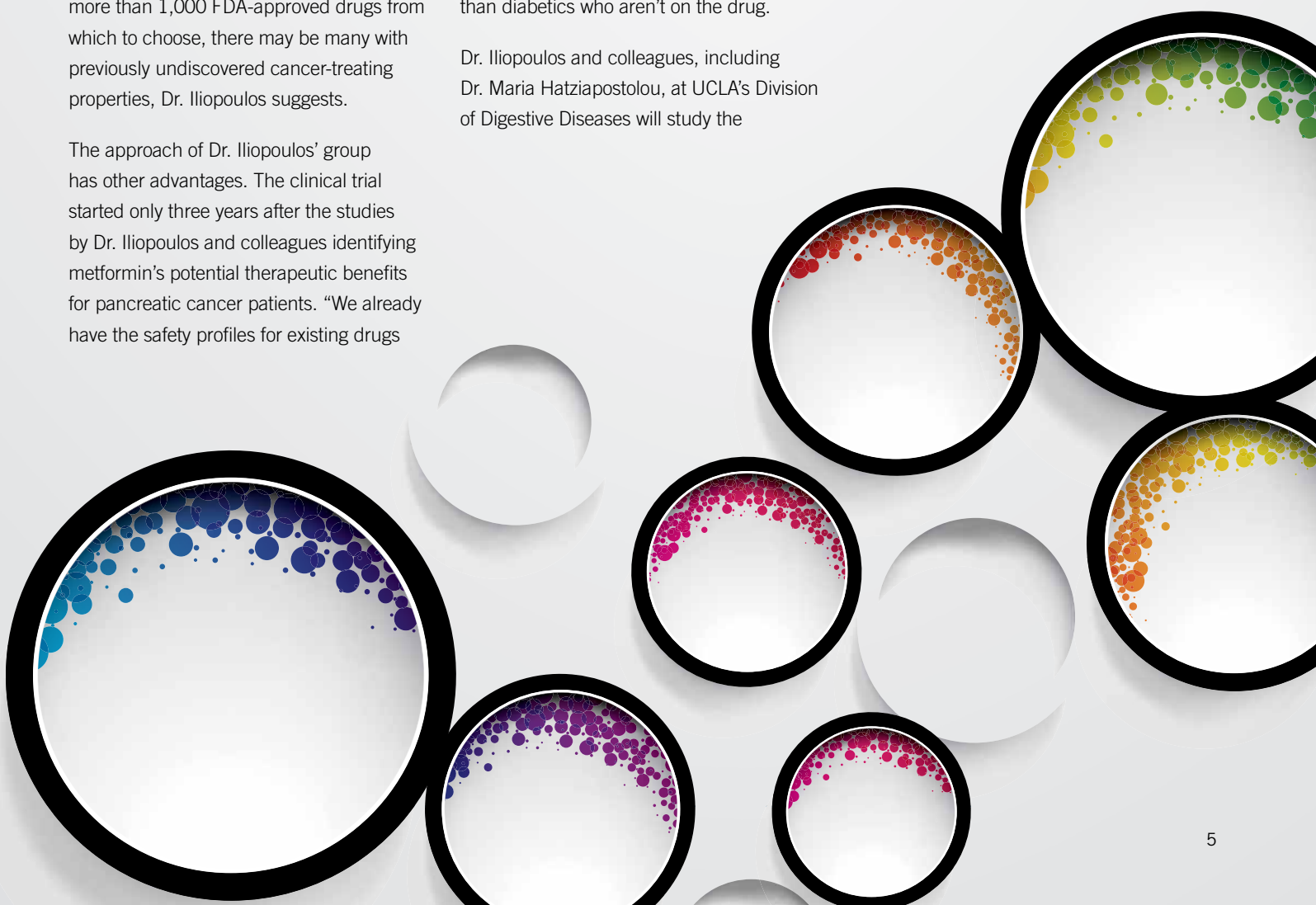
like metformin,” says Dr. Iliopoulos. “That means that when we find out one of these drugs might be effective in cancer, it can go to the clinic much faster, saving years of time and the significant cost associated with conducting Phase I trials.” In addition, he notes, a dose of metformin costs just a few dollars – far less expensive than the typical cost of novel drugs that are developed for cancer, which can run thousands of dollars per dose.

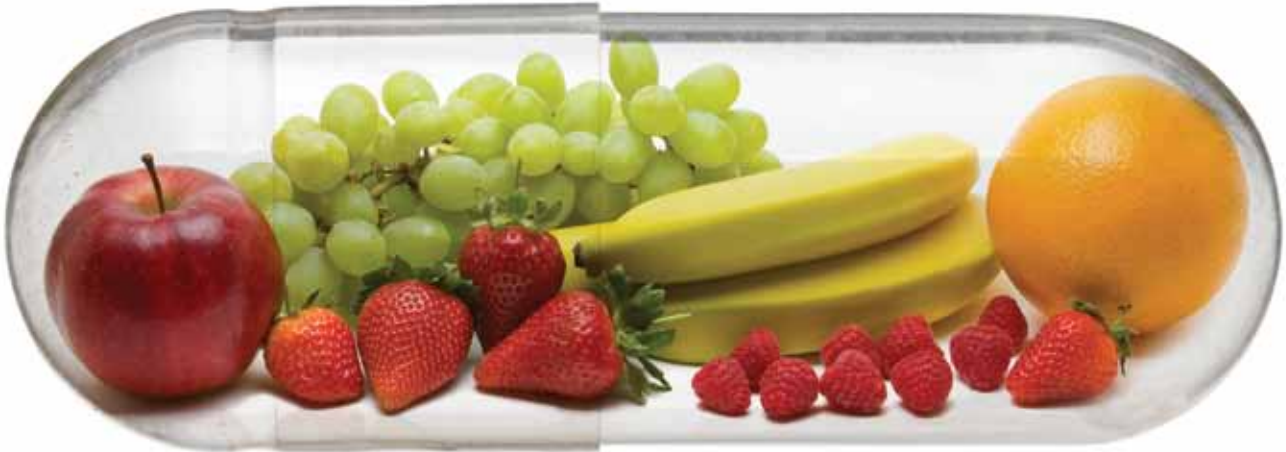
For the clinical trial, Dr. Iliopoulos is hopeful that metformin will increase the median survival time for patients who have no other treatment options beyond standard chemotherapy. The epidemiological evidence is encouraging: With metformin having been used by many diabetes patients for more than a decade, retrospective studies have shown that these patients have a lower risk of developing pancreatic cancer than diabetics who aren’t on the drug.

Dr. Iliopoulos and colleagues, including Dr. Maria Hatziapostolou, at UCLA’s Division of Digestive Diseases will study the

molecular changes in the patients who are treated with metformin to learn more about how the drug is working. The goal is to use that information to develop even better drugs, or identify targets that are important for other cancers. Already, the group has identified evidence that metformin suppresses inflammatory responses, a finding with relevance to cancer.

Dr. Iliopoulos is excited not only about the current clinical trial, but also about the future of this approach in expediting new treatments. “The type of screen we did at Harvard was just the beginning,” he says. “At the Center for Systems Biomedicine at UCLA, we will be able to take advantage of our infrastructure and powerful new technologies to perform experiments that will help us identify new therapies for inflammatory bowel diseases and other conditions in the near future.”





Role of Nutrition Emphasized in Treatment of Digestive Disorders

Registered Dietitian with Special Expertise Assists Patients

Although diet is known to play an important role in conditions involving the gastrointestinal tract, it is often not given the attention it deserves, according to Dr. Lin Chang, professor of medicine in the Division of Digestive Diseases. One prominent exception is at UCLA, where the division's Digestive Health and Nutrition Clinic, under Dr. Chang's direction, has brought on a registered dietitian as a key member of the clinical care team.

For conditions such as reflux and chronic constipation, the importance of nutritional interventions has been well established. But Dr. Chang notes that a growing body of evidence is now available on how food can affect bowel sensitivity and symptoms in other chronic digestive disorders characterized by pain and discomfort, such as irritable bowel syndrome, functional dyspepsia, chronic diarrhea, gastroparesis, fecal incontinence

and cyclical vomiting syndrome; more is now known about the types of diets that can help reduce symptoms in these patients. And for patients with celiac disease, the dietary route — specifically, a gluten-free diet — is the only effective treatment.

Because many gastroenterologists have a limited background in nutrition, they tend to focus on other aspects of digestive disorders and are less likely to delve deeply into the role of diet in their assessment or to stress nutritional strategies in treating patients, Dr. Chang says. They may refer to a dietitian when they believe diet is playing a role in symptoms such as constipation, diarrhea, bloating or reflux, but many patients fail to follow through on the referral.

At the Digestive Health and Nutrition Clinic, patients can see their physician and the

dietitian on the same visit as part of a multidisciplinary team approach designed to bring another dimension to the practice. Moreover, the dietitian, Nancee Jaffe, comes with a specific focus and expertise in gastrointestinal disorders and GI health. Jaffe also has personal knowledge of the dietary challenges patients with GI conditions face, having lived with celiac disease.

Jaffe typically sees patients after they have visited their physician, then works with the doctor in developing a care plan. At the initial appointment she discusses the patient's history with the illness and goes through a dietary history, seeking to understand the foods that might be producing or exacerbating the GI symptoms. Often, patients will be asked to keep logs of all symptoms and everything they eat for a period of time in an effort to learn more about their individual triggers.

“For most digestive conditions, changing the diet isn’t going to be the main treatment, but it’s part of a protocol that helps the medications work better, reduces symptoms and can improve the patient’s emotional state and quality of life,” Jaffe says.

While some patients have chronic GI symptoms solely based on food intolerances or sensitivities, more often food is one of many factors in bringing on or worsening symptoms. “For most digestive conditions, changing the diet isn’t going to be the main treatment, but it’s part of a protocol that helps the medications work better, reduces symptoms and can improve the patient’s emotional state and quality of life,” Jaffe says.

The types of dietary concerns presented at the clinic vary greatly. Some patients have lactose intolerance or fructose malabsorption. Often, irritable bowel syndrome (IBS) patients are prescribed a low-FODMAP (Fermentable Oligosaccharides, Disaccharides, Monosaccharides and Polyols) diet, limiting difficult-to-digest sugars. Patients with acid reflux may be instructed to limit certain trigger foods, such as caffeine, alcohol, mint or fatty foods, while counseling for those with short bowel syndrome focuses on ways to assist in proper digestion and absorption, adequate intake and nutritional balance

Unlike most of the other conditions, when it comes to celiac disease, nutrition – avoiding gluten in the diet – is the mainstay of treatment: The gluten-free diet is the only effective therapy for celiac disease, notes Dr.

Chang, and even if new medications become available, they are unlikely to replace the need for a gluten-free diet.

Having a dietitian as part of the team treating celiac disease patients is critical, because many patients who try to follow the strategy on their own make mistakes and continue to accidentally consume gluten – which is most commonly found in foods containing wheat, barley and rye. Problems occur because reading food labels can be complicated, and there is no law in place to require the labeling of foods containing gluten. “Dietary education is particularly important for these patients,” says Dr. Chang. “They benefit from someone with expertise who can provide specific examples on how to best follow the diet.”

Without proper education, Jaffe notes, some celiac disease patients’ efforts to avoid gluten steer them toward diets that are unhealthy for other reasons – high in cholesterol, for example. Patients with IBS or other diet-restrictive conditions often face the same balancing act as they seek to maintain eating habits that are both nutritionally sound and healthy for their GI tracts. There is no “one-size-fits-all” approach, Jaffe says. Besides the fact that even patients with the same diagnosis may respond differently to certain

foods, it’s also important to help patients find a healthy dietary strategy that works within their lifestyle and preferences.

“A lot of my job is about compassion,” she says. “I let patients know that we have a team working with them – that they’re not alone – and provide support and resources to ensure they maintain their quality of life, even while taking these new steps to make themselves healthier. We have to recognize that food isn’t just about feeding the body; it also feeds the psyche and the soul. We are social creatures, and food is an important part of our culture. So if patients are cutting something out of their diet, I help them find healthy alternatives that not only fit into their diet protocol, but that are palatable and pleasing to them.”

“A multidisciplinary approach is very important in treating patients with digestive diseases, and nutrition is part of the armamentarium that can help them, along with things like medication, education, behavioral therapy and lifestyle changes,” says Dr. Chang. “It’s a healthy intervention, and it’s something that patients can do to feel they have some control over their symptoms. Given what we know about the role of nutrition in these disorders, it makes a great deal of sense to have a dietitian as an integral part of the care team.”



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GENOMIC SEQUENCING

Personalized Medicine Poised to



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 Santa Monica
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 in Gastrointestinal and
 Personalized Surgery
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When something is very big and moving very fast, the laws of physics tell us that it will strike with great impact. This could also hold true for personalized medicine, the application of genomic information to the understanding and treatment of medical conditions. “Personalized medicine represents a transformation of healthcare for humanity — and it’s happening faster than anyone ever anticipated,” declares F. Charles Brunicaudi, MD, Moss Foundation Chair in Gastrointestinal and Personalized Surgery.

While the field of personalized medicine is, according to Dr. Brunicaudi, still in its infancy, he and others are working to increase our understanding of genomic information and expand its use in providing clinical care. “A year ago, we had a portfolio of about eight genes that we could use to guide patient care; our portfolio now includes over 200.”

Examples from the field of digestive diseases include the CDH and APC genes. The CDH gene encodes for the E-cadherin protein. Patients with the CDH-1 gene are at increased risk for developing gastric cancer. Patients who are identified by their CDH gene can be put into a high-risk protocol and followed with regular biopsies, or treated prophylactically with total gastrectomy.

Mutations of the APC gene, which encodes a protein of the same name, along with a family history of

colonic polyps, are associated with a high risk of colorectal cancer. Again, patients identified by their APC gene can be followed in a high-risk protocol or can undergo total colectomy to prevent colon cancer.

In both cases, knowledge of the patient’s genetic code can lead to early cancer detection or preemptive treatment. A further step will be the development of targeted therapies that directly combat the disease based on the patient’s genomic profile, or even gene therapy to replace the defective gene.

To cite an example, Dr. Brunicaudi was part of a team whose analysis of pancreatic-cancer-patient genomes revealed aberrations in genes that control the axon guidance pathways. Those findings were recently reported in the journal *Nature*. “Our next step is to try to develop targeted therapies to the axon guidance genes that might be effective for pancreatic cancer,” states Dr. Brunicaudi.

New Center to Bring Personalized Medicine to Digestive Disease Patients

UCLA is launching a new treatment and research center, the UCLA-Santa Monica GI Neuroendocrine Center, that will focus on providing care guided by the patient’s GI neuroendocrine profile, including their genomic profile. Genomic sequencing of the patient’s blood and tumor tissue will augment standard immunohistochemistry and pathologic analysis of



disease specimens in determining which therapies are most appropriate for individual patients.

Research will include the use of genomic sequencing information to identify oncogenes and suppressor genes in order to develop targeted therapies. Another principal goal of the new center will be to develop targeted molecular imaging, such as PET-CT, optical imaging and radionuclide imaging to supplement current imaging modalities

A Furious Pace of Progress

Since the first draft of the human genome was sequenced in 2001, the speed of sequencing has increased by about 10,000 fold while the cost has decreased by about 10,000 fold. “Each run of our sequencing equipment takes about two weeks and generates about 20 times as much data as was generated during the entire 15-year period of the Human Genome Project,” states Stanley F. Nelson, MD, professor of human genetics and pathology and laboratory medicine.

Thus far, genetic testing has often been used to establish the genetic basis of rare and dramatic conditions, such as Mendelian genetic forms of diarrhea and malabsorption disorders. Dr. Nelson points out, “What these rare syndromes tell us about the genes and proteins needed to make the intestines fully develop and function normally

ultimately impacts more common diseases like Crohn’s disease, ulcerative colitis and diverticulitis.”

The next great step in personalized medicine will be to develop informatics tools to help physicians extract clinical meaning from the raw material of gene sequencing. “We know about 2,000 different locations in the genome that influence some health trait in everybody, but they each influence a person’s health only a little bit,” explains Dr. Nelson. The ability to effectively process all this information can ultimately yield insights about caring for individual patients — choosing and dosing medications more appropriately or knowing on an individual basis the risks of rare adverse drug reactions.

Bracing for Impact

“It’s been said that the genome is the anatomy of the 21st century. How can we take care of patients if we don’t know their anatomy?” asks Dr. Brunickardi. “To take the idea a step further, epigenetics and signaling pathways are the physiology of the 21st century. Physicians should know their patients’ physiology before they implement care.”

Twelve years after the first draft of the human genome was sequenced, Dr. Brunickardi points out that personalized medicine is still in a very early stage of development. But it is already very big. And it is moving very fast.

Twelve years after the first draft of the human genome was sequenced, Dr. Brunickardi points out that personalized medicine is still in a very early stage of development. But it is already very big. And it is moving very fast.

Faculty, researchers and fellows from the UCLA Division of Digestive Diseases will present more than 90 accepted abstracts at the upcoming Digestive Disease Week. Please join us at the following sessions:

MAY 18

Phosphatase and Tensin Homolog PTEN is an Essential Regulatory Factor in Toll-like Receptor 5-elicited Inflammatory Responses
Distinguished Abstract Plenary
Eunok Im, Jane Jung, Charalabos Pothoulakis, Sang H. Rhee

Predictors of Recurrent Barrett's Esophagus After Successful Radiofrequency Ablation in a Nationwide, Multicenter Cohort: Results from the U.S. RFA Registry
AGA/ASGE Presidential Plenary
WJ Bulsiewicz, ES Dellon, WD Lyday, A Ertan, DS Camara, S Komanduri, GW Chmielewski, **V. Raman Muthusamy**, NJ Shaheen

What Causes "Functional" Bowel Disorders? Recent Insights and What It Means for the Clinician
Postgraduate Course
Lin Chang

The "Impossible" Abdominal Pain Patient: Treatment Strategies and Helpful Hints
Postgraduate Course
Lin Chang

How to Achieve the Optimal Bowel Preparation: What Diet, What Solution, What Intervals?
Clinical Symposium
Brennan M. Spiegel

Human Monoclonal Antibodies Against Clostridium Difficile Toxin A and B Inhibit Inflammatory Responses and Epithelial Cell Damage to Toxins A and B in Human Peripheral Blood Monocytes and Human Colonic Tissues
Research Forum
T Hing, **Hon Wai Koon**, DQ Shih, JH Yoo, S Ho, X Chen, CP Kelly, SR Targan, **Charalabos Pothoulakis**

GERD Symptoms in the General Population: Prevalence and Severity vs. Care Seeking Patients
Research Forum
ER Cohen, **Roger Bolus**, D Khanna, **Lin Chang**, GY Melmed, P Khanna, **Brennan M. Spiegel**

Introduction – Putting Patients First: Actionable Evidence for Clinical Practice (AGPG)
Postgraduate Course
Brennan M. Spiegel

Biodegradable Stents are Superior to Fully Covered Metal Stents in the Endoscopic Management of Refractory Benign Esophageal Strictures: A Meta-analysis
Poster Session

Stephen Kim, Martijn G. van Oijen, Nikhil Agarwal, Chris M. Hamerski, Rabindra R. Watson, V. Raman Muthusamy

Characteristics of Viral Breakthrough with Direct Acting Agents for Chronic Hepatitis C Treatment in Clinical Practice
Poster Session
K Zhou, J Ferguson, S Bau, **Sammy Saab**

Crosstalk Between PKD1 and β -catenin Signaling Pathways in Intestinal Epithelial Cells
Poster Session
Y Ni, **James Sinnett-Smith**, SH Young, **Enrique Rozengurt**

Effects of Urocortin 2 and Corticotropin-Releasing Hormone Receptor 2 in Colorectal Cancer Growth and Metastasis
Poster Session
J Rodriguez, **Charalabos Pothoulakis, Stavroula Baritaki**

Estrogens Promote Development of Colitis-associated Cancer
Poster Session
J Heijmans, MC Wielenga, S Rosekrans, JF van Lidth de Jeude, JJ Roelofs, P Groothuis, A Ederveen, ES de Jonge Muller, I Biemond, JC Hardwick, **Daniel W. Hommes**, V Muncan, GR van den Brink

Fidaxomicin and OPT-1118 Inhibit Clostridium Difficile Toxin A – Mediated Inflammation in Mouse Ileum
Poster Session
T Hing, S Ho, **Hon Wai Koon**, JH Yoo, X Chen, CP Kelly, **Charalabos Pothoulakis**

Helicobacter Pylori Infection and Apical Acidity Alter Transepithelial Resistance, Paracellular Permeability, and Inflammatory Response in Gastric Epithelial Cells
Poster Session
EA Marcus, O Vagin, E Tokhtaeva, **George Sachs**, DR Scott

Identification of Protein Kinase D1 as a Mediator of Feedback Inhibition of PI3K/Akt Activation in Intestinal Epithelial Cells Stimulated with G Protein-coupled Receptor Agonists
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Y Ni, **James Sinnett-Smith, Enrique Rozengurt**

Identifying the Ideal Strategy for the Management of Refractory Benign Esophageal Strictures: A Cost-minimization Analysis
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Stephen Kim, Martijn G. van Oijen, Rabindra R. Watson, Chris M. Hamerski, PD Siersema, V. Raman Muthusamy

Independent Predictors of Lesion Localization and Outcomes in Cirrhotic and Non-cirrhotic Patients with Severe Hematochezia by Bivariate and Multivariate Analyses
Poster Session
Marine Camus, Dennis M. Jensen, Mary Ellen Jensen, Daniela Markovic, Jeffrey Gornbein

Intracellular Ca^{2+} Oscillations Produced by the Ca^{2+} -sensing Receptor are Mediated by Negative Feedback by Protein Kinase C at Thr888
Poster Session
SH Young, **Oswaldo Rey, James Sinnett-Smith, Enrique Rozengurt**

Neurotensin-HIF-1 α -microRNA 210 Axis Orchestrates Hypoxia, Colonic Inflammation and Intestinal Angiogenesis.
Poster Session
Kyriaki Bakirtzi, Christos Polyarchou, Maria Hatzia Apostolou, Dimitrios Iliopoulos, Charalabos Pothoulakis

Primary Myfibroblasts Maintain Short-term Viability Following Submucosal Injection in Syngeneic, Immune-competent Mice Utilizing Murine Colonoscopy
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HA Khalil, W Nie, **Enrique Rozengurt**, MG Stelzner, MG Martin, J Dunn, J Yoo

Protein Kinase D1 is an Upstream Kinase for Class II Histone Deacetylases (HDAC) 4, 5 and 7 in Intestinal Epithelial Cells
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James Sinnett-Smith, RK Kui, **Enrique Rozengurt**

Protein Kinase D1 (PKD1) Promotes Migration of Intestinal Epithelial Cells
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SH Young, **James Sinnett-Smith**, **Enrique Rozengurt**

The Impact of Arthropathies in Inflammatory Bowel Diseases is Significant: Results from a Longitudinal Analysis in a Multi-disciplinary IBD Clinic
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Daniel W. Hommes, H Fidler, AE van der Meulen-de Jong, L Brakenhoff

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Bloating and Distension: Understanding the Mechanisms and Optimizing Management
Meet the Professor Session
Lin Chang, F Cremonini

Endoscopic Treatment of Foreign Bodies and Food Impactions
Meet the Expert
Bennett Roth

Human Gut Microbiota Modulates Gut Serotonergic Pathway and Motility
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PC Kashyap, CS Reigstad, A Marcobal, **Muriel H. Larauche**, S Higginbottom, **Yvette Taché**, DR Linden, G Farrugia, J Sonnenburg

Durability of Reversion to Squamous Mucosa After Successful Eradication of Barrett's Esophagus (BE) with Radiofrequency Ablation (RFA): Results from the U.S. RFA Registry
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WJ Bulsiewicz, S Pasricha, S Komanduri, **V. Raman Muthusamy**, RI Rothstein, HC Wolfsen, CJ Lightdale, BF Overholt, DS Camara, NJ Shaheen

Hands-on Stations – Barretts and Esophageal Cancer
Research Forum
TH Baron, ML Davila, KS Dua, JB Klapman, CJ Lightdale, **V. Raman Muthusamy**, JN Shah, NJ Shaheen, VM Shami

Racial Differences in the Characteristics of Barrett's Esophagus (BE) and Response to Radiofrequency Ablation (RFA) Treatment: Results from the U.S. RFA Registry
Research Forum
N Li, WJ Bulsiewicz, CJ Lightdale, RD Madanick, G Triadafilopoulos, WD Lyday, **V. Raman Muthusamy**, A Infantolino, BF Overholt, NJ Shaheen

Dr. Twitter and Dr. Google at Your Service: Real-life Examples of Using Social Media for GI Patient Care and Clinical Research
Postgraduate Course
Martijn G. van Oijen

Managing Ascites in 2013: Evolving Approaches to an Age-old Problem
Postgraduate Course
Bruce A. Runyon

Putting Patients First – Top "Take Home" Points from the Meeting to Bring Back to Your Patients
Postgraduate Course
Brennan M. Spiegel

The Health Technology Revolution: Get Up to Speed, or Get Passed By & the Quantified Patient: Using Apps and Wireless Sensors to Monitor Your Patients Between Visits
Postgraduate Course
Brennan M. Spiegel

Hands-on Stations – Luminal Stenting and Ablation (HW5)
Hands-on Workshop
V. Raman Muthusamy

A Multi-national Investigation of Attachment, Catastrophizing and Negative Pain Beliefs in Irritable Bowel Syndrome
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MJ Gerson, C Gerson, **Lin Chang**, E Corazziari, D Lucian Dumitrascu, UC Ghoshal, P Porcelli, MJ Schmulson, WA Wang, MR Zali

Alterations in Regional Brain Network Properties in Irritable Bowel Syndrome
Poster Session
Jennifer S. Labus, JD Van Horn, C Torgerson, **Cody Ashe-McNalley**, A Irimia, MC Chambers, **Kirsten Tillisch**, **Emeran A. Mayer**

Differences in Resting-state BOLD Oscillation Signals Between Healthy and IBS Subjects
Poster Session
Jui-Yang Hong, Lisa A. Kilpatrick, **Jennifer S. Labus**, **Zhiguo Jiang**, Arpana Gupta, **Cody Ashe-McNalley**, Jean Stains, Bahar Ebrat, **Kirsten Tillisch**, **Bruce D. Naliboff**, **Emeran A. Mayer**

Gender and Group Differences in Gastrointestinal Symptom Severity Between Irritable Bowel Syndrome and Inflammatory Bowel Disease Patients and the General Population
Poster Session
Lin Chang, **Roger Bolus**, GY Melmed, RD Hays, D Khanna, P Khanna, **Brennan M. Spiegel**

High-intense Rectal Urgency and its Representation in the Brain
Poster Session
SA Walter, M Lowén, **Emeran A. Mayer**, **Kirsten Tillisch**, M Engström, AD Craig

Measuring Health Related Quality of Life (HRQOL) in Crohn's Disease Using Twitter: A Pilot Study of Social Media as a Novel Tool to Assess Disease Burden
Poster Session
DE Strom, **Victoria Sheen**, C Arnold, **Brennan M. Spiegel**, **Martijn G. van Oijen**

Qualitative Assessment of Symptom Experience in Patients with Irritable Bowel Syndrome for the Development of Patient-reported Outcome Instruments
Poster Session
MJ Baird, R Carson, C Ervin, **Lin Chang**, **Brennan M. Spiegel**, NJ Norton, JM Lackner, K Lasch, S Fehnel

Regional Neuroplastic Brain Changes in Patients with Inflammatory Bowel Diseases (IBD) and Irritable Bowel Syndrome (IBS)
Poster Session
Jui-Yang Hong, **Jennifer S. Labus**, **Zhiguo Jiang**, **Cody Ashe-McNalley**, Jean Stains, Bahar Ebrat, **Kirsten Tillisch**, I Dinov, Y Shi, **Emeran A. Mayer**

Resting State Brain Changes in Patients with Inflammatory Bowel Disease
Poster Session
Kirsten Tillisch, **Cody Ashe-McNalley**, **Sneha Shaha**, **Jennifer S. Labus**, Jean Stains, **Emeran A. Mayer**

Use of Twitter as a Platform for Health Information Exchange about Viral Hepatitis
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K Shahedi, **Martijn G. van Oijen**

Wide Disparities in Attitudes and Practices Regarding Type II Sphincter of Oddi Dysfunction: A Survey of Expert U.S. Endoscopists
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Rabindra R. Watson, AK. Jain, JN Shah, S Komanduri, JB Klapman, **V. Raman Muthusamy**

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HBV: HBIG Out, Antivirals In
Clinical Symposium
Sammy Saab

Management of Surgical Risk in Patients
with Cirrhosis
Combined Clinical Symposium
Bruce Runyon, S Cleary

G Protein-coupled Bile Acid Receptor TGR5 is
Expressed in the Colon and Increases Distal
Colonic Transmembrane Ion Exchanges in Rats
Research Forum
H Duboc, **Muriel Larauche, Pu-Qing Yuan,
Million Mulugeta, Yvette Taché**

Doppler Ultrasound Probe (DUP) Detection
of Arterial Blood Flow in Severe Delayed
Post-polypectomy Induced Ulcer Hemorrhage
(PPIUH): Relationship to Stigmata & Implications
for Primary Prevention
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**Gordon V. Ohning, Kevin A. Ghassemi,
Dennis M. Jensen, Thomas O. Kovacs, GA
Machicado, GS Dulai, Rome Jutabha**

Randomized Controlled Trial (RCT) of Hemoclip
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(PPIU's) for Prevention of Delayed Hemorrhage
in Patients on Chronic Warfarin: Initial Results,
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Gordon V. Ohning, Thomas O. Kovacs**

Urgent Capsule Endoscopy for Bleeding Site
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Topic Forum
**Marine Camus, Dennis M. Jensen, Gordon V.
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Kevin A. Ghassemi**

Corticotropin Releasing Hormone Receptor 1
(CRH-R1) and Progesterone Receptor (PGR)
Polymorphisms Interact with Early Life Trauma
in Healthy Controls (HC) and Patients with
Irritable Bowel Syndrome (IBS)
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**Lisa A. Kilpatrick, Arpana Gupta, Nuwanthi
Heendeniya, Jennifer S. Labus, Emeran A. Mayer**

Corticotropin Releasing Hormone Receptor 1
(CRH-R1) Polymorphisms are Predictive
of Irritable Bowel Syndrome (IBS) Status
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M Gadd, W Shih, AP Presson, **Nuwanthi
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Distinct effects of Ifn- γ and IL-17A on
TL1a-modulated Murine Regional Inflammation
and Fibrosis
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L Zheng, X Zhang, R Ichikawa, J Chen, K Wallace,
**Charalabos Pothoulakis, Hon Wai Koon,
SR Targan, DQ Shih**

Early Adverse Life Events: Influence on Resting
State Connectivity in Somatosensory, Cognitive
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Jennifer S. Labus, Kirsten Tillisch, Jui-Yang Hong,
Jean Stains, Suzanne R. Smith, Bahar Ebrat,
Cody Ashe-McNalley, Bruce D. Naliboff,
Emeran A. Mayer**

A Systematic Review of Patient, Provider and
System Barriers to Colorectal Cancer Screening
with Colonoscopy in African-Americans
Poster Session
EG Bromley, **Folasade P. May, L Federer,
Brennan M. Spiegel, Martijn G. van Oijen**

Effect of Ghrelin Agonist, Anamorelin on
Feeding, Meal Structure and Body Weight
in Alpha-synuclein Over-expressing Mice
Poster Session
**Lixin Wang, C Pietra, Honghui Liang,
SR Northrup, MF Chesselet, Yvette Taché**

Effect of Site Volume on Eradication of
Barrett's Esophagus (BE): Results from the
U.S. RFA Registry
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S Pasricha, WJ Bulsiewicz, **V. Raman Muthusamy,
S Komanduri, HC Wolfsen, RE Pruitt, A Ertan,
GW Chmielewski, NJ Shaheen**

Effects of Substance P on Pro- and Anti-
inflammatory Responses of Human Mesenteric
Preadipocytes Isolated from IBD Patients
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P Fleshner, DQ Shih, Iordanis Karagiannidis,
Charalabos Pothoulakis**

Initial Covered Metal Stent Placement is Less
Expensive Than Serial Plastic Stenting for
Biliary Decompression in Patients Receiving
Downstaging Chemotherapy for Locally
Advanced Pancreatic Cancer: A One Year
Cost Minimization Study
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**Nikhil Agarwal, Martijn G. van Oijen,
Chris M. Hamerski, Rabindra R. Watson,
V. Raman Muthusamy**

Irritable Bowel Syndrome Symptoms are Related
to the Resting Brain's Sensorimotor Network
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**Michelle P. Chen, SA Walter, M Lowén, Jennifer
S. Labus, Lisa A. Kilpatrick, Emeran A. Mayer,
Kirsten Tillisch**

Liver Transplant Referral at an Urban Public
Hospital: Opportunities for Improvement
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A Datta, **Brennan M. Spiegel,
Simon W. Beaven, VE Eysselein**

Low Uptake of Colorectal Cancer Screening
Among African-Americans in an Integrated
Veterans Affairs Healthcare Network
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**Folasade P. May, EG Bromley, MD Baek,
JL Yoon, ER Cohen, A Lee, MW Reid,
Martijn G. van Oijen, Brennan M. Spiegel**

Opioid Stimulation of Mitogen-activated Protein
Kinase (MAPK) in Enteric Neurons is Mediated
by Dynamin-dependent μ Opioid Receptor
(μ OR) Endocytosis
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CC Duraffourd, **Laura Anselmi, Catia Sternini**

Outcomes of Plastic Biliary Stent Placement
in Patients with Biliary Obstruction Secondary
to Locally Advanced Pancreatic Neoplasms
Receiving Downstaging Chemotherapy
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**Chris M. Hamerski, PS Ge, Rabindra R. Watson,
S Komanduri, K Bidari, BB Cinnor, JB Klapman,
CL Lin, SC Zhang, TR Donahue,
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Pituitary Adenylate-Cyclase Activating
Peptide (PACAP) Injected Intraperitoneally (IP)
Suppresses Ghrelin Release and Appetite
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Transplant Referral at an Urban Public Hospital:
Opportunities for Improvement
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A Datta, **Brennan M. Spiegel, Simon W. Beaven,
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Vasoactive Intestinal Peptide (VIP) Plays a Role
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IBS: What are the Best Proven Therapies?
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Outcome Measurement in FGID Clinical Trials:
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Brennan M. Spiegel

Albumin Predicts Mortality and Other Outcomes
in Acute Gastrointestinal Bleeding (GIB)
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C Nordstrom, **Sundip S. Karsan**, MW Reid,
Brennan M. Spiegel

Further Validation of a Novel Patient
Educational Booklet to Enhance Colonoscopy
Preparation: Benefits in Single-dose, but Not
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A Lee, M Vu, DA Fisher, R Modi, MD Baek,
MR Johnson, **Brennan M. Spiegel**

Independent Risk Factors of 30-day Outcomes
in Peptic Ulcer Bleeding (PUB's) by Multivariate
Analyses: Is Ulcer Size a Predictor of Worse
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Marine Camus, **Thomas O. Kovacs**,
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Neurotensin-induced Tumor Formation is
Regulated by Neurotensin Receptor 1 (NTR1)/
MicroRNA-133a-associated NTR1 Recycling
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Dimitrios Iliopoulos, **Charalabos Pothoulakis**

Preparing for the Affordable Care Act in
Inflammatory Bowel Diseases: A 2010-2012
US Insurance Claims Analysis
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Jennifer M. Choi, **Daniel W. Hommes**,
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KD Myers, **Martijn G. van Oijen**

The Efficacy and Safety of Radiofrequency
Ablation (RFA) for Treatment of Barrett's
Esophagus Containing Intramucosal Carcinoma
(IMC): Results from the U.S. RFA Registry
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KE Hathorn, WJ Bulsiewicz, ES. Dellon,
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The Inpatient Economic and Mortality
Assessment for Liver Transplantation:
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Data from 2005 to 2009
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M Stepanova, H Wai, MK Srishord, **Sammy Saab**,
M Erario, ZM Younossi

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Dimitrios Iliopoulos

Anti-fibrogenic Roles of Cathelicidin in Chronic
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T Hing, DQ Shih, R Gallo, **Charalabos Pothoulakis**,
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Corticotropin-releasing Factor (CRF)-
Proopiomelanocortin (POMC)- β -endorphin
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Corticotropin-releasing Hormone Receptors
Activate Inflammatory Pathways in Mesenteric
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Differences in Gastrointestinal Symptom Severity
Between Irritable Bowel Syndrome (IBS) and
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the General Population
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Lin Chang, **Roger Bolus**, GY Melmed, RD Hays,
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Effect of Satiety Hormone Analog, Exenatide,
on Resting State Brain Activity
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Kristen Coveleskie, **Emeran A. Mayer**, **Cody
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How Well Do Physicians Perceive Severity
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D Khanna, **Lin Chang**, P Khanna,
Brennan M. Spiegel, GY Melmed

Preadipocyte-specific Effects on Human
Colonocyte Proinflammatory Responses
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Protection of the Enteric Nervous System
in Colitis: A Therapeutic Approach for IBD?
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The Combined Nutrient and Lactulose Challenge
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The Isoquinoline Alkaloid Berberine Inhibits
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Twitter Offers Insight into Health Related Quality
of Life (HRQOL) in Ulcerative Colitis
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ER Cohen, **Brennan M. Spiegel**,
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Twitter-based "Virtual Focus Group" Yields
Similar Results as Traditional Face-to-face
Focus Groups: A Pilot Study in GERD Patients
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MD Baek, CB Whitman, **Brennan M. Spiegel**,
G Fuller, **Roger Bolus**, J Talley, **Martijn G. van Oijen**



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