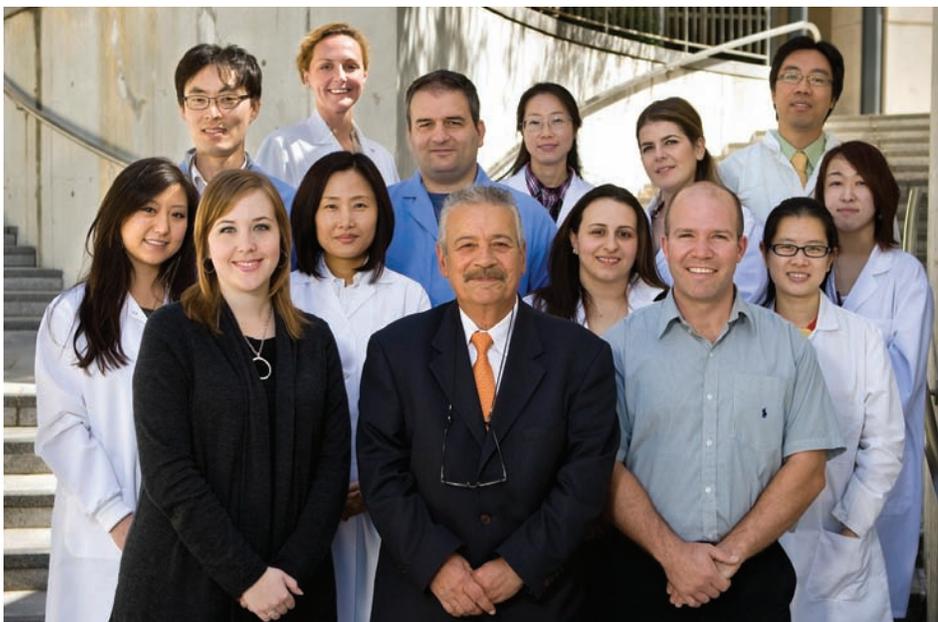


Division of Digestive Diseases

David Geffen School of Medicine at UCLA

Spring 2011 Newsletter

Closing in on the Root Causes of IBD, Crohn's Disease, and Ulcerative Colitis



The team at the UCLA Inflammatory Bowel Disease (IBD) Neuropeptide Center. Left to Right: (Front Row) Kathryn Moriarty; Charalabos "Harry" Pothoulakis, M.D.; James Bugni, Ph.D. (2nd Row) Elise Ma; Eunok Im, Ph.D.; Leina Al-Rabadi, M.D.; Ivy Law, Ph.D.; Jane Jung (3rd Row) Sang Hoon Rhee, Ph.D.; Iordanis Karagiannides, Ph.D.; Aristeia Sideri, M.D. (4th Row) Kyriaki Bakirtzi, Ph.D.; Yoon Jeong Choi, Ph.D.; Hon Wai "Micheal" Koon, Ph.D. Not Pictured: Christopher Fink, M.D.; Jorge Rodriguez, M.D.; Dimitris Stavrakis

Thanks in part to discoveries he and others have made, Charalabos "Harry" Pothoulakis, M.D., is leading a multidisciplinary program that is homing in on the root causes of inflammatory bowel disease (IBD), which could lead to new therapies for conditions that can cause considerable discomfort throughout patients' lifetimes.

The UCLA Inflammatory Bowel Disease (IBD) Neuropeptide Center, part of the

Division of Digestive Diseases, is among the first in the world to bring together researchers with a wide range of expertise – in fields that include neuroscience, inflammation, immunology, endocrinology, and obesity. The purpose is to study how neuropeptides and hormones interact with the immune system and the gut in the development of IBD and other disorders.

"This is an area that people have just started to recognize as being important

Dr. and Mrs. E. Raymond Borun

A Long-time Commitment to Medicine

Dr. and Mrs. E. Raymond Borun have been generous contributors to UCLA's Division of Digestive Diseases for more than a decade, as well as long-time supporters of the university's gerontology, cardiology, and scholarship programs. In these philanthropic endeavors, Dr. Borun has been committed to the interests of his late parents Anna and Harry Borun.

Anna and Harry Borun were residents of Los Angeles from the early 1900s and part of a family partnership that established a wholesale drug and sundry business in 1919 by the name of Borun Brothers. Ten years later, the founding partners opened their first retail outlets under the Thrifty Drug Store name. By the time Mr. Borun died in 1969, there were 323 stores.

In 1957, Mr. and Mrs. Borun made a donation of stock from their business to establish the Anna and Harry Borun Foundation. But it was only after their death that the value of the stock began to soar. After his mother's death in 1975, Dr. Borun, a retired cardiologist, assumed leadership of the foundation. "My wife and I and our three daughters

[Continued on page 7](#) ▶

[Continued on page 4](#) ▶

From the Division Chief

UCLA Division of Digestive Diseases
David Geffen School of Medicine at UCLA
Gary Gitnick, M.D.

During the coming year, our Division will undergo many changes designed to ensure the continued excellence of our programs and sustain the strong foundation that has allowed us to grow and achieve excellence over the last 58 years.

In the last two years, we have worked to develop a new strategic plan – one that differs

markedly from our previous approaches. It is intended both to position our division for growth in traditional directions and to meet the requirements of the new National Institutes of Health roadmap. The plan aims to more readily promote translation of laboratory findings to better treatments by bringing clinicians and basic scientists together in administrative units that can effectively complement existing and new programs.

The plan requires changes in the division's administrative core, which facilitates the growth of each of our academic sections or units. Toward that end, while our physician-scientists will retain their leadership roles, we also will be expanding the leadership responsibilities of others.

Additionally, the strategic plan has placed great importance on developing a

program for retention and bridge funding and expanding our infrastructure and space to meet our growth-related needs.

Last, I am happy to report that we have successfully completed our search for a director of interventional endoscopy; V. Raman Muthusamy, M.D., comes to us from UC Irvine Medical Center, where he has been Associate Clinical Professor of Medicine. He brings a long list of accomplishments in his field and an impressive academic career.

With enormous gratitude to the division's institutional, public, and private funders and to the many individuals who have made our success possible, we look forward to a solid future, working together to ensure the excellence of our existing and new programs. ■

New Booklet on Colonoscopies Helps Improve Exam Quality

A booklet based on results from a first-of-its kind, comprehensive study by Brennan Spiegel, M.D., M.P.H., Associate Professor in the Division of Digestive Diseases, will help patients better prepare for their colonoscopy exam.

The colonoscopy is an essential screening exam beginning at age 45-50 to identify and remove polyps that can lead to colorectal cancer, the leading nonsmoking-related cancer killer of Americans. The effectiveness of the procedure, however, depends as much on what happens in the hours before the patient arrives as on the skill of the healthcare team. Doctors have found that inadequate preparation is common, limiting the completeness of the procedure.

In their study, Dr. Spiegel and colleagues set about to address this concern by asking patients what information would help them better prepare. Based on their

findings, they developed a user-friendly booklet addressing the knowledge gaps, then tested its impact in a study. Patients were randomized into either a group that received the booklet or one that received usual instructions for their colonoscopy preparation. The study found that patients who were given the booklet were far more likely to arrive for their colonoscopy with a "good" preparation (68 percent) than patients who had received the usual preparation instructions (46 percent).

"Unlike every other screening test in medicine, the ability of the colonoscopy to reduce the risk for cancer is associated with the physical preparation by the patients themselves," says Dr. Spiegel. "The worse the prep is, the fewer polyps we can identify and remove. This booklet is inexpensive, easy to hand out, and can be used for anyone preparing for a colonoscopy. Most important, its content is now supported by evidence. We believe something so simple can save lives."



Booklets are available in packs of 25 from SLACK Incorporated: 800.257.8290 or www.slackbooks.com/colonprep.

Going with That Gut Feeling

Jonathan Jacobs, M.D.

Fellow studies communication between the gut and intestinal bacteria

As early as high school, Jonathan Jacobs, M.D., eyed a career in biomedical research. At first, the reasons were personal. “My mother has rheumatoid arthritis, which got me interested in autoimmunity,” Dr. Jacobs explains. “I saw how it affected her and wanted to learn more about why the immune system would attack the body.”

Dr. Jacobs, who joined the UCLA Division of Digestive Diseases last July as part of a Ph.D. fellowship program, has continued to be interested in the immune system, but his focus now is on the gut. Working in the laboratory of Jonathan Braun, M.D., Ph.D., Professor of Pathology and Laboratory Medicine and of Molecular and Medical Pharmacology, Dr. Jacobs will be studying the interactions between the immune system and the bacteria that live in the intestine and colon. His research has implications for inflammatory bowel disease (IBD), which is diagnosed in an estimated 600,000 people in the United States each year.

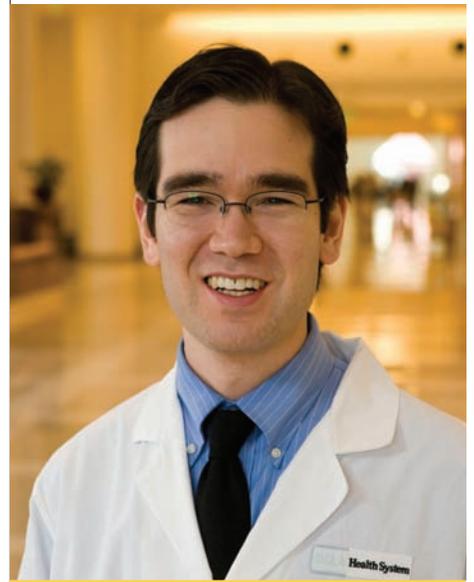
“Our hypothesis, and that of many people in the field, is that IBD arises from an inappropriate response to the bacteria that live in the gut,” Dr. Jacobs explains. “There is wide variation in these microbes, and we believe that some communities may predispose people to the development of IBD.” He and his colleagues are embarking on laboratory studies to explore whether or not certain genes can result in preferential colonization of the gut by disease-causing bacteria. This research aims to gain insight into the still poorly understood process by which gut inflammation is

triggered in IBD patients. “We still don’t have a great grasp of how these diseases develop,” he notes.

Dr. Jacobs followed his initial interest in science by pursuing a degree in biochemistry as an undergraduate at Harvard University, with an emphasis on immunology and cell biology. He remained in the same laboratory while in medical school at Harvard and during a fellowship year through the Howard Hughes Medical Institute, studying how autoimmunity develops in an arthritis model. Ultimately, his clinical interests veered toward gastroenterology, which resulted in his focus on the immune pathways in the gut that lead to IBD.

After completing an internal medicine residency at Stanford, Dr. Jacobs came to UCLA for a gastroenterology fellowship through STAR (Specialty Training and Advanced Research), a program at the David Geffen School of Medicine at UCLA, in which physician-scientists undergo combined clinical fellowship and research training. “The STAR program allows me to have protected research time to pursue ambitious long-term projects that I hope will launch my career,” Dr. Jacobs explains.

He sees great potential for progress in his area of interest. “Understanding how the immune system is regulated and how its dysfunction can lead to disease makes for really exciting science,” Dr. Jacobs says. “I anticipate that during my research career, there will be huge progress in clarifying the interplay of the immune system and gut microbes and that this work will lead to new treatment strategies for IBD.” ■



Jonathan Jacobs, M.D.

“Understanding how the immune system is regulated and how its dysfunction can lead to disease makes for really exciting science,” Dr. Jacobs says.



Mr. and Mrs. E. Raymond Borun

“I remember my father telling me that the UCLA medical school was destined to become one of the finest in the country,” Dr. Borun recalls.

[Dr. and Mrs. E. Raymond Borun continued from page 1](#)

have seen ourselves as conduits, contributing to the types of causes that were of interest to my parents.”

Since 1999, those causes have included the Division of Digestive Diseases – mostly to support the Division’s fellowship program. In carrying out Anna and Harry Borun’s wishes, the Boruns also have maintained a strong interest in aging – its social, psychological, and biological aspects. In 1989, they established the UCLA Borun Center for Gerontological Research to promote research and education programs aimed at improving the lives of the elderly. In 2003, they directed the family foundation to endow the Anna and Harry Borun Chair in Geriatrics/Gerontology to support the director of the Borun Center. Reflecting Harry Borun’s interest in education, the Boruns also have funded student scholarships.

For a number of reasons, supporting programs at the David Geffen School of Medicine at UCLA – including those of the Division of Digestive Diseases – has flowed naturally from a decision-making process driven by the interests of Anna and Harry Borun.

Anna Borun’s passion was in causes that assisted the elderly. Harry Borun was interested in medical research and healthcare, particularly for those unable to afford it. He was on the board of directors at Cedars of Lebanon Hospital (the predecessor to Cedars-Sinai Medical Center in Los Angeles). His vision for the future was that a world-class medical school would be at UCLA.

“I remember my father telling me that the UCLA medical school was destined to become one of the finest in the country,” Dr. Borun recalls. “I said, ‘You’re crazy!’ Here was a school that didn’t yet exist, and he was saying it would soon be comparable to Stanford and all of these schools in the East that had much more of a history. But he was an optimist and an enthusiastic advocate for Southern California, and he thought it had unlimited possibilities.”

After graduating from Stanford University School of Medicine during

World War II, Raymond Borun served in the U.S. Army, then returned after the war to complete his internship and medical residency at Los Angeles County Hospital (now LAC+USC Healthcare Network). In 1949, while he was assigned to the diabetic ward, he met and fell in love with a nurse who had recently come to work at the hospital from Staten Island, NY. “I moved to the operating room, and he went back East for a few years, but we stayed in touch,” Ruth recalls. Three years later, in 1952, Raymond and Ruth were married.

In 1954, Dr. Borun affiliated with UCLA as an assistant clinical professor of medicine, specializing in cardiovascular disease. At the time, the school was only three years old, but it was well on its way to living up to the prediction of Harry Borun. Dr. Borun remained affiliated with the medical school throughout his career – during which time it ascended to the ranks of the world’s leading medical institutions.

Over the years, Dr. Borun has developed relationships with the leaders of the Division of Digestive Diseases, including the current Chief, Gary Gitnick, M.D., and Vice Chief, Eric Esrailian, M.D., M.P.H. The connection has been personal as well as professional. “I have been very favorably impressed with the philosophy of care exhibited in my relationships with the Division,” says Dr. Borun. “We feel it is outstanding in both medical care and research and deserves support.”

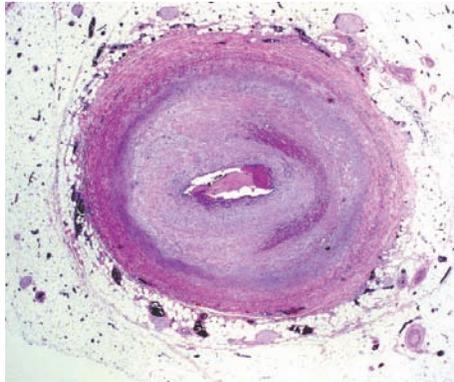
“Because my husband and I were both in healthcare, we are familiar with the fact that many of these programs will not run without outside help,” adds Ruth Borun. “We are in an enviable position to be able to provide support.”

Dr. Borun says that for all of his parents’ generosity, they never discussed the importance of philanthropy with him. “It was something that came naturally,” he reflects. That generosity is now being practiced by their three children Nancy, Barbara, and Amy; more recently, Dr. Borun stepped down as chair of the foundation, transferring the leadership responsibilities to his youngest daughter Amy. ■

UCLA Team Uncovers Mechanism behind Organ Transplant Rejection

UCLA researchers have pinpointed the culprit behind chronic rejection of heart, lung, and kidney transplants. Published in the Nov. 23 edition of *Science Signaling*, their findings suggest new therapeutic approaches for preventing transplant rejection and sabotaging cancer growth.

The team focused on the mechanism behind the narrowing of the donor's grafted blood vessels, which blocks blood from reaching the transplanted organ. Starved of oxygen and other nutrients, the organ eventually fails, forcing the patient back on the transplant waiting list. In the study, Elaine Reed, Ph.D., Director of the UCLA Immunogenetics Center and Professor of Pathology at the David Geffen School of Medicine at UCLA, and her colleagues looked at how human leukocyte antigen (HLA) molecules on donor tissue provoke an immune response in the patient. The team



examined how the patient's antibodies trigger signals that spark overgrowth of the cells lining the inner blood vessels of the grafted organ.

The scientists discovered that HLA's ability to stimulate cell growth and movement depends upon a quid pro quo relationship with another molecule called integrin beta 4. Dr. Reed's UCLA coauthors included Xiaohai Zhang, Ph.D. and CURE Director Enrique Rozengurt, D.V.M., Ph.D., of the UCLA Division of Digestive Diseases. ■

Schwarzenegger Appoints Division Member to State Medical Board



Eric Esraillian, M.D., M.P.H.

Then-Governor Arnold Schwarzenegger appointed **Eric Esraillian, M.D., M.P.H.**, Vice Chief of the UCLA Division of Digestive Diseases, to the Medical Board of California in June 2010.

Its mission is to protect healthcare consumers through the proper licensing and regulation of physicians and surgeons and certain allied healthcare professions and through the vigorous, objective enforcement of the Medical Practice Act and to promote access to quality medical care through the Board's licensing and regulatory functions.

In addition to panel review of physician cases, Dr. Esraillian was also appointed to the Education Committee and the Special Task Force on International Medical School Recognition.



Ronald Reagan UCLA Medical Center Receives Magnet Designation



The Magnet Recognition Program, a subdivision of the American Nurses Credentialing Center, awarded the re-designation of Magnet facility to Ronald Reagan UCLA Medical Center (RRUCLAMC), including Mattel Children's Hospital. The decision was unanimous between the appraisers and the commission. Only five percent of U.S. hospitals have achieved this prestigious designation, the premier award recognizing and promoting excellence in nursing practice and patient care services.

Being a Magnet hospital exemplifies the outstanding care provided to patients, professionalism, the knowledge of staff, and a commitment to excellence. The program especially commended RRUCLAMC's commitment to the community, including service to the most vulnerable populations, as well as the hospital's high patient satisfaction scores.

Division of Digestive Diseases Donor Luncheons

Gary Small, M.D., and Gerald Kominski, Ph.D., spoke at recent luncheons sponsored by the UCLA Division of Digestive Diseases, where donors and friends had an opportunity to meet some of the division's faculty and physician-scientists and listen to lectures on memory and the recently enacted healthcare reform.

Dr. Small, who spoke on memory and aging, is the Parlow-Solomon Professor on Aging, Professor of Psychiatry and Biobehavioral Sciences, and Director of the UCLA Center on Aging at the David Geffen School of Medicine at UCLA. Dr. Kominski, who spoke on healthcare reform, is Professor of Health Services and Associate Director of the UCLA Center for Health Policy Research.



Left to right: Lynn Booth, Ronald Mandell, Gerald and Gail Oppenheimer

John Zaylor and Dr. Yvette Taché

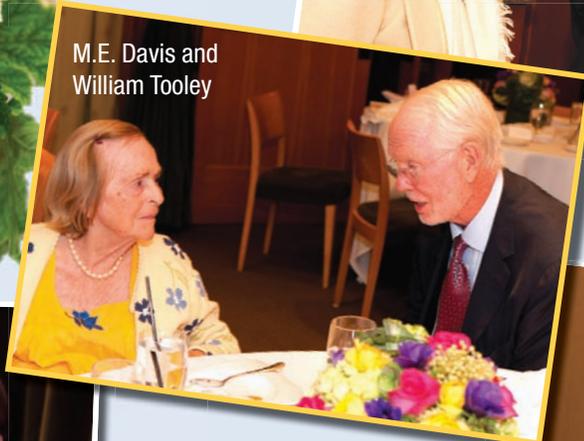


Margo Peck and Sandy Climan

Ruth Berliner and Dr. Joseph Pisegna



M.E. Davis and William Tooley

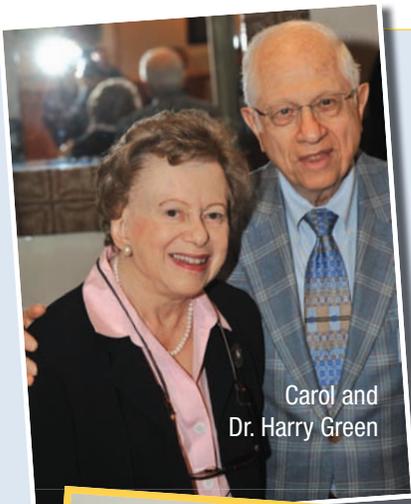


Bud Knapp

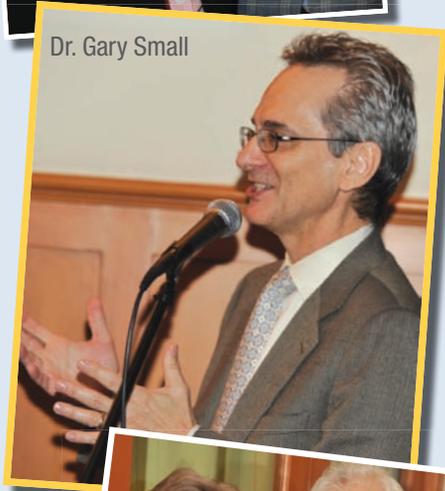


Dr. Gerald Kominski





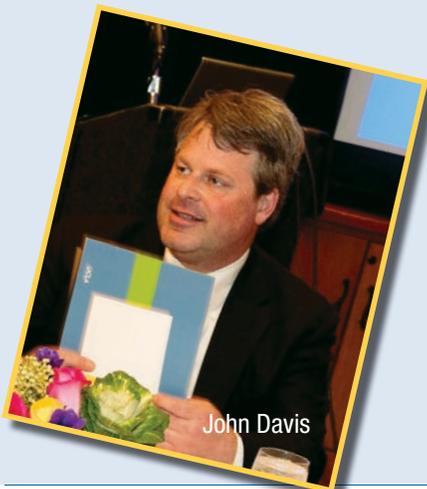
Carol and
Dr. Harry Green



Dr. Gary Small



▲ Ruth Borun
and Dr. E. Raymond Borun



John Davis

Crohn's, continued from page 1

in IBD," says Dr. Pothoulakis, the Eli and Edythe L. Broad Foundation Chair and Professor of Medicine, Pathology and Laboratory Medicine at UCLA, as well as Director of the center.

IBD refers to multiple conditions affecting the gastrointestinal tract, the most prominent of which are Crohn's disease and ulcerative colitis. Each year in the United States alone, 600,000 new cases of IBD are diagnosed, along with many more throughout the world. These chronic inflammatory conditions cause many people to become incapacitated and, in some cases, require advanced abdominal surgeries for survival. Symptoms tend to wax and wane but typically include abdominal cramps and pain, bloody diarrhea, fever, loss of appetite, and weight loss. "These are life-changing diseases," says Dr. Pothoulakis.

He notes that although environmental, genetic, and immune-system factors as well as bacteria in the intestine are all believed to play a role, researchers have had difficulty pinpointing the precise causes of these conditions. As a result, Dr. Pothoulakis says, "The management of IBD is currently inadequate."

That's where the work of Dr. Pothoulakis and his colleagues at the UCLA IBD Neuropeptide Center comes in.

Neuropeptides are small molecules that help transmit information between neurons in the brain as well as in peripheral organs, including the gastrointestinal tract. Neuropeptides are actively involved when the smooth muscle in the gut contracts, resulting in abdominal pain or diarrhea.

In recent years, Dr. Pothoulakis and his associates have made major discoveries that have contributed to a new understanding of neuropeptides' role in IBD. They found that neuropeptides are involved in the inflammatory response and that these molecules actually become more abundant during inflammation of the gut in IBD. "If we take a biopsy from a patient with IBD and compare it with a biopsy of a healthy individual or someone with another colonic disorder such as irritable bowel syndrome (IBS), only in the biopsies of patients with IBD do we see increased neuropeptide

expression," Dr. Pothoulakis explains. Moreover, his group has shown in animal models that attacking these neuropeptides reduces inflammation and the symptoms of IBD. The understanding that neuropeptides regulate inflammation in the gut has made a dramatic impact in the field, and Dr. Pothoulakis is now focused on translating that understanding into clinical trials of new treatments to inhibit inflammation in IBD patients.

More recently, Dr. Pothoulakis' group discovered the presence of neuropeptide receptors in fat cells and presented evidence that when there is inflammation in the intestine, the fat tissue surrounding it is also inflamed. "This inflammation of the fat tissue is significantly mediated by neuropeptide receptors," he explains. Now, Dr. Pothoulakis and colleagues are examining how neuropeptides modulate fat tissue and thereby affect abdominal inflammation, particularly as it relates to progress and symptoms of IBD. Their research has significance beyond this disease. "Obesity is one of the most prominent public health problems around the world," says Dr. Pothoulakis. "Our findings linking obesity with inflammation and neuropeptide function also could be very important in efforts to find ways to tackle this growing problem."

Dr. Pothoulakis graduated from the Aristotelian University of Thessaloniki Medical School in Greece and completed a research fellowship at Boston University School of Medicine before joining the faculty of Harvard Medical School in 1996. He served as director of the Gastrointestinal Neuropeptide Center at Boston's Beth Israel Deaconess Medical Center. There, he became well-known for his discoveries and insights regarding the function of gastrointestinal neuropeptides, for which he was bestowed the prestigious Janssen Award in Basic Research in Gastrointestinal Motility by the American Gastroenterological Association. In 2008, he was recruited to UCLA's Division of Digestive Diseases to head the IBD Neuropeptide Center.

The center continues to receive generous support from the Blinder Research

[Continued on page 8](#) ▶

UCLA Health System

Division of Digestive Diseases

405 Hilgard Avenue
100 Medical Plaza, Suite 265
Los Angeles, CA 90095

TR23

NON-PROFIT
ORGANIZATION
U.S. POSTAGE
PAID
UCLA



UCLA Medical Group ranks as one of California's top-performing physician organizations.

[Crohn's continued from page 7](#)

Foundation for Crohn's Disease. Recently, it received a significant boost to its efforts to translate basic science research findings into new IBD treatments with the Eli and Edythe L. Broad Foundation's pledge of \$2.5 million in support of the division's new IBD clinical center. The gift to establish the Eli and Edythe L. Broad IBD Clinical Care and Clinical Research Program, as well as the Eli and Edythe L. Broad IBD Clinical Care and Clinical Research Laboratory, will facilitate the development of new clinical trials and therapeutic targets for the disease, according to Dr. Pothoulakis.

Dr. Pothoulakis believes one of the strengths of the UCLA IBD Neuropeptide Center is its emphasis on translating laboratory findings to better treatments. He is also applying his expertise in that area to the entire division in his new roles as Chief of Research Integration and as Associate Chief for Training and Education. "I will be bringing all of the division's experts together to better communicate, share data, and begin to develop tissue banks that will strengthen the division's research," he explains. "To tackle these complex diseases, we need to have everyone sharing their expertise – molecular biologists, clinicians, and those in between, from all of the relevant disciplines. By doing so, I am confident we can make a difference that will improve patients' lives." ■

Gary Gitnick, MD
Chief, Division of Digestive Diseases

Eric Esrailian, MD, MPH
Vice Chief,
Division of Digestive Diseases

Steve Ramirez
Director of Development

Dan Gordon
Writer/Editor

Ginny King Supple
Contributing Editor

Michelle Moeck
Graphics/Production

Reed Hutchinson, Don Liebig
Photography