Treating GI Disorders through Non-Surgical Means

At major medical centers, a wide variety of gastrointestinal (GI) conditions – from certain cancers to esophageal, pancreatic, small bowel, and bile duct disorders – are increasingly being diagnosed and treated through non-surgical approaches. “Many procedures that were once the domain of the surgeon can now be done in a more minimally invasive way,” says V. Raman Muthusamy, M.D., one of the leaders in the emerging field known as interventional endoscopy.

The Joneses have a history of donations to UCLA, contributing to the Jonsson Comprehensive Cancer Center and UCLA Anderson School of Management and giving smaller donations to the Division of Digestive Diseases in the past, but recently they decided to support the Division in a more significant way. They had known Drs. Gary Gitnick and Eric Esrailian, Division chief and vice chief, respectively, and Mr. Jones had told Dr. Esrailian that he would be happy to provide support for the right program, which turned out to be Dr. Beaven’s lab.

Dr. Beaven is seeking to understand how metabolic syndrome – a cluster of conditions that include excess body fat, high blood pressure, high blood sugar, and high cholesterol – causes liver disease in the earliest stages and the process by which the disease progresses to the end stages of cirrhosis. One in three Americans is believed...

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Mr. and Mrs. Brad Jones
Philanthropy: An Excellent Investment

When Brad Jones asserts that philanthropy is “the best use of one’s money,” he knows of what he speaks.

Mr. Jones, who with his wife Joan has provided generous funding in support of Dr. Simon Beaven’s research on metabolic syndrome within UCLA’s Division of Digestive Diseases, has achieved considerable success choosing the right investments in his career as a venture capitalist. A founding partner of Redpoint Ventures and previously a general partner with Brentwood Venture Capital, he has managed successful investments in biotechnology, communications, Internet commerce and infrastructure, medical devices, semiconductors, software, and wireless products. Currently, he focuses on technology opportunities located in Southern California.

“We were fortunate enough to make a fair amount of money, and there are really only two things you can do with it when you die – leave it all to your children or give it to charities,” Mr. Jones explains. “We certainly will provide some money for our kids, but as [billionaire investor and philanthropist] Warren Buffett has said, each child needs only a certain amount, and giving them more doesn’t really benefit them, or society, the way philanthropy does. Joan and I felt that a good use of our money would be to put it toward helping other people, and Simon’s lab has the potential to be extraordinarily helpful to people through scientific advancement.”

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Celiac Disease: Working to Improve Diagnosis and Treatment

Much remains to be learned about why celiac disease is becoming increasingly common. An autoimmune disorder in which consumption of gluten (found in wheat, barley, and rye) sets off a toxic response characterized by damage to the small intestine, celiac disease has increased five-fold in the last 50 years. Once thought to be a rare pediatric disorder, it is now believed to affect nearly 1 percent of the U.S. population.

“Celiac disease is caused by a combination of genetic and environmental factors, and our genes don’t change that quickly, so clearly something about our environment has changed,” says Gregory Harmon, M.D., who recently joined the Division of Digestive Diseases as Director of UCLA’s celiac disease program. Scientists have hypothesized about several contributing factors, ranging from the improving cleanliness (leaving the immune system out of balance from the reduced exposure to infections) to the changing bacteria milieu in people’s gastrointestinal tracts to the increasing gluten content of the wheat from today.

Dr. Harmon is one of the leading experts of the science and treatment of celiac disease. He completed gastroenterology training at UC San Diego and worked with Dr. Martin Kagnoff, an internationally known celiac-disease expert, to build UC San Diego’s program. He will now work to build a clinical research and treatment program at UCLA. In his new position, Dr. Harmon will also take on the role of directing the adult gastroenterology care for patients in UCLA’s small intestinal transplant program.

“More than 95 percent of people who have celiac disease are not yet diagnosed,” Dr. Harmon says. Because the symptoms are so common and range from very mild to severe, many patients are never tested for the disease.

As we move forward in strengthening our research, training, and clinical components, the support of our friends in the community continues to be vital to this effort. We are especially thrilled to share with you some exciting news about the Gerald Oppenheimer Family Foundation’s involvement with the newly named Gail and Gerald Oppenheimer Family Center for Neurobiology of Stress at UCLA. Additionally, the Division is enormously grateful to Mr. and Mrs. Brad Jones for their vision as well as commitment to Dr. Simon Beaven’s research on metabolic syndrome.

Please read on for detailed information about these and other exciting developments. We continue to be grateful for your support and partnership in this success.
In recent years, researchers at UCLA's Center for Neurobiology of Stress have been studying the links between the brain and digestive system in the development and treatment of common chronic digestive disorders in adults and children. Now, with the support of the Gerald Oppenheimer Family Foundation, the newly renamed Gail and Gerald Oppenheimer Family Center for Neurobiology of Stress will expand its activities to include research of brain-body interactions in other chronic medical disorders and the biology underlying mind-based therapies.

The first reception, held in June, took place at the Center’s new 6,000-square-foot facility. It features labs and clinic areas and houses the 30 faculty and staff, who had previously been located throughout the campus. Different programs within the center are dedicated to studying different aspects of mind-brain-body interactions, one of them focusing on yoga, meditation, hypnosis, and cognitive behavioral approaches.

Supported by annual federal grants, the Center will receive additional support from the Oppenheimer family’s 2002 gift, directed to underwrite both this facility and the UCLA Center for East-West Medicine. Half of the gift has been established to meet these programs’ long-term objectives.

The endowed funding will help investigators explore mind-brain-body interactions in several stress-sensitive conditions, including persistent pain disorders, such as irritable bowel syndrome and interstitial cystitis, obesity, inflammatory diseases of the liver and intestine, and chronic cardiovascular disorders. It also will fund studies of the biological mechanisms underlying the effectiveness of various mind-body therapies.

“We are pleased to support this new field that addresses the mind-body connections and the role of stress in chronic disease that ultimately may be able to offer more treatment and care options for patients,” said Gail and Jerry Oppenheimer. “We believe these complementary approaches are the future of medicine. We have been supporting alternative medicine with a focus on mind-body connections for around 10 years but are just beginning to incorporate the role of stress. We know there is a long way to go before practitioners are able to achieve the goal of a breakthrough, so we hope other people will join us in supporting this innovative center.”

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Early-stage cancers and polyps that would have previously required surgical removal are now often treated endoscopically, he notes, through a technique called endoscopic mucosal resection. Stents can be placed to create openings, when patients' tumors are obstructing the GI tract. Interventional endoscopists are accessing the bile duct and pancreas to remove gallstones that might otherwise require surgical exploration or to treat disorders such as chronic pancreatitis.

The small bowel, the area between the stomach and the colon, was historically difficult to access with scopes; now, through a new device, Dr. Muthusamy and his interventional endoscopy colleagues can perform a procedure called spiral enteroscopy, enabling them to treat disorders deep in the small bowel. He was involved in a major advance that enables patients who have Barrett's esophagus with dysplasia (early cellular changes that can signal cancer) to undergo a much-less-invasive endoscopic treatment.

"We are covering the full spectrum of digestive diseases through a broad set of endoscopic techniques that, in some ways, are approaching surgical capabilities," Dr. Muthusamy says.

Dr. Muthusamy, who came to the Division from UC Irvine, completed his residency at Duke University Medical Center and trained at the Centre for Evidence-Based Medicine in Oxford, England. He completed his fellowship in gastroenterology at UC San Francisco, did additional training in advanced endoscopy at UCI, and then returned to UCSF, where he was director of endoscopic ultrasound and conducted clinical research.

An engineering major as an undergraduate, he was already inclined toward devices and technology when he went into medicine. “What drew me to gastroenterology in particular was its blend of diagnostic challenges and direct applications,” Dr. Muthusamy says. “Interventional endoscopy was particularly attractive because it involved both technology and the engineering of devices.”

At UCI and UCSF, he pursued clinical research, focusing on the evaluation of existing and new endoscopic technologies for the diagnosis and treatment of digestive disorders. This work included Dr. Muthusamy’s key role in the development of an endoscopic technique for treating Barrett’s esophagus with dysplasia. Until recently, the condition often required surgical removal of the esophagus to head off the development of cancer. The technique that Dr. Muthusamy helped to develop and successfully test in clinical trials uses radiofrequency ablation to effectively burn off the dysplasia, eliminating the need for surgery.

“I always felt that if the dysplasia involved a very small area of the esophagus, it would be much better to eliminate it locally than to remove the entire organ, and it’s been quite satisfying to see this approach come to fruition,” says Dr. Muthusamy. “The same goes for other types of pre-cancerous lesions – it’s much better if we can effectively treat them before surgery is required.”

Dr. Muthusamy also is exploring the clinical applications of endoscopic ultrasound, which is used to diagnose digestive disorders – often on the same visit as the treatment. “A suspected pancreatic tumor, for example, can now be diagnosed and biopsied, the tumor can be staged, the nerves can be injected with medications to relieve pain, and radioactive seeds can be placed to prepare the patient for effective radiation therapy all in one session,” he says.

In addition to continuing with his research and clinical efforts, Dr. Muthusamy is now aiming to build a comprehensive interventional endoscopy program. “There are people at various centers who do some of these procedures, but very few centers have a full-service, cohesive team,” he says. Ultimately, the plan calls for several interventional endoscopists working in conjunction with other surgical and medical teams to provide the most effective and least invasive care tailored to each patient’s circumstances. In addition

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New Endoscopic Approaches for Obesity and Pancreatic and Biliary Diseases

More than a million people in the United States have undergone bariatric surgery for weight-loss. The most common forms are gastric bypass procedures, which create a small upper pouch that is reconnected to the small intestine as a physiological strategy for reducing food intake. But a vast majority of these patients begin to re-gain weight after a period of time, in part because their surgically created gastric pouch begins to stretch, allowing for increased consumption.

For the past year, Rabindra R. Watson, M.D., has been part of a group that has developed non-surgical techniques to improve the results of bariatric weight-loss surgery, either by reducing the volume of the pouch through the injection of sclerosing agents that harden the tissue or by re-sewing the pouch to counter the stretching. Now, Dr. Watson has brought these techniques to UCLA; the clinical instructor of medicine started in September, after being recruited to join the Division of Digestive Diseases’ new interventional endoscopy team.

After completing his residency in internal medicine and a fellowship in gastroenterology at UC San Francisco, Dr. Watson spent the last year in an advanced endoscopy Harvard University fellowship at Massachusetts General Hospital and Brigham and Women’s Hospital. He will continue to pursue research he began there – developing new endoscopic approaches for obesity, as well as pancreatic and biliary diseases.

“Endoscopy represents a natural progression of medicine and technology,” Dr. Watson says of the non-surgical approach now being used for a growing list of GI conditions (see the accompanying article on Dr. V. Raman Muthusamy). “We have progressed from performing surgery through large incisions to the keyhole incisions of laparoscopy. The next step is to perform these types of interventions through natural orifices via endoscopy, which is now possible thanks to new technology, new devices, and the refinement of endoscopic skills.”

For example, Dr. Watson is currently involved in research that uses endoscopic techniques, rather than surgery, to remove nonviable and infected material from around the pancreas following bouts of severe pancreatic inflammation. This form of endoscopic therapy represents a significant step forward in the treatment of this highly morbid condition. In addition to being much less invasive, the approach promises to improve patient safety and recovery times. UCLA has been selected as a participating site in a forthcoming national multicenter clinical trial of this treatment modality, in which Dr. Watson and his colleagues will be involved.

Dr. Watson says he was drawn to UCLA by its academic reputation, as well as the emphasis by the Division of Digestive Diseases on building a world-class interventional endoscopy program. “It was clear, through the funding and facilities being devoted to launch this program, that the Division has made it a priority,” he says. “It is an exciting time for innovation in minimally invasive endosurgery, as we are now pushing the boundaries of what we have thought possible. That’s what we’re going to be focusing on at UCLA.”

Faculty Paper Published in Genetics in Medicine

Terri Getzug, M.D., faculty member with the UCLA Division of Digestive Diseases, recently co-authored a paper with Wayne Grody, M.D., Ph.D., and Neda Zadeh, M.D., which appeared in Genetics in Medicine, the official journal of the American College of Medical Genetics. The title of the paper is “Diagnosis and management of familial Mediterranean fever: Integrating medical genetics in a dedicated interdisciplinary clinic.” This article, one of the only reviews of its kind from the United States, provides clinicians with the presenting features of familial Mediterranean fever, methods of diagnosis including molecular testing, and current management based on this team’s extensive experience with hundreds of affected individuals over the last 50 years.
those with active celiac disease. It is diagnosed by endoscopic biopsy of the small intestine.

The only current treatment is to eliminate gluten from the diet. Dr. Harmon notes that most patients do well as long as they stay away from the offending proteins. Some patients, however, are sensitive to trace amounts of gluten that inadvertently contaminate their food.

“Being diagnosed with celiac disease is a life-changing event,” says Dr. Harmon. After being diagnosed with the disease, patients need to avoid gluten in all the things they ingest, including medications. “We need new therapeutics to help these patients become less sensitive to gluten,” he says. As Dr. Harmon builds the celiac disease program at UCLA, he intends to explore new treatment options.

Dr. Harmon will also apply his laboratory background to collaborate with scientists who are conducting the basic experiments that can lead to future clinical advances. In addition to his clinical work at UC San Diego, Dr. Harmon conducted studies in the lab focusing on inflammation in the gastrointestinal tract. Among other things, his research group reported key findings in a model of cystic fibrosis that identified novel targets for treating that disease. Dr. Harmon will draw upon his prior experience to help bring new scientific advances in celiac disease from the laboratory bench to the bedside.

Dr. Harmon says he was drawn to gastroenterology by the challenges involved in working with patients to identify the cause of their unclear symptoms. “When a patient has stomach pain, several different diagnoses may be causing it,” he notes. “Celiac disease is one of the potential explanations for numerous abdominal complaints.” Dr. Harmon notes that working at a state-of-the-art institution such as UCLA helps him to provide the best care for his patients.

Celiac Disease, continued from page 2

Division of Digestive Diseases Donor Luncheon

Andrew Da Lio, M.D., F.A.C.S., spoke at a recent luncheon sponsored by the UCLA Division of Digestive Diseases. Dr. Da Lio is clinical professor and director of microsurgery in the Division of Plastic and Reconstructive Surgery at the David Geffen School of Medicine at UCLA. Attendees had an opportunity to listen to a lecture on the latest thinking and treatments in the field of plastic surgery and meet some of the Division’s faculty and physician-scientists.
to have metabolic syndrome, an early warning sign for some of the leading causes of death, including diabetes, heart disease, and stroke. Dr. Beaven's research could help lead to preventative treatments.

“Gary and Eric told me they had this brilliant young physician-scientist who needed funding to start his own lab in order to further his research,” Mr. Jones recalls. “I heard about the research that Simon was doing and what the goals were, and it seemed to me to be a really important area of medicine. Simon clearly has the credentials and the capability to move research forward in this area, so we decided to help fund the lab.”

Mr. Jones has deep roots in Los Angeles. Though he was born in Ohio, his family moved here when he was eight, settling in Palos Verdes. He went to Harvard University to study science, earning a bachelor’s degree in chemistry and a master’s in physics, and then went to Stanford University for both his M.B.A. and J.D. degrees.

Brady and Joan met when both were students at Stanford Law School in 1977. After graduating, they returned to Los Angeles, married, and raised two daughters and a son, now 27, 25 and 22, in Manhattan Beach. After spending time practicing law, Joan was elected to the Manhattan Beach City Council and went on to serve as the city’s mayor; she now runs a retail store in the area.

Although they support each other’s philanthropic decisions, Brad and Joan each pursue their own charitable endeavors. Among others, Joan’s interest has been in providing scholarships to the community college system for people from low-income backgrounds who otherwise wouldn’t be able to afford fees and textbooks.

Philanthropy may be a great investment, but as Mr. Jones well knows, there are many worthy philanthropic investments from which to choose. “When [Microsoft founder] Bill Gates was criticized early in his career for not giving away enough, his response was that he had worked really hard to make the money, and he wanted to take the time and work just as hard to figure out the right way to give it away,” Mr. Jones says. “How we allocate resources in the private sector for the benefit of the economy and in the nonprofit sector for the benefit of people is very important. You can give money to things that can have an astounding impact.”

In deciding where to invest his philanthropic dollars, Mr. Jones says he takes into account the same two criteria as when he is considering which small tech companies to support in his venture capital business. Both led him to enthusiastically support Dr. Beaven’s lab.

The first is the qualifications and capabilities of the people who are being supported. “In my business, you look carefully at the quality of the management teams and if they can build the company and be successful,” Mr. Jones says. “Similarly, if you’re funding something that’s nonprofit, it’s important to look at the people and see if they can accomplish something significant with the money you’re providing. I think Simon can do that.”

The second: “When you’re investing in a company, you want to know about the market opportunity,” says Mr. Jones. “How important is the product? How much demand will there be for it? How big is the market size? In the nonprofit sector it’s the same sort of thing: How important is the technology in terms of providing better solutions for people, and how many will benefit from that? On both questions, metabolic syndrome is very worthy of support: The technology needs to be further developed to create solutions for people, and a huge number can benefit from any breakthroughs that are made.”

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Million Mulugeta, M.V.Sc., D.V.M., Ph.D., received the 2011 International Foundation for Functional Gastrointestinal Disorders (IFFGD) Research Award in Basic Science. Adjunct professor in the Division of Digestive Diseases, he is conducting research on understanding the processes underlying stress-related GI disorders in order to develop effective therapies. Dr. Mulugeta also is examining the molecular basis of compounds related to the body’s reaction to stress to clarify the impact they have on digestive functioning and pain response. IFFGD awards support and encourage the participation of clinicians and scientists in multidisciplinary efforts aimed at advancing the understanding of these disorders in adults and in children.
Venkataraman Raman Muthusamy, M.D. continued from page 4

to patient care, Dr. Muthusamy says the program will train future interventional endoscopists for practice in the United States and abroad, while serving as a focal point for the development and testing of new techniques and technologies.

Endoscopists are increasingly venturing into territory that was once the domain of surgeons, while surgeons are continuing to adopt more minimally invasive approaches. “We were once distinct entities, black and white, and increasingly we are morphing into shades of gray,” Dr. Muthusamy says. As the two disciplines meet near the middle, he adds, new opportunities for collaboration will arise. He also foresees his program working closely with medical and radiation oncologists, as endoscopic techniques continue to become more important to the diagnosis and treatment of GI cancers.

“Our goal is to coordinate all of the relevant programs – surgery, medical and radiation oncology, radiology, pathology, and interventional gastroenterology – to develop a specialized center for complex GI care,” Dr. Muthusamy says. “At this world-class institution, we are ideally situated to do that.”