

UCLA Division of Digestive Diseases

Spring 2008 Newsletter

David Geffen School of Medicine at UCLA

Probiotics: From Bugs to Drugs



Grocery products containing probiotics.

Increasingly, we see rows upon rows of refrigerated products containing live bacteria in supermarkets and health food stores. What could live bacteria possibly do for you? Advertisers tout the benefits of yogurt and other foods containing live cultures that you can eat to shorten or prevent illness. With the myriad claims many commercial enterprises make, how do you know what to believe? Although “good bugs” can protect your stomach from a variety of ills, there is more than meets the eye when you look deeper into the science surrounding their potential use.

The gastrointestinal (GI) tract is the largest source of our immune system, and keeping it healthy is vitally important. The human GI tract is inhabited by a little more than four pounds of bacteria, representing more than 400 different species. These bacteria are critical for normal development of the intestine and for defense against infections – and are critical for our

health. Probiotics are live microorganisms that, when consumed in proper amounts, can provide you with health benefits and a protective effect against potentially harmful bacteria that also live in the GI tract. Including probiotics in your diet can support healthy gut flora, and some can help in treating diseases.

There is plenty of “food for thought” as you face the heavy advertising of probiotics. Dr. Fergus Shanahan says, “Everything has to be put in perspective. In healthy people, they probably aren’t necessary, but probiotics would be helpful if you are taking antibiotics.” Dr. Shanahan and his colleagues are investigating how to cure and prevent illnesses in the GI tract, carefully conducting scientific studies and clinical trials to use probiotics as an ally to treat these and other specific diseases. The aim is to transform “bugs to drugs” – in other words, to make sure variables such as dosages, strains, product quality, and stability are

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From the Division Chief

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

I am proud. Once again, U.S. News & World Report rated the UCLA Division of Digestive Diseases as best in the Western United States and among the top five in the nation. This standing reflects the remarkable and talented faculty on board, who are productive leaders and whose numbers continue to increase. Our division has grown to the point where we have expertise throughout the field. Moreover, our research programs reflect unparalleled depth, covering myriad basic science and clinical pursuits.

We have several new additions to our division. Dr. Kirin Bhat is an advanced biliary endoscopist with training in endoscopic ultrasonography. Dr. Wendy Ho, from Massachusetts General Hospital/Harvard Medical School, is a clinician and educator in general gastroenterology. Dr. Daniel Cho, from

UCLA, is a clinician and educator in general gastroenterology.

The team of seven scientists from Harvard headed by Dr. Charalabos "Harry" Pothoulakis is flourishing at UCLA, having built an extremely strong program. The IBD Affinity Group, which has been successfully developed, includes 12 senior investigators and their colleagues from multiple disciplines on campus. In addition, many of our faculty members have been recognized for their outstanding work, for example, Dr. Brennan Spiegel and Dr. Emeran Mayer.

The advances in signal transduction of Dr. Enrique Rozengurt and his group are defining the basic mechanisms in the development of cancer and other chronic diseases; their publications are among the most widely quoted. In addition, Dr. Peter Anton and his associates have built a program in mucosal immunology

unlike that seen anywhere in the world. Our training program is thriving, and we are now in the midst of a transition in leadership. Dr. Wilfred "Fred" M. Weinstein is handing over the reins to Dr. Spiegel and Dr. Bennett Roth. They anticipate continued growth and excellence in producing the next generation of top clinicians and scientists in this field.

The progress and success in clinical care and research that come out of this division are made possible in large part by the generosity of our donors. Their funds underwrite the infrastructure that allows us to thrive. Federal, state, and university resources are not available for essential positions, such as secretaries and fund managers, who keep the organization strong and productive. In addition, our donors support the largest part of our training program budget and provide the moneys necessary to recruit new faculty. Thus, I am proud, as well, that the UCLA Division of Digestive Diseases continues to merit the encouragement and commitment of our friends in the community and beyond. ■

DDD Faculty Inform Patients in the Community

Physicians in the UCLA Division of Digestive Diseases, such as Dr. Sammy Saab and Dr. Eric Esrailian, dedicate themselves to community service in the normal course of their careers in medicine.

Seminars for Patients with Liver Disease

Soon after Dr. Sammy Saab, Associate Professor of Medicine and Surgery and a former Fellow in the Division, came to UCLA eight years ago, he established a yearly seminar for patients and families to discuss problems they are having with liver disease. The seminars are taught in English and Spanish, and he looks forward to plans to expand into Arabic and other languages, as well. The half-day meetings are conducted at UCLA and are free for all attendees, with breakfast provided. The presenters are

doctors, surgeons, and oncologists from UCLA, and other high-profile individuals. From 150 to 200 people usually attend, and the numbers have

been growing every year.

The presenters try to tell the story about the liver: what it does, how it functions, how to know when it's damaged (based on blood test results), and how to take care of it when being treated.

IBD Hot Topics

Among his many other community involvements, Dr. Eric Esrailian is co-chair of a yearly symposium for several hundred patients with Crohn's disease and ulcerative colitis.

The half-day course is free, and the lectures highlight the latest on inflammatory bowel disease (IBD) treatment, management, research, psychosocial support, and patients' rights. Also, health professionals get an up-to-date education on these diseases.

The Greater Los Angeles/Orange County Chapter of the Crohn's and Colitis Foundation of America (CCFA) sponsors the yearly symposium, as well as walks and other events. Patients can go to the CCFA Website

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First-Rate Fellows Aspire to Make an Impact in Treating Digestive Diseases

Exemplary doctors Karen Simon and Omid Shaye aim high to shape the future treatment and prevention of digestive diseases with the skills they have learned through their experience in basic science and clinical research at UCLA.

Dr. Karen Simon

Dr. Simon thought she would become a doctor like her father but wanted to experience the work world first. She grew up in Ohio outside of Cincinnati and then went to Stanford University, where she majored in Art History. She taught for a year in Santa Barbara and then decided to apply to medical school. After graduating from Northwestern University Medical School, Dr. Simon came to Los Angeles for her residency. She joined the UCLA Division of Digestive Diseases Fellowship Program in July 2005, pursuing her interest in inflammatory bowel disease (IBD). She says that training at UCLA provides a lot of opportunity to work with the “big names in the field” in a cutting-edge environment.

A pivotal experience in her patient relationships came three years ago, when Dr. Simon’s one-year-old daughter had open-heart surgery. Being the family or patient as opposed to a doctor for the first time made her realize what it feels like to be a patient hanging on a doctor’s every word. A phrase like “Everything will most likely be fine” does not give patients much confidence, when there are numerous medications and possible complications. When she talks to patients, she gives as much information as she can, such as, “We will take every precaution to make sure you do fine on this medication.”

In September, Dr. Simon will start her career as a gastroenterologist – the only woman in a private practice in Camarillo. Up to now, there were



Karen Simon, M.D.

practically no female role models in General Gastroenterology. “Nowadays, private practices are becoming more aware that they are behind the times, with numerous patients asking for a woman to handle their cases.” Regarding her journey in medicine, Dr. Simon reflects, “From the time you decide to apply to med school to the start of your career is a dozen years, and now I am here, ready to follow in my father’s firmly established footsteps after all.”

Dr. Omid Shaye

From the revolution in Tehran to the basketball courts at UCLA, Dr. Omid Shaye has quite an interesting background. Born in Tehran shortly after the revolution, he and his family were smuggled out of Iran in 1982 when he was age five. After a two-week journey in which they ran out of food and were shot at and ambushed, they finally arrived in Israel, where they lived for 3-1/2 years before coming to Los Angeles. A product of local public schools, Dr. Shaye says, “Growing up, UCLA was like a second home. I practically lived at the John Wooden Center, on the men’s basketball court.” He naturally gravitated to UCLA, where he majored in Neuroscience with a minor in Education.



Omid Shaye, M.D.

Dr. Shaye attended the UC San Diego School of Medicine. He developed a passion for Gastroenterology “because it is an area with a wide variety of different diseases and does so much. The intellectual aspect of medicine mixes with the technical, surgical, and anatomical approach to fixing things.” Dr. Shaye is dedicated to improving care in medicine, and “being in research allows you to affect the lives of countless people.”

He recognizes that almost every GI disease is affected by obesity, and wants to focus on halting it through effective treatments. Dr. Shaye points out, “In recent decades, all innovations in technologies have been because of the Baby Boomers. Now that age group of 80-million people between 40-60 years old wants to prevent diseases, prolong life, and know how to live better. We cater to their needs.”

It is important to Dr. Shaye to be a positive role model for the doctor/patient relationship. He would like to inspire patients to take more active roles in their own health. “It also makes our job more fun, since they get healthier and better in a positive environment.”

After his fellowship ends in another year, Dr. Shaye intends to pursue academics and do clinical GI and clinical research. He wants to teach and get involved in many aspects of medicine. “I love building and creating things, and I have great energy,” states Dr. Shaye – even off the basketball court.



Dr. Fergus Shanahan

more predictable. Standardization and regulation are also of utmost importance.

Dr. Shanahan received his training at UCLA as a Fellow in the Division of Digestive Diseases and is now a world-renowned expert on inflammatory bowel disease (IBD). He has conducted extensive research in the area of probiotics in treating patients with a wide range of clinical disorders. Dr. Shanahan is now Chief of the Department of Medicine at University College Cork and Cork University Hospital.

“Probiotics are most simply defined as bacteria that can be harnessed for therapeutic benefit,” Dr. Shanahan explains. The most commonly used probiotics are lactobacilli and bifidobacteria.

Some products have exaggerated and unproven claims attached to them. More of a good thing is not necessarily better: Eating seven containers of yogurt per day will not cure your GI problem. Dr. Shanahan emphasizes that good science is important in evaluating the positive aspect of probiotics. He says, “It is

4 important to separate the science from the commercial ventures that make wild

and unsubstantiated claims for the effectiveness of probiotics. These claims cannot be justified or validated at the present time and can sometimes obscure or retard the progress made by established scientists and studies.”

Dr. Shanahan reports that there is solid evidence for the effectiveness of some probiotics in certain conditions. By far, the best is in the treatment or prevention of acute diarrheal infections, such as childhood gastroenteritis and antibiotic-associated diarrheal disease. Another emerging indication for probiotic usage is in the prevention of a serious bacterial overgrowth syndrome called necrotizing enterocolitis (NEC) that affects premature babies weighing less than 3.3 pounds at birth. Also, some – but not all – probiotics have been shown in rigorous controlled clinical trials to be effective in irritable bowel syndrome (IBS). In the largest clinical trial of any probiotic in any setting conducted to date, it has been shown that *Bifidobacterium infantis* 35624 was clinically superior to the placebo.

A molecular mechanism is shown in some probiotic effects. Listeriosis is a rare but very serious food-borne infection that has a high mortality rate. One particular probiotic (*Lactobacillus salivarius* UCC118) has been shown conclusively to protect against infection by producing an antibacterial molecule (a bacteriocin named salivaricin) that kills listeria; however, this mechanism is not how probiotics protect against other infections, such as that caused by *Salmonella* organisms. Moreover, in reference to IBD, Dr. Shanahan says, “We all thought the use of probiotics would help in Crohn’s disease, but so far it hasn’t.” Also, findings with ulcerative colitis have been mixed; those trials are continuing.

“There is no such thing as zero risk,” Dr. Shanahan states. “While probiotics are generally and correctly regarded as being relatively safe, there is always the potential for hazard depending on the setting.” Recently, a

study conducted in Utrecht, Holland, using probiotics vs. placebo in the treatment of pancreatitis, generated results suggesting that the particular probiotic mixture was actually harmful and was associated with a higher mortality rate than in the placebo-treated patients. This work underscores the importance of being specific about the type of probiotic used and conducting more research.

Once normal host-flora interactions in the gut and the molecular mechanisms of probiotic action in IBS and other disorders are better understood, the move from “bugs to drugs” will become a reality.

Are probiotics the latest magic potion that promises good health for all? According to Dr. Shanahan, the message to clinicians is to “select pharmabiotic strategies only on the basis of solid science. Consumers should avoid products that lack true scientific backing.” In other words, be sure to follow that “gut feeling” the

Faculty Awards & Presentations

- Dr. Dennis Jensen will receive a new award from the American Society of Gastrointestinal Endoscopy (ASGE), the Distinguished Endoscopic Mentoring Award. It will be presented at the national Digestive Diseases Week conference. He also has received funding for a new five-year Veterans Administration Merit Review Randomized Controlled Trial (Doppler Ultrasound Probe for Blood Flow Detection in Severe UGI Bleeding). This study will be conducted with UCLA’s CURE Hemostasis Research Group.



Kelsey and Camille Grammer

Why Philanthropy Matters

example, patients – not just physicians – are invited to seminars and luncheons, where they gain knowledge of cutting-edge research and applications in such areas as nutrition and diet, irritable bowel syndrome (IBS), inflammatory bowel disease (IBD), hepatitis, transplantation, and more. In addition, she enjoys the semiannual newsletters that highlight Division people and programs.

The couple realize that teaching by example will motivate the next generation of donors, who witness how the “circle of giving” makes a difference for both the supporter and the charitable organization. This mutually rewarding relationship calls to mind the poetry of W. H. Auden, Mr. Grammer’s favorite writer. Mr. Grammer points out that Auden’s body of work reflects love, religion and morals, and the relationship between human beings in a tumultuous world. The Grammers have been able to experience the value of the human experience and wish to share their good fortune with others.

In addition to supporting the Division of Digestive Diseases, Mrs. Grammer also contributes to such causes as ovarian cancer and breast cancer because of a family history with these diseases. Early on, Mr. Grammer became involved with Toys for Tots due to its upbeat nature, and he also gives to Teach for America in gratitude for what his education meant to him.

They sum up their involvement with the Division of Digestive Diseases as being part of “a wonderful family at UCLA.” They are pleased to lend their support, knowing where each donation is being directed and how it is being realized. For themselves, for this field of medicine at UCLA, and for everyone else, Camille and Kelsey Grammer assure us that “as big as you can dream is as big as you can get.” Just don’t let your eyes get bigger than your stomach...

—Ginny King Supple

Cheers to the quote that rolls off the tongue of Kelsey Grammer: “I believe that every right implies a responsibility, every opportunity an obligation, every possession a duty.” It is part of the plaque quotation by John D. Rockefeller, Jr., at Rockefeller Center.

Camille and Kelsey Grammer firmly believe that the privilege of success from their own efforts imparts an obligation to give back to the world – and they do. The Grammers are philanthropic, often preferring to be anonymous and to contribute without any reward. Moreover, what would we do without the “gifts” that Mr. Grammer provides as an accomplished actor, producer, director, writer, voice artist, and family man and those that Mrs. Grammer offers as a devoted wife, mother, and friend of Digestive Diseases?

Mr. and Mrs. Grammer readily note that their lives have been changed through the services available at the UCLA Division of Digestive Diseases. The doctors and staff are not only experts in the field, but they also express an energy and enthusiasm that patients eagerly embrace. Among them is Dr. Eric Esrailian, Director of UCLA’s General Gastroenterology & Digestive Diseases Center, who states, “Mr. and Mrs. Grammer are true friends of the Division on every level, and we appreciate their continued support and encouragement.”

Regarding the Division’s outreach activities, Mrs. Grammer finds that they have a particular impact, as well; for

UCLA Division of Digestive Diseases Mission Statement

Our mission is to advance scientific knowledge and understanding that lead to cures and improved patient care for gastrointestinal disorders and to provide advanced training for future generations of clinicians and scientists.

You Can Make a Difference!

The UCLA Division of Digestive Diseases has many pressing needs to continue our mission. You can direct your charitable gift of cash, securities, real estate, art, or other tangibles to our greatest needs, under the direction of Dr. Gary Gitnick, Chief of the Division, or to specific research, training, laboratory, or recruitment programs. For more information, please contact Patricia Roderick, Director of Development – Office # 310.267.1837 or # 310.825.7501, or email at proderick@support.ucla.edu.



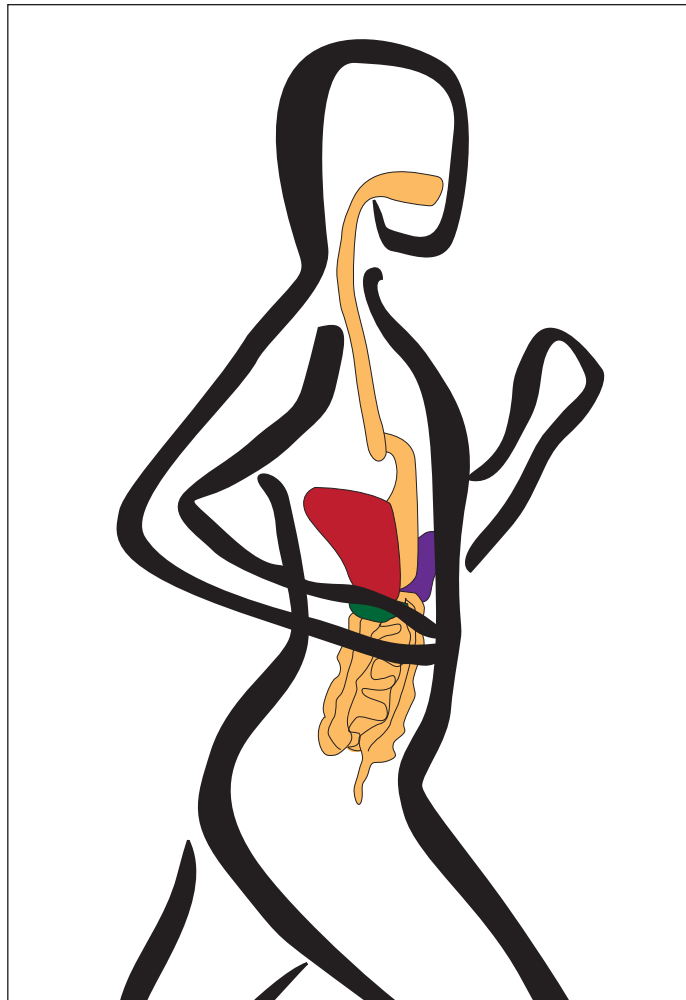
Obesity and the Digestive Tract: What's Your Risk?

By Simon Beaven, M.D.

Natural selection clearly favors the accumulation and storage of fat in humans. In his 2004 award-winning documentary, "Super Size Me," Morgan Spurlock personally demonstrates how easy it was to gain weight, decimate a good cholesterol profile, and inflict damage on his own liver after just a few days of eating nothing but fast food. The reverse process – losing weight and improving cholesterol – is substantially more difficult. Fat-laden foods taste great. Cholesterol is plentiful in diets derived from animal products. High fructose corn syrup (along with other additives) in our food supply makes our meals calorie-dense. Average portion sizes are bigger than ever. Lack of exercise and inactivity are rampant, too. These and other forces are aligned against us in the "Battle of the Bulge."

The ongoing National Health and Nutrition Examination Survey (NHANES) estimated the prevalence of obesity in the United States at one in three adults in 2003-2004 – three times the 1970 level, and almost one in five children is, at least, overweight. Obesity is no longer a disease of the aging population; it is happening to more people and at younger ages.

The complications of obesity include diabetes, high blood pressure, poor cholesterol profiles (known as dyslipidemia), and susceptibility to heart disease and atherosclerosis. Other, less obvious consequences



can directly affect your digestive health. First, the liver can become fatty just like the rest of the body. In the United States, fatty liver has emerged as one of the most common reasons to consult a liver doctor (hepatologist). It is usually asymptomatic and may present as simple abnormalities in blood tests. Strikingly, fatty liver may be as common as obesity itself. A recent large study pegged the prevalence at 34 percent (one in three) of U.S. adults. A different study that looked at liver biopsies of 100 healthy people being evaluated as living donors for transplantation found significant fat in one-third of the samples.

We don't know which people with fatty liver will go on to develop liver inflammation and scarring, even cirrhosis. Even a small percentage – say 5% – puts 3.5-million people at risk, and 1% (35,000) might experience liver failure and need liver transplantation. In 2001, the waiting list for liver transplantation in the U.S. peaked at 14,897, and while the number of operations increases every year, there were just 6,441 transplants in 2005. Moreover, new reports show that cirrhosis from fatty liver has surpassed alcoholic liver disease as the second most common indication for liver transplantation. It is clearly only a matter of time before it meets and beats chronic hepatitis C as the number-one cause.

Obesity predisposes you to developing acid reflux disease, which can make the existing heartburn even worse. Excessive weight also negatively affects the organs outside the digestive tract, raises your overall risk of dying prematurely, and puts you at extra risk for any procedure involving anesthesia. It is associated with the development of obstructive sleep apnea, which disturbs your sleeping patterns and may lead to cardiopulmonary complications later in life. The most ominous point is that obesity has been firmly linked with cancers of the digestive tract: colon, esophagus, pancreas, liver, and gallbladder.

Doctors now recognize that common obesity-related conditions are

interconnected, often going hand-in-hand to make up the “super disease” we call the metabolic syndrome (previously syndrome X). Of course, these diseases can exist by themselves, and not everyone with obesity has diabetes or vice versa. More than ever before, physicians trained in Gastroenterology, Cardiology, Endocrinology, and Nutrition have to think outside the confines of their respective specialties and learn to recognize and manage the metabolic syndrome and its links to metabolism, inflammation, and cancer.

It has been known that 1) fat-derived compounds (lipids) are important for normal cellular processes and interactions throughout the body, 2) lipid signaling pathways are often deranged in the chronic diseases related to obesity and aging, and 3) fat tissue is not just inert, extra baggage but rather a complex endocrine organ, making and secreting factors that communicate with the liver, muscle, and brain. Even our dietary behaviors are linked to factors secreted by fat tissue and the stomach, and our individual cells are programmed to recognize and respond to our diet’s basic nutritional components, meaning that there are specific fatty acid and cholesterol sensors.

In the laboratory, I study the mechanisms and actions of the body’s cholesterol sensor, known as the liver X receptor (LXR). We are working to reveal the relationships between cholesterol and the development of diabetes, obesity, and liver disease and to uncover new targets to treat metabolic diseases.

You may wish to talk to your doctor about specific risk factors for metabolic syndrome, but in the meantime:

- eat smaller, less-processed meals that are balanced in the food groups and minimal in cholesterol and trans fats;
- keep the total calories down;
- exercise more and turn off the television;
- avoid high-sugar soft drinks and juices.

Many professionals already have dedicated themselves to the obesity problem, but all doctors need to be diligent in addressing it with their patients. Hospitals and health plans have implemented exercise and nutrition classes and promote healthy living in advertising and mailings. The requirement to publish nutrition facts on the labels of food items is important, but further research is needed into the effects of food additives, preservatives, and sweeteners. Such data will take time to accumulate and analyze, requiring substantial research funding and personnel.

At present, there are no blockbuster medical therapies for fatty liver or obesity itself; however, a recent premier review on fat signaling lists at least 63 individual drugs that are in preclinical or clinical trials to target the metabolic syndrome and its related inflammatory state. Our healthcare system is increasingly taxed with the chronic diseases of aging: obesity, diabetes, heart disease, and cancer – perhaps the toll we pay for having greater longevity. I firmly believe that the key to making further advances requires an understanding of the molecular basis of metabolic processes in health and disease. At UCLA, the Division of Digestive Diseases is committed to being at the forefront of these discoveries and bringing them to our patients. ■

Passing Two Hats: Fellowship Program Director Dr. Fred Weinstein Steps Down

At the end of June, Dr. Wilfred “Fred” M. Weinstein will step down from wearing his two leadership hats in the UCLA Division of Digestive Diseases – as Training Program Director and Chief for Training and Education. Dr. Gary Gitnick says, “Because of Fred, our program is certainly among the best in Digestive Diseases in the world. He has built an integrated program that is exemplary and one of which our faculty and fellows can be proud.” Thanks, Dr. Weinstein, for doing so much and for devoting your personal time, as well, to this effort!

Dr. Brennan Spiegel will become Chief for Training and Education. Bringing a new perspective and remarkable background in evidence-based medicine, Dr. Spiegel will greatly enhance the needs of our growing education effort. He was the creator of a core curriculum lecture series for Internal Medicine residents at the Greater Los Angeles Veterans Administration Medical Center. In 2005, he also developed a curriculum in outcomes research for fellows in the UCLA Affiliated Program in Gastroenterology. He has presented his annual board review series, developed for fellows in Gastroenterology, since 2004. At the request of a publisher, he has now converted this series

into a book to be published this year. Even more important, he has served as a mentor for 18 students in the past four years and published papers with 10 of them. Dr. Gitnick says, “I know that he will bring to our division a unique perspective that will further enhance our overall program in training and education.”

Dr. Bennett Roth has accepted a one-year appointment as Director of the UCLA Integrated Training Program in Digestive Diseases. He has served the Division in many capacities and has consistently done an outstanding job in building programs and acting as a leader in many areas and activities. In addition, Dr. Roth has undertaken significant roles in the Department of Medicine, the School of Medicine, and UCLA Medical Center. His exceptional skills as a clinician and educator qualify him to lead the Training Program in a creative fashion and as a role model. “Together, Dr. Roth and Dr. Spiegel will carry on Dr. Weinstein’s tradition of excellence in promoting a great training and educational effort for all of our fellows,” says Dr. Gitnick. “We commend them for their willingness to take on these important new responsibilities and look forward to working with them in helping to build a training program for the future.” ■



In Memoriam

Mary Gianopulos passed away on December 16, 2007. She pursued a successful career in women's fashion in New York, working on collections for couture designer Mary McFadden. Throughout her youth and adult life, Mrs. Gianopulos also was active in Greek cultural and church activities. She retired in 1986, spending time with her husband, Nicholas, before his passing in 1996. Mrs. Gianopulos moved to Los Angeles in 2003 to be near her grandchildren, with whom she adored spending time and cooking their favorite Greek food. She is survived by her children James, Despina, and Peter and grandchildren Mimi, Alexa, Niki, and Sophia. The Gianopulos and Landers families set up the Mary Gianopulos Memorial Fund (fund # 618060) for the UCLA Division of Digestive Diseases. Her warm presence, embracing hospitality, and her many kindnesses to family and friends will be greatly missed.

Georgia R. Frontiere, the owner of the National Football League's Rams for nearly three decades and the first woman to take control of a league franchise, passed away on January 18, 2008. A sometime night-club singer and chorus-line performer who hoped to become an opera singer, Mrs. Frontiere was thrust into the football world when her husband, Carroll Rosenbloom, died and left most of the Rams' ownership to her. She put her personal stamp on the franchise when she moved the team to St. Louis, her home town, and received wide media attention as a woman running a football team. She was divorced from her husband, Dominic Frontiere, in 1980. She is survived by son Dale, daughter Lucia Rodriguez, six grandchildren, and her companion Earle Weatherwax. In the spirit of Mrs. Frontiere's history of extensive charitable donations, the Rosenbloom and Rodriguez families established a fund in her memory (fund # 618210) to benefit the UCLA Division of Digestive Diseases.

Roland Arnall, founder of Orange-based Ameriquest Mortgage Co., passed away on March 17, 2008, at the age of 68. Mr. Arnall, who recently resigned as U.S. Ambassador to the Netherlands, died of cancer at UCLA Medical Center. A Jewish native of France, he and his family moved to the United States after surviving World War II. He sold flowers on the streets of Los Angeles and then went into real estate in the 1970s, before founding Long Beach Savings in 1979. That banking institution split into Ameriquest and a publicly traded subsidiary that was sold in 1999 to become a part of Washington Mutual. One of his senior vice presidents from the 1990s praised Mr. Arnall's philanthropy, which included support of the Simon Wiesenthal Center in Los Angeles, the Fulfillment Fund, and the family's long-time support of the UCLA Division of Digestive Diseases. Mr. Arnall also served 16 years as a trustee of the California State University system. He is survived by his wife

UCLA Specialist in Pancreatic Cancer Leads Multi-Site Clinical Trial

Dr. James Farrell of the Division of Digestive Diseases heads a multi-center screening study that focuses on the early detection of pancreatic cancer. The first of its kind in the United States, the Cancer of the Pancreas (CAPS3) Screening Study is being conducted at five institutions – UCLA Medical Center, The Johns Hopkins Hospital, Mayo Clinic, The University of Texas M. D. Anderson Cancer Center, and Dana Farber Cancer Institute.

The CAPS3 study will screen for pancreatic cancer and its precursors, using state-of-the-art imaging tests – MRI, CT, and endoscopic ultrasound. It will help determine which screening test is the best, which individuals are likely to benefit most from screening, and what biomarkers in pancreatic secretions (containing a variety of enzymes) and blood may be helpful in diagnosing early, curable pancreatic cancer or its precursors. Dr. Farrell predicts that in 2008, there will be 37,680 new cases of pancreatic cancer and 34,290 deaths.



A twofold goal is to find the most sensitive screening procedures for very small precancerous pancreatic lesions and to treat these lesions before they turn into cancer. Another goal is to search for a gene mutation that is linked with the development of pancreatic cancer. The study covers the cost of a genetic counseling session and pancreatic screening for participants.

Subjects included in the study are patients (ages 30-80) diagnosed with Peutz-Jeghers syndrome; patients (ages 40-80) with verified BRCA 2 or FAMMM/p16 gene mutations with at least one first-degree or second-degree relative with pancreatic cancer; and patients with a verified family history of pancreatic cancer involving two first-degree relatives, or if three relatives have the disease, at least one must be a first-degree relative and the others a cousin, aunt, uncle, niece, nephew, or grandparent on the same family side.

Early detection is the key to fighting pancreatic cancer, and the CAPS3 Screening Study will go a long way toward improving the treatment of and finding a cure for this disease. ■

GRACIOUS PHILANTHROPIST

Tamar and Robert Manoukian's philanthropy is a very important part of their lives. Mr. Manoukian is a successful businessman and a true citizen of the world. He is Armenian by birth, Lebanese by nationality, and British by residence and spends significant time at their home in Beverly Hills.

Recently, Mr. Manoukian made a \$1,000,000 pledge to the UCLA Division of Digestive Diseases to be allocated under the direction of Dr. Gary Gitnick for projects in greatest need. "Our Division is very grateful to Mr. Manoukian for these unrestricted funds. Due to the cutbacks in federal and state funding, unrestricted gifts are invaluable to our division" says Dr. Gitnick. ■



Dr. Gary Gitnick and Mr. Robert Manoukian

Meet Our Alumni: Dr. Michael Jones

Many esteemed graduates of the Fellowship Program in the UCLA Division of Digestive Diseases have gone on to careers in far-flung places, from Ireland to Nebraska. One of the most important results of this program has been to produce outstanding community clinicians, who have applied their training and expertise in treating and educating patients.

Dr. Michael Jones of Omaha is an excellent example of a UCLA graduate, who went back to his home state for clinical practice. He did his undergraduate work at Southern Methodist University in Dallas, Texas, and then went to the University of Nebraska for medical school. After serving his fellowship at UCLA from 1978-80, Dr. Jones began his practice in Omaha as a solo practitioner. He now has 12 partners and will add three more in another year.

Specializing in General Gastroenterology, Dr. Jones follows a large number of patients with inflammatory bowel disease (IBD). He is on the board of the local Crohn's and Colitis Foundation of America (CCFA) and through it participates in patient education conferences. His next big push is to establish a GI wellness center for patients, as well as a specific IBD clinic. "We want to see the patient as a whole, taking into consideration the patient's physical and emotional needs together," he says.

Of his experience as a fellow, he says, "There was no question in my mind that it was the best program in the

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world. The faculty taught us to think critically about the literature and the care." Two faculty members in particular made an impression on Dr. Jones with their "extraordinary bedside manners" – Dr. Gary Gitnick and Dr. Sherman Mellinkoff, Dean Emeritus of UCLA's medical school (1962-1986). Dr. Jones remembers, "Dr. Mellinkoff was a master. He had an uncanny ability to come into a patient's room, introduce himself, and in a sweet way put the patient and family at ease. Getting to see that grace and compassion from those doctors was pretty amazing."

With many fond memories of his tenure at UCLA, Dr. Jones continues to work with people from the Division and keeps in touch with others. He notes that while he was developing and growing his practice in Gastroenterology, "I always tried to set the highest standard of care, which was instilled during my fellowship training at UCLA." Maybe Omaha isn't so far-flung after all. ■



Michael Jones, M.D.



Friends of Digestive Diseases Luncheon: "Good Bacteria"

The UCLA Division of Digestive Diseases held its quarterly luncheon on Tuesday, April 29, 2008. The luncheons honor Division supporters and their families and feature presentations on current topics in medicine and patient care. The featured guest speaker was Dr. Fergus Shanahan, who gave a presentation on "Making Bacteria Work for You." Dr. Shanahan, a former Fellow in the Division of Digestive Diseases and an acclaimed expert on inflammatory bowel disease (IBD), heads a team of scientists and postgraduate students at the Alimentary Pharmabiotic Centre (APC) in Ireland, studying how to harness the benefits of the natural gut flora for use in the treatment and prevention of disease.

It is known that the beneficial bacteria found in the digestive tract help to keep the "bad" bacteria at bay. The natural, or "good," bacteria that live in your gut help crowd out or

counteract harmful germs, speed the digestion of food, and keep your immune system functioning properly.

Good bacteria, in the form of probiotics, also can be used for treatment. Dr. Shanahan's main concerns are that researchers conduct careful studies and scientific trials in this area, because different strains of bacteria react differently with various diseases of the digestive tract. Dr. Shanahan cautions that, "Not all probiotics are the same. In the same way that one would never think of saying that pills are 'good for you' without specifying the particular pill and the particular ailment for which it might be required – so too, one should not speak of probiotics as some form of panacea for all things or for all people. Different probiotics have different properties." More investigations must be conducted on how to standardize and use probiotics for medical applications. ■



**Agi Hirshberg,
Mitch and Sheri Stein**



**Eric Esrailian, Mr. Hugh Cassar
and Mrs. Keets Cassar.**



Mr. and Mrs. Oppenheimer

UCLA Clinic Treats a Genetic Disorder Familial Mediterranean Fever

by Terri Getzug, M.D.

For more than 500 registered patients at the UCLA Familial Mediterranean Fever (FMF) clinic, Dr. Terri Getzug, Director, is a source of information and inspiration. The facility is one of the only such clinics in the country, and since its inception in the early 1960s, has served as a major referral center for this under-recognized, prevalent, and very treatable condition.

FMF is a genetic disorder that affects primarily ethnic groups of Middle Eastern and Mediterranean origin, mainly Jews, Armenians, Turks, and Arabs. Although the disease is highly prevalent among Sephardic Jews and Armenians, it also has been reported rarely in Japanese and other groups. FMF is inherited in an autosomal recessive

manner, meaning that the likelihood for offspring of an asymptomatic couple carrying the gene to be affected is one in four (25%) with each pregnancy.

One of the key problems is that FMF often is not diagnosed, and there can be confusion between peritonitis from FMF and other disorders. Patients may undergo unnecessary operations such as appendectomies and gallbladder removal as a result. The disease can be quite disabling, especially if undiagnosed and untreated. Children can have growth retardation, failure to thrive, and multiple school absences. Adults can miss many days of work and have problems with fertility, pain medicine addiction, and depression.

FMF is characterized by sporadic attacks of inflammation affecting the serosal surfaces, or linings, of body

cavities. The pathogenesis of FMF is unclear but relates to a self-limited dysregulation of the inflammatory response in the body (inflammation running unchecked). Symptoms include recurrent bouts of fever and severe abdominal, chest, or joint pain usually lasting no more than three days. In between attacks, patients are generally completely well and without symptoms. Attack frequency is extremely variable, ranging from just a few times a year to weekly. The onset of symptoms in 90% of individuals is before age 20.

If untreated, besides having a negative effect on one's lifestyle and potential unnecessary surgeries, certain FMF patient populations are prone to the development of amyloidosis. With this condition, a special type of protein is deposited in the kidneys and other

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organs including the digestive tract, liver, spleen, and thyroid. It can lead to end-stage renal disease with the subsequent need for hemodialysis and kidney transplantation, as well as cause malnutrition through malabsorption of nutrients and diarrhea. Amyloidosis is generally irreversible, but in FMF it has the unique feature of being reversible if caught and treated early. Additionally, this form of amyloidosis can be prevented or arrested by the proper treatment of FMF. Interestingly, the frequency of amyloidosis differs among various ethnic groups, with FMF being highest in Turks and North African Jews and less common in Armenians (in the United States) and Ashkenazi Jews. Usually it develops before age 40.

Since 1972, colchicine, an old drug used to treat gout (a form of arthritis), has been the first-line treatment for patients with FMF. Colchicine use prevents attacks in greater than 90% of patients and prevents amyloidosis. It is a very safe and effective remedy, which, for the majority of patients, has major beneficial effects. In the absence of amyloidosis, the life expectancy of patients with FMF is normal.

An exciting development in FMF research has been the identification of the genetic defect responsible – the MEFV gene that has been mapped to chromosome 16. Since the MEFV gene's discovery in 1992, more than 30 genetic mutations have been described and can now be detected through blood testing. Future research into the function of the MEFV gene product will lead to a better understanding of the pathogenesis of FMF and its treatment and ultimate prevention.

Because there are no definitive diagnostic tests for FMF, the diagnosis is primarily a clinical one. Refreshingly, an accurate patient history with specific questioning related to current and past symptoms, family history, and ethnic background is the key to making the proper diagnosis! Supportive genetic testing also can be helpful in selected individuals. Dr. Getzug welcomes questions about the disease and is available for patient referrals. ■

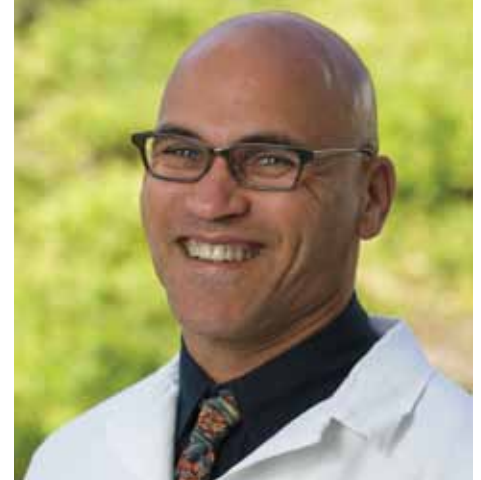
Meet a Pioneering Researcher

Dr. Adrian Lunn's passion for research has led him to a unique way of studying cancer. He focuses on using good cells to mobilize and kill cancer cells by revealing how normal cells are policing other cell growth.

A gastroenterologist and Assistant Professor in the UCLA Division of Digestive Diseases, Dr. Lunn also serves as a clinical instructor in the Division. He came to the United States in 1997 from the Bahamas in search of combining a medical degree with a Ph.D. in research. After being a foreign exchange pre-med student at Columbia College in New York, he was accepted at the Yale School of Medicine, where he received his M.D. degree and Master of Science degree in Experimental Pathology. He then returned to Columbia-Presbyterian Hospital in Internal Medicine before applying to UCLA to specialize in Gastroenterology under Dr. Enrique Rozengurt, who directs research in the Division.

Dr. Lunn earned his Ph.D. in Molecular Biology in UCLA's Specialty Training and Advanced Research (STAR) Program. It was created in 1994 to enable young academicians to complete clinical training in Internal Medicine or a subspecialty and to obtain a Ph.D. degree or postdoctoral fellowship. Dr. Lunn comments that "STAR graduates serve as a bridge between the two worlds of the clinic and the laboratory."

"I think a lot about the spread of cancer and how tissue structure controls cell behavior," states Dr. Lunn. He says that the bulk of cancer research has been focused on the cells themselves and less on how cancer cells interact with normal cells. "People think that once cancer cells encounter normal ones, the normal cells then turn bad." He thinks normal cells keep cancer cells in check and may have



J. Adrian Lunn, MD

a role in killing off abnormal ones. In the lab, he looks at how cancer cells invade tissue and is attempting to see how he can stop that process. Instead of growing cells in plastic dishes, Dr. Lunn is placing them in three-dimensional containers in substances resembling Jell-o. He cuts the cells in half to observe them for movement and programmed cell death.

By studying stomach and intestinal cancers, Dr. Lunn wonders if distortion of the cell structure – not chronic inflammation – causes cancer. He provides the example that cirrhosis of the liver can cause the destruction or distortion of cells; cirrhosis itself is a key but elusive player in cancer. There is also a link between inflammatory bowel disease (IBD) and cancer. "If you remove a polyp and send it to a pathologist, you can see the difference between normal cells and cancer cells, which have big nuclei and are distorted structurally. Cancer is part of the distortion. We do not yet have the proper tools to understand this mechanism," he says.

As a researcher, Dr. Lunn is concerned that the National Institutes of Health recently funded only 8% of scientists who applied for grants, down 33% from a few years ago. If more private support were available, he also would like to do clinical work. He enjoys caring for patients, noting that "they force you to be humble

Division of Digestive Diseases Alumni Directory:

Good things are worth waiting for. The UCLA Division of Digestive Diseases' first Alumni Fellowship Directory has arrived. Our goal was to create a way for our outstanding graduates of the Gastroenterology Fellowship Program to reconnect. The directory lists graduates from 1960-2008 and from six countries and more than 33 states.

All alumni who submitted information to the directory will receive a complimentary copy by mail. If you are an alumnus interested in receiving a copy, please contact Patricia Roderick at # 310.267.1845 or by email at proderick@support.ucla.edu .



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