STONY BROOK UNIVERSITY MEDICAL CENTER

FALL 2011

Retroflections

DIVISION OF GASTROENTEROLOGY

CONTENTS

For information on referrals, call (631) 444-5220.

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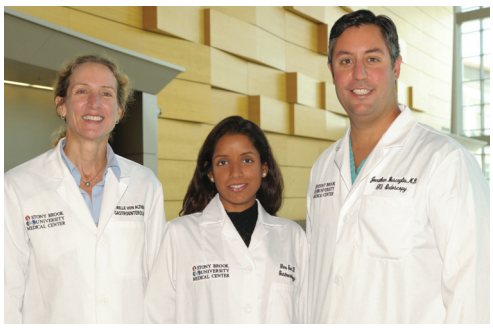
THREE NEW CENTERS OPEN

Centers of Excellence Strengthen GI Program

To further fulfill a commitment to meet Long Island's growing demand for expertise in all aspects of gastroenterology, three Centers of Excellence at Stony Brook University Medical Center have been named. This milestone came to fruition under the leadership of Basil Rigas, MD, DSc, Chief of the Division of Gastroenterology and Hepatology, through the recruitment of highly trained physicians with expertise in key GI areas, coupled with the acquisition of gold-standard diagnostic technology.



Pictured (I to r): Dr. Isabelle von Althen, Dr. Gina Sam and Dr. Jonathan Buscaglia.

The Advanced Endoscopy Center, with Jonathan Buscaglia, MD, at the helm as Director, offers several diagnostic procedures and treatments available on Long Island only at Stony Brook. Since endoscopy has taken on a larger role in therapeutic treatment beyond its traditional role as a diagnostic tool, there has been an increased need for expertise in all facets of advanced endoscopy.

continued on page 2

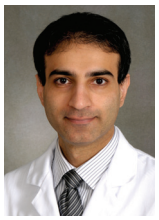
EDITOR'S NOTE

Welcome to the latest issue of *Retroflections*. The recent opening of the Division of Gastroenterology's three new Centers of Excellence—the Advanced Endoscopy Center, the Gastrointestinal Women's Center and the Gastrointestinal Motility Center—has truly strengthened our overall GI program, allowing our GI experts to better serve our patients in need of specialized services.

Our ongoing quest for improvement includes the recruitment of faculty with excellent training and updating our clinical facilities. The Endoscopy Unit has undergone expansion with a new pre-operative area and the addition of new procedure rooms. Also, the first phase of an extensive renovation and expansion of our outpatient facilities has been completed at 3 Technology Drive.

This issue of *Retroflections* not only highlights some of our accomplishments, one of which is our GI Program being nationally ranked in the top 50 in *U.S.News & World Report's* "2010-11 Best Hospitals" issue. It also provides an insight into some of the clinical issues we manage on a day-to-day basis.

We welcome your questions and comments regarding the content in this issue and about our Program. With your support, we will continue our mission to provide the best in patient care as well as serve as an effective, collaborative tertiary referral center. ■



Asim Khokhar, MD
Assistant Professor
of Medicine

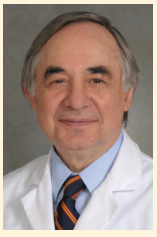
CHIEF'S CORNER

I am pleased to announce the opening of our newly created Centers of Excellence: the Advanced Endoscopy Center, the Gastrointestinal Women's Center and the Gastrointestinal Motility Center. Each new center employs a multidisciplinary approach and provides access to state-of-the-art equipment and highly trained GI faculty. The establishment of these centers demonstrates our commitment to provide to our patients exceptional and specialized GI care.

The Division's growth and expansion continues in other areas as well. To deal with specific and sometimes complex issues within our or any referring GI practice, our inpatient Endoscopy Unit, which has received the American Society for Gastrointestinal Endoscopy recognition as a center of excellence, has undergone expansion. In addition, renovation and expansion of our outpatient facilities has begun.

The future looks even brighter. We're expanding efforts into patient-centered clinical research; we're growing our drug discovery program; and we've initiated a study of the human microbiome, the bacteria that inhabit our intestinal tract and which seem to influence or even trigger several diseases. We are also further streamlining our clinical activities to be more responsive to the needs of patients and their referring physicians.

Our Division was ranked among the top 50 GI Divisions in the nation in *U.S.News & World Report's* "2010-11 Best Hospitals" issue. I congratulate the faculty, nurses, staff, trainees, students and institutional administration who worked tirelessly to help achieve this goal. Our Division has evolved into "the place to be" for effective, efficient and compassionate care.



Basil Rigas, MD, DSc
Professor and Chief, Division of Gastroenterology and Hepatology

Centers of Excellence Strengthen GI Program *(continued from page 1)*

Leading-edge procedures, including endoscopic ultrasound, endoscopic retrograde cholangiopancreatoscopy, sphincter of Oddi manometry and radiofrequency ablation are available to patients at the Center. Collaborating with the patient's referring physician is a high priority for our professionals. Other key specialists who work closely with the Center's staff include advanced biliary and pancreatic surgeons and interventional radiologists.

Isabelle von Althen, MD, an expert in women's gastrointestinal health, serves as the Director of the GI Women's Center. Four board-certified female gastroenterologists and a nurse practitioner evaluate, diagnose and treat GI disorders and conditions that are unique to or more prevalent in women. These include irritable bowel syndrome (IBS), functional dyspepsia, pregnancy-related GI disorders and certain immune-mediated liver diseases and gallbladder stones. Rounding out the team's highly specialized expertise are advanced endoscopists, urologists and radiologists. This multidisciplinary team works closely with patients and their referring physicians to plan the best possible outcomes.

The GI Motility Center provides individualized treatments for patients with disorders that affect the movement, or motility, in their digestive tracts. Director Gina Sam, MD, MPH, is a motility expert with extensive training in esophageal manometry, pH testing, anorectal manometry and biofeedback. The team also performs therapeutic endoscopy procedures. The healthcare professionals' overall goal is to help patients regain normal GI motility and improve their quality of life. Patients and referring physicians receive timely communication during the process.

With more than 8,000 endoscopic procedures performed annually by a team of experts in state-of-the-art facilities, using gold-standard diagnostic technology and supported by a committed staff of dedicated healthcare professionals, these three new GI Centers of Excellence reflect Stony Brook's ongoing commitment to deliver "the best ideas in medicine" to the Long Island community. ■

2010-11 NATIONAL RANKING

Among *U.S.News & World Report's* Top 50

Stony Brook's Gastroenterology Program was nationally ranked in the Top 50 in *U.S.News & World Report's* "2010-11 Best Hospitals" issue. Best Hospitals 2010-11 includes rankings of 152 medical centers nationwide in 16 specialties. Of the 1,892 hospitals that qualified for ranking, Stony Brook was one of only 152 medical centers that scored high enough to be ranked.

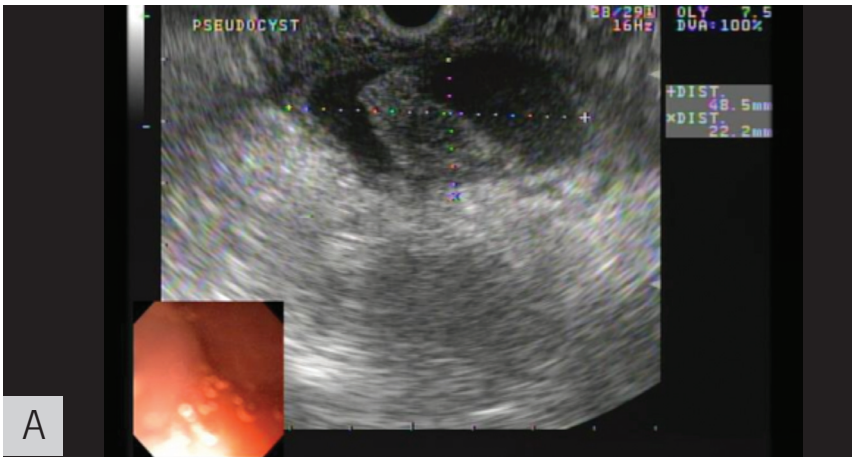
Led by Basil Rigas, MD, DSc, physicians provide world-class care in all aspects of gastroenterology, including cancer screenings, motility, women's gastrointestinal health, inflammatory bowel diseases, diagnosis of pre-malignant conditions, advanced endoscopic interventions, nutrition and weight loss, and liver, pancreatic and biliary diseases. In addition to patient care, Stony Brook University Medical Center physicians and researchers conduct cutting-edge research in the development of novel drugs against cancer, use nanotechnology to diagnose diseases earlier and more accurately, and apply stem cells to treat patients with Crohn's disease.

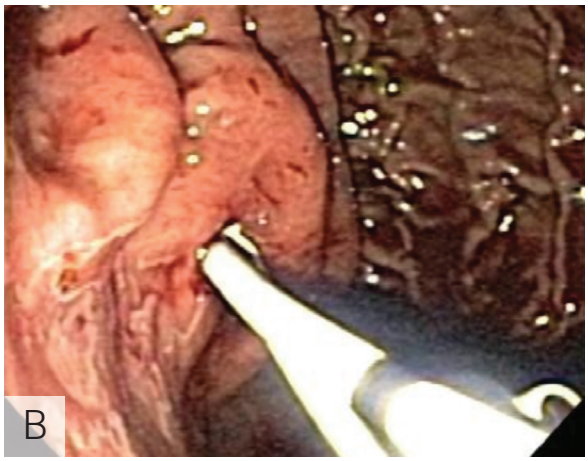
At Stony Brook, patients are treated with respect and compassion by a team of renowned GI physicians whose joint goal is to provide the best possible and most effective treatment. For more information, call (631) 444-4000. ■

CASE REPORT

Satish Nagula, MD

Endoscopic Management of Pancreatic Pseudocysts





A 45-year-old male with a history of heavy alcohol abuse was referred to Stony Brook University Medical Center for evaluation of a several-week history of progressive abdominal pain with radiation to the back. He also had progressive dyspnea on exertion, early satiety and significant pain associated with oral intake. A CT scan revealed an 8.5 cm pseudocyst adjacent to the gastric body, as well as a 3 cm pseudocyst in the pancreatic tail with a tract to the left lung with an associated pleural effusion, consistent with a pancreatico-pleural fistula.

The patient had endoscopic ultrasound (EUS) guided-pseudocyst drainage and an endoscopic retrograde cholangiopancretography (ERCP). The EUS revealed the 8.5 cm pseudocyst adjacent to the proximal stomach [Image A]. Under direct endosonographic guidance, the pseudocyst was punctured with a 19-gauge FNA needle. The needle tract was ultimately dilated to 12 mm, and two 10 Fr double-pigtail stents (cyst-gastrostomy) were placed, draining the cyst into the stomach [Image B]. The ERCP demonstrated the 3 cm pseudocyst in the pancreatic tail; a pancreatic sphincterotomy was performed and a pancreatic stent was placed.

Over the subsequent four weeks, the patient's abdominal pain, early satiety and dyspnea all gradually improved. A repeat CT scan revealed complete resolution of both pseudocysts, as well as resolution of the pancreatico-pleural fistula. The pancreatic stent and the cyst-gastrostomy drains were all removed, and the patient has had complete resolution of his symptoms. The patient was instructed that alcohol cessation is critical to prevent recurrence of these symptoms.

Discussion

Pancreatic pseudocysts are common sequelae of pancreatitis. Indications for pseudocyst drainage have evolved over the past 20 years. Size is no longer a firm indication for drainage; indications include abdominal pain, recurrent pancreatitis/cholangitis, and cyst superinfection. Historically, pseudocysts were drained surgically, with operative creation of a cyst-gastrostomy or a cyst-duodenostomy. With the advent of interventional endoscopic ultrasound, EUS-guided pseudocyst drainage is rapidly becoming the standard of care in the initial management of pseudocysts. Pancreatic stent placement remains an important tool in the management of pseudocysts in direct communication with the pancreatic duct. The stent facilitates the flow of pancreatic juices toward the ampulla, thus minimizing flow into the pseudocyst.

These EUS and ERCP techniques are minimally invasive alternatives to operative pseudocyst drainage procedures. While surgery remains a critical tool for certain patients, endoscopic techniques offer an effective, minimally invasive initial approach to the management of pancreatic pseudocysts. ■

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KEY **Image A:** Endoscopic ultrasound view of pseudocyst **Image B:** Endoscopic view of cyst-gastrostomy drains

CASE REPORT

Gina Sam, MD, MPH

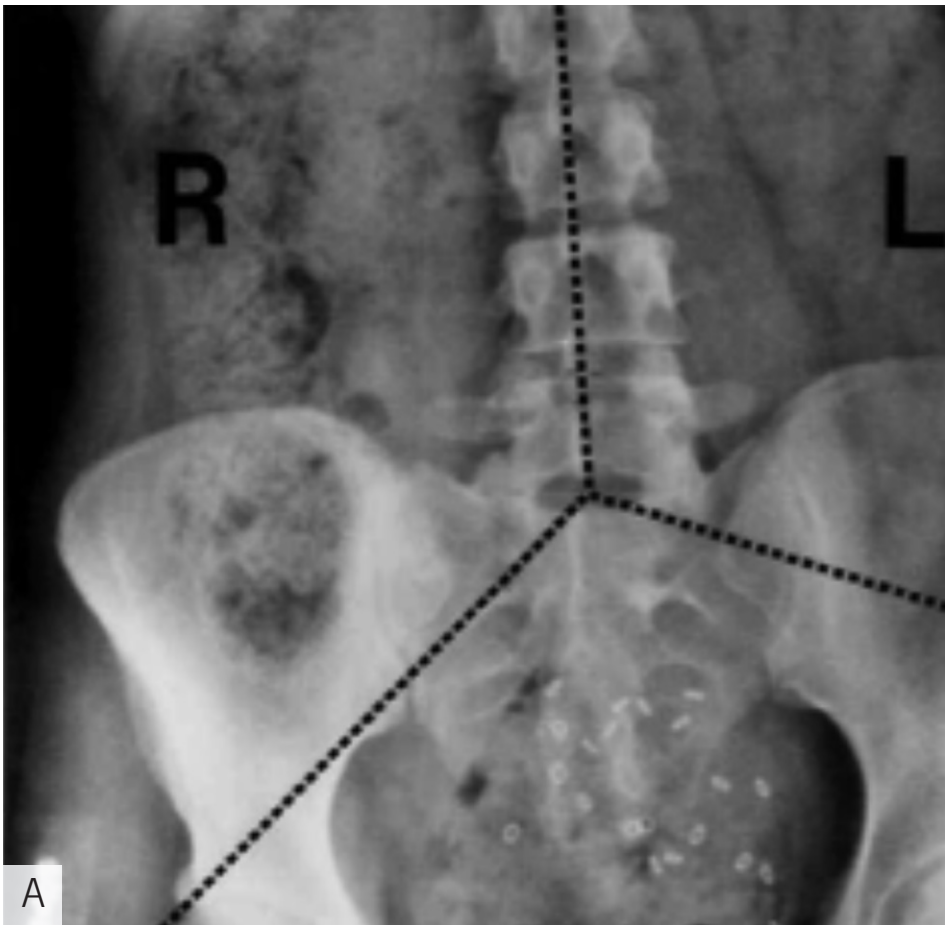
Biofeedback as a Treatment Method for Constipation due to Pelvic Floor Dyssynergia

A 31-year-old female presented with a chief complaint of constipation, which dated back to the beginning of her college years. She reported having a bowel movement once every two to three weeks. She described her stool as hard and pellet like and usually had to use a Fleet® enema to have a bowel movement.

She also has to strain excessively with incomplete evacuation and usually had to perform self-digital disimpaction. She had tried many laxatives including Milk of Magnesia®, Dulcolax®, Senokot®, Lactulose® and Fleet enemas without any improvement in her constipation. She also had been seen by two gastroenterologists and recently had a normal colonoscopy.

The patient had no other medical history, no surgeries, and had no pregnancies. She denied any trauma or accidents involving the pelvic floor or back. She was not taking any medications.

On physical exam, the patient was a well-appearing female in no acute distress. Her abdomen was distended and stool could be palpated along her transverse and descending colon. She did not have any rebound or guarding. On rectal exam, she did not have any hemorrhoids or anal fissures. Stool was palpated in the rectal vault and her baseline external sphincter pressure was normal. On bearing down, she was contracting her anal sphincter. She underwent a Sitz Marker study and by day five she had all of the markers at her rectosigmoid junction. [Image A.]

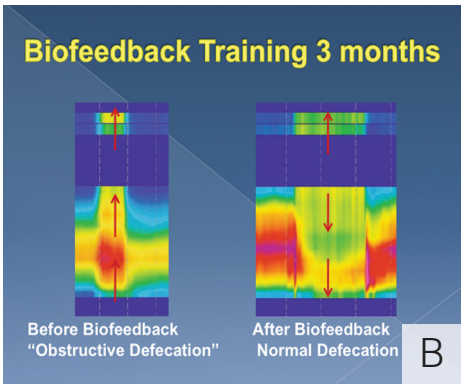


Discussion

The patient underwent a high-resolution anorectal manometry, which revealed pelvic floor dyssynergia, where during the Valsalva maneuver she was increasing her rectal pressure as well as anal sphincter pressure causing an obstruction. After undergoing three months of biofeedback training, she had a complete resolution of her constipation.

Constipation is a common problem with a prevalence of about 20 percent in the population. One third of patients with constipation have an evacuation disorder called dyssynergic defecation. This term is often referred to as anismus or pelvic floor dyssynergia or obstructive defecation. Dyssynergic defecation occurs when there is a problem coordinating the rectal, abdominal, pelvic and anal sphincter muscles during defecation. During normal defecation, a patient increases the rectal muscle pressure and relaxes the anal sphincter muscle to facilitate a bowel movement. Patients with dyssynergic defecation often complain of excessive straining, incomplete evacuation and hard stools, along with infrequent bowel movement and almost 40 percent of these patients have to use digital maneuvers to assist with a bowel movement. The cause of dyssynergic defecation is not completely understood but is probably multifactorial. It is thought to be an acquired, learned dysfunction rather than an organic or neurogenic disease. These patients do not respond to laxatives or an increase in dietary fiber.

KEY **Image A:** Sitz Marker study **Figure B:** Biofeedback images **Image C:** Dr. Gina Sam, with Grace Walker, RN, explains the biofeedback diagram to her patient.



Anorectal manometry is a test where a catheter with multiple electrodes is inserted into the rectal vault to measure the pressures of the rectum and the anal sphincter muscle during several maneuvers, which reproduce the act of having a bowel movement. In a patient with normal defecation, during a Valsalva maneuver a patient's rectal pressure should rise and his or her anal sphincter muscle pressure should relax. In a patient with one form of dyssynergic defecation, the rectal pressure may rise but the anal sphincter does not relax.

Biofeedback is a type of treatment that involves teaching the patient how to coordinate the rectoanal muscles. A manometry catheter is placed in the rectal vault and a patient is able to perform exercises to strengthen the rectal muscles and coordinate the rectal muscles with the anal sphincter muscle. Three randomized controlled trials have shown that in patients with this disorder, biofeedback was superior to conservative treatment and lasted up to three months [Figure B]. In the April 2010 issue of *The American Journal of Gastroenterology*, Satish Rao, MD, observed that patients had sustained improvement in their bowel symptoms and anorectal function and this continued up to one year after treatment. Patients who had conservative management had no change in symptoms. ■

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Successful Treatment for Barrett's Esophagus

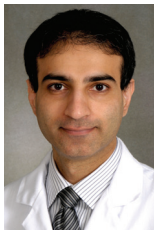
Barrett's esophagus is a precancerous condition that develops as a consequence of long-standing gastroesophageal reflux (GERD). Treatment for this condition with radiofrequency ablation (RFA) is quite effective and helps to prevent development of esophageal cancer. RFA is a minimally invasive procedure that uses highly targeted heat energy to irradiate and eliminate precancerous tissue in the esophagus. The patient shown here has a long history of GERD, and was diagnosed with Barrett's esophagus several years ago. Previous biopsies demonstrated early signs of dysplasia. She underwent RFA last year at Stony Brook, and her most recent endoscopy demonstrated that her Barrett's esophagus has been successfully eradicated. The experts at Stony Brook have been performing RFA for Barrett's esophagus for the past 18 months. More than 50 patients have been successfully treated, including those with dysplasia and non-dysplastic Barrett's esophagus. ■

Satish Nagula, MD, (right) begins the procedure, while John Fredriksen, RN, monitors the patient.

CASE REPORT

To B or not to B

Asim Khokhar, MD
Shaheen Rasheed, MD



A 44-year-old Asian woman was referred to our hepatology clinic for evaluation of elevated liver enzymes. At age 23, when her mother died of hepatocellular carcinoma, she was diagnosed with chronic hepatitis B. She apparently was followed with normal liver enzymes and deemed a chronic inactive carrier of hepatitis B. It's unclear what her hepatitis B DNA levels had been. A previous liver biopsy showed minimally active chronic hepatitis with grade 0-1 and stage 0-1. Two months prior to her presentation, her liver enzymes were elevated, with ALT as high as 1,500.

The patient reported recent increasing fatigue and joint pain. She denied any alcohol history, any history of jaundice, IV drug use, tattoos or blood transfusions. On physical examination her vitals were stable, she was anicteric and her abdomen was soft, non-tender and non-distended.

Lab work showed CBC and basic metabolic panel were within normal limits and that her liver synthetic function was good. AST and ALT were elevated, hepatitis B DNA level was greater than 1 billion, hepatitis B e-antigen was positive, and e-antibody was negative. She was negative for hepatitis A, C and D. A work-up for other causes for elevated liver enzymes found no other etiology. Most recent liver enzymes were an ALT of 1,255 and AST of 737, billirubin was 0.69 and PT was 10.7.

The patient was started on entecavir 0.5 mg QD, with a goal to seroconvert from e-antigen positive to e-antigen negative, and continue therapy for about six months to a year after seroconversion. Within a few weeks of treatment she showed improvement in liver enzymes, her hepatitis B DNA level was down to the thousands and she seroconverted to e-antigen negative and e-antibody positive. Six months into treatment, her e-antigen was reported as indeterminate while e-antibody was positive. Her liver enzymes had normalized and her hepatitis B DNA level was undetectable. She was continued on entecavir.

About a year into treatment, her e-antigen was reported as negative again and e-antibody as indeterminate. The viral load remained undetectable. Eighteen months into treatment she became e-antigen positive and e-antibody negative (HBeAg reversion) again. She had a persistently undetectable viral load and normal transaminases. In the subsequent year, she fluctuated between the e-antigen and e-antibodies being negative, indeterminate or positive. Unable to achieve a sustained seroconversion from e-antigen to e-antibody, she is continued on entecavir. Throughout her course, she is screened for hepatocellular carcinoma with six monthly AFPs and abdominal imaging.

Discussion

An estimated 400 million people are affected by the hepatitis B virus worldwide, 75 percent of whom are Asian in origin. Most of the infection in that part of the world is acquired at birth or within the first few years after birth[1].

Since its discovery in the early '70s, hepatitis B e Ag (HBeAg) has been extensively studied to understand chronic hepatitis B infection[2]. HBeAg serocoversion is considered an important end point in treating chronic hepatitis B (eAg pos wild type virus), and it is suggested that treatment continue six months after HBeAg loss and the appearance of antibodies to HBeAg.[3] However, in a number of cases, as in this case history, the e-antigen to e-antibody seroconversion is not durable. There are suggestions that the criterion and the end point for the treatment of chronic hepatitis B should be reevaluated.

Reasons to treat hepatitis B are several-fold, mainly to prevent progression to cirrhosis, hepatocellular carcinoma and liver failure. A high HBV DNA level is an independent predictor for cirrhosis and hepatocellular carcinoma[4]. Decreasing the viral load should decrease their incidence. Also, elevation of ALT levels has shown to be directly related to the risk of hepatocellular carcinoma and cirrhosis[5]. Development of cirrhosis and HCC are not limited to e-antigen positive hepB[5], casting some doubt on dependence on its seroconversion as a reliable marker. Due to the unpredictability of HBeAg seroconversion, there are thoughts about using HBsAg loss or seroconversion from HBsAg-positive to hepatitis B surface antibody as an end point for the treatment of chronic hepatitis B[6]. Although less frequent than eAg seroconversion, it is a more robust measure of response.

Comments

This case underscores the importance of frequent follow-up of patients with chronic hepatitis B, with active disease (should be on treatment) and for "inactive carriers," since the course of disease is unpredictable and may activate at any time. Follow-up should continue even after eAg seroconversion. Our primary goal in the treatment of chronic hepatitis B should be normalization of liver enzymes, loss of hep B viral DNA and HBsAg seroconversion. ■

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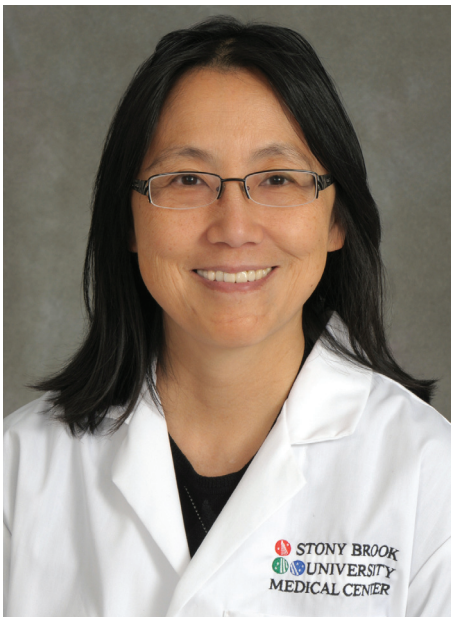
FACULTY INTERVIEW

Interviewed by Vijay Jayaraman, MD

Ellen Li, MD, PhD

Professor of Medicine and Microbiology and Molecular Genetics



Dr. Ellen Li is a board-certified gastroenterologist and world-class scientist with expertise in inflammatory bowel diseases (IBD). Her specialty as a scientist is in translational research. In Stony Brook's Division of Gastroenterology and Hepatology, she leads a major translational research initiative to analyze the effects of two key genes on the microscopic bacteria (microbia) that are present in the lining of the intestines and to explore how these microbia interact with the lining in the gut. Dr. Li is a Professor of Medicine and Molecular Genetics and Microbiology.

Q Could you please enlighten us on some of the research projects that you are currently involved in?

A We are currently involved in several interesting and rapidly evolving areas of research related to the gastrointestinal system. One of our studies involves studying the interaction of the bacteria that commonly reside within the intestine with the human host and assessing its role in contributing to the development of IBD. We are also part of a Crohn's & Colitis Foundation of America (CCFA)-funded consortium studying the human microbiome, working along with leading investigators across the country. We are now establishing Stony Brook University as the data analysis center for these consortia.

I also have an ongoing CCFA-funded investigation to determine the molecular markers of post-operative Crohn's disease (CD) recurrence in patients. Additionally, we have a National Institute of Diabetes and Digestive and Kidney Diseases (NIH/NIDDK)-funded investigation into the effect of CD risk alleles on enteric microbiota.

Q Can you please explain what translational research is and what your goals are regarding it at Stony Brook?

A Translational research is a way of thinking about and conducting scientific research to make the results of research applicable to the population under study. In the field of medicine, for example, it is used to translate the findings in basic research more quickly and efficiently into medical practice and, thus, meaningful health outcomes, whether those are physical, mental or social.

Over the past five years, the focus of my research efforts has been to build patient data/tissue repositories that will facilitate clinical translational research in digestive diseases. I was the driving force in organizing the Washington University Digestive Disease Research Core Center Tissue Procurement Facility. This group has systematically collected intestinal tissues linked to detailed patient clinical data (that is periodically updated for longitudinal follow-up). We also began systematically genotyping all of the patients with and without IBD for highly reproducible CD risk alleles. This allowed us to rapidly translate observations in mice that were deficient in expressing Atg16l1, which is the mouse homologue of the human gene ATG16L1. This gene is associated with an increased risk of developing CD involving the ileum. It was found that the Paneth cells, a specialized intestinal lining cell that secretes antimicrobial peptides, were abnormal in the mice with deficient Atg16l1 expression. In a matter of days we were able to confirm that ileal CD patients that were homozygous for the ATG16L1T300A risk allele exhibited a similar Paneth cell morphology. In contrast, the ileal CD patients who were homozygous for the non-risk allele exhibited normal Paneth cell morphology. This led to a breakthrough in our understanding about the genetics of IBD and resulted in a landmark article published in *Nature*, November 2008.

Because we had used the same patient database/tissue repository in parallel projects, we were in a unique position to integrate the microbiome dataset with the datasets generated by concurring projects that link genotype/phenotype, clinical outcome data to whole human genome expression profiling and ileal histological data.

Now that I have joined Stony Brook University, I have begun collaborating extensively with Wei Zhu, PhD, in the Department of Applied Mathematics and Statistics to develop new methods of integrating the microbiome datasets with genome profiling data and histological data.

Q What is your vision for the future of Stony Brook University in the management of colon cancer?

A At Stony Brook, we have strengths in engineering and applied mathematics and statistics that we plan to take advantage of in developing new approaches to personalized medicine with the new genetic data. My vision is that we all work together within this University and break through silos in creating interdepartmental centers of excellence on IBD, high-risk colon cancer and functional bowel diseases. We are working towards this now by combining the efforts of the adult and pediatric GI Departments, Colorectal Surgery and the Department of Pathology (Tissue Bank), in order to build a Digestive Disease Research Tissue Procurement Facility. ■

STONY BROOK UNIVERSITY MEDICAL CENTER

Division of Gastroenterology
Stony Brook, NY 11794-8173

Retro*flections*

FALL 2011

The Gastroenterology and Hepatology Team

Pictured here are faculty in the Division of Gastroenterology and Hepatology at Stony Brook University Medical Center. Top row (l to r): Robert J. Richards, MD, MSc, Associate Professor; Asim Khokhar, MD, Assistant Professor; Chris Lascarides, MD, Assistant Professor; Edward Cheng, MD, Associate Professor; Robert Shaw, MD, Associate Professor; Leah Lieber, MD, Assistant Professor; and Juan Carlos Bucobo, MD, Assistant Professor. Bottom row (l to r): Jonathan Buscaglia, MD, Director, Advanced Endoscopy Center, Assistant Professor; Ramona Rajapakse, MD, Associate Professor; Ellen Li, MD, PhD, Professor; Douglas Brand, MD (emeritus); Isabelle von Althen, MD, Director, Gastrointestinal Women's Center, Director, Fellowship Program, Assistant Professor; Basil Rigas, MD, DSc, Chief, Division of Gastroenterology and Hepatology, Professor; Gina Sam, MD, MPH, Director, Gastrointestinal Motility Center, Assistant Professor; and Satish Nagula, MD, Director, Endoscopy, Assistant Professor. (Not pictured: Atul Kumar, MD, Assistant Professor).

Something to Share with Your Patients

On Tuesday, December 13, Gina Sam, MD, MPH, Director, Gastrointestinal Motility Center, and Satish Nagula, MD, Director, Endoscopy, will present "The 'Burning' Question: Is It Heartburn or Something More?" The general public is invited to attend to learn more about heartburn, gastroesophageal reflux disease (GERD), Barrett's esophagus and esophageal cancer. A question-and-answer session will follow the presentation.

Time: 7 pm
Place: Longwood Public Library
800 Middle Country Road
Middle Island, NY

Those planning to attend are asked to call (631) 924-6400, ext. 250.