



UCSD

Division of Gastroenterology

Newsletter



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Letter from the Chief

Since our last newsletter in Spring 2007, a number of very positive things have happened in our Gastroenterology Division. First, the Division was awarded a competitive renewal of its NIH Training Grant for another 5 years, which commenced its 32nd year of existence as of July 2007. This grant is important in our mission of training academic gastroenterologists, affording fellows protected time for focused research. Second, the Division competed for and will be awarded its first-ever Digestive Diseases Center Grant from the NIH in December 2007. This grant is important to support and grow the research mission of the Division, and will greatly enhance developing junior and established investigators in conducting basic research. The Center grant is focused on the continuum of inflammation to repair to transformation that occurs in all GI organs, and will contain animal, imaging, and gene expression cores. Third, we have moved our Grand Rounds to Tuesday evenings at 6:30PM weekly at the VA, and have recruited some fantastic speakers, including David Brenner, Steph Targan, Loren Laine, Gail Hecht, Tom Imperiale and John Allen from the AGA Task Force on Quality in GI Practice. Dates for speakers can be obtained from Olivia Hernandez (ohernandez@ucsd.edu). Fourth, we have commenced the training of 4 fantastic new fellows in July 2007, and have recruited 5 outstanding fellows through the GI Match for July 2008, all of whom are highlighted elsewhere in this newsletter. Additionally, Martin F. Kagnoff, M.D. moved up to Professor Emeritus status, and a reception honoring his 35 years of faculty service was held on September 5, 2007. Marty will remain active through his research and administering the Warren Celiac Center for Research in the GI Division.

The Division will host a research retreat focused on infection, inflammation, and IBD on October 27, 2007 from 8:30a-2:30p at the Eucalyptus Point Conference Center on the UCSD Campus. All are welcome, and breakfast and lunch will be served. Please RSVP with Karen Kasser (kkasser@ucsd.edu) before October 20, 2007.

The clinical aspects of our Division continue to grow, and in 2006-2007, the Division recorded its highest productivity ever. Patent access continues to improve with the growth of our clinical programs in IBD, advanced endoscopy, motility, hepatology, celiac disease, and cancer genetics.

The UCSD GI Division continues to amaze me with its innovation, research, and faculty, and it is these items that will allow this Division to become stronger as we serve the local, national, and research community.



**Division of Gastroenterology
Program Highlights.....Advanced Endoscopy Center**

**Interventional Endoscopy Highlights, Part I –
Double Balloon Small Bowel Enteroscopy**

The UCSD Advanced GI Endoscopy Center is the first in San Diego, and one of only a few places in the United States, to perform double balloon enteroscopy to evaluate the small bowel for lesions, and the BARRX balloon ablation system for Barrett’s esophagus.

Case 1. Jejunal Adenocarcinoma.

A 44-year-old woman with one-year history of unexplained intermittent abdominal pain and iron deficiency anemia was referred to UCSD Interventional Endoscopy for further evaluation. She previously had non-diagnostic CT scan x 4, capsule endoscopy x 2, EGD x 2, colonoscopy x 2, push enteroscopy with colonoscope, tagged RBC scan, and angiogram. Wireless small bowel capsule endoscopy revealed a narrowing with possible mass in the proximal small intestine. Fuji double balloon enteroscopy revealed a retained capsule and a stricture. The stricture had heaped borders, and the scope could barely pass through. Submucosal tattoo was placed. Endoscopic biopsies revealed adenocarcinoma. The patient subsequently underwent a laparoscopic resection of the lesion. The final pathology was a 1 cm T3, N0 jejunal adenocarcinoma. The patient received post-surgical chemotherapy, and is doing well.

This highlights how evaluation of the small intestine has markedly advanced with small bowel capsule endoscopy to screen for lesions, and then double balloon enteroscopy (DBE) to reach lesions in the jejunum and ileum. Double balloon endoscopy uses a special tube with a balloon on the tip, together with an overtube with a balloon on the distal end, to pleat small intestine over an endoscope (as shown in Figure 1a and 1b). Cases have been reported of the scope passing from the mouth to the cecum, although usually the proximal small intestine is seen from the oral route, and the distal small intestine seen from the colonic route.

UCSD is one of only three centers in Southern California to have Double Balloon Enteroscopy, with the other two being Cedars-Sinai and USC.

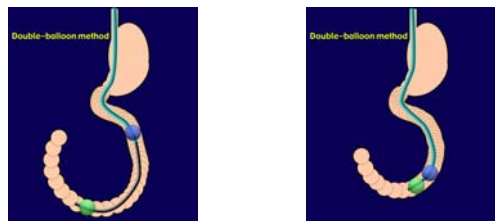


Figure 1a and 1b. Cartoons of double balloon endoscope.



Figure 2. Capsule endoscopy showing possible mass or stricture in the jejunum.

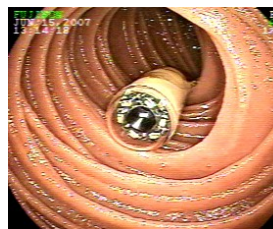


Figure 3. DBE showing retained capsule in jejunum.

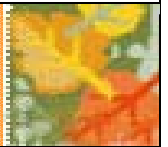


Figure 4. DBE showing jejunal stricture.



Figure 5a and 5b. DBE showing jejunal mass.





Interventional Endoscopy Highlights, Part 2- Endoscopic Ablation of Barrett's Esophagus

Case 2. Endoscopic Treatment of Superficial Esophageal Adenocarcinoma in Barrett's Esophagus using EMR and BARRX.

A 74-year-old patient with 6 cm Barrett's esophagus with high grade dysplasia and a focal nodule was referred for BARRX. Endoscopic ultrasound (EUS) revealed no deep wall lesions and no peri-esophageal lymph nodes. Endoscopic mucosal resection of the nodule revealed carcinoma which just barely invaded into the submucosa. The patient was felt not to be a surgical candidate due to multiple medical problems. He underwent two sessions of BARRX balloon thermal ablation, followed by two additional sessions of endoscopic mucosal resection of residual Barrett's at the gastroesophageal junction. After 2-years of follow-up the patient continues to be free of any residual Barrett's esophagus.

For the past 2 years, UCSD Interventional Endoscopy has been using a combination of balloon thermal ablation (BARRX corporation) along with endoscopic mucosal resection to eradicate Barrett's esophagus with high grade dysplasia and/or intramucosal carcinoma. BARRX is a balloon which delivers a computer calculated 12 Joules/cm² of energy in a 360-degree cylinder to ablate esophageal mucosa. UCSD contributed data to a study presented at DDW 2007 titled "Halo 360 Circumferential Ablation is Safe and Effective for the Treatment of Barrett Esophagus and High-Grade Dysplasia: A U.S. Multi-Center Registry". Besides UCSD, the other centers included Duke, Mayo Clinic, and Stanford, among others. A total of 85 patients were in the study. The study found that 88% had complete regression of all Barretts without any complications. Among the 3 patients contributed to the study from UCSD, all currently have no evidence of any residual ablation, and the two who had intramucosal cancer have no evidence of residual cancer.

For further information or patient referrals to the UCSD Interventional GI Endoscopy Program, contact Margie Lewis at phone 858-657-6882 or fax 858-657-6881.



Figure 6. Cartoon of BARRX
Halo-360 balloon thermal ablation



Figure 7. Endoscopic view of whitened coagulated mucosa after circumferential balloon thermal ablation.

Division Highlights....

- The GI Division Welcomes 2007-2010 Fellows : Andrew Bain, M.D. , (Emory University), Rohit Loomba, M.D., (NIH/NIDDK), Raymond Tang, M.D., (UCLA) and Cristina Wiese, M.D., (UCLA).
- The GI Division Welcomes the following new faculty : Masayuki Adachi, Ph.D., David Brenner, M.D., Tatayana Kisseleva, Ph.D., Alexander Kuo, M.D. , Brad Moore, M.D., Robert Lee, M.D., Heather Patton, M.D., Ekhiro Seki, Ph.D., Khalid Selim, M.D. A reception for the new fellows/faculty will be held September 23, 2007 .
- On September 5, 2007, the GI Division honored Dr. Martin F. Kagnoff's transition to Professor Emeritus. (see photos of the reception in this newsletter)
- On October 27 the Division will host the 2nd Annual UCSD Gastrointestinal Research Symposium. This years title; " Infection, Inflammation and IBD." Keynote speaker will be Jonathan Braun, M.D., Ph.D. ,Professor and Department Chair, UCLA Pathology and Laboratory Medicine.
- As of July 1, 2007 GI Grand Rounds and Conferences have a new venue and time. Meetings are now held in the VA Medical Center, Conference Room B, 1st Floor, every Tuesday, from 5:30 - 6:30pm for Conferences and 6:30 - 7:30pm for GI Grand Rounds. Hope to see you there!
- The Division completed the Fellows Match for 2008 are: Mamie Dong, M.D., (UCLA), Marianne Fahmy, M.D., (UCSD), and James Lin, M.D., (University of Michigan), Ingrid Gonzalez, M.D., (Mass General Hospital), Benjamin Cohen, M.D., (Mount Sinai, NY).
- The Division had another successful DDW and enjoyed seeing everyone who joined us at the Alumni Reception in Washington, D.C. The 2008 DDW will be here in San Diego and we are currently making plans for a great Reception on Sunday Evening, May 18, 2008 please hold that date.
- The Annual Isenberg Lecture will be held on January 22, 2008 at 5:00pm, in Garren Auditorium; This years speaker will be Daniel Podolsky, M.D. from Massachusetts General Hospital/Harvard. All are invited!
- The Division wishes Scott Naugler, M.D. well as he joins the faculty of Oregon Health Sciences University and John Garvie, M.D., who joined a hospital practice in Phoenix, AZ.

Awards & Honors....

- Dr. Lars Eckmann was awarded an NIH UO1 Grant entitled Next-generation 5-nitroimidazoles against giardiasis. Dr. Eckmann will be collaborating with Barry Sharpless, (Scripps), Frances Gillin, (UCSD, Dept. of Pathology), Diane Smith, (San Diego State) Jacqui and Peter Upcroft, (Queensland Institute of Medical Research, Australia). The goal of the project is to develop derivatives of the commonly used drug metronidazole with improved activity against diverse Mz-sensitive and Mz-resistant Giardia.
- In July 2007 John Carethers, M.D. and the GI Division received notification of an outstanding score and will be awarded a Digestive Diseases Research Development Center Grant from NIH. The Center will be the first ever for the UCSD GI Division, becoming one of 20 NIH-funded Digestive Centers in the U.S. The Center will commence in December 2007, and has a focus on inflammation to repair to transformation in the GI tract. The Center will have 28 inaugural faculty members, and fund three cores to support basic research: Animal, imaging, and gene expression.
- Declan McCole, Ph.D., received an American Physiological Society GI & Liver Section Research Recognition Award at the Experimental Biology 2007 meeting in Washington D.C. in May.
- Hui Dong, M.D., Ph.D. received a competitive score on his NIH R21 proposal on duodenal bicarbonate secretion.
- Declan McCole, Ph.D., received top-scoring on an abstract at the FASEB Summer Conference 2007: Gastrointestinal Tract XII, held at Snowmass, Colorado on August 11-16.

Recent Division Publications...

- Hamilton JP, Xie G, Raufman J-P, Hagan S, Griffin TL, Packard CA, Chatfield DA, Hagey LR, Steinbach JH, **Hofmann AF**. Bile acids of human cecal contents: concentration and spectrum *Amer J Physiol* 2007;293:G256-63.
- Gass J, Vora H, **Hofmann AF**, Gray GM, Khosla C. Enhancement of dietary protein digestion by conjugated bile acids. *Gastroenterology* 2007;133:16-23.
- **Ho SB**, Dvorak LA, Moor RE, Jacobson AC, Frey MR, Corredor J, Polk DB, Shekels LL. Cysteine-rich domains of muc3 intestinal mucin promote cell migration, inhibit apoptosis, and accelerate wound healing. *Gastroenterology*. 2006 Nov;131(5):1501-17.
- Boles S, Chau E, **Jung B**. ACVR2 (Activin Receptor Type 2). *Atlas Genet Cytogenet Oncol Haematol*. June 2007. URL:<http://AtlasGeneticsOncology.org/Genes/ACVR2ID567ch2q22.html>
- **Ghosh P**, Olson RK, **Harmon G**. Sugar Rush in the Colon: Why Incidental Findings on PET scan Justify Colonoscopy? *Am J Gastroenterology*, in press, 2007.
- Lee, JK and **Ghosh, P**. Non-metastatic cancer of the colon associated with pyogenic liver abscess. Accepted in Press, *Amer J of Gastroenterology*, 2007.
- Beck SE, **Carethers JM**. BMP suppresses PTEN expression via RAS/ERK signaling. *Cancer Biol & Ther* 6, 2007 (in press).
- **Jung B** and **Carethers JM**. Gastrointestinal Cancers. In: Digestive Diseases Self Education Program (DDSEP) 2007.
- Hagedorn H, Dieperink E, Dingmann D, Durfee J, **Ho SB**, Isenhardt C, Rettmann N, Willenbring M. Integrating hepatitis prevention services into a substance use disorder clinic. *J Subst Abuse Treat*. 2007;32:391-8.
- **Chow JYC**, Quach KT, Cabrera BL, Cabral JA, Beck SE, **Carethers JM**. RAS/ERK modulates TGFbeta-regulated PTEN expression in human pancreatic adenocarcinoma cells. *Carcinogenesis*, 2007 (in press).
- Shin SK, Nagasaka T, **Jung BH**, Matsubara N, Kim WH, **Carethers JM**, Boland CR, Goel A. Epigenetic and genetic alterations in Netrin-1 receptors UNC5C and DCC in human colon cancer *Gastroenterology*, 2007 (accepted).
- Boland CR, Koi M, Chang DK, **Carethers JM**. The Biochemical Basis of Microsatellite Instability and Abnormal Immunohistochemistry and Clinical Behavior in Lynch Syndrome: from bench to bedside. *Familial Cancer* 2007. (in press).
- Mencin A, Seki E, Osawa Y, Kodama Y, De Minicis S, Knowles M, **Brenner DA**. Alpha-1 antitrypsin Z protein (PiZ) increases hepatic fibrosis in a murine model of cholestasis. *Hepatology*. 2007 (in press)
- Hagedorn H, Dieperink E, Dingmann D, Durfee J, **Ho SB**, Isenhardt C, Rettmann N, Willenbring M. Integrating hepatitis prevention services into a substance use disorder clinic. *J Subst Abuse Treat*. 2007;32:391-8.
- **Hassanein TI**, Hilsabeck RC, Perry W. Introduction to the Hepatic Encephalopathy Scoring Algorithm (HESA). *Dig Dis Sci*. 2007 (in press)
- Perry W, Hilsabeck RC, **Hassanein TI**. Cognitive Dysfunction in Chronic Hepatitis C: A Review. *Dig Dis Sci*. 2007 (in press)
- Weinstein MM, Jung SA, Pretorius DH, Nager CW, den Boer DJ, **Mittal RK**. The reliability of puborectalis muscle measurements with 3-dimensional ultrasound imaging. *Am J Obstet Gynecol*.
- Jung SA, Pretorius DH, Padua BS, Weinstein MM, Nager CW, den Boer DJ, **Mittal RK**. Vaginal high-pressure zone assessed by dynamic 3-dimensional ultrasound images of the pelvic floor. *Am J Obstet Gynecol*. 2007; 197:52.e1-7.
- Lee JH, Pretorius DH, Weinstein M, Guaderrama NM, Nager CW, **Mittal RK**. Transperineal three-dimensional ultrasound in evaluating anal sphincter muscles. *Ultrasound Obstet Gynecol*. 2007; 30:201-9.
- Tipnis NA, Rhee PL, **Mittal RK**. Distension during gastroesophageal reflux: effects of acid inhibition and correlation with symptoms. *Am J Physiol Gastrointest Liver Physiol*. 2007; 293:G469-74.
- **Kagnoff MF**. 2007 William K. Warren, Jr., prize for excellence in celiac disease research awarded to professor Ludvig M. Sollid of Oslo, Norway. *Gastroenterology*. 2007; 133:9-10.
- **Buck M**, **Chojkier M**. C/EBP{beta} Phosphorylation Rescues Macrophage Dysfunction and Apoptosis Induced by Anthrax Lethal Toxin. *Am J Physiol Cell Physiol*. 2007 (in press)
- **Kisseleva T**, **Brenner DA**. Role of hepatic stellate cells in fibrogenesis and the reversal of fibrosis. *J Gastroenterol Hepatol*. 2007; 22:S73-8.
- Tacke F, Trautwein C, Yagmur E, Hellerbrand C, Wiest R, **Brenner DA**, Schnabl B. Up-regulated eotaxin plasma levels in chronic liver disease patients indicate hepatic inflammation, advanced fibrosis and adverse clinical course. *J Gastroenterol Hepatol*. 2007; 22:1256-64.
- Lee J, Kum J, **Ghosh P**. Gastrointestinal: Glycogenic acanthosis. *J Gastroenterol Hepatol*. 2007;22:1550.

Kagnoff Emeritus Reception September 5, 2007



Professor Emeritus Martin Kagnoff, M.D. Career Highlights

1965

M.D., Harvard Medical School

1965-1967

Intern, Junior Resident in Medicine, Peter Bent Brigham Hospital

1967-1969

Lt. Commander, U.S. Navy; Principal Investigator, Dept. of Experimental Biology, Armed Forces Radiobiology Research Institute, National Naval Medical Center, Bethesda, M.D.

1969-1970

Senior Resident in Medicine, New York Hospital, Cornell University

1970-1972

NIH-supported GI Fellowship, Boston Univ. School of Medicine

1972-1974

Visiting Scientist, Salk Institute

1972-2007

Assistant, Associate, and Full Professor of Medicine

2003-2007

Professor of Pediatrics

2005-present

Director, William K. Warren Medical Research Center for Celiac Disease

2007-present

Professor Emeritus, Depts. of Medicine and Pediatrics

CONGRATULATIONS, MARTY!

Organization Statement

The UCSD GI Division will provide the best clinical care to those afflicted with gastrointestinal and liver diseases, investigate at the clinical and basic levels the best way to improve those diseases, and educate trainees on how to best approach the care of patients with those diseases. The UCSD GI Division will strive to be nationally recognized through its faculty as well as innovations that will improve the care of patients with gastrointestinal and liver diseases nationwide.

The UCSD GI Division was founded in 1970 by Henry Wheeler, M.D. who served as its first Division Chief. Later, Jon I. Isenberg, M.D. led the Division from 1979 to 1993, followed by C. Richard Boland, M.D. from 1995 to 2003, and currently by John M. Carethers, M.D., since 2004. The GI fellowship Training Program commenced in 1974 and the NIH Training Grant was initially funded in 1976. The Division has trained several local gastroenterologists in San Diego, as well as developed several academicians at University-based medical schools, including some with leadership and administrative positions.

Main Campus - GI Academic Offices

Division of Gastroenterology
9500 Gilman Drive - 0063
La Jolla, CA 92093-0063

UC303
Tel:(858)534-2757
Fax:(858) 534-3338

Medical Center-Hillcrest

Division of Gastroenterology
200 W. Arbor Drive-8413
San Diego, CA 92103

350 Dickinson Street, Suite 342
Tel: (619) 543-3622
Fax: (619) 543-2766

Thornton Hospital

9300 Campus Point
La Jolla, CA 92037
Tel: (858) 657-7000

VETERANS ADMINISTRATION MEDICAL CENTER

Gastroenterology Section (111D)
3350 La Jolla Village Drive
San Diego, CA 92161
Tel: (858) 552-8585 x2631
Fax: (858) 552-4327

Information concerning this newsletter or requests for additional copies can be directed to Karen Kasser at kkasser@ucsd.edu or (858) 534-2757.
Visit our website at <http://gastro.ucsd.edu>

