



UCSD Division of Gastroenterology Newsletter



April 2008

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Letter from the Chief

Dear Friends:

It is a great pleasure to be the city “host” for our premier annual meeting, Digestive Diseases Week (DDW), held in San Diego from May 17-21, 2008. DDW was last in San Diego in May 2000, and is anticipated to return to San Diego in May 2012 at last check. The meeting, jointly sponsored by the AGA, AASLD, ASGE, and SSAT, attracts more than 19,000 participants. Many of our GI faculty are intimately involved in the planning, programming, and execution of this large meeting, and several local scientific experts from UCSD and surrounding institutions will give State-of-the Art lectures, highlighting the outstanding crop of academic thought-leaders in San Diego. UCSD will host a first-ever all University of California DDW reception, linking the five medical UC campuses’ GI alumni all in the same place. The UCSD GI Division has 15 oral presentations from its faculty and fellows, higher than most years in the past, and will present more than 30 posters. The meeting will certainly spotlight the outstanding San Diego community, PETCO Park, local restaurants, and Southern California weather.

During DDW, Kim Barrett, Ph.D., Professor of Medicine and Dean of Graduate Studies, will receive one of the inaugural 2008 Outstanding AGA Women in Science awards. Kim is one of 24 women named because of their exemplary contributions to digestive disease science, education, scholarship and research. These awards are linked to a fund drive to honor the first women president of the AGA, Sara Jordan, MD (AGA President 1942, 1943) for a Research Scholar Award, a 3-year award nationally made to developing junior faculty. The Division congratulates Kim on this honor!

The GI Division continues to be prosperous, with a newly NIH-funded Digestive Diseases Center (one of only 20 in the United States), and several individual grants awarded to faculty and fellows for their research plans. Research breakthroughs in liver fibrosis, hepatic encephalopathy, advanced endoscopy, motility, mucosal immunology and GI cancer have recently been published by Division members. The Division’s clinical activity remains busy, and its productivity has grown. I expect the upcoming academic year to be even more fruitful in these arenas.



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Division of Gastroenterology Program Highlights.....Inflammatory Bowel Disease (IBD) Center

To provide superior treatment options to patients, the Division of Gastroenterology developed the UCSD Inflammatory Bowel Disease (IBD) Center. Led by **Dr. Michael Docherty**, an expert in the treatment of complicated cases of Crohn's disease and ulcerative colitis, the center offers state-of-the-art care for people with all forms of inflammatory bowel disease. Dr. Docherty, along with **Dr. Derek Patel**, have received extra training in IBD management above their normal gastroenterology fellowship at nationally-recognized IBD centers.

The UCSD IBD Center's purpose is to provide outstanding care for patients with IBD, including Crohn's disease and ulcerative colitis. A key aspect is to provide access to novel therapies, including newer biological agents and offer patients first-hand access to clinical trials with not-yet released cutting-edge therapies. For example, UCSD is a site for the COSPAR study evaluation the anti-TNF antibody Cimzia. Additionally, for those who need surgeries for these diseases, minimally invasive and novel robotic surgical approaches are offered through **Drs. Sonia Ramamoorthy** and **Mark Talamini**, Center faculty from the Department of Surgery.

The UCSD IBD Center will be the first organized and full service Center for San Diego patients with Inflammatory Bowel Disease. The Center combines outstanding and coordinated clinical care, in the outpatient and inpatient settings, utilizes a modern infusion center for biological therapy, provides remarkable surgical and radiological expertise, and offers participation in nationally-run clinical trials. Other diagnostic features include capsule endoscopy and double-balloon enteroscopy capable of visualizing nearly the entire small bowel endoscopically.

Center faculty have been raising awareness of these diseases as well as the existence of the UCSD IBD Center. In addition to educational presentations to physicians and patients in San Diego, Dr. Docherty has developed a patient education webcast entitled, "The Pros and Cons of Biologics for Colitis" that is available on iTunes, and presented by Healthtalk.com.

The UCSD IBD Center has developed an IBD registry, an expanding database that is currently coordinated by **Sandra Woods, BSN**, GI Case Manager at Thornton Hospital. The database documents current and past patient treatment histories, and serves as a determinant for eligibility for some clinical trials. The location of the UCSD IBD Center is Thornton Hospital, but there are clinics at both Thornton and Hillcrest locations.



Michael Docherty, M.D.



Derek Patel, M.D.

You can get more information about the UCSD Inflammatory Bowel Disease (IBD) Center at their website:
<http://health.ucsd.edu/specialties/gastro/inflammatory-bowel-disease/>

For Referrals, please contact 858-657-8440

Division Highlights....

Thomas Savides, M.D., Professor of Clinical Medicine and Director of Advanced Endoscopy participated with UCSD Surgeons Mark Talamini, M.D. and Santiago Horgan, M.D. in what is believed to be the Country's first removal of a diseased appendix through the mouth for a patient. The NOTES procedure was performed on March 12, 2008 at UCSD's Thornton Hospital. UCSD Medical Center is one of the national sites for NOTES research, and UCSD has done more than 18 transvaginal cholecystectomies in humans, and has an active animal lab. The surgery has received national attention, and was featured in Time Magazine in April 2008.

The GI Division will welcome **Denise Kalmaz, M.D.** and **David Owens, M.D.** to the faculty beginning July 2008. Both Dr. Kalmaz and Dr. Owens are completing their GI fellowship training at UCSD as of June 2008.

Martina Buck Ph.D., Assistant Professor and **Mario Chojkier, M.D.** Professor of Medicine, were highlighted in the press regarding a RSK-inhibiting peptide that blocks liver fibrosis and published in PLoS ONE in December 2007.

The **UCSD GI Division** will present 15 oral presentations and more than 25 posters at DDW 2008, held in San Diego from May 18-21, 2008

The GI Division welcomes **Maureen Quinn** as new Division Assistant at our Hillcrest offices. Ms. Quinn will support several of our academic Gastroenterologists as well as various Division-wide projects.

The **2008 Digestive Diseases Week** will be in San Diego May 18 -21, 2008. The UCSD GI Division along with UCLA, UCSF, UCI and UCD GI Divisions will host an All University of California Alumni Reception at the San Diego Maritime Museum. Invitations will be mailed in April 2008 and will require RSVP.

Alexander Kuo, M.D. has been named Director of Hepatology for the GI Division. Dr. Kuo will supervise the liver clinics, including hepatitis C treatment clinics a UCSD. **Tarek Hasanein, M.D.** remains the Director for Medical Liver Transplant.

New Hepatology staff includes, **Deborah Beyer, NP** who will coordinate hepatitis C patient care, and **Abigail Padilla**, who will support the hepatology hospital related administrative roles.

The **UCSD Digestive Disease Research Development Center**, one of 20 NIH funded Digestive Centers in the United States, begins operation in May 2008. The Center will operate three research cores for members of the Center performing research in the thematic areas of the Center. A website highlighting the functions and operation of the Center will commence over the next few months.

The GI Division held its **2nd Annual Research Retreat** on February 23, 2008 at UCSD. Lars Eckmann, M.D. coordinated the program which focused on Infection, Inflammation, and IBD. The retreat highlighted research at UCSD from several Departments and is a focus of the Division's newly-obtained NIH Digestive Diseases Center grant..

Awards & Honors....

John Carethers, M.D., Professor of Medicine and Chief of the GI Division, was elected to the American Society for Clinical Investigation (ASCI). ASCI, which publishes the Journal of Clinical Investigation, was established in 1908 and is one of the oldest and most respected medical honor societies. Since its inception, 2800 physician-scientists have been elected to ASCI for their outstanding record in scholarly achievement in biomedical research. Many members are widely-recognized leaders in academic medicine. Dr. Carethers joins **Drs. Eliot Alpert, David Brenner, Mario Chojkier, Alan Hofmann, and Marty Kagnoff** as UCSD GI Divisional members of this prestigious society.

Declan McCole, Ph.D., Assistant Project Scientist, received a travel award to attend the Second International Symposium on Pediatric Inflammatory Bowel Disease, to be held in Irvington, VA April 13-16, 2008.

Kim Barrett, Ph.D., Professor of Medicine and Dean of Graduate Studies, was selected nationally as one of the inaugural AGA Women in Science, 2008. She will receive her award at a ceremony to be held during DDW in San Diego In May 2008.

Barbara Jung, M.D., Assistant Professor of Medicine, received notice that she will be awarded an NIH R03 Grant for her research entitled "Activin and Intestinal Polyp Progression," slated for funding in July 2008 for 2 years.

Bernd Schnabl, M.D., visiting third year fellow from Columbia University and anticipated faculty member as of July 2008, was awarded a grant from the American Liver Foundation, beginning July 2008. Dr. Schnabl currently holds a Fellow-to-Faculty Transition Award from the Foundation for Digestive Health and Nutrition.

Pradipta Ghosh, M.D., third year GI fellow, was awarded a Research Scholar Award from the Foundation for Digestive Health and Nutrition. The three-year award is entitled "The Role of G_i Proteins and GIV/Girdin in Cell Migration: Implications for Colon Cancer Metastases." and begins July 2008.

Rohit Loomba, M.D., MHSC, first year GI fellow, was awarded the 2008 San Diego GI Society Abstract Award for fellows. Dr. Loomba was selected after a presentation in March 2008 with competition from fellows from Scripps Green, Navy, and UCSD. **Dr. Loomba** was also awarded a 2008 GI/Hepatology Fellows Travel grant to the 59th Annual meeting of the American Association for the Study of Liver Diseases, for Fall 2008.

Recent Division Publications...

Kakiyama G, Tamegai H, Iida T, Mitamura K, Ikegawa S, Goto T, Mano N, Goto J, Holz P, **Hagey LR, Hofmann AF**. Isolation of a Major Novel Dominant Biliary Bile acid in the Wombat: 15 α -hydroxylithocholic acid. *J Lipid Res* 2007;48:2682-92.

Cooke JR, Behling CA, Perricone A, **Savides TJ**. Using Trans-Esophageal Endoscopic Ultrasound-Guided Fine Needle Aspiration to Diagnose Sarcoidosis in Patients with Mediastinal Lymphadenopathy. *Clinical Pulmonary Medicine*, January 2008;15(1):13-17

Chappell AE, Bunz M, **Dong H**, Seol E, Lytle C, **Barrett KE & McCole DF**. 2007. Hydrogen peroxide inhibits Ca²⁺-dependent chloride secretion across colonic epithelial cells via distinct kinase signaling pathways and ion transport proteins. *FASEB Journal*. June Issue; 22 (6). (in press)

Lee JK, **Ghosh P**, McWhorter V, Payne M, Olson RK, **Krinsky ML**, Ramamoorthy SL, **Carethers JM**. Evidence for colorectal sarcomatoid carcinoma arising from tubulovillous adenoma. *World Journal of Gastroenterology*, 2008. (in press)

Chow JYC, Dong H, Quach KT, Nguyen PNV, Chen K, **Carethers JM**. TGFbeta mediates PTEN suppression and cell motility through calcium-mediated PKCalpha activation in pancreatic cancer cells. *Am J Physiol Gastrointest Liver Physiol*, 2008; 294 : G899 - G905.

Jung BH, Beck SE, **Carethers JM**. Bone morphogenetic protein (BMP) and activin signaling in colon cancer. *Colorectal Cancer Reports* 4(2): 71-76, 2008.

Seki E, Brenner DA. TLR and adaptor molecules in liver disease: Update. 2008; (in press)

Seki E, Kondo Y, Iimuro Y, Naka T, Son G, Kishimoto T, Tsutsui H, Fujimoto J, Nakanishi K. Demonstration of cooperative contribution of MET- and EGFR-mediated STAT3 phosphorylation to liver regeneration by exogenous suppressor of cytokine signaling. *J. Hepatol* 2008; 48: 237-45.

Hruz P, **Eckmann L**. Caspase recruitment domain-containing sensors and adaptors in intestinal innate immunity. *Curr Opin Gastroenterol*. 2008 Mar;24(2):108-14.

Ringqvist E, Palm JE, Skarin H, Hehl AB, Weiland M, Davids BJ, Reiner DS, Griffiths WJ, **Eckmann L**, Gillin FD, Svärd SG. Release of metabolic enzymes by Giardia in response to interaction with intestinal epithelial cells. *Mol Biochem Parasitol*. 2008 (in press)

Jung SA, Pretorius DH, Weinstein M, Nager CW, Den-Boer D, **Mittal RK**. Closure Mechanism of the Anal Canal in Women: Assessed by Three-Dimensional Ultrasound Imaging. *Dis Colon Rectum*. 2008. (in press)

Korsapati H, Babaei A, Bhargava V, **Mittal RK**. Cholinergic stimulation induces asynchrony between the circular and longitudinal muscle contraction during esophageal peristalsis. *Am J Physiol Gastrointest Liver Physiol*. 2008; 294(3):G694-8.

Babaei A, Bhargava V, Korsapati H, Zheng WH, **Mittal RK**. A Unique Longitudinal Muscle Contraction Pattern Associated With Transient Lower Esophageal Sphincter Relaxation. *Gastroenterology*. 2008 (in press)

Barrett KE. New ways of thinking about (and teaching about) intestinal epithelial function. *Adv Physiol Educ*. 2008; 32(1):25-34.

Chen T, Zhang W, Wang J, **Dong H**, Wang M. Eimeria tenella: Analysis of differentially expressed genes in the monensin- and maduramicin-resistant lines using cDNA array. *Exp Parasitol*. 2008 Mar 7;

Perry W, Hilsabeck RC, **Hassanein TI**. Cognitive dysfunction in chronic hepatitis C: a review. *Dig Dis Sci*. 2008 ;53(2):307-21.

Cheung RC, Currie S, Shen H, Bini EJ, **Ho SB**, Anand BS, Hu KQ, Wright TL, Morgan TR; for the VA HCV-001 Study Group. Can We Predict the Degree of Fibrosis in Chronic Hepatitis C Patients Using Routine Blood Tests in Our Daily Practice? *J Clin Gastroenterol*. 2008 (in press)

Lee JK, Kum J, **Ghosh P**. Nonmetastatic cancer of the colon associated with pyogenic liver abscess. *Am J Gastroenterol*. 2008; 103(3):798-9.

Groom H, Dieperink E, Nelson DB, Garrard J, Johnson JR, Ewing SL, Stockley H, Durfee J, Jonk Y, Willenbring ML, **Ho SB**. Outcomes of a Hepatitis C screening program at a large urban VA medical center. *J Clin Gastroenterol*. 2008; 42(1):97-106.

Ganz RA, Overholt BF, Sharma VK, Fleischer DE, Shaheen NJ, Lightdale CJ, Freeman SR, Pruitt RE, Urayama SM, Gress F, Pavey DA, Branch MS, **Savides TJ**, Chang KJ, Muthusamy VR, Bohorfoush AG, Pace SC, Demeester SR, Eysselein VE, Panjehpour M, Triadafilopoulos G. Circumferential ablation of Barrett's esophagus that contains high-grade dysplasia: A U.S. multicenter registry. *Gastrointest Endosc*. 2008 (in press)

Buck M, Chojkier M. A Ribosomal S-6 Kinase-Mediated Signal to C/EBP-beta Is Critical for the Development of Liver Fibrosis. *PLoS ONE*. 2007; 2(12):e1372.

Savides TJ. EUS-guided ERCP for patients with intermediate probability for choledocholithiasis: is it time for all of us to start doing this? *Gastrointest Endosc*. 2008; 67(4):669-72.

DDW 2008 Oral Presentations...

Jung B, Cabral J, Beck S, Gomez J, Carethers JM. **Dichotomous signaling mechanisms for activin-induced growth suppression and migration in colon cancer cells.**

Jung B, Gomez J, Chau E, Cabral J, Ream-Robinson D, Shin SK, Goel A, Carethers JM. **Activin signaling in microsatellite stable (MSS) colon cancers is disrupted by a combination of genetic and epigenetic mechanisms.**

Chung H, Young DJ, Le T-AT, Lee JK, Ream-Robinson D, Carethers JM. **Determination of mutation frequency and rate of activin receptor 2 (ACVR2) and transforming growth factor receptor 2 (TGFR2) in colorectal cells with different DNA mismatch repair (MMR) defects.**

Tuo B, Wen G, Wei J, Zhang Y, and Dong H. **Gender Differences in Duodenal Bicarbonate Secretion Cause Gender Differences in Human Duodenal Ulcer.**

Scharl M, Barrett KE, McCole DF. **The Crohn's disease candidate gene protein tyrosine phosphatase N2 (PTPN2) is activated by gamma interferon (IFN-g) in intestinal epithelial cells (IECs) in an adenosine-monophosphate kinase (AMPK) dependent manner.**

Weinstein MM, Pretorius DH, Jung S-A, Wan JJ, Nager CW, Mittal RK. **Assessment of Anatomy and Function of the Puborectalis and Anal Sphincter Muscles in Asymptomatic Parous Women.**

Babaei A, Bhargava V, Aalam S, Scadeng M, Mittal RK. **Effect of Proton Pump Inhibitor on the Gastric Volume: Assessed by Magnetic Resonance Imaging.**

Korsapati HR, Dohil R, Quin AM, Bhargava V, Mittal RK. **Normal Circular Muscle but Dysfunctional Longitudinal Muscle in Eosinophilic Esophagitis**

Chappell AE, Bunz M, Scharl M, Lytle C, Barrett KE, McCole DF. **Hydrogen peroxide inhibits Calcium-stimulated colonic epithelial ion transport via activation of adenosine monophosphate-activated protein kinase and inhibition of NKCC1.**

Resta-Lenert S, Maruggi M, and Ho C. **Synbiotics protect against oxidative stress in inflammatory bowel disease (IBD) by inducing phase 2 response enzymes.**

Kodama Y, Taura K, Miura K, Osawa K, Brenner DA. **Anti-apoptotic effect of JNK1 through Mcl-1 stabilization in TNF α -induced hepatocyte apoptosis**

De Minicis S, Seki E, Osterreicher CH, Kodama Y, Johannes K, Scwabe RF and Brenner DA. **Phagocytic and non-phagocytic NADPH-oxidase isoforms differentially regulate fibrosis but not steatosis in the liver.**

Miura K, Taura K, Kodama Y, Brenner DA. **HCV-induced oxidative stress suppresses basal and IL6-stimulated hepcidin expression in human hepatoma cell lines**

Kisseleva T, Notas G, Taura K, Kodama Y, De Minicis S, Kramer M, Hesson DP, Pelura T, Brenner DA. **Human Serum Amyloid P (hSAP) inhibits bile duct ligation induced liver fibrosis in mice.**

Ho SB, Krinsky ML. **Quality Polyp Research in Colonoscopy. Are We Achieving Polyp Clearance?**

*2008 Endowed Isenberg Lecture
January 22, 2008*

*Lecturer: Daniel K. Podolsky, M.D.
Massachusetts General Hospital/ Harvard University*

Title: "Making Innate Good Sense: Tolls and CARD Tricks in the Epithelium"



Post-Lecture Reception in BSB Hallway

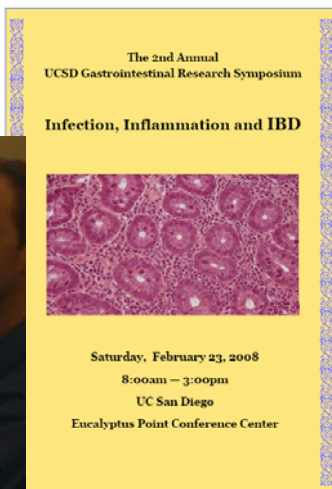


Dr. Kim Barrett, Dr. David Brenner (rear), Dr. Daniel Podolsky
Ms Birgitta Martensson, Dr. John Carethers

*2nd Annual Gastrointestinal Research Symposium
Infection, Inflammation and IBD
February 23, 2008*



Attendees taking in a presentation



Dr. Lars Eckmann highlights a point on the PowerPoint presentation

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) 534-3320
Visit our website at <http://gastro.ucsd.edu>