

Focus on Research, Member's Profile: Mike Smith, PhD

INSIDE THIS ISSUE

- 1 Focus on Research: Mike Smith, PhD
- 2 Focus on Research Contd
- 3 DHRC Pilot Grants Awarded
- 4 News from the Cores
- 5 DHC Seminar Series Winter Schedule

...Identify correlates of protection in order to translate A_{2A}R agonist function correlates ...

Dr. Smith joined the UVA Division of Gastroenterology in 1996. His primary research focus is in characterizing how cells involved in the innate immune system sense and respond to microbial infection. His current interrelated projects include studies of Toll- Like Receptor structure and function (with focus on identification and characterization of regions within the TLR2 TIR domain essential for signaling activity, recruitment of signaling adapter proteins and dimerization with TLR1 or TLR6), the role of heparin sulfate proteoglycans syndecan-1 and syndecan-4 in the host response to *Helicobacter pylori* infection, and modulation of macrophage function through the adenosine A_{2A} receptor. Stimulation of cells through the A_{2A}R can generally be viewed as a mechanism to dampen the inflammatory response and acts to inhibit the production of pro-inflammatory cytokines while enhancing the production of anti-inflammatory mediators. He is a co-Investigator along with Peter Ernst, Barbara Mann, Joel Linden, Richard Guerrant, William Scheld, other UVA faculty and Adenosine Therapeutics LLC on a recently awarded UO1 grant to study the utility of "Adenosine Receptor Agonists as an Immunotherapy for Biodefense". Dr. Smith's role in this project is to test a variety of tissue culture models to identify correlates of protection in order to translate A_{2A}R agonist function from animal models to applications in humans. Dr. Smith is a permanent member of the NIH study section on innate immunity and inflammation (III) since 2005 and council member and treasurer of the Society for Leukocyte Biology

Dr. Smith's former post doc, Jitendra Gautam, recently won the President's Award for best work by a trainee at the annual



Focus on Research

meeting of the Society for Leukocyte Biology for his studies on TLR2 structure/function. Dr. Gautam has recently accepted an instructor of research position in Nephrology with Dr. Kline Bolton's laboratory. We would also like to congratulate Mike on his recent strong showing in the 42nd Annual [Head of the Charles](#) (one of the biggest rowing events of the year) master's doubles race on October 21-22. He and his teammate completed the 3 mile course in a blistering 22:18 for their fourth consecutive victory!

Recent Publications:

1. **MF Smith, Jr.**, JL Novotny, V.S. Carl and LD Comeau. 2006. *Helicobacter pylori* and Toll-like receptor agonists induce syndecan-4 expression in an NF- κ B-dependent manner. *Glycobiology* 16:221-229.
2. **MF Smith, Jr.**, J.K. Gautam, S.G. Black, and P.B. Ernst. 2006. Microbial-induced regulation of syndecan expression: Important host defense mechanism or an opportunity for pathogens? *TheScientificWorldJOURNAL*. 6:442-445
3. JK Gautam, Ashish, LD Comeau, JK Krueger, and **MF Smith, Jr.** 2006 Structural and functional evidence for the role of the TLR2 DD loop in TLR1/2 heterodimerization and signaling. *J. Biol. Chem.* 281:30132-30142.
4. AM O'Hara, A Bhattacharyya, RC Mifflin, **MF Smith**, KA Ryan, K G-E Scott, M Naganuma, A Casola, T Izumi, S Mitra, PB Ernst, and SE Crowe. 2006. Interleukin-8 induction by *Helicobacter pylori* in gastric epithelial cells is dependent on apurinic/aprimidinic endonuclease-1/redox factor-1. *J. Immunol.* In press.
5. S-Z Ding, **MF Smith, Jr.** and JB Goldberg. 2006. *Helicobacter pylori* Infection and Mitogen-Activated Protein Kinases Modulate Cell Cycle Machinery and Cell Cycle Progression in Gastric Epithelial Cells. *J. Gastroenterology and Hepatology* In press.



Mike Smith, PhD

DHRC Pilot Grants Awarded 2006-07

We are proud to announce this year's winners of the pilot feasibility award program. After careful selection by the center's advisory board six awards were given of up to \$25,000/year to provide initial funds for the development of digestive health related research initiatives leading to the submission of competitive grants to traditional funding sources. Selection criteria included applicants without current or past NIH research support, no previous digestive health related work, and the testing of new innovative ideas with excellent potential. Current winners include three investigators from the Department of Internal Medicine: Gastroenterology and three from other Medical and Academic Departments.

Department of Internal Medicine Winners:

Dr. Brian Behm will study Pravastatin in Moderate to Severe Crohn's Disease, **Dr. Diklar Makola** will initiate a randomized study of gastric versus jejunal feeding in patients with acute severe pancreatitis, and **Dr. Michael Smith** is investigating Heparan sulfate proteoglycans and host response to *Helicobacter pylori*.

Department of Pathology:

Dr. Janet Cross will test the role of a novel cytokine, Macrophage Migration Inhibition Factor (MIF), in *H. pylori* pathogenesis.

Department of Biology:

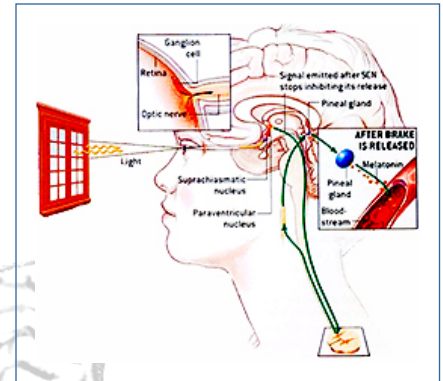
Dr. Carla Green while studying circadian clock mechanisms has recently led her (somewhat unexpectedly!) into the field of metabolism and digestion.

Department of Pharmacology:

Dr. William McIntire aims to investigate the effect of G protein α , β and γ Adenosine A2b receptor signaling in intestinal epithelial cells.

Applications for next year's awards are now being accepted, for more information go to:

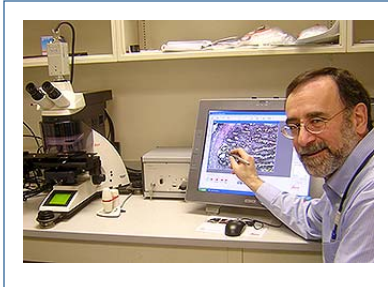
www.uvadigestivehealth.org/dhrc/pilot.cfm



Circadian Clock

*Six awards were given of
up to \$25,000/year*

News from the Cores: Molecular Biology/Gene Expression



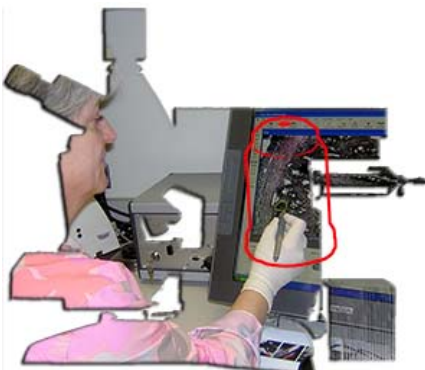
Steven Cohn demonstrating the Leica LMD 6000

Dr. Steven Cohn, director of the molecular biology/gene expression core, is pleased to announce the acquisition of a new 2006 Leica LMD 6000 Laser Capture Microdissection system through a joint purchase by the DHRC and the Cancer Center. The Leica LMD 6000 enables high-precision, high-velocity collection of very small objects, such as individual cells or groups of cells. The instrument features a 355 nm UV laser enabling fast cutting of specimens from tissue sections. The isolated material falls directly into one of four tubes positioned below the tissue. The system's interface features a hand held stylus that interacts with the screen to easily isolate complex shapes for laser cutting (see illustration below). Sample isolation requires only a few mouse clicks and all experiment parameters can be stored for annotation purposes, including digital images. Charges for machine use and technical services are currently pending approval in the Dean's office. The core personnel are available to center members for consultation regarding experiment design, sample preparation, instrument training and will also assist in the use of the LMD 6000.

The core also currently offers:

- i) Access to gene array methodology through the Biomolecular Research Core Facility, affimetrix human and mouse chips for purchase . Members receive discounts on the cost of statistical and bioinformatics consulting for gene array experiments .
- ii) Real-time PCR services including consultation and training in the design of primers for real time PCR, training in the use of the Applied Biosystems SDS7000 and the Biorad iCycler, running real time PCR assays with the option of performing SYBR Green or TaqMan (the reagents needed for these assays are on site and Celera pre-calibrated assays for many genes of interest are available at a discount to Center members) assay validation for both SYBR Green and Taqman, staff assistance in data analysis, interpretation and troubleshooting.

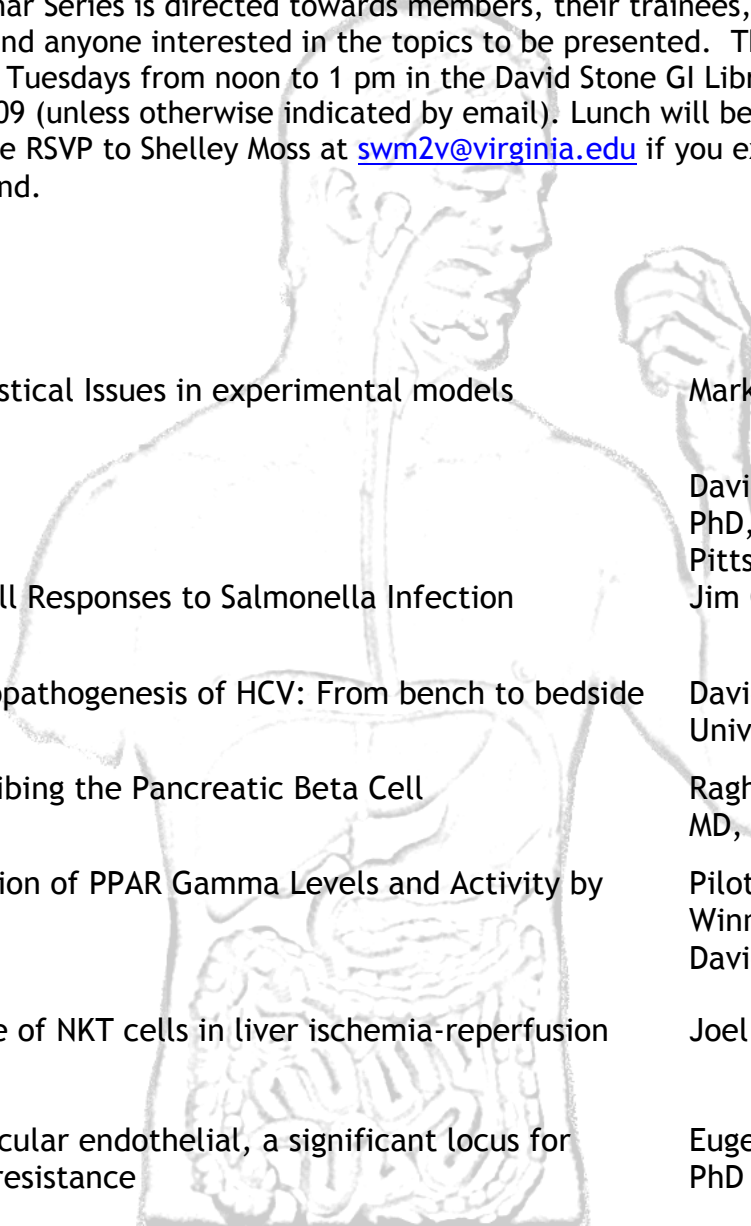
Please contact Dr. Alda Vidrich at av4x@virginia.edu and drop by for a visit, the core is located in MR4 RM 1001.



DHC Seminar Series Winter Schedule

The 2006-07 DHC Seminar Series is directed towards members, their trainees, laboratory personnel, GI Fellows and anyone interested in the topics to be presented. The series is CME accredited and held on Tuesdays from noon to 1 pm in the David Stone GI Library, West Complex, 2nd Fl RM 2109 (unless otherwise indicated by email). Lunch will be provided for the Seminar Series so please RSVP to Shelley Moss at swm2v@virginia.edu if you expect a group larger than two to attend.

Winter 2007



Jan 9	Biostatistical Issues in experimental models	Mark Conaway, PhD
Jan 23	TBA	David Whitcomb, MD, PhD, University of Pittsburgh
Jan 30	Host Cell Responses to Salmonella Infection	Jim Casanova, PhD
Feb 13	Immunopathogenesis of HCV: From bench to bedside	David R Nelson, M.D. University of Florida
Feb 20	Transcribing the Pancreatic Beta Cell	Raghavendra Mirmira, MD, PhD
Feb 27	Regulation of PPAR Gamma Levels and Activity by TGIF	Pilot Feasibility Winner David Wotton, PhD
March 6	The role of NKT cells in liver ischemia-reperfusion injury	Joel Linden, PhD
March 13	The vascular endothelial, a significant locus for insulin resistance	Eugene Barrett, MD, PhD
March 20	1. Source of Protective IL-10 in Innate Intestinal Inflammation (25 min) 2. Regulations of Ghrelin Structure and Function by Protein Kinase C (25 min)	Pilot Feasibility Winners Eric Houpt, MD Julie Sando, PhD