

New Leadership for the DHC



Jorge Bezerra, MD



Mitchell Cohen, MD



Ted Denson, MD



Aaron Zorn, MD

In June 2003 the Digestive Health Center (DHC) was established by Mitchell Cohen, MD (Director) and Jorge Bezerra, MD (Associate Director). Under Dr. Cohen's leadership the center has increased the number of members, expanded core services, and established a Pilot and Feasibility Program. Recently, Dr. Cohen accepted the position as Vice Chair for Clinical Affairs at Cincinnati Children's Hospital Medical Center (CCHMC). Due to his new role at CCHMC, Dr. Cohen will become an Associate director of the center devoting his effort as Director of the Clinical Component. Dr. Bezerra will become the DHC director.

Additionally, two current DHC members, Lee (Ted) Denson, MD and Aaron Zorn, PhD will become Associate Directors of the center. Dr. Denson will take primary responsibility for organizing the Seminar Enrichment Program and Dr. Zorn will oversee the Pilot and Feasibility Program.

Pilot and Feasibility Recipients

The Digestive Health Center (DHC) is pleased to announce the recipients of its 2009 Pilot and Feasibility grants. We received a large number of competitive applications and faced a difficult task to have to select three recipients among so many high level applications. Below we display the abstracts of the three selected grant applications.

Kasper Hoebe, PhD; CCHMC Division of Molecular Immunology

In the current proposal, we describe a novel recessive mutation termed sphinx that disrupted both lymphocyte survival and normal hematopoiesis in the mouse. Homozygotes are born at normal Mendelian ratios, but succumbed to premature death by 100 days of age. The onset of hematopoietic abnormalities occurred immediately after birth, as HSCs failed to fully migrate from the neonatal liver. Extramedullary hematopoiesis occurred in the liver, which became fibrotic and hyperplastic in adults. The mice lacked functional lymphocytes and exhibited dynamic changes in immune homeostasis, marked by progressive lymphopenia, neutrophilia,



Pilot and Feasibility Awardees continued

Kasper Hoebe, PhD continued

anemia and wasting disease. The causative mutation was found to reside in the GTPase of the immunity-associated protein 5 (GIMAP5)-a member of the GTP-binding superfamily with poorly defined functions. The current proposal aims to identify the physiological role of GIMAP5 in the development of colitis.

Kevin Hommel, PhD; CCHMC Division of Behavioral Medicine and Clinical Psychology

Treatment nonadherence is associated with increased morbidity and mortality across various pediatric chronic illness groups. Prevalence rates (i.e., % of patients taking less than 80% of doses) of nonadherence across disease groups range from 50% in children to 65-75% in adolescents. Medication nonadherence in pediatric inflammatory bowel disease (IBD) is a significant health issue, with prevalence rates ranging from 50-88% and frequency rates (i.e., % of doses not taken) ranging from 38-49%. Risk of relapse in IBD is 5.5 times greater in nonadherent IBD patients. An individually-tailored behavioral treatment approach that enables accurate patient- and family-specific functional analysis of behaviors that contribute to nonadherence and that can be adapted to meet each family's individual and unique needs is needed to optimize adherence and health outcomes in pediatric IBD. Thus, the proposed study aims to evaluate the efficacy/magnitude of effect, feasibility, and acceptability, of an individually-tailored, family-based behavioral treatment to improve medication adherence, disease severity, and patient quality of life in adolescents (ages 11-18) with IBD. It is anticipated that the results of this pilot and feasibility study will provide support for a larger randomized controlled trial to examine efficacy of this intervention to improve self-management behavior in adolescents with IBD.



Alexander Miethke, PhD; CCHMC Division of Gastroenterology, Hepatology, and Nutrition

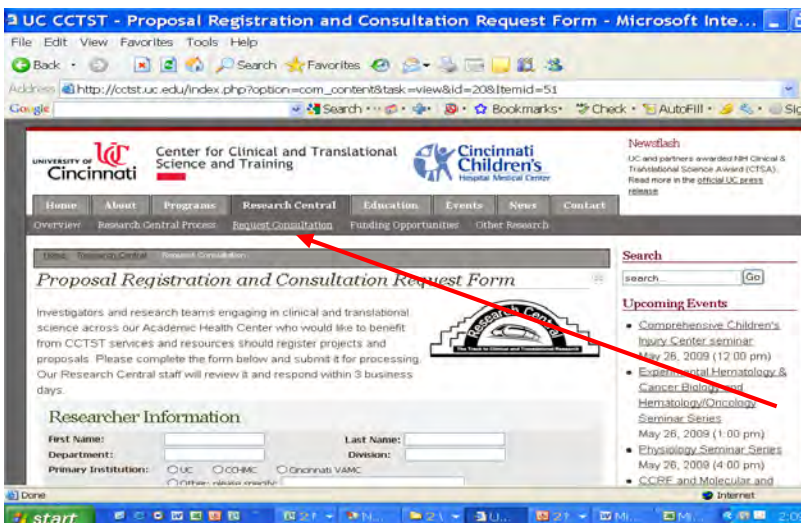
Previous studies revealed an activation of pro-inflammatory genes and presence of autoreactive cells in children with biliary atresia (BA). However, the cellular and molecular basis of this autoreactivity remains largely undefined. Here I will determine whether regulatory T (Treg) cells are capable of reducing the bile duct damage mediated by innate immune cells in a rotavirus-induced murine model of BA. In preliminary studies, I found that the liver is devoid of Treg cells during the early immune response to postnatal rotavirus infection in newborn mice, and that Treg cells effectively suppress dendritic cell (DC)-dependent activation of NK cells. These studies identified a tri-cellular network in the hepatic ecosystem whose interaction regulates early phases of neonatal biliary injury. By using a cell specific co-culture assay that recapitulates this cellular network, I will determine a) which subtype of DCs are the target of Treg cell mediated suppression, and b) which contact-dependent or cytokine-mediated mechanisms are employed by Treg cells in the regulation of NK cell activation. Furthermore, I will investigate whether the adoptive transfer of Treg cells prior to rotavirus infection suppresses NK activation by DCs in vivo and prevents the initiation of bile duct injury in experimental BA. Collectively, these studies may identify cellular targets that may be used to block the initiation and/ or progression of the disease.



New Biostatistical Support for DHC Members

The DHC is partnering with the Center for Clinical and Translational Science and Training (CCTST) to provide members ready access to research methods and biostatistical support. **BioMETrCS** (Biostatistics, Methods and Ethics in Translational and Clinical Studies) faculty and staff are experienced at coordinating a broad array of interdisciplinary clinical and translational research projects, applying biostatistical, methodological, and ethical principles to complex research studies. BioMETrCS services include a broad range of activities spanning the methodological, biostatistical and ethical domains of clinical and translational research. A few examples include:

- Advising on research designs, including project implementation and data collection methods
- Providing guidance on appropriate statistical methods for individual situations
- Calculating power analyses for usual designs
- Analyzing existing datasets
- Creating randomization plans
- Developing data safety and monitoring plans
- Creating data collection instruments, including surveys and questionnaires



When seeking support from BioMETrCS, DHC members should be present at the initial meeting. The first 10 hours of work with a BioMETrCS faculty or 20 hours with a BioMETrCS staff member will be paid by the CCTST per DHC grant fiscal year (June 1 to May 31). For Projects that go beyond this initial period, DHC members will receive a 50% discounted rate up to \$800 per DHC member, per DHC grant fiscal year (June 1 to May 31). To obtain assistance you must complete the request form by going to the “Research Central” tab at the CCTSA website: <http://cctst.uc.edu/>.

Revised Morphology Core Charges

The Research Pathology Service of the Integrative Morphology Core provides routine and specialized histological services. Starting June 1, 2009 charges for morphology services (see table below) will be per DHC member, per DHC grant fiscal year (June 1 to May 31).

Service	Initial Charges for DHC Member	Additional Services for DHC Member
Tissue Processing & Embedding	No Charge for the first 1,500 blocks	\$15 minimum (1st 15 blocks) \$1 per additional block
Paraffin or Cryostat Sectioning	\$1.50 for the first 4,500 slides	\$2.00 per slide
H&E Staining	\$2.50 for the first 1,000 slides	\$4.50 per slide
Special Staining	\$3.50 for the first 500 slides	\$6.50 per slide
Immunohistochemistry	\$10.00 for the first 500 slides	\$18.00 per slide
In Situ Hybridization	\$20.00 for the first 100 slides	\$30.00 per slide

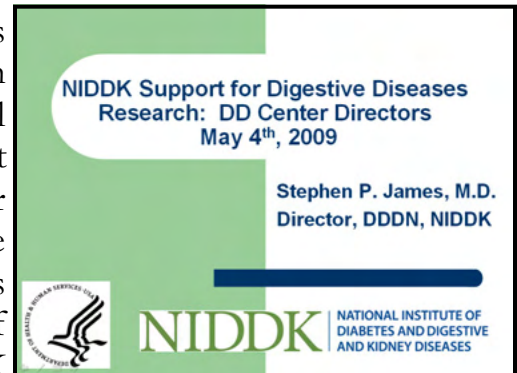
DHC Seminar Series

There will be no seminars in July or August. Our fall seminar series will begin on **Tuesday September 1** in which **Anna Mae Diehl, MD** from Duke University will present her work on fatty liver diseases.

Our seminars are held **on Tuesdays at noon in Location S Room 6.125**. Bring your lunch; soft drinks and cookies are provided. The enrichment series includes distinguished speakers from outside the Academic Medical Center, as well as conferences by investigators and research fellows from Cincinnati, and journal clubs. For current information see: <http://www.cincinnatichildrens.org/dhc/seminar.htm>

Cincinnati Hosted the 2009 Digestive Disease Center Directors Meeting

The DHC hosted the annual Digestive Disease Center Directors meeting May 3-4, 2009. Each year the 16 Digestive Diseases Research Core Centers, 4 Development Centers, and staff from National Institute of Diabetes & Digestive & Kidney Diseases (NIDDK) meet at one of the centers. **Judy Podskalny, PhD** (Director, Career Development, Research Fellowship, & Digestive Disease Centers Programs) provided a Digestive Disease Center Director's Update. Additionally, **Stephen James, MD** (Director, Division of Digestive Diseases and Nutrition) presented an overview of NIDDK support for Digestive Disease Research. Current and past Pilot and Feasibility Recipients presented their work. This was a great opportunity to showcase the outstanding scientific research of our members.



New DHC Members

The DHC is pleased to welcome a 2 new Members:

William Ridgway, MD is an Associate Professor and Director of Division of Immunology, Allergy, and Rheumatology, Department of Medicine at the University of Cincinnati. Dr. Ridgway explores the immunogenetic mechanisms of spontaneous autoimmune biliary disease in NOD congenic mice.

Roger Worrell, PhD is an Assistant Professor in the Department of Molecular and Cellular Physiology at the University of Cincinnati. Dr. Worrell's research interest are focused in two broad areas: 1) Mechanisms and regulation of fluid secretion and absorption primarily in gastrointestinal and renal systems and 2) The mechanisms of intestinal injury and repair.

For all publications, please acknowledge the DHC as follows:

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For more information regarding the DHC please contact one of the following:

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