Mary K. Estes, Ph.D., is the 2010 Vanderbilt Digestive Disease Center Retreat Keynote Speaker. Her presentation entitled “Norovirus Vaccine Development: A Bench to Bedside Story” will be delivered on April 19, 2010.

Dr. Estes earned her B.A. from Elmira College in Elmira, New York and her Ph.D. in bacteriology and immunology from the University of North Carolina at Chapel Hill. At Baylor College of Medicine in Houston, Texas, she completed a postdoctoral fellowship in virology.

She is currently the Director of the Texas Medical Center Digestive Diseases Center, Co-Director of Translational Biology and Molecular Medicine, the Cullen Endowed Chair of Molecular and Human Virology at the Baylor College of Medicine.

Her clinical and research interests include GI virus-host interactions, pathogenesis and immunity, translational biology, molecular mechanisms, viral diarrhea, Norwalk virus, mucosal immunity, and vaccines for rotaviruses and calciviruses.

Her laboratory is studying the effects of two particular viruses. Rotaviruses are the leading cause of severe diarrhea among infants and children, and noroviruses cause more than 90% of epidemic non-bacterial outbreaks of gastroenteritis around the world. Her laboratory focuses on evaluating how to effectively deliver virus-like particles subunit vaccines to induce a mucosal immune response and protection from virus infection.

VDDRC Retreat Keynote Speaker

Mary K. Estes, Ph.D.

Pilot/Feasibility Projects for 2010

*Naji Abumrad, M.D. Proteomic Analysis of Liver Tissue in NAFLD
Claudia Andl, Ph.D. E-cadherin and TGFβ receptor II loss in the esophagus
*Charles Flynn, Ph.D. Lipid abundance and spatial distribution in NAFLD
*Stephen McElroy, M.D. Effects of TNF on Epithelial Barrier Function During Development
Michael Rosen, M.D. STAT6 as a Therapeutic Target in Ulcerative Colitis
Amar Singh, Ph.D. Role of Claudin-2 in Inflammatory Bowel Disease and Cancer
*Benjamin Spiller, Ph.D. Structural & Functional Study of VirA in Shigellosis
John Stafford, M.D., Ph.D. Reversal of fatty liver by activating fat storage with adiponectin
*Saraswathi Viswanathan, Ph.D. Fish oil and COX modulate adipose tissue-specific inflammation
Christopher Williams, M.D., Ph.D. Modulation of junctional signaling by Bves in colorectal carcinoma
*Weisong Zhou, Ph.D. PGE2 and differentiation in inflammatory bowel diseases

*American Recovery and Reinvestment Act (ARRA) Recipients

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POINTS OF INTEREST:

• 2010 VDDRC Retreat Keynote Lecture - Mary K. Estes, Ph.D.
• 11 P&F Recipients 2010
• Spotlight, Young Investigator Award Recipient - Michael Rosen, M.D.
Dr. Manuel R. Amieva, M.D., Ph.D.

Dr. Manuel R. Amieva is an Assistant Professor of Pediatrics and Microbiology & Immunology at Stanford University School of Medicine in Stanford, CA.

Dr. Amieva earned his medical degree and completed his internship, residency and fellowship at the Stanford University School of Medicine. He is board certified in pediatrics and pediatric infectious diseases.

His laboratory is investigating the strategies pathogens utilize to colonize and subvert the epithelial barrier. They focus on the epithelial junctions as a target for bacterial pathogens, since the cell-cell junctions serve as both a barrier to infection and also a major control site for epithelial function.

They are especially interested in how the gastric pathogen Helicobacter pylori may cause cancer by interfering with cell signaling at the epithelial junctions.

On Tuesday, January 19, 2010, Dr. Amieva gave a presentation for the DDRC Seminar Series titled “Life on the Cell Junctions”.

Abstract of Dr. Amieva’s presentation: Several bacteria mucosal colonizers adhere to and intimately interact with the epithelial junctions. Some of these interactions lead to invasive disease or chronic illness.

We will discuss novel roles for two major virulence factors from Helicobacter pylori and Listeria monocytogenes involved in colonizing and breaching the epithelial junctions.

Young Investigator, Michael Rosen, M.D.

Dr. Rosen completed fellowship training in Pediatric Gastroenterology, Hepatology and Nutrition at Vanderbilt and joined the faculty in 2009. Working under the mentorship of Brent Polk, he is interested in the role of Th2 inflammation in ulcerative colitis and the effect of Th2 cytokines on colon epithelium.

IL-13 is an important cytokine in the pathogenesis of ulcerative colitis, and is known to directly impair colon epithelial permeability by inducing apoptosis and the expression of the pore-forming tight junction protein claudin-2.

Dr. Rosen has been exploring the role of signal transducer and activator of transcription 6 (STAT6), the main transcription factor activated by IL-13, in ulcerative colitis. Through immunohistochemical staining of endoscopic biopsies, Dr. Rosen first found increased phosphorylated STAT6 in pediatric patients at diagnosis with ulcerative colitis.

Using HT29 colon epithelial cells as a model system, he has shown STAT6 is necessary for the induction of apoptosis and claudin-2 expression by IL-13.

Dr. Rosen then explored the potential for the FDA-approved histone deacetylase inhibitor SAHA to mitigate the effects of IL-13 on colon epithelium. SAHA had previously been shown to inhibit constitutive STAT6 activation in several forms of lymphoma. He has demonstrated that SAHA is able to potently inhibit IL-13-induced STAT6 activation, apoptosis and claudin-2 expression in HT29 cells.

Through these studies funded by a Vanderbilt Digestive Disease Research Center Pilot and Feasibility Grant, Dr. Rosen has procured the two-year George Ferry Young Investigator Development Award from the Children’s Digestive Health and Nutrition Foundation.

Going forward, Dr. Rosen will further evaluate the potential of SAHA for treating a Th2 mouse model of colitis.
Cynthia L. Sears, M.D.

Dr. Cynthia L. Sears is a Professor of Medicine in the Division of Infectious Diseases and Gastroenterology at Johns Hopkins University School of Medicine in Baltimore, MD.

Dr. Sears earned her medical degree at Thomas Jefferson Medical School in Philadelphia, PA. She then completed her residency at The New York Hospital-Cornell Medical Center.

She was also a fellow at the Cornell Medical Center/Sloan-Kettering Cancer Institute at the University of Virginia School of Medicine. She is board certified in internal medicine and infectious diseases. Her interests include infectious diarrheal diseases, cryptosporidiosis, food borne disease, and *bacteroides fragilis* infections.

On Tuesday, December 1, 2009, Dr. Sears gave a presentation for the VDDRC Seminar Series titled “A Microbial Trigger for Colon Oncogenesis”.

Abstract of Dr. Sears’s presentation: The colonic microbiota are proposed as one potential trigger for colon tumor formation. The human colonic bacterium, *enterotoxigenic Bacteroides fragilis* (ETBF), that secretes *B. fragilis* toxin (BFT), causes human inflammatory diarrhea but also asymptptomatically colonizes a proportion of the population. ETBF triggers colitis and strongly induces colonic tumors in multiple intestinal neoplasia (Min) mice, in part, through Stat3/Th17-dependent mechanisms.

These results suggest a specific mucosal immune-mediated pathway for inflammation-induced cancer by a common human commensal bacterium, providing new mechanistic insight into human colon carcinogenesis.

William Grady, M.D., Ph.D.

Dr. William Grady is an Associate Professor and Clinical Research Division Section Chief in the Division of Gastroenterology at the Fred Hutchinson Cancer Research Center in Seattle, Washington.

Dr. Grady earned his medical degree from the University of Michigan. He was a postdoctoral fellow in the Department of Molecular Biology at the Fred Hutchinson Cancer Research Center. In 1999, he was appointed Assistant Professor of Gastroenterology at Case Western University, and in 2000 he was appointed to the same position at Vanderbilt University.

Dr. Grady is a member of the American Association for Cancer Research, American Association for the Study of Liver Disease and the American Gastroenterological Association. In 2008, he was awarded the Burroughs Wellcome Clinical Scientist Award in Translational Research from the Fred Hutchinson Cancer Research Center.

His research interests include molecular and cell biology of gastrointestinal cancer and the genetic and epigenetic alterations in cancer. He focuses on the clinical management of gastrointestinal cancer family syndromes and the prevention of colon cancer.

On Thursday, November 5, 2009, Dr. Grady gave a presentation for the DDRC Seminar Series titled “Epigenetics and Colon Cancer”.

Abstract of Dr. Grady’s presentation: Epigenetic and genetic alterations are common in a variety of cancers, including gastrointestinal cancer. These alterations deregulate a variety of cell functions and lead to the promotion of tumor formation in the GI tract.

The role of epigenetic alterations in the initiation and progression of colon neoplasms will be discussed as will the functional consequences of these epigenetic alterations.
Dana Philpott, Ph.D.

Dr. Dana Philpott is an Assistant Professor in the Department of Immunology at the University of Toronto in Ontario, Canada.

Dr. Philpott earned her B.S. in cellular, molecular and microbial biology from the University of Calgary in Alberta, Canada. She was a postdoctoral fellow studying cellular microbiology at McMaster University in Ontario, Canada and then the Institut Pasteur in Paris, France.

In 1996, she completed her Ph.D. in the Department of Molecular and Medical Genetics at the University of Toronto.

She has received many awards for her research including the Canadian Institutes for Health Research New Investigator Award and the European Molecular Biology Organization Young Investigator award.

She has recently published articles related to Nod proteins in well-known journals including Autophagy, Nature Medicine, Nature Immunology, and Cell Microbiology.

On Tuesday, October 27, 2009, Dr. Philpott gave a presentation for the DDRC Seminar Series entitled “Nod proteins in infection and immunity”.

Abstract of Dr. Philpott’s presentation: Nod proteins are innate immune detectors of bacterial peptidoglycan.

Our work focuses on how these proteins are implicated in innate and adaptive immune responses following infection and how dysregulation of these proteins might impact on barrier diseases, such as Crohn’s disease and asthma.

D. Scott Merrell, Ph.D.

Dr. D. Scott Merrell is an Associate Professor in the Department of Microbiology and Immunology at the Uniformed Services University, in Bethesda, MD.

Dr. Merrell earned his B.S. in biology from Lyon College in Batesville, AR. He then completed his M.S. in microbiology at the University of Arkansas and his Ph.D. in molecular biology at Tufts University School of Medicine in Boston, MA. Following this, he was a postdoctoral fellow for three years at the Stanford School of Medicine.

He has recently published articles related to Helicobacter pylori in journals such as Gastroenterology, Journal of Clinical Microbiology, Antimicrobial Agents and Chemotherapy and The Journal of Antibiotics.

On September 30, 2009, Dr. Merrell gave a presentation for the DDRC Seminar Series titled “Learning to Hide and Wait: Helicobacter pylori Life in the Stomach”.

Abstract of Dr. Merrell’s presentation: Helicobacter pylori chronically infects fifty percent of the population and is associated with development of gastritis, peptic ulcer disease and gastric cancer.

Pathogenesis is intricately linked to the ability to persist within the stomach as well as the elaboration of subsets of virulence factors. Strategies for survival within the gastric niche and the role of environmental signals in disease and pathogenesis will be discussed.

The art of healing comes from nature, not from the physician. Therefore the physician must start from nature, with an open mind.

~Philipus Aureolus Paracelsus
The VDDRC News Digest is the official publication of the VDDRC. Each issue features research interest area and highlights core laboratories’ research activities. The Digest also includes news, a VDDRC member’s feature publication, and upcoming events. If you have suggestions for a future issue of the VDDRC News Digest, please contact us.

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**The Vanderbilt Digestive Disease Research Center Mission and Goals**

The DDRC is a multidisciplinary center at Vanderbilt University Medical Center developed to serve the following purposes:

- Promote digestive disease-related research in an integrative, collaborative and multidisciplinary manner
- Enhance the basic research capabilities of established DDRC investigators
- Attract investigators not involved in digestive diseases-related research to pursue these lines of investigation
- Develop and implement programs for training and establishment of young investigators in digestive diseases-related research
- Facilitate the transfer of basic research findings to the clinical area

We’re on the Web!
http://mc.vanderbilt.edu/ddrc