Complex Traits Group

VERTEX
THE SCIENCE of POSSIBILITY

Crohn's and Colitis Canada
Crohn et Colite Canada

Workshop Series: **Inflammation at Barrier Surfaces: From Bench to Bedside**

R. Balfour Sartor, M.D.

Midget Distinguished Professor of Medicine, Microbiology & Immunology / Director, Multidisciplinary Center for IBD Research and Treatment, University of North Carolina at Chapel Hill

Ernest Seidman, M.D.

Professor of Medicine & Pediatrics, Canada Research Chair in Immune Mediated Gastrointestinal Disorders / Bruce Kaufman Endowed Chair in IBD at McGill, Digestivelab, Research Institute of MUHC, MGH Campus

"Microbiome in IBD: Insights into pathogenesis and target for improved therapy."

The community structure of resident enteric bacteria in Crohn's disease, ulcerative colitis and chronic immune-mediated experimental colitis is abnormal (dysbiosis), with reproducible decreases in putative protective commensals, such as *Clostridium* and *Bacteroides* subsets, and expansion of *Enterobacteriaceae*, *Fusobacteriia* and other aggressive species.

Studies of gnotobiotic rodents demonstrate that resident bacteria are essential for chronic, immune-mediated intestinal inflammation with both bacterial and host genetic- specific responses.

Specific bacterial subsets can induce protective (regulatory) immune responses and reverse established disease, supporting the concept that selective therapeutic manipulation of resident microbiota could provide novel nontoxic approaches to treating UC and Crohn's disease. Manipulating the microbiota with novel probiotic, antibiotic and dietary strategies promise more physiologic and longer lasting therapeutic approaches beyond current immunosuppressive therapy.

"Potential Roles of Vitamin D in Crohn Disease: From Pathogenesis to Treatment and Prevention"

- Incidence of Crohn Disease in Canada is Highest Reported Worldwide
- Pathogenesis of Crohn Disease Believed to be Due to Combination of Genetic, Microbial and Environmental Factors
- Polymorphisms of NOD2 Gene Most Common Genetic Risk Factor for Crohn disease
- vD Deficiency Influences the Development and Progression of Autoimmunity
- Vitamin D (vD) Deficiency Associated With Impaired Innate Immunity
- vD Induces Expression of NOD2 Gene, Resulting in Enhanced Innate Immunity & Increased Bacterial Isolation & Killing
- vD modulated cytokine responses in Crohn disease, increasing production induced by NOD2 activation and decreasing TLR-induced cytokines
- In macrophage-dendritic cells, vD nearly abolished IL-12p70 production but increased levels of IL-10 and IL-23
- Our results suggest that CD patients who do not have a NOD2 mutation may have NOD2 dysfunction if vD deficient
- However, patients homozygous for 1007fs NOD2 mutation have no response to vD
- Higher vD Status is Associated with Reduced Risk of Crohn Disease

Wednesday, April 22, 2015 at 4:00 PM

Martin Amphitheatre, Room 504

McIntyre Medical Sciences Bldg | 3655 Promenade Sir William Osler

Followed by a *Wine and Cheese* mixer | Bellini Atrium - 5:30 PM

Hosted by the Complex Traits Group

This seminar is mandatory for Biochemistry Graduate Students

Sponsored by:

Vertex Pharmaceuticals & Crohn's and Colitis Canada