

# Diagnostics and Prognostics for Crohn's Disease & Ulcerative Colitis

## TECHNICAL FIELD

Diagnostic: Crohn's disease, Ulcerative Colitis (2007-0105)

## BACKGROUND

Approximately 1 million Americans suffer from Inflammatory Bowel Disease (IBD), a group of disorders that cause the intestines to become inflamed. Two subtypes of IBD, Crohn's disease (CD) and Ulcerative Colitis (UC), are marked by an abnormal immune response to bacteria in the intestinal tract. CD most often affects the small intestine and/or colon, while UC typically affects only the colon and rectum. CD is primarily found in adolescents and young adults between the ages of 15 and 35, with ~10% of the overall cases of CD being in people less than 18 years old. Because CD and UC present as very similar diseases, it is often difficult to definitively diagnose a patient.

Currently, there are some diagnostic serological assays available; however, more biomarkers need to be identified to distinguish CD and UC. These biomarkers could also be used as a non-invasive method for determining the likelihood of response to therapeutics, creating the ability to treat CD or UC on a patient-specific basis.



## TECHNOLOGY

Several defects in neutrophil function have been noted in CD, including reduced phagocytosis, adhesion, chemotaxis, and oxidative burst. This has been shown to reduce neutrophil accumulation at sites of injury, promoting the accumulation of bacterial products and stimulation of the mucosal adaptive immune system. To enhance neutrophil response to bacteria, granulocyte-macrophage colony-stimulating factor (GM-CSF) is required.

Currently, GM-CSF is in Phase II clinical trials in CD. In order to determine which patients would benefit from GM-CSF activity modulation, the expression levels of GM-CSF need to be defined for specific subtypes of IBD. Drs. Denson and Trapnell have discovered that patients with small bowel CD exhibit high levels of anti-GM-CSF antibodies, while patients with UC exhibit low levels of the antibodies.

For the first time, a biomarker exists to distinguish between CD and UC. This biomarker can also be used to predict whether a patient will benefit from GM-CSF modulation through administration or neutralization.

## APPLICATIONS

1. Diagnostic tool for Crohn's disease
2. Predictor of treatment response for Crohn's disease

## ADVANTAGES

- Distinguishes Crohn's disease and Ulcerative Colitis
- Non-invasive
- Increases likelihood of therapeutic success

## INVESTIGATOR

Lee Denson, MD  
Department of Gastroenterology,  
Hepatology, and Nutrition  
Cincinnati Children's Hospital Medical  
Center

Bruce Trapnell, MD, MS  
Department of Pulmonary Biology  
Cincinnati Children's Hospital Medical  
Center

## STATUS

Patent applications pending.

## CONTACT

Korie Counts, PhD  
Technology Manager  
[korie.counts@cchmc.org](mailto:korie.counts@cchmc.org)  
513-636-6736

# Diagnostics and Prognostics for Crohn's Disease & Ulcerative Colitis

## THE INVENTOR

Lee Denson, MD  
Department of Gastroenterology, Hepatology, and Nutrition

## BACKGROUND

**MD:** Medical College of Virginia, Richmond, VA, 1993

**Residency:** Pediatrics, Yale-New Haven Hospital, New Haven, CT, 1993-96

**Certification:** Pediatrics, 1996 & 2002

**Fellowship:** Pediatric Gastroenterology, Yale University School of Medicine, New Haven, CT, 1996-99



The primary focus of Dr. Lee A. Denson's laboratory is to determine the molecular basis for alterations in growth hormone signaling in inflammatory bowel diseases (IBD).

Normal growth and development are dependent upon the ability of growth hormone to regulate IGF-1 expression. Evidence from studies in children with IBD and mouse models of colitis indicates that inflammatory cytokines which are up regulated in this setting may cause an acquired GH resistance. Consequences may include growth failure, altered body composition and impaired mucosal healing.

Dr. Denson's lab is using complementary experimental and patient-based approaches to investigate regulation of growth hormone signaling in mouse models of colitis and in children with Crohn's disease. These include down regulation of the growth hormone receptor and up regulation of a family of post-receptor inhibitory proteins, the Suppressors of Cytokine Signaling (SOCS). These studies should lead to the development of more effective therapies for children with IBD and other chronic inflammatory conditions.

## RECENT PUBLICATIONS:

Puppin, C., A. D'Élia, L. Pellizzari, D. Russo, F. Arturi, I. Presta, S. Filetti, C. Bogue, L. Denson, and G. Damante. **Thyroid-specific transcription factors control Hex promoter activity.** 2003 *Nucleic Acids Research*, 31:1845-1852.

Held, MA., W. Cosme-Blanco, LM. DiFedele, EL. Bonkowski, RK. Menon, and LA. Denson. **Alterations in growth hormone receptor abundance regulate growth hormone signaling in murine obstructive cholestasis.** 2005. *Am J Physiol Gastrointest Liver Physiol*, 288:G986-G993.

DiFedele, LM., J. He, EL. Bonkowski, X. Han, MA. Held, A. Bohan, RK. Menon, and LA. Denson. **Tumor necrosis factor alpha blockade restores growth hormone signaling in murine colitis.** 2005. *Gastroenterology*, 128:1278-91.

Han, X., D. Sosnowska, EL. Bonkowski, and LA. Denson. **Growth hormone inhibits signal transducer and activator of transcription 3 activation and reduces disease activity in murine colitis.** 2005. *Gastroenterology*, 129:185-203.