

Diagnostics and Prognostics for Crohn's Disease

TECHNICAL FIELD

Diagnostic: Crohn's Disease (2006-0202)

BACKGROUND

Crohn's disease, a type of inflammatory bowel disease (IBD), is a chronic, episodic disorder that affects between 400,000 and 600,000 people in North America. Crohn's disease often develops in the teenage years, though individuals in their 60s and 70s are also at increased risk. There is a genetic component to susceptibility with highest relative risk in siblings, affecting males and females equally. Unlike other major types of IBD, such as ulcerative colitis, there is no known cure for Crohn's disease, and therefore the treatment goal is to attain a remission status of the disease. However, as there is no reliable predictor of response to any standard therapies, the treatment course may not be appropriate for that particular patient. This leads to a trial-and-error type of approach to treating the patient, and illustrates the need for a genetic-based test that could determine the best course of treatment for a patient with Crohn's disease.



APPLICATIONS

1. Diagnostic and Prognostic for Crohn's Disease

2. Research tool

ADVANTAGES

- Provides efficient, personalized approach to identifying a therapy course

INVESTIGATOR

Lee A. Denson, M.D.
Division of Gastroenterology, Hepatology
and Nutrition
Cincinnati Children's Hospital Medical
Center

STATUS

Patent applications pending.

CONTACT

Korie Counts, PhD
Technology Manager
korie.counts@cchmc.org
513-636-6736

TECHNOLOGY

Current standard therapies for IBD include steroids and immunomodulators, and both of these lead to a sustained remission in approximately 50% of patients. There are no reliable predictors of response, and thus Dr. Denson and colleagues have prepared and stratified patient samples to directly address this deficiency. Obtaining colon biopsies from children with IBD at diagnosis, children with chronic IBD which has not responded to standard therapies, and normal controls, the analysis demonstrated a marked difference in the gene signatures for each sample set. More importantly, there exists a gene set that distinguishes between samples obtained at diagnosis from patients who ultimately responded to standard therapy versus those who were refractory to standard therapy over the first year following diagnosis. Some of these genes code for chemokines and matrix proteins which have been previously implicated in the pathogenesis of IBD; however, the majority of the genes in the signature have no known role in this pathology. Analysis of four responders and six refractory patients has shown that this assay will predict the refractory patients with 85% specificity and 100% sensitivity using the pattern of gene expression detected in one colon biopsy upon diagnosis. This assay would be ideal in the determination of therapy course upon IBD diagnosis.

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THE INVENTOR

Lee A. Denson, MD
Assistant Professor
Division 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.

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.