Therapeutic Approach for Inflammatory Bowel Disease by Targeting Microbial Proteases

Tech ID: 31914 / UC Case 2020-159-0

BACKGROUND

Ulcerative colitis (UC), an inflammatory bowel disease (IBD), is characterized by chronic inflammation of the colon, with severity of mucosal inflammation being associated with a higher risk of work disability, hospitalization, colorectal cancer, and colectomy. Non-specific immunosuppressive agents targeting the host, such as steroids, thiopurines, and/or biologics, are used to offset the natural history of disease in patients with moderate-severe inflammation. These therapies are, however, associated with significant risks and often ineffective in adequately managing disease. Genomic technologies have identified associations between microbial dysbiosis, or temporal shifts in composition, and UC severity. While recent efforts extended profiling of microbiota in UC beyond genomics, it remains poorly understood if these shifts are causal or associative in nature, and which mechanisms govern pathogenic roles of the microbiome in UC.

TECHNOLOGY DESCRIPTION

Researchers at UC San Diego undertook a study to analyze fecal and serum samples from 40 patients with Ulcerative Colitis (UC) by performing a series of genomics, metabolomics, metapeptidomics, and multiplexed metaproteomics analyses, whereby researchers found that *Bacteroides vulgatus* induced proteolysis, was enriched in the gut of these UC patients. A separate 200-person validation cohort confirms the connection between B. vulgatus proteases and UC severity. Moreover, the multi-omics analysis of the 200 patient cohort extends our observations to Crohn's disease. *Bacteroides vulgatus* disrupted intestinal epithelial permeability *in vitro,* but protease inhibition was sufficient to restore the epithelial barrier. When fecal material from UC patients are transplanted into germ-free mice, these mice ended up with increased colitis. However, oral administration of protease inhibitors attenuated disease severity. This means that targeting microbial proteases can ameliorate the intestinal barrier dysfunction and restore mucosal integrity.

APPLICATIONS

The inventors have provided methods that target microbial proteases (MP) to ameliorate the intestinal barrier dysfunction and restore mucosal integrity. MP are useful to treat and prevent diseases and disorders caused by pathogenic bacteria in the gastrointestinal system of a subject.

ADVANTAGES

Drugs on the market target human proteins and not the microbe as we are proposing. Our findings highlight the potential therapeutic approach for IBD by targeting microbial proteases to ameliorate intestinal barrier dysfunction and restore mucosal integrity.

STATE OF DEVELOPMENT

The state of development is at the experimental stage

INTELLECTUAL PROPERTY INFO

The technology is patent pending and available for licensing.

RELATED MATERIALS

- R Mills, P Dulai, Y Vázquez-Baeza, Q Zhu, G Humphrey, L DeRight Goldasich, R Quinn, A Gewirtz, B Chassaing, H Chu, W Sandborn, P Dorrestein, R Knight, D Gonzalez. OP31 Meta–omics reveals microbiome-driven proteolysis as a contributing factor to the severity of ulcerative colitis disease activity Journal of Crohn's and Colitis, Volume 14, Issue Supplement_1, January 2020, Pages S030–S031 - 01/15/2020

PATENT STATUS

Patent Pending

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OTHER INFORMATION

KEYWORDS

therapeutics, microbiome, proteases, IBD, Ulcerative colitis, mucosal integrity, intestinal barrier dysfunction

CATEGORIZED AS

- **Medical**
  - Disease: Digestive System
  - Therapeutics

RELATED CASES

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