Microbiome Theranostic for Sulfasalazine Treatment in Patients with IBD-Associated Spondyloarthritis

Lead Inventor:

Randy Longman, M.D., Ph.D.
Associate Professor of Medicine, Medicine, Weill Cornell Medical College

Business Development Contact:
Brian Kelly
Director, Technology Licensing

(646) 962-7041
bjk44@cornell.edu
Microbiome Theranostic for Sulfasalazine Treatment in Patients with IBD-Associated Spondyloarthritis

### Background & Unmet Need
- Patients with Inflammatory Bowel Disease (IBD) frequently experience rheumatic manifestations of disease, most commonly spondyloarthritis (SpA)
- There is no widely accepted standard of care for IBD-associated spondyloarthritis (IBD-SpA)
- Sulfasalazine is one of the earliest medications to demonstrate efficacy for inducing IBD remission, but is only effective in reducing rheumatic symptoms in a subset of patients with IBD-SpA
- Sulfasalazine is a prodrug consisting of sulfapyridine (SP) and 5-aminosalicylate, linked by a diazo bond which is cleaved by colonic microbiota
- The antibacterial capability of SP to disrupt bacterial synthesis of folate has led to the hypothesis that the microbiome may play a role in the efficacy of SAS
- **Unmet Need**: Methods for determining which IBD-SpA patients will respond to Sulfasalazine to increase patient response rates to this therapy

### Technology Overview
- **The Technology**: A theranostic for predicting and rescuing treatment response to Sulfasalazine in patients with IBD-SpA
- **The Discovery**: A small clinical trial identified enrichment of *Faecalibacterium prausnitzii* (*F. prau*) and other ‘folate trap’ bacteria as a biomarker for Sulfasalazine response in IBD-SpA patients
- Mechanistically, Sulfasalazine therapy enhances butyrate synthesis via *F. prau*, which limits colitis in responder microbiomes
- **PoC Data**: Relative abundance of *F. prau* alone and with additional taxa demonstrates strong ability to discriminate between Sulfasalazine responders and non-responders (AUC of ROC curve: 0.78, p<0.05 and 0.095, p<0.01, respectively)
- Administration of folate trap bacteria *F. prau* in non-responder mouse models of IBD rescues response to Sulfasalazine, marked by reduced weight loss and cecal lipocalin, a biomarker of intestinal inflammation

**Inventors:**
Randy Longman
Svetlana Lima

**Patents:**
Provisional Filed

**Publications:**

**Biz Dev Contact:**
Brian Kelly
646-962-7041
bjk44@cornell.edu

**Cornell Reference:**
D-11070
Microbiome Theranostic for Sulfasalazine Treatment in Patients with IBD-Associated Spondyloarthritis

Technology Applications

- Method to predict response to Sulfasalazine in IBD-SpA patients by measuring relative abundance of folate-trap bacteria
- Method for treating IBD-SpA patients who lack a functional folate trap by administering Sulfasalazine in combination with one or more folate trap bacteria, such as *F. prausnitzii*

Technology Advantages

- Theranostic test measuring relative abundance of bacteria can be completed via standard PCR-based procedures and at low cost
- Sample collection for theranostic test is non-invasive and standard for IBD patients
- Can increase speed to correct treatment selection for IBD-SpA patients, which is essential due to the progressive nature of the disease

Supporting Data / Figures

**Figure 1:** Graphical abstract representing relationship between folate trap bacteria in the microbiome of Spondylarthritis patients and responsiveness of Sulfasalazine therapy.

Inventors:
- Randy Longman
- Svetlana Lima

Patents:
- Provisional Filed

Publications:

Biz Dev Contact:
- Brian Kelly
  - 646-962-7041
  - bjk44@cornell.edu

Cornell Reference:
- D-11070
Microbiome Theranostic for Sulfasalazine Treatment in Patients with IBD-Associated Spondyloarthritis

Supporting Data / Figures

**LEfSe of Baseline Microbiome: Primary Cohort**
- **Responders**
- **Non-responders**

- *Faecalibacterium prausnitzii*
- *Roseburia inulivorans*
- *Bacteroides nordii*
- *Alistipes onderdonkii*
- *Collinsella aerofaciens*
- *Ruminococcus callidus*
- *Streptococcus salivarius*

*P < .05*

**Validation Cohort**

*F. prau, AUC 0.78 *

*F. prau + R. callidus, AUC 0.95 **

**Figure 1: Left:** Bar plot displays the differentially abundant microbial species between responders and non-responders in the clinical trial. Most notably, folate trap microbe *F. prau* is enriched in responders (*p < 0.05*)

**Right:** ROC curves demonstrating the ability of the indicated bacterial taxa in discriminating responders from non-responders in a separate validation cohort (*n = 16*) (*p ≤ 0.05 and **p ≤ 0.01*).
Microbiome Theranostic for Sulfasalazine Treatment in Patients with IBD-Associated Spondyloarthritis

Supporting Data / Figures

Figure 1: Administration of F. prausnitzii rescues response to Sulfasalazine treatment in gnotobiotic mice colonized with non-responder microbiomes

(A) Schematic of experimental setup. Germ-free mice received fecal microbial transplants (FMTs) from three non-responder subjects. The experimental group was administered F. prausnitzii prior to DSS exposure to induce colitis (B) Mice receiving F. prausnitzii with Sulfasalazine demonstrated reduced weight loss (B) and cecal lipocalin content (C) compared to controls. *p < 0.05, **p < 0.01, and ***p < 0.0001.