Weill Cornell Medicine

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:
Lima et al. *Cell Rep Med*. 2024.

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

Cornell Reference:
D-11070

Weill Cornell Medicine

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. prau*

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

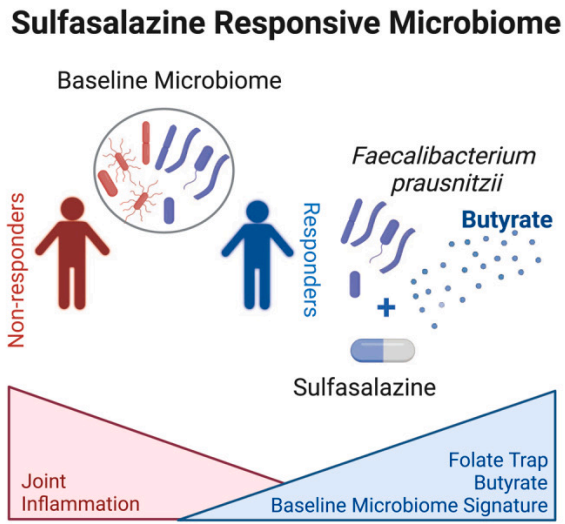


Figure 1: Graphical abstract representing relationship between folate trap bacteria in the microbiome of Spondylarthritis patients and responsiveness of Sulfasalazine therapy.

Inventors:
Randy Longman
Svetlana Lima

Patents:
Provisional Filed

Publications:
Lima et al. *Cell Rep Med*. 2024.

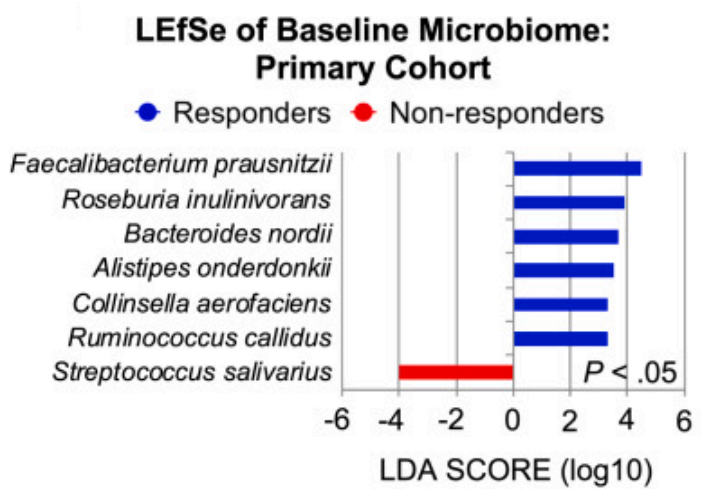
Biz Dev Contact:
Brian Kelly
646-962-7041
bjk44@cornell.edu

Cornell Reference:
D-11070

Weill Cornell Medicine

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

Supporting Data / Figures



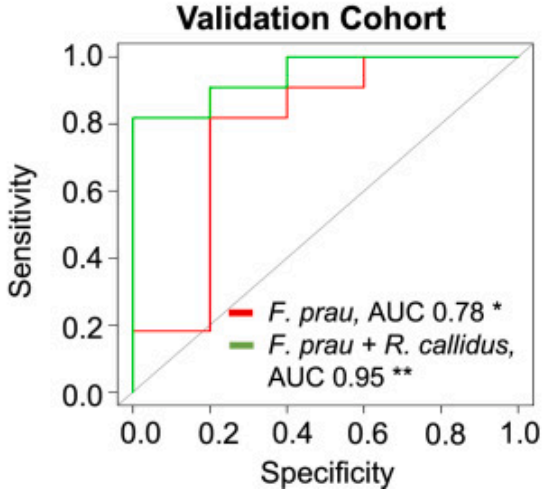


Figure 1: Left: Bar plot displays the differentially abundant microbial species between responders and non-responders in the clinical trial. Most notably, folate trap microbe *F. prau* is enriched in responders ($p<0.05$) **Right:** ROC curves demonstrating the ability of the indicated bacterial taxa in discriminating responders from non-responders in a separate validation cohort (n = 16) ($*p \leq 0.05$ and $**p \leq 0.01$).

Inventors:
Randy Longman
Svetlana Lima

Patents:
Provisional Filed

Publications:
Lima et al. *Cell Rep Med*. 2024.

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

Cornell Reference:
D-11070

Weill Cornell Medicine

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

Supporting Data / Figures

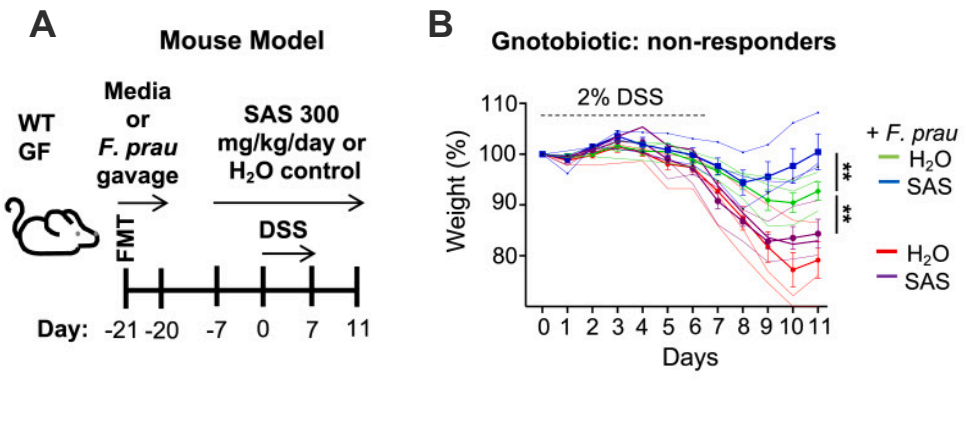


Figure 1: Administration of *F. prau* rescues response to Sulfasalazine treatment in gnotobiotic mice colonized with non-responder microbiomes **(A)** Schematic of experimental setup. Germ-free mice received fecal microbial transplants (FMTs) from three non-responder subjects. The experimental group was administered *F. prau* prior to DSS exposure to induce colitis **(B)** Mice receiving F. prau with Sulfasalazine demonstrated reduced weight loss **(B)** and cecal lipocalin content **(C)** compared to controls. $*p < 0.05$, $**p < 0.01$, and $****p < 0.0001$.

Inventors:
Randy Longman
Svetlana Lima

Patents:
Provisional Filed

Publications:
Lima et al. *Cell Rep Med*. 2024.

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

Cornell Reference:
D-11070

Weill Cornell Medicine

Weill Cornell Medicine