

Transferable Microbiota for the Treatment of Ulcerative Colitis

Lead Inventor:

Randy Longman, M.D., Ph.D.

Associate Professor of Medicine, Weill Cornell Medical College Director, Jill Roberts Center for Research in IBD

Business Development Contact:

Brian Kelly
Director, Technology Licensing

(646) 962-7041

bjk44@cornell.edu

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Background & Unmet Need

- Fecal microbiota transplantation (FMT) has emerged as a promising new treatment for patients with disrupted microbiota, such as those with ulcerative colitis (UC)
- However, large-scale clinical trials have demonstrated that FMT is only effective in a subset of patients, limiting the utility of treatment
- FMT relies on healthy donor samples that have poorly defined microbiota compositions, and thus the microbial mechanisms for engraftment and clinical response are poorly understood
- Unmet Need: Identification of specific microbial strains associated with therapeutic benefit in FMT for the treatment of UC and related disorders

Technology Overview

- The Technology: Method for treating UC by administration of immune-reactive microbiota (TIM)
- The inventors analyzed fecal samples from UC patients before and 4 weeks post-FMT
- Single cell sorting was used to culture individual IgAcoated bacteria that were then identified by 16S rDNA gene sequencing
- Analysis of the sequencing data revealed a core TIM that correlated with clinical response
- PoC Data: Colonization of germ-free mice with the core TIM strains Odoribacter splanchnicus and Alistipes finegoldi reduced the severity of T cell colitis through an IL-10-dependent mechanism
- The identified microbial compositions may lead to improved treatment of UC and other disorders associated with imbalanced gut microbiota

Inventors:

Randy Longman Lasha Gogokhia Svetlana Lima

Patents:

US Application Filed

Publications:

Lima et al. Gastro. 2022. Lima et al. Gastro. 2020. Gogokhia et al. Gastro. 2019.

Biz Dev Contact:

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Technology Applications

- Efficient and efficacious method of microbial transfer to treat UC and related disorders
- Screening tool for therapeutically active microbial communities

Technology Advantages

- Defined microbial composition improves control and reproducibility compared to FMT therapy
- IgA-reactive strains protect against colitis via a defined IL-10-dependent mechanism

Supporting Data / Figures A Mono-colonization of GF C57BL/6 WT P Rag2-/DD D20 GF Odoribacter Alistipes Foxp3 P value < 0.0001 B Page 32 Antibiotics P P value < 0.0001 Foxp3 P value < 0.0001 B Page 32 Antibiotics P P value < 0.0001 B Page 32 Antibiotics P P value < 0.0001 B Page 32 Antibiotics P P value < 0.0001 B Page 32 Antibiotics P P value < 0.0001 B Page 32 Antibiotics P P value < 0.0001 B Page 32 Antibiotics P P value < 0.0001 B Page 32 Antibiotics P P value < 0.0001 B Page 32 Antibiotics P P value < 0.0001 B Page 32 Antibiotics P P value < 0.0001 B Page 32 Antibiotics P P value < 0.0001 B Page 32 Antibiotics P P value < 0.0001 B Page 32 Antibiotics P P value < 0.0001 B Page 32 Antibiotics P P value < 0.0001 B Page 32 Antibiotics P P value < 0.0001 B Page 32 Antibiotics P P value < 0.0001 B Page 32 Antibiotics P P value < 0.0001 B Page 32 Antibiotics P P value < 0.0001 B Page 32 Antibiotics P P value < 0.0001 B Page 32 Antibiotics P P value < 0.0001 B Page 32 Antibiotics P P value < 0.0001 B Page 32 Antibiotics P P value < 0.0001 B Page 32 Antibiotics P P value < 0.0001 B Page 32 Antibiotics P P P value < 0.0001 B Page 32 Antibiotics P P Value < 0.0001 B Page 32 Antibiotics P P Value < 0.0001 B P P Value < 0.0001 B

Figure 1: Germ-free mice were colonized with patient-derived *O. splanchnicus* or *A. finegoldii* isolates. Colonization of germ-free mice induced RORgt+/Foxp3+ iTreg cells and reduced the severity of transfer T cell colitis in Rag-/- mice.

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