Weill Cornell Medicine

Platform for Targeted Genetic Manipulation of Non-Model Gut Microbes

Lead Inventor:

Chun-Jun Guo, Ph.D.

Assistant Professor of Immunology in Medicine,
Weill Cornell Medical College

Business Development Contact:

Brian Kelly   (646) 962-7041

Director, Technology Licensing   bjk44@cornell.edu

Platform for Targeted Genetic Manipulation of Non-Model Gut Microbes

Background & Unmet Need

- Hundreds of microbiota genes are associated with host biology/disease

- However, unraveling the causal contribution of a microbiota gene to host biology remains difficult as many of the genes are encoded by nonmodel gut commensals and are not genetically targetable

- While genetic toolsets are readily available for model bacteria, many nonmodel gut bacteria (e.g., *Lachnospiraceae* and *Prevotella*) are not genome sequenced, and it is unknown how to introduce exogenous DNA or which gene manipulation tool to use

- **Unmet Need:** A generalizable approach to identify gene transfer methodology and build gene manipulation tools for nonmodel microbes in the gut

Technology Overview

- **The Technology:** Genetic manipulation pipeline to identify gene transfer methodology and build a genetic tool for nonmodel human gut commensals

- The pipeline efficiently identified the gene transfer methods for 88 (mostly nonmodel) gut bacterial isolates and built their tool for targeted gene manipulation

- Via a multifactorial optimization of their conjugation/transformation conditions, gene transfer methods were identified for 38 nonmodel gut *Clostridia,* with genetic tools successfully implemented in 27 of the *Clostridia* strains

- **PoC Data:** Using the platform, the team demonstrated that deletion of a commensal gene for bile acid synthesis (*bai*) in a *Clostridia* commensal uncovered a role for the *bai* gene in mediating colon inflammation and host gut microbiome composition

Inventors:
Chun-Jun Guo

Patents:
PCT Application Filed

Publications:
Jin et al. *Cell.* 2022.

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

Cornell Reference:
D-9388

Weill Cornell Medicine

Platform for Targeted Genetic Manipulation of Non-Model Gut Microbes

Technology Applications

- Enables precise control of microbiome molecular output to interrogate effects on host biology
- Genetic engineering toolkit for therapeutic and synthetic biology applications using nonmodel gut bacteria

Technology Advantages

- Gene manipulation tools were implemented without requiring prior knowledge of genome sequences
- Provides a library of targetable gut isolates and validated genetic tools
- Expands the scope of commensals that may be employed as "live biotherapeutics"
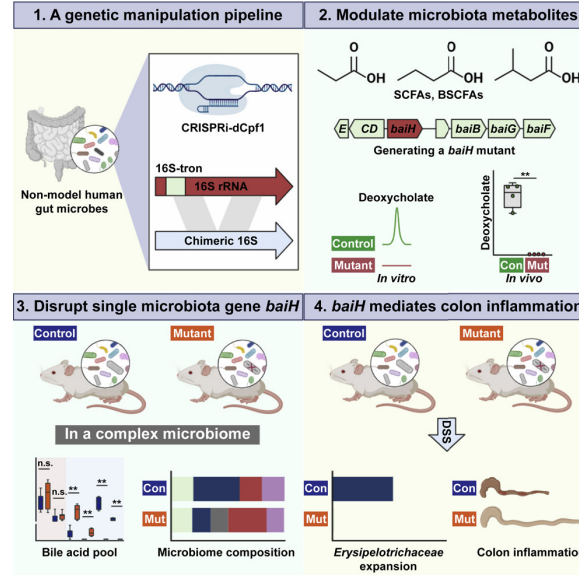
Supporting Data / Figures

Figure 1: Overview of the platform for genetic manipulation for non-model microbes in the gut.

Inventors:
Chun-Jun Guo

Patents:
PCT Application Filed

Publications:
Jin et al. *Cell.* 2022.

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

Cornell Reference:
D-9388

Weill Cornell Medicine