

## Precision Microbiome Modulation: Using discrete fiber structures to precisely modulate gut microbiomes

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December 7<sup>th</sup>, 2020




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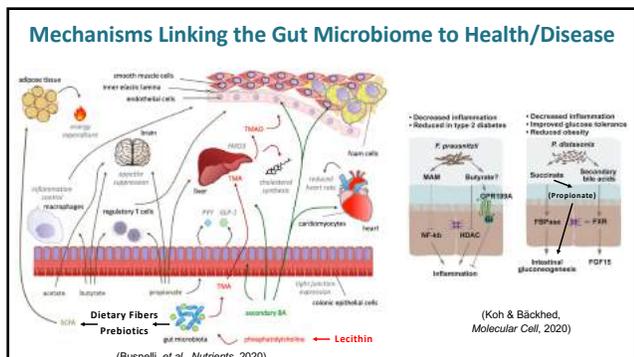
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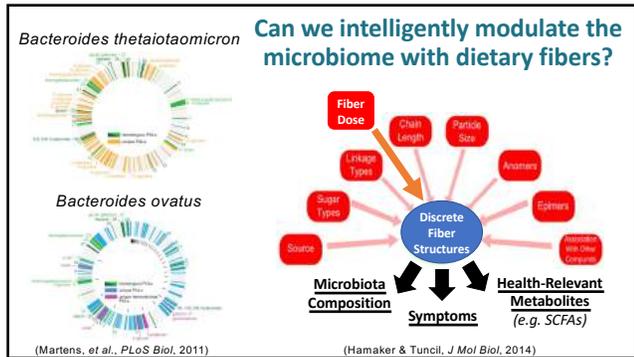
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### Intelligent Modulation may not be Feasible when Considering Ecological Constraints of the Gut Microbiota



Highly evolved ecosystem that is remarkably stable in healthy adults

1. **Inter-individual differences** in what microbes are present and in their response to fiber.
2. **Functional redundancy**: Unrelated species utilize the same substrate or produce the same metabolite.
3. **Phylogenetic niche conservatism may not apply** as strains of the same species can use different substrates.
4. **Fiber degradation** is the result of complex **cross-feeding networks** of primary degraders, secondary fermenters, & metabolite utilizers.
5. **Individualized environmental factors** can influence microbial responses (e.g. pH, inflammation, nutrients).

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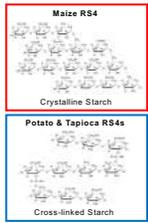
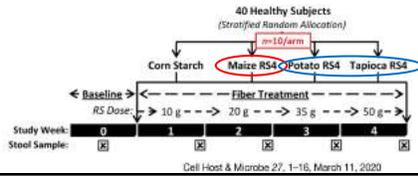
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### RS4 Intervention Study Design



**Important Questions:**

- Can discrete fiber structures obtain predictable changes in microbiota composition and health relevant functions?
- What are the dose-response relationships in these effects?



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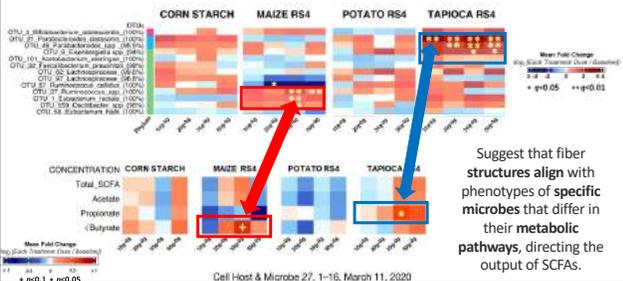
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### RS4-Structure Dependent Effects on Microbiota Composition & Function



Suggest that fiber structures align with phenotypes of specific microbes that differ in their metabolic pathways, directing the output of SCFAs.

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### How do we obtain discrete fiber structures?

- Modify existing carbohydrates/fibers with chemical and enzymatic approaches.
- Develop designer carbohydrates by synthesizing fiber structures that precisely align with the genomes of specific microbes.
- Extract and purify fibers from various agricultural residuals (grains, fruits, vegetables, legumes, fungal, or animal).
  - Up to 40% of our food supply is wasted, with ~30% of it lost during agricultural production (www.fao.org)



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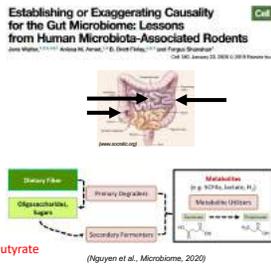
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### Considerations when Identifying Target Microorganisms and Metabolites

- Targeted expansion of a microorganism or production of a metabolite is causally linked health in humans.
- Target location along the GI tract and the magnitude of response required.
  - Jejunum - Distal Ileum - Cecum - Distal Colon
- Consider environmental constraints.
  - Target metabolites and microbes that use public goods released by primary degraders.
  - Crystalline Starch → *Ruminococcus* spp. → *E. rectale* → Butyrate



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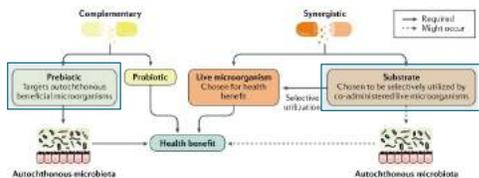
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### Using Discrete Fiber Structures for the Development of Next-Generation Prebiotics & Synergistic Synbiotics

The International Scientific Association for Probiotics and Prebiotics (ISAPP) consensus statement on the definition and scope of synbiotics

Willy E. Burdick<sup>1,2</sup>, Clara F. Gray<sup>3</sup>, Robert A. Hutcheon<sup>4</sup>, Rogan A. Pendergast<sup>5</sup>, Diego Arellano<sup>6</sup>, Brian K. Klotzel<sup>7</sup>, Kevin P. Sandberg<sup>8</sup>, Manuel D. Mendez<sup>9</sup>, Stephen B. Auer<sup>10</sup>, Anshu M. Deshpande<sup>11</sup> and Mary Ellen Sandberg<sup>12</sup>



*Faecalibacterium prausnitzii*; *Eubacterium rectale*; *Clostridium* spp., *Prevotella copri*; *Parabacteroides distans*

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### Conclusions & Implications

- **Discrete fiber structures** offers tremendous potential for the development of **next-generation prebiotics** that precisely target gut microbes in an attempt to promote health and treat disease; providing an approach for both **personalized nutrition** and **precision medicine**.
- **Residual agricultural materials** offer an exciting opportunity for the isolation of discrete fiber structures and development of **novel** and **sustainably-sourced** prebiotics and synbiotics.
- To successfully develop discrete fiber structures, further research is needed to determine *i) what microorganisms and metabolites* to targeted in humans, *ii) where along the GI tract* is the ideal, and *iii) what microbial response magnitude* is required to be efficacious.

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### Acknowledgements

- Jens Walter
- Chen Yang
- Maria Elisa Perez-Muñoz
- Zhengxiao (Terry) Zhang
- Nguyen Nguyen
- Lucila Triador
- Christopher Cheng
- Jeffrey Bakal




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### Questions?

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