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Prebiotics for effective gut microbiota and health outcomes

Thaisa M. Cantu-Jungles, Ph.D. and Bruce R. Hamaker, Ph.D.
Ali Keshavarzian, MD – Rush Medical College, Chicago

Disclosure – RiteCarbs LLC

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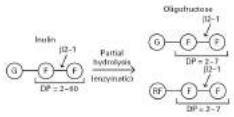
1

Prebiotics – what are they?

- Although not defined as such, prebiotics started as FOS, inulin and GOS
- Now, other fibers are considered "prebiotic", such as resistant maltodextrins and RS, other oligosaccharides (e.g. AXOS, HMOs), pectins



ISAPP - "a substrate that is selectively utilized by host microorganisms conferring a health benefit" (Gibson et al., 2017)

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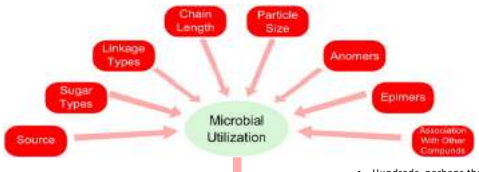
2

2

Dietary fibers : vast array of *discrete structures*



- Hundreds, perhaps thousands, of diverse chemical structures
- Different physical structure types
  - Cell wall matrices
  - Extracellular polysaccharides/biofilms
  - Designed/modified physical structures

(Tuncil & Hamaker, 2014)

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3

3

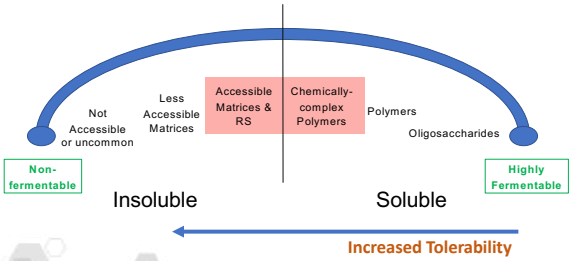
Dietary fiber chemical and physical structure

- Fermentable *vs* non-fermentable
- Soluble *vs* insoluble
- Tolerable *vs* non-tolerable:
  - Fermentability rate

4

4

Fiber Fermentability Spectrum



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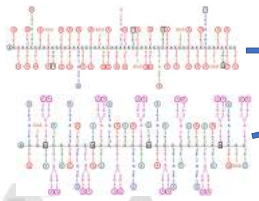
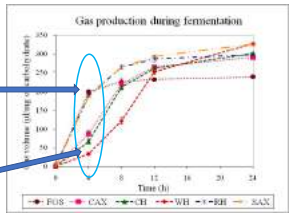
Tolerability

Complex fibers are potentially more tolerable





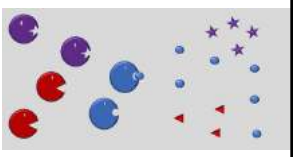
Rumpagaporn et al., *Carb. Polymers* 2015

6

6

Concept: Prebiotic dietary fibers can be aligned to gut bacteria

Fermentable dietary fibers
- Oligosaccharides (FOS, GOS..)
- Soluble fibers (β-glucans, pectins, inulin..)
- Insoluble matrix fibers (arabinoxylans, xyloglucans, fungal β-glucans, cellulose)
- Resistant starches
- Other manufactured fibers (resistant maltodextrins, polydextrose..)



(Tuncil & Hamaker, 2014)

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7

7

Strategies to find alignment of prebiotic fibers to bacteria

Alignment of chemical structures
- Look at the ability that different bacteria have to **degrade** fiber CHOs
  - The genomic presence of Carbohydrate-Active Enzymes, which are specific to the sugar moiety and linkage type in the molecule

Alignment of physical matrix structures
- Look at the machinery that different bacteria have to **access** fiber CHOs
  - Some have to physically bind to substrates (e.g. SUS-like systems, gram (-) bacteria, such as *Bacteroides spp.*)
  - Some have long appendages (cellulosomes) with enzymes attached to "reach in" and get CHOs from insoluble fiber matrices (e.g. Clostridia, such as *Ruminococcus spp.*)
  - Some have ports that directly and efficiently take in oligosaccharides (e.g. *Bifidobacterium spp.*)

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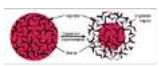
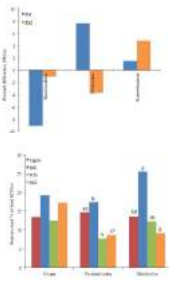
8

8

Aligning physical structure to butyrogenic Firmicutes



- **Mouse study** – 2 types resistant starch - physically accessible (RS2) and inaccessible (starch microspheres, SM)
  - **Phyla shift to Firmicutes**
  - **>2x mol% butyrate for SM group in distal colon**



RESEARCH ARTICLE

Physical Inaccessibility of a Resistant Starch Shifts Mouse Gut Microbiota to Butyrogenic Firmicutes

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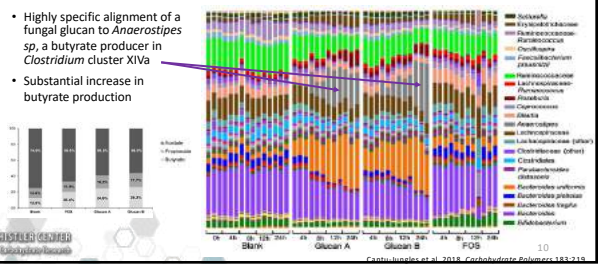
9

9

Insoluble β-glucan aligns to butyrogenic species

- Highly specific alignment of a fungal glucan to *Anaerostipes sp*, a butyrate producer in *Clostridium* cluster XIVa
- Substantial increase in butyrate production



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10

Cantu-Jungles et al. 2019. Carbohydrate Polymers 183:219

10

Fermentable dietary fibers aligned to promote key gut bacteria:

Does it work in everyone?

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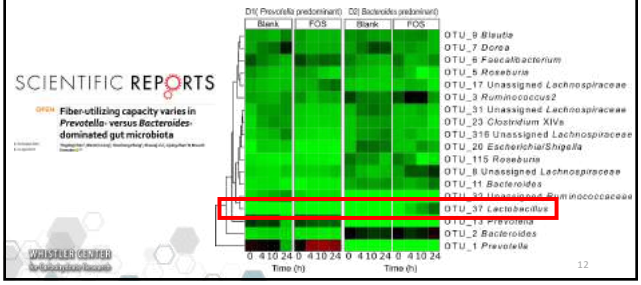
11

11

Usually no! Different gut microbiota communities respond differently to fibers



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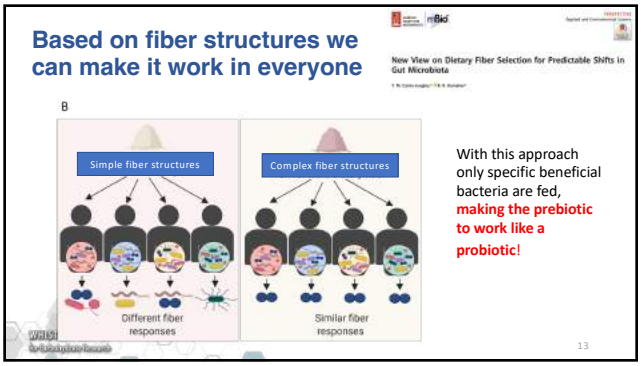
12

12

Based on fiber structures we can make it work in everyone



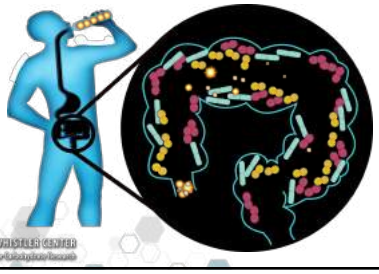
New View on Dietary Fiber Selection for Predictable Shifts in Gut Microbiota

With this approach only specific beneficial bacteria are fed, **making the prebiotic to work like a probiotic**!

13

13

Prebiotics that work like probiotics



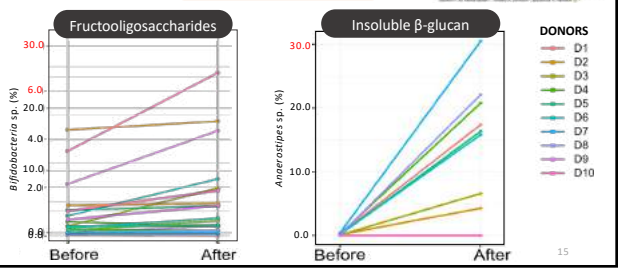
Specifically promote intestinal probiotic bacteria in a targeted way

14

14

Prebiotics that work like probiotics

Robust Responses



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15

Prebiotics that work like probiotics

How is it better than prebiotics?

- Targets specific microbes
- Consistent result in different individuals
- Robust microbiota response

How is it better than probiotics?

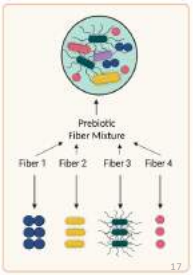
- Increases probiotic bacteria already present in the gut (including those sensitive to oxygen and hard to cultivate)
- Lower manufacturing cost
- Proven safety

16

16

Prebiotic fiber mixtures to promote a balanced gut microbiome and health

- Different bacterial groups in the gut are important to its homeostasis and function
- To support the core microbiome, a better option is mixing fibers that align to important health-related gut bacteria



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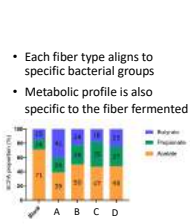
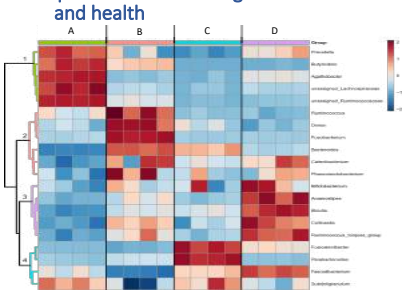
17

Prebiotic fiber mixtures to promote a balanced gut microbiome and health

- Each fiber type aligns to specific bacterial groups
- Metabolic profile is also specific to the fiber fermented

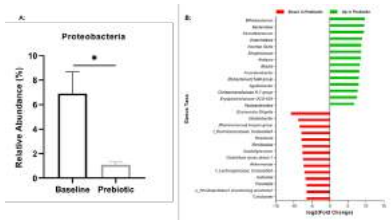




18

18

Clinical study - Prebiotic mixture promotes beneficial microbiota

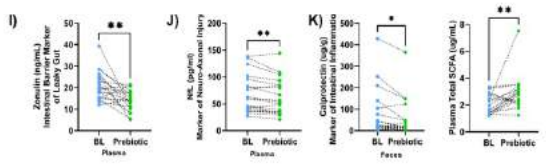


(A) Putative pro-inflammatory phyla Proteobacteria was significantly lower (P = 0.031) in PD Prebiotic treatment, compared to Baseline; mean ± SD. (B) Bar plot showing differentially abundant taxa, where genera taxa are grouped along the y-axis and the x-axis indicates the log2 fold-change following PD Prebiotic treatment. Prebiotic predominately increased short-chain fatty acids (SCFA) taxa (green); decreased certain keystone putative pathogenic PD bacteria (red). N-of-7 PD subjects (before vs. after prebiotic supplementation).

19

19

Clinical study - Prebiotic mixture improved gut permeability and "brain health"



20

20

What does the future hold for dietary fiber prebiotics?

- Complex fibers aligned to bacteria for targeted, predicted, common responses across individuals (**prebiotics that support intestinal probiotics**)
  - From material side, **use of processing techniques to make a new generation of highly specific prebiotics** specially through design/modification of physical structure
- Fibers designed to match and promote ingested probiotics (**synbiotics**)
- More holistic approach that uses a **mixture of fiber prebiotics aligned to different health-related microbial groups** to shape the core community and promote health

21

21

For gut microbiota work, thanks to …

- Purdue
  - Haidi Xu
  - Like Hasek
  - Amandeep Kaur
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  - Nusebye Bulut
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  - John Patterson
  - Cindi Nakatsu
  - Steve Lindenmann
- University of Michigan Medical School
  - Eric Martens
- Rush Medical School
  - Ali Keshavarzian
- Shanghai Jiao Tong University/Rutgers University
  - Liping Zhao

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22

22

Q&A

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23