



Prebiotic mechanisms and immunity

Stephen Fleming

GLOBAL
PREBIOTIC
ASSOCIATION

TRAVERSE
SCIENCE



Definitions

Probiotic

“live microorganisms which when administered in adequate amounts **confer a health benefit on the host**”

Hill *et al.* 2014. *Nat Rev Gastroentero* **11**, 506–514

Prebiotic

“A nutritional product and/or ingredient selectively utilized in the microbiome producing health **benefits.**”

Global Prebiotic Association

Postbiotic

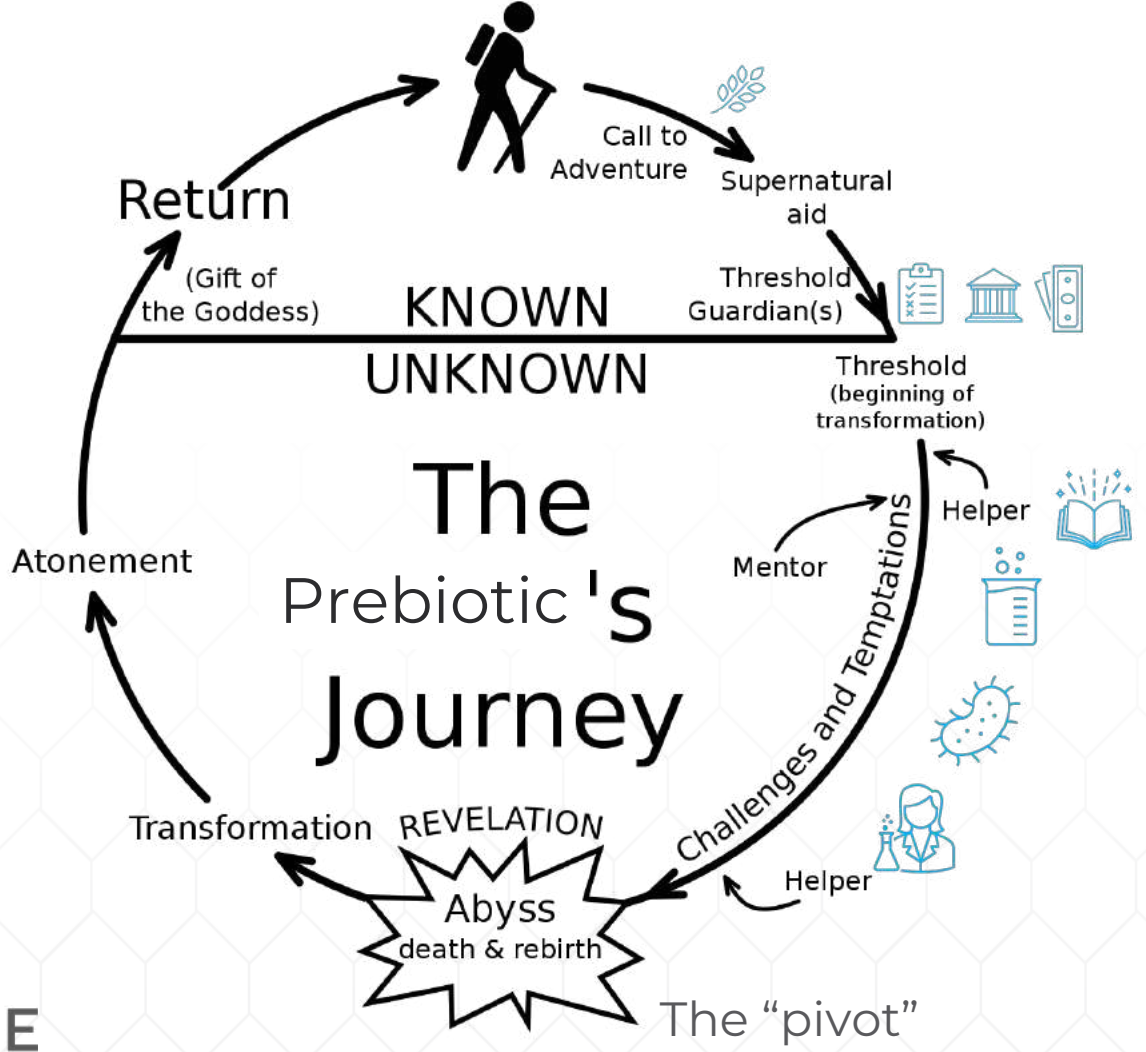
“preparation of inanimate microorganisms and/or their components that **confers a health benefit on the host**”

Salminen, S. *et al* 2021. *Nat Rev Gastroentero* 1–19

Where do mechanisms fit in this?



Both Science and Business are a journey

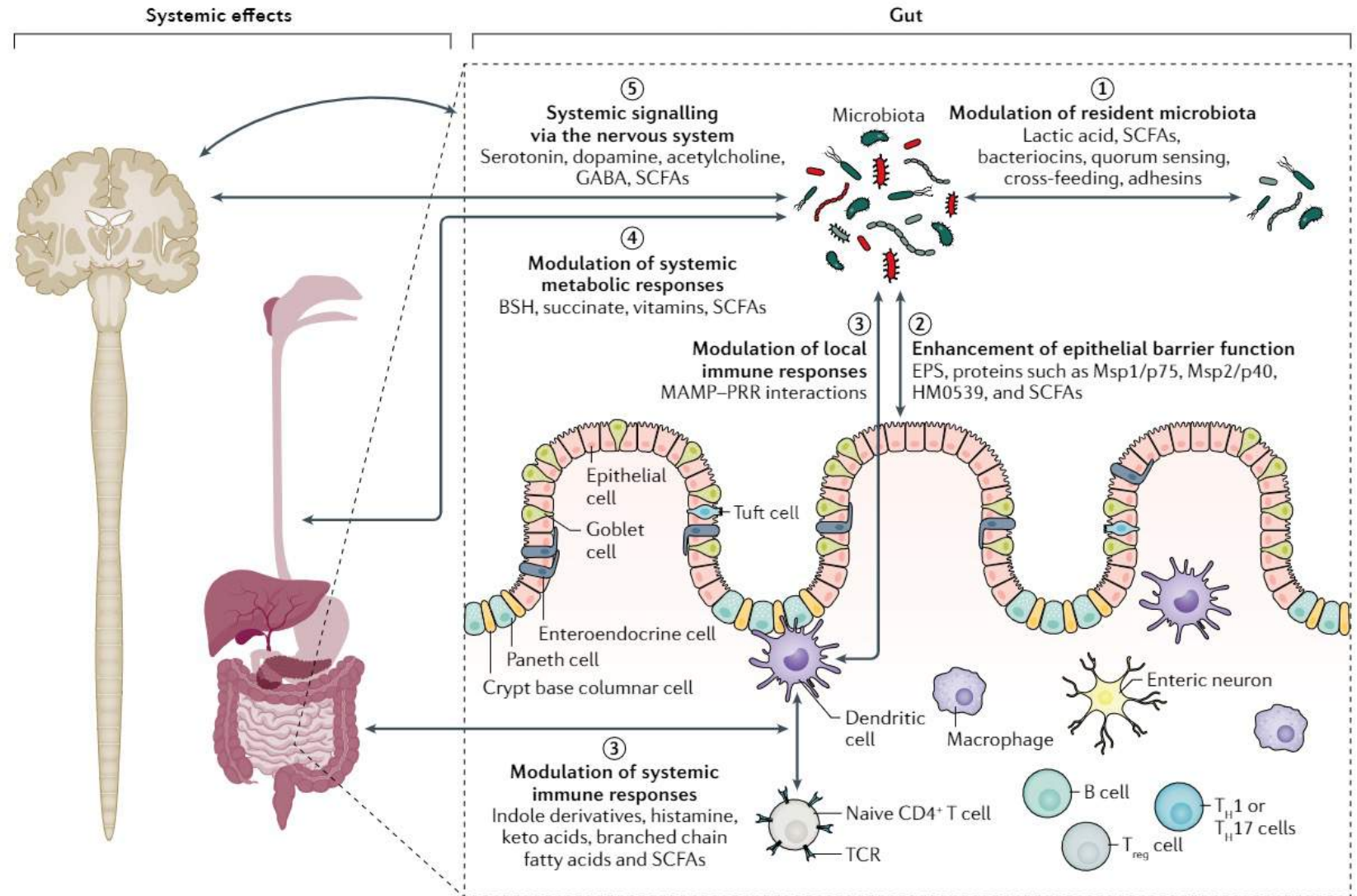


- Mechanisms can...
- Build trust/understanding
 - Drive R&D
 - Help creation of derivatives
 - Expend time/\$
 - Be confusing
 - Raise more ?? than answers



Where are we in the journey?

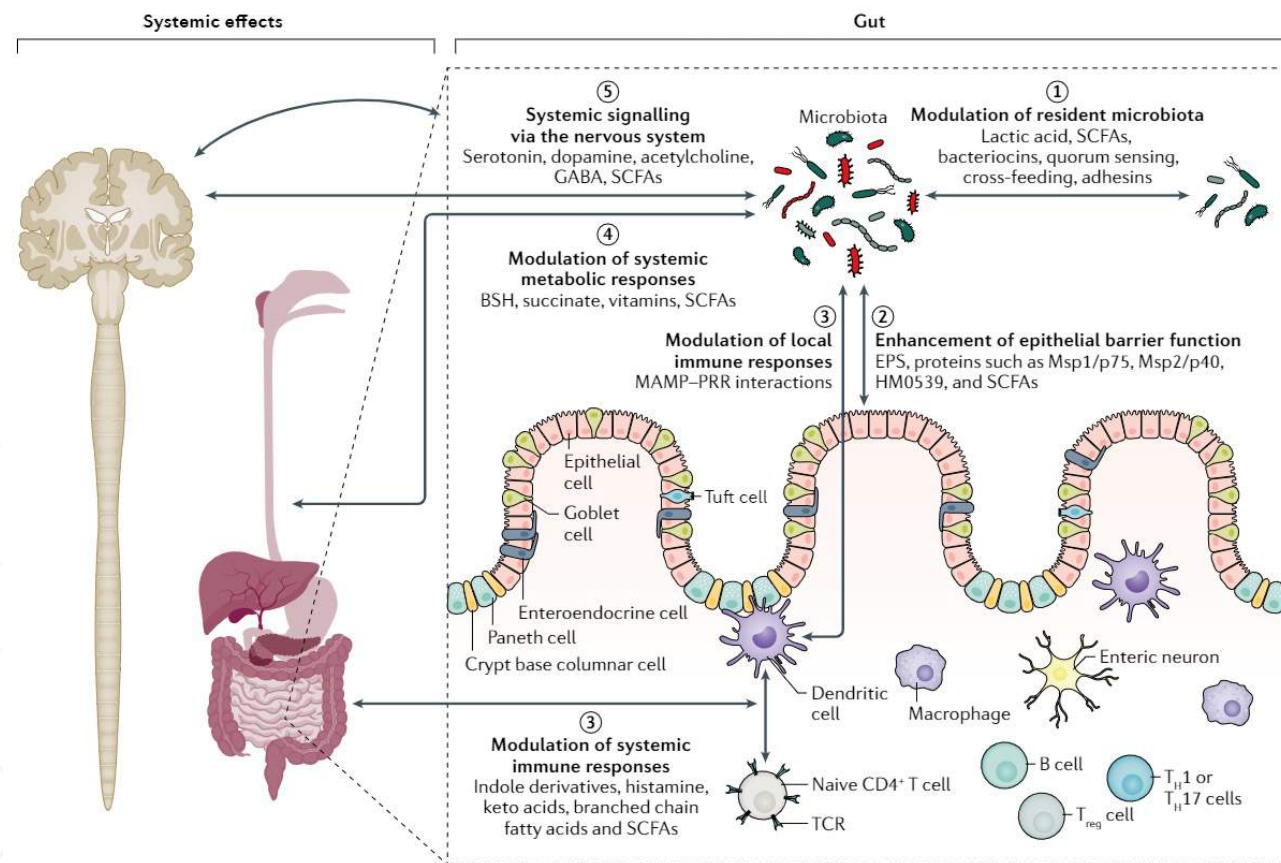
- ...not far
– A lot of opportunity!





Context is key

- *When and where* are biomarkers...biomarkers?
 - Mechanisms are contextual
- Question
 - Is changing the microbiome required to modulate the nervous system?





Article

A Mediation Analysis to Identify Links between Gut Bacteria and Memory in Context of Human Milk Oligosaccharides

Stephen A. Fleming ^{1,*}, Jonas Hauser ², Jian Yan ³, Sharon M. Donovan ^{4,5}, Mei Wang ⁴ and Ryan N. Dilger ^{1,5,6,7}

Take home:
Prebiotics had little impact on relative abundance of genera

Young pigs fed...

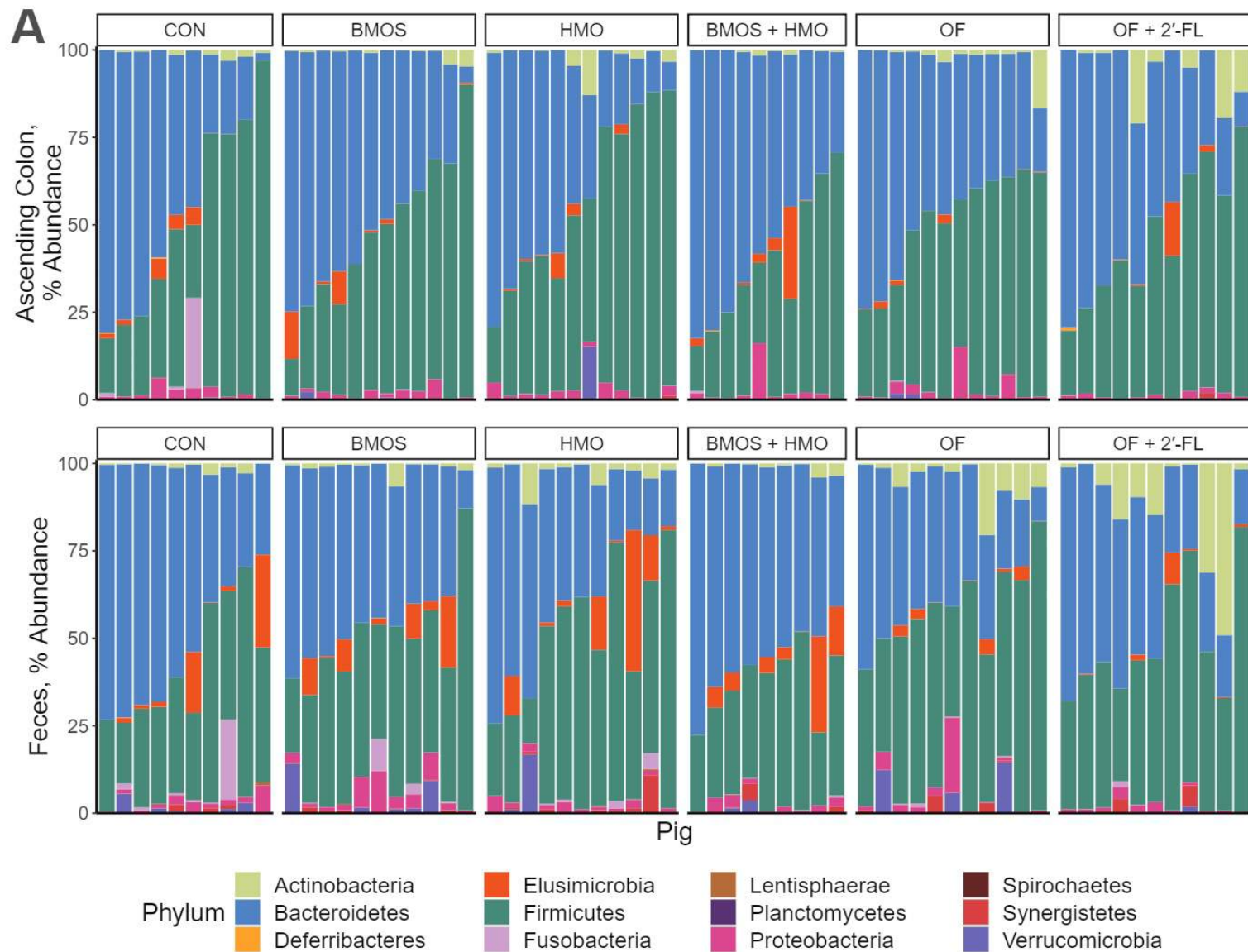
Con: No oligosaccharides

BMOS: Bovine Milk Oligosaccharides

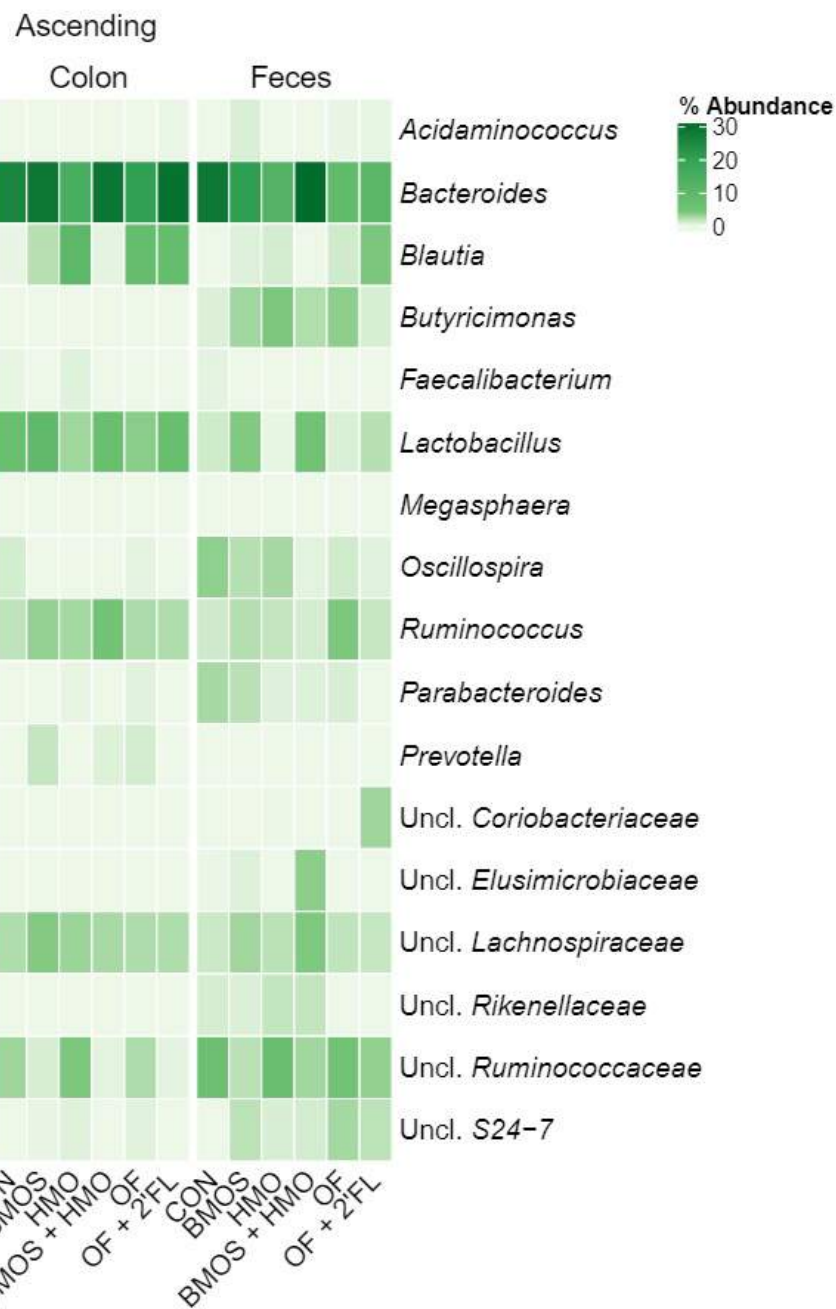
HMO: Human Milk Oligosaccharides

OF: Oligofructose

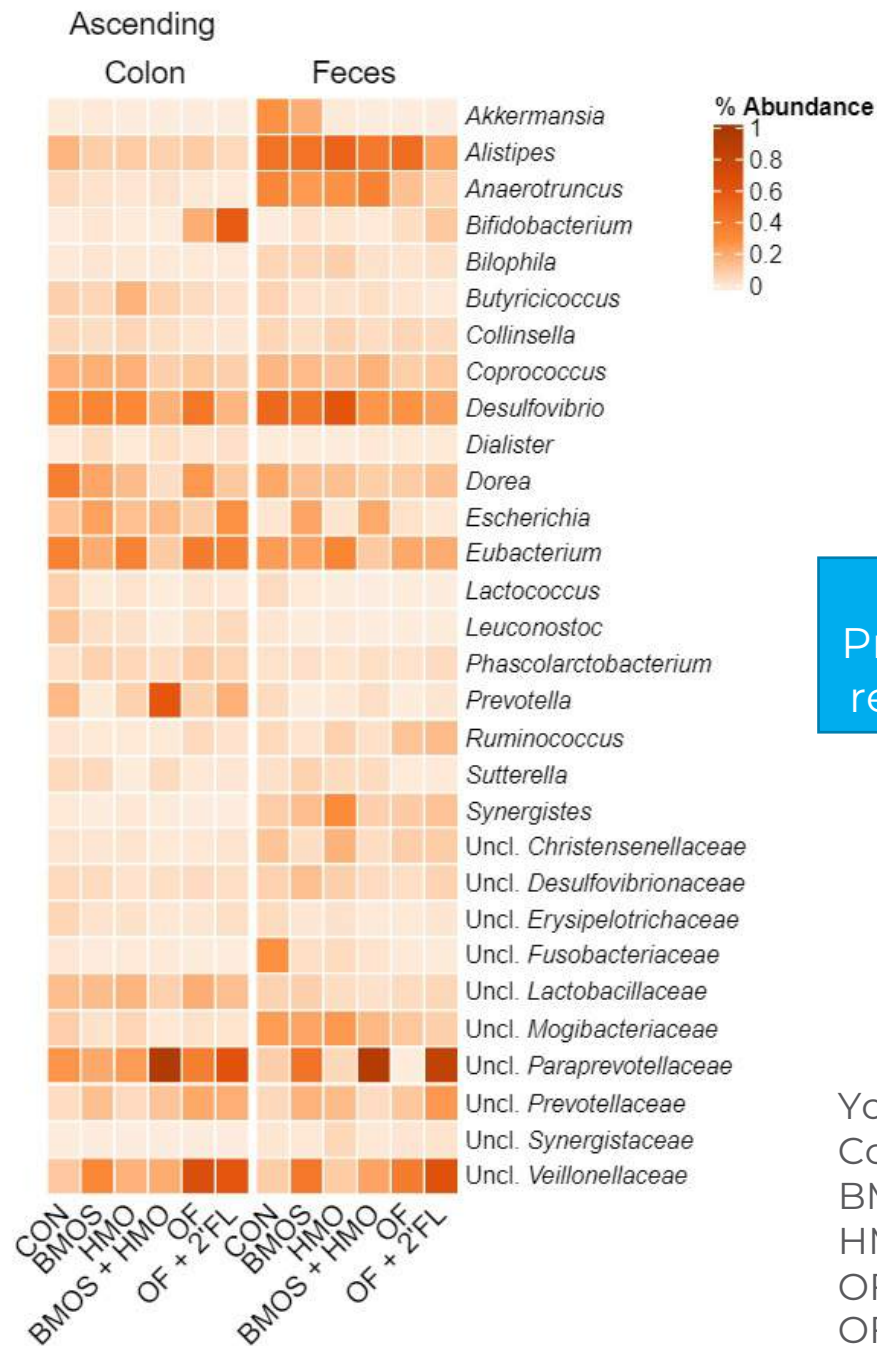
OF + 2'FL: OF + 2'fucosyllactose




Median Relative Abundance of Common Genera, >1%



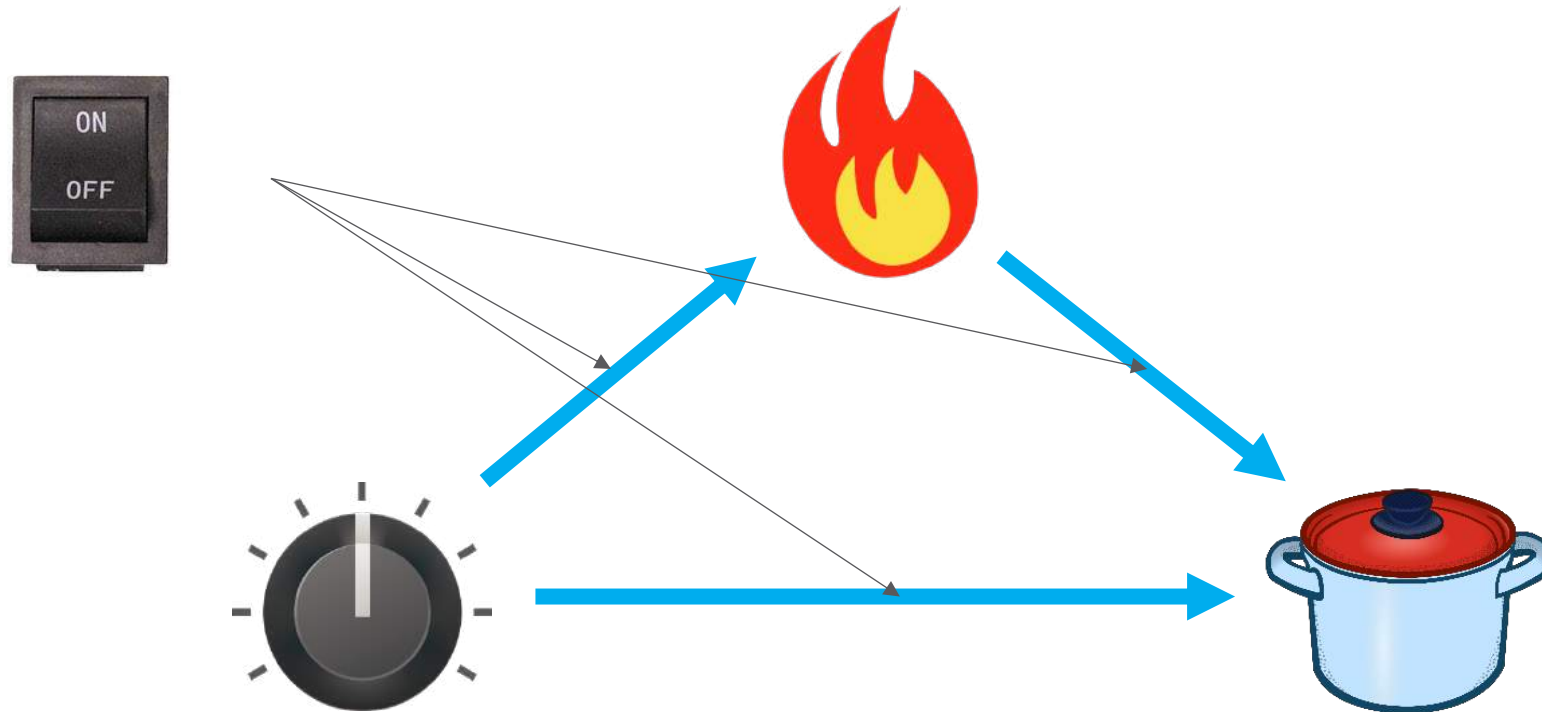
Median Relative Abundance of Uncommon Genera, 0.05–1%



Take home:
Prebiotics had little impact on relative abundance of genera

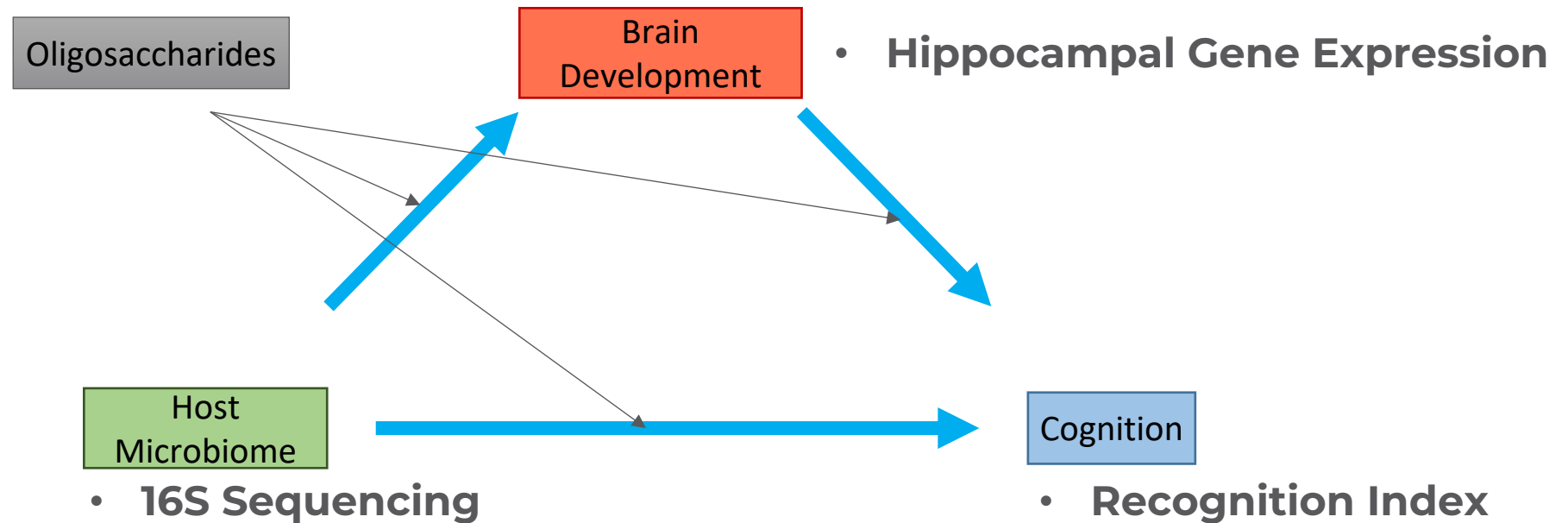
Young pigs fed... 
 Con: No oligosaccharides
 BMOS: Bovine Milk Oligosaccharides
 HMO: Human Milk Oligosaccharides
 OF: Oligofructose
 OF + 2'FL: OF + 2'fucosyllactose

Mediations vs. Moderations



1. The **flame** *mediates* the relationship between the **knob** and **water temperature**
 - Although the knob strongly predicts water temperature, it exerts its effect through its action on the flame
2. The **power** moderates the magnitude of the above relationship
 1. When the power is off, there is zero correlation between above variables

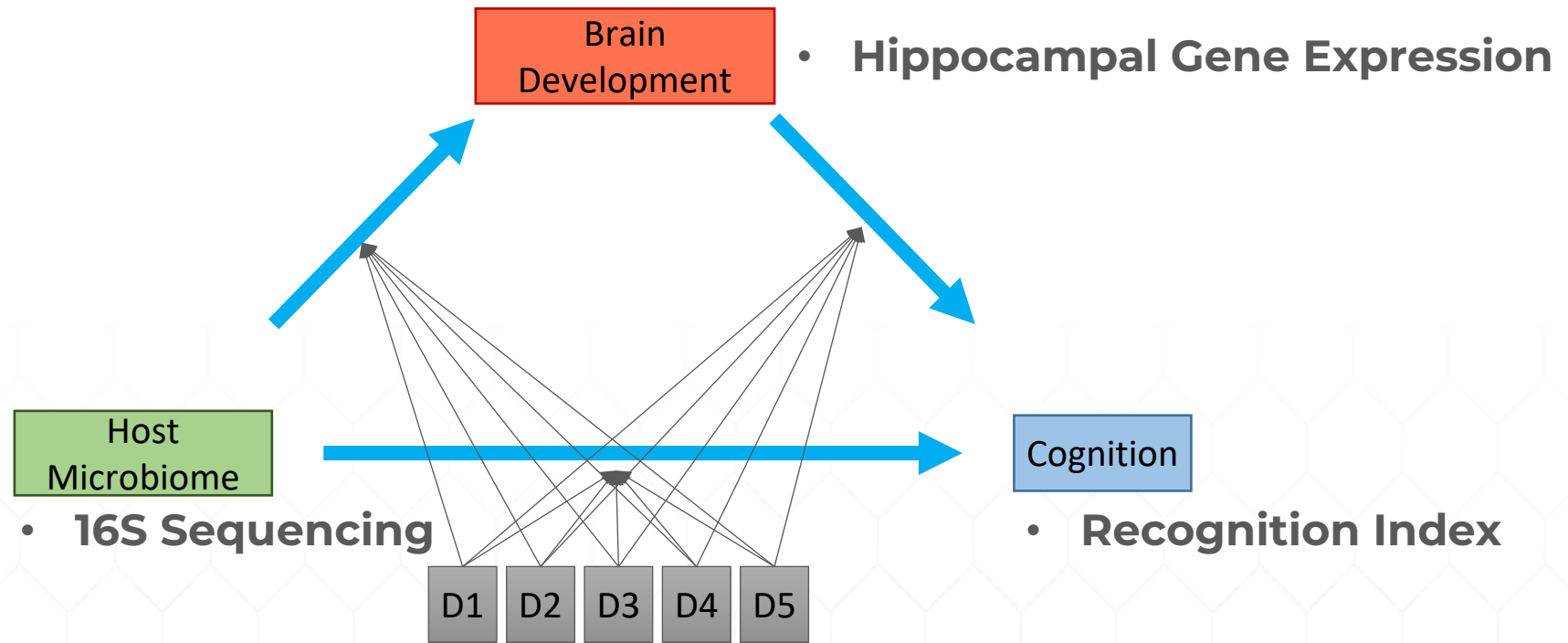
Mediation and Moderation



1. Does **brain development** *mediate* the relationship between **host microbiome** and **cognition**?
2. Do **oligosaccharides** *moderate* the magnitude of the above relationships?



The diet introduces complexity

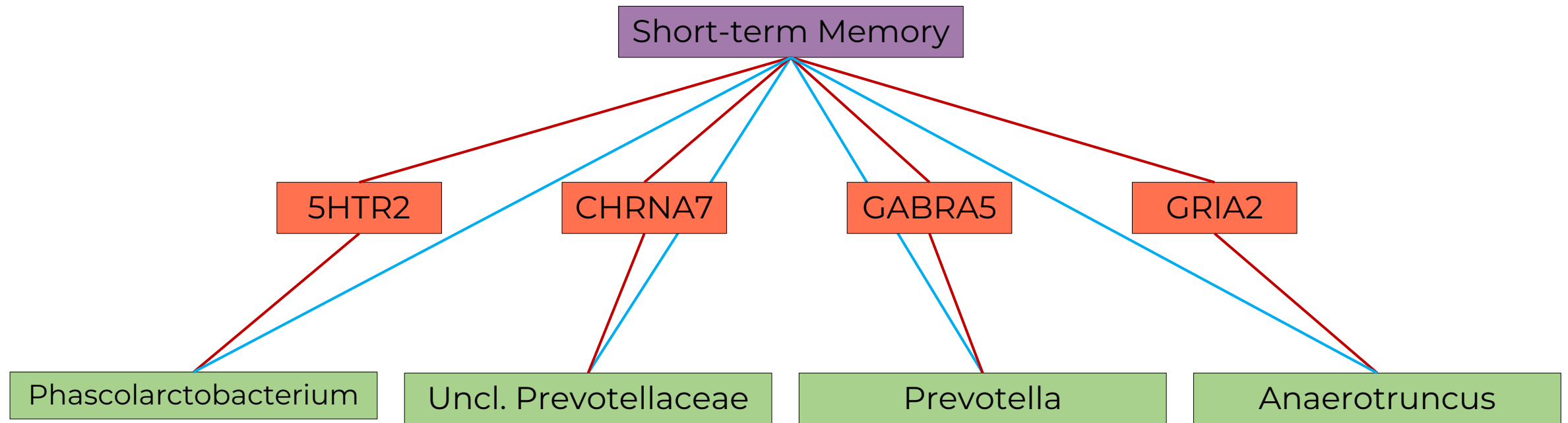


For pigs fed oligofructose and 2'fucosyllactose...

Genera were **negatively** related to gene expression

Gene expression was **negatively** related to short-term memory

Genera were **positively** related to memory



Take-Home

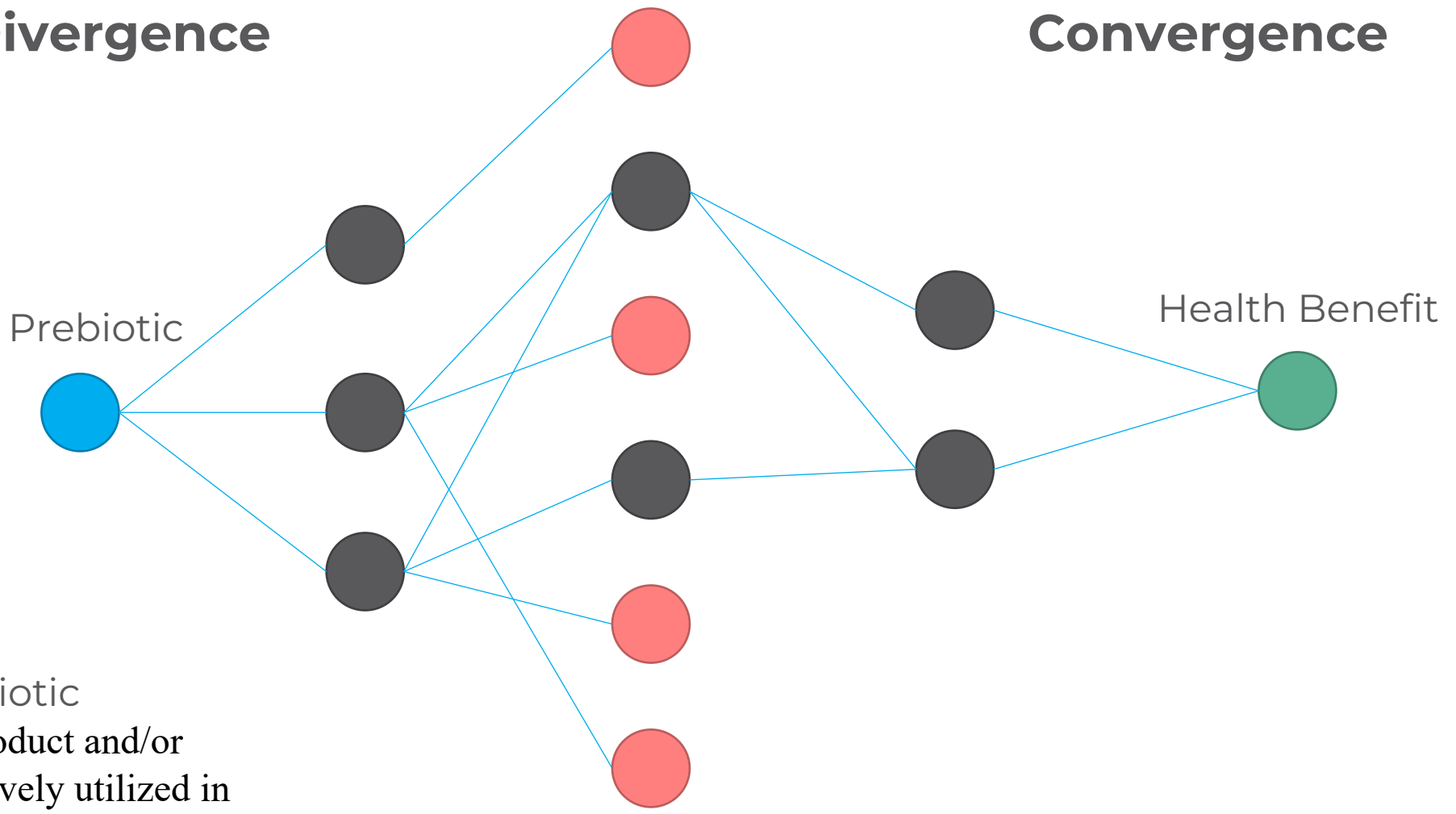
No relationships to **Long**-term memory!
Different genera predicted memory for different diets

— Negative Relationship
— Positive Relationship

Mechanisms

Divergence

Convergence



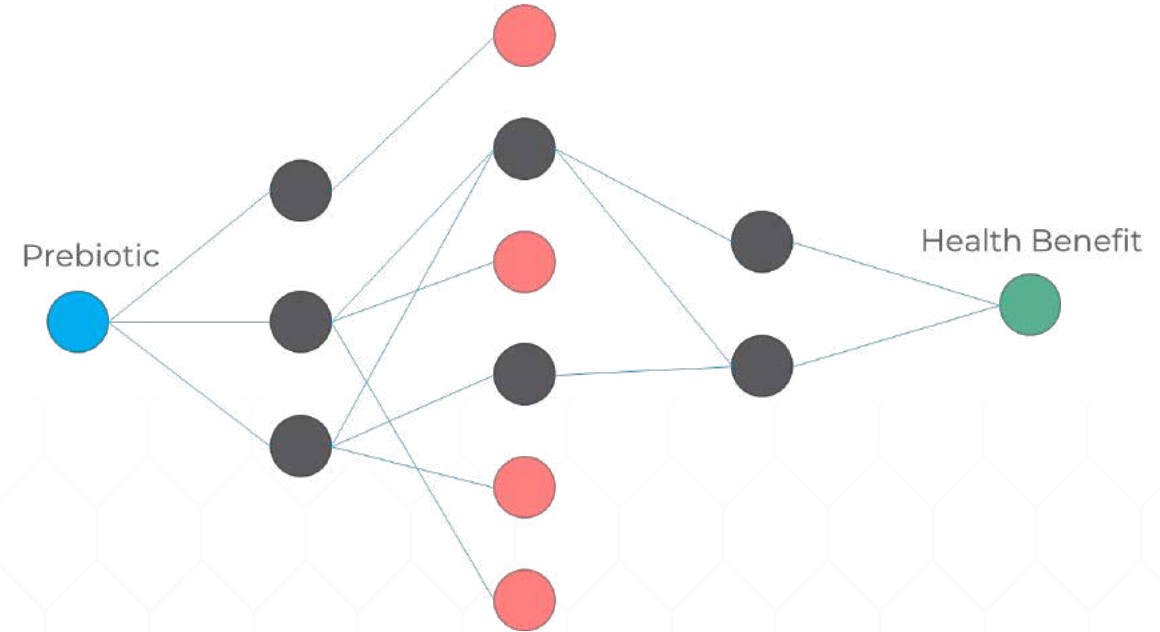
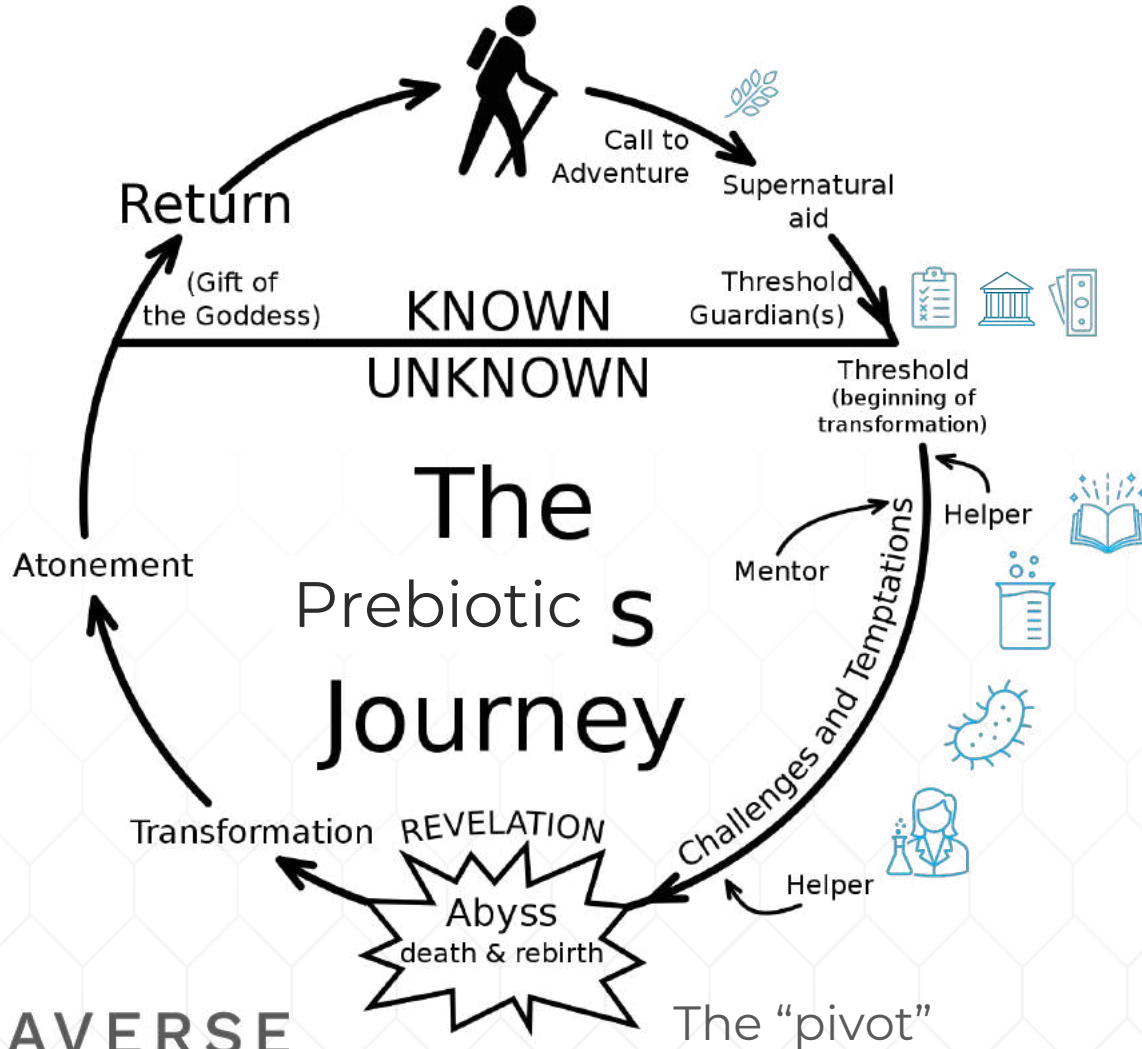
Prebiotic

“A nutritional product and/or ingredient selectively utilized in the microbiome producing health benefits.”

Global Prebiotic Association



Both Science and Business are a journey



Academics:
Middle = opportunity
Ends = boring

Business:
Middle = risk
Ends = reward



**Thank you for
choosing to Traverse
Science with us**



Questions?

engage@traversescience.com