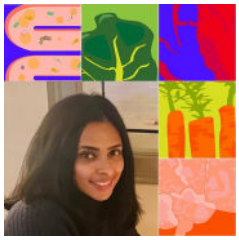
Microbiome, Gut and Systemic Health: New Frontiers in Personalised Nutrition



Dr. Amrita Vijay

The Role of the Gut in Modulating Systemic Inflammation

12:00-12:45pm

An event by: Nutritional Medicine Institute

Platinum sponsors: regenerus labs, VIRIDIAN Effective | Ethical | Pure, pure encapsulations

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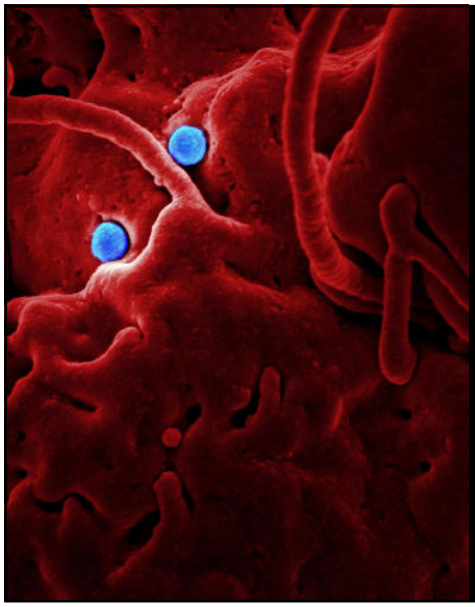

The Role of the Gut Microbiome in Modulating Systemic Inflammation

Dr Amrita Vijay (PhD), Research Fellow
University of Nottingham

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Conflict of interest

No conflict of interest to disclose as part of this presentation

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This presentation will provide an overview of the role the gut microbiome in modulating systemic inflammation

Key topics:

- The role of gut dysbiosis and increased intestinal permeability in chronic low-grade inflammation
- A comparison of dietary interventions targeted towards modulating inflammation via the gut microbiome

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Section 1

Systemic inflammation and the gut microbiome

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Systemic Inflammation

Systemic inflammation occurs when inflammation spreads throughout the body beyond a local site of injury or infection.

This can happen due to a hyperactive immune system or bacteria and toxins entering the bloodstream.

Systemic inflammation leads to widespread tissue damage and NCDs

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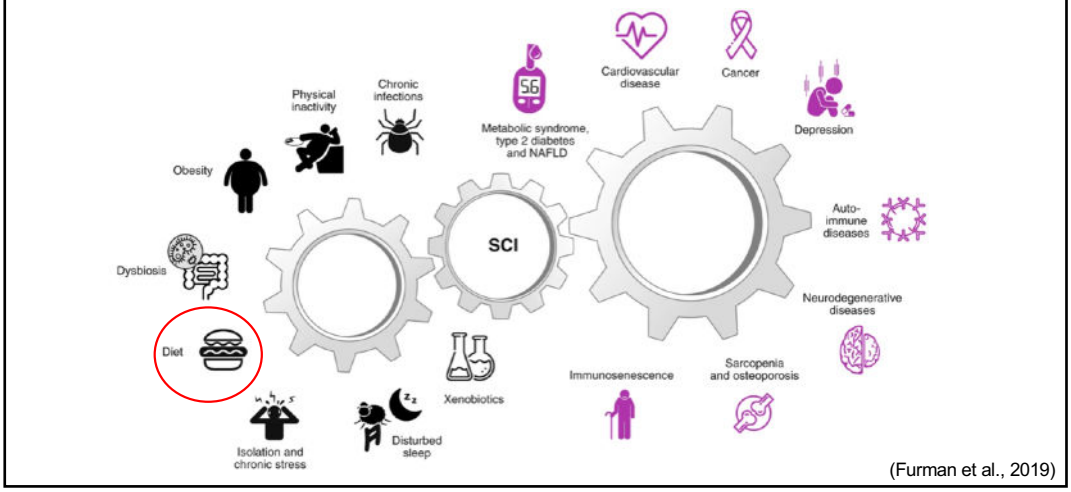
Causes and consequences of systemic chronic inflammation



(Furman et al., 2019)

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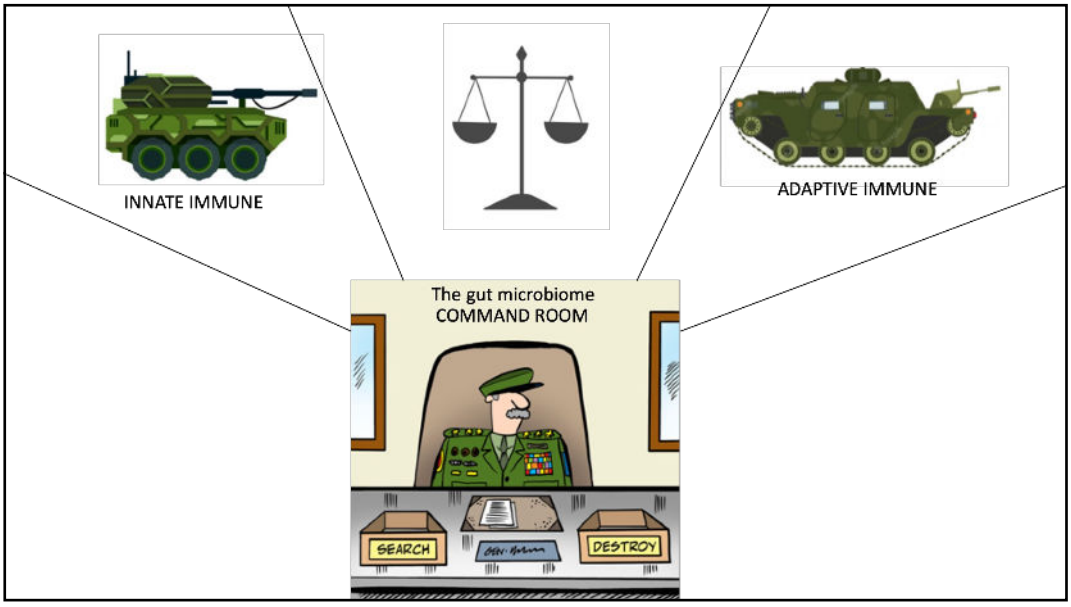

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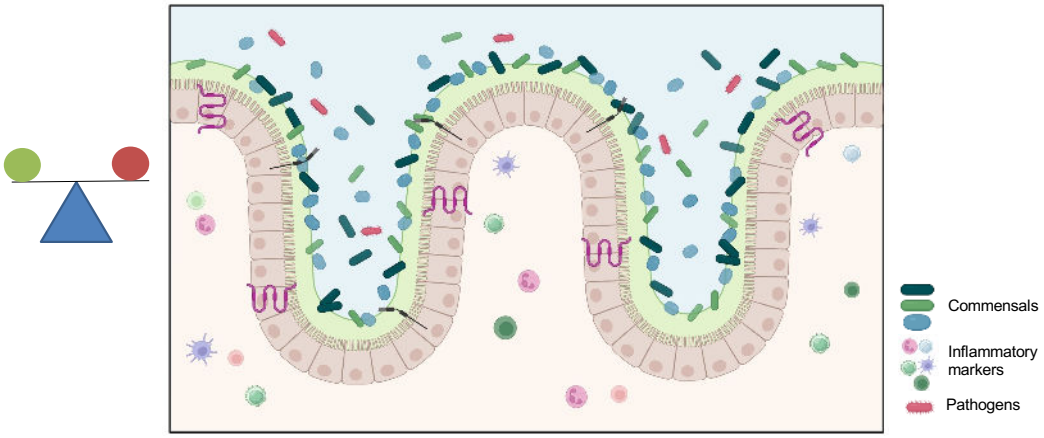
Gut homeostasis

Intact barrier function



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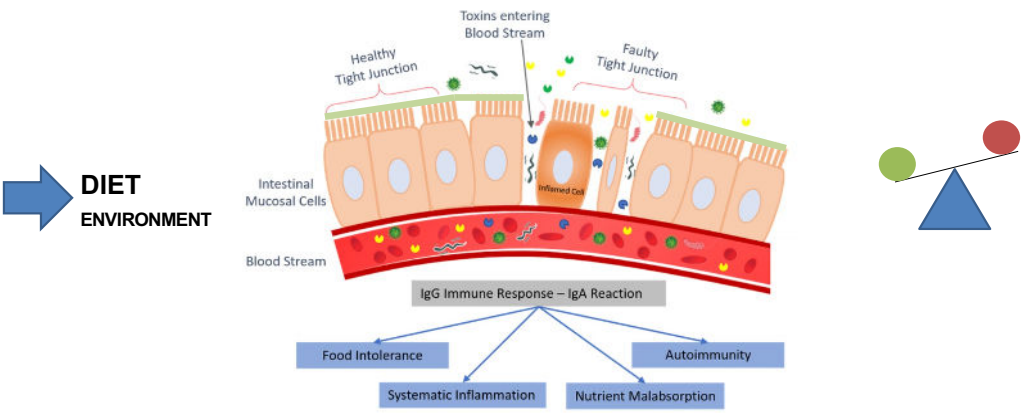
Gut dysbiosis

Compromised barrier function



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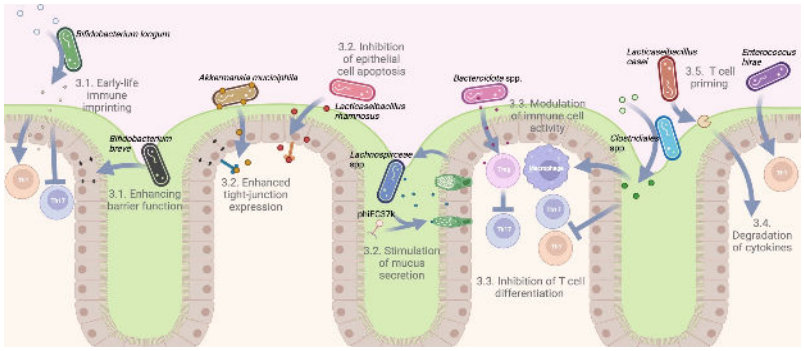
Mechanisms of how microbiome-based interventions can modulate the immune system



Microbes → Immune ← Metabolites

(Hitch et al., 2022)

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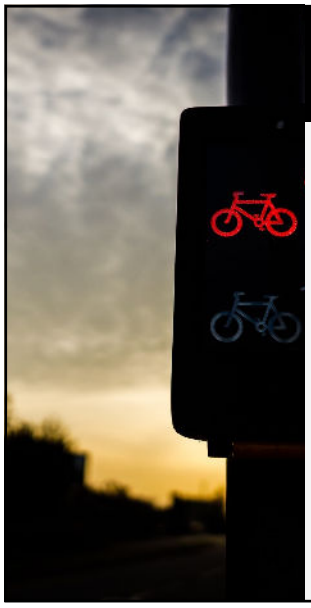

All inflammatory disease begins with the (leaky) gut?

- Limited mechanistic insight to prove that it is the single unifying cause of specific inflammatory diseases
- Limited repeatable and reliable measures of intestinal permeability
- Limited information on measure of who/ what is being translocated through these virtual barriers
- The inflammatory response to the barrier injury is what is important and this can vary from person to person

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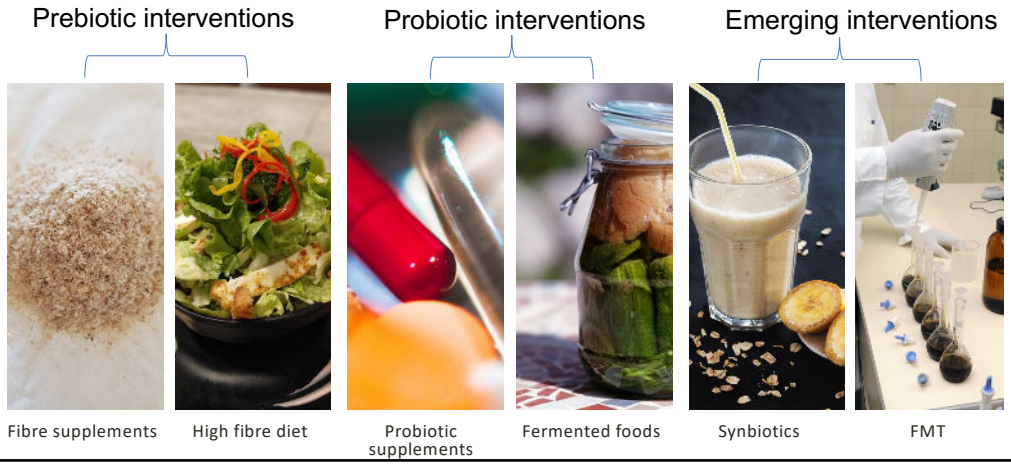
Common microbiome-based intervention methods targeting inflammation



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Section 2

High fibre diet versus fibre supplements

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Effect of a High-Fiber Diet vs a Fiber-Supplemented Diet on inflammatory markers

VS

psyllium

25-30g/ day for 3 weeks

Inflammatory markers

What was found:

- *Overall decrease in CRP in both groups with no difference between groups*
- *Fibre supplement group showed a greater reduction*
- *The CRP levels changed to a greater percentage in lean participants than in obese participants*
- *The reduction in CRP levels occurred regardless of fibre source (diet or supplement)*
- *Effect however influenced by individual characteristics*

(King et al., 2007)

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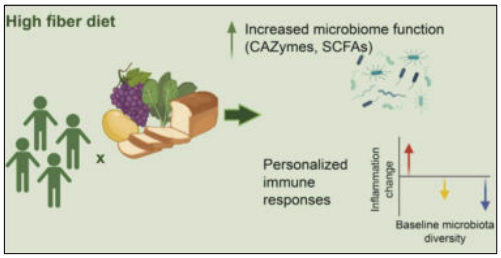
High fibre diet changes microbiome function and elicits personalised immune responses

- Increased fibre intake by 20g/day by incorporating fibre rich foods for 6 weeks
- Detailed instructions were provided to encourage participants to include a variety of fibre sources



What was found:

- *No significant changes in microbiome composition & stool SCFAs*
- *Shifts in functional attributes such carbohydrate-processing capacity*
- *Immune changes were divergent and based on baseline inflammatory status of the individual*
- *Trend towards higher microbiome diversity in the low inflammation group compared to high inflammation group*

(Wastyk et al., 2021)

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The effect of single source fibre supplementation on gut microbiome and inflammatory profiles

6-week dietary intervention of 20g inulin supplementation → 34 healthy individuals consuming <10g of fibre/ day → Changes in gut microbiome and inflammatory profiles

(Vijay et al., 2021)

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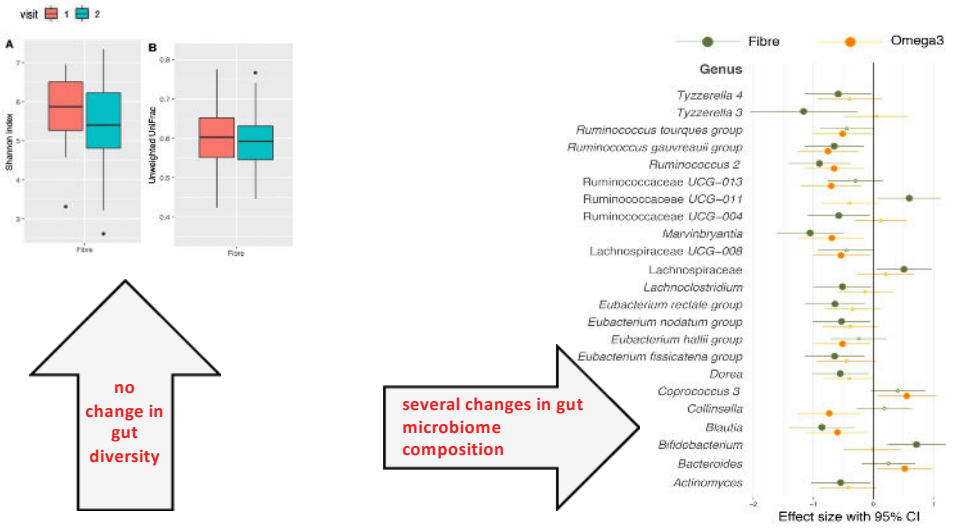

(Vijay et al., 2021)

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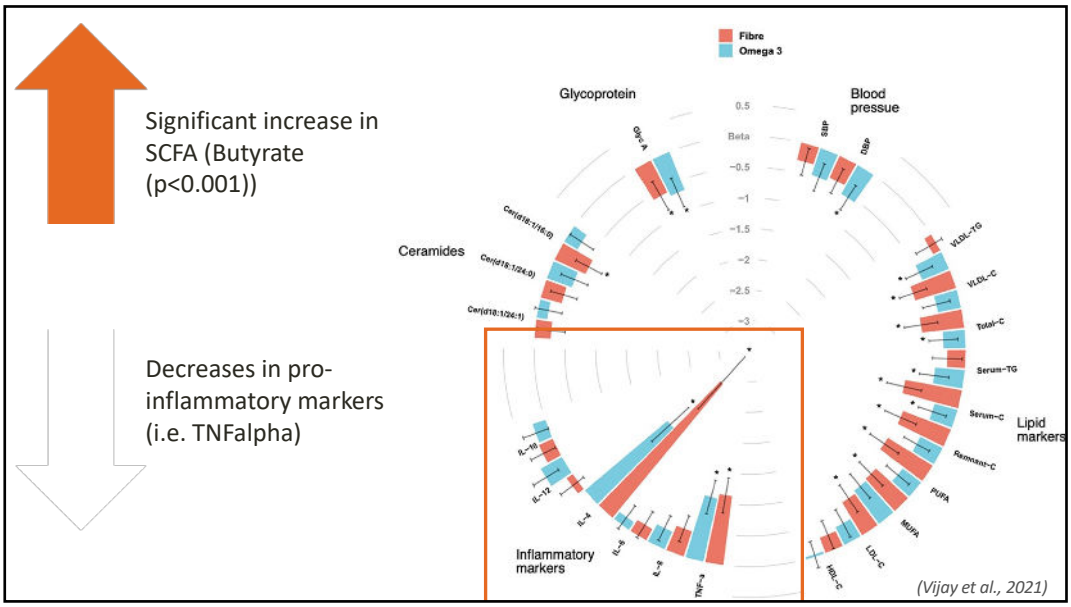
Significant increase in SCFA (Butyrate (p<0.001))
Decreases in pro-inflammatory markers (i.e. TNFalpha)
Fibre
Omega 3
Glycoprotein
Blood pressue
Ceramides
Lipid markers
Inflammatory markers
(Vijay et al., 2021)

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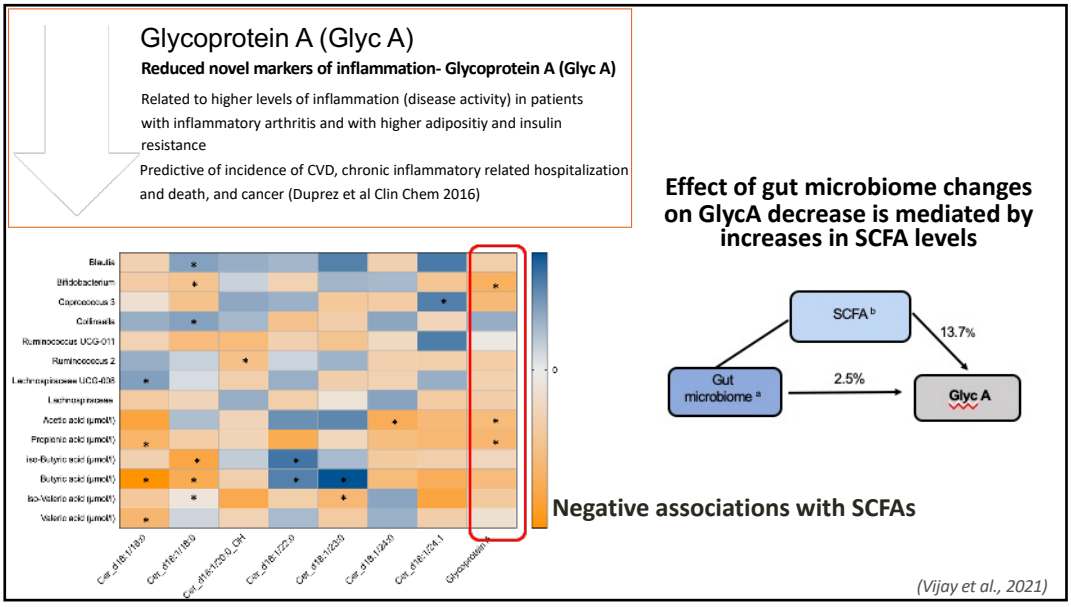
Glycoprotein A (Glyc A)
Reduced novel markers of inflammation- Glycoprotein A (Glyc A)
Related to higher levels of inflammation (disease activity) in patients with inflammatory arthritis and with higher adipositiy and insulin resistance
Predictive of incidence of CVD, chronic inflammatory related hospitalization and death, and cancer (Duprez et al Clin Chem 2016)
Effect of gut microbiome changes on GlycA decrease is mediated by increases in SCFA levels
SCFA b
13.7%
Gut microbiome a
2.5%
Glyc A
Negative associations with SCFAs
(Vijay et al., 2021)

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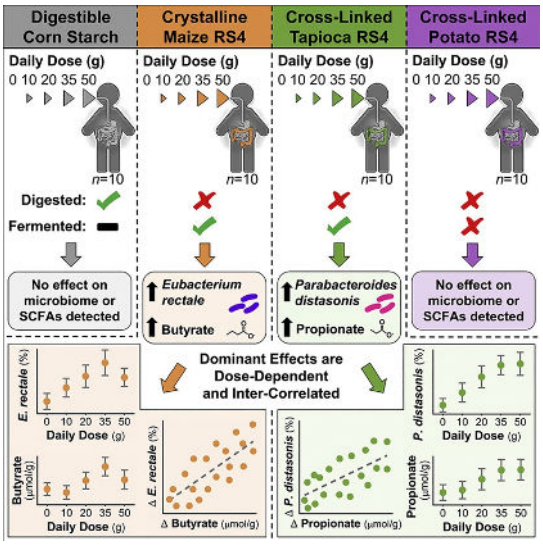
Modulation of the gut microbiome is dependent on the structure and source of dietary fibres



(Deehan et al., 2021)

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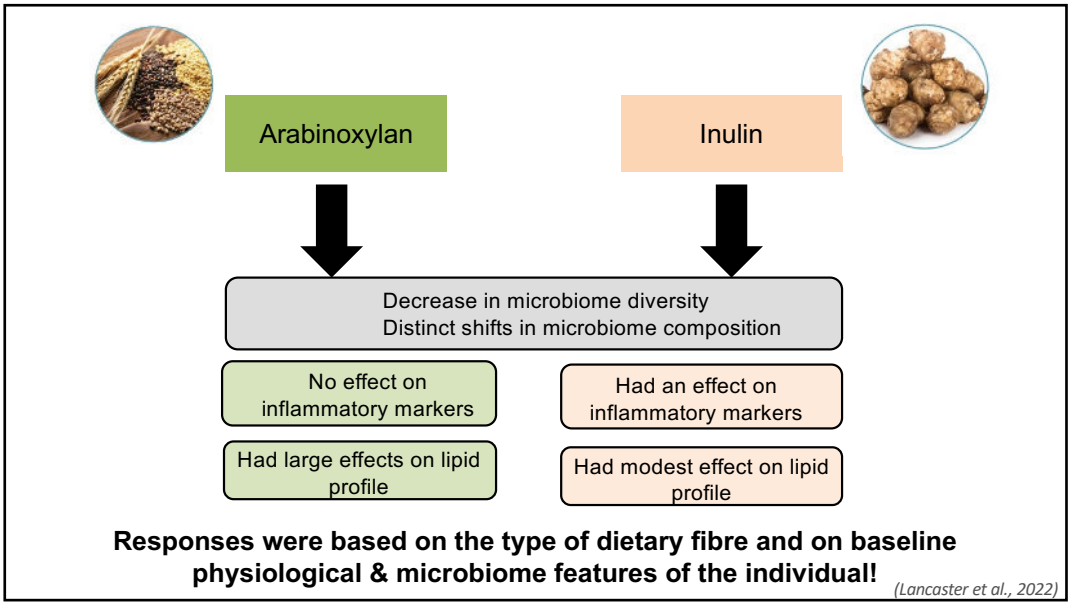

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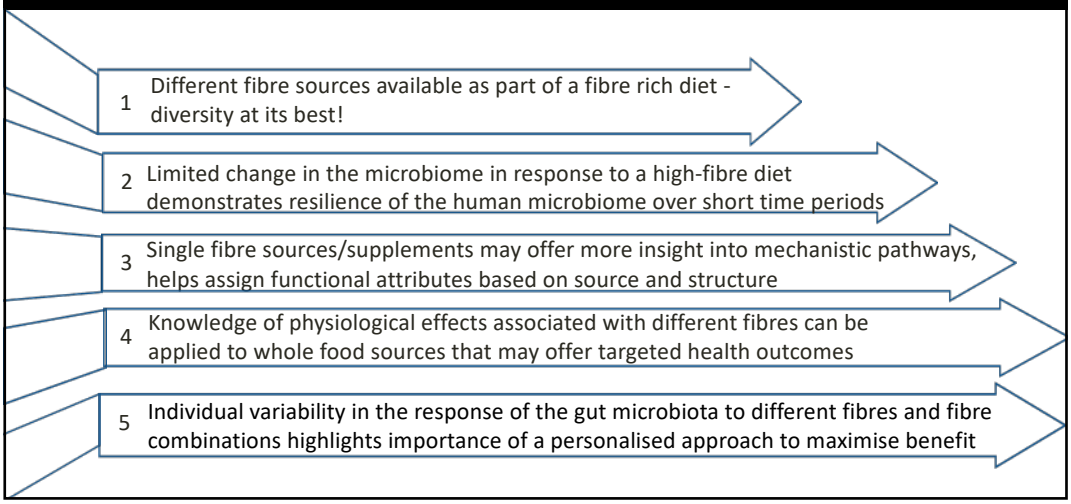
Key takeaways



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Section 3

Fermented foods versus probiotic supplements

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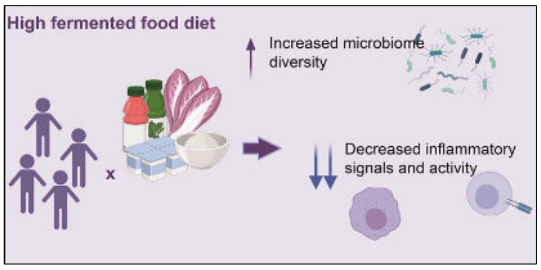
Fermented food diet increases microbiome diversity and decreases markers of inflammation

Consumed 6 servings a day of fermented foods/day (Kombucha, yogurt, kefir, kimchi, sauerkraut, veg brine drink) for 6 weeks



What was found:

- *Increased microbiota diversity and altered functionality (SFCA)*
- *Decrease in markers of host inflammation*
- *19 of 93 cytokines, chemokines, and other inflammatory serum proteins decreased*
- *The magnitude of these changes was not significantly different between "high" and "low" fermented food consumers*
- *Significant correlations between immune changes and SCFAs*

(Wastyk et al., 2021)

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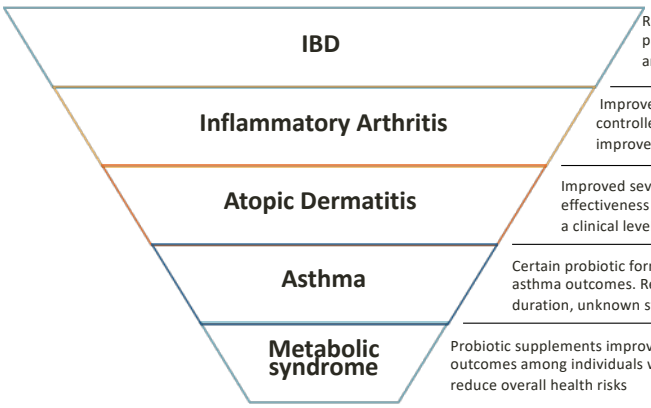
Effectiveness of probiotic supplementation

Meta-analysis of RCTs on inflammatory diseases



Reduced the inflammatory potential of the gut in patients with mild-moderately active ulcerative colitis and patients already in remission
Plaza-Díaz et al., 2017

Improved symptoms of pain in patients. More randomized controlled trials needed to determine optimal dosing and improve efficacy
Zeng et al., 2022

Improved severity of AD however, strong evidence to support the effectiveness of the administration of probiotic supplements at a clinical level remains elusive
Umborowati et al., 2022

Certain probiotic formulations more effective than others in improving asthma outcomes. Results are conflicting due to discrepancy in dosage, duration, unknown strains used
Ciprandi et al., 2023

Probiotic supplements improved specific anthropometric and biochemical outcomes among individuals with MetS however, not sufficient evidence to reduce overall health risks
Dong et al., 2019

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Different strains present with different functionalities

Based on in vitro & in vivo models

Production of bioactive compounds (SCFAs)

Bifidobacterium longum subsp, infantis 157F, **L. reuteri**, L. pentosus, **L. rhamnosus I**, L. paracasei subsp. paracasei, **L. plantarum**

Maintenance of barrier integrity

L. rhamnosus strain GG, **L plantarum**, Bifidobacterium dentium N8, Lactobacillus strains

Bioconversion of substrates and biodegradation of toxins

Bifidobacterium animalis subsp. lactis HN019, **L. reuteri**, Saccharomyces boulardii and Saccharomyces cerevisiae

Immune modulation/anti-inflammatory potential

L. plantarum, Apilactobacillus kosoi 10HT, A. kunkeei JCM16173T, and A. apinorum JCM30765T

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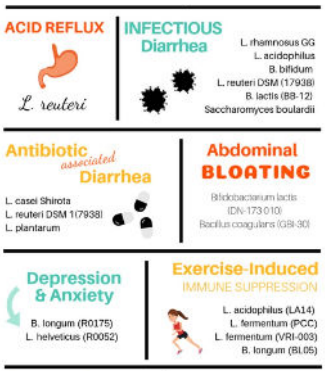
Personalised approaches to improve efficacy



1. STRAIN SPECIFICITY

- Efficacy of probiotics are both strain and disease specific
- Different bacterial strains may have varying effects on specific heath outcomes
- Bacterial strains have distinct functions and mechanisms of action
- Using a personalised approach based on profiles of candidate microbial strains with known mechanisms of action and specific health benefits

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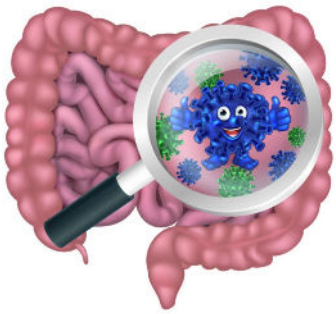
Personalised approaches to improve efficacy



2. BASELINE FEATURES OF HOST MICROBIOME

- Stable engraftment of specific probiotics depend on individualised features of the host gut microbiome
- Example- oral administration of *B.longum* AH1206 persisted in the gut of 30% of individuals for 6 months
- Lower levels of *B.longum in the baseline gut – Darwin's naturalization hypothesis!*
- Indicates the importance of considering baseline microbiome features for precise and personalized microbiome reconstitution

(*Maldonado-Gómez et al., 2016*)

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Key takeaways

1. Both Fermented foods and supplements confer positive effects in modulating inflammatory profiles
2. Fewer studies have directly assessed the role of fermented foods on clinical health outcomes
3. Fermented foods consists of a heterogenous mixture of microbes and other actives offering a synergetic effect over shorter durations
4. Probiotic properties are both strain and disease-specific need for personalisation!
5. Considering the functional capacity of probiotics, a given preparation could not be all-encompassing in a given condition

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Emergence of synbiotic interventions

Products in which the prebiotic compound(s) selectively favour the probiotic organism(s)

- Complementary Synbiotics
- Synergistic Synbiotics
- More than just a commercial formulation
- Effective in disease & healthy states
- Synbiotic effect based on microbial enterotypes

(Kazemi et al.,2020)

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Faecal microbiota transplantation (FMT)

The close evolutionary relationship between our microbiome and the cells of our immune system explained by FMT

- Wider application of FMT on inflammatory diseases
- Most promising treatment for IBS with long term benefit
- FMT combined with an anti-inflammatory diet may improve efficacy
- Success may depend on a 'well-defined donor'

(El-Salhy et al., 2022; Kedia et al., 2022)

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Key takeaways

1. Mechanisms of how FMT works is still underway and long term risks are not yet understood
2. The identification of 'super doners'- currently microbiome signatures have yet to be identified
3. Unlike *C. Diff*, the impact of FMT is less clear in chronic inflammatory disease states, where the cause of the disease hasn't been proven (i.e. bacteria or other factors)

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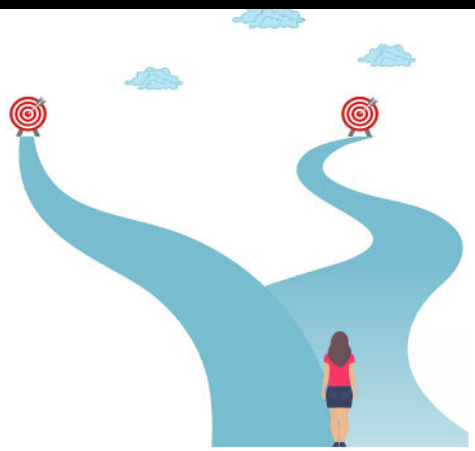
Key considerations for next steps



- Microbiota-targeted diets can change immune status, providing a promising avenue for decreasing inflammation in relation to healthy & disease states
- Precision insight into how one type of dietary intervention may differentially impact individuals, enabling diet to be leveraged in numerous, individual-specific clinical contexts
- Move away from blanket recommendations as the importance of personalisation is becoming more evident in gut microbiome research

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Thank you!

Nutritional Medicine Institute

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UK | CHINA | MALAYSIA

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Dr Afroditi Kouraki
Dr Liz Simpson

CDRF

UKRI Medical Research Council

NIHR | Nottingham Biomedical Research Centre

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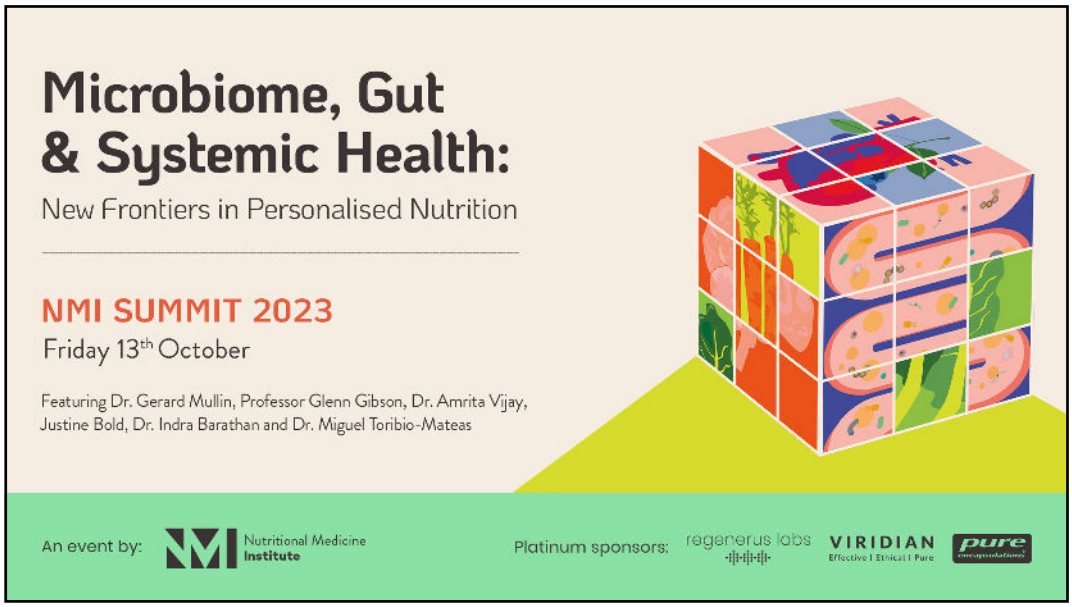
Microbiome, Gut
& Systemic Health:
New Frontiers in Personalised Nutrition
NMI SUMMIT 2023
Friday 13th October
Featuring Dr. Gerard Mullin, Professor Glenn Gibson, Dr. Amrita Vijay,
Justine Bold, Dr. Indra Barathan and Dr. Miguel Toribio-Mateas
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