



Precision Microbiome Strategies: Building Gut Resilience Through Accurate Testing

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Elena Panzeri, MSc Genetics and Nutrition, BSc Nutritional Therapy, Naturopath, PhD student at UCL
(oral-gut-brain axis disorders), Head of Clinical Education at GutID, UK

The Gut Microbiome: A New Frontier in Personalised Medicine.

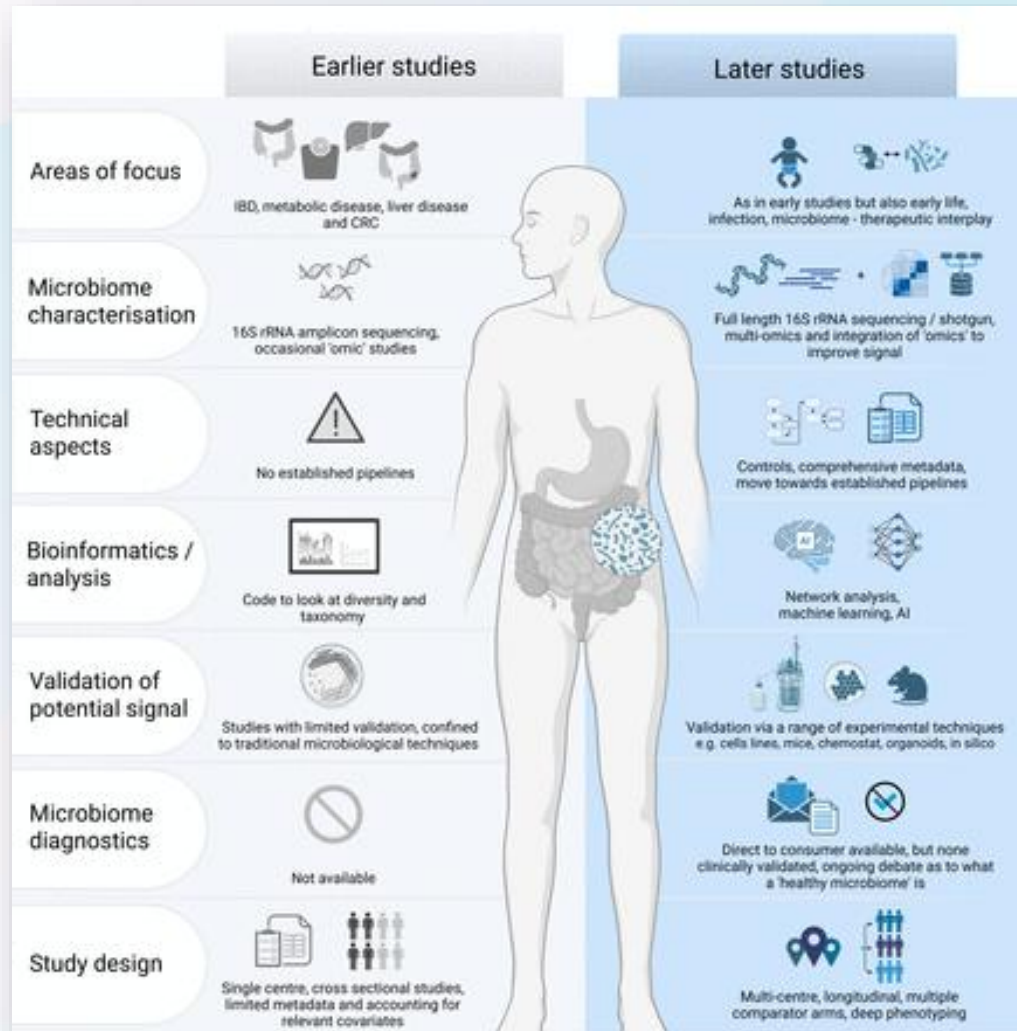


Figure 1-Alexander JL, Mullish BH, Thomas L, *et al*
Recent advances in our understanding of the gut microbiome: an analysis from the Gut Microbiota for Health Expert Panel of the British Society of Gastroenterology

Gut 2026 Jun 2;gutjnl-2026-338252

In just a decade, the microbiome has become one of the most rapidly advancing fields in personalised healthcare.

- Influences **immunity, metabolism, inflammation and gut barrier function**
- Helps explain why **individuals respond differently** to the same intervention
- Links **nutrition, host physiology and health outcomes**
- Provides a potentially **modifiable target** for personalised care

Increasingly recognised as a source of clinically actionable insights!

Few biological systems are simultaneously so influential, so individual, and so modifiable.

How Can the Gut Microbiome Influence Health?

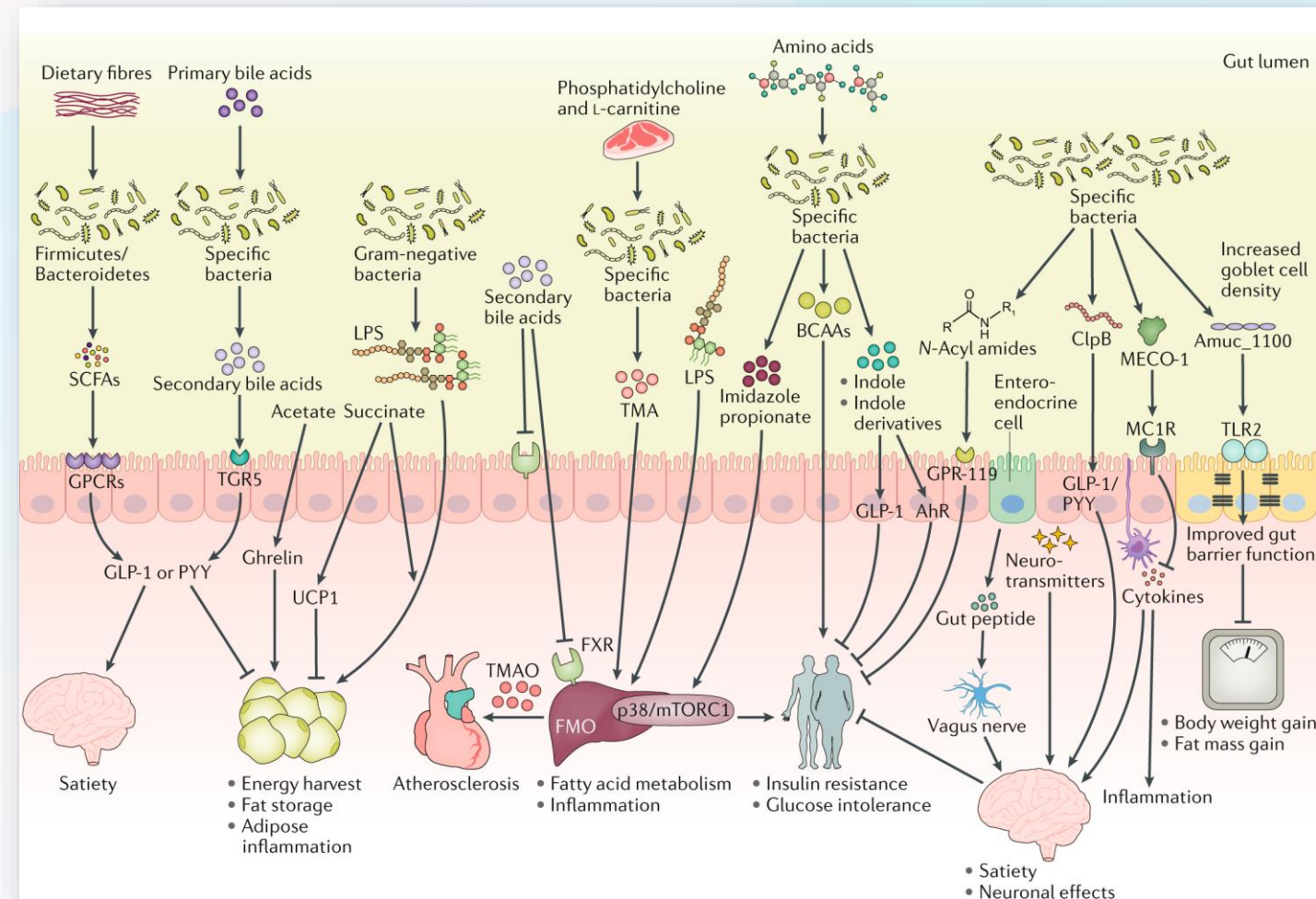


Figure 2- Fan Y, Pedersen O. **Gut microbiota in human metabolic health and disease.** *Nat Rev Microbiol.* 2021 Jan;19(1):55-71

Gut microbes interact with the host primarily through microbial metabolites and signalling molecules.

Health-supporting pathways

SCFAs → energy metabolism, immune regulation, gut barrier integrity

Secondary bile acids → FXR/TGR5 signalling, metabolic homeostasis

Indoles & tryptophan metabolites → AhR activation, mucosal and immune function

Neuroactive compounds → gut–brain communication and neuroendocrine signalling

Potentially adverse pathways

LPS (lipopolysaccharide) → immune activation and inflammatory signalling

TMA → **TMAO** → cardiovascular and metabolic risk pathways

Microbial metabolites provide a mechanistic link between diet, the microbiome, and host physiology.

Why Traditional Microbiome Interpretation Often Falls Short

WHAT WE USED TO THINK

- ❌ Good bacteria = good
- ❌ Bad bacteria = bad
- ❌ More diversity = always better
- ❌ Focus on individual organisms



WHAT WE NOW KNOW

- ✅ Context determines significance 
- ✅ Balance matters more than abundance alone 
- ✅ Function matters more than taxonomy alone 
- ✅ Microorganisms act within an ecosystem 

CLINICAL REALITY



Elevated “beneficial” bacteria may indicate **imbalance**



Low abundance does not always indicate **dysfunction**



The same organism can have different significance in **different ecosystems**



Health depends on the **ecosystem**, not a single player



KEY MESSAGE

Microbial health is determined by **ecosystem balance and function**—not by the presence of individual organisms alone.

From **reductionist interpretation** to **ecosystem-based microbiome assessment**

Gut Resilience: A Key Determinant of Microbiome Health.

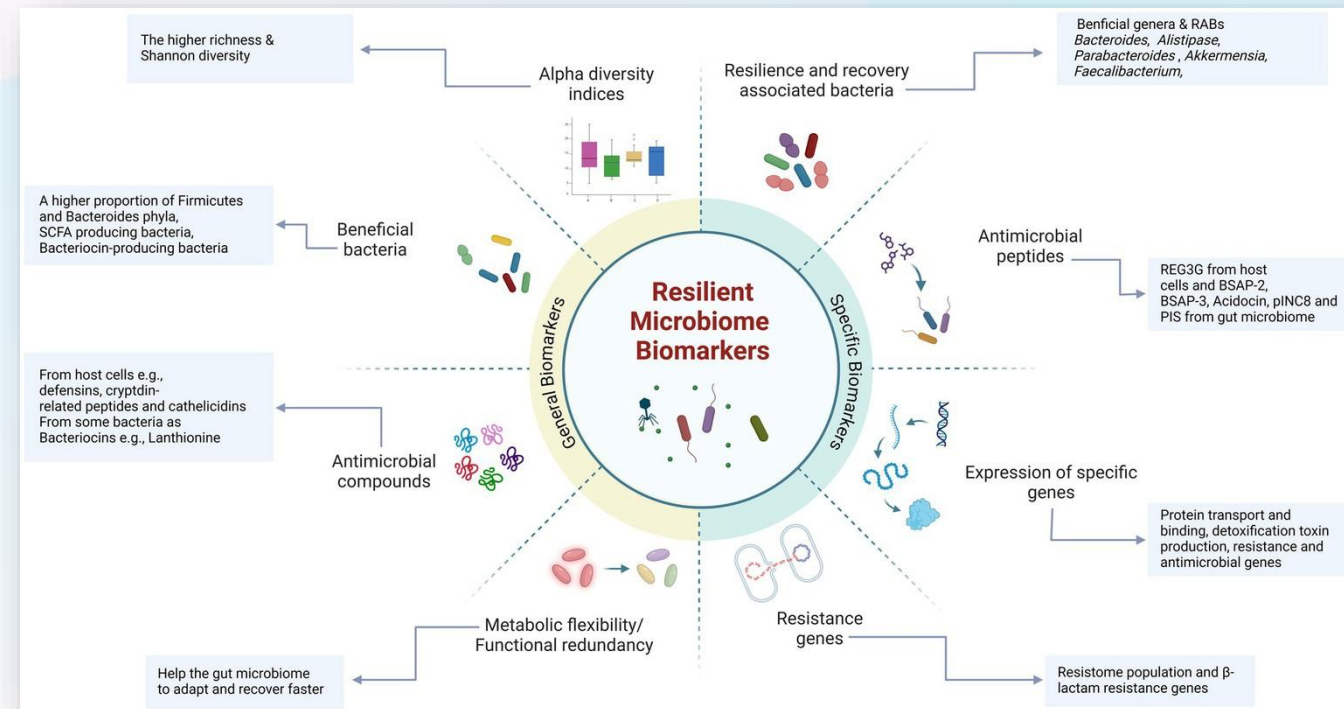


Figure 3- Safarchi A, Al-Qadami G, Tran CD and Conlon M **Understanding dysbiosis and resilience in the human gut microbiome: biomarkers, interventions, and challenges.** *Front. Microbiol.* 2025 16:1559521

The defining feature of a healthy microbiome is not just “who” is present, but how effectively the ecosystem maintains function, adapts, and recovers under pressure!

Resilience = ability of the microbiome to maintain function despite challenges

- Resist disturbance
- Recover after perturbation
- Maintain key functions
- Adapt to change

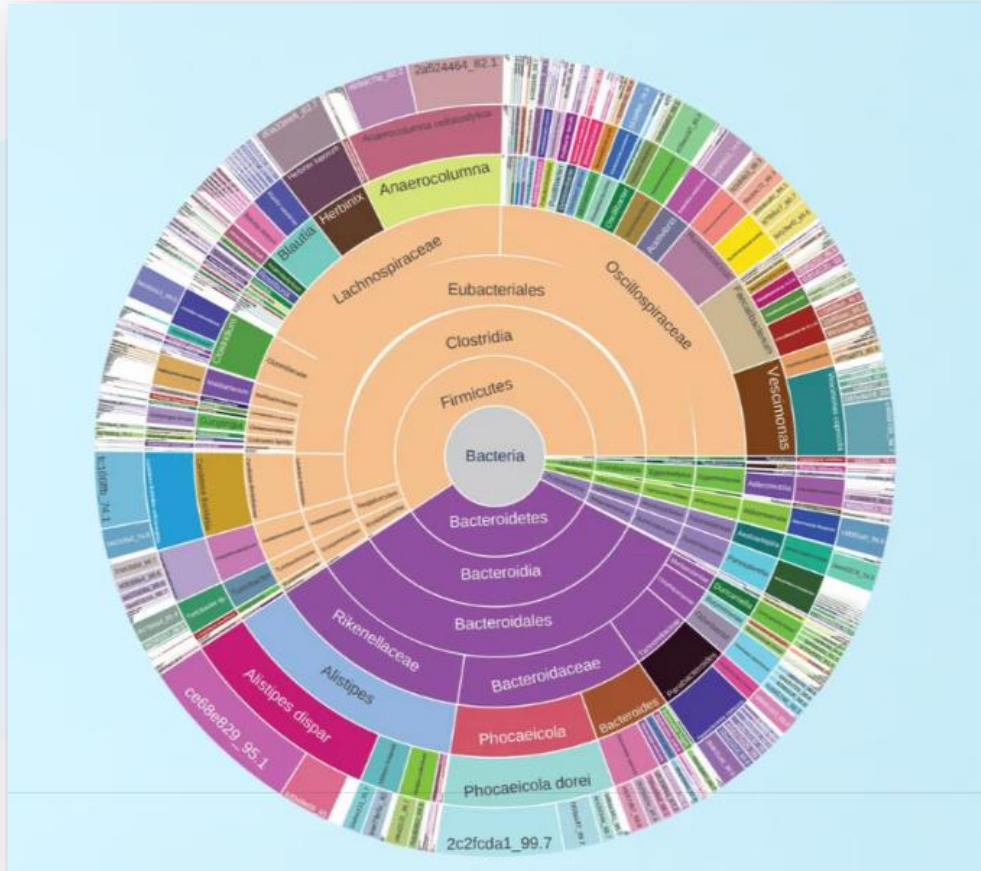
Influenced by

- Diversity and ecological interactions
- Functional redundancy
- Diet, medications and lifestyle

Biomarkers of resilience

- Higher microbial diversity
- SCFA-producing bacteria and balanced “beneficial” bacteria
- Functional redundancy
- Recovery-associated taxa (e.g. *Akkermansia*, *Faecalibacterium*)
- Metabolic flexibility

The GutID Ecosystem Approach.



Target Plot: ecosystem structure and microbial composition across taxonomic levels

Integrated analysis: resilience, functional potential, and host-microbiome interactions (gut-axes).

Ecosystem-level interpretation: moving beyond individual organisms toward clinically meaningful patterns

Gut-Brain Axis

- ✓ Mood Disorders
- ✓ Alzheimer's Disease (AD) Risk
- ⚠ Parkinson's Disease (PD) Risk
- ✓ Irritable Bowel Syndrome

Beneficial Bacteria

- ✓ Probiotics
- ✓ Mucosa Protection
- ⚠ Short-Chain Fatty Acids (SCFAs) Production

Gut-Gastrointestinal Axis

- ✓ Small Intestinal Bacterial Overgrowth (SIBO)
- ✓ Inflammatory Bowel Disease (IBD)
- ✓ Bile Acids (BAs) Metabolism

Gut-Metabolism Axis

- ✓ Obesity
- ✓ Type 2 Diabetes (T2D)
- ⚠ Non-Alcoholic Fatty Liver Disease (NAFLD)

Gut-Heart Axis

- ✓ Hypertension (HTN)
- ✓ Atherosclerosis
- ✓ Trimethylamine (TMA) Production

Gut-Immune Axis

- ✓ Lipopolysaccharide (LPS) Production
- ✓ Histamine Production
- ✓ Eczema & Atopic Dermatitis

Resilience & Biodiversity

- ✓ Alpha Diversity
- ✓ Richness
- ✓ Evenness
- ✓ Beta Diversity
- ✓ Firmicutes/Bacteroidetes (F/B) Ratio
- ✓ Firmicutes/Bacteroidetes (F/B) Total
- ✓ Fusobacteria
- ⚠ Mycoplasma
- ✓ Resistome Score
- ✓ Enterotype
- ⚠ Proteobacteria
- ⚠ Pathogens
- ✓ Top 10 Species

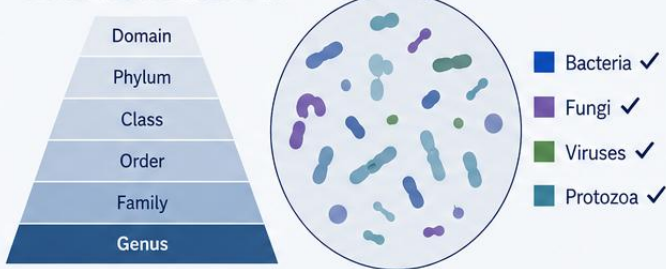
Why Accurate Testing Matters!

From Detection to Understanding

Ecosystem interpretation depends on accurate microbial identification.

BROAD BUT LOWER RESOLUTION

TAXONOMIC RESOLUTION



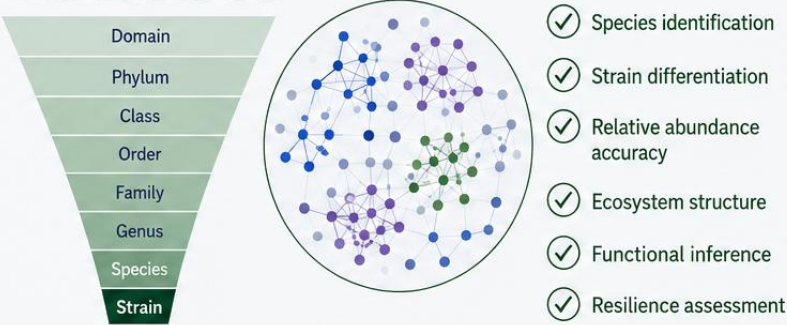
LIMITATIONS

- ✗ Limited species resolution
- ✗ Limited strain resolution

What is present?

HIGH-RESOLUTION BACTERIAL ECOSYSTEM PROFILING

TAXONOMIC RESOLUTION

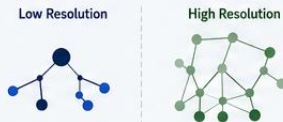


How is the ecosystem functioning?

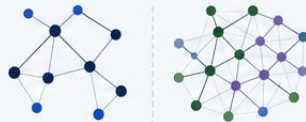
RELATIVE ABUNDANCE ACCURACY



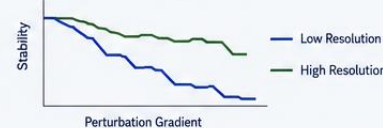
STRAIN-LEVEL DIFFERENTIATION



ECOSYSTEM STRUCTURE



RESILIENCE ASSESSMENT



Clinical insight depends not only on breadth of detection, but also on the **accuracy and resolution** of microbial identification.

Why accuracy matters

- Many microbial functions are species- and strain-specific
- Ecosystem resilience depends on accurate community profiling
- Functional interpretation is only as reliable as the organisms identified

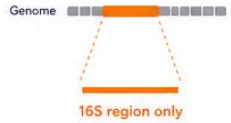
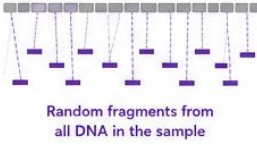
Clinical consideration

Greater taxonomic resolution may provide more ecological insight than broader but lower-resolution microbial surveys.

A high-resolution assessment of bacterial communities may provide greater ecosystem-level insight than a broader but lower-resolution survey of multiple microbial kingdoms

Comparing Microbiome Testing Technologies.

Different Technologies Answer Different Questions

1. PCR TARGETED PCR (qPCR / PCR)	2. 16S rRNA 16S rRNA SEQUENCING	3. TITAN-1 LONG-READ RIBOSOMAL SEQUENCING	4. SHOTGUN METAGENOMICS (SHORT- OR LONG-READ)
What it analyzes 	What it analyzes 	What it analyzes 	What it analyzes 
What it measures Presence or absence of the targeted organism, gene, or marker	What it measures Bacterial taxa (groups) present in the sample	What it measures Bacterial species and strains, and their relative abundance	What it measures All genetic material, including: • Bacteria • Fungi • Viruses • Potential host DNA
Key strengths ✓ Very sensitive ✓ Highly specific	Key strengths ✓ Bacterial overview ✓ Diversity assessment	Key strengths ✓ High-resolution bacterial profiling ✓ Species-level identification ✓ Strain-level differentiation ✓ Accurate relative abundance	Key strengths ✓ Broadest scope ✓ Functional potential assessment
Limitations ✗ Only detects what is specifically targeted ✗ No ecosystem assessment ✗ No diversity information	Limitations ✗ Limited species differentiation ✗ Strain identification generally not possible	Limitations ✗ Focused on bacteria only	Limitations ✗ More computationally complex ✗ Dependent on reference databases ✗ May reduce sensitivity for low-abundance organisms
Clinical Question  Is a specific organism or gene present?	 Which bacterial groups are present?	 Which bacterial species and strains are present, and in what abundance?	 What DNA is present in the sample?

IN SUMMARY

 PCR
Is a specific organism or gene present?

→

 16S rRNA
Which bacterial groups are present?

→

 TITAN-1
Which bacterial species and strains are present, and in what abundance?

→

 Shotgun Metagenomics
What DNA is present in the sample?

Key Clinical Questions

PCR: Is a specific organism or gene present?

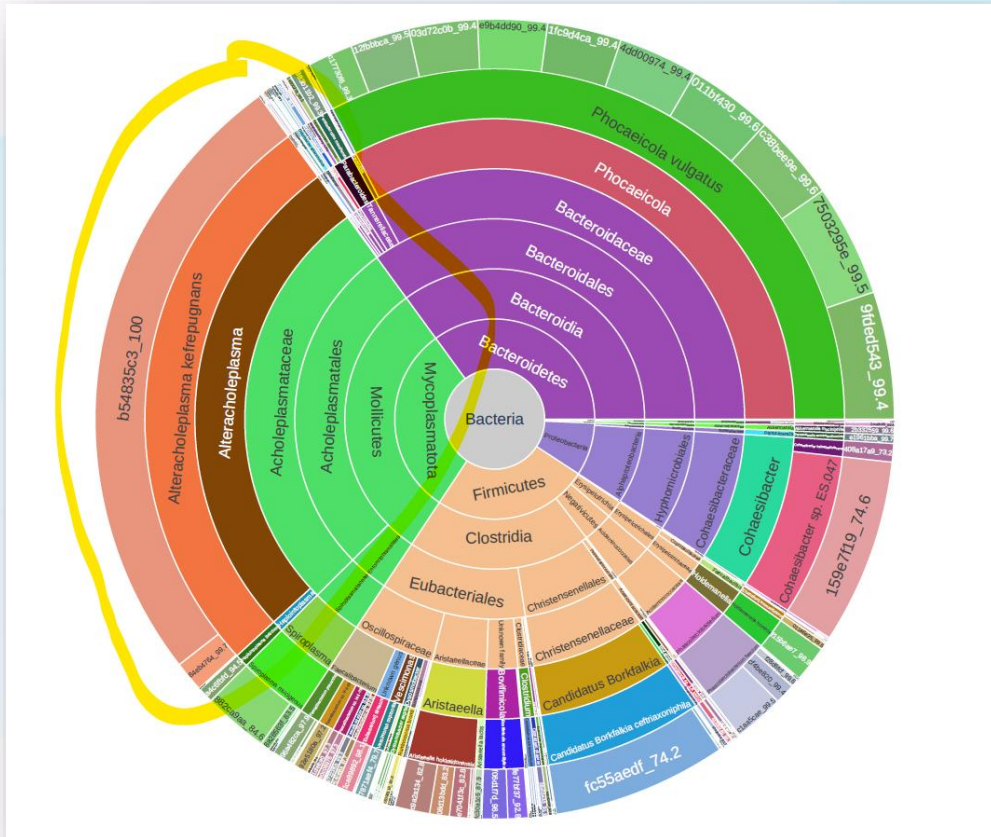
16S rRNA: Which bacterial groups are present?

Titan-1 (gut-ID): Which bacterial species and strains are present, and in what abundance?

Shotgun Metagenomics: What DNA is present in the sample?

Different technologies answer different biological questions and provide different levels of ecological insight.

Case Study: A Healthy Diet Does Not Guarantee a Resilient Microbiome!



GutID Findings

~35% of the ecosystem dominated by uncommon or poorly characterised taxa

Alteracholeplasma kefrepuagnans (26.8%) Reduced abundance of protective species. **Evidence of reduced ecosystem resilience despite an apparently microbiome-supportive diet.**

Species	Relative Abundance (%)	Reference Range (%)	Flag
<i>Phocaeicola vulgatus</i>	32.68	1.16 - 45.59	
<i>Alteracholeplasma kefrepuagnans</i>	26.78	0 - 0.01	high
<i>Cohaesibacter</i> sp. ES.047	7.49	0 - 0.01	high
<i>Candidatus Borkfalkia ceftriaxoniphila</i>	7.29	0.01 - 4.62	high
<i>Phascolarctobacterium faecium</i>	3.30	0.43 - 8.61	
<i>Spiroplasma mucigenus</i>	3.24	0 - 0.13	high
<i>Aristaeella hokkaidonensis</i>	3.15	0.03 - 3.36	
<i>Bovifimicola ammoniilytica</i>	1.89	Not Established	high
<i>Holdemanella hominis</i>	1.46	0.39 - 37.8	
<i>Faecalibacterium prausnitzii</i>	0.95	0.3 - 6.32	

Clinical Background.

Female, 36 years

Fibre-rich, polyphenol-rich whole-food diet

Regular fermented foods

Daily bowel movements

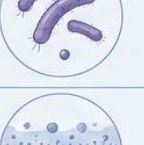
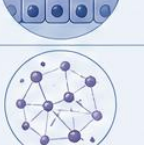
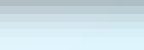
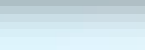
Persistent gastritis symptoms

Significant stress and disrupted sleep Extensive lifetime antibiotic exposure

Why This Matters

- ✓ Ecosystem structure may be missed when dominant organisms are not accurately identified
- ✓ Diet quality alone does not determine microbiome resilience
- ✓ Host factors, life history, stress, sleep, and previous antimicrobial exposure shape ecosystem function
- ✓ Accurate microbial identification may fundamentally alter ecosystem interpretation and intervention strategy

Building Resilience: From Interpretation to Intervention.

KEY FINDING	CLINICAL SIGNIFICANCE	INTERVENTION
 Dominance of Mycoplasmatota <i>(Alteracholeplasma kefrepuans 26.8%)</i>	 Major ecosystem distortion	 Black walnut husk + Olive leaf extract
 Elevated Proteobacteria <i>(Cohaesibacter spp.)</i>	 Increased inflammatory potential (LPS burden)	 Antimicrobial strategy + polyphenols
 Low SCFA-producing bacteria	 Reduced resilience and metabolic function	 Psyllium husk + pomegranate + green tea
 Low <i>Lactobacillus</i> / probiotic-associated taxa	 Reduced colonisation resistance	 Sauerkraut + kefir
 Reduced mucosal protection <i>(Faecalibacterium, Akkermansia)</i>	 Impaired barrier support	 DGL + slippery elm
 Reduced ecosystem resilience	 Lower capacity to recover from perturbation	 Increase microbial diversity and functional redundancy
 Sleep disruption & chronic stress	 Host drivers of dysbiosis	 Glycine + sleep optimisation
 Frequent snacking & late eating	 Disrupted ecological rhythms	 Time-restricted eating, no food after 7:30 pm

What changed the clinical management?

Without accurate identification:

"Healthy diet → continue current approach"

With accurate ecosystem assessment:

Target dominant Mycoplasmatota

Address inflammatory Proteobacteria

Support mucosal integrity

Rebuild resilience and SCFA production

The Future of Microbiome Testing in Personalised Medicine.

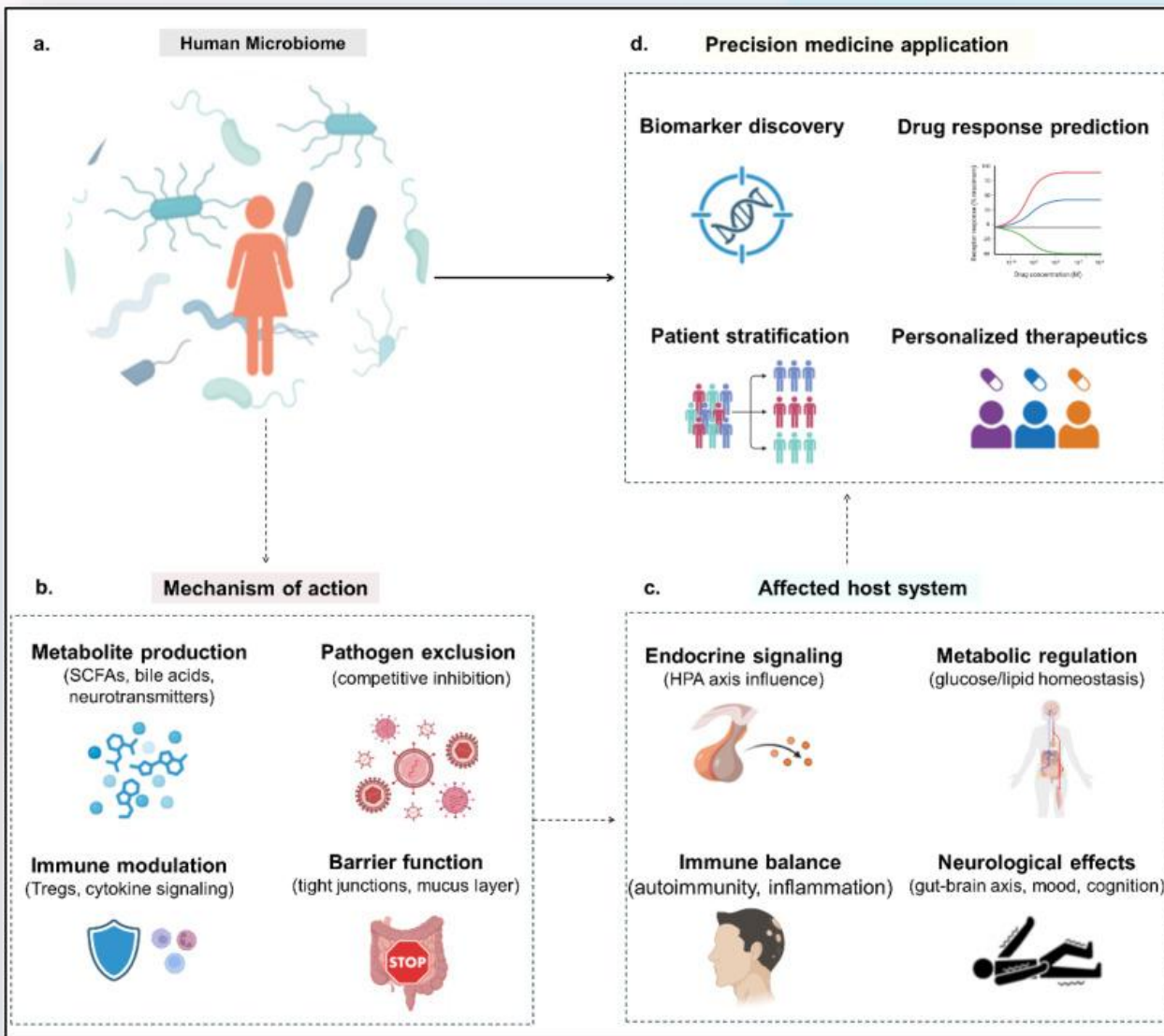


Figure 4-Umama Shahid, Microbiome-guided precision medicine: Mechanistic insights, multi-omics integration, and translational horizons, *The Journal of Precision Medicine: Health and Disease*, Volume 3, 2025

Emerging direction of microbiome testing in PM:

- Moving beyond organism detection toward **ecosystem-level interpretation**
- Integrating **microbial composition, functional potential, host physiology, and clinical data**
- Increasing emphasis on **accuracy, taxonomic resolution, and ecological context**
- Multi-omics approaches (metagenomics, metabolomics, transcriptomics) will improve mechanistic understanding
- Microbiome-informed interventions may support **patient stratification, prevention, and personalised care**

The future of microbiome testing is not simply identifying which microbes are present, but understanding how microbial ecosystems influence human biology and translating that knowledge into precise, clinically meaningful interventions.

References.

Alexander, J.L., Mullish, B.H., Thomas, L., Weersma, R.K., Sokol, H., Roberts, L.A., Edwards, L.A., Emmanuel, A., Gerasimidis, K., Hall, L.J., Iqbal, T.H., Kinross, J.M., McIlroy, J., Monaghan, T.M., Sergaki, C., Shawcross, D.L., Stewart, C.J., Lamb, C.A., Williams, H.R.T. and Hansen, R. (2026). Recent advances in our understanding of the gut microbiome: an analysis from the Gut Microbiota for Health Expert Panel of the British Society of Gastroenterology. *Gut*, [online] p.gutjnl-2026-338252. doi:<https://doi.org/10.1136/gutjnl-2026-338252>.

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