LIVE WEBINAR

Unlocking the Inner Ecosystem

Decoding the Gut Microbiome for Clinical Application

Wednesday, Mar 29 | 7 - 8PM AEDT

CO-BIOME By MICROBA

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Meet your speakers

Hayley Parcell
Nutritionist and Head of Co-Biome™ Healthcare

Dr Brad Leech
Nutritionist and Lead Clinical Educator

Krystyna Sullivan
Naturopath and Clinical Application Specialist

All participants have been muted

There is an optional 15 minutes for questions at the end

Add your questions in the chat and we will come back to them at the end

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Acknowledgement of Country

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Disclaimers

- The information provided in this webinar is for the use of qualified healthcare professionals.
- The information contained in this webinar is in no way to be taken as prescriptive or to replace a healthcare professional's duty of care and personalised care practices.
- The clinical opinions and patient case studies shared by presenters are solely those of the individual presenters and do not necessarily represent the view of Co-Biome.

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What we'll be covering

- Introducing Co-Biome™
- The role of the gut microbiome in clinical practice
- Decoding the gut microbiome for clinical application
- The Co-Biome™ MetaXplore™ range
- Case study: Interpreting a MetaXplore™ GI Plus report
- Q & A

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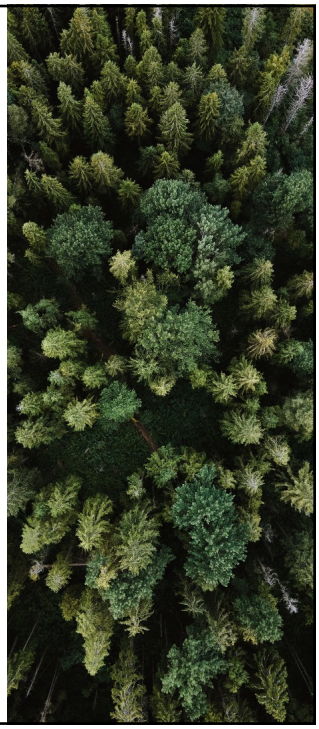
Introducing Co-Biome™

Hayley Parcell



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Improving human health through precision microbiome testing

Co-Biome™ believes that the future of good health lies within us and through accurately unlocking the complexity of the gut microbiome, we can better manage patient health for the future.

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What's the Co-Biome difference?

Contribution
We are contributing to improve human health

Whole gut microbiome analysis through metagenomic assessment of over 28,000 species

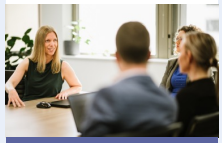
Connection
We are connecting with healthcare professionals and their patients

Supportive team of clinical application specialists

Commitment
We are committed to clinically useful information

Developed by a team of clinicians, specifically for clinicians

Courage
We show courage to pioneer evidence-based solutions



Scientifically graded statements on the evidence

Conscious
We are conscious of our impact

Local Australian NATA accredited lab with world-class technology

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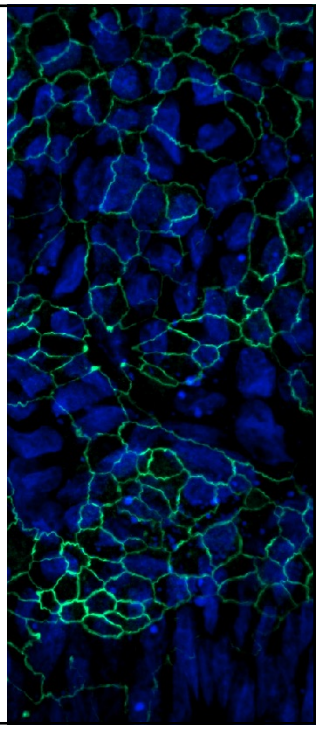
The role of the gut microbiome in clinical practice

Dr Brad Leech



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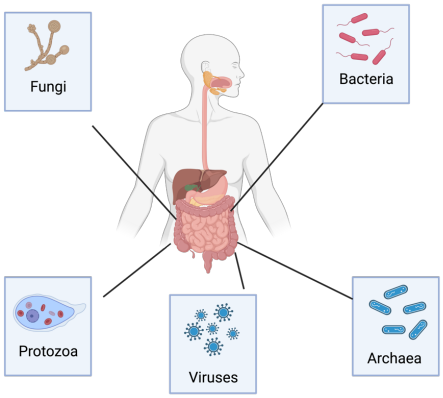
What is the Microbiome

The microbiome is defined as “a characteristic microbial community occupying a reasonably well-defined habitat which has distinct physio-chemical properties” (*Whipps et al, 1988*)



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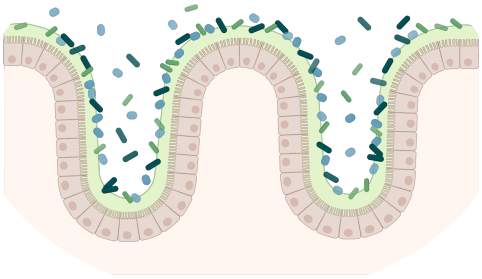
The colonic mucus provides a home and a fuel source for the microbiome



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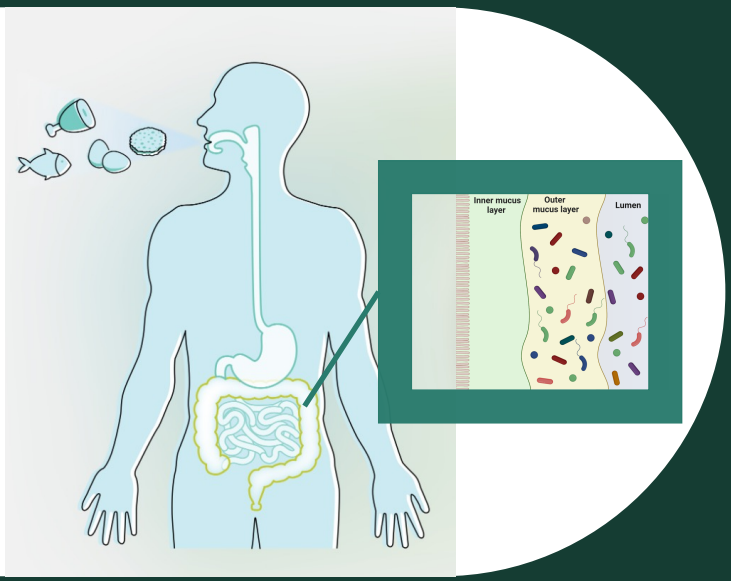
The microbes within the gut microbiome consume:

- dietary fibre and resistant starch
- excess dietary protein
- host proteins
- mucin glycans



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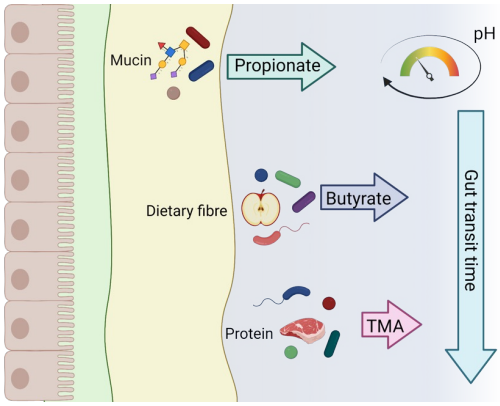
The amount of metabolite produced by the microbiome reflects:

- the number of microbial genes that produce different metabolites
- availability of fuel sources
- environmental conditions in the gut



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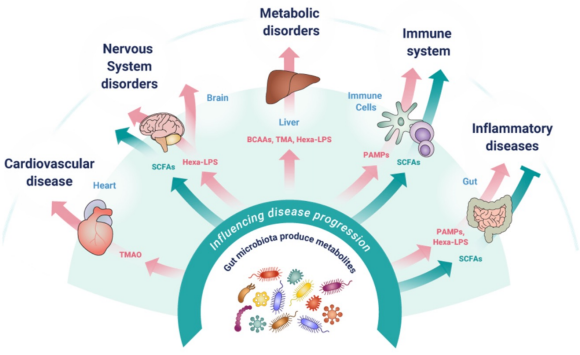
How can the gut microbiome influence health?



Gebrayel, 2022

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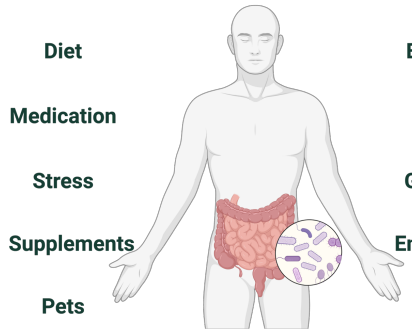
What can influence a patient's microbiome health?



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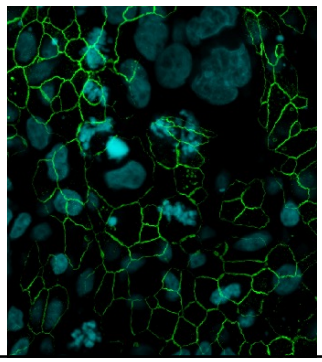
Decoding the gut microbiome for clinical application

Dr Brad Leech



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gastrointestinal health

- Gastrointestinal disorders, including irritable bowel syndrome (IBS), intestinal permeability, and inflammatory bowel disease (IBD)
- Digestive complaints, including constipation, diarrhoea, bloating and abdominal pain
- Hormonal imbalance
- Metabolic and weight concerns
- Immune system health concerns
- Chronic inflammation

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How can gut microbiome analysis help us?

Microbiome's contribution to health	Dietary direction	Supplements	Patient compliance
How is my patient's microbiome contributing to their clinical presentation? What is the severity of my patient's gut health? How is my patient's microbiome contributing to health or disease risk?	What personalised dietary advice should I provide my patient? How is my patient's diet impacting their microbiome?	What are the prebiotic, probiotic and polyphenol supplements which should be used or avoided for my patient? Which supplements should I prioritise?	Allow us to monitor and support patient compliance and treatment over time.

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"Test don't guess"

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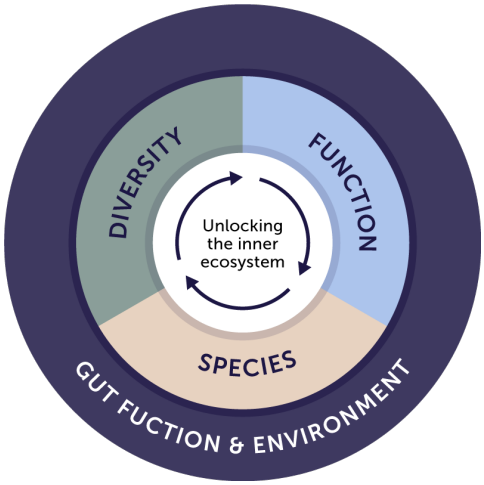
Decoding the gut microbiome for clinical application



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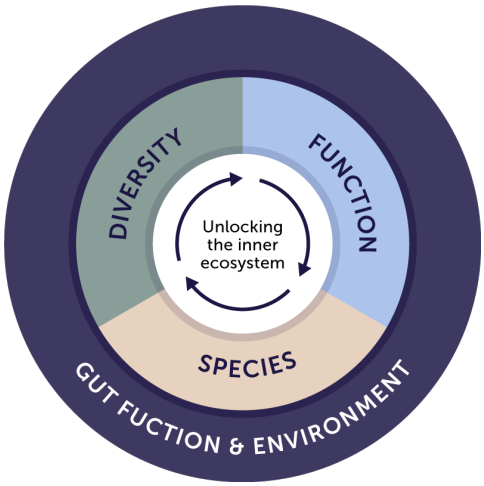
6 key questions to answer

1. What is the microbial diversity and richness?

2. What is the whole microbiome's capacity to produce or consume metabolites associated with health?

6. Are there alterations in gut function or environment?



3. Are pathogenic bacteria or protist parasites present? (if required)

4. Who makes up the whole ecosystem – bacteria, archaea, fungi, protists?

5. Which species are present and what is their abundance?

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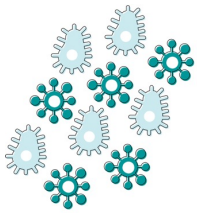
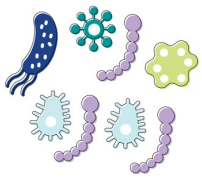
1. What is the microbial diversity and richness?

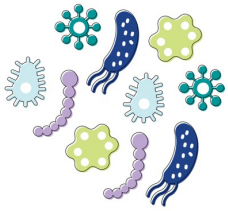
DIVERSITY



LOW DIVERSITY:
Low richness
High evenness



LOW DIVERSITY:
High richness
Low evenness



HIGH DIVERSITY:
High richness
High evenness

A healthy person's sample will contain between 110 – 244 species.[1]

Higher microbial diversity is predictive of a more stable microbiome.[2]

Low diversity may be associated with increased systemic inflammation.[3, 4]

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1. Data from Microba's Future Insights program. 2. Byrd, 2021 3. Mokkala, 2020, 4. Zhernakova, 2016

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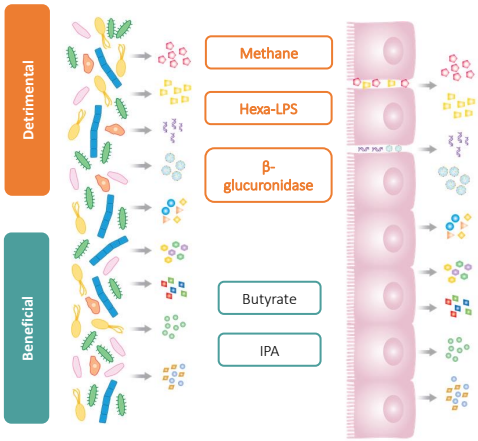
2. What is the microbiome's capacity to produce or consume metabolites associated with health?

FUNCTION



Slow intestinal motility	Constipation
Drive systemic inflammation	Obesity
Disrupt hormone detox	Hormonal imbalance
Protect intestinal barrier	Good digestion
Reduce intestinal inflammation	Gut healing

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2. What is microbiome's capacity to produce or consume metabolites associated with health?

FUNCTION

	MICROBIAL MARKER	CLINICAL RELEVANCE
Short chain fatty acids	Butyrate	Main fuel source for gut cells. Low levels associated with intestinal and systemic inflammation and impaired intestinal barrier integrity.
	Acetate	Most abundant SCFA produced in the gut. Can be converted by some species to butyrate. Low levels associated with intestinal inflammation.
	Propionate	SCFA produced by the gut microbiome. Optimal production associated with normal gut transit time and immune balance within the GIT.
Health indicators	3-indolepropionic acid (IPA)	Beneficial substance produced by some gut bacteria when they break down tryptophan. Low levels may be associated with intestinal and systemic inflammation and impaired barrier integrity.
	Mucin	Component of the mucous layer that lines and protects the epithelial gut barrier. High levels of mucin consuming microbes may be associated with intestinal inflammation.
	Oxalate consumption	Key component of calcium oxalate kidney stones. Low microbial oxalate consumption associated with increased urinary oxalate excretion. May be reduced in patients with recurrent kidney stones.
	Hydrogen sulphide	Produced by gut microbes when they break down sulphur-containing compounds. It is responsible for the rotten egg smell of flatulence. Can be protective of the gut at low levels. At high levels can disrupt intestinal barrier integrity.
	Methane	Gas produced by some species of the gut microbiome, primarily through reduction of carbon dioxide and hydrogen. Elevated levels associated with increased intestinal transit time and constipation.
	B. fragilis toxin	Normal inhabitant of the human gut. Small proportion can secrete a toxin called fragilysin. High levels may impair intestinal barrier integrity.
	Beta-glucuronidase	Bacterial enzyme that can re-activate a wide variety of drugs and hormones. High levels may affect drug response and toxicity.
	Branched-chain amino acids (BCAAs)	Derived from the diet and produced by the gut microbiome which can contribute to elevated plasma BCAAs levels. High levels associated with systemic inflammation. Muscle important in regulating BCAA levels through regular physical activity.
	Hexa-acylated lipopolysaccharide (hexa-LPS)	Inflammatory compound produced by some species of bacteria within the Proteobacteria phylum. High levels associated with intestinal and systemic inflammation and impaired intestinal barrier integrity, via activation of immune receptor TLR4.
	Trimethylamine (TMA)	Compound produced by some microbes from breakdown of choline and carnitine. TMA produced in gut transported to liver, where it can convert to TMAO. High level of TMAO in blood plasma is strongly associated with cardiometabolic disease.

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Green = positively associated Grey = scale dependent Red = negatively associated

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Clinical Application of Hexa-LPS

Clinical Relevance

Hexa-acylated lipopolysaccharides (hexa-LPS) are bacterial cell wall components of bacteria within the Gammaproteobacteria class.

High hexa-LPS may be associated with intestinal and systemic inflammation and impaired intestinal barrier integrity.

Treatment Considerations

Clinicians may want to prescribe galacto-oligosaccharides (GOS) or the probiotic combination of *Lactobacillus gasseri* KS-Y3, *Bifidobacterium bifidum* G9-Y and *Bifidobacterium longum* MM2 to reduce hexa-LPS.

An increased omega-3 to saturated fat ratio in the diet may reduce blood levels of hexa-LPS after meals.

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Lyte, 2016; Ahola, 2017

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Clinical Application of IPA

Clinical Relevance

3-indolepropionic acid (IPA) is a beneficial substance produced by some gut bacteria when they break down the amino acid tryptophan.

Low levels of IPA may be associated with intestinal and systemic inflammation and impaired intestinal barrier integrity.

Treatment Considerations

Clinicians may want to suggest foods rich in ellagic acid (e.g., chestnuts, blackberries, and ellagic acid enriched pomegranate juice), as well as a Mediterranean diet for patients with low IPA production.

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Yang, 2020; Tuomainen, 2018; de Mello, 2017

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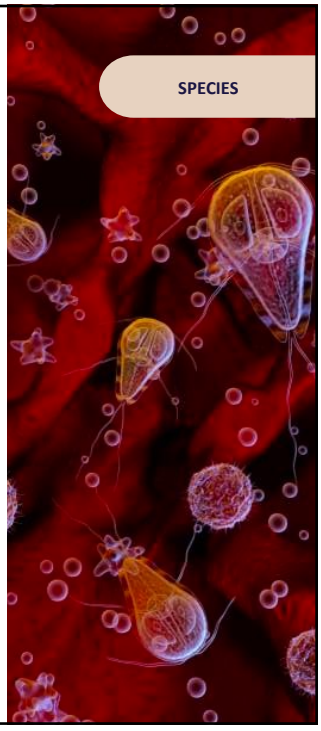
3. Are pathogenic bacteria or protist parasites present?

Clinical consequence	Exposure
Nausea, vomiting, diarrhoea, abdominal discomfort, bloody stool, gas.[1] Impacts gut environment.[2]	Contaminated food, drinking water, animals, waste, soil.

Pathogenic bacteria	Protist parasites
Yersinia enterocolitica *Aeromonas spp.* *Campylobacter spp.* *Salmonella spp.* *Vibrio spp.* *Clostridium difficile toxin B* Hypervirulent *Clostridium difficile* *E. coli* pathotypes x 6	*Giardia lamblia* *Entamoeba histolytica Cryptosporidium spp.* *Dientamoeba fragilis* *Cyclospora cayetanensis*



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1. McHardy, 2014; 2. Naveed, 2021

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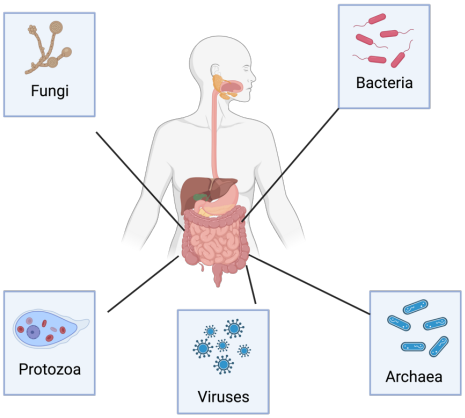
4. Who makes up the whole ecosystem – bacteria, archaea, fungi, protists?

SPECIES



Shotgun metagenomics can report on all species that make up the whole gut microbiome community^

It's important to consider individual species in the context of the whole microbiome

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^ Shotgun metagenomics can report on all species with a relative abundance above 0.01% including non-diagnostic eukaryotes (fungi and protist parasites).

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5. What species are present and what is their abundance?

SPECIES

- Bacteroidota = 23.98%
- Firmicutes_A = 58.14% → *Faecalibacterium prausnitzii C* 1.98% of patient's microbiome
- Proteobacteria = 2.66%
- Verrucomicrobiota = 1.33% → *Akkermansia muciniphila*, 1.33% of patient's microbiome
- Firmicutes = 0.48%
- Firmicutes_C = 0.45%
- Desulfobacterota_A = 0.15% → *Bilophila wadsworthia*, 0.15% of patient's microbiome
- Cyanobacteria = 0.16%
- Actinobacteriota = 0.84% → *Bifidobacterium longum*, 1.47% of patient's microbiome

Data from Microba case study.

There are no species a healthy microbiome must contain

The most common species, *Blautia_A wexlerae*, is found in 98% of healthy cohort[1]

The **amount of microbes** doing the job is more important than **which species** are doing the job

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1. Data from Microba healthy cohort.

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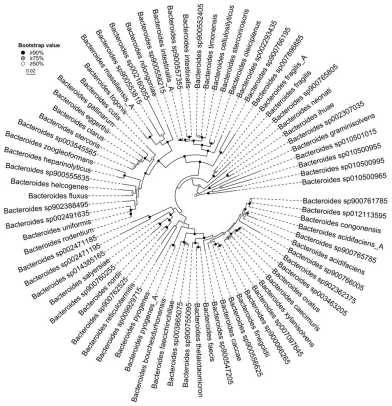
Why species level view matters

SPECIES



Species within the same genus can have different functions and play very different roles

***Bacteroides* genus**

Bacteroides vulgatus

Associations: IBD, liver fibrosis, insulin resistance, and polycystic ovarian syndrome.

Bacteroides uniformis

Associations: production of anti-inflammatory compounds and improved immune function

Strains within same species can also play different roles, e.g. ***Escherichia coli***

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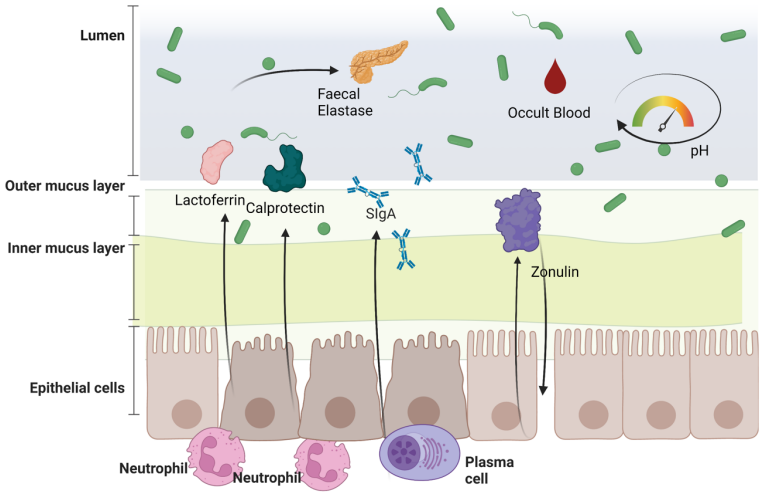
6. Are there alterations of gut function or environment?

GUT FUNCTION & ENVIRONMENT



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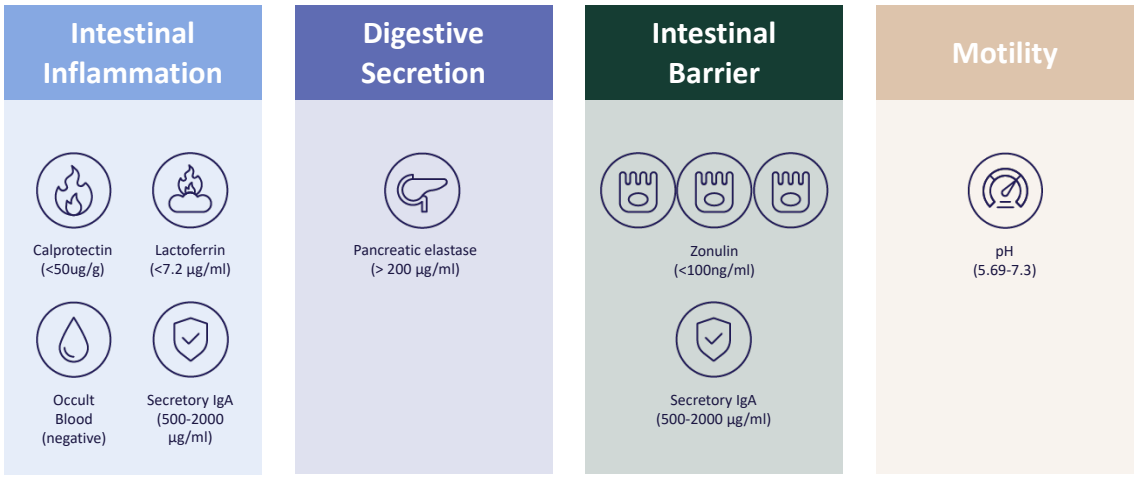
6. Are there alterations of gut function or environment?

GUT FUNCTION & ENVIRONMENT



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Clinical Application of Functional Markers

GUT FUNCTION & ENVIRONMENT

Functional Marker	Clinical indication	Clinical relevance
Calprotectin	• Acute intestinal inflammation and estimated degree of inflammation	• Distinguish active IBD from IBS • Monitor disease activity and relapse in IBD and colorectal cancer
Lactoferrin	• Intestinal inflammatory activity	• Monitor disease activity /treatment /relapse in IBD
Faecal pH	• Gut transit time	• Elevated pH may indicate longer transit time • Low pH may indicate rapid transit time • Seen in patients with lactose intolerance • Estimates absorption of short-chain fatty acids (SCFAs)
Faecal Occult Blood	• Intestinal bleeding	• Early diagnosis can significantly reduce risk of a serious colorectal disease
Pancreatic elastase	• Pancreatic exocrine function	• Diagnosis or exclusion of exocrine pancreatic insufficiency • Monitor exocrine pancreatic function in cystic fibrosis, diabetes mellitus, chronic pancreatitis
Zonulin	• Increased intestinal permeability	• Allows substances from gut lumen to pass across the epithelium and activate immune reactions
Secretory IgA	• Intestinal inflammation and increased intestinal permeability	• Major role in preventing adherence of microbes to mucosal sites, activation of the alternative complement pathway and inflammatory reactions

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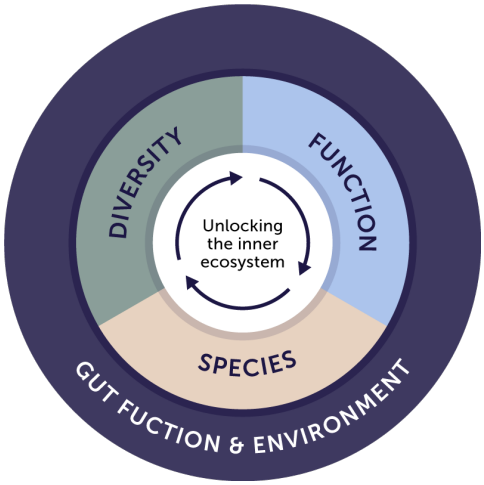
Key Take Aways

1. Assess microbial diversity and richness

2. Assess the whole microbiome's capacity to produce or consume metabolites associated with health
butyrate, acetate, propionate, 3-indolepropionic acid (IPA) hexa-acylated lipopolysaccharide (hexa-LPS), trimethylamine (TMA), hydrogen sulphide, branched-chain amino acids (BCAA), B.fragilis toxin, methane, beta-glucuronidase

6. Assess alterations of gut function or environment
faecal calprotectin, faecal occult blood, faecal pH, lactoferrin, pancreatic elastase, secretory IgA, zonulin



3. Identify pathogenic bacteria and protist parasite presence using qPCR when necessary

4. Assess the WHOLE microbiome using metagenomics

5. Understand the presence and abundance at a species-level view using metagenomics

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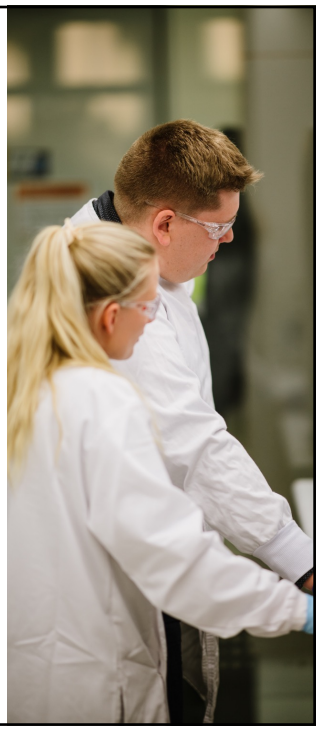
The Co-Biome MetaXplore range

Krystyna Sullivan



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Introducing the MetaXplore™ range

MetaXplore™
MetaXplore™ provides a metagenomic driven gut microbiome profile, together with the latest research insights for healthcare professionals.
Technology: metagenomics

$369

MetaXplore™ GI
MetaXplore™ GI provides the same comprehensive microbiome profile as MetaXplore™ as well as reporting on seven gastrointestinal health markers and science backed clinical insights to assist clinical decision-making and intervention.
Technology: metagenomics + diagnostic GI health markers + faecal pH

$489

MetaXplore™ GI Plus
MetaXplore™ GI Plus is Co-Biome's most comprehensive functional gut microbiome profile. It provides all the features found in MetaXplore™ and MetaXplore™ GI, plus targeted bacteria and parasite panels using quantitative polymerase chain reaction (qPCR) technology for diagnostic pathogen detection.
Technology: metagenomics + diagnostic GI health markers + faecal pH + qPCR

$529

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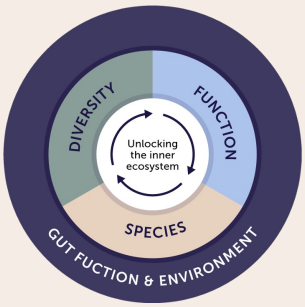
MetaXplore™ range test indications:

- Gastrointestinal disorders, including irritable bowel syndrome (IBS), intestinal permeability and inflammatory bowel disease (IBD)
- Digestive complaints, including constipation, diarrhoea, bloating and abdominal pain
- Hormonal imbalance
- Metabolic and weight concerns
- Immune system health concerns
- Chronic inflammation

What does the MetaXplore™ range measure?

- Diversity
- Species
- Function
- Gut function & environment[1]



What insights can the MetaXplore™ range provide?

The MetaXplore™ range can show how the gut microbiome and gastrointestinal health is impacting health categories including:


Intestinal inflammation


Systemic inflammation


Detox / retox


Intestinal motility


Digestive secretions


Intestinal barrier

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How is their ecosystem functioning?

Gut microbiome and gastrointestinal health impact on health categories

	Intestinal inflammation	Digestive secretions	Intestinal motility	Systemic inflammation	Detox / retox	Intestinal barrier
MICROBIOME FUNCTION	Acetate Butyrate Hexa-LPS IPA Mucin consumption Propionate		Diversity Methane Propionate Richness	BCAAs Butyrate Diversity Hexa-LPS IPA Richness Trimethylamine	Beta-glucuronidase Oxalate consumption	*B.fragilis* toxin Hexa-LPS IPA Hydrogen sulphide
GUT FUNCTION & ENVIRONMENT (optional)	Calprotectin Lactoferrin Occult blood Secretory IgA	Pancreatic elastase	Faecal pH			Secretory IgA Zonulin

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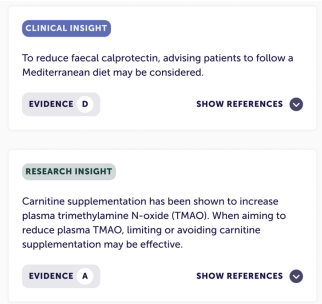
The MetaXplore™ range provides **personalised clinical and research insights** using scientifically graded statements on the evidence for **diet** and **lifestyle** interventions **plus probiotic**, **prebiotic**, **nutrient** and **polyphenol** supplementation



Grades / Code	Description
A	Body of evidence can be trusted to guide practice
B	Body of evidence can be trusted to guide practice in most situations
C	Body of evidence provides some support for recommendation, but care should be taken in its application
D	Body of evidence is weak, and recommendation must be applied with caution
PP, H	Body of evidence is observational only and must be applied with caution
PP, IV	Body of evidence is in vitro and must be applied with a high degree of caution

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TEST	WHEN TO REFER

MetaXplore™ 	• Easiest swab collection and return process
	• Reason for test is to explore role of microbiome in:
	  ○ systemic inflammation, e.g. cardiovascular disease, obesity
	  ○ detox/ retox, e.g. hormone imbalance, oxalate processing

MetaXplore™ GI 	• Provides combination of microbial markers to assess impact of microbiome, and gastrointestinal health markers to assess gut function and environment
	• Reason for test may be related to:
	  ○ altered intestinal motility, e.g. constipation, diverticular disease
	  ○ compromised intestinal barrier function, e.g. autoimmune disease, food sensitivities
	  ○ intestinal inflammation, e.g. Inflammatory bowel disease, allergy
	  ○ pancreatic function, e.g. weight loss, alcoholism

MetaXplore™ GI Plus 	• Most comprehensive test available
	• Provides qPCR diagnostic panel for pathogenic bacteria and protist parasites
	• Recommended for patients:
	  ○ wanting comprehensive gold standard test
	  ○ with symptoms of pathogen infection, e.g. abdominal pain, blood in stool, travel history
	  ○ who may have post-infective irritable bowel syndrome

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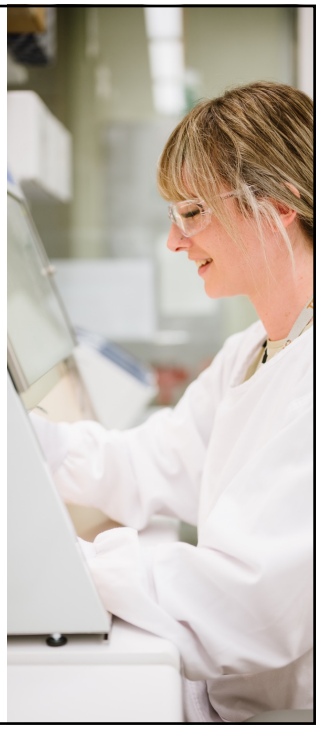
Case study: Interpreting MetaXplore™ GI Plus Reports

Dr Brad Leech



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Patient Case Study

Chronic autoimmune disease and gastrointestinal symptoms

Age - 52

BMI - 27.5 (overweight)

Diagnosis - Hashimoto's disease, systemic lupus erythematosus, Sjögren's syndrome, Raynaud's syndrome, fibromyalgia, migraine headache

Gastrointestinal - nausea, food sensitivities, burning indigestion pain, chronic diarrhoea, reflux, intermittent constipation

Family history - heart disease, colon cancer

Systemic - chronic pain, high blood pressure

Dietary - low carbohydrate diet, low fibre intake

Medication - Nexium 40mg, Gaviscon b.d.

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Patient Centred Care

Important considerations when using research and clinical insights

- The patient's clinical presentation including:
  - Symptoms
  - Medical history
  - Physical examination
- Additional pathology results
- Any patient sensitivities or preferences
- Important areas of the report to address first
- Any conflicting insights suggested

Based on the patient's clinical presentation and MetaXplore™ results the clinician should determine the most appropriate course of treatment.

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Patient treatment plan

Supplement	Dosage	Duration	Related condition
Fish oil with SPM	Two with breakfast and lunch	3 months	Pain and inflammation
Curcumin	Two with breakfast and dinner	2 months	Intestinal and systemic inflammation
PEA	One with breakfast and dinner	2 months	Pain and inflammation

Dietary/ Lifestyle	Related condition
High plant-based diet	Low diversity, high TMAO
Breakfast: rolled oats with blackberries and walnuts	Low butyrate, low IPA (contains beta glucan) and ellagic acid
Increase fermented foods	Low microbial diversity
Weekly gardening	Low microbial diversity
Green banana flour	Low butyrate

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Key takeaways

- Assessing a patient's gut microbiome and gastrointestinal health should be a consideration for many of your patients
- Consider diversity, function, species and gut function and environment when assessing a patient's gut microbiome and gastrointestinal health
- Co-Biome's MetaXplore™ range provides three comprehensive gut microbiome and gastrointestinal health tests to support clinical decision making
- Using Co-Biome's MetaXplore™ range of tests combined with your clinical expertise can support informed prescribing and patient outcomes

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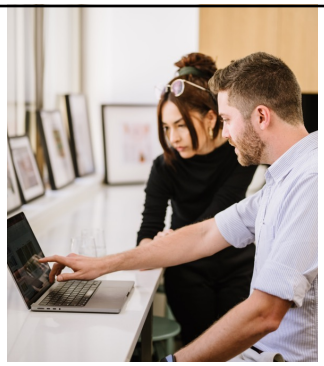

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Introductory offer

- **30% discount** off the MetaXplore™ range available only to webinar attendees
- A discount link will be emailed to you
- The introductory offer will be available until 30 April 2023

To gain referral access:

- Register: co-biome.com/register/

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15 minutes

Q&A from the chat

Hayley Parcell
Dr Brad Leech
Krystyna Sullivan

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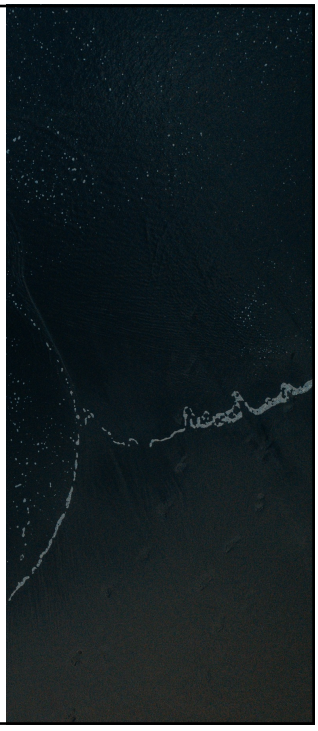

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LIVE WEBINAR

Thank you for attending

Additional resources:

- MetaXplore™ Range Brochure
- How to refer handout
- Interpretation Guide (coming soon)
- Patient brochure (coming soon)

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