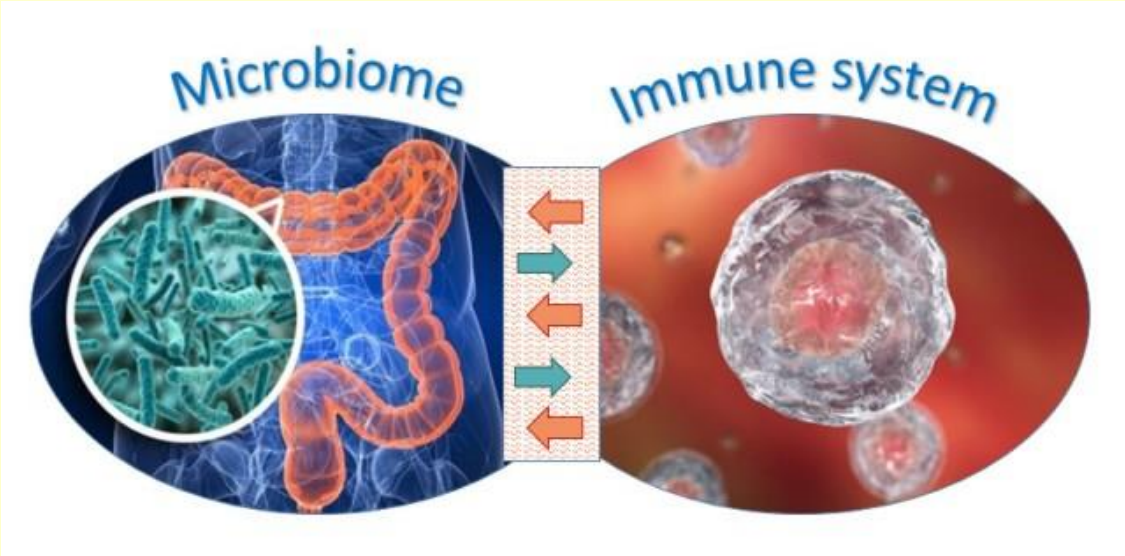
The Microbiome, Human Gut and Immune Regulation



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Overview

1. Why the gut microbiome is crucial for immune regulation

2. The interplay among gut barrier, the gut microbiota, immune cells and health outcomes

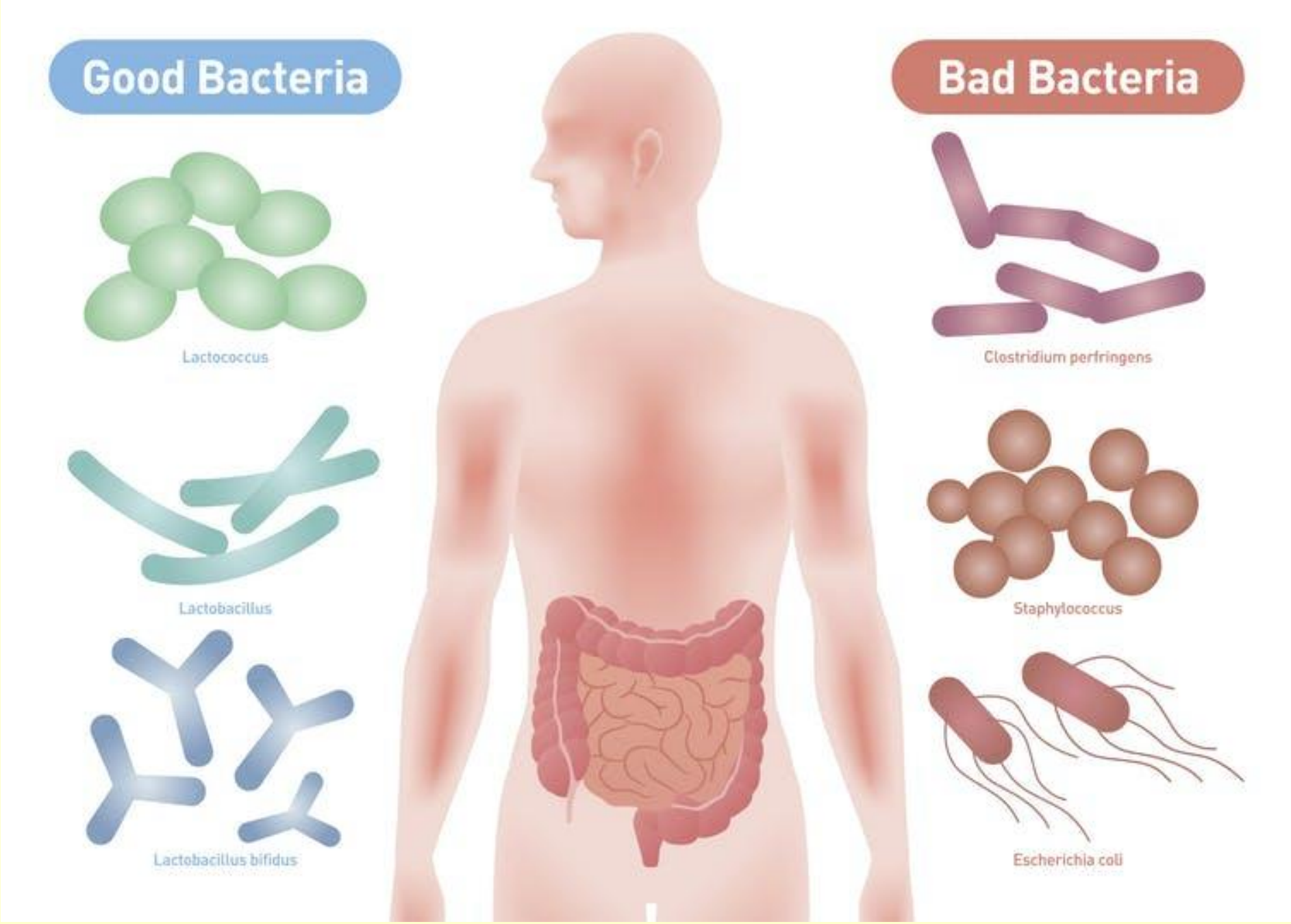
3. Role of gut microbiome in immune development

4. Nutritional factors implicated in gut microbiome/immune function

The Gut Microbiome and Immune Regulation

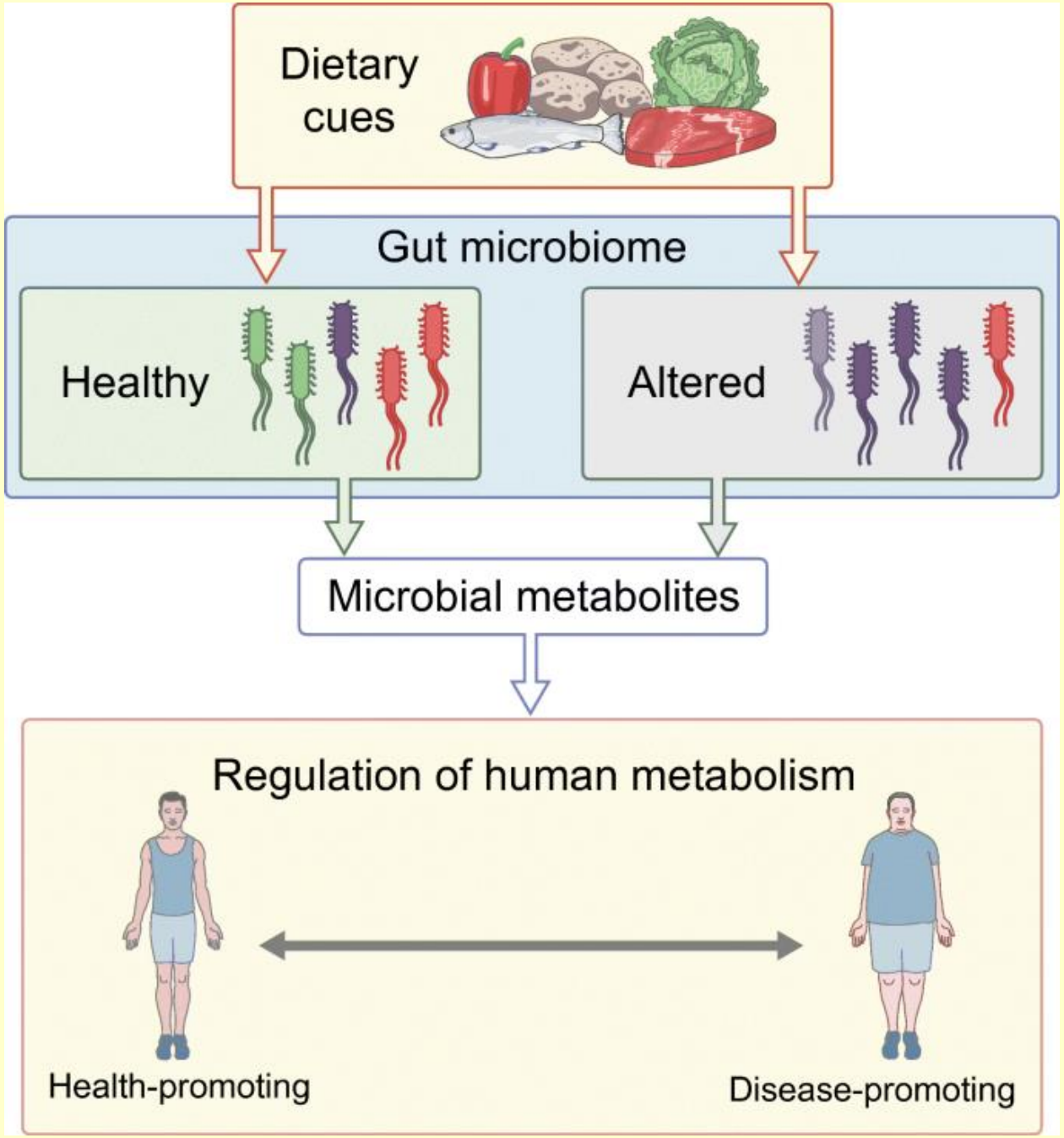
The Microbiome

- Trillions of bacteria are distributed in complex and site-specific communities on the skin and at mucosal surfaces
- Historically, these bacteria were considered to be harmful
- Now clear that this ‘microbiome’ is integral to human physiology and health, as well as disease
- Largest community is found in the distal gut

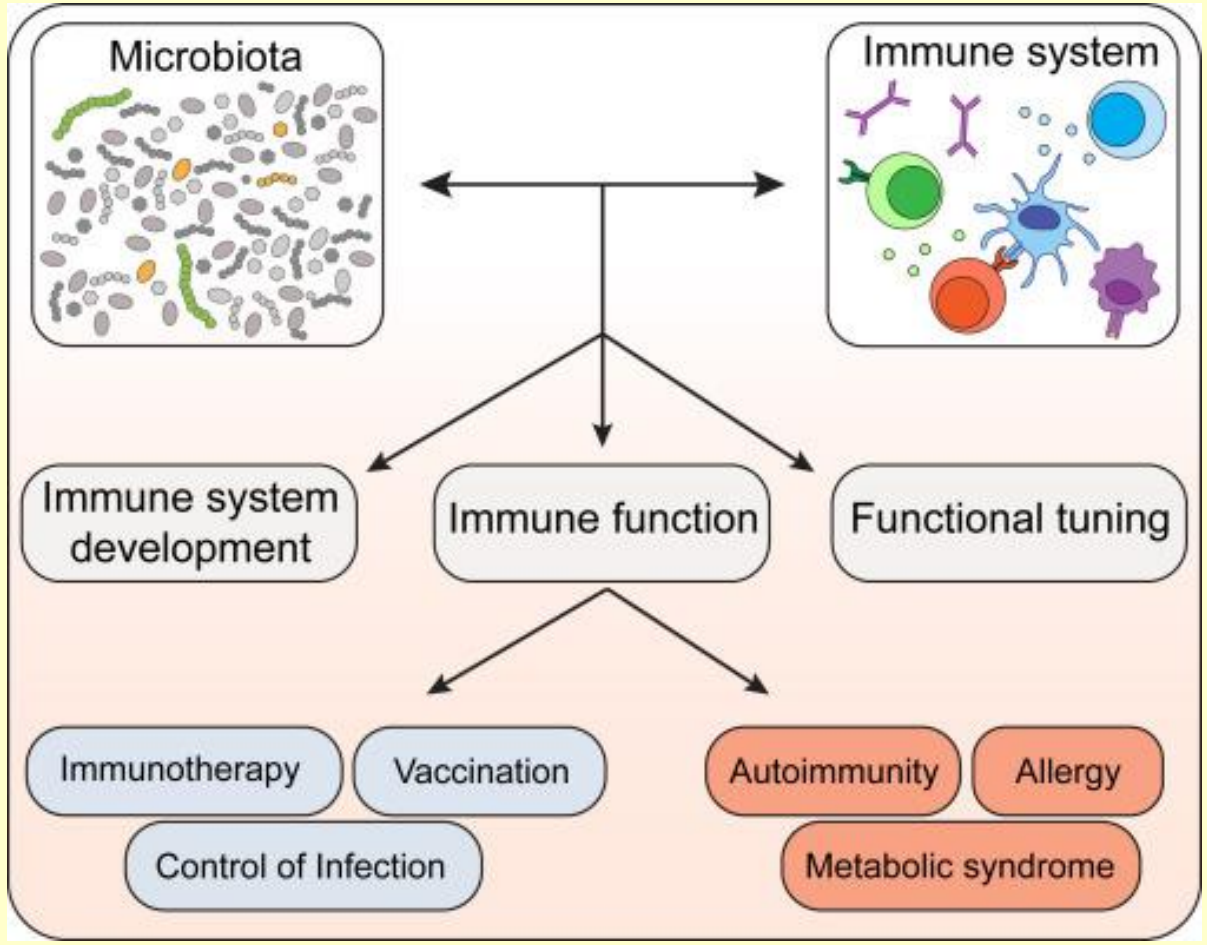

Good Bacteria
Lactococcus
Lactobacillus
Lactobacillus bifidus
Bad Bacteria
Clostridium perfringens
Staphylococcus
Escherichia coli

The Human Gut Microbiome

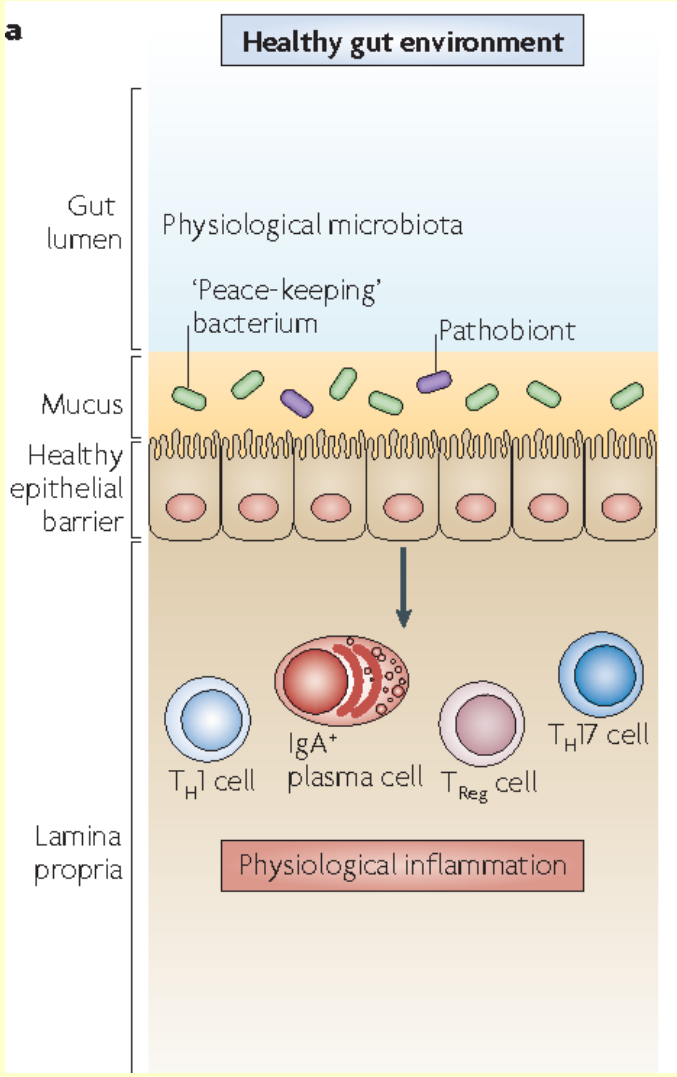
- Human gut contains ~10^{14} bacteria
- Close link with other mucosal sites
- Key regulator of immune system
- Also plays role in other key processes:
  - → Gut development
  - → Gut integrity
  - → Cognitive health
  - → Metabolic health


Dietary cues
Gut microbiome
Healthy
Altered
Microbial metabolites
Regulation of human metabolism
Health-promoting
Disease-promoting

Interaction Between the Microbiome and the Immune System

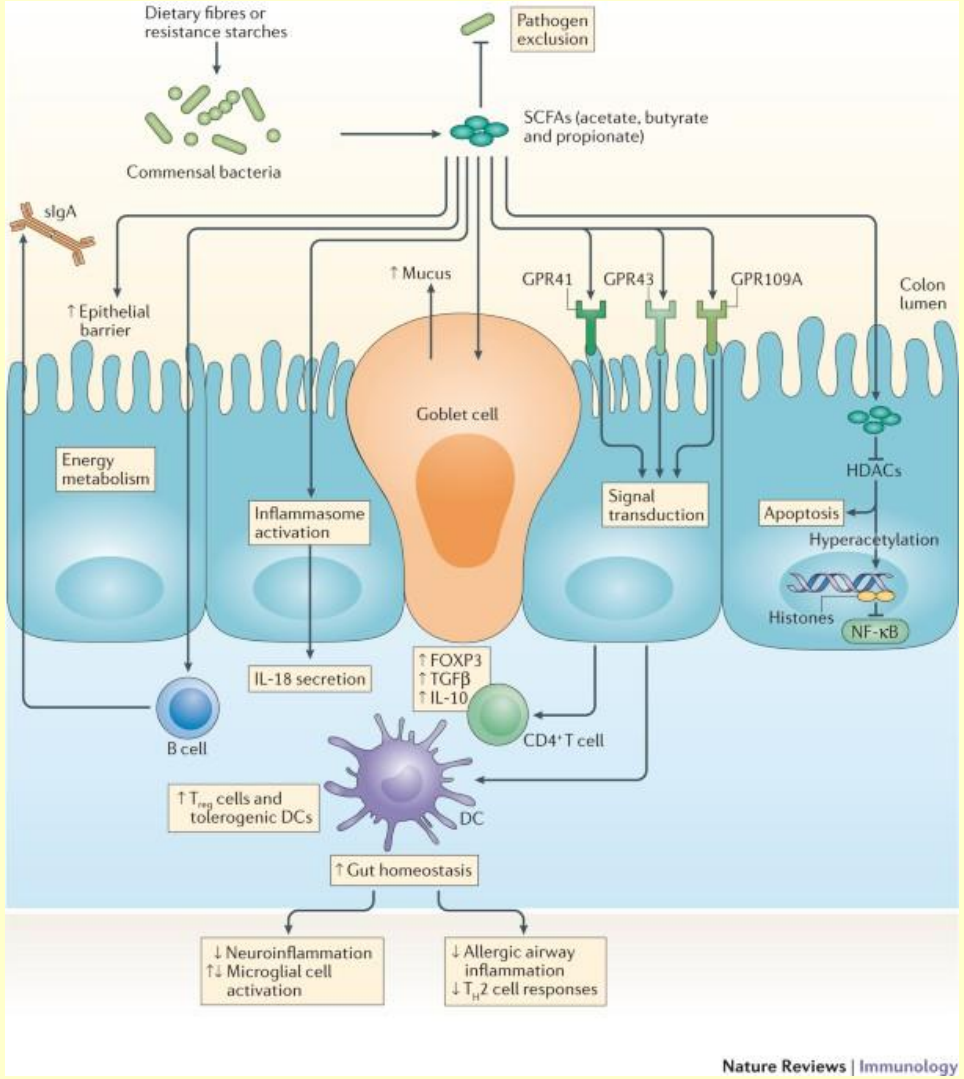


Maintaining a Healthy Gut Environment

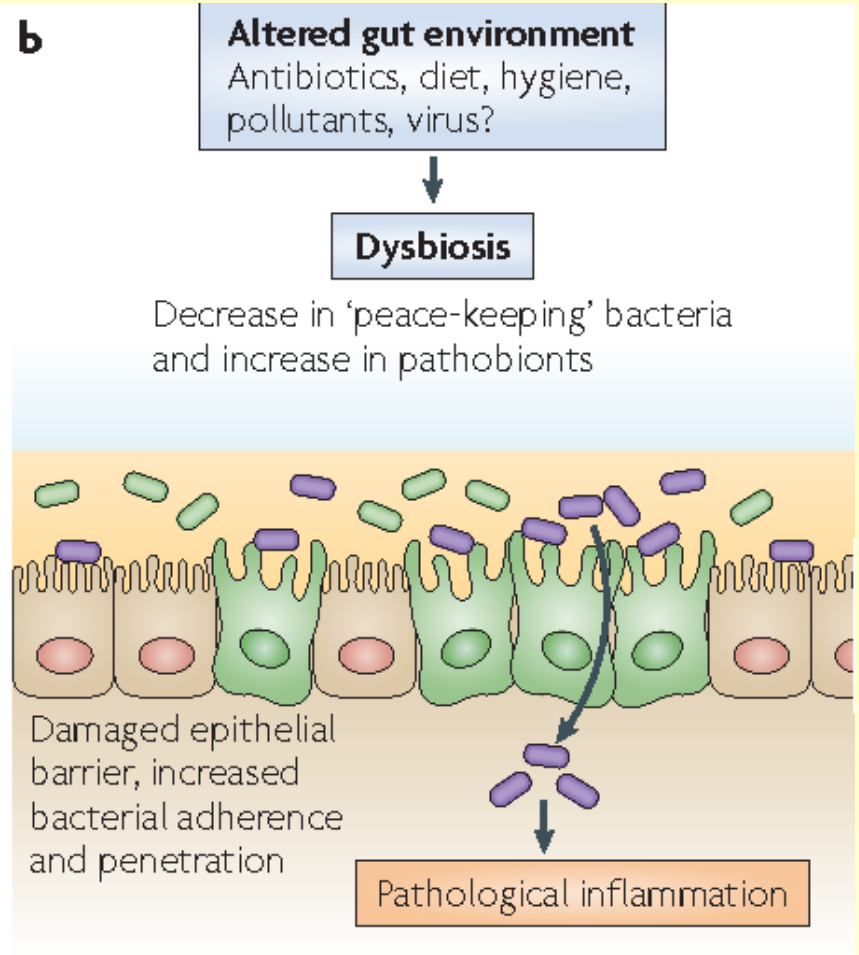


- Efficient barrier to contain the microbiota in the gut lumen and appropriate microbial balance
- Feedback mechanisms avoid excessive activation of host immune responses
- 'Peacekeeping' bacteria release anti-inflammatory products – help tune host responses towards tolerance
- Also help to prevent the pro-inflammatory effects of any pathogenic bacteria – to maintain intestinal homeostasis.

Gut Microbiome and Immune Signalling

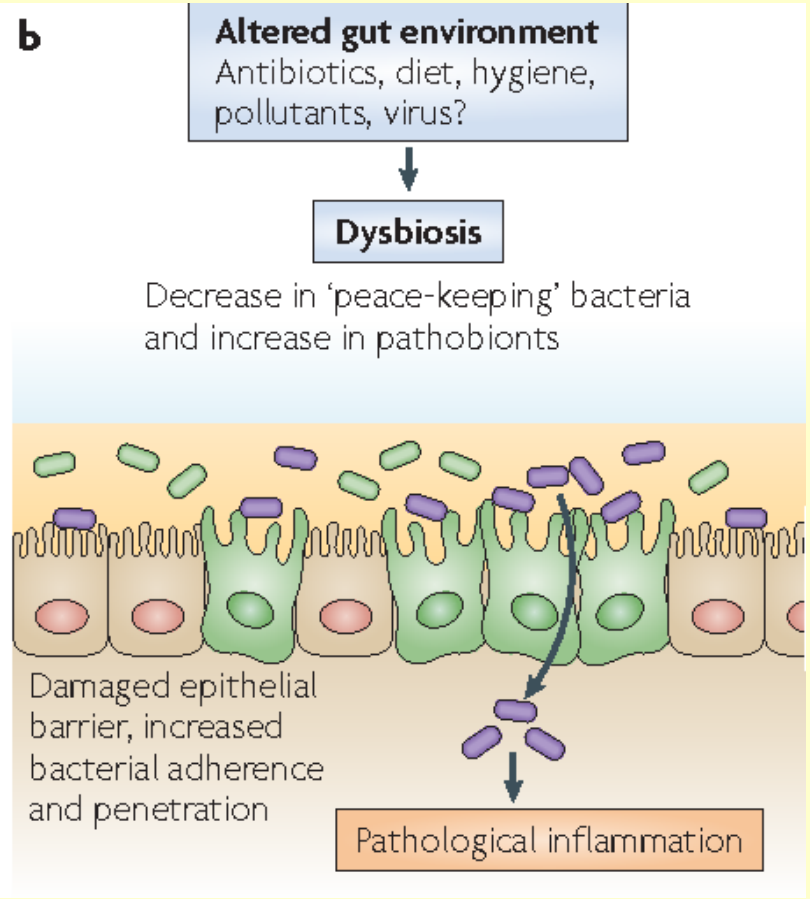


Impact of an Altered Gut Environment



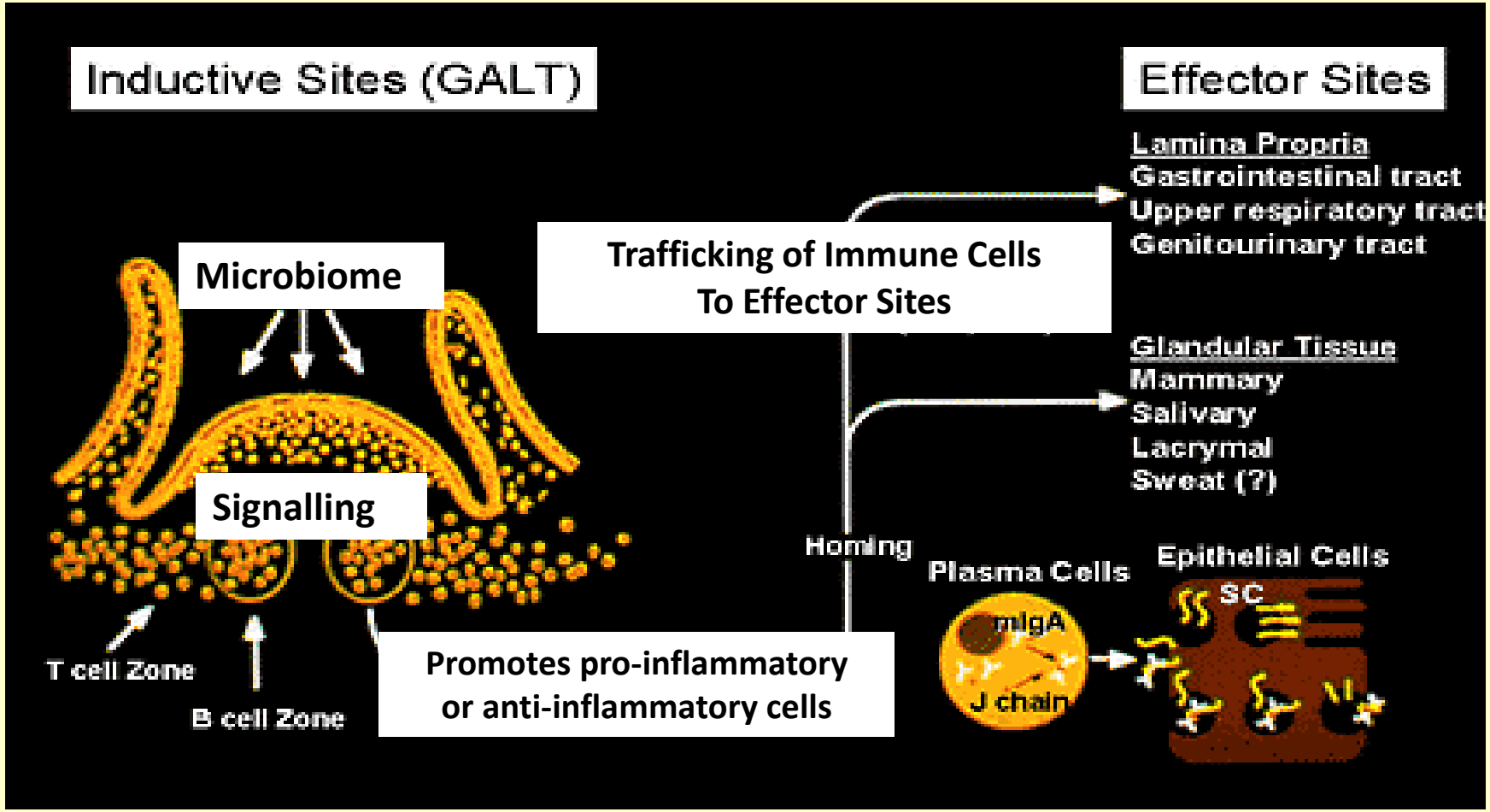
- Loss of integrity of gut barrier or inappropriate balance of bacteria ('dysbiosis')
- Associated with 'leakage' of bacteria from the gut lumen and increased inflammatory signalling
- Promotes immune activation in lamina propria
- Causes pathological inflammation – locally and systemically

Long-term Impacts of an Altered Gut Environment



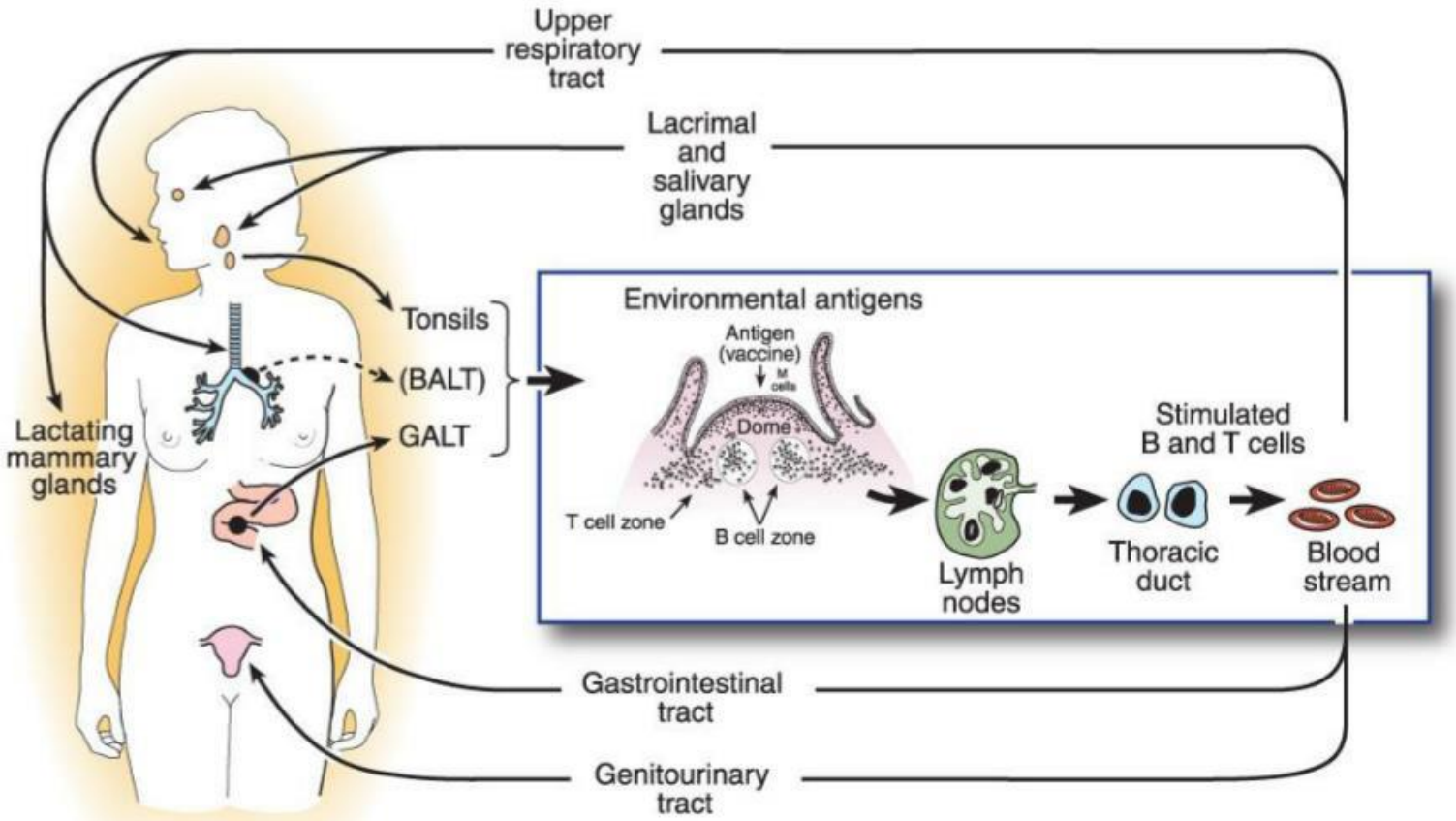
- Intestinal inflammation results in:
  - →Increased bacterial adherence
  - →Epithelial damage
  - →Increased entry of bacteria into the intestinal lamina propria
- Can also alter the balance of pro-inflammatory vs commensal bacteria
- Creates a vicious inflammatory cycle of inflammation pathobionts

The Common Mucosal Immune System



Systemic
Inflammation

The "Common" Mucosal Immune System



Role of the Microbiome in Immune Development

Early Immune System Development

- Immune cells are present from just a few weeks of pregnancy

- After birth - a baby's immune system needs to be able to fight infection, but this isn't immediate

Passive immunity

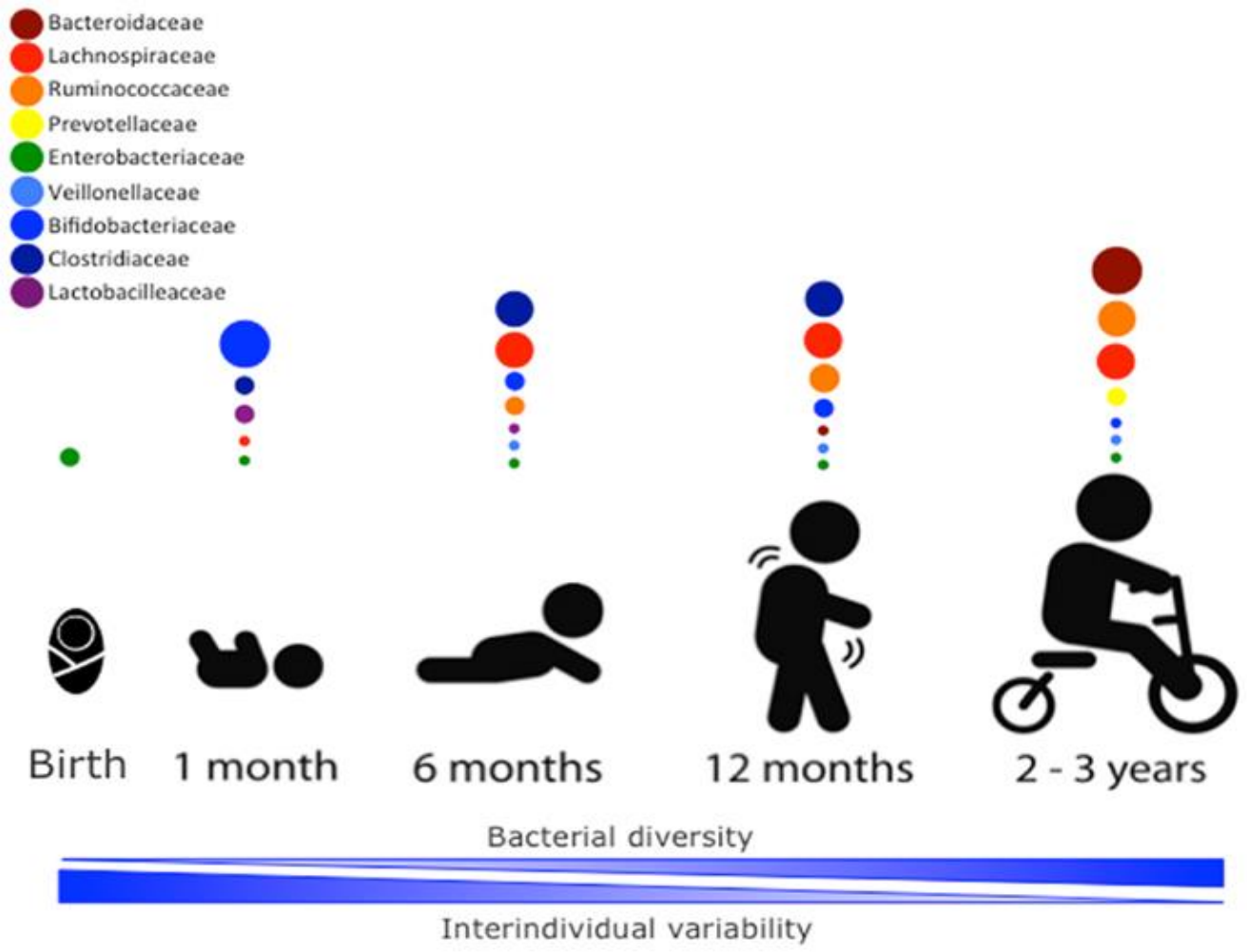
- Antibodies transferred from mum via placenta and breast milk provide passive immunity
- This protects the baby while its immune system finishes developing
- A few months after birth, the baby's immune system is able to fight infections

The Role of the Infant Microbiome

- Maturation of the gut is critical to establish a physical barrier to minimise infection

- The development of the infant immune system is closely relate to the development of the infant microbiome

Infancy: A Critical Window in the Development of the Microbiome

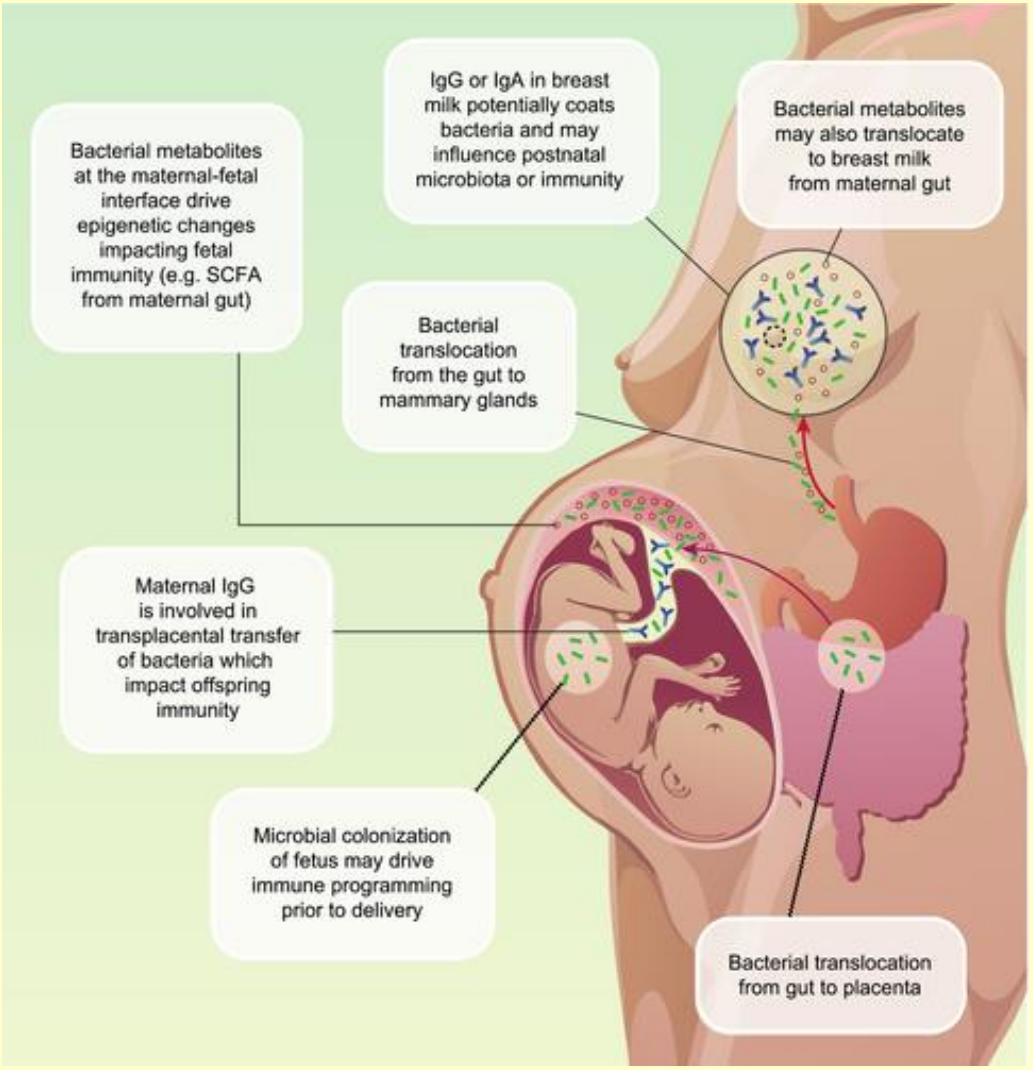


Infancy: A Critical Window in the Development of the Microbiome

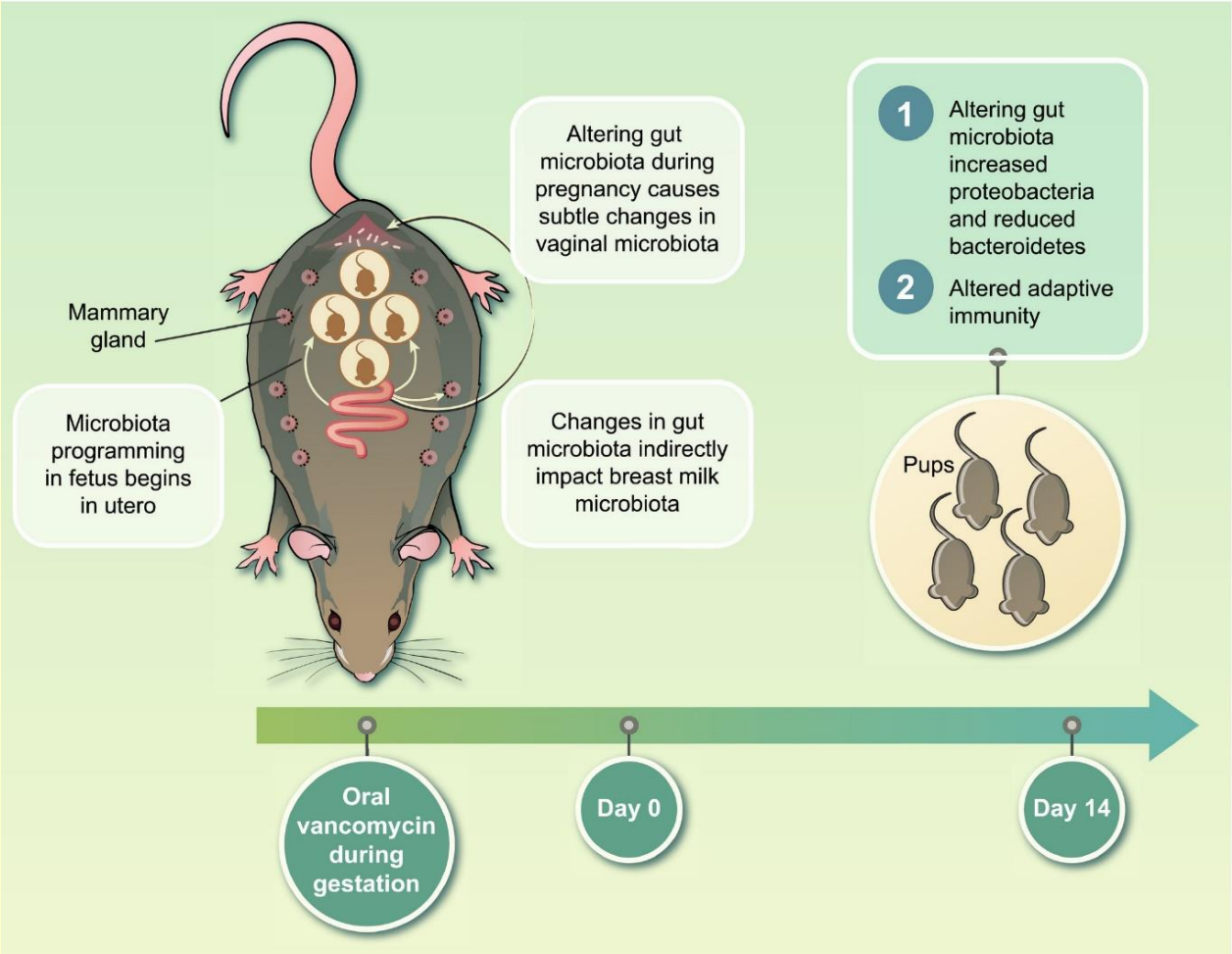
- Inappropriate colonisation in infancy:
  - → Delayed gut development
  - → Delayed immune development
  - → Increased susceptibility to infection
  - → Adverse long-term health outcomes

- Important to optimise early microbial colonisation

The Maternal Microbiome Influences Immune Development *in utero*

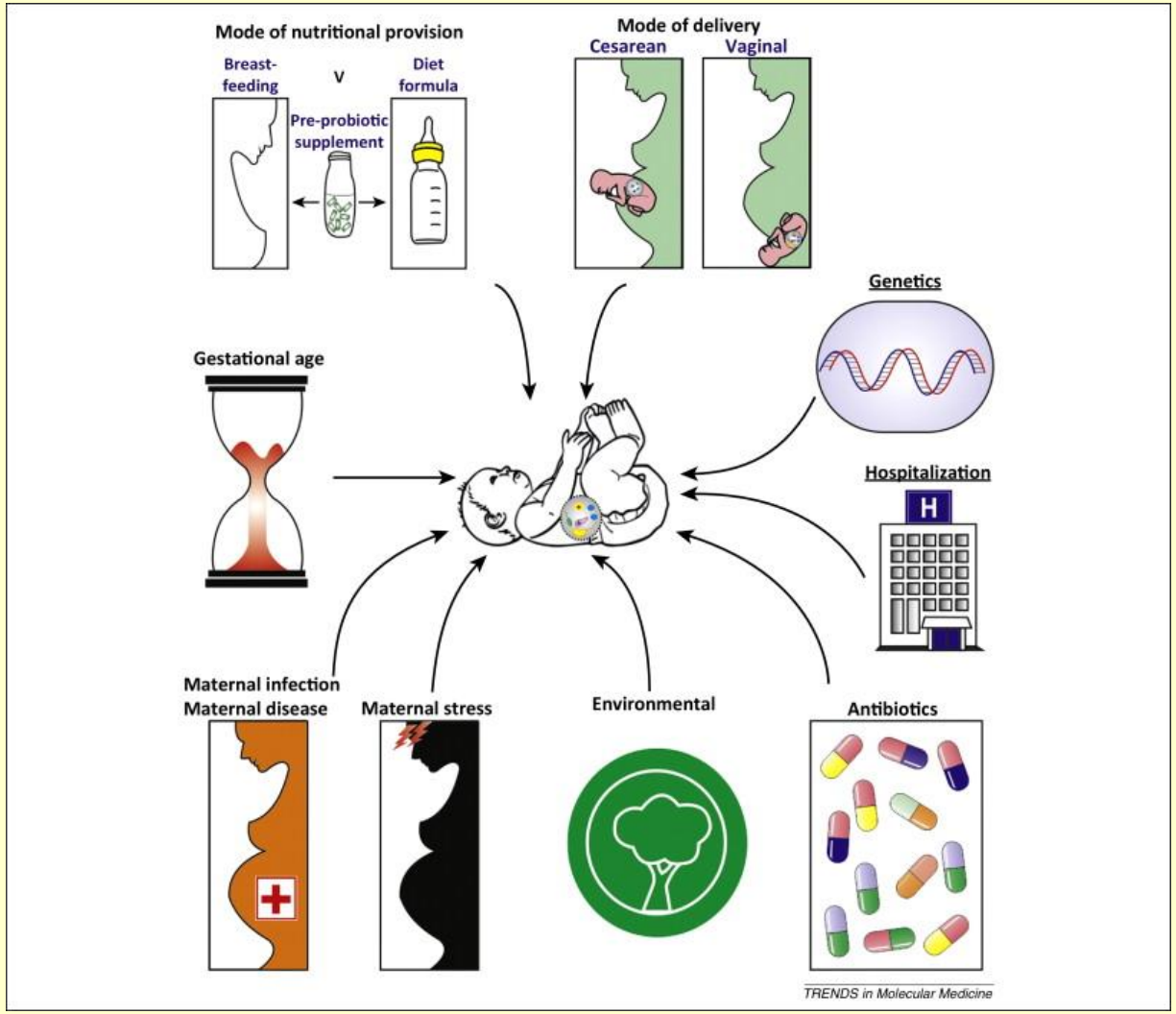


Experimental Evidence for the Link Between Maternal and Infant Microbiome



Nyangahu *et al*. *Microbiome* 2018

Factors Influencing Microbiome Development



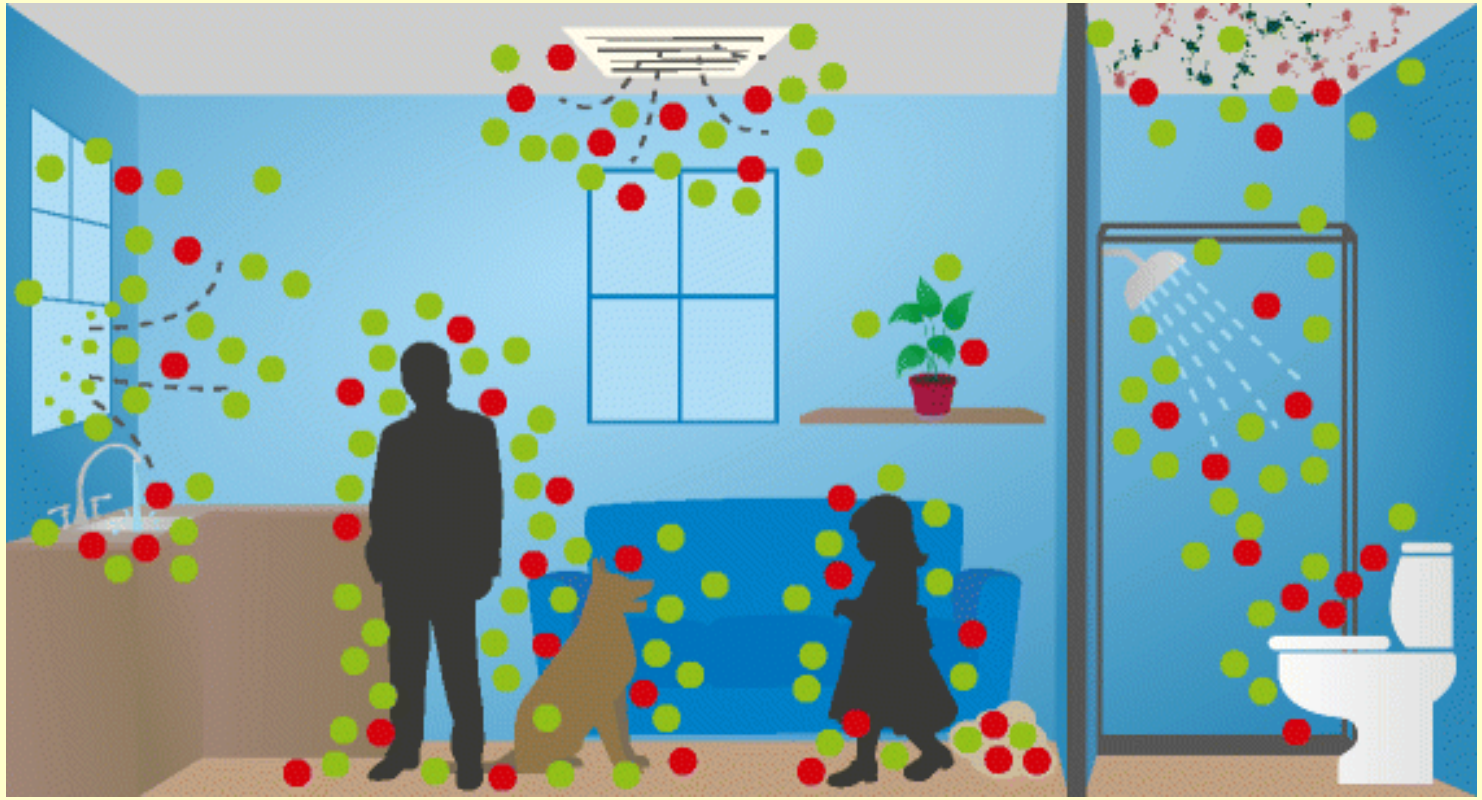
Factors Influencing Microbiome Development

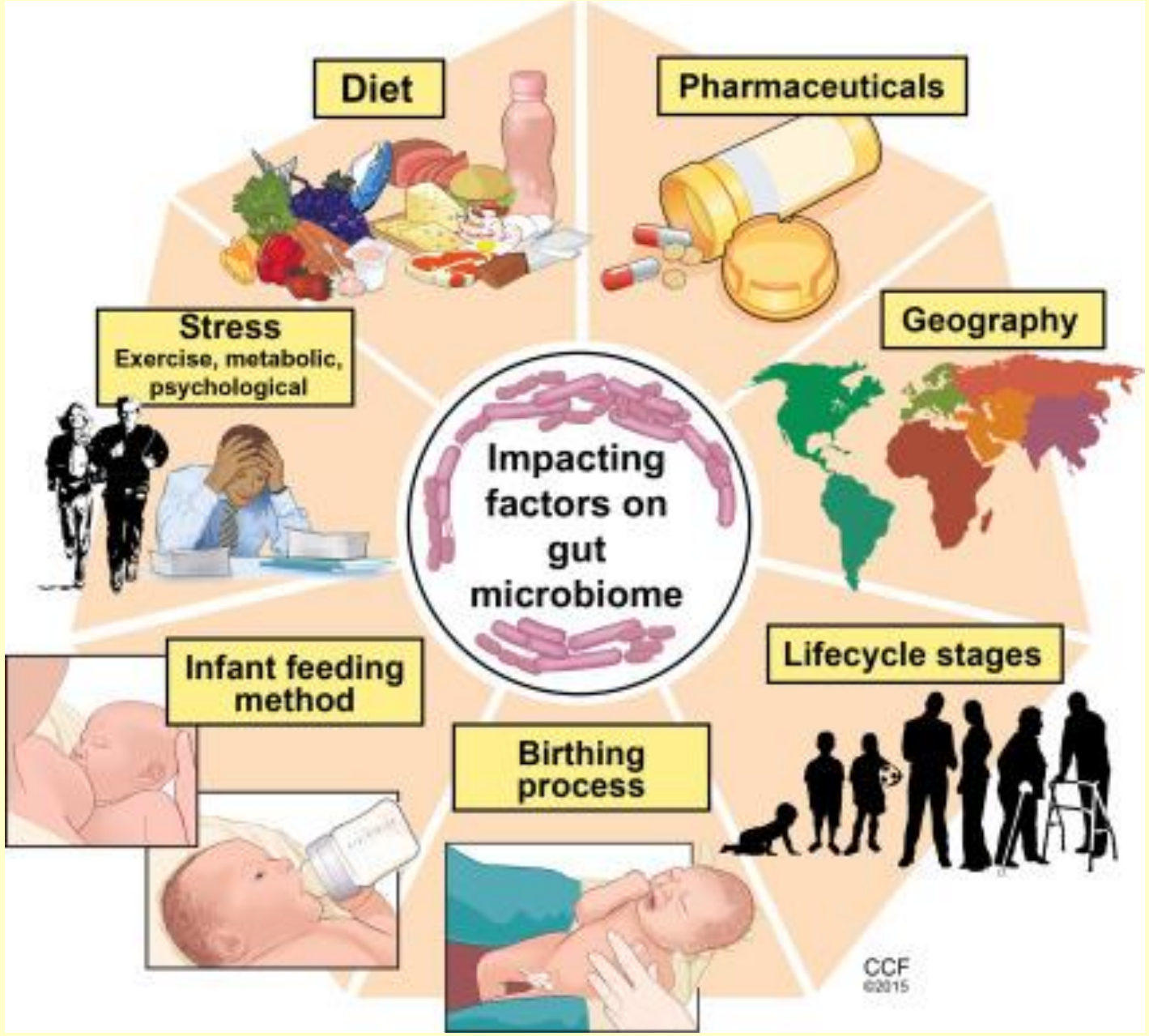
- **C-section delivery** - tends to delay development of the microbiome
- **Formula feeding** – significantly alters microbiome development and tends to be associated with increased numbers of inflammatory bacteria
- **Antibiotics** – delay microbiome development (kill off good as well as bad bacteria)
- **Probiotics** – can support microbiome development

The Breast Milk Microbiome

- Breast milk once thought to be sterile
- Now clear that it has its own distinct microbiome – and that this can influence microbiome and immune development in the breastfed infant
- Source of breastmilk microbiome still not fully understood

Factors Influencing Microbiome Composition




Diet
Pharmaceuticals
Stress
Exercise, metabolic, psychological
Geography
Impacting factors on gut microbiome
Infant feeding method
Lifecycle stages
Birthing process
CCF
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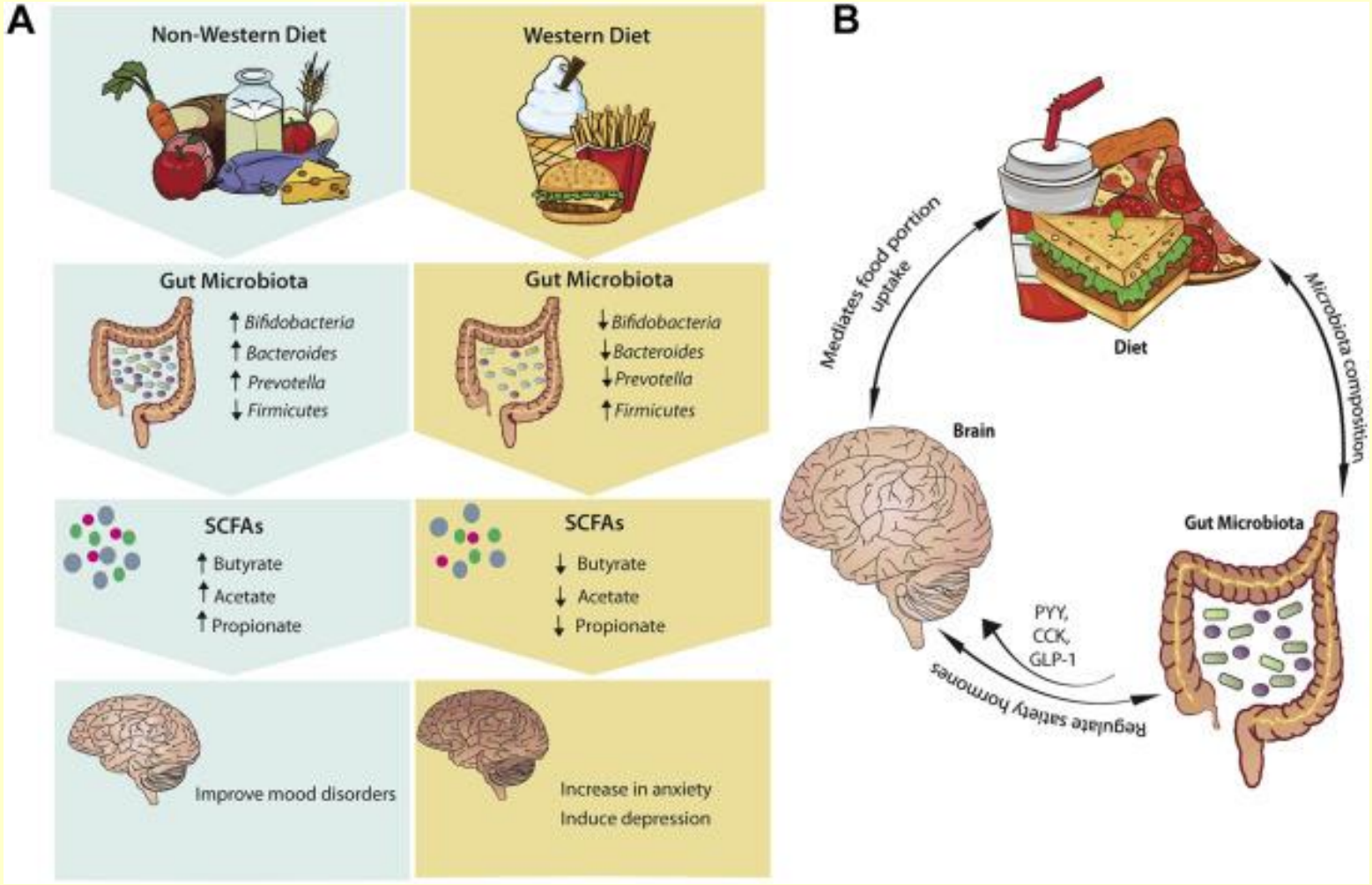
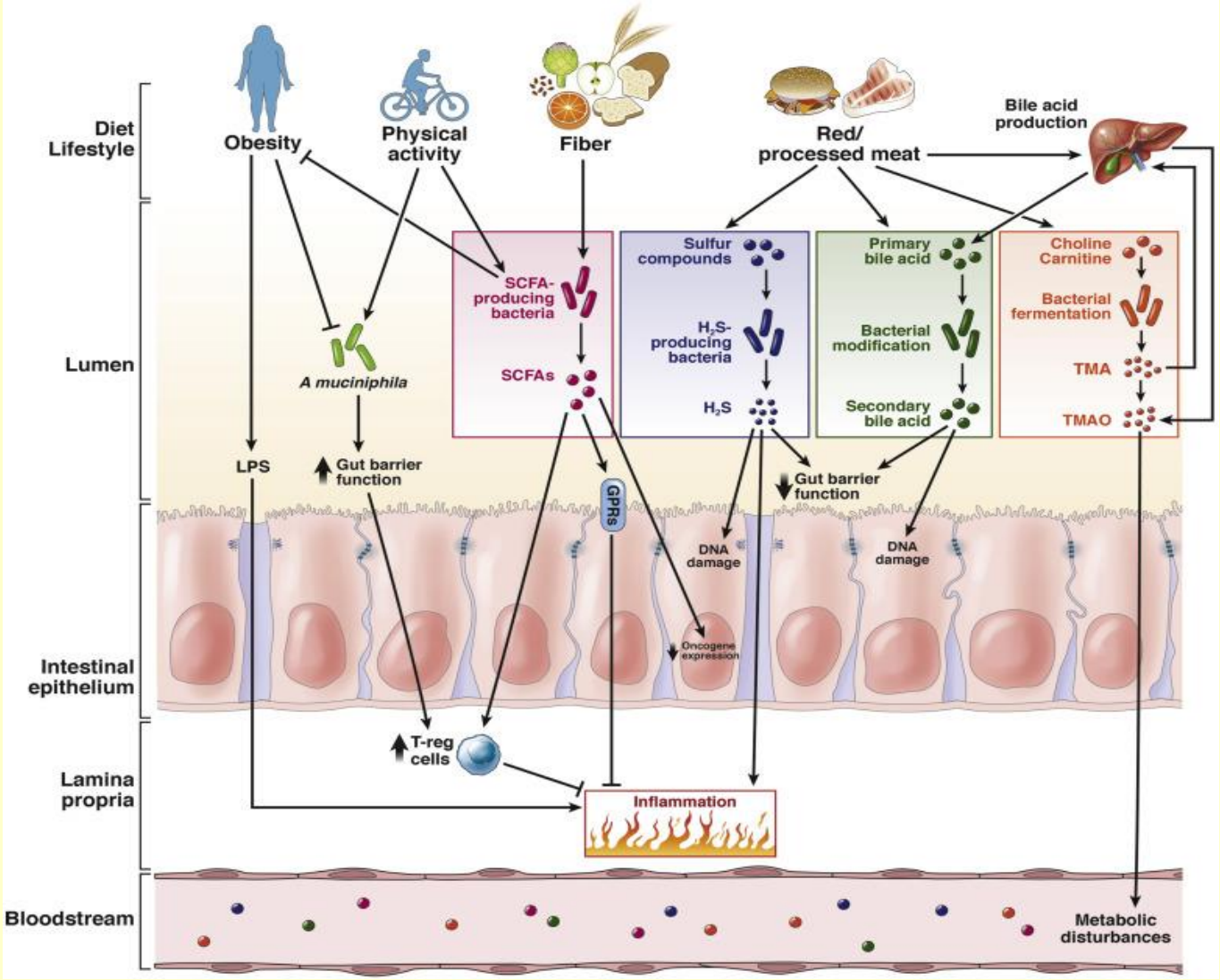
Diet Quality Impacts Microbiome Composition



The Link Between Diet/Lifestyle and the Microbiome

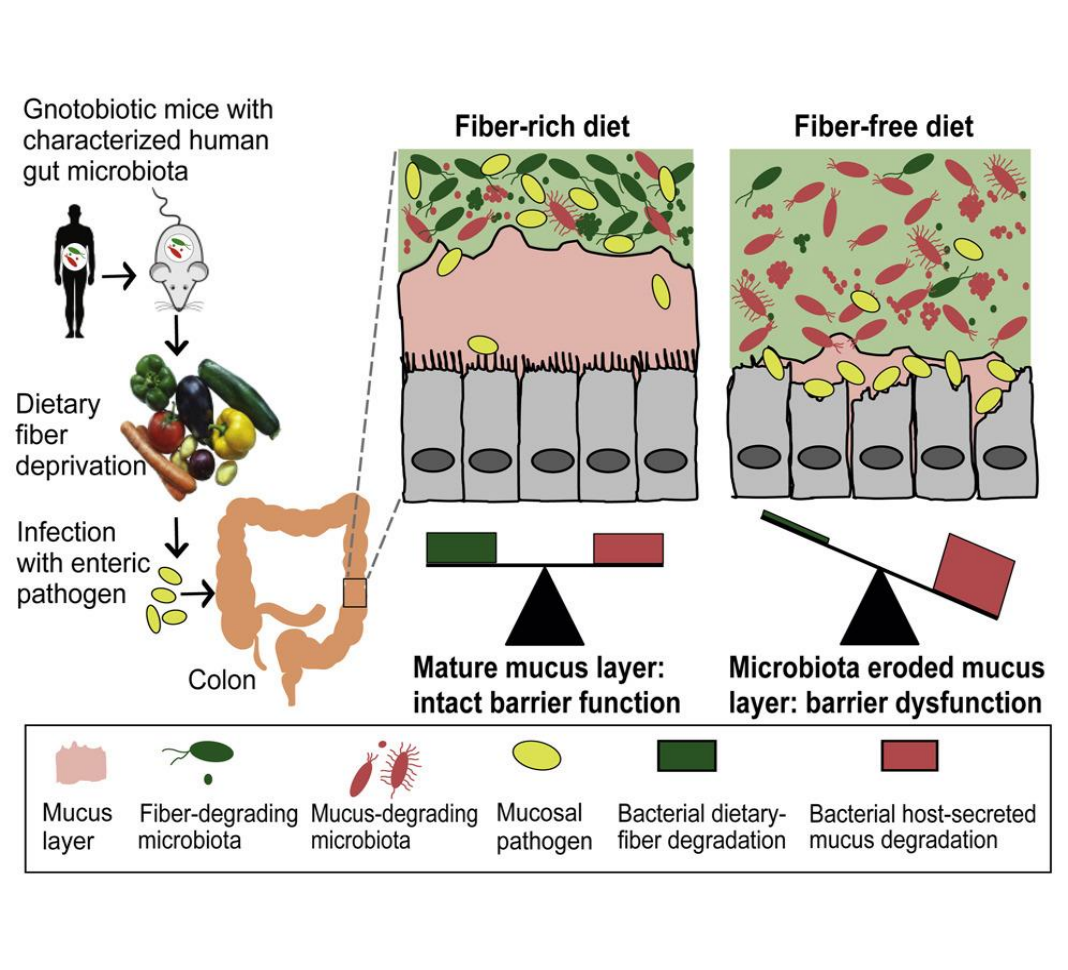


Important Dietary Components for the Gut Microbiome

- Nutritious balanced diet can support a healthy microbiome

- Key nutrients:
  - Fibre (resistant starch)
  - Probiotics & Prebiotics
  - Phytosterols
  - Polyphenols
  - Omega-3 fatty acids
  - Vitamins A, B, D, E, K
  - β-carotene

Fibre and the Microbiome



- Fibre persists in the digestive tract and reaches the lower gut
- Metabolised by specific bacteria encoding fibre-degrading enzymes
- Fibre digestion results in the accumulation of short-chain fatty acids (SCFAs) and other metabolic by-products that support positive health outcomes

PROBIOTICS vs. PREBIOTICS

Both Are Necessary for A Healthy Gut

Probiotics are the good bacteria living in your gut. They help your body break down food and support gut health, as well as overall wellness.

PLANT-BASED PROBIOTIC FOODS


NATTO


COCONUT KEFIR


SAUERKRAUT


TEMPEH


KIMCHI


MISO


PICKLED VEGGIES (NON-PASTEURIZED)


NON-DAIRY YOGURT

Prebiotics are the food for the good bacteria. They come from the non-digestible fiber in certain foods.

PLANT-BASED PREBIOTIC FOODS


ASPARAGUS


GARLIC


BANANAS


JICAMA


CHICORY ROOT


JERUSALEM ARTICHOKE


ONION/ LEEKS


LEAFY GREENS & DANDELION GREENS

FOOD REVOLUTION NETWORK

Probiotics

- The WHO defines probiotics as “live microorganisms which when administered in adequate amounts confer a health benefit for the host”
- Probiotics:
  - Survive stomach acid and bile
  - Reach the lower gut (intestines)
  - Confer health benefits

Probiotic Foods

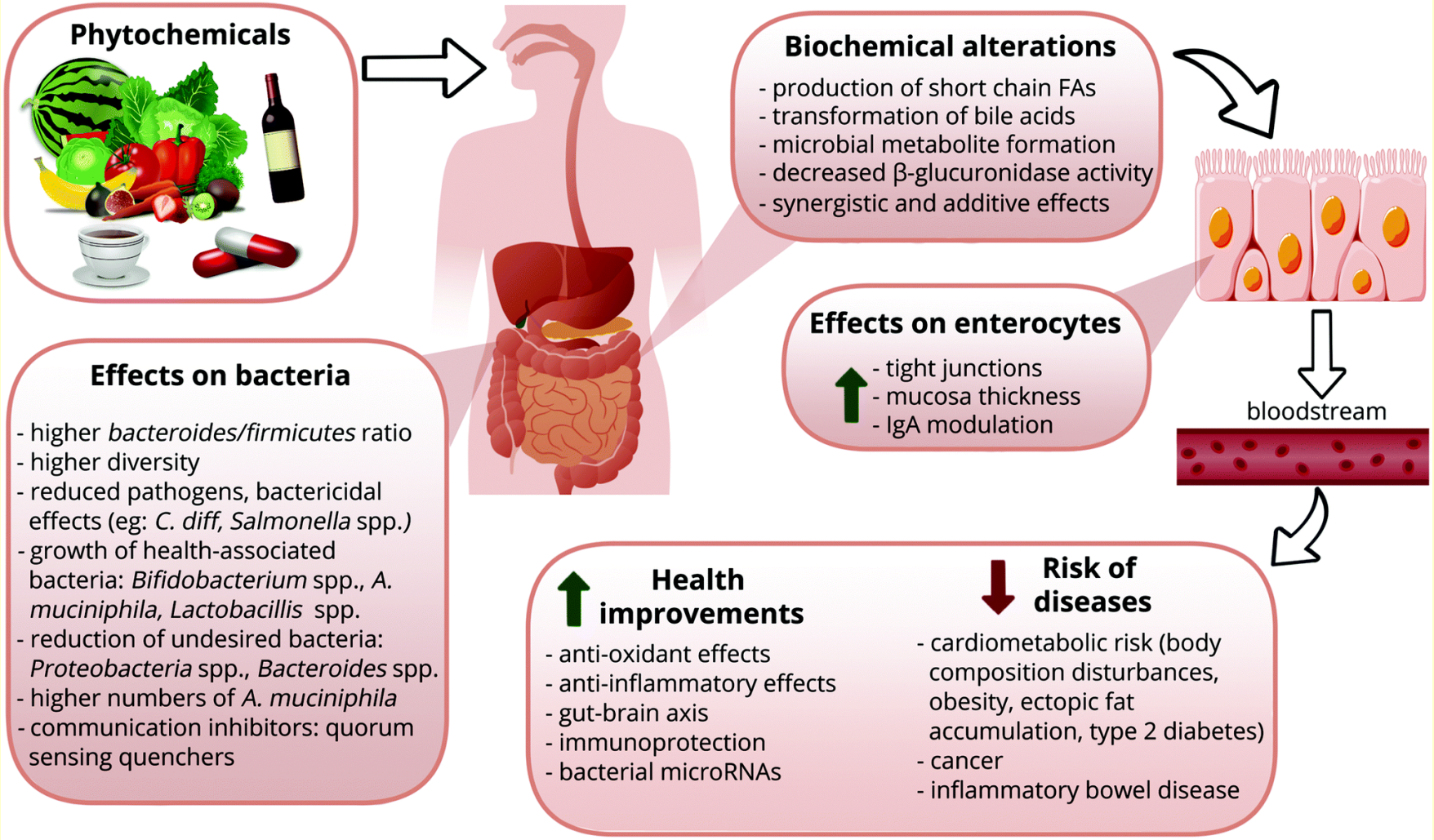
Human Milk Oligosaccharides

- Breastmilk contains about 200 different types of HMOs
- These act as prebiotics- and feed good bacteria in the gut
- Most abundant HMO in human milk is 2’FL
- Several studies show benefits to immune development of supplementing infant formulas with 2’FL
- 2’FL can also have beneficial effects in adults

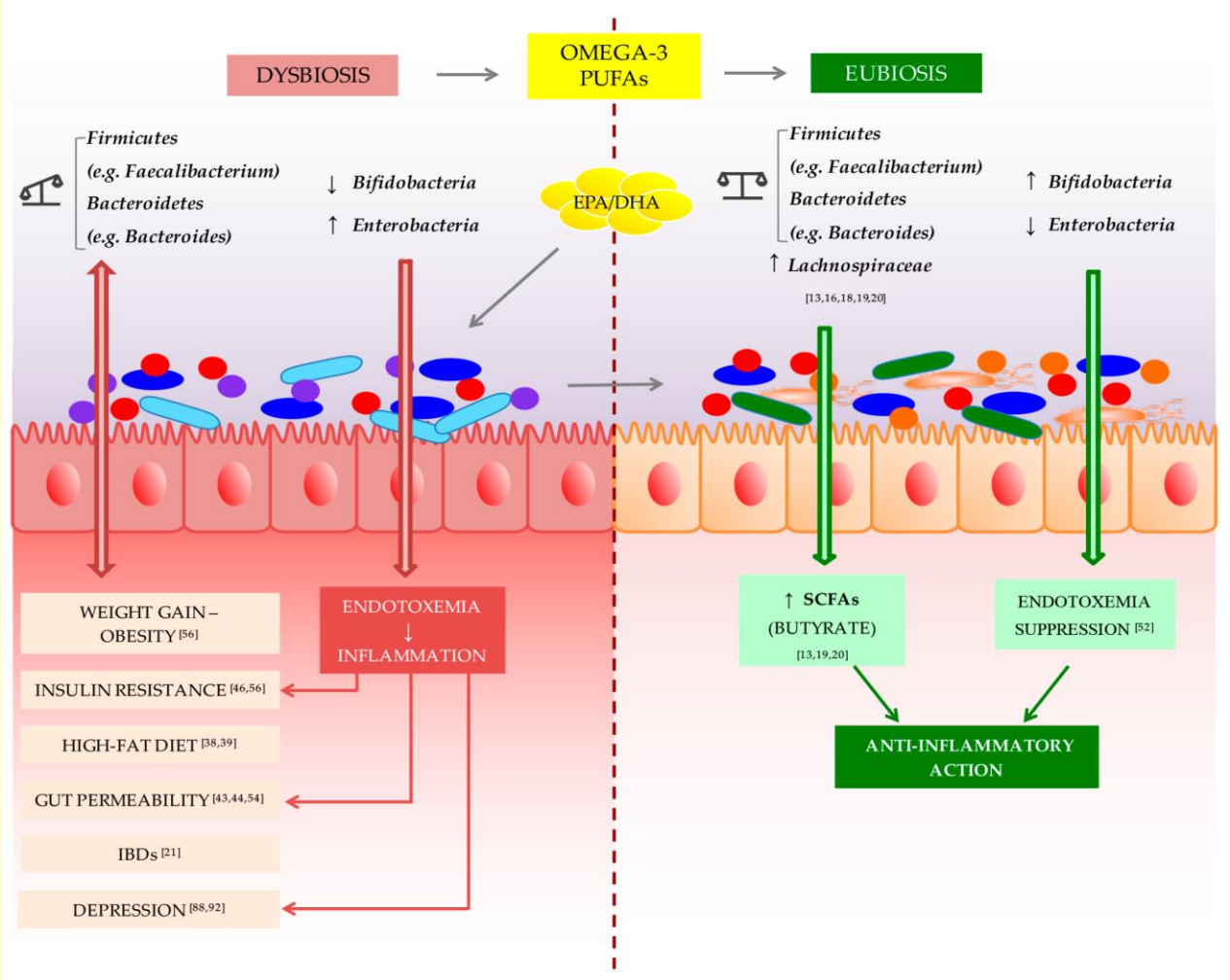
Important Micronutrients for the Gut Microbiome

- Phytosterols
- Omega-3 fatty acids
- Polyphenols
- Vitamins A, B, D, E, K
- β-carotene

Important Micronutrients for the Gut Microbiome: Phytosterols



Important Micronutrients for the Gut Microbiome: Omega-3 Fatty Acids



Important Micronutrients for the Gut Microbiome

Polyphenols

- promote a greater abundance of beneficial bacteria
- Some also exert prebiotic activity
- Gut bacteria also increase the bioavailability of the beneficial polyphenols so they can exert their health benefits

Vitamin D

- Positively affects gut microbiota composition by increasing beneficial bacteria (e.g. *Lacnobacterium*)
- Modulates the immune response, and reduces incidence/severity of asthma and allergic disease

Important Micronutrients for the Gut Microbiome: Vitamins

- Several Vitamins (A, C, D, K, B) have been shown to favourably affect microbiome composition
- Gut microbiota can also synthesise various B vitamins and vitamin K
- The gut microbiome also plays a role in synthesis of β-carotene - regulates its antioxidant effects

Summary

- The composition of the gut microbiome plays an integral role in the function of the immune system and in human health and disease
- The gut microbiome plays a central role in immune regulation – and microbiome health is critical for optimal immune health
- The development of the immune system is closely linked to the development of the infant microbiome
- Diet and environmental factors are important regulators of microbiome composition – and thus immune function and immune-related conditions