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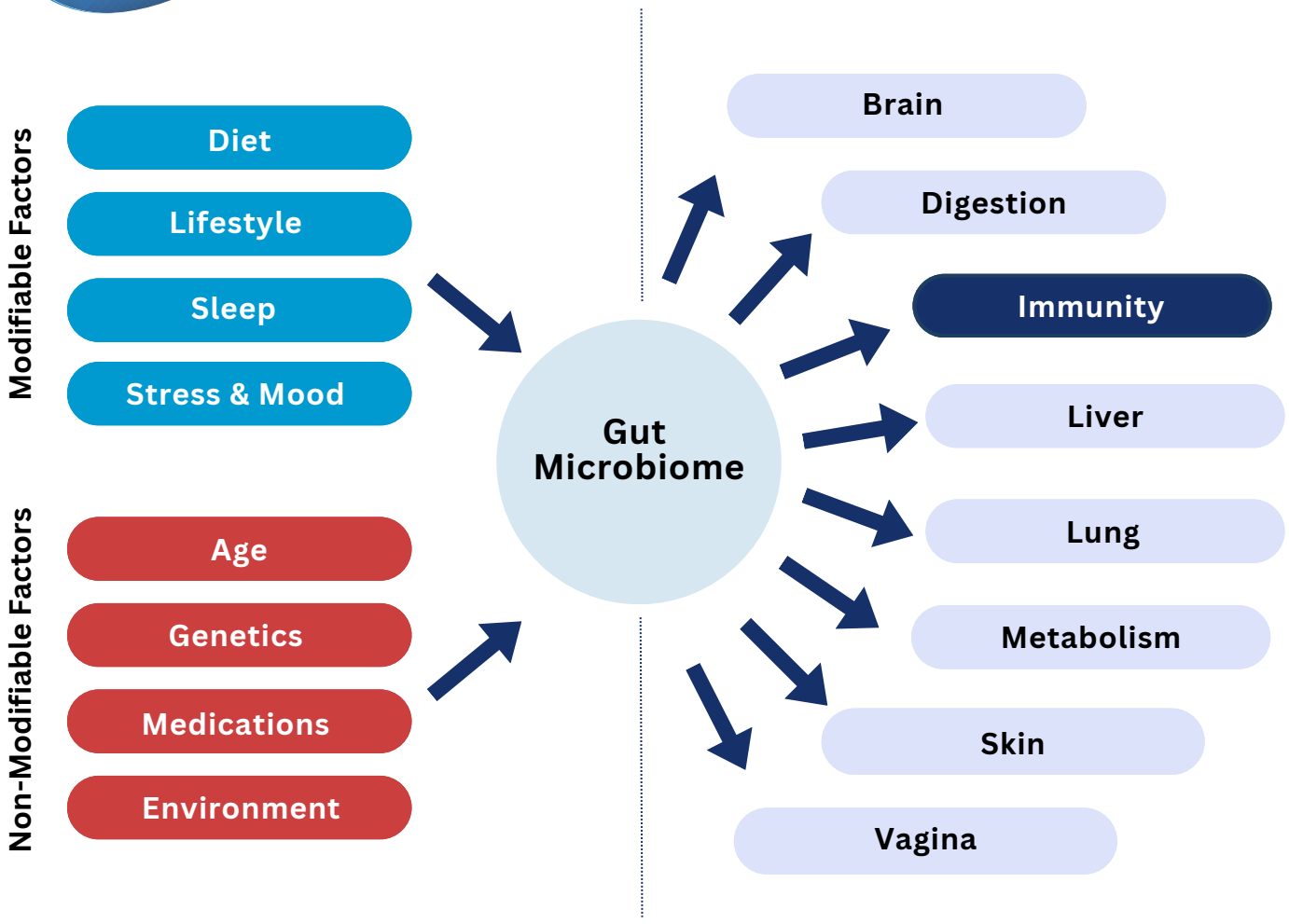
Science for Health

GUT-IMMUNE AXIS HCP RESOURCE

The gut microbiome could be considered as "the conductor of health", orchestrating with organs and systems in the human body, via different axes, to maintain homeostasis and optimal health.

The diagram below outlines some of the main axes whereby the gut communicates with other organs and systems in the body.



Gut Microbiome: The whole environment and the genetic make-up of the human microbiota (i.e., the microbes, their collective genetic material present and the by-products that they produce).

This resource explains the relationship between the gut microbiota and immune system, known as the gut-immune axis. An overview of the gut microbiota and immune system is provided before diving into the gut-immune axis, outlining the pathways of communication and how to support the body's defence system, with a particular focus on dietary approaches.

Yakult Science - making the science of the gut microbiota easy to digest

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CONTENTS

KEY POINTS

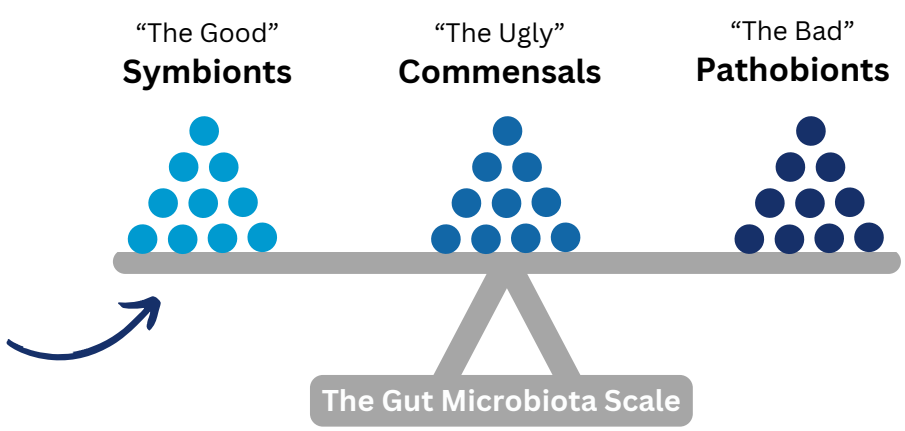
- **Good gut health** is essential to supporting the immune system.
- The gut microbiota (the trillions of microbes living along the digestive tract) play a major role in the **body's defence system**.
- **70-80%** of immune cells reside in the gastrointestinal (GI) tract.
- Via the gut-immune axis, the gut microbiota **trains, educates and constantly communicates** with the immune cells situated in the gut to support long-term immunity.
- Gut microbial **diversity** is key to a healthy gut microbiota and, in turn, a healthy immune system. Many modifiable (e.g., diet, physical activity) and non-modifiable factors (e.g., age, genetics) influence gut diversity.
- An **imbalanced gut microbiota** may have system-wide effects and contribute to poor immune health.

GUT MICROBIOTA

What is the gut microbiota?

The gut microbiota is the **collection of microbes** (e.g., bacteria, archaea, fungi and viruses) living throughout the **gastrointestinal tract**. Everyone has a **unique** gut microbiota.

There is no core "healthy" microbiota that is common to all individuals. Instead, a gut microbiota is considered to be optimal when balanced (a state called **symbiosis**). A balanced gut microbiota is important for supporting immunity.



IMMUNE SYSTEM

What is the immune system?

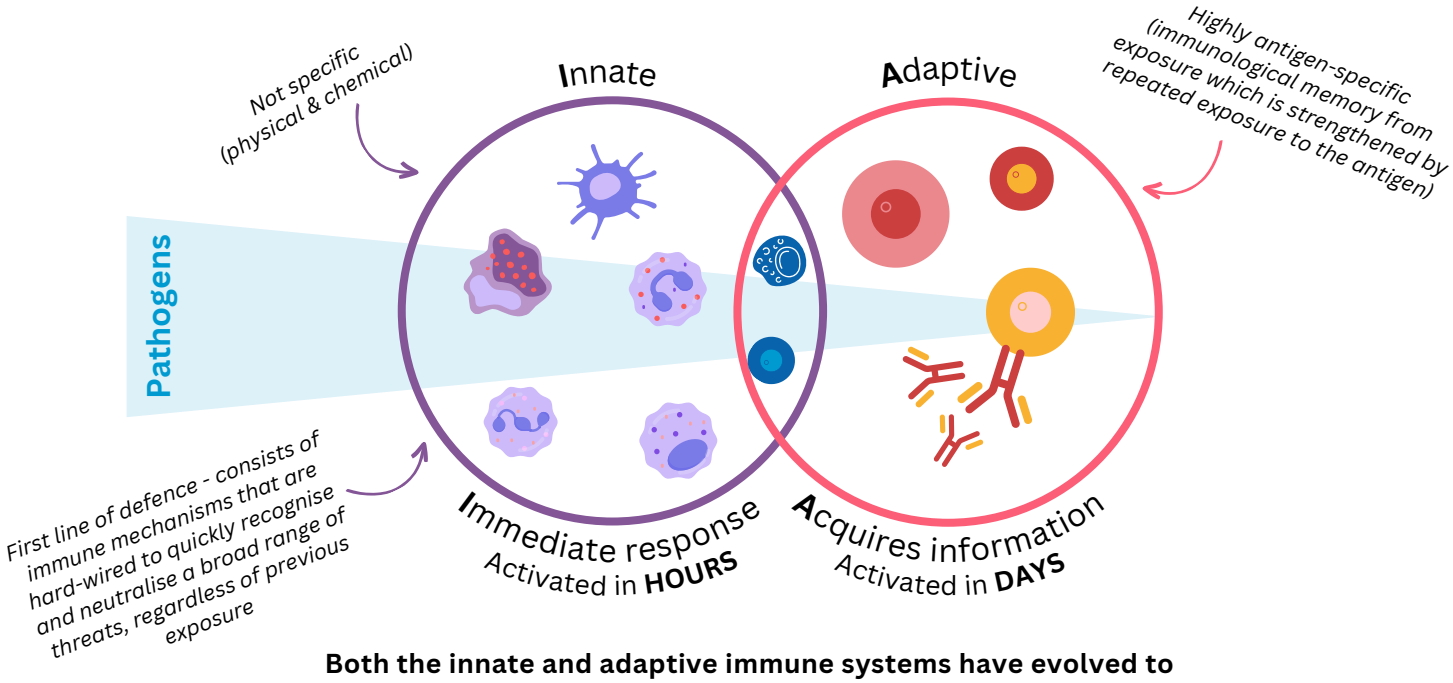
The immune system is the body's natural defence mechanism and comprises of two systems – the **innate** and **adaptive** immune responses.

It is a complex network of organs, cells and proteins that **defends the body against infections and viruses**, whilst protecting the body's own cells.

As long as your immune system is running smoothly, you don't notice that it's there. But if it stops working properly – because it's weak or can't fight particular germs – you can become unwell.

The goal should always be a 'balanced' immune system.

Innate & Adaptive Immune Responses



Both the innate and adaptive immune systems have evolved to require microbial interactions during their development.[1–3]

FACT CHECKER

MYTH: ***"It's good to boost our immunity"***

THE FACTS: Whilst we want to support our immune system to ensure it is functioning optimally, "boosting" it is undesirable.

When the immune system overreacts or underreacts this can cause health problems. Ideally, the immune system should be in a healthy, balanced state to maintain normal functioning, ready to respond to infections as needed. Overstimulated immune cells may lead to chronic inflammation, allergies and autoimmune diseases.[4]

ABOUT THE GUT-IMMUNE AXIS

Our gut health and immune health are closely linked, meaning an imbalance in one can affect the other.

GUT HEALTH

Trainer, mediator & regulator of host immunity

IMMUNE HEALTH

Regulator of microorganism colonisation (harmless vs harmful microbes)

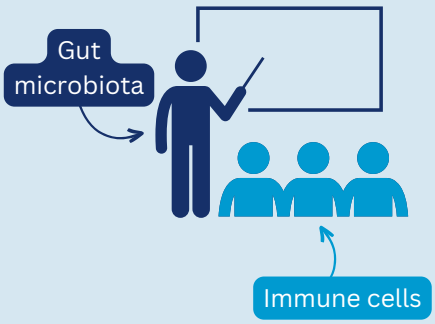
How do the gut and immune system communicate?

The gut-immune axis involves intimate **bidirectional communication** between the **commensal bacteria microbiota** and **immune system**. Research shows commensals and their by-products (e.g., short-chain fatty acids) have an important role in immune development and homeostasis, and communicate with immune cells via **direct and indirect pathways** (see page 4). Simultaneously, the immune system maintains host-microbe symbiosis and regulates healthy microbe colonisation (see page 4).[3,5–8]

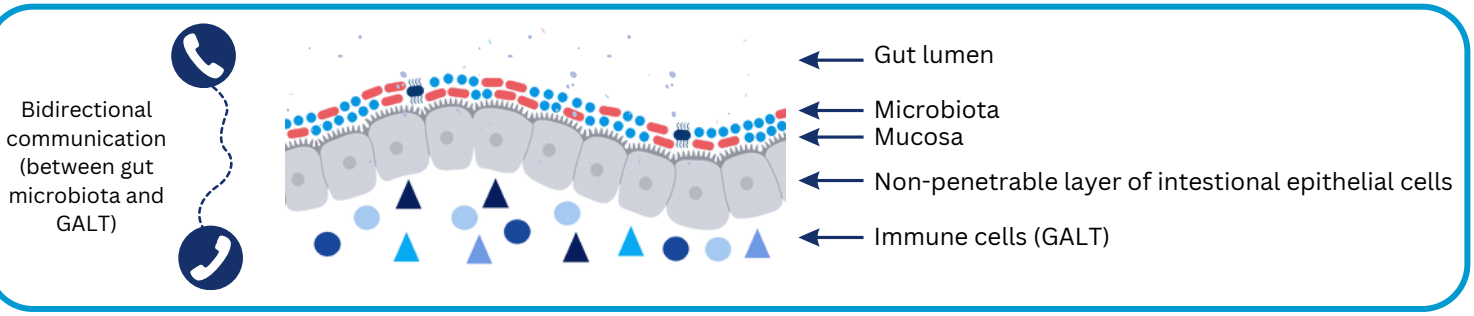
Role of GALT

Gut-associated lymphoid tissue (GALT) is the largest immune organ in the body and consists of an extensive network of innate and adaptive immune cells. GALT forms an important part of the immune response by **protecting the body from foreign pathogens** (e.g., viruses), while **allowing tolerance to non-pathogenic microorganisms** (e.g., commensals) and dietary proteins.[4]

70-80% of immune cells are in the gut[5–7]



However, without the gut microbiota, the GALT (and thus the immune system) would be inefficient at identifying and defending the body against harmful pathogens. Evidence suggests that an **imbalanced gut microbiota** (a state called **dysbiosis**) can lead to a "poorly trained" immune system.[9–10] For example, it could lead to the immune system overreacting to "innocent bystanders" (e.g., proteins in certain foods causing an allergy) or underreacting to harmful "real culprits" (e.g., a virus resulting in contracting an upper respiratory tract infection).



COMMUNICATION PATHWAYS

There are many mechanisms by which the commensal gut microbiota and immune cells communicate and interact with one another.[3,5–8]

1. **The gut microbiota indirectly supports the immune system by optimising food digestion** (and thus ensuring the full nutritional benefits are obtained from foods consumed) via:
   - **Fermentation of dietary fibre**, generating metabolites such as short-chain fatty acids (SCFAs, a type of postbiotic) - see below.
   - **Synthesis of vitamins** e.g., vitamin K, biotin, folate and vitamin B12 (which are important for the maintenance of normal function of the immune function).
   - **Absorption of nutrients** e.g., calcium, magnesium and iron.

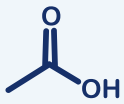
2. **Gut microbiota supports biotransformation** whereby toxic chemical compounds are biochemically modified into less toxic forms.

3. **Gut epithelial cells, reinforced by a mucus lining, provide a barrier** to bacterial invasion. This mucus lining also retains antimicrobial substances e.g., secretory IgA (an antibody and key feature of the mucosal immune system).

ROLE OF SCFAs IN THE GUT-IMMUNE AXIS[7,11–13]

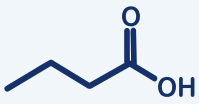
Short-chain fatty acids (SCFAs) are **by-products from gut microbiota fermentation of non-digestible dietary fibre** e.g., acetate, butyrate, propionate and lactate. SCFAs are amongst the most well-researched postbiotics and have been shown to:

- Provide energy to gut epithelial cells
- Act as an anti-inflammatory agent
- Help to maintain layers of mucus and secretory IgA to prevent pathogens entering the bloodstream
- Generate regulatory T-cell production, function and maturation
- Support intestinal homeostasis
- Ensure colonisation resistance



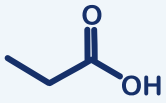
Acetate

- Regulates pH of gut
- Nourishes bacteria which produce butyrate



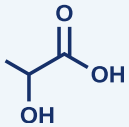
Butyrate

- Main energy source for gut epithelial cells
- Supports integrity of barrier thus preventing leaky gut
- Balance inflammation



Propionate

- Regulates inflammation
- Stimulates satiety via release of hormones peptide YY and GLP-1



Lactate

- Maintains immune function
- Protects against opportunistic bacteria
- Acts as feed for beneficial bacteria

GUT-IMMUNE AXIS THROUGHOUT LIFE

This flowchart describes the development of the immune system and compositional changes in the gut microbiota throughout life. Early-life microbiota can determine and predict ↑ or ↓ risk of developing certain health conditions (e.g., allergies, autoimmune conditions and inflammatory disease) later in life.[14–16]

Up to **~3 years** is the **critical window of opportunity** to modulate the GM composition with greatest intra- and inter-variability. After this age, the microbiota is more **stable** and **mature** (40%-60% similarity with the adult microbiota).[17–19]

Pregnancy: Maternal microbiota is the major influence on neonatal GM. Immune cells have receptors for many of the key hormones involved in pregnancy (e.g., oestrogen and progesterone).[20]

Birth delivery mode: Impacts neonatal GM. Babies born by vaginal delivery show increased *Bifidobacterium*,[21–22] which is associated with a lower risk of childhood infections, atopic disorders, and obesity.[23–24]

Milk source: Influences infant GM.[25–26] Greater amounts of *Bifidobacterium* and *Bacteroides*, and lower amounts of *Streptococcus* and *Enterococcus* are seen in breastfed babies compared to those consuming formula milk.[27]

Childhood: Increased hygiene measures and broad-spectrum antibiotic usage reduces GM.[28–29]

Adolescence/ adulthood: GM and immunity is dependent on diet and lifestyle factors.[30]

Menopause: GM becomes less diverse and reflects the male gut microbiota.[31] Changes to immunity either directly (e.g., elevated inflammatory serum markers) or indirectly (e.g., poor sleep, changing appetites), are largely owed to oestrogen deprivation.[32–33]

Older adults: Innate and adaptive immune function, as well as GM diversity, decline with age.[34]

Environment: GM is influenced by those you live with (including pet ownership) and those in the same household will have a more similar microbiota.[35–36] Exposures such as pollution and pathogens will also affect GM.[37–39]

GM = Gut Microbiota

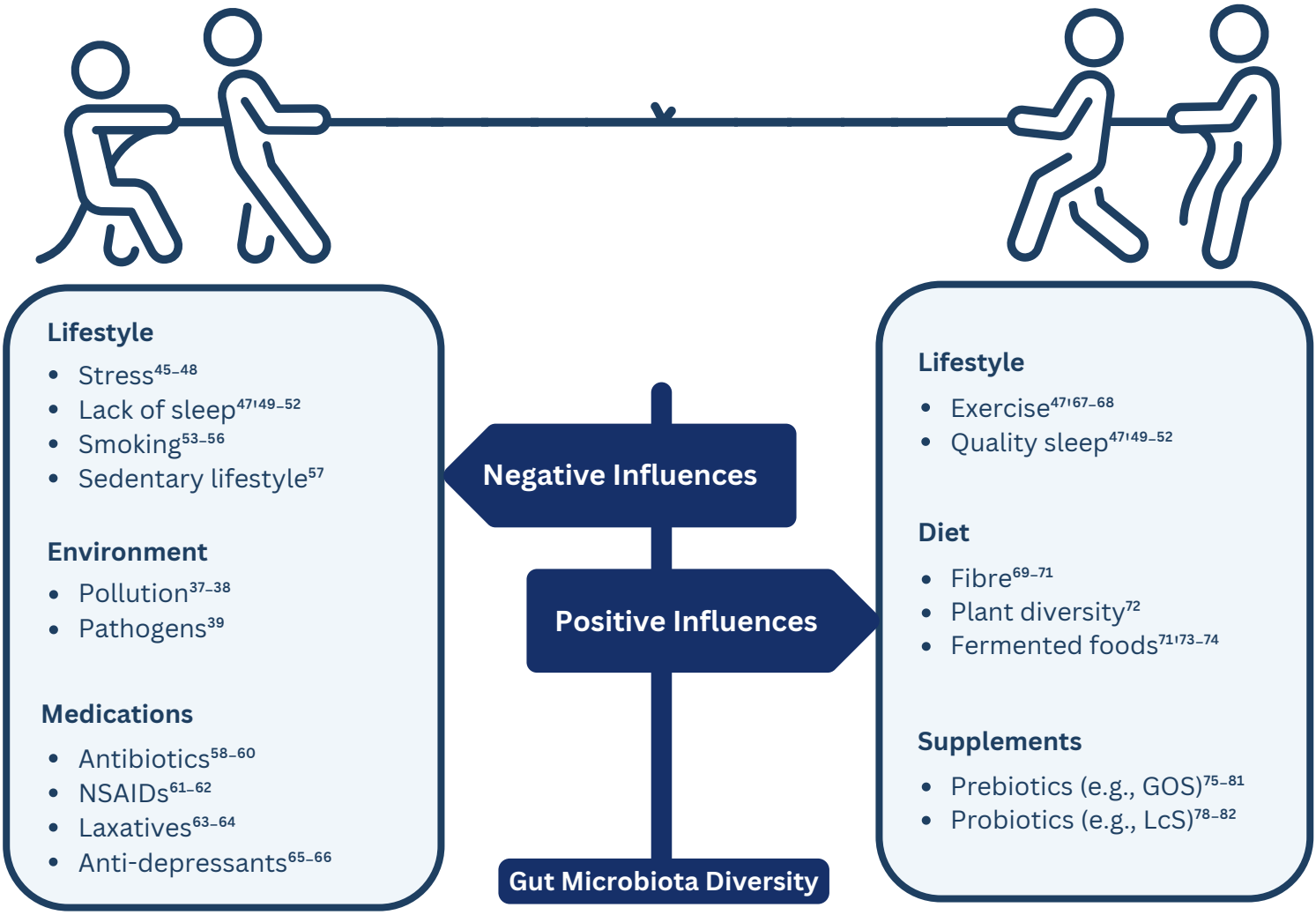
HOW TO SUPPORT THE GUT-IMMUNE AXIS

Good gut health is essential to supporting the immune system. The term gut health has been defined as the "absence of gastrointestinal symptoms (e.g., abdominal pain, diarrhoea) and disease (e.g., inflammatory bowel disease, colon cancer)".[40] However, microbiology research focuses on the composition of the gut microbiota and its role in health.

Although it isn't possible to define a "healthy" microbiota, a **diverse gut microbiota** is associated with health and longevity.[41] A diverse gut microbiota has also been associated with positive immune health outcomes.[3] Alternatively, gut dysbiosis (i.e., imbalanced gut microbiota) induces immune dysregulation.[42–43]

There are a number of **factors** (modifiable and non-modifiable) which **affect the diversity** of the gut microbiota and, in turn, **the immune system** (see image below).

Diet and lifestyle choices can promote immune health by supporting the gut microbiota.[44]



NSAIDs; Non-steroidal anti-inflammatory drugs

With age, digestion and nutrient absorption are altered and the immune system weakens, all of which can lead to a decreased diversity of the gut microbiota.[83] Genetics can also affect the microbes that live in the gut.[44] In addition, composition of the gut microbiota can fluctuate based on the time of year (e.g. summer or winter), ethnicity, geography, urbanisation and culture.[84–86]

IMPORTANCE OF DIET FOR SUPPORTING THE GUT-IMMUNE AXIS

Animal studies have provided insight into the complex interplay between diet, the gut microbiota and immune function.[83–84]

When it comes to immunity, diet and the gut we can connect the three corners of the triangle:

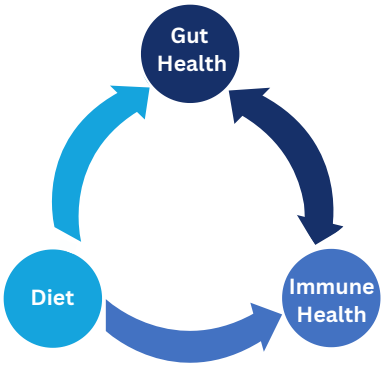
1) **Diet affects gut health**

2) **Diet affects immunity**

3) **Gut health affects immunity**

4) **Immunity affects gut health**

5) **Diet affects gut health which affects immunity**



THE POWER OF NUTRITION

Food choice is key to shaping the gut microbiota – it is one of the most important easily modifiable factors determining which bacterial species reside in the gut.[89] The gut microbiota composition can be altered within a matter of weeks, and even days (although there is both intra- and inter-individual variation).[90] Collectively, human studies show that dietary changes can have a significant and meaningful effect on the gut microbiota composition.

Research is beginning to support the notion that manipulation of gut microbes may be a powerful means to alter diverse aspects of human health, given the integral role of the gut microbiota in immune processes.[74] As research continues in this area, diets targeting the gut microbiota to introduce or eliminate specific bacterial species, could prove a powerful avenue for realising the possibilities of improving health through nutrition.

FACT CHECKER

MYTH: ***"Eating oranges can prevent cold and flus"***

THE FACTS: Oranges are well known for their vitamin C (ascorbic acid) content with many upping their intake to prevent colds. A systematic review showed vitamin C supplementation is not effective in preventing the common cold (based on 29 studies), however it can reduce symptom duration and severity (based on 31 studies).[91] In comparison, another systematic review of 23 studies showed probiotic administration prevented the occurrence of at least one episode of upper respiratory tract infections (URTIs) and reduced the average duration of an acute URTI episode (compared to placebo).[92]

FOODS IN FOCUS

Read our **Diet Diversity Guide**

FIBRE

Dietary fibres are fermented by the gut microbiota, producing SCFAs. SCFAs play an important role in the gut-immune axis. Diets high in fibre are associated with greater microbial richness and diversity.[93] Sources of fibre include fruits, vegetables, wholegrain carbohydrates, beans and lentils, nuts and seeds, herbs and spices.

DIVERSITY

Restrictive diets can starve the gut microbiota, whereas a diet focused on adding more – more plants, more variety, and more fibre – can increase gut microbial diversity. Research has shown that those who ate more than 30 different plant-based foods per week, had a far more diverse gut microbiome compared to those who ate less than 10.[94]

MEDITERRANEAN DIET

The Mediterranean diet is characterised by an abundance of high-fibre plant foods and contains sources of omega-3 fatty acids, vitamin D and polyphenols which have been shown to increase gut microbiota diversity and support immunity.[95-101]

FERMENTED FOODS

Fermented foods (e.g., fermented milk drinks, kimchi, sauerkraut, kombucha) can be a source of live dietary microbes and are thought to support gut health. Some human studies have shown that fermented foods can play a part in modulation of the gut microbiota.[71,73-74,102]

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Scan here for our Microbiome Matters podcast

Season 6, Episode 3 - Immunity

"What we do now can really help us decades down the line. Having that long-term view of immune function is something I really encourage."

Dr Jenna Macciochi, Immunologist

Microbiome Matters Podcast (Season 6, Episode 3)

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November 2023

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