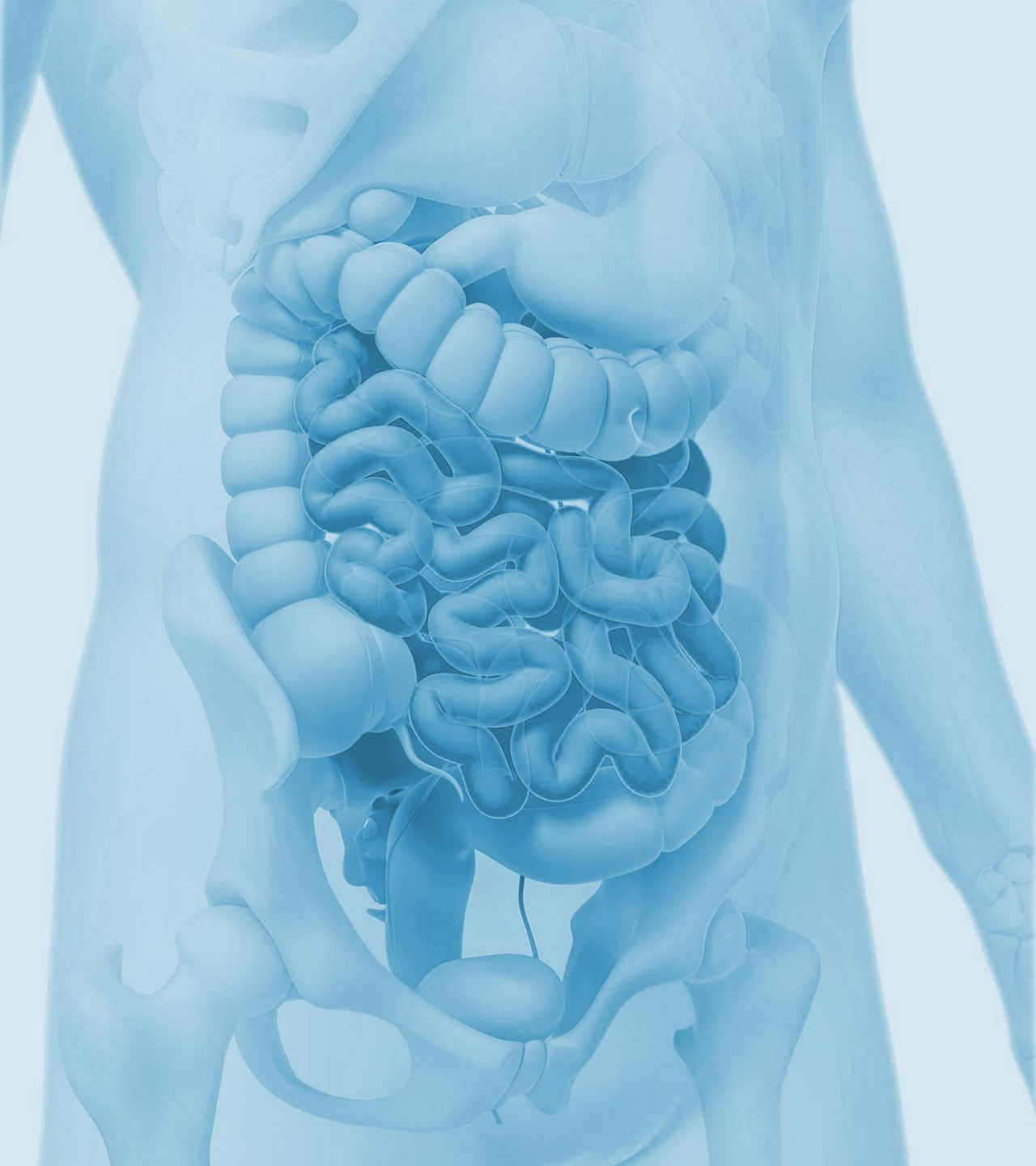




GUT MUSCLE AXIS

Start 

Section title

- Section sub-heading



Click on the chapter title to return to the main screen where all sections of that chapter are displayed.

This button will take you back to the general index of the module, from where you can access all the chapters and sections.

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Use this button to return to the help/instruction slide.

HELP



Use the navigation arrows to move the slides forward or backward.

NEXT



Note that this action affects the linear order of the module.

BACK



Instructions

In this screen you will find the instructions to navigate correctly through the module.

Remember that underlined text and the following icons mean that you can click on them to open a pop-up or navigate to a related slide.



EXTRA INFO

This button will open a large popup with extra relevant information.



CLOSE

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GUT MICROBIOTA

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Definition of gut microbiota

- All the microbes in the gut are collectively known as “gut microbiota”, and genomes associate with them represent the “gut microbiome”.¹
- The composition is highly variable among individuals but remains relatively stable over time in healthy adults.²
- These microorganisms produce a variety of metabolites from the anaerobic fermentation of exogenous dietary components and endogenous compounds generated by microorganisms and host.²



Short Chain Fatty Acids (SCFAs) result from fiber fermentation in the colon and include acetic acid, butyric acid, and propionic acid.

Did you know?

Microorganisms include bacteria, viruses, fungi, and other microbes; however, in the context of the gut microbiome, we most often refer primarily to bacteria.¹



Characteristics of gut microbiota

A healthy adult gut microbiota includes bacteria from **7-9 different phyla**.¹

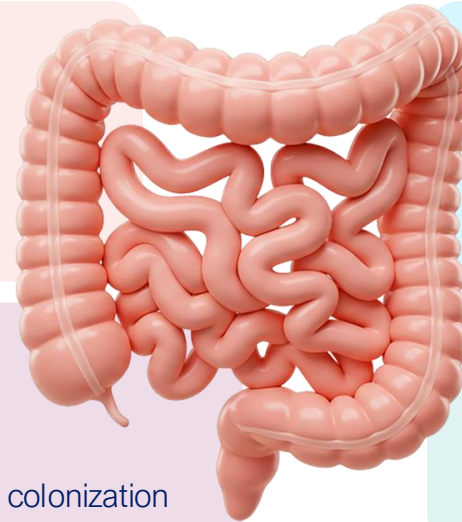
- Mostly: Firmicutes, Bacteroidetes, Actinobacteria and Proteobacteria.
- Bacteroidetes and Firmicutes account for **most dominant phyla**.
 - Older adults:
 - ↓ Bacteroidetes,
 - ↓ Firmicutes

Firmicutes
e.g., *F. prausnitzii*

- Inhibition of production of pro-inflammatory cytokines
- Butyrate production

Bacteroides
e.g., *E. coli*

- Bacteriocin production
- Protection against pathogen colonization



Proteobacteria
e.g., *B. thetaiotaomicron*

- Nutrient absorption
- Maturation and maintenance of epithelial cells

Actinobacteria

e.g., *Bifidobacterium longum*

- Improves intestinal barrier function
- Inhibits inflammation

Role of the most abundant microorganisms within the gut microbiota. Modified from reference³

Disturbances in the intestinal microbial population (Dysbiosis) ⇔ imbalance of the homeostasis ⇔ development of pathologies.²

1. Eckburg PB, et al. Diversity of the human intestinal microbial flora. *Science* 2005;308:1635-1638.
2. Yang Y, et al Microbial imbalance and intestinal pathologies: connections and contributions. *Dis Model Mech.* 2014 Oct;7(10):1131-42.
3. Maciel-Fiuza MF, et al Role of gut microbiota in infectious and inflammatory diseases. *Front Microbiol.* 2023 Mar 27;14:1098386.

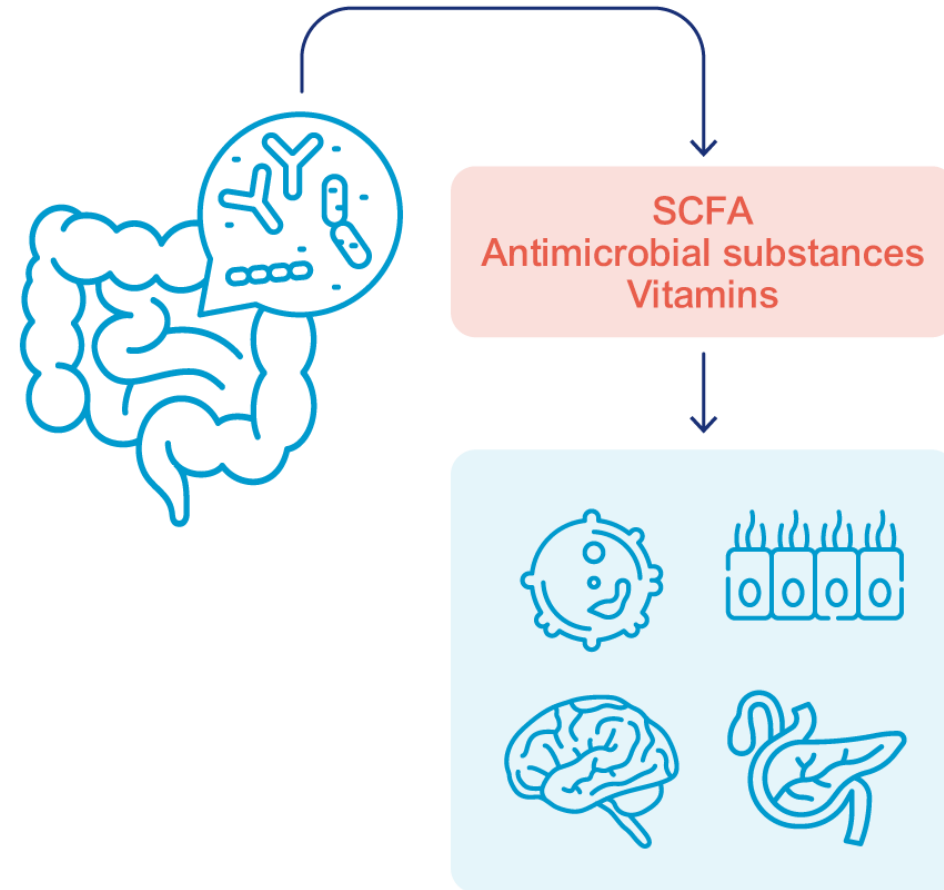
Overview of gut microbiota functions

The gut microbiota exerts a wide range of activities, such as:

- Aids in digestion and metabolism e.g., of non-digestible carbohydrates (fibers)¹
- Produces SCFA²
- Synthesizes vitamins (B vitamins, Vitamin K)²
- Produces antimicrobial substances³

These impact on multiple physiological systems, such as:

- Promoting gut barrier function⁴
- Protecting against pathogens³
- Balancing the immune system⁵
- Influencing host neurological functions e.g., cognition (gut –brain axis)⁶
- Reducing insulin resistance⁷



1. Rothschild D, et al. Environment dominates over host genetics in shaping human gut microbiota. Nature. 2018 Mar 8;555(7695):210-215.
2. Rowland J, et al. Gut microbiota functions: metabolism of nutrients and other food components. Eur J Nutr. 2018 Feb;57(1):1-24.
3. Mills S, et al. Precision Nutrition and the Microbiome, Part I: Current State of the Science. Nutrients. 2019 Apr 24;11(4):923.
4. Wiley NC, et al. The microbiota-gut-brain axis as a key regulator of neural function and the stress response: Implications for human and animal health. J Anim Sci. 2017 Jul;95(7):3225-3246.
5. Sharma A, et al. Gut microbiota in regulatory T cell generation and function: mechanisms and health implications. Gut Microbes. 2025 Dec;17(1):2516702.
6. Cryan JF, et al. The Microbiota-Gut-Brain Axis. Physiol Rev. 2019 Oct 1;99(4):1877-2013.
7. Kelly CJ, et al. Crosstalk between Microbiota-Derived Short-Chain Fatty Acids and Intestinal Epithelial HIF Augments Tissue Barrier Function. Cell Host Microbe. 2015 May 13;17(5):662-71.

Summary

- ✓ The gut microbiota, composed of trillions of microbes, varies between individuals but remains stable in healthy adults and produces metabolites through anaerobic fermentation
- ✓ Gut microbiota and its metabolites play **key roles** in:
 - **Metabolism** (fiber, bile acid, amino acid metabolism; production of SCFAs and vitamins)
 - **Protection** (immune activation, antimicrobial secretion)
 - **Structural maintenance** (mucus regulation, tight junction integrity)
 - **Downstream signaling** (immune, endocrine, neural and metabolic pathways)





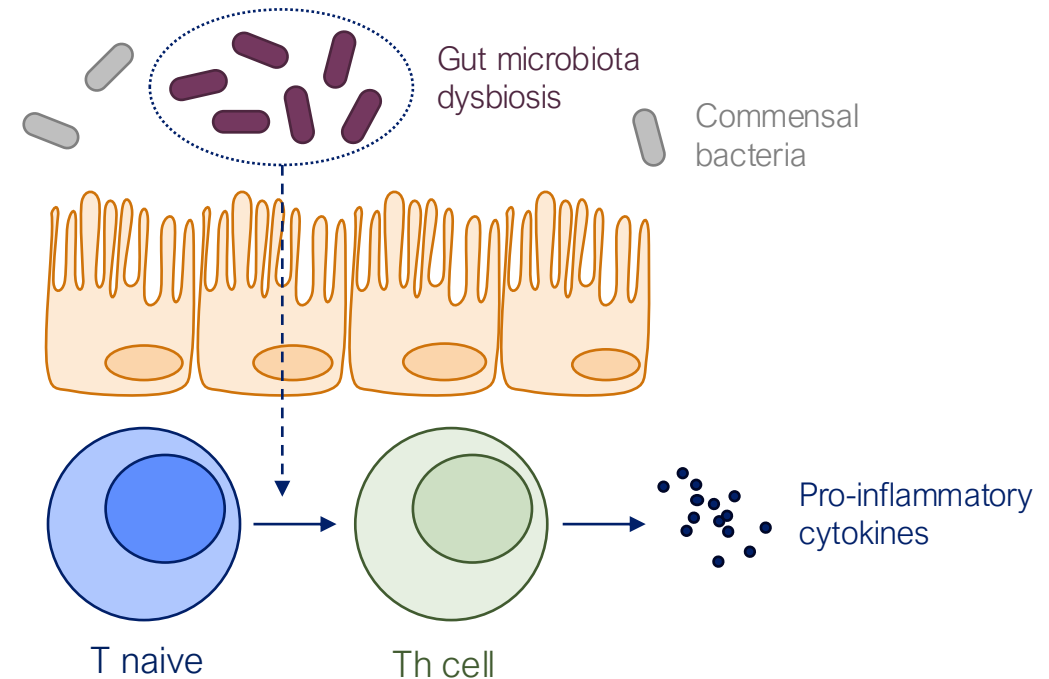
GUT MUSCLE AXIS

- [2.1. How gut microbes modulate inflammation](#)
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-

How gut microbes modulate inflammation

Gut microbes modulate inflammation in various ways:

- Producing anti-inflammatory metabolites (e.g., SCFA), which have downstream effects such as promoting **regulatory T cell (Treg)** differentiation.¹
- Maintaining gut barrier function.²
- Maintaining the immune system balance (e.g., between pro-inflammatory Th17 cells and anti-inflammatory Treg cells).³
- In dysbiosis, the microbiota may also drive Th cell responses and proinflammatory cytokine production.⁴



1. Furusawa Y, et al. Commensal microbe-derived butyrate induces the differentiation of colonic regulatory T cells. *Nature*. 2013 Dec 19;504(7480):446-50.
2. Chelakkot C, et al. Mechanisms regulating intestinal barrier integrity and its pathological implications. *Exp Mol Med*. 2018 Aug 16;50(8):1-9.
3. Belkaid Y, et al. Role of the microbiota in immunity and inflammation. *Cell*. 2014 Mar 27;157(1):121-41.
4. Maciel-Fiuza MF, et al. Role of gut microbiota in infectious and inflammatory diseases. *Front Microbiol*. 2023 Mar 27;14:1098386.

How gut microbiota metabolites modulate inflammation (1/2)

Gut microbiota–derived metabolites have properties that allow them to interact with their host’s immune system.¹



Click here to view some examples of immune-modulatory actions mediated by microbiota metabolites

The gut microbiota promotes immune tolerance.²



Immune tolerance

Is the immune system's remarkable ability to not attack the body's own cells (self-tolerance) or harmless foreign substances (like food or beneficial microbes), preventing autoimmune disease and allergies, while still fighting pathogens.²



How gut microbiota metabolites modulate inflammation (1/2)

Examples of immune-modulatory actions mediated by microbiota metabolites

Short-chain fatty acids

Help conserve integrity of intestinal mucosa and balance between Treg and Th17 cells.¹

Indole derivatives

Promote integrity of enteric epithelium inducing multiplication of intestinal goblet cells.²

Tryptophan derivatives

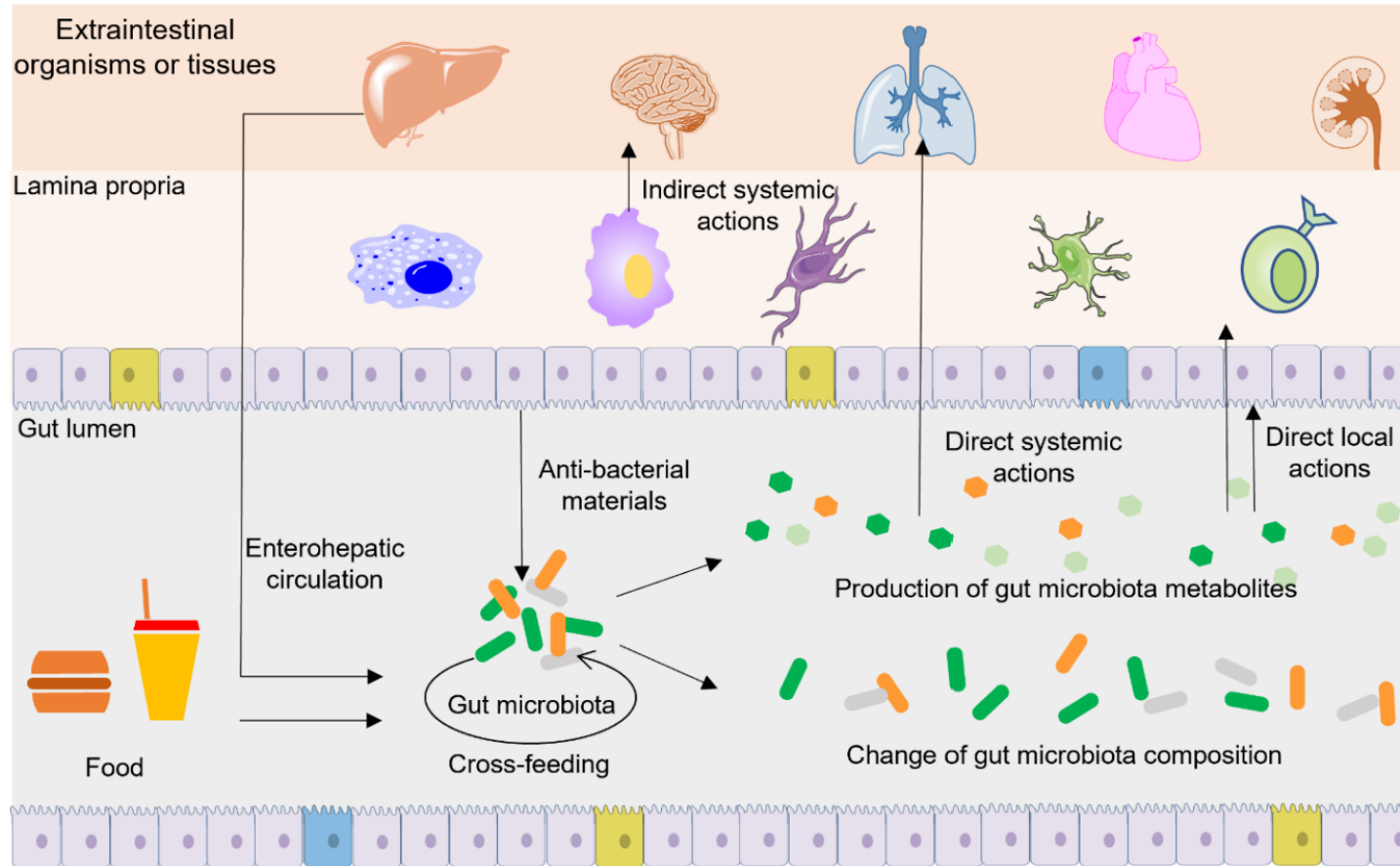
Promote differentiation and function of anti-inflammatory macrophages, Treg cells and IL-22.¹

Polysaccharide A.

Influence T cell activation through interaction with Toll-like Receptor 2 (TLR2) ➡ favoring immune tolerance.³

1. Maciel-Fiuza M. F. et al Role of gut microbiota in infectious and inflammatory diseases. Front Microbiol. 2023 Mar 27;14:1098386.
2. D'Amelio P. et al Gut Microbiota, Immune System, and Bone. Calcif Tissue Int. 2018 Apr;102(4):415-425.
3. Round J.L. et al. The Toll-like receptor 2 pathway establishes colonization by a commensal of the human microbiota. Science. 2011 May 20;332(6032):974-7.

How gut microbiota metabolites modulate inflammation (2/2)

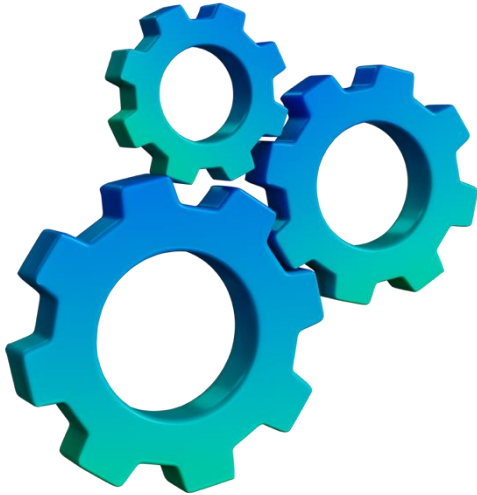


Functions of gut microbiota metabolites.¹

1. Liu J, et al, Functions of Gut Microbiota Metabolites, Current Status and Future Perspectives. Aging Dis. 2022 Jul 11;13(4):1106-1126.



Gut muscle axis: Key mechanisms of interaction



The gut microbiota influences muscle metabolism through:¹

- Regulation of energy availability and muscle protein metabolism via SCFA production (including role in anabolic resistance with age)
- Inflammation modulation
- Nutrient availability including amino acids, and nitrogen balance
- Mitochondrial functions and oxidative capacity
- Endocrine and gut-muscle signaling
- Interaction with exercise

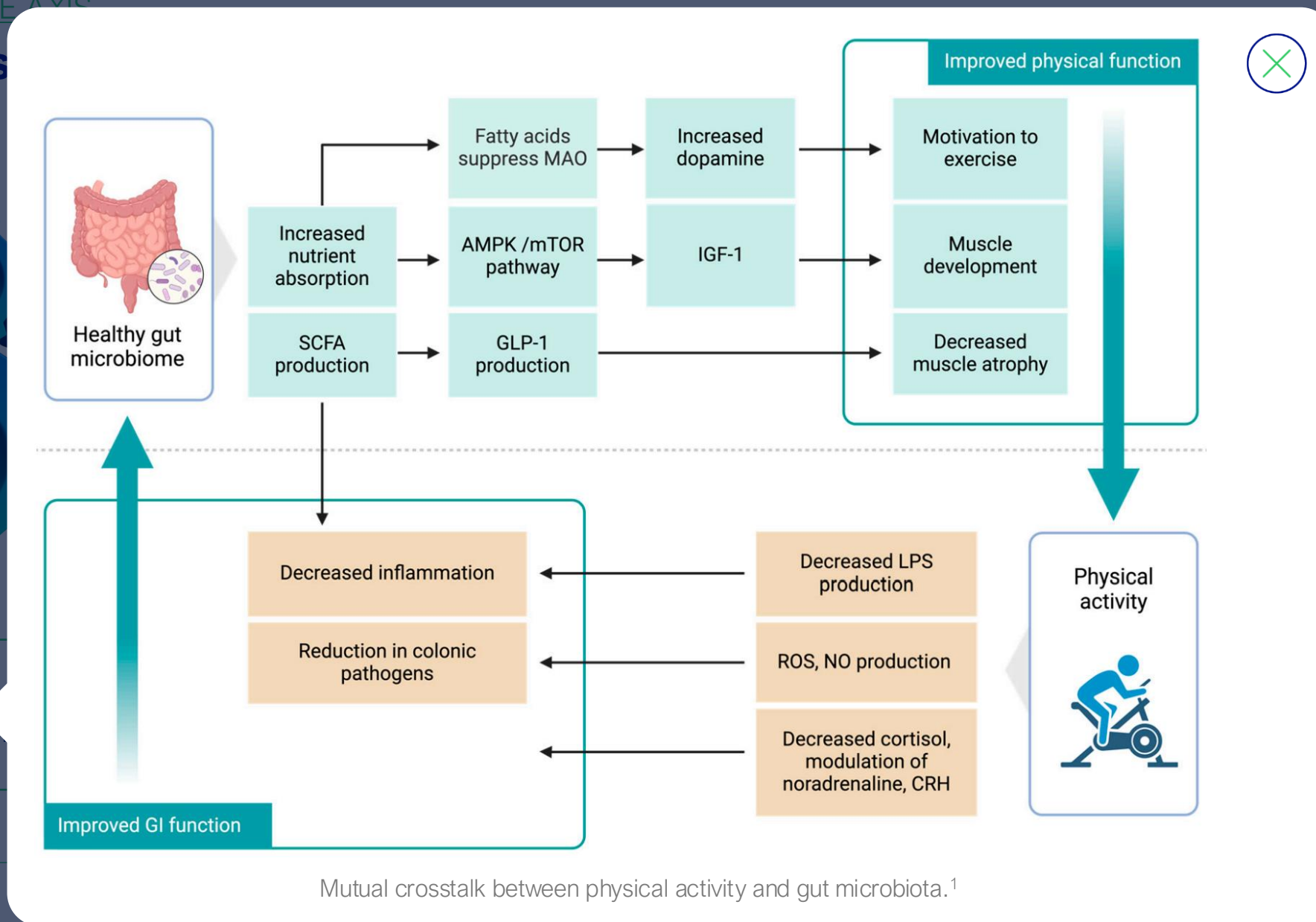


Click here to see a mutual crosstalk between physical activity and gut microbiota

Did you know?

There is a strong correlation between SCFAs and muscle strength.¹





1. Varghese S, et al Physical Exercise and the Gut Microbiome: A Bidirectional Relationship Influencing Health and Performance. *Nutrients*. 2024 Oct 28;16(21):3663.

Gut muscle axis: Effects of microbial metabolites on muscle

Substances generated by the gut microbiota can reach the bloodstream and affect skeletal muscle cells.



Folate and Vit B12

Improve muscle anabolism and prevent hyperhomocysteinemia-induced oxidative stress and endothelial damage, that lead to reduced muscle function.¹

Tryptophan

Stimulates the Insulin-like Growth Factor 1 (IGF-1) / Ribosomal protein S6 kinase, 70 kDa, polypeptide 1(p70s6k) / mTor pathway in muscle cells, promoting expression of genes involved in myofibrillar synthesis.²

Betaine

Has potential to drive muscle fiber differentiation and increase myotube hypertrophy by activating IGF-1 pathway.³

Butyrate (SCFA)

Supports aerobic metabolism in skeletal muscle by boosting mitochondrial activities and promotes the release of glucagon-like peptide 1 reducing muscle atrophy.⁴

1. Kuo HK, et al. Relationship of homocysteine levels to quadriceps strength, gait speed, and late-life disability in older adults. J Gerontol A Biol Sci Med Sci. 2007 Apr;62(4):434-9.

2. Lin R, et al. A review of the relationship between the gut microbiota and amino acid metabolism. Amino Acids. 2017 Dec;49(12):2083-2090.

3. Senesi P, et al. Betaine supplement enhances skeletal muscle differentiation in murine myoblasts via IGF-1 signaling activation. J Transl Med. 2013 Jul 19;11:174.

4. Tolhurst G, et al. Short-chain fatty acids stimulate glucagon-like peptide-1 secretion via the G-protein-coupled receptor FFAR2. Diabetes. 2012 Feb;61(2):364-71.

Influence of exercise on the gut microbiome



Exercise ↔ Gut

Exercise influences gut microbiome via:¹⁻³

- Enhancing gut microbiome diversity
- Increasing SCFA production
- Improving nutrient utilization, insulin sensitivity and blood-sugar regulation,
- Modulating neural and hormonal pathways, improving gut barrier integrity.
- Reducing inflammation by effects on bile acid metabolism



Click here if you want to see graphic on the impact of exercise on gut microbiota.¹

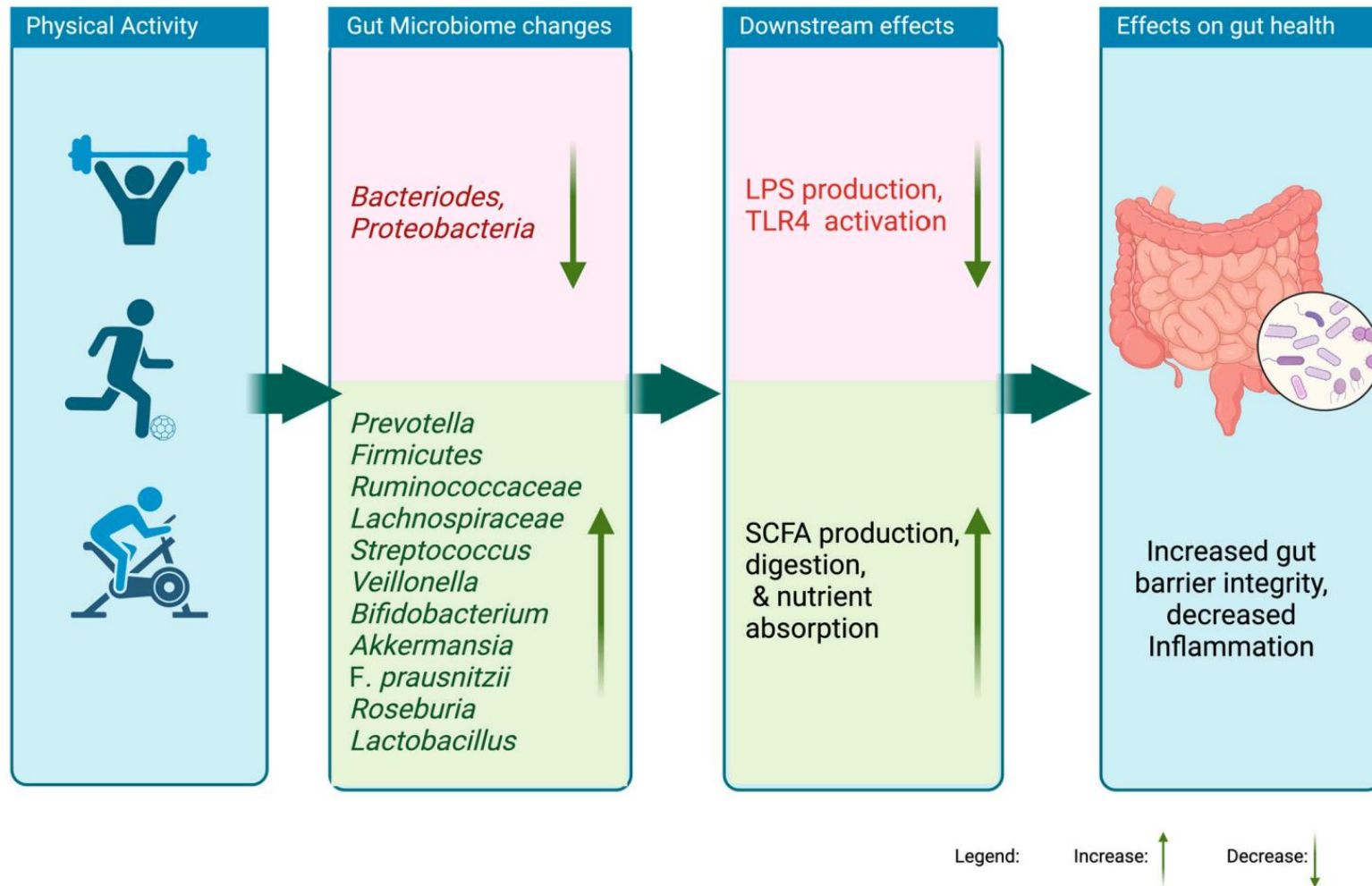
1. Varghese S, et al. Physical Exercise and the Gut Microbiome: A Bidirectional Relationship Influencing Health and Performance. *Nutrients*. 2024 Oct 28;16(21):3663.
2. Houttu V, et al. The role of the gut microbiome and exercise in non-alcoholic fatty liver disease. *Therap Adv Gastroenterol*. 2020 Sep 15; 13:1756284820941745.
3. Molina-Molina E, et al. Exercising the hepatobiliary-gut axis. The impact of physical activity performance. *Eur J Clin Invest*. 2018 Aug;48(8):e12958.

Influence

Exercise

Exercise influ

- Enhancing
- Increasing
- Improving sensitivity
- Modulating pathways,
- Reducing acid metab

Impact of exercise on gut microbiota.¹

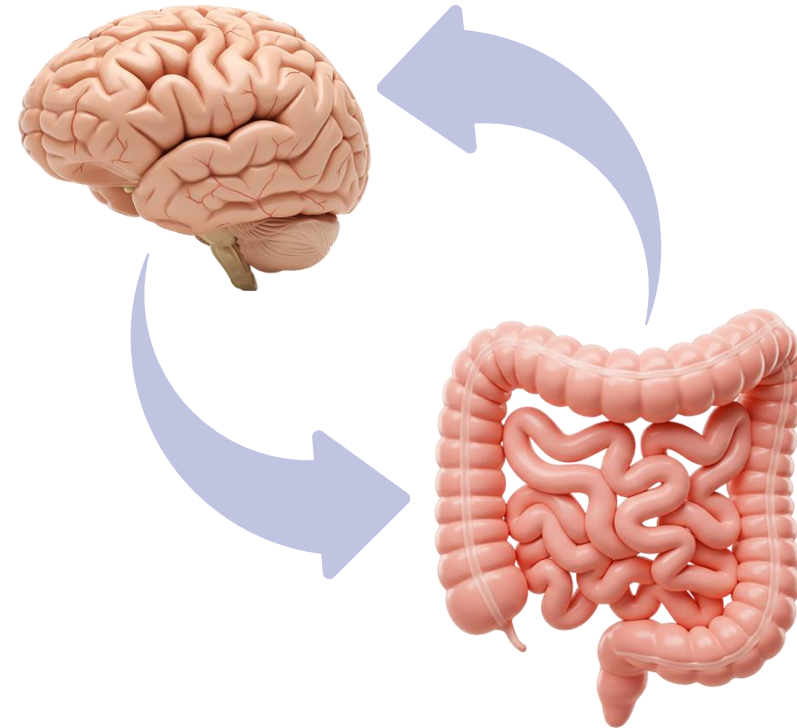
1. Varghese S, et al. Physical Exercise and the Gut Microbiome: A Bidirectional Relationship Influencing Health and Performance. *Nutrients*. 2024 Oct 28;16(21):3663.

1. Varghese S, et al. Physical Exercise and the Gut Microbiome: A Bidirectional Relationship Influencing Health and Performance. *Nutrients*. 2024 Oct 28;16(21):3663.
2. Houttu V, et al. The role of the gut microbiome and exercise in non-alcoholic fatty liver disease. *Therap Adv Gastroenterol*. 2020 Sep 15;13:1756284820941745.
3. Molina-Molina E, et al. Exercising the hepatobiliary-gut axis. The impact of physical activity performance. *Eur J Clin Invest*. 2018 Aug;48(8):e12958.

Gut brain axis

Exercise-induced neurochemical changes in the brain.

- In mice, microbiome-driven production of endocannabinoid metabolites in the gut ➔ increases dopamine levels during exercise.¹
 - Improves exercise performance
 - Incentive-driven pleasure ➔ Stimulates engagement.
- In mice, depletion of the microbiome ➔ inhibition of peripheral endocannabinoid receptors:¹
 - Dopamine blockade
 - Impair exercise capacity.



Influence of some specific exercise types on gut microbiome



Type of exercise	Effects on gut health ¹⁻³
Regular moderate intensity exercise	Reduces circulating levels of lipopolysaccharides (LPS) and decreases expression of Toll like receptors ➡ decreased inflammation and improved gut barrier function.
Moderate aerobic exercise	Promotes IgA production in the gut ➡ enhancing gut microbiota ability to prevent intestinal pathogen colonization
Combining aerobic and resistance training	Affects bacterial diversity by increasing families such as Ruminococcaceae and Lachnospiraceae among others ➡ lower prevalence of chronic metabolic disorders.

1. Varghese S, et al. Physical Exercise and the Gut Microbiome: A Bidirectional Relationship Influencing Health and Performance. *Nutrients*. 2024 Oct 28;16(21):3663.

2. Wiertsema SP, et al. The Interplay between the Gut Microbiome and the Immune System in the Context of Infectious Diseases throughout Life and the Role of Nutrition in Optimizing Treatment Strategies. *Nutrients*. 2021 Mar 9;13(3):886.

3. Tveit KM, et al. Polyphenol-induced improvements in glucose metabolism are associated with bile acid signaling to intestinal farnesoid X receptor. *BMJ Open Diabetes Res Care*. 2020 Aug;8(1):e001386.

Effects of aerobic exercise on healthy, active adults

A 12-week aerobic exercise training with brisk walking increased intestinal *Bacteroides*, as well as trunk muscle strength and cardiopulmonary function in elderly women.¹

Exercise

- Increases the blood flow in the gut
- Strengthens contraction of abdominal muscles
- Accelerates release of gastrointestinal hormones, speeding up peristalsis of food and shortening time to pass through the colon
- Increases the content of short-chain fatty acids (SCFA) in the feces, which can reduce the intestines' pH, promoting *Bacteroides* growth



Summary

- ✓ Gut microbiota shapes inflammation and immune tolerance via metabolites and barrier support; dysbiosis can trigger pro-inflammatory cytokines.
- ✓ Immunoactive metabolites promote Treg/Th17 balance and epithelial integrity.
- ✓ Gut muscle axis: microbial metabolites reach circulation and may influence skeletal muscle cells processes (e.g., IGF-1/mTOR, GLP-1).
- ✓ Exercise remodels the microbiome: ↑ diversity and SCFAs, improved barrier and metabolic/immune regulation; effects vary by exercise type.
- ✓ Exercise may induce neurochemical changes in the brain that enhance motivation/performance.





AGE-RELATED CHANGES IN THE MICROBIOME

[3.1. Age-related changes in the gut microbiota](#)

[3.2. Age and gut microbiota composition](#)

[3.3. Gut dysbiosis and aging](#)

[3.4. The role of microbiota in sarcopenia](#)

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[3.6. Summary](#)

Age-related changes in the gut microbiota (1/2)

With increasing age:¹

- Typically, gut microbial diversity declines and its function in metabolism and regulation of the immune system is reduced
- The microbiota is more vulnerable to lifestyle and psychosocial changes
- Changes in living arrangements (e.g., moving to a care home)
- Increased social isolation
- Dietary change



Other age-related contributing factors¹

- Antibiotics and polypharmacy
- Multi-morbidity
- Reduced appetite
- ↓ mastication ability ↓ salivary function
- Loss of dentition
- ↓ Nutrient intake and absorption
- ↑ Gastroesophageal reflux
- Hypochlorhydria

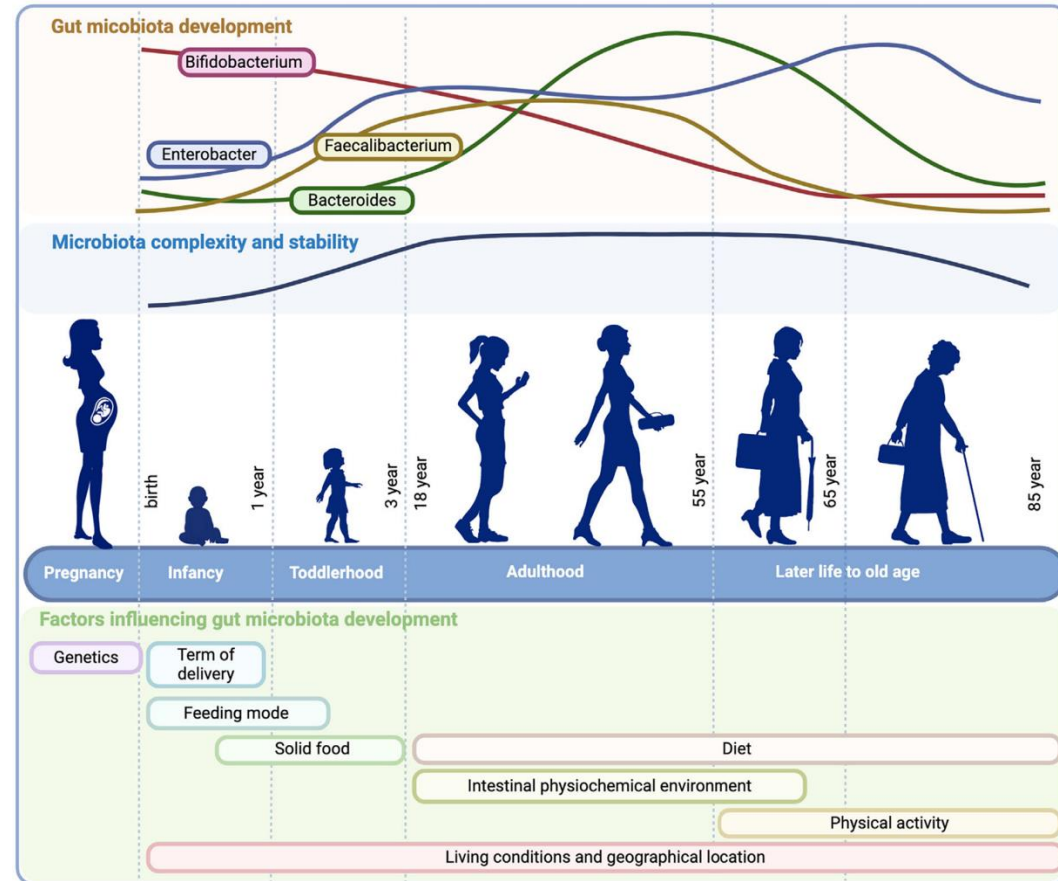


Age-related changes in the gut microbiota (2/2)

From birth to old age microbial communities:¹⁻²

- Are dynamic and shaped by a combination of genetic, environmental, and lifestyle factors
- In early life they are highly variable
- They stabilize during most of adulthood
- Become more variable in old age, with greater individual differences

Diagram showing gut microbiota changes across the lifespan.¹



1. Schoultz I, et al. Gut microbiota development across the lifespan: Disease links and health-promoting interventions. J Intern Med. 2025 Jun;297(6):560-583.
2. Martino C, et al. Microbiota succession throughout life from the cradle to the grave. Nat Rev Microbiol. 2022 Dec;20(12):707-720.

Age and gut microbiota composition

The inter-individual variability in human microbiota increases with age.

- The relative ratio of *Bacteroides* and *Prevotella* ➔ biomarker of healthy and active aging, diet, and lifestyle.¹
- Abundance of *Akkermansia*, *Bifidobacterium* and *Christensenella* ➔ positive signature of healthy ageing and longevity.²
- ↓ Abundance of SCFAs producers (e.g., *Faecalibacterium prausnitzii*, *Roseburia*) ➔ weaker physical barrier that leads to decreased immune tolerance.³
- ↑ Abundance of pathobionts (e.g., proteobacteria)

Relative
ratio

Core microbiota¹⁻³

- Ruminococcaceae
- Lachnospiraceae
- Bacteroidaceae

Relative
ratio

Subdominant genera and families^{2,3}

- Eggerthella
- Akkermansia
- Anaerotruncus
- Bilophila
- Christensenella
- Synergistaceae



1. Gorvitovskaia A, et al. Interpreting *Prevotella* and *Bacteroides* as biomarkers of diet and lifestyle. *Microbiome*. 2016 Apr 12;4:15.
2. Biagi E, et al. Gut Microbiota and Extreme Longevity. *Curr Biol*. 2016 Jun 6;26(11):1480-5.
3. Vemuri R. Gut Microbial Changes, Interactions, and Their Implications on Human Lifecycle: An Ageing Perspective. *Biomed Res Int*. 2018 Feb 26;2018:4178607.

Gut dysbiosis and aging

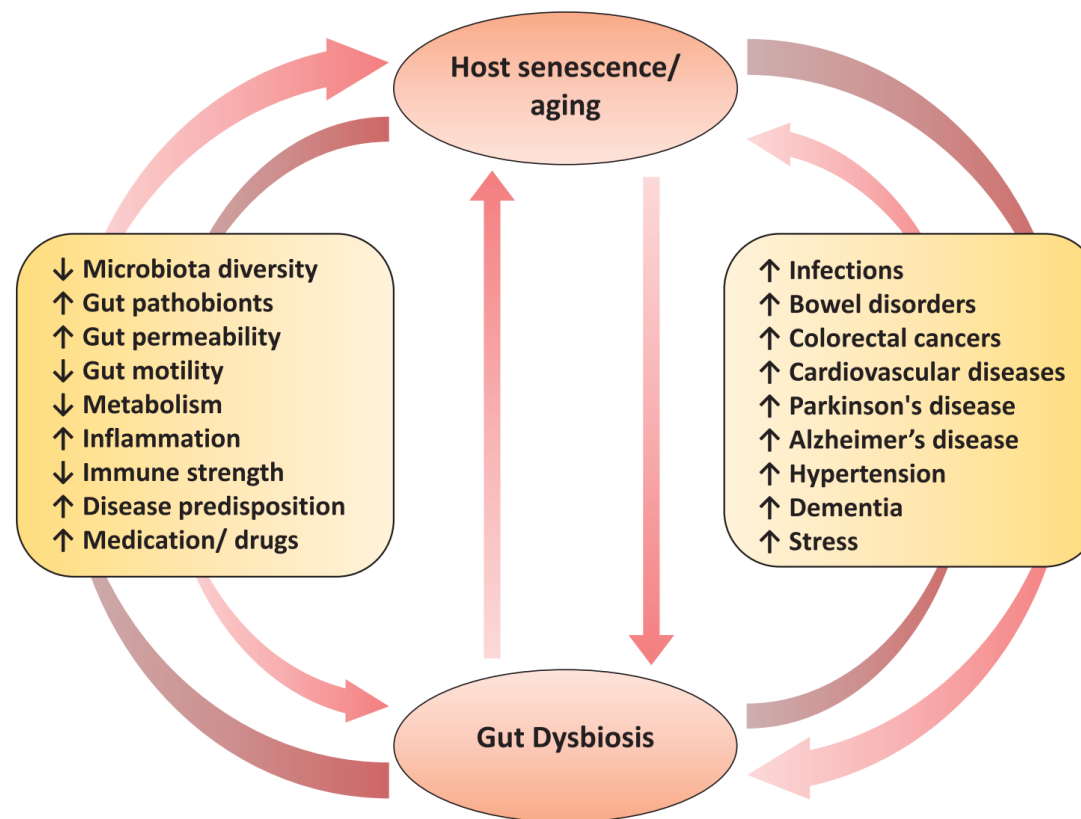
Dysbiosis: Alteration in the typical composition and function of the gut microbiota linked to disease¹

Altered gut microbiota diversity and compromised gut barrier integrity lead to:²

An abnormal leakage of LPS, histamines and serotonin ➡ inflammatory response

With age this is associated with:

- Irregular bowel transit
- Reduced appetite
- Frailty
- Weight loss
- Cognitive decline
- Hypertension
- Vitamin D deficiency



The bidirectional relationship between the human gut microbiome and aging, along with potential contributing factors.²

1. Lynch SV, et al. The Human Intestinal Microbiome in Health and Disease. N Engl J Med. 2016 Dec 15;375(24):2369-2379.
2. Nagpal R, et al. Gut microbiome and aging: Physiological and mechanistic insights. Nutr. Healthy Aging. 2018;4:267-285.



The role of microbiota in sarcopenia

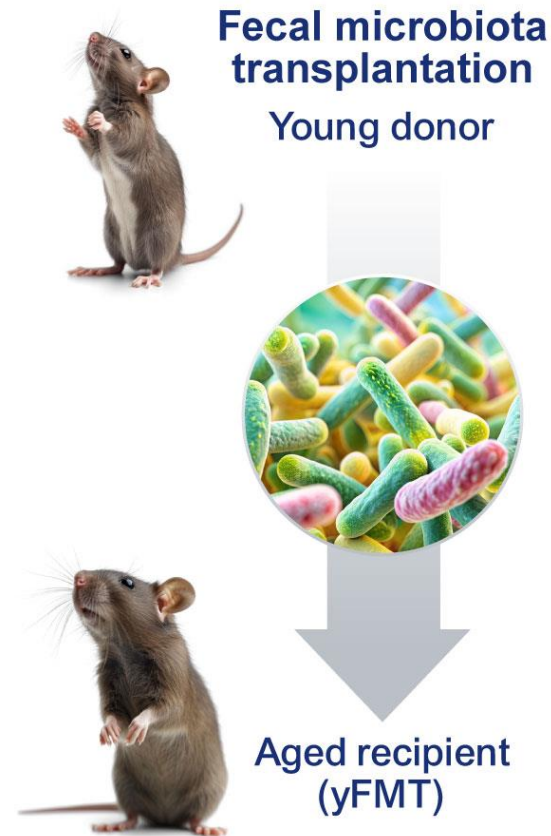


Age-related alterations in the gut microbiota can contribute to the onset of frailty and sarcopenia.¹

- Gut microbiome ➡ anabolic resistance and chronic inflammation affects gut barrier and the availability of absorption of dietary proteins.²
- Microbiota metabolites modulate satiety and appetite through signals in the enteric nervous system.¹
 - Age-related anorexia ➡ loss of appetite with age that can lead to malnutrition.
 - Malnutrition can lead to general wasting, including muscle loss, contributing to sarcopenia.



Future strategies for mitigating sarcopenia



Gut microbiota plays a key role in the development of sarcopenia via the 'gut-muscle' axis, and probiotics-based therapy such as fecal microbiota transplantation might be a strategy for sarcopenia.

Fecal microbiota was transplanted from either young (yFMT) or old donor rats into aged recipient rats for a duration of 8 weeks.

Microbiota transplantation from young donors to aged rats was found to mitigate:¹

- Muscle mass loss
- Muscle strength weakness
- Muscle function impairment
- Age-related atrophy
- Poor regeneration capacity in fast-and slow-switch muscles



Summary

- ✓ With age the gut microbiota's overall diversity and metabolic/immune regulatory capacity decline, and the microbiota becomes more vulnerable to lifestyle/psychosocial and dietary changes.
- ✓ Across the lifespan, microbiota dynamics follow a characteristic trajectory: high inter-individual variability in early life, relative stability through adulthood, and renewed variability/instability in later life.
- ✓ Gut dysbiosis in older age is associated with compromised intestinal barrier integrity and increased translocation of inflammatory mediators (e.g., LPS), GI dysfunction and systemic age-related phenotypes (e.g., frailty, cognitive decline, hypertension, vitamin D deficiency) among others.
- ✓ Healthy aging is associated with higher levels of *Akkermansia*, *Christensenella*, and *Bifidobacterium*, while aging decreases core taxa like Ruminococcaceae and Bacteroidaceae.
- ✓ Gut microbiota alterations may contribute to frailty and sarcopenia via anabolic resistance, chronic inflammation, and reduced dietary protein availability/absorption.





NUTRITIONAL INTERVENTIONS TO ENSURE A HEALTHY GUT MICROBIOME

[4.1. Definition of probiotic](#)

[4.2. Probiotics for muscle health](#)

[4.3. The role of *Lactobacillus* species and muscle metabolism](#)

[4.4. Definition of Prebiotic](#)

[4.5. Prebiotics: Inulin and fructooligosaccharides \(FOS\)](#)

[4.6. Prebiotics and their role in cognition](#)

[4.7. Summary](#)

Definition of probiotic

Probiotics are defined as live microorganisms that, when administered in adequate amounts, confer a health benefit on the host (according to ISAPP).¹

- The strongest evidence for probiotics that impact muscle health pertains to *Lactobacillus* and *Bifidobacterium*.²



Want to know more on the definition of Probiotic?

Criteria to be a probiotic:³

1. Identified at the genus, species, or strain level;
2. Safe for food and clinical use;
3. Able to survive intestinal transit;
4. Able to adhere to mucosal surfaces;
5. Able to colonize in the human intestine or vagina;
6. Produces antimicrobial substances;
7. Able to antagonize pathogenic bacteria;
8. Possesses clinically documented and validated health effects;
9. Stable during processing and storage.



Probiotics for muscle health

Probiotic supplementation can improve muscle mass, strength and muscle function in adults.^{1,2}

Some mechanisms through which probiotics influence muscle function:³

- **Release proteases and peptidases** ➡ enhance protein digestion and increase amino acid availability for muscle protein synthesis
- **Maintain gut integrity** ➡ reduce leakage of bacteria and their proinflammatory toxins into the bloodstream that can trigger inflammation and subsequent catabolic effect on muscle
- **Production of SCFAs**

**DID
YOU
KNOW?**

Fermented food is an important source of probiotics. It contains thousands of live bacteria.



1. Shokri-Mashhadi N, et al. A meta-analysis of the effect of probiotic administration on age-related sarcopenia. Food Sci Nutr. 2023 Aug 9;11(9):4975-4987.

2. Prokopiadis K, et al. Impact of probiotics on muscle mass, muscle strength and lean mass: a systematic review and meta-analysis of randomized controlled trials. J Cachexia Sarcopenia Muscle. 2023 Feb;14(1):30-44.

3. Ebner N, et al. Recent developments in the field of cachexia, sarcopenia, and muscle wasting: highlights from the 11th Cachexia Conference. J Cachexia Sarcopenia Muscle. 2019;10:218-225.

The role of *Lactobacillus* species and muscle metabolism

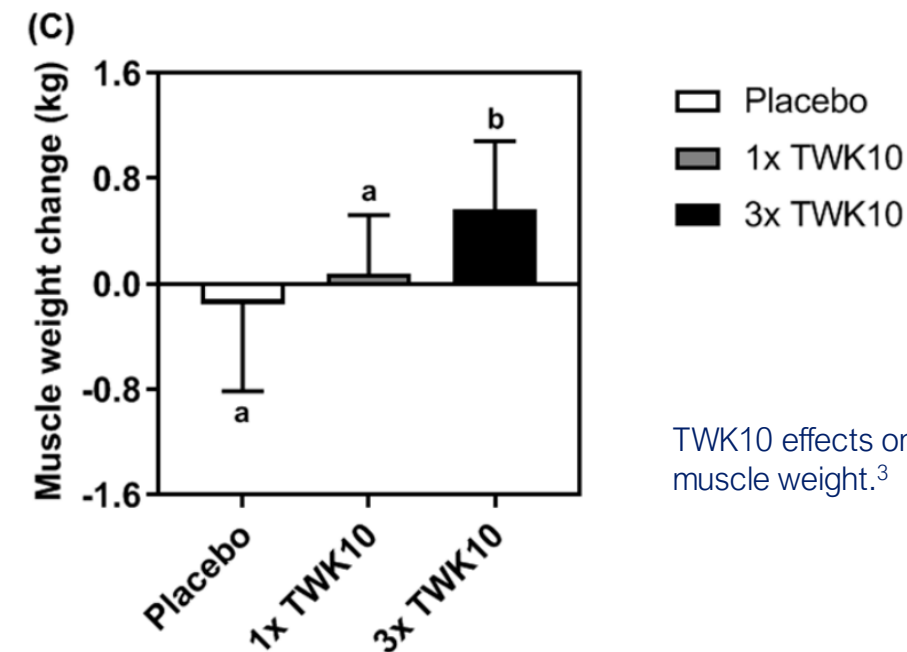
Higher gut *Lactobacillus* levels are positively correlated with skeletal muscle mass index.¹

Effects of supplementation with *Lactobacillus plantarum* TWK10 in humans for > 6 weeks and $>2 \times 10^{10}$ CFU/day resulted in:^{2,3}

- Improved muscle mass
- Increased left hand grip strength
- Increased lower limb muscle strength, and gait speed
- Incremented exercise performance
- Decreased body fat
- Increased muscle mass



Click here to view some examples of the protective mechanisms of *Lactobacillus*



TWK10 effects on muscle weight.³



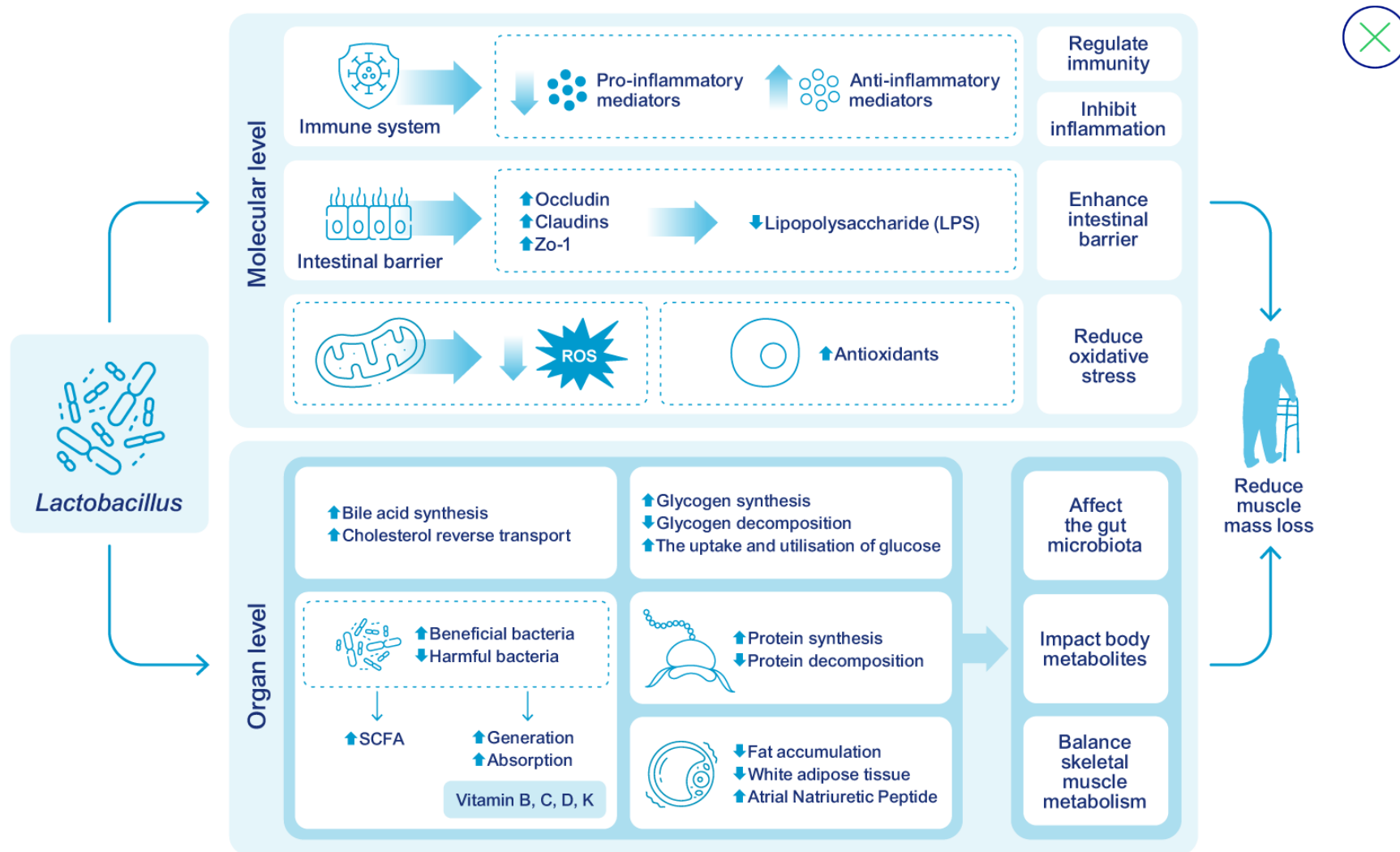
1. Lou J, et al. Changes and correlation analysis of intestinal microflora composition, inflammatory index, and skeletal muscle mass in elderly patients with sarcopenia. *Geriatr Gerontol Int*. 2024 Jan;24(1):140-146.
 2. Lee MC, et al. *Lactobacillus plantarum* TWK10 Improves Muscle Mass and Functional Performance in Frail Older Adults: A Randomized, Double-Blind Clinical Trial. *Microorganisms*. 2021 Jul 8;9(7):1466.
 3. Huang WC, et al. Effect of *Lactobacillus plantarum* TWK10 on Exercise Physiological Adaptation, Performance, and Body Composition in Healthy Humans. *Nutrients*. 2019 Nov 19;11(11):2836.

The role of metabolites

Higher gut *Lactobacillus* levels are associated with skeletal muscle mass and function.

Effects of supplementing with *Lactobacillus* in humans for > 6 weeks:

- Improved muscle mass and function
- Increased left ventricular mass
- Increased low-density lipoprotein cholesterol
- Incremented energy expenditure
- Decreased body fat mass
- Increased muscle mass and function



Protective mechanisms of *Lactobacillus* on Inflammation, oxidative stress, and muscle metabolism. Adapted from¹

1. Zhu J, et al. Probiotics and muscle health: the impact of *Lactobacillus* on sarcopenia through the gut-muscle axis. *Front Microbiol.* 2025 Mar 14;16:1559119.

2. Lee MC, et al. *Lactobacillus plantarum* TWK10 Improves Muscle Mass and Functional Performance in Frail Older Adults: A Randomized, Double-Blind Clinical Trial. *Microorganisms.* 2021 Jul 8;9(7):1466.

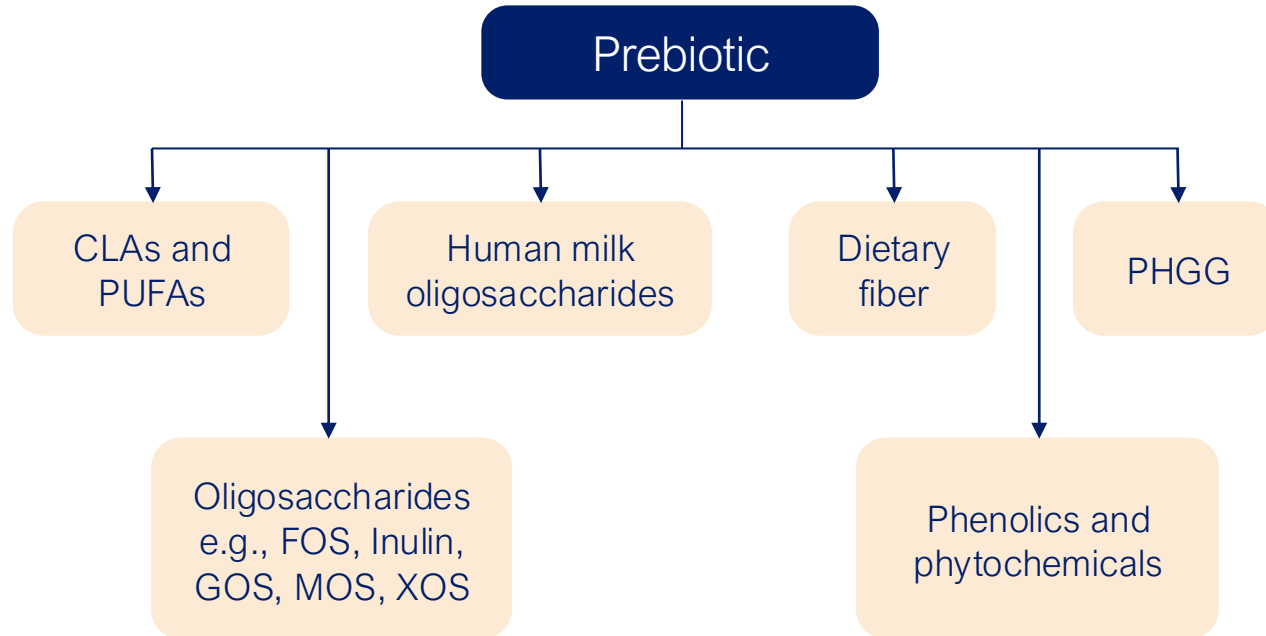
3. Huang WC, et al. Effect of *Lactobacillus plantarum* TWK10 on Exercise Physiological Adaptation, Performance, and Body Composition in Healthy Humans. *Nutrients.* 2019 Nov 19;11(11):2836.

Definition of Prebiotic

Prebiotics are substrates that are selectively utilized by host microorganisms conferring a health benefit (according to ISAPP)¹



Want to know more on the definition of Prebiotic?



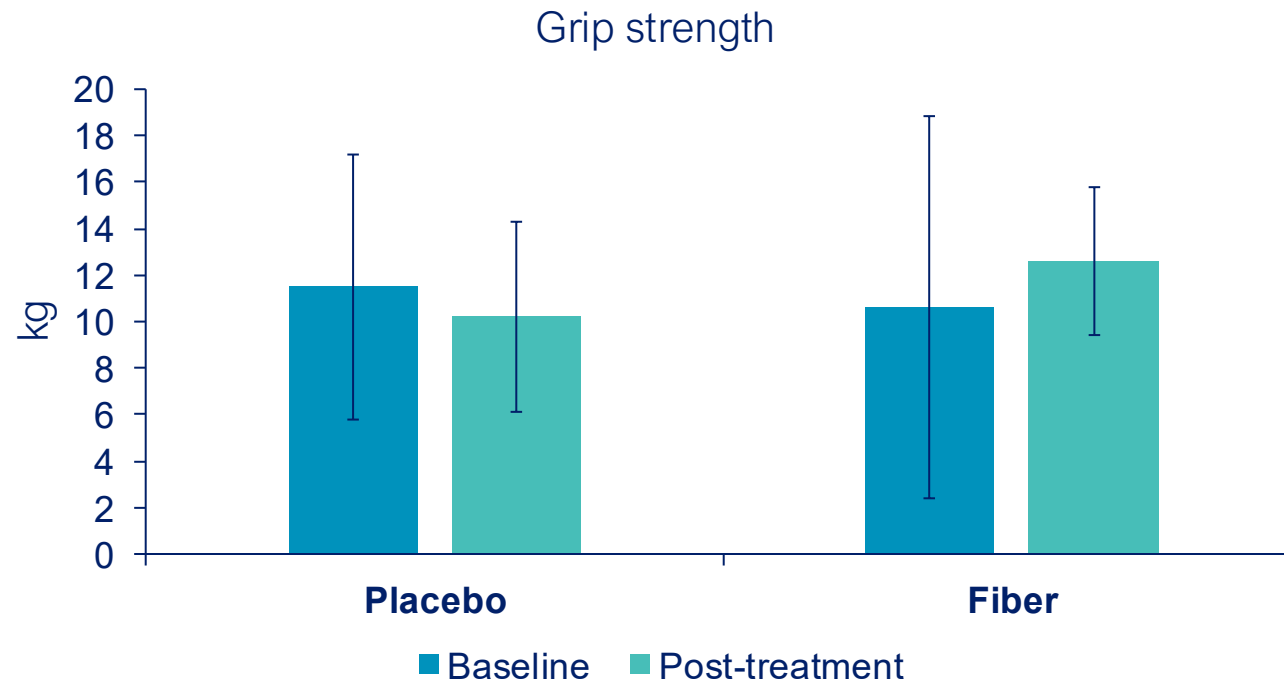
Types of prebiotics. CLA, conjugated linoleic acid; PUFA, polyunsaturated fatty acid; FOS, fructooligosaccharides; GOS, galactooligosaccharides; MOS, mannanoligosaccharide; PHGG, partially hydrolyzed Guar Gum; XOS, xylooligosaccharide. Figure based on data described in^{1,2}

1. Gibson GR, et al. Expert consensus document: The International Scientific Association for Probiotics and Prebiotics (ISAPP) consensus statement on the definition and scope of prebiotics. Nat Rev Gastroenterol Hepatol. 2017 Aug;14(8):491-502.
2. Chaplin A, et al. Conjugated Linoleic Acid Supplementation under a High-Fat Diet Modulates Stomach Protein Expression and Intestinal Microbiota in Adult Mice. PLoS One. 2015 Apr 27;10(4):e0125091.



Prebiotics: Inulin and fructooligosaccharides (FOS)

- Prebiotic supplementation (inulin + FOS) has been shown to increase muscle strength (handgrip) and endurance (exhaustion) in frail older adults.¹
- Inulin-type prebiotics may help to increase calcium absorption and support bone health.²



Grip strength in the right hand. $p < 0.05$. Figure based on data described in¹

1. Buigues C, et al. Effect of a prebiotic formulation on frailty syndrome: a randomized, double-blind clinical trial. *Int J Mol Sci*. 2016;17(6):932.

2. Abrams SA, et al. Young adolescents who respond to an inulin-type fructan substantially increase total absorbed calcium and daily calcium accretion to the skeleton. *J Nutr*. 2007 Nov;137(11 Suppl):2524S-2526S.



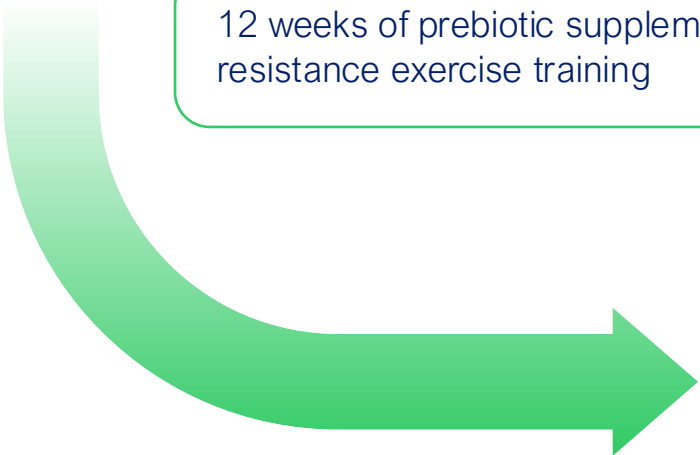
Prebiotics and their role in cognition

The PROMOTe randomized controlled double-blind trial of 36 pairs of twins found that prebiotic supplementation improved cognition, a key component of future frailty, in adults over 60.¹

12 weeks of prebiotic supplementation (inulin and FOS) +
resistance exercise training

VS

placebo
+ resistance exercise training

- 
- 40 microbiome features changed between baseline and study end for the prebiotic group, while only 1 changed in placebo.
 - Main change in intervention group ➡ increased Bifidobacterium
 - Positive association between the rise in cognitive factor scores and the relative abundance of Actinobacteria at the end of the study.



Summary



- ✓ **Probiotics** are live microorganisms that, when administered in adequate amounts, confer a health benefit.
 - ✓ Probiotics may enhance protein digestion and amino acid bioavailability, strengthen gut barrier integrity, and increase SCFA production.
 - ✓ Muscle-health evidence is strongest for *Lactobacillus* and *Bifidobacterium*; meta-analyses report improvements in muscle mass, strength and function in adults.
- ✓ **Prebiotics** are substrates that are selectively utilized by host microorganisms conferring a health benefit.
 - ✓ In older adults, they have shown improvements in muscle strength, endurance and cognitive outcomes, alongside measurable shifts in the gut microbiome (↑ *Bifidobacterium* / Actinobacteria).



PRACTICAL GUIDANCE TO SUPPORT A HEALTHY GUT MICROBIOME

[5.1. How to prevent dysbiosis and nutritional imbalance](#)

[5.2. From science to plate](#)

[5.3. Summary](#)



How to prevent dysbiosis and nutritional imbalance (1/2)

- Avoiding high-fat diet (HFD), as HFD induces microbial dysbiosis.¹
- Consuming a healthy varied diet to help with microbial diversity.
- Ensuring adequate intakes of proteins, vitamin D, antioxidant nutrients, and long-chain polyunsaturated fatty acids to promote protein synthesis and modulate inflammation.²
- Avoiding unnecessary antibiotics and limiting polypharmacy where possible.
- Engaging in regular exercise training to promote beneficial changes in gut microbial health and support the maintenance of muscle mass and function.³
- Having good sleep and stress management.



1. Adak A, et al. An insight into gut microbiota and its functionalities. Cell Mol Life Sci. 2019 Feb;76(3):473-493.

2. Ticinesi A, et al. Nutrition and Inflammation in Older Individuals: Focus on Vitamin D, n-3 Polyunsaturated Fatty Acids and Whey Proteins. Nutrients. 2016 Mar 29;8(4):186.

3. Grosicki GJ, et al. Gut Microbiota Contribute to Age-Related Changes in Skeletal Muscle Size, Composition, and Function: Biological Basis for a Gut-Muscle Axis. Calcif Tissue Int. 2018 Apr;102(4):433-442.

How to prevent dysbiosis and nutritional imbalance (2/2)

- Regular and healthy bowel movements.
- Meet fiber recommendations ➡ Most older adults do not consume adequate amounts of fibre.¹
 - US adequate intake (AI) for adults > 50 years is 30 g/day for men and 21 g/day for women.²
 - EU recommendations state that individuals should consume >25 g/day.¹

Did you know?

Despite a growing evidence base across multiple health settings, there is no current guidance recommending probiotics for the general population. Recommendations are indication-specific (e.g., *C. difficile*-related settings, post-antibiotic diarrhea), and optimal strain/dose/duration remain inconsistent across conditions.

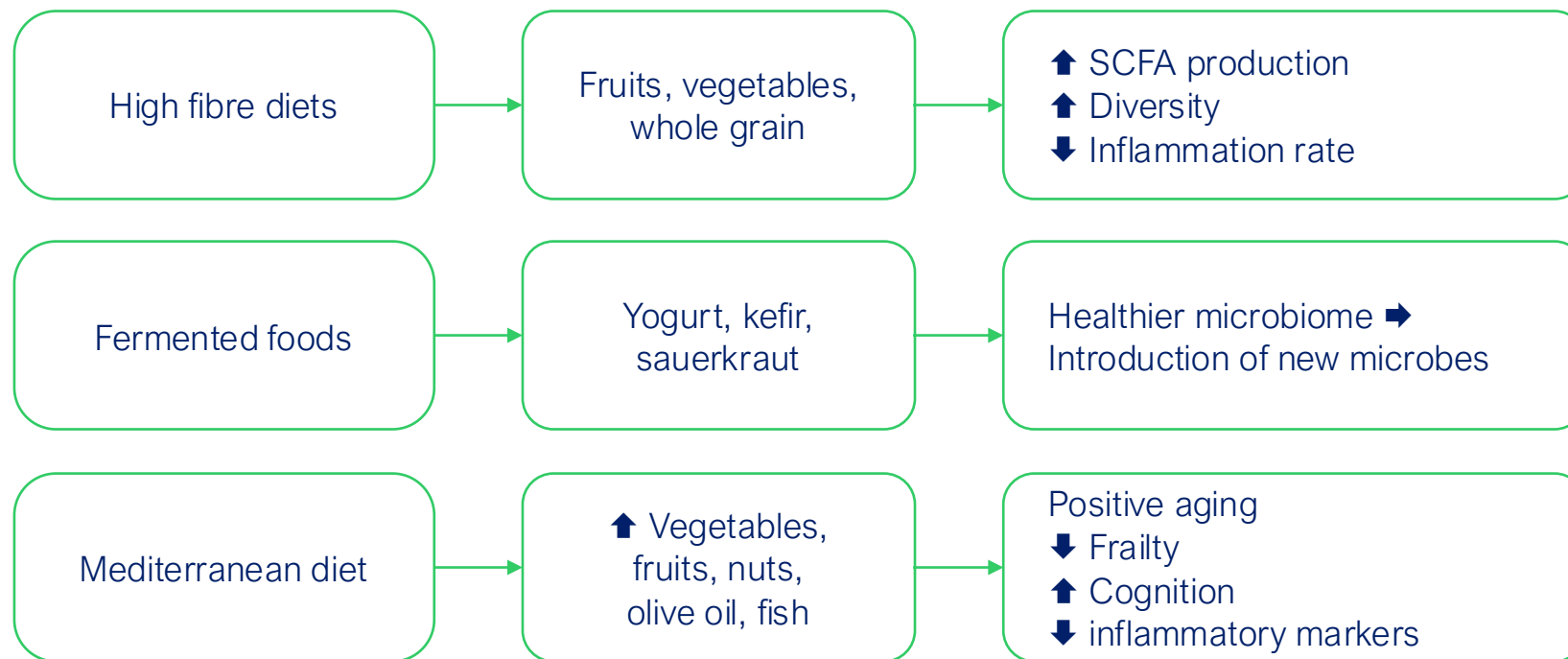


1. EFSA Panel on Dietetic Products, Nutrition, and Allergies (NDA); Scientific Opinion on Dietary Reference Values for carbohydrates and dietary fibre. EFSA Journal 2010; 8(3):1462.

2. Akbar A, et al. The Role of Dietary Fiber in Health Promotion and Disease Prevention: A Practical Guide for Clinicians. StatPearls Publishing; 2025 Available from: <https://www.ncbi.nlm.nih.gov/books/NBK559033/> [Accessed 27-01-2026].

From science to plate

How to influence the gut microbiome through diet.^{1,2}



1. Ni Lochlainn. Impact of gut microbiota on Nutritional Health in Older Adults. In: The Nutritional landscape of aging: gut microbiota, protein patterns and micronutrient shifts. European Geriatric Medicine Society (EuGMS) Congress 2025; September 24th -26th, Reykjavik Iceland. Available from: https://www.youtube.com/watch?v=iv7ppmEdQ_4 [Accessed 27-01-2026].

2. Ghosh TS, et al. Mediterranean diet intervention alters the gut microbiome in older people reducing frailty and improving health status: the NU-AGE 1-year dietary intervention across five European countries. Gut. 2020 Jul;69(7):1218-1228.

Summary



- ✓ The following strategies can help prevent dysbiosis and nutrition-related imbalance:
 - ✓ Avoid high-fat diets; prioritize high-fiber, plant-rich diets (fruit/veg/whole grains) to ↑ microbial diversity.
 - ✓ Meet fiber recommendations: US AI >50 y = 30 g/day (men), 21 g/day (women); EU recommendation >25 g/day.
 - ✓ Consume adequate protein and micronutrients, keep an active lifestyle and include adequate sleep and stress management.
 - ✓ Minimize unnecessary antibiotics and polypharmacy.
- ✓ There is no recommendation on pre/probiotics for general population and no standardized dosing; use is typically indication-specific (e.g., *C. difficile* contexts, post-antibiotic diarrhea).



CONCLUSIONS



- ✓ **Gut microbiota** ferment dietary substrates to produce metabolites such as SCFAs, synthesize some vitamins and transform bile acids, all of which influence host metabolism, immune function and gut barrier integrity.
- ✓ **Aging** can reduce microbial diversity and SCFA production, leading to LPS leakage, inflammation, anabolic resistance, insulin resistance, and muscle loss.
- ✓ **Gut–muscle axis:** microbiota-derived metabolites modulate immunity and metabolism which impact on muscle health, while exercise enhances microbial diversity and barrier function.
- ✓ **Probiotics and prebiotics** can increase SCFA production, reduce inflammation, and improve muscle metabolism, strength, and functional performance.



Want to know more?
Watch “The impact of gut microbiota on
Nutritional Health in Older Adults”

This training material has been reviewed for scientific accuracy and relevance by Mary Ní Lochlainn – King's College London. It is intended for educational purposes only and does not replace clinical judgment or institutional guidelines.



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- Was awarded the British Geriatric Society's **Rising Star in Research** award in 2021 and the Dhole-Eddlestone prize for **best paper of the year** in Age and Ageing.
- Her research focuses lie in prevention and delay of age-associated morbidity, including sarcopenia and frailty, ultimately aiming to improve the lives of older adults.
- She is now leading the "It's Getting Hot in Here" study on the impact of heatwaves on older people, including on their microbiome.

Thank you!

