

The role of exercise in modulating the gut muscle axis: Implications for performance and recovery

Nicholas Mwebaze¹ , Roland Shimey Mukana¹ , Loyce Nahwera¹ , Annet Nankwanga² , Ricky Richard Ojara³ , Elyvania Nabaggala¹ , Linika Lumbuye¹ , Milton Chebet⁴ , Timothy Makubuya¹ 

¹ Department of Sport Science, Kyambogo University, Kampala, Uganda. ² Department of Physiotherapy, Soroti University, Soroti, Uganda. ³ Department of Sport and Exercise Science, Gulu University, Gulu, Uganda. ⁴ Department of Sports Science, Faculty of Science, Kabale University, Kabale, Uganda.

Abstract

Received:
March 26, 2026

Accepted:
June 11, 2026

Online Published:
June 30, 2026

Keywords:
Exercise physiology,
fatigue, gut muscle axis,
gut microbiota, recovery,
sports performance.

Background & Objective: The gut muscle axis has lately emerged as an important relationship between exercise physiology, microbiome research, and nutrition. This systematic review investigated how exercise alters gut microbial composition and function, and how these changes influence muscular performance, recovery, and overall health. **Key Findings:** Current studies suggest that both acute and chronic exercise result to beneficial changes in microbial diversity, increasing the production of metabolites such as short chain fatty acids, bile acids, and tryptophan derivatives that aid in energy metabolism, mitochondrial efficiency, and anti-inflammatory pathways. Also, gut-derived signals appear to affect muscle adaptation, immunological regulation, and fatigue resistance, indicating a bidirectional link. **Nutritional Implications:** Nutritional techniques such as probiotic, prebiotic, and symbiotic supplementation can influence the gut-muscle axis, which has implications for protein metabolism, amino acid availability, and tissue repair. Studies in athletes suggest that gut microbial composition is linked to endurance ability, recovery rates, and resilience to overtraining-related inflammation. **Limitation:** However, methodological limitations, such as heterogeneity in study designs and limits in microbiome sequencing, restrict the generalizability of current findings. This review highlights important limitations in the integration of gut microbial profile-based exercise prescription, tailored nutrition, and multi-omics techniques. **Conclusion & Future Directions:** Future studies should use systems biology and precision medicine frameworks to further describe the functional effects of gut muscle interactions in various populations, such as clinical groups with metabolic problems or sarcopenia. The gut muscle axis is a promising area of study in sports and exercise science that may help develop tailored interventions that improve long-term health outcomes, speed up recovery, and maximize performance.

Introduction

The gut muscle axis refers to a bidirectional communication network linking the intestinal microbiota and its metabolic products with skeletal muscle physiology. Gut microbes generate key metabolites such as short chain fatty acids, branched chain amino acid derivatives, bile acid products, and microbial peptides. These compounds influence nutrient availability, gut barrier integrity, and systemic inflammation, which in turn affect insulin sensitivity, immune activity within muscle tissue, mitochondrial function, and muscle protein turnover. At the same time, skeletal muscle regulates the internal environment through the release of myokines and exerkines, together with exercise induced alterations in metabolism and gut motility that shape microbial composition and activity.

These continuous exchanges form a dynamic communication loop that influences whole body homeostasis relevant to health, ageing, and exercise performance.

Interest in the gut muscle axis has grown because exercise, diet, and recovery strategies appear to modulate this system in several important ways. First, exercise consistently emerges as one of the strongest behavioural modifiers of gut microbiota composition and function. Human studies show that habitual aerobic and resistance training are associated with a more diverse microbiome, greater abundance of short chain fatty acid producing taxa, and enrichment of gene pathways involved in carbohydrate and amino acid metabolism. These changes relate to improved substrate utilisation, mitochondrial efficiency, and energy

✉ N. Mwebaze, e-mail: mwebazen17@gmail.com

To Cite: Mwebaze, N., Mukana, R. S., Nahwera, L., Nankwanga, A., Ojara, R. R., Nabaggala, E., Lumbuye, L., Chebet, M., & Makubuya, T. (2026). The role of exercise in modulating the gut muscle axis: Implications for performance and recovery. *Adv Health Exerc*, 6(2), 77-88.

production, suggesting that exercise shaped microbial communities may support endurance, strength, or recovery capacity. Secondly, experimental work demonstrates that gut derived metabolites such as butyrate and propionate influence insulin sensitivity, mitochondrial biogenesis, and inflammatory pathways that determine recovery and adaptation. Thirdly, practical interventions involving diet, probiotics, prebiotics, or structured training programs provide promising tools for optimising the gut muscle axis in both athletes and clinical populations.

The purpose of this review was to synthesise mechanistic and applied evidence on how exercise modulates the gut muscle axis and to consider implications for performance and recovery. The review first outlines the major microbial and host derived mediators involved in gut muscle communication, including short chain fatty acids, amino acid metabolites, myokines, and immune signals. It then evaluated human studies and animal studies separately in order to distinguish observational patterns from mechanistic finding. Human research focused on exercise related shifts in microbial diversity, metabolite profiles, and associations with performance or recovery outcomes. Animal studies provide controlled experimental evidence that clarifies causal pathways linking microbial activity to muscle metabolism, adaptation, and endurance capacity. The review appraises dietary, probiotic, prebiotic and exercise-based intervention strategies, while identifying limitations in current methodology and priorities for future studies. Through this structured approach, the review aims to offer researchers and practitioners clear insights into the mechanistic foundations and practical applications of the gut muscle axis in performance, recovery, and rehabilitation contexts.

Method

This study was conducted as a systematic review following PRISMA guidelines to synthesize evidence on the role of exercise in modulating the gut-muscle axis and its implications for performance, recovery, and musculoskeletal health. A comprehensive search of PubMed, Scopus, Web of Science, and Google Scholar was undertaken for studies published between 2010 and 2025. Search terms combined concepts related to gut microbiota, exercise, skeletal muscle, microbial metabolites, and immune regulation. Other studies

were identified through manual screening of reference lists from key articles and reviews.

Studies were included if they examined exercise-induced changes in gut microbiota, investigated microbial influences on muscle physiology, or evaluated microbiome-targeted interventions such as probiotics, prebiotics, symbiotic, or postbiotics in relation to performance and recovery. Human and animal studies published in peer-reviewed English-language journals were eligible. Studies lacking relevance to the gut-muscle axis, non-peer-reviewed publications, conference abstracts, and articles with insufficient methodological detail were excluded. Following duplicate removal, titles, abstracts, and full texts were screened according to predefined eligibility criteria, with the selection process documented using a PRISMA flow diagram.

Data extraction was performed using a standardized template that captured study characteristics, participant information, exercise interventions, microbiome assessment methods, and key outcomes related to microbial composition, metabolite production, muscle performance, and recovery. To assess methodological accuracy, study quality was evaluated using appropriate risk-of-bias tools according to study design. Particular attention was given to sample size, study duration, dietary control, microbiome analytical techniques, and consistency of reported outcomes when interpreting the evidence.

Due to substantial heterogeneity across populations, exercise protocols, microbiome assessment methods, and outcome measures, a meta-analysis was not feasible. Therefore, findings were synthesized narratively and organized into thematic areas, including exercise-induced microbial adaptations, microbial metabolites and muscle physiology, performance outcomes, and recovery mechanisms. The strength of evidence was critically appraised by comparing findings across human and animal studies, highlighting methodological limitations, conflicting results, and current research gaps to provide a balanced assessment of the gut-muscle axis literature. Other studies were identified through citation tracking of seminal and high impact reviews, including those by Chew et al. (2023), Mach and Fuster Botella (2017), and Wang et al. (2023). Only peer reviewed articles published in English were included using a criterion shown in Figure 1.

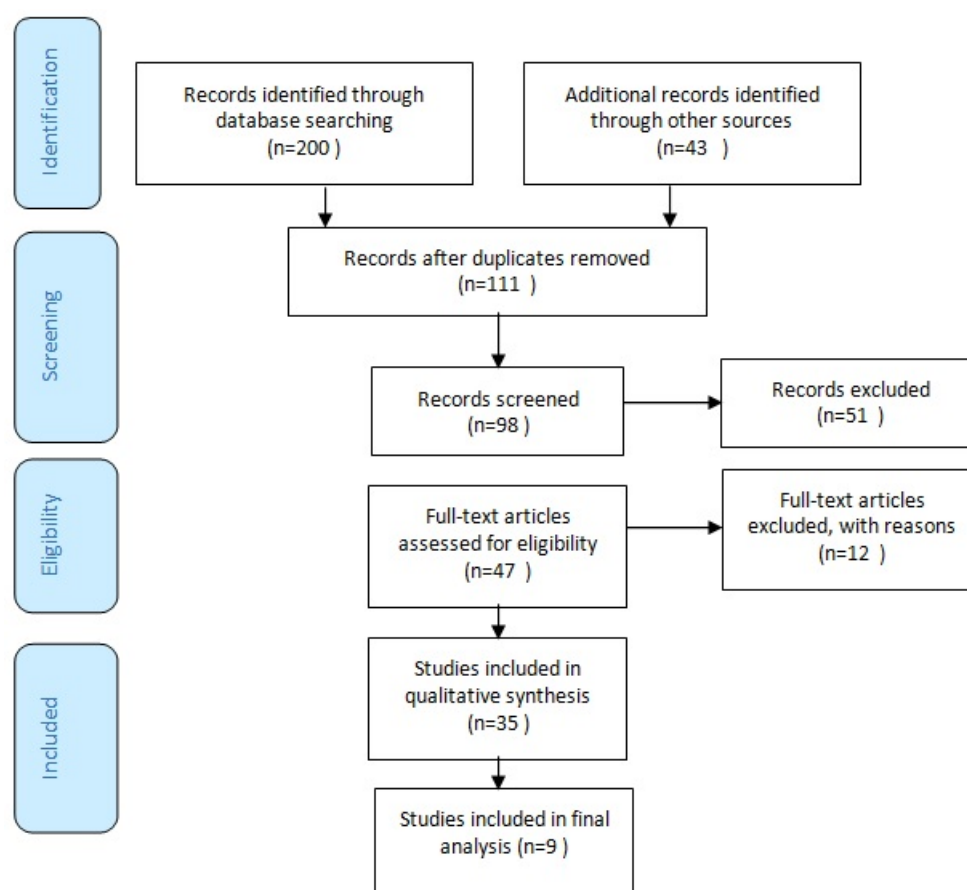


Figure 1. PRISMA Flowchart showing the selection of articles.

Inclusion and Exclusion Criteria

Inclusion criteria

Studies were included if they investigated exercise related changes in gut microbiota, the influence of microbial metabolites on muscle physiology, or microbiome targeted interventions relevant to performance or recovery. Both human and animal studies were eligible, consistent with previous integrative reviews (Clarke et al., 2014; Scheiman et al., 2019; Cullen et al., 2023).

Exclusion criteria

Studies were excluded if they lacked a specific focus on the gut muscle axis, did not provide full text, had insufficient methodological detail, or focused primarily on unrelated disease states. Conference abstracts and non-peer reviewed reports were not considered.

Synthesis and Analysis

A qualitative narrative synthesis was used to integrate results across study types. Analysis focused on several core areas:

- mechanistic pathways linking gut microbiota, microbial metabolites, and muscle function (Chew et al., 2023; Saponaro et al., 2024)
- acute versus chronic exercise effects on microbial diversity and metabolite output (Cullen et al., 2023; Petersen et al., 2017)
- implications for performance and recovery across human and animal research (Scheiman et al., 2019; Clarke et al., 2014)
- methodological limitations and gaps in the evidence base

Comparative tables were developed to summarise key findings from human and animal studies, including microbial changes, intervention types, and observed effects on muscle performance or recovery (Clarke et al., 2014; Mach and Fuster Botella, 2017). Evidence quality was evaluated with attention to sample size, assessment methods, and consistency of reported outcomes.

Limitations of the Review

This review has several limitations. Publication bias may have favoured studies reporting positive associations between exercise and gut microbiota.

Included studies varied widely in design, populations, sequencing methods, and exercise protocols, introducing heterogeneity similar to that noted in previous reviews (Clauss et al., 2021; Cullen et al., 2023). The scarcity of longitudinal human trials restricts causal inference, particularly in distinguishing whether microbial changes drive or simply reflect improved physiological outcomes. Despite these constraints, the approach provided a comprehensive synthesis of current understanding of the gut muscle axis in relation to exercise, nutrition, and recovery key studies selected are shown in Table 1 (human study) and Table 2 (animal study).

Results

Conceptualising the Gut Muscle Axis

The gut muscle axis refers to a complex, bidirectional communication system linking the intestinal microbiota

and skeletal muscle through a network of metabolic, immune, and neuroendocrine pathways (Chew et al., 2023; Saponaro et al., 2024). This framework positions the gut as both a digestive and an endocrine immune interface that influences systemic physiology. Skeletal muscle also functions as an endocrine organ that releases myokines, which act on distant tissues including the gut (Tremaroli and Bäckhed, 2012). Central to this relationship is the idea that gut derived metabolites and inflammatory mediators regulate muscle metabolism, mitochondrial biogenesis, and protein synthesis, while exercise induced muscle activity can reshape microbial composition and strengthen intestinal barrier integrity (Li, 2024). These interactions create an integrative model connecting microbial ecology with musculoskeletal health, performance, and recovery.

Table 1
Human studies investigating exercise and the gut-muscle axis.

Study	Population	Study Design	Exercise Modality	Microbiome Assessment Method	Key Gut Microbiota Findings	Muscle/Performance Outcomes	Major Limitations
Clarke et al. (2014)	40 professional rugby players and sedentary controls	Cross-sectional	Habitual elite training	16S rRNA sequencing	Greater microbial diversity and increased abundance of health-associated taxa in athletes	Improved metabolic profile and lower inflammatory markers	Cross-sectional design prevents causal inference
Petersen et al. (2017)	Competitive cyclists	Cross-sectional	Endurance cycling	Metagenomic sequencing	Enrichment of carbohydrate- and amino acid-metabolizing bacteria	Enhanced energy metabolism and exercise adaptation	Small sample size and limited dietary control
Scheiman et al. (2019)	Marathon runners	Observational human study	Endurance running	Metagenomics and metabolomics	Increased abundance of <i>Veillonella</i> following competition	Association with improved endurance capacity	Human findings largely associative
Huang et al. (2019)	Healthy adults	Randomized intervention trial	Structured exercise training	Microbial profiling	Probiotic supplementation altered microbial composition	Improved exercise performance and body composition	Limited duration and sample size
Barton et al. (2018)	Professional athletes and controls	Cross-sectional	Mixed athletic disciplines	Metagenomics and metabolomics	Enhanced microbial functional capacity in athletes	Greater metabolic flexibility and energy utilization	Potential dietary confounding
de Paiva et al. (2023)	Athletic populations	Systematic review	Aerobic and resistance exercise	Multiple methods	Probiotics associated with favorable microbial changes	Improvements in recovery and performance markers reported in some studies	High heterogeneity among included studies

SCFA: Short-chain fatty acid; 16S rRNA: 16S ribosomal RNA sequencing.

Table 2
Animal studies investigating mechanistic pathways of the gut-muscle axis.

Study	Animal Model	Study Design	Intervention /Exercise Model	Mechanistic Focus	Key Findings	Muscle/Performance Outcomes	Translational Significance
Scheiman et al. (2019)	Mouse model	Experimental	Administration of <i>Veillonella atypica</i>	Lactate metabolism and propionate production	<i>Veillonella</i> converted exercise-derived lactate into propionate	Significantly increased treadmill endurance	Demonstrated direct microbial contribution to performance
Aoi et al. (2023)	Mouse model	Experimental	Exercise-acclimated microbiota transfer	Bile acid metabolism	Altered circulating bile acid profiles improved muscle metabolism	Enhanced skeletal muscle metabolic function	Identified microbiota-mediated metabolic signalling pathway
Kim et al. (2014)	Multiple animal models	Mechanistic review	SCFA-focused interventions	Immune regulation and inflammation	SCFAs regulated T-cell activity and inflammatory pathways	Improved muscle repair environment	Established immunological links between gut and muscle
Li et al. (2024)	Rodent studies	Mechanistic synthesis	Exercise and microbiota modulation	SCFA signalling and mitochondrial biogenesis	Exercise-induced microbial changes activated AMPK and PGC-1 α pathways	Improved muscle metabolism and reduced sarcopenia risk	Supports exercise-based microbiome interventions
Giron et al. (2022)	Various animal models	Experimental evidence synthesis	Probiotic and microbiota interventions	Muscle regeneration and immune signalling	Gut-derived metabolites influenced muscle repair and regeneration	Enhanced recovery and muscle function	Supports therapeutic microbiome modulation
Saponaro et al. (2024)	Multiple preclinical models	Mechanistic review	Myokine-microbiota interactions	Endocrine communication pathways	Identified bidirectional signalling between myokines and microbial metabolites	Enhanced adaptation and recovery mechanisms	Expands understanding of gut-muscle crosstalk

AMPK: Adenosine monophosphate-activated protein kinase; PGC-1 α : Peroxisome proliferator-activated receptor gamma coactivator 1-alpha; SCFA: Short-chain fatty acid.

At the automotous level, gut muscle communication is mediated through microbial metabolites, immune signalling pathways, and neural circuits. One of the most extensively studied groups of metabolites are the short chain fatty acids acetate, propionate, and butyrate, produced from the fermentation of dietary fibres. These compounds act as energy substrates for colonocytes, modulate systemic lipid and glucose metabolism, and activate the AMPK PGC 1 α signalling axis, which promotes mitochondrial biogenesis and oxidative capacity in muscle (Li, 2024; Wang et al., 2023). Immune signalling plays an equally important role. Dysbiosis can lead to increased intestinal permeability and the translocation of lipopolysaccharides (LPS) into circulation, triggering cytokine release that impairs insulin signalling and muscle anabolism (Chew et al., 2023; Zhao et al., 2022). In contrast, a balanced microbial environment supports regulatory immune responses that limit inflammation and allow more efficient muscle repair. Neural and hormonal pathways further integrate this system through the gut brain

muscle axis, with vagal signalling and enteroendocrine mediators such as glucagon like peptide 1 and serotonin influencing nutrient absorption, metabolic regulation, and muscle physiology (Saponaro et al., 2024).

The gut microbiota plays a critical role in energy metabolism and inflammatory control, processes that strongly influence exercise performance and adaptation. Beneficial taxa such as *Faecalibacterium prausnitzii* and *Akkermansia muciniphila* are associated with improved insulin sensitivity, greater SCFA production, and reduced oxidative stress (Wang et al., 2023). These microbial processes improve substrate utilisation during exercise, support mitochondrial efficiency, and aid glycogen replenishment during recovery. Microbial synthesis of B vitamins, amino acids, and bioactive peptides further supports protein turnover and antioxidant defence in skeletal muscle (Tremaroli & Bäckhed, 2012). Chronic disruptions to the gut ecosystem can impair these processes and lead to increased fatigue, slower recovery, and reduced

metabolic efficiency (Chew et al., 2023). Strategies that support microbial balance such as structured exercise, balanced diets, and probiotic or prebiotic interventions therefore offer potential to improve performance and recovery outcomes.

Exercise and Gut Microbiota: A Two-Way Relationship

The interaction between exercise and gut microbiota is inherently bidirectional and reflects ongoing adaptations between host physiology and microbial ecology. Exercise functions as both a modulator and a beneficiary of microbial composition and metabolic activity (Wegierska et al., 2022). Regular physical activity is associated with enhanced microbial diversity and increased abundance of beneficial taxa such as *Akkermansia muciniphila*, *Faecalibacterium prausnitzii*, and *Roseburia* spp., which support gut barrier integrity, energy metabolism, and anti-inflammatory signalling (Mach & Fuster Botella, 2017; Li, 2024). Conversely, the gut microbiota influences the host's exercise capacity by regulating nutrient bioavailability, immune balance, and resistance to oxidative stress (Scheiman et al., 2019). This reciprocal relationship forms a mutualistic feedback loop in which exercise shapes microbial activity through changes in intestinal motility, immune responses, and hormone release, while the microbiota contributes to performance and systemic adaptation through metabolite mediated pathways (Sonnenburg & Bäckhed, 2016; Clarke et al., 2014).

Acute vs. Chronic Exercise Effects on Microbial Composition and Diversity

Acute exercise, defined as a single bout of activity, produces transient changes in microbial activity and intestinal permeability. High intensity or prolonged exercise can temporarily increase gut permeability and allow LPS and other components to enter circulation, triggering short term inflammatory responses (Keirns et al., 2020). These responses are usually reversible and may support adaptive immune modulation when exposure is moderate. Chronic exercise has more sustained effects. Long term aerobic or resistance training consistently increases microbial alpha diversity, enhances populations of SCFA producing bacteria, and enriches functional genes involved in carbohydrate and amino acid metabolism (Cullen et al., 2023; Petersen et al., 2017). Athletes typically show a richer and more metabolically capable microbiome than sedentary individuals, suggesting cumulative training exposure supports a stable and health promoting microbial ecosystem (Clarke et al., 2014).

Exercise Induced Shifts in Microbial Metabolites

Exercise also alters microbial metabolite profiles, particularly SCFAs, bile acids, and tryptophan derived compounds. SCFAs such as acetate, propionate, and butyrate are key mediators between the microbiota and muscle metabolism (Nogal et al., 2021). Chronic endurance exercise increases the abundance of SCFA producing taxa such as *Roseburia* and *Eubacterium rectale*, elevating circulating SCFA concentrations that activate AMPK and promote fatty acid oxidation, mitochondrial biogenesis, and anti-inflammatory effects in skeletal muscle (Li, 2024; Mach & Fuster Botella, 2017). Exercise related shifts in bile acid metabolism arise from microbial changes in bile salt hydrolase activity, which influences lipid absorption and energy regulation (Aoi et al., 2023). Tryptophan metabolites, including indole derivatives, activate aryl hydrocarbon receptor pathways that help modulate oxidative stress and inflammatory responses during adaptation and recovery (Zhao et al., 2022). Collectively, these metabolite shifts produce a biochemical environment favourable for metabolic flexibility and muscle resilience.

Gut Derived Signals Influencing Muscle Physiology and Systemic Adaptation

Gut derived signals influence muscle physiology through metabolic, immune, and endocrine pathways. SCFAs directly enhance muscle glucose uptake and glycogen storage through G protein coupled receptor activation and reduce proinflammatory cytokines such as TNF α and IL 6 (Chew et al., 2023). Microbial metabolites shape myokine production, and higher availability of butyrate may enhance the secretion of irisin and IL 15, which contribute to mitochondrial health and muscle hypertrophy (Saponaro et al., 2024). Gut derived serotonin and secondary bile acids also influence muscle contractility and energy expenditure through enteroendocrine signalling pathways (Aoi et al., 2023). Together, these mechanisms support improved insulin sensitivity, reduced oxidative stress, and enhanced endurance. The synergistic interactions between exercise and the microbiota therefore create integrated physiological adaptations that underpin performance, recovery, and rehabilitation potential.

Nutritional Modulation of the Gut Muscle Axis

Nutrition is a central regulator of the gut muscle axis because it shapes microbial activity, metabolite production, and skeletal muscle metabolism. The gut microbiota responds rapidly and dynamically to dietary composition. Macronutrient balance, fibre intake, and

bioactive compounds strongly influence microbial diversity and the production of functionally relevant metabolites (Jardon et al., 2022). Diets rich in plant-based fibres, polyphenols, and omega 3 fatty acids typically increase beneficial taxa such as *Bifidobacterium*, *Akkermansia*, and *Faecalibacterium prausnitzii*, promoting gut barrier integrity and reducing systemic inflammation (Mach & Fuster Botella, 2017; Li, 2024). In contrast, high fat and high sugar Western style diets disrupt microbial balance, suppress short chain fatty acid (SCFA) production, and increase metabolic endotoxemia, which impairs muscle insulin sensitivity (Clarke et al., 2014; Chew et al., 2023). Nutritional approaches that enhance microbial diversity and SCFA output therefore have direct implications for exercise performance. SCFAs such as butyrate and propionate improve mitochondrial efficiency, enhance energy metabolism, and support fatigue resistance in active muscle (Saponaro et al., 2024). Collectively, these findings highlight that dietary quality shapes the microbiome muscle communication axis in ways that directly influence training, endurance, and recovery.

Probiotics, Prebiotics, and Synbiotics as Ergogenic Aids

The strategic use of probiotics, prebiotics, and synbiotics has gained increasing recognition as a means of supporting the gut muscle axis and improving exercise outcomes. Probiotics, which are live microorganisms administered in adequate amounts, can enhance barrier integrity, improve nutrient absorption, and reduce systemic inflammation (Jäger et al., 2019). Certain strains including *Lactobacillus plantarum* TWK10 and *Bifidobacterium breve* B 3 have been shown to increase endurance capacity, elevate glycogen storage, and reduce muscle damage markers in both animal and human studies (de Paiva et al., 2023; Chen et al., 2019). Prebiotics, typically non digestible fibres such as inulin and fructooligosaccharides, selectively feed SCFA producing microbes and support improved lipid oxidation and insulin sensitivity during prolonged exercise (Mach and Fuster Botella, 2017). Synbiotics, which combine probiotics and prebiotics, produce additive or synergistic effects by stabilizing the gut ecosystem, buffering exercise induced perturbations, and improving energy metabolism (Jäger et al., 2019). Together, these microbiome targeted interventions show ergogenic potential by reducing oxidative stress, modulating cytokine responses, and supporting recovery after intense physical exertion.

Nutrient Microbiome Interactions in Recovery and Protein Metabolism

Recovery following exercise depends heavily on nutrient microbiome interactions that influence amino acid availability, protein synthesis, and inflammatory balance. The gut microbiota contributes to protein digestion and amino acid metabolism, generating metabolites such as branched chain fatty acids and bioactive peptides that activate muscle anabolic pathways (Neis et al., 2015; Zhao et al., 2022). Microbial species such as *Clostridium sporogenes* and *Peptostreptococcus anaerobius* convert tryptophan and tyrosine into indole derivatives and phenolic compounds that fortify gut barrier integrity and modulate immune tone, which indirectly supports muscle recovery (Aoi et al., 2023). SCFAs produced from fermentable fibres can also enhance muscle protein synthesis through AMPK and mTOR signalling pathways, promoting regeneration after strenuous exercise (Li, 2024; Saponaro et al., 2024). Consuming high-quality proteins together with fermentable fibres therefore supports both microbial fermentation and skeletal muscle repair. This synergy provides a biochemical rationale for nutritional periodisation whereby dietary composition is aligned with training demands to optimise microbial balance, energy availability, and recovery efficiency in athletic and physically active populations.

Gut Muscle Axis and Performance Outcomes

A growing body of evidence links gut microbiota composition and function with performance phenotypes such as endurance, strength, and fatigue resistance. These effects arise largely from microbial metabolites that influence host energetics, inflammatory regulation, and muscle adaptation (Chew et al., 2023; Li, 2024). Observational studies consistently report that elite athletes and highly active individuals harbour more diverse and functionally versatile microbiomes compared with sedentary controls, including enrichment of taxa involved in SCFA production, lactate metabolism, and amino acid biosynthesis (Clarke et al., 2014; Petersen et al., 2017). These microbial patterns correlate with improved insulin sensitivity, enhanced substrate switching between fats and carbohydrates, and reduced systemic inflammation, all of which support sustained aerobic output and recovery (Wang et al., 2023). Conversely, dysbiosis or loss of key microbial functions is associated with impaired metabolic flexibility and slower recovery after intense exercise (Chew et al., 2023). Although

human studies are often associative and subject to dietary and environmental confounders, animal studies provide clear mechanistic evidence supporting causal links between microbiota and performance (Scheiman et al., 2019; Saponaro et al., 2024).

Microbial metabolites play a central role in shaping mitochondrial function and muscle adaptation. SCFAs such as butyrate, propionate, and acetate act as metabolic substrates and signalling molecules that promote mitochondrial biogenesis, enhance oxidative metabolism, and suppress proinflammatory pathways that hinder adaptation (Chew et al., 2023; Wang et al., 2023). Microbial conversion of exercise generated metabolites provides an additional layer of cross talk. For example, *Veillonella* species metabolize lactate into propionate, and administration of *Veillonella atypica* has been shown to enhance treadmill endurance in mice, demonstrating a clear microbiota derived ergogenic mechanism (Scheiman et al., 2019). Amino acid related microbial metabolites, including branched chain amino acid derivatives and proteolysis products, influence mTOR and other anabolic pathways that underpin hypertrophy and strength gains when combined with resistance training (Neis et al., 2015; Saponaro et al., 2024). Together, these pathways create a biochemical environment that can support or hinder mitochondrial efficiency, protein turnover, and the inflammatory conditions required for optimal adaptation.

Human and athlete focused studies further illustrate the translational relevance of the gut muscle axis. Scheiman et al. (2019) identified *Veillonella atypica* as enriched in marathon runners after races and confirmed its ergogenic potential in murine models. Clarke et al. (2014) reported that professional rugby players show greater microbial diversity and enrichment of functionally beneficial taxa compared with controls, findings supported by larger profiling studies of elite athletes (Petersen et al., 2017; Barton et al., 2018). Although human intervention trials remain limited, early evidence suggests that probiotics and prebiotics may reduce fatigue, support immune stability, and lessen gastrointestinal distress during heavy training. Some small studies have also reported improvements in time to exhaustion and reductions in muscle damage markers, although effects are strain specific and vary considerably (Jäger et al., 2019; Chen et al., 2019). These findings suggest that microbiome modulation may complement traditional training and nutritional strategies, though more rigorous and

standardised trials are required to confirm efficacy and identify optimal microbial or functional targets.

Recovery and Immune Modulation

The gut microbiota plays a central role in regulating post exercise inflammation by shaping both the magnitude and duration of immune responses following strenuous activity. Exercise triggers a transient activation of inflammatory pathways that mobilise neutrophils, macrophages, and cytokines essential for tissue repair. However, persistent or excessive inflammation can hinder recovery (Varghese et al., 2024). A balanced microbiome supports anti-inflammatory signalling through the production of metabolites such as SCFAs that act on immune cells to suppress proinflammatory cytokine release and to enhance regulatory pathways (Kim et al., 2014). In contrast, dysbiosis or increased intestinal permeability during intense exercise facilitates the translocation of microbial products such as lipopolysaccharide into circulation, amplifying systemic inflammation and delaying muscle repair (Dmytriv et al., 2024). These gut immune interactions collectively influence the recovery trajectory by determining how rapidly exercise induced damage is resolved.

Beyond inflammation control, gut derived signals contribute to muscle repair, oxidative balance, and tissue regeneration. Microbial metabolites including SCFAs, indole derivatives, and microbial peptides modulate redox balance by upregulating antioxidant systems and limiting excessive reactive oxygen species formation, thereby protecting regenerating muscle fibres from oxidative damage (Facchin et al., 2024; Kim et al., 2014). Emerging evidence also shows that immune cells educated in the gut migrate to injured muscle, where they regulate fibrosis and support myogenic progenitor activity, providing a mechanistic link between intestinal immunity and muscle regeneration (Giron et al., 2022). SCFAs, particularly butyrate, also influence HDAC and AMPK related signalling cascades that promote mitochondrial biogenesis and protein sparing processes that facilitate recovery.

There is growing evidence that the gut muscle axis contributes to overtraining, chronic low-grade inflammation, and impaired performance. Prolonged high intensity training without adequate recovery can disrupt gut barrier integrity and sustain endotoxemia, contributing to fatigue, mood disturbances, and symptoms characteristic of overtraining syndrome (Varghese et al., 2024; Al Beltagi et al., 2025). Athletes

exposed to heavy training loads, hot environments, or low energy availability exhibit elevated markers of intestinal permeability and lipopolysaccharide, which correlate with slower recovery and reduced performance (Ghaffar et al., 2024; Clauss et al., 2021). These findings suggest that maintaining microbial eubiosis and gut barrier function through nutrition, structured recovery, and microbiome targeted interventions can reduce maladaptive inflammation and improve training sustainability.

Collectively, mechanistic and clinical evidence positions the gut microbiota as both a mediator and an indicator of recovery quality. Microbiome derived metabolites and immune cells contribute to the resolution of inflammation, protection against oxidative stress, and enhancement of muscle repair, while dysbiosis prolongs inflammatory responses and increases overtraining risk. Practical implications include the need to monitor factors that impair gut barrier integrity such as heat stress or low energy availability and to incorporate dietary and probiotic strategies that support SCFA production and anti-inflammatory balance.

Emerging Therapeutic and Practical Applications

Advances in gut muscle axis research have generated growing interest in microbiome targeted strategies to support performance, recovery, and overall metabolic health. Athletes can benefit from dietary approaches that enhance microbial diversity and metabolite production. Diets rich in plant-based fibres, polyphenols, and omega 3 fatty acids increase beneficial taxa such as *Faecalibacterium prausnitzii* and *Akkermansia muciniphila*, which enhance SCFA synthesis and anti-inflammatory signalling (Clauss et al., 2021; Ghaffar et al., 2024). Supplementation with probiotics, prebiotics, and symbiotic offers another promising intervention avenue. Strains such as *Lactobacillus plantarum*, *Bifidobacterium longum*, and *Lactobacillus casei* have shown potential in improving gut barrier integrity; reducing exercise induced gastrointestinal distress, and lowering systemic inflammation (Clauss et al., 2021). Post biotics, which include non-viable microbial components and metabolites, present a stable alternative, offering benefits related to immune modulation and recovery (Kumar et al., 2024).

A frontier within sports science involves personalising training and nutrition based on individual microbiome profiles. Interindividual differences in microbial composition appear to contribute to variation

in training responses (Petersen et al., 2023). For example, individuals with higher *Prevotella* abundance often demonstrate superior endurance capacity and carbohydrate metabolism, likely facilitated by enhanced SCFA production (Mach et al., 2017). Integrating microbiome sequencing with metabolomic and physiological data may support personalised exercise programming. Such programs could tailor training loads and dietary strategies to promote microbial taxa or metabolic functions that enhance desired performance outcomes.

Beyond athletic applications, the gut muscle axis presents opportunities within clinical populations.

Dysbiosis and reduced SCFA production in older adults contribute to mitochondrial dysfunction, chronic inflammation, and muscle atrophy characteristic of frailty and sarcopenia (Picca et al., 2023). Resistance training combined with probiotic or prebiotic supplementation may restore microbial balance and enhance muscle anabolic sensitivity (Kim et al., 2014). Similarly, individuals with metabolic disorders may benefit from interventions that modulate systemic inflammation and improve insulin signalling (Li et al., 2024). Emerging therapeutics such as faecal microbiota transplantation and engineered probiotics highlight the potential of microbiome restoration as a tool for musculoskeletal health. These developments underscore the significance of gut muscle axis interventions in both performance enhancement and broader rehabilitation and disease management contexts.

Methodological Considerations and Research Gaps

Despite growing evidence supporting gut muscle interactions, several methodological limitations constrain current understanding and translational potential. A major challenge is the gap between animal and human research. Many mechanistic findings relating to SCFA signalling, immune metabolic crosstalk, or barrier function originate from animal models (Kim et al., 2014). Although these models provide strong experimental control, they cannot fully reflect human variability in diet, environment, and lifestyle (Clauss et al., 2021). Human studies, meanwhile, often have small sample sizes, short follow up periods, and limited dietary standardisation, which restrict causal inference (Clauss et al., 2021). Longitudinal and interventional human trials are needed to clarify how chronic training, diet, and microbiome manipulation influence muscle performance over time.

Technological constraints also limit progress. Standard microbiome sequencing methods, particularly 16S rRNA profiling, provide limited functional resolution and fail to capture strain level differences that may significantly impact host outcomes (Li et al., 2024). Advanced techniques such as metagenomics, metabolomics, and proteomics offer deeper insights but are costly and inconsistently applied. Additionally, faecal sampling remains the standard proxy for microbial activity, yet may not adequately represent metabolic processes in more physiologically active regions such as the small intestine (Idrisa et al., 2025). Metabolomic measurements of gut derived metabolites are further complicated by host metabolism, diet, and circadian factors. Lack of standardised protocols in data collection, normalisation, and bioinformatics hinders meaningful cross study comparisons.

Another challenge lies in integrating multi-level biological data to understand complex host microbe interactions. The gut muscle axis operates across metabolic, immune, neural, and transcriptional pathways, requiring systems biology approaches for comprehensive interpretation. Multi omics integration combining metagenomics, metabolomics, transcriptomics, and proteomics offers a promising direction (Petersen et al., 2023). Linking microbial gene expression with muscle transcriptomic responses could identify causal pathways that shape endurance, hypertrophy, or recovery outcomes. However, such approaches require large, multi-ethnic cohorts and accessible computational infrastructure.

To advance the field, harmonised study methodologies and longitudinal, mechanistically oriented human trials are essential. Without these improvements, progress in translating mechanistic insights into practical applications will remain limited.

Future Directions

Future research on the gut muscle axis will move toward personalised microbiome informed exercise and nutrition interventions. Recognising individual variability in both microbiome composition and exercise responses highlights the need for tailored strategies rather than generalised recommendations (Petersen et al., 2023). Identifying microbial signatures associated with distinct performance phenotypes such as endurance capacity, hypertrophy potential, or fatigue resistance will be essential. These signatures can guide dietary and exercise prescriptions tailored to microbial function, such as increasing fibre intake for individuals with low SCFA producing capacity or incorporating

anti-inflammatory diets for those with more inflammation prone profiles (Clauss et al., 2021).

Artificial intelligence, machine learning, and systems biology will play an increasingly important role in mapping the complex communication that characterises the gut muscle axis. Integrating multi omics datasets can reveal hidden patterns, predict responses to interventions, and identify biomarkers that inform training and nutrition decisions (Li et al., 2024). As computational models advance, personalised training loads, dietary plans, and recovery strategies may be dynamically adjusted based on real time gut microbial and physiological feedback (Clauss et al., 2021).

Translational opportunities extend beyond sport. In clinical contexts, microbiome-based interventions may improve rehabilitation outcomes in conditions such as sarcopenia, metabolic disease, or neurological impairment (Picca et al., 2023). Next generation probiotics, microbial consortia, and faecal microbiota transplantation present promising avenues for restoring microbial ecosystems and promoting musculoskeletal health. Collaboration across microbiology, exercise physiology, nutrition, and clinical practice will be crucial for translating mechanistic insights into practical interventions.

The field is moving toward a data driven paradigm where precision microbiome science informs personalised exercise and nutrition strategies. This shift will redefine how performance, recovery, and rehabilitation are supported across athletic and clinical populations.

Conclusions

The available evidence highlights the gut muscle axis as a central bidirectional communication network linking exercise, nutrition, and skeletal muscle physiology. Studies consistently show that gut microbiota composition and function influence energy metabolism, inflammatory regulation, and muscle adaptation, while exercise modifies microbial diversity and metabolite production in ways that support physical performance. Microbial metabolites such as short chain fatty acids, bile acids, and amino acid derivatives act as important modulators of mitochondrial function, fatigue resistance, and anabolic signalling, providing a mechanistic basis for the interplay between gut health and musculoskeletal function. Nutritional strategies that include dietary fibre, polyphenols, probiotics, prebiotics, and symbiotic further reinforce this system

by supporting recovery, reducing oxidative stress, and mitigating post exercise inflammation.

The implications for performance and recovery are wide reaching. Maintaining a diverse and metabolically capable microbiome can enhance endurance, strength, and recovery kinetics while reducing the risk of overtraining, systemic inflammation, and exercise induced gastrointestinal disturbances. Practical applications such as personalised nutrition, microbiome informed training approaches, and targeted supplementation provide promising pathways for both elite and recreational athletes seeking to optimise performance. Beyond sport, therapeutic opportunities exist in clinical contexts. Microbiome focused interventions may support management of sarcopenia, metabolic diseases, and muscle injury rehabilitation, demonstrating the broader relevance of gut muscle axis research to public health and clinical practice.

Despite considerable progress, important gaps remain. Longitudinal human studies, mechanistic investigations, and standardised analytical frameworks for microbiome and metabolomic research are still limited. Addressing these gaps will require interdisciplinary collaboration across exercise physiology, microbiology, nutrition, and computational biology. Integrative multi omics, systems biology modelling, and artificial intelligence approaches offer promising tools for identifying predictive biomarkers, tailoring personalised interventions, and translating mechanistic insights into practice. With continued coordinated research, the field is well positioned to advance understanding of the gut muscle axis and to unlock its potential for improving performance, recovery, and long-term musculoskeletal health.

Author Contributions

NM, RSM, NL, AN, ORR, EN, LN, MC, and TM contributed to the conceptualization, writing, and revision of the manuscript. All authors participated in the development of the review, contributed to the interpretation of the literature, critically reviewed the manuscript for important intellectual content, and approved the final version for publication.

Ethical Approval

N/A

Funding

The authors declare that the study received no funding.

Conflict of Interest

The authors hereby declare that there was no conflict of interest in conducting this research.

References

- Al-Beltagi, M., Saeed, N. K., Bediwy, A. S., El-Sawaf, Y., Elbatarny, A., & Elbeltagi, R. (2025). Exploring the gut-exercise link: A systematic review of gastrointestinal disorders in physical activity. *World J Gastroenterol*, 31(22), 106835. <https://doi.org/10.3748/wjg.v31.i22.106835>.
- Aoi, W., Inoue, R., Mizushima, K., Honda, A., Björnholm, M., Takagi, T., & Naito, Y. (2023). Exercise-acclimated microbiota improves skeletal muscle metabolism via circulating bile acid deconjugation. *IScience*, 26(3), 106251. <https://doi.org/10.1016/j.isci.2023.106251>.
- Barton, W., Penney, N. C., Cronin, O., Garcia-Perez, I., Molloy, M. G., Holmes, E., Shanahan, F., Cotter, P. D., & O'Sullivan, O. (2018). The microbiome of professional athletes differs from that of more sedentary subjects in composition and particularly at the functional metabolic level. *Gut*, 67(4), 625–633. <https://doi.org/10.1136/gutjnl-2016-313627>.
- Chew, W., Lim, Y. P., Lim, W. S., Chambers, E. S., Frost, G., Wong, S. H., & Ali, Y. (2023). Gut-muscle crosstalk. A perspective on influence of microbes on muscle function. *Front Med*, 9, 1065365. <https://doi.org/10.3389/fmed.2022.1065365>.
- Clarke S. F., Murphy, E. F., O'Sullivan, O., Lucey, A. J., Humphreys, M., Hogan, A., Hayes, P., O'Reilly M., Jeffery, I. B., Wood-Martin, R., Kerins, D. M., Quigley, E., Ross, R. P., O'Toole, P. W., Molloy, M. G., Falvey, E., Shanahan F., & Cotter, P. D. (2014). Exercise and associated dietary extremes impact on gut microbial diversity. *Gut*, 63(12), 1913–1920. <https://doi.org/10.1136/gutjnl-2014-307305>.
- Clauss, M., Gérard, P., Mosca, A., & Leclerc, M. (2021). Interplay between exercise and gut microbiome in the context of human health and performance. *Front Nutr*, 8, 637010. <https://doi.org/10.3389/fnut.2021.637010>.
- Cullen, J. M., Shahzad, S., & Dhillon, J. (2023). A systematic review on the effects of exercise on gut microbial diversity, taxonomic composition, and microbial metabolites: Identifying research gaps and future directions. *Front Physiol*, 14, 1292673. <https://doi.org/10.3389/fphys.2023.1292673>.
- de Paiva, A. K., de Oliveira, E. P., Mancini, L., Paoli, A., & Mota, J. F. (2023). Effects of probiotic supplementation on performance of resistance and aerobic exercises: a systematic review. *Nutr Rev*, 81(2), 153–167. <https://doi.org/10.1093/nutrit/nuac046>.
- Dmytriv, T. R., Storey, K. B., & Lushchak, V. I. (2024). Intestinal barrier permeability: the influence of gut microbiota, nutrition, and exercise. *Front Physiol*, 15, 1380713. <https://doi.org/10.3389/fphys.2024.1380713>.
- Facchin, S., Bertin, L., Bonazzi, E., Lorenzon, G., De Barba, C., Barberio, B., Zingone, F., Maniero, D., Scarpa, M., Ruffolo, C., Angriman, I., & Savarino, E. V. (2024). Short-Chain Fatty Acids and Human Health: From Metabolic Pathways to Current Therapeutic Implications. *Life*, 14(5), 559. <https://doi.org/10.3390/life14050559>.
- Ghaffar, T., Ubaldi, F., Volpini, V., Valeriani, F., & Romano Spica, V. (2024). The role of gut microbiota in different types of physical activity and their intensity: Systematic review and meta-analysis. *Sports*, 12(8), 221. <https://doi.org/10.3390/sports12080221>.

- Giron, M., Thomas, M., Dardevet, D., Chassard, C., & Savary-Auzeloux, I. (2022). Gut microbes and muscle function: can probiotics make our muscles stronger? *J Cachexia Sarcopenia Muscle*, 13(3), 1460-1476. <https://doi.org/10.1002/jcsm.12964>
- Huang, W. C., Lee, M. C., Lee, C. C., Ng, K. S., Hsu, Y. J., Tsai, T. Y., ... & Huang, C. C. (2019). Effect of *Lactobacillus plantarum* TWK10 on exercise physiological adaptation, performance, and body composition in healthy humans. *Nutrients*, 11(11), 2836. <https://doi.org/10.3390/nu11112836>
- Idrisa, K., GATO, E., & Agossou, J. A. (2025). Postbiotics and musculoskeletal health: emerging applications in bone, muscle, and joint care. *International Journal of Research Publication and Reviews*, 6(5), 18334-18339. <https://doi.org/10.55248/gengpi.6.0525.2025>
- Jäger, R., Mohr, A. E., Carpenter, K. C., Kerksick, C. M., Purpura, M., Moussa, A., ... & Antonio, J. (2019). International society of sports nutrition position stand: probiotics. *J Int Soc Sports Nutr*, 16(1), 62. <https://doi.org/10.1186/s12970-019-0329-0>
- Jardon, K. M., Canfora, E. E., Goossens, G. H., & Blaak, E. E. (2022). Dietary macronutrients and the gut microbiome: a precision nutrition approach to improve cardiometabolic health. *Gut*, 71(6), 1214-1226. <https://doi.org/10.1136/gutjnl-2020-323715>
- Keirns, B. H., Koemel, N. A., Sciarrillo, C. M., Anderson, K. L., & Emerson, S. R. (2020). Exercise and intestinal permeability: another form of exercise-induced hormesis? *Am J Physiol Gastrointest Liver Physiol*, 319(4), G512-G518. <https://doi.org/10.1152/ajpgi.00232.2020>
- Kim, C. H., Park, J., & Kim, M. (2014). Gut microbiota-derived short-chain fatty acids, T cells, and inflammation. *Immune Netw*, 14(6), 277. <https://doi.org/10.4110/in.2014.14.6.277>
- Kumar, A., Green, K. M., & Rawat, M. (2024). A comprehensive overview of postbiotics with a special focus on discovery techniques and clinical applications. *Foods*, 13(18), 2937. <https://doi.org/10.3390/foods13182937>
- Li, T., Yin, D., & Shi, R. (2024). Gut-muscle axis mechanism of exercise prevention of sarcopenia. *Front Nutr*, 11, 1418778. <https://doi.org/10.3389/fnut.2024.1418778>
- Mach, N., & Fuster-Botella, D. (2017). *Endurance exercise and gut microbiota: A review. J Sport Health Sci*, 6(2), 179-197. <https://doi.org/10.1016/j.jshs.2016.05.001>
- Neis, E. P., Dejong, C. H., & Rensen, S. S. (2015). The role of microbial amino acid metabolism in host metabolism. *Nutrients*, 7(4), 2930-2946. <https://www.mdpi.com/2072-6643/7/4/2930>
- Nogal, A., Valdes, A. M., & Menni, C. (2021). The role of short-chain fatty acids in the interplay between gut microbiota and diet in cardio-metabolic health. *Gut microbes*, 13(1), 1-24. <https://doi.org/10.1080/19490976.2021.1897212>
- O'Brien, M. T., O'Sullivan, O., Claesson, M. J., & Cotter, P. D. (2022). The athlete gut microbiome and its relevance to health and performance: a review. *Sports Med*, 52(1), 119-128. <https://doi.org/10.1007/s40279-022-01785-x>
- Petersen, L. M., Bautista, E. J., Nguyen, H., Hanson, B. M., Chen, L., Lek, S. H., Sodergren, E., & Weinstock, G. M. (2017). Community characteristics of the gut microbiomes of competitive cyclists. *Microbiome*, 5(1), 98. <https://doi.org/10.1186/s40168-017-0320-4>
- Picca, A., Fanelli, F., Calvani, R., Mulè, G., Pesce, V., Sisto, A., Pantanelli, C., Bernabei, R., Landi, F., & Marzetti, E. (2018). Gut dysbiosis and muscle aging: searching for novel targets against sarcopenia. *Mediators Inflamm*, 2018, 7026198. <https://doi.org/10.1155/2018/7026198>
- Saponaro, F., Bertolini, A., Baragatti, R., Galfo, L., Chiellini, G., Saba, A., & D'Urso, G. (2024). Myokines and microbiota: new perspectives in the endocrine muscle-gut axis. *Nutrients*, 16(23), 4032. <https://doi.org/10.3390/nu16234032>
- Scheiman, J., Lubner, J. M., Chavkin, T. A., MacDonald, T., Tung, A., Pham, L. D., ... & Kostic, A. D. (2019). Metabolomics analysis of elite athletes identifies a performance-enhancing microbe that functions via lactate metabolism. *Nat Med*, 25(7), 1104-1109. <https://doi.org/10.1038/s41591-019-0485-4>
- Sonnenburg, J. L., & Bäckhed, F. (2016). Diet-microbiota interactions as moderators of human metabolism. *Nature*, 535(7610), 56-64. <https://doi.org/10.1038/nature18846>
- Tang, Y., Wang, Y. D., Wang, Y. Y., Liao, Z. Z., & Xiao, X. H. (2023). Skeletal muscles and gut microbiota-derived metabolites: novel modulators of adipocyte thermogenesis. *Front Endocrinol (Lausanne)*, 14, 1265175. <https://doi.org/10.3389/fendo.2023.1265175>
- Tremaroli, V., & Bäckhed, F. (2012). Functional interactions between the gut microbiota and host metabolism. *Nature*, 489(7415), 242-249. <https://doi.org/10.1038/nature11552>
- Varghese, S., Rao, S., Khattak, A., Zamir, F., & Chaari, A. (2024). Physical exercise and the gut microbiome: a bidirectional relationship influencing health and performance. *Nutrients*, 16(21), 3663. <https://doi.org/10.3390/nu16213663>
- Wang, Y., Li, Y., Bo, L., Zhou, E., Chen, Y., Naranmandakh, S., Xie, W., Ru, Q., Chen, L., Zhu, Z., Ding, C., & Wu, Y. (2023). Progress of linking gut microbiota and musculoskeletal health: casualty, mechanisms, and translational values. *Gut Microbes*, 15(2), 2263207. <https://doi.org/10.1080/19490976.2023.2263207>
- Wegierska, A. E., Charitos, I. A., Topi, S., Potenza, M. A., Montagnani, M., & Santacroce, L. (2022). The Connection Between Physical Exercise and Gut Microbiota: Implications for Competitive Sports Athletes. *Sports Med*, 52(10), 2355-2369. <https://doi.org/10.1007/s40279-022-01696-x>
- Xu, Y., & He, B. (2025) The gut-muscle axis: a comprehensive review of the interplay between physical activity and gut microbiota in the prevention and treatment of muscle wasting disorders. *Front Microbiol*, 16, 1695448. <https://doi.org/10.3389/fmicb.2025.1695448>