

Impiego dei probiotici per il contrasto della sarcopenia fisiologica: razionale e risultati

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Age-related sarcopenia: facts and figures

Sarcopenia is a systemic and progressive disorder of skeletal muscle characterized by an age-related decline in muscle mass, strength, and/or function (Rosenberg 1989).

Its prevalence is alarmingly high, affecting 5 -13% of adults aged 60–70 and rising to 11–50% in those over 80 (Wang, 2025)

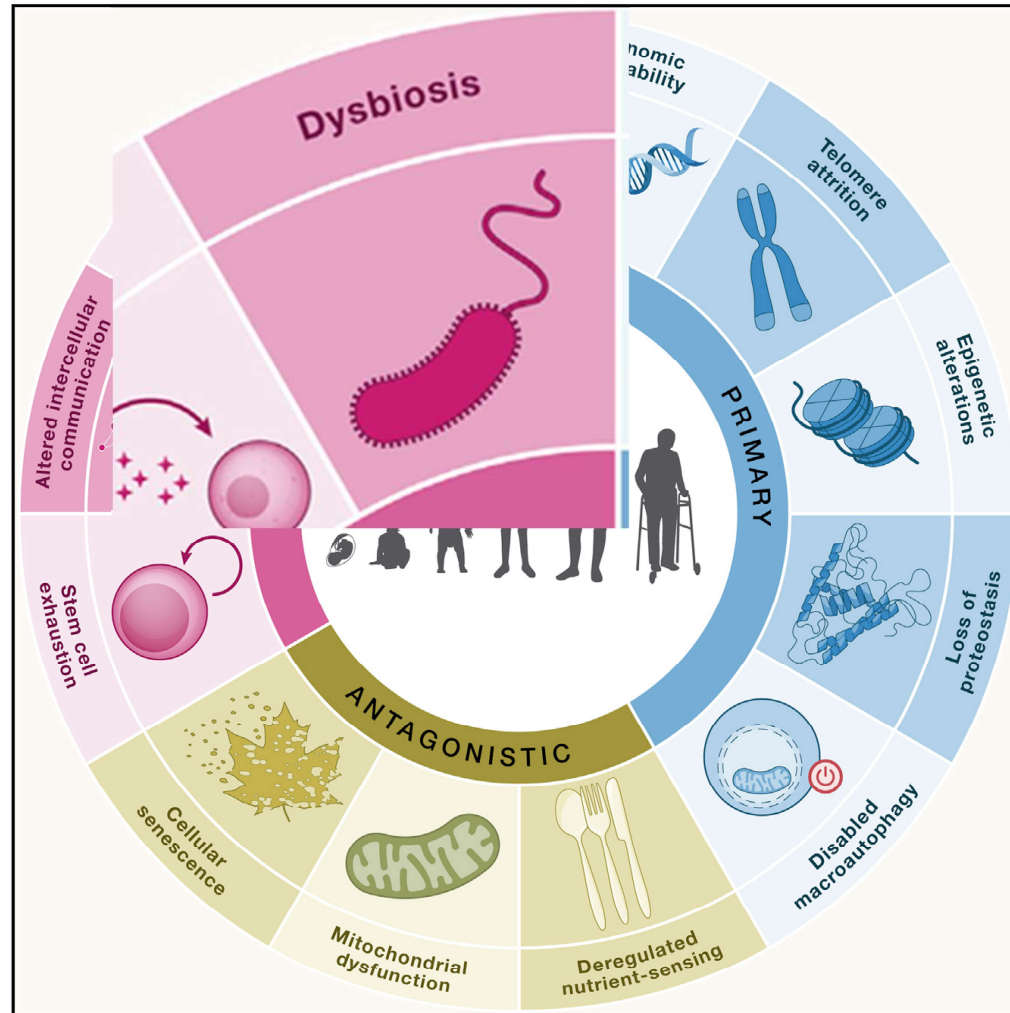
Sarcopenia increases vulnerability to adverse outcomes such as heightened risk of falls and mortality, decline in physical function, and frailty, which significantly impacts the quality of life for the elderly population (Wang, 2025).

MECHANISMS ?

Hallmarks of ageing

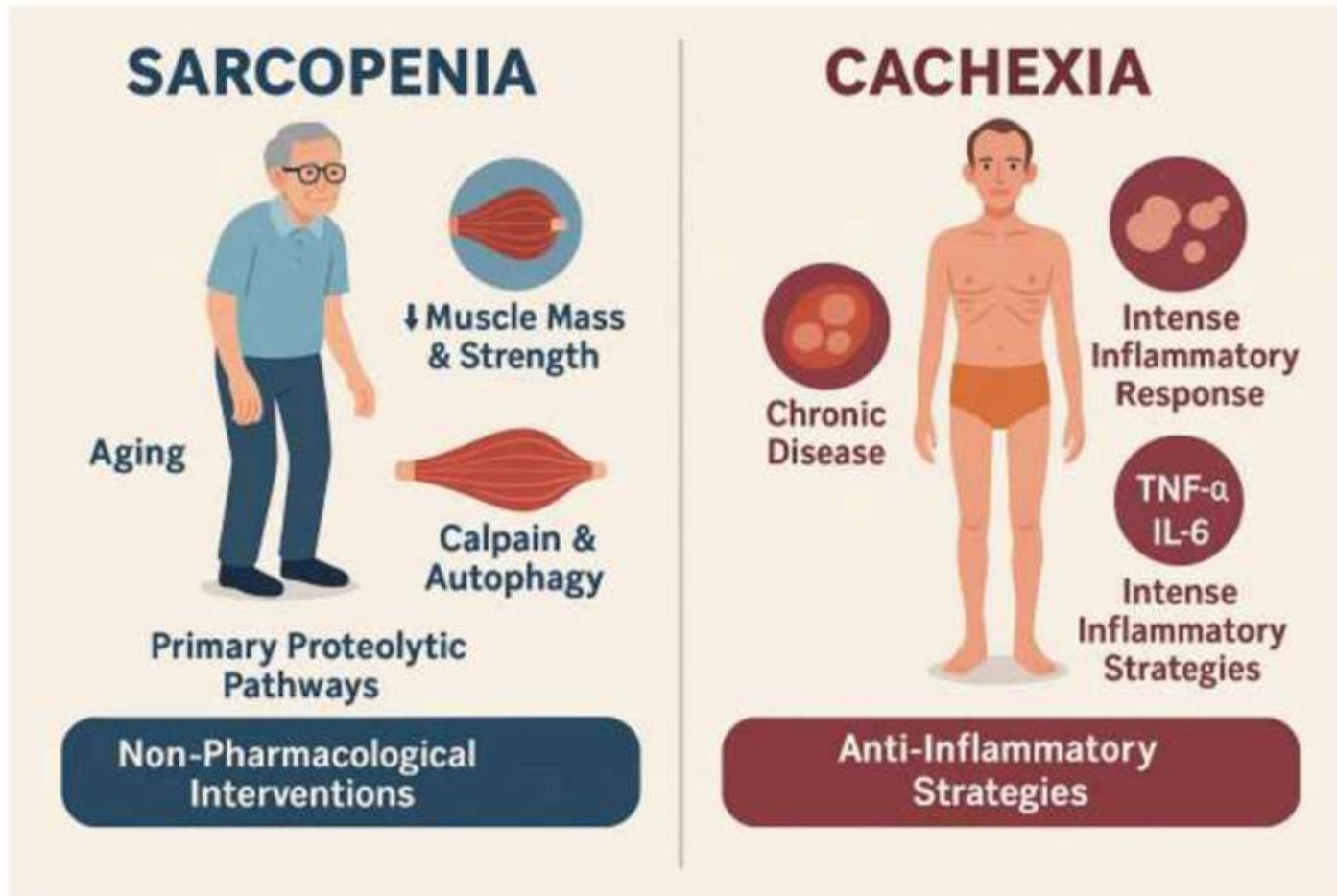
Criteria

(1) the time-dependent manifestation of alterations accompanying the aging process, (2) the possibility to accelerate aging by experimentally accentuating the hallmark, and—most decisively—(3) the opportunity to **decelerate, halt, or reverse aging** by therapeutic interventions on the hallmark.



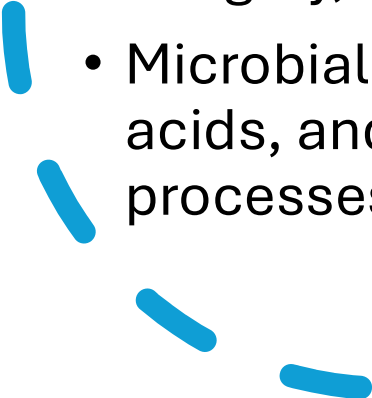
Lopez-Otin, *Cell*
2023;186:243-78

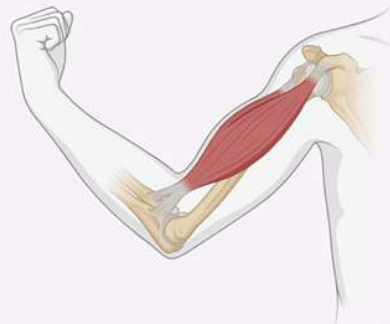
Differences between sarcopenia and cachexia



The gut-muscle axis

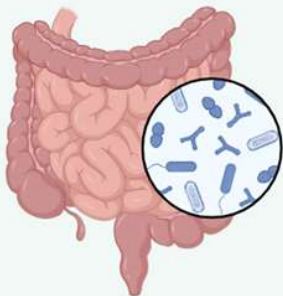


- The **gut microbiota–muscle axis** is now recognized as a bidirectional system in which gut microbial composition and metabolites directly influence skeletal muscle mass, strength, and function, particularly in the context of aging and muscle wasting disorders such as sarcopenia and cachexia.
 - Key mechanisms include modulation of muscle protein turnover, inflammation, mitochondrial function, neuromuscular junction integrity, and insulin sensitivity.
 - Microbial metabolites—especially short-chain fatty acids (SCFAs), bile acids, and amino acid derivatives—play central roles in these processes.
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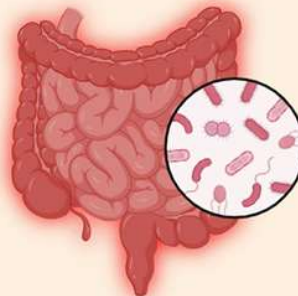
Gut-muscle axis

Healthy



- ↓ Intestinal inflammation
- ↑ Intestinal mucosal barrier function
- ↑ Antioxidants production
- ↑ SCFAs
- ↑ Immune regulatory performance
- ↑ Endocrine regulatory performance

Sarcopenia

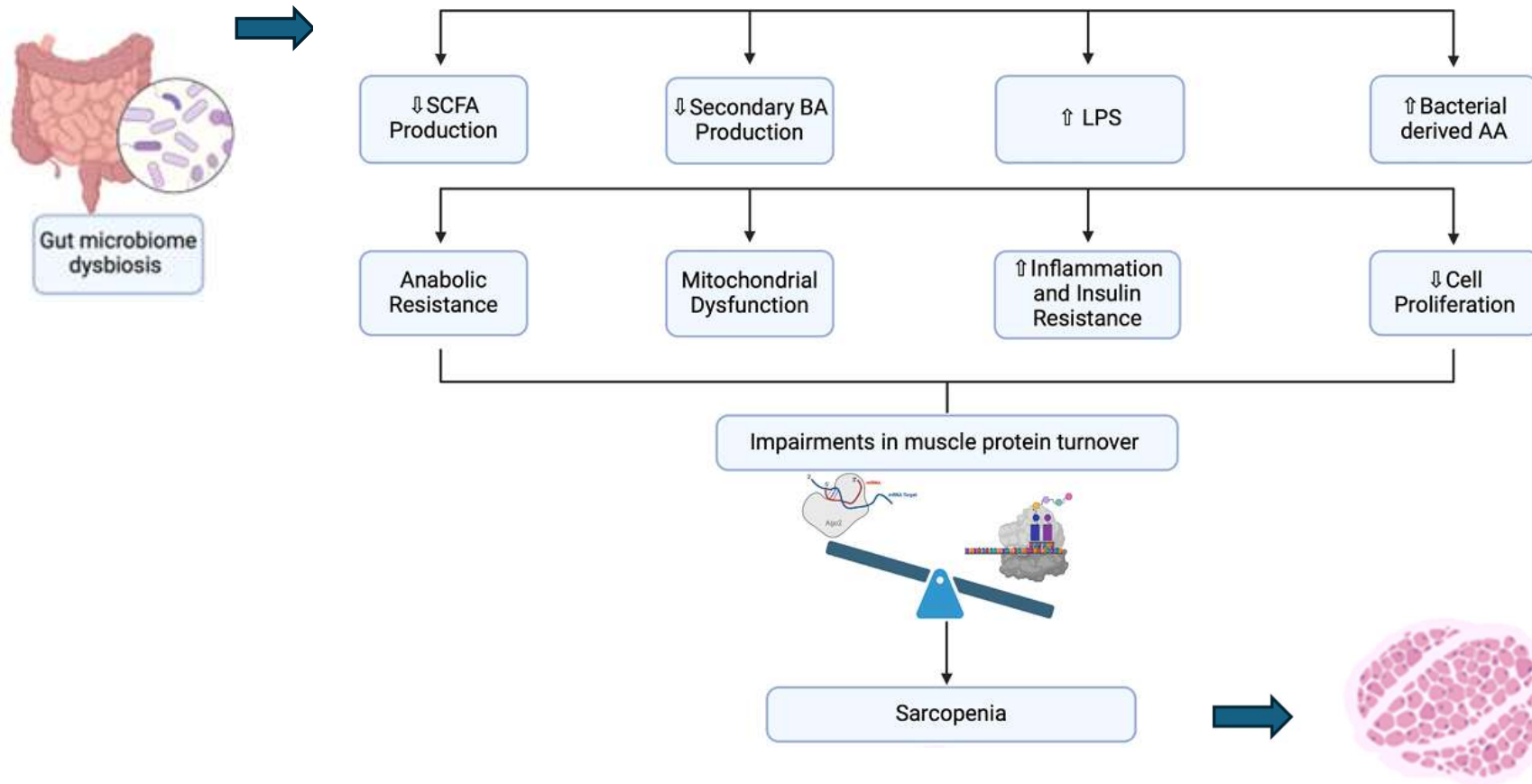


- ↑ Intestinal inflammation
- ↓ Intestinal mucosal barrier function
- ↑ LPS production
- ↓ SCFAs
- ↓ Immune regulatory performance
- ↓ Endocrine regulatory performance

Regulatory mechanism of gut microbiota on sarcopenia based on gut-muscle axis

Li W et al. *Food Sci Nutr* 2024;21: 8779-8792

Age-related alterations in gut-muscle axis



The aged-type gut microbiota

AGED-TYPE MICROBIOTA

- LOW BIODIVERSITY
- INCREASE IN PRO-INFLAMMATORY PATHOBIONTS:
Enterobacteriaceae, Staphylococcus, Streptococcus
- REDUCTION IN IMMUNOMODULATORY GROUPS:
Clostridium cluster IV
- REDUCTION IN SCFA PRODUCERS:
Clostridium cluster XIVa

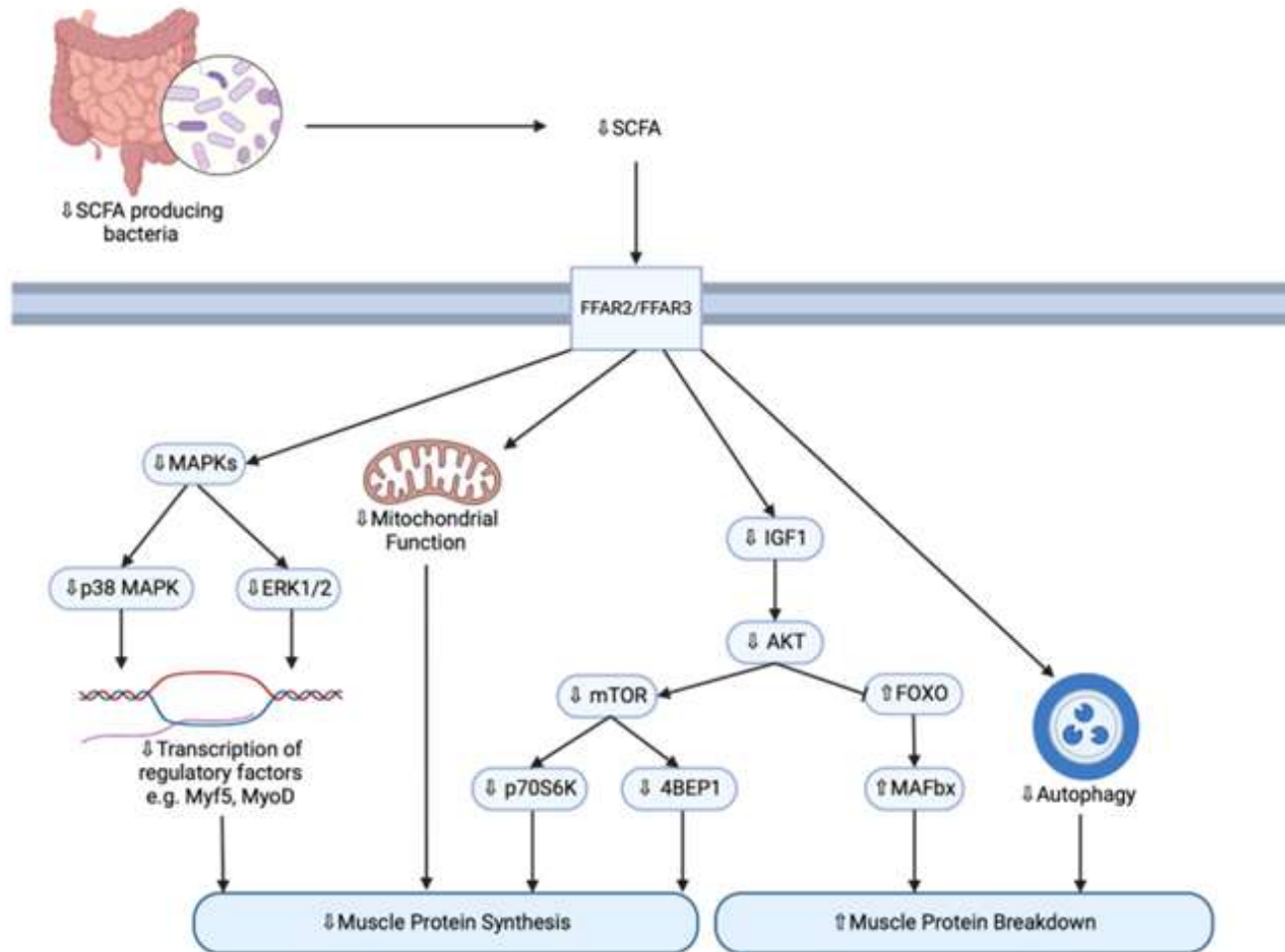
- **DETERIORATION IN NUTRIENT INTAKE AND ABSORPTION** (including dentition, salivary function and intestinal transit time)
- **SENSORY CHANGES IN TASTE AND SMELL**



- **PHYSICAL CHANGES TO THE INTESTINAL EPITHELIAL BARRIER** (leaky gut)
- **INFLAMMAGING**
- **IMMUNOSENESCENCE**

From a decline in SCFA concentrations to sarcopenia

Ageing is associated with a decline in SCFAs. SCFAs can be up taken by the FFAR2/FFAR3 receptors in skeletal muscle which in turn may alter cellular proliferation, mitochondrial function, decrease muscle protein synthesis and increase muscle protein breakdown.



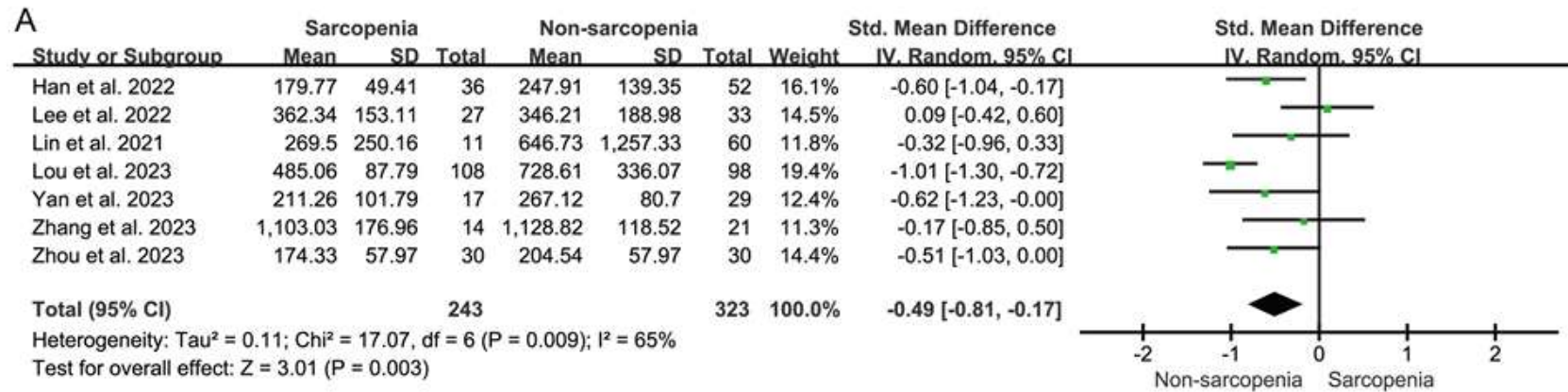
Gut microbiota in patients with sarcopenia: a systematic review and meta-analysis

Guangning Wang^{1†}, Yujie Li^{2†}, Huisong Liu³ and Xinjuan Yu^{4*}

Results: Ten studies, including 421 cases of sarcopenia and 1,642 cases of controls, were included in the meta-analysis. Patients with sarcopenia showed significantly reduced gut microbiota in α diversity, and β diversity was significantly different in 8/9 of included studies. We also found more abundance of phylum Proteobacteria and genus *Escherichia-Shigella*, and less abundance of phylum Firmicutes and genus *Faecalibacterium*, *Prevotella 9*, *Blautia* in the sarcopenia group.

Conclusion: The gut microbiota composition in patients with sarcopenia has undergone alterations, serving as a fundamental reference for further investigation into the potential pathogenic mechanisms and treatment strategies for sarcopenia.

Alpha diversity in sarcopenia vs non sarcopenia

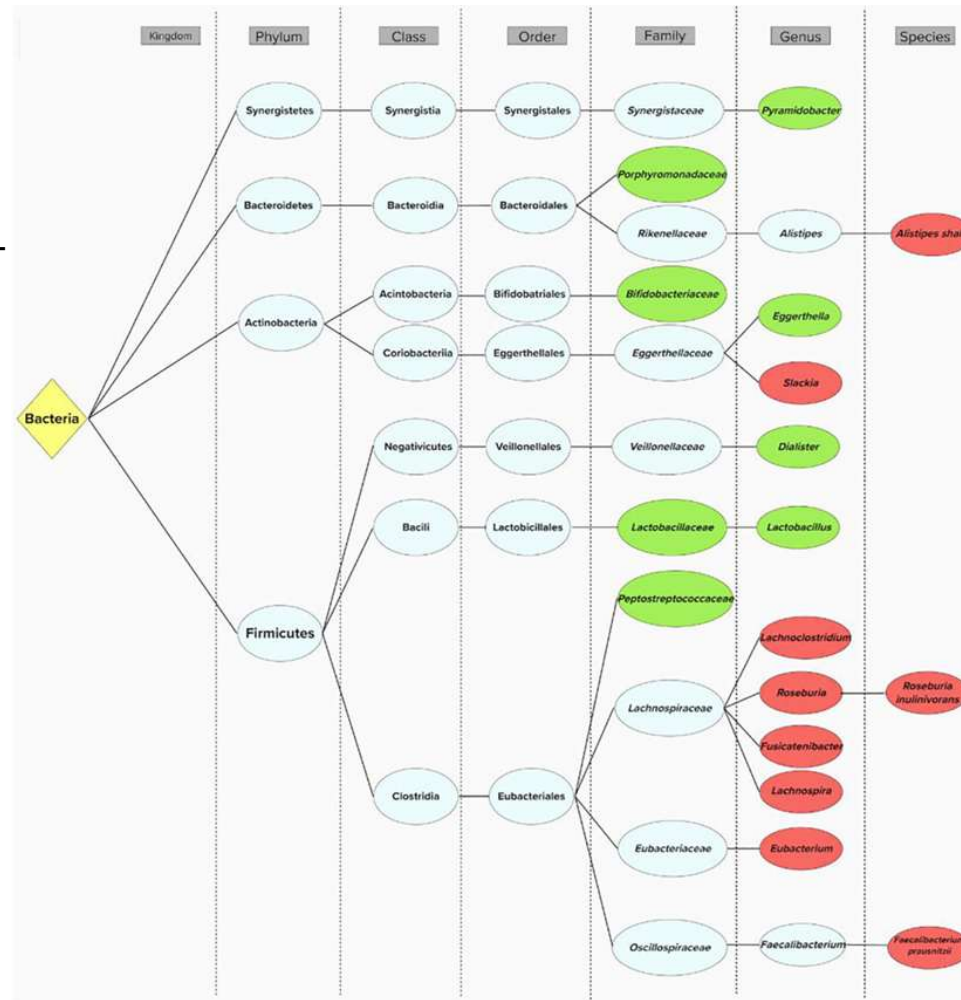


Beta diversity in sarcopenic patients among different studies

Study	β diversity	Findings	Statistic value
Almohaisen et al. (2022)	PCoA based on Bray–Curtis dissimilarity	No significant difference in gut microbial composition among S and NS	$p = 0.360$
Han et al. (2022)	PCoA based on Bray–Curtis dissimilarity	A significant difference in gut microbial composition among S and NS	$p = 0.037$
He et al. (2023)	PCoA based on Bray–Curtis dissimilarity	A significant difference in gut microbial composition among S and NS	$p < 0.050$
Lee et al. (2022)	PCoA based on Bray–Curtis dissimilarity	A significant difference in gut microbial composition among S and NS ^a	$p = 0.049$
	PCoA based on Bray–Curtis dissimilarity	No significant difference in gut microbial composition among S and NS ^b	$p = 0.200$
Liu et al. (2021)	PLS-DA	A significant difference in gut microbial composition among S and NS	$p = 0.0001$
	Unweighted UniFrac distances matrix	A significant difference in gut microbial composition among S and NS	NR
	PCoA based on Unweighted UniFrac distances	No significant difference in gut microbial composition among S and NS	$p = 0.080$
Wang X. et al. (2022) and Wang Y. et al. (2022)	PCoA based on Bray–Curtis dissimilarity	A significant difference in gut microbial composition among S and NS ^c	$p = 0.004$
	PCoA based on Bray–Curtis dissimilarity	A significant difference in gut microbial composition among S and NS ^d	$p = 0.020$
Yan et al. (2023)	PCoA based on Bray–Curtis dissimilarity	A significant difference in gut microbial composition among S and NS	$p < 0.050$
Zhang et al. (2023)	PCoA based on Bray–Curtis dissimilarity	A significant difference in gut microbial composition among S and NS	$p = 0.001$
Zhou et al. (2023)	PCoA based on Bray–Curtis dissimilarity	A significant difference in gut microbial composition among S and NS	$p = 0.004$

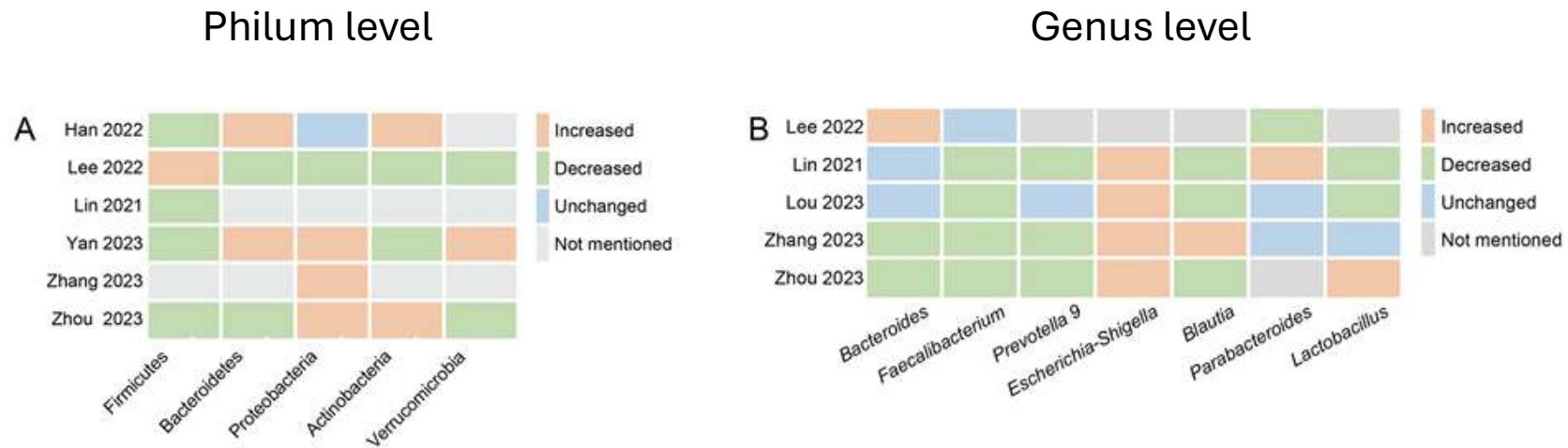
Bacterial taxonomy of altered gut microbiota composition in age-related sarcopenia among human studies

The principal alteration in age-related sarcopenia was a reduction in short-chain fatty acids (SCFAs)-producing bacteria, in particular of Lachnospiraceae family. Also decreased were some bacterial species, such as *Alistipes shahi* and *Faecalibacterium prausnitzii*, which are butyrate-producers

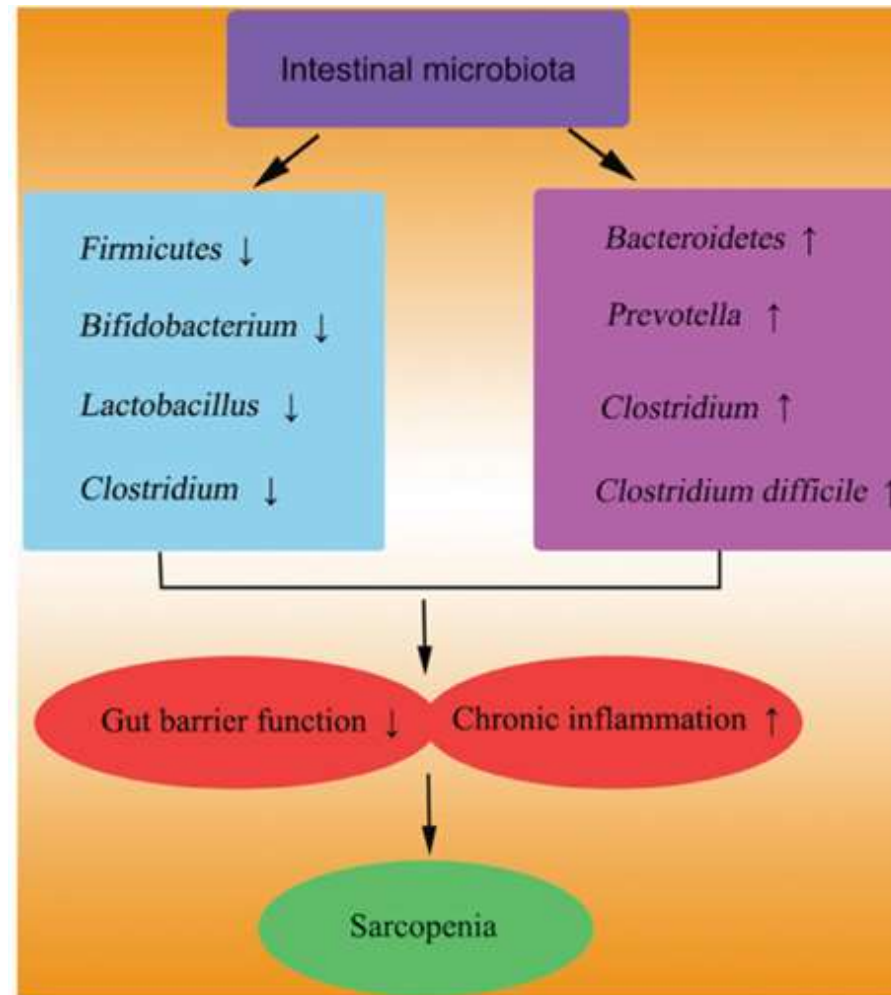


Nikkah A. *J Appl Microbiol* 2022;134:1-11

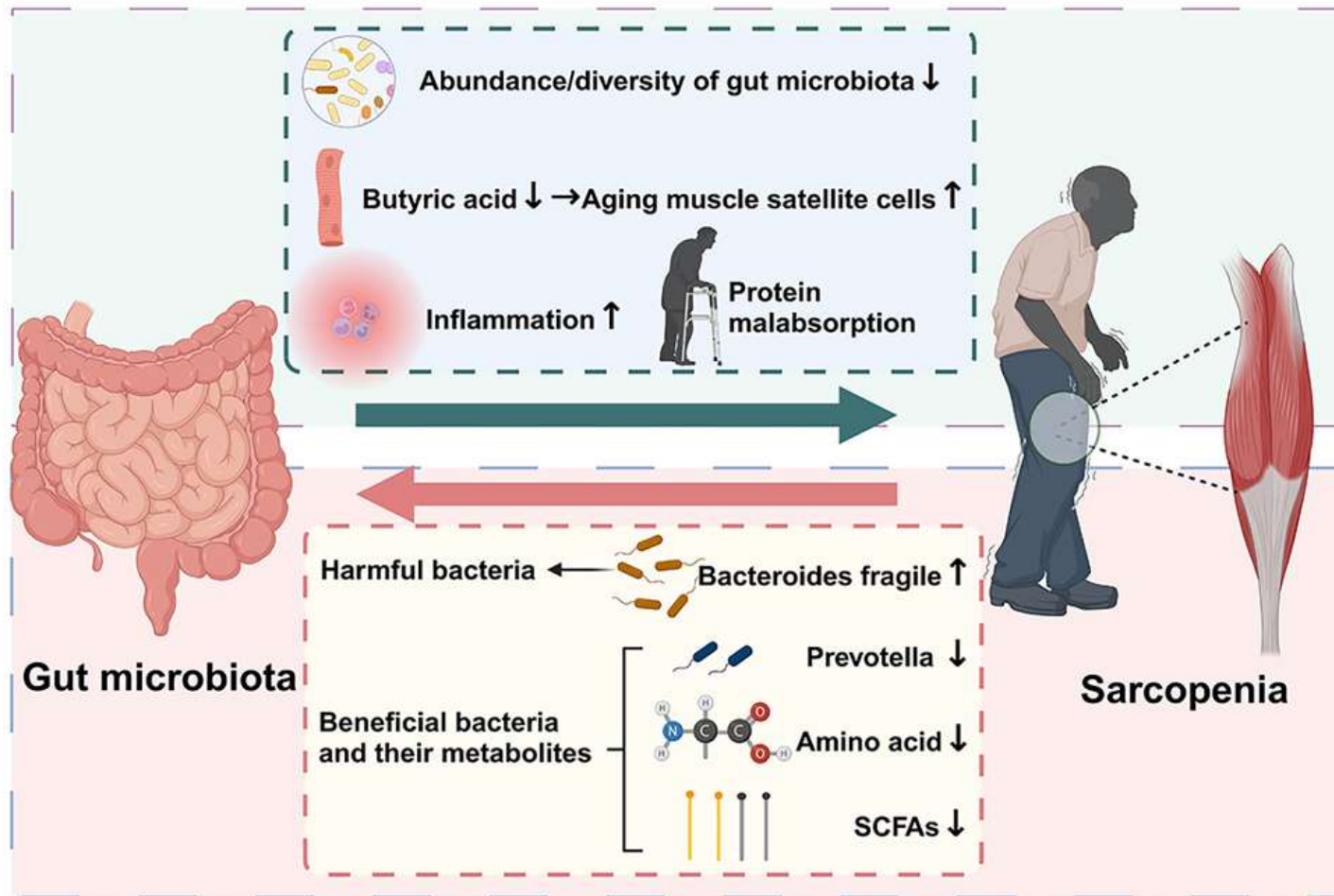
Changes in the relative abundance of the microbiota in patients with sarcopenia compared with those of non-sarcopenia controls



From dysbiosis to sarcopenia



Potential mechanisms of the gut dysbiosis leading to sarcopenia

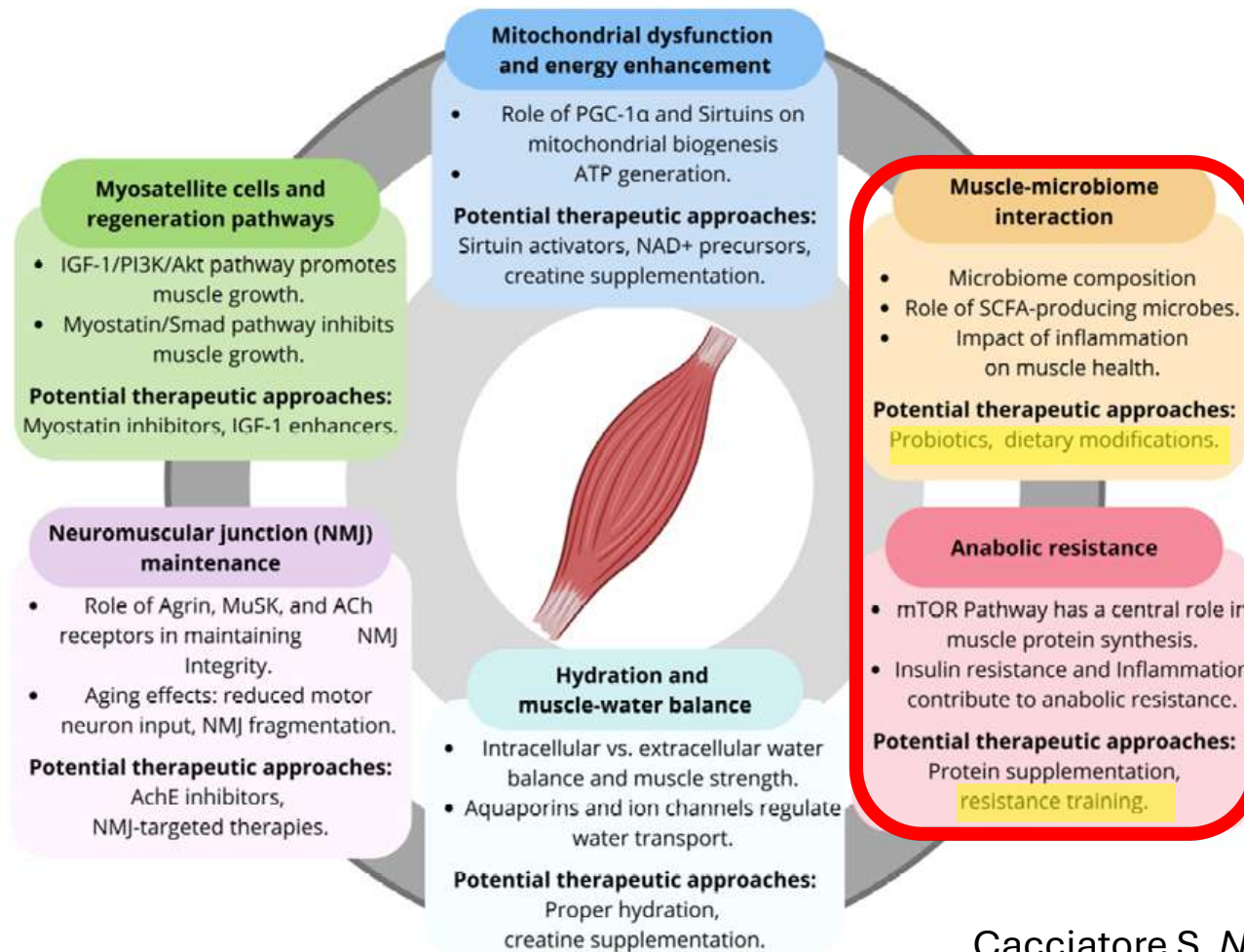


Li W et al. *Food Sci Nutr* 2024;21: 8779-8792

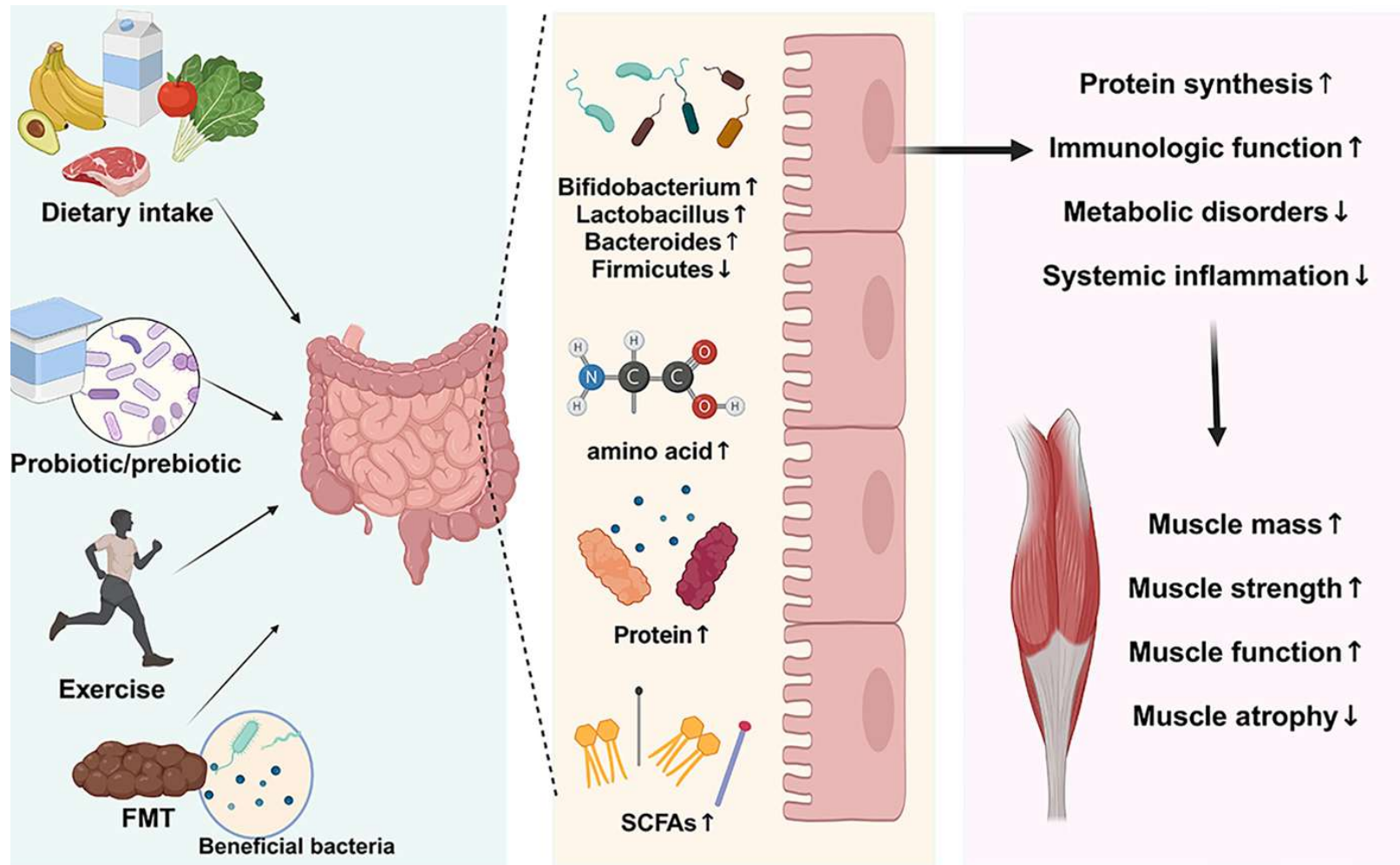
Modulation of sarcopenia pathways by microbial metabolites: the case of SCFA

Microbial metabolites	Physiological function	Modulation of sarcopenia pathways	Trends in sarcopenia	References
SCFAs	Inhibiting the NF- κ B signaling pathway	Protection from inflammaging	↓	Hu et al., 2024 ; Qu et al., 2025 ; Tang et al., 2022 ; Wang et al., 2012 ; Wu et al., 2020 ; Ye et al., 2024
	Activating PGC-1 α	Enhancement of mitochondrial function	↓	
	Increasing expression of IRS-1 gene	Improvement of insulin sensitivity	↓	
	Upregulating Occludin and ZO-1	Enhancement of intestinal barrier integrity	↓	
	Activating AMPK signaling pathway	Improvement of protein synthesis	↓	

Overview of emerging pathways and potential therapeutic approaches for age-related sarcopenia



Potential methods to alleviate sarcopenia by modulating gut microbiota



Evidence-based interventions against sarcopenia

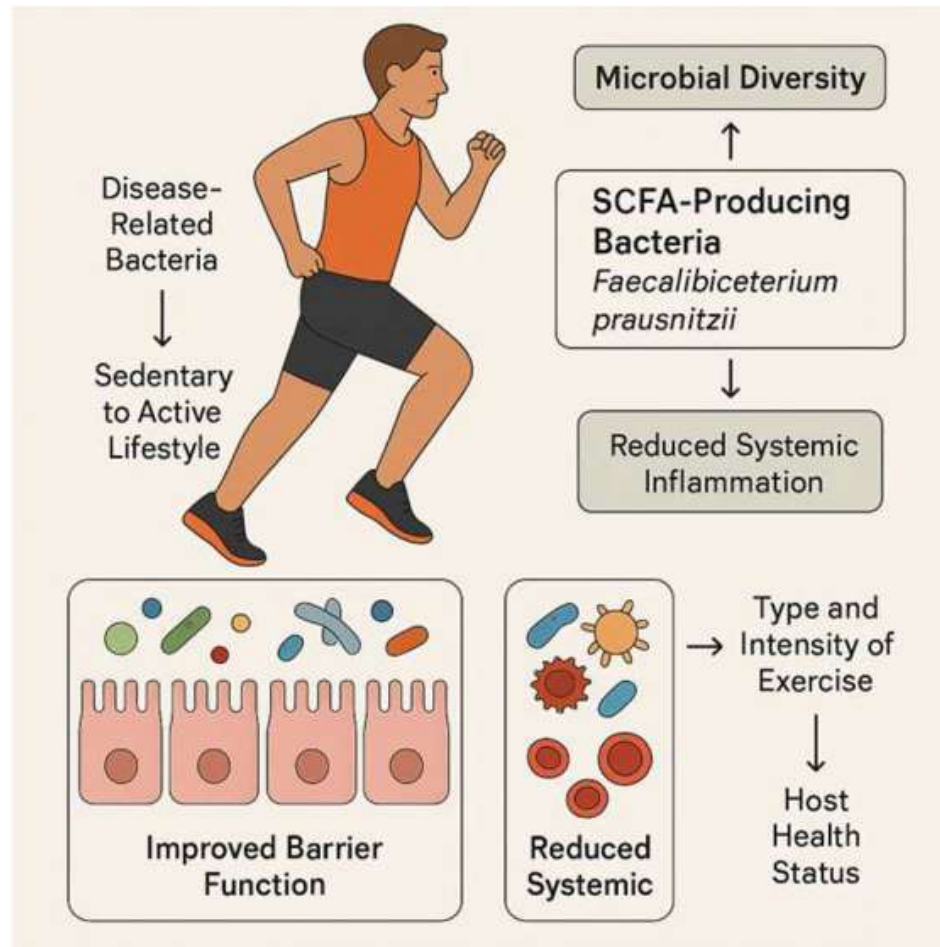
Intervention	Strategies	Evidence-Based Outcomes	References
Physical exercise	- Resistance training; - Moderate aerobic exercise.	- ↑ Muscle mass; - ↑ Strength.	[277–279]
Protein Supplementation	- 1.2–1.5 g/kg/day protein; - Leucine-rich sources (whey).	- ↑ Gait speed.	[280]
Vitamin D	- Supplementation (800 IU).	- ↑ Appendicular muscle mass.	[281]
Mediterranean diet	- Omega-3, MUFA, and fiber.	- ↓ Systemic inflammation; - Bone-muscular protection.	[282,283]
Gut Microbiota Modulation	- Probiotics (e.g., <i>Lactobacillus</i>); - Prebiotics.	- ↓ Muscle atrophy.	[265,266]
Multimodal Combination	- Exercise + protein + vitamin D.	- Synergistic effects (↑ muscle mass).	[263]

↑: Increase; ↓: Decrease; MUFA: Monounsaturated fatty acid.

Harnessing the gut-muscle axis: multimodal approaches to combat sarcopenia

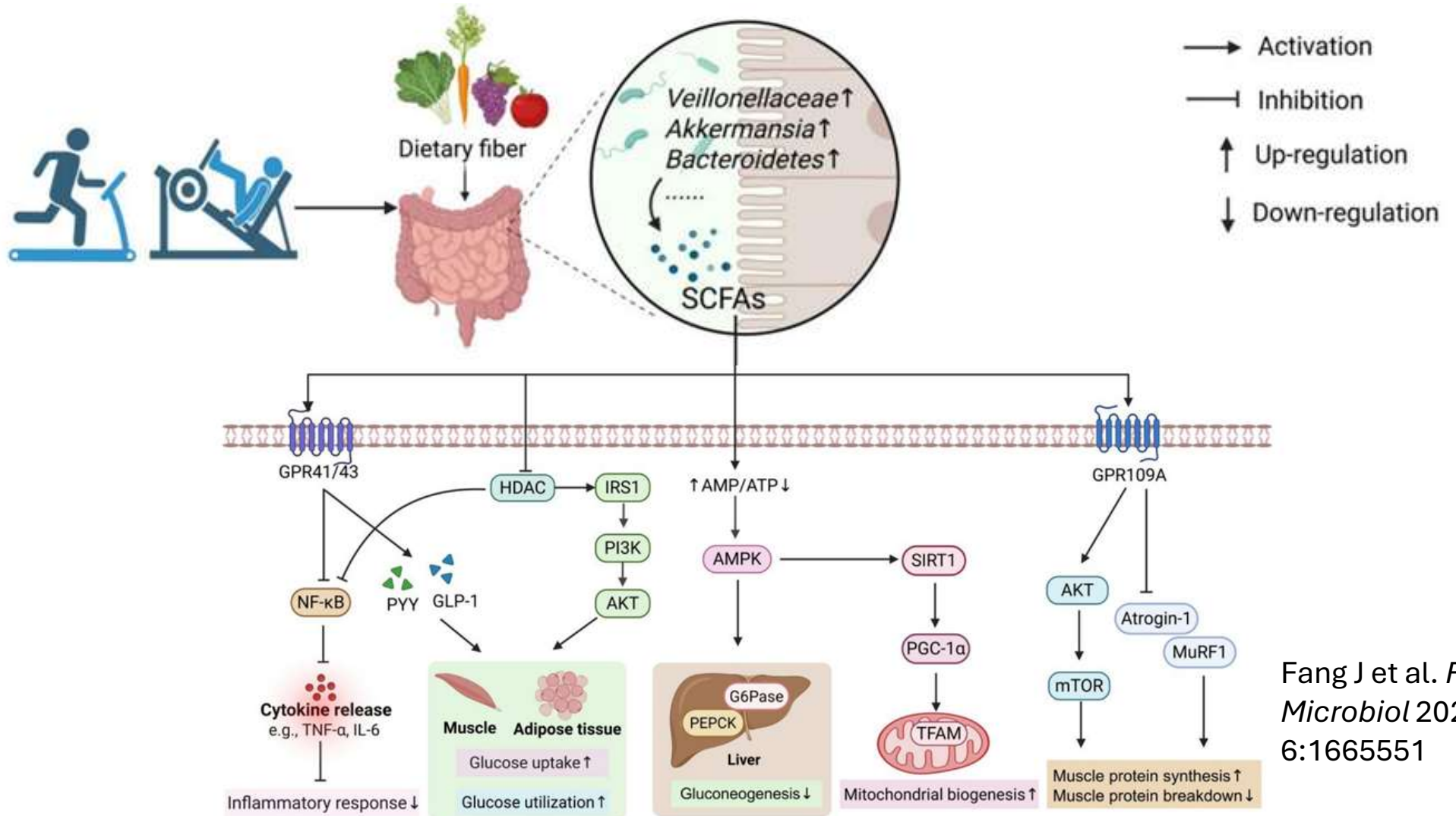
Intervention	Muscle effects	Microbiome effects	Evidence
Aerobic exercise	Increased Aerobic capacity and Muscle endurance	Increased abundance of <i>Oscillospira</i> <i>Bacteroides</i> and reduced abundance of <i>Clostridium difficile</i>	Human RCTs ranging from 5 to 12 weeks duration in healthy aged participants [Taniguchi et al. (2018); Morita et al. (2019)]
Resistance exercise	Increased muscle mass and function	No changes in gut microbiota composition and alpha diversity reported	Human RCT of 8 weeks duration in healthy young participants [Bycura et al. (2021)]
Combination of resistance and aerobic exercise	Increased muscle mass and function	Increased abundance of <i>Actinobacteria</i> and reduced abundance of <i>Firmicutes</i> and <i>Bacteroidetes</i>	Human RCT of 8 weeks duration in healthy sedentary aged participants [Zhong et al. (2021)]
Probiotics	Increased Muscle mass and function and mitochondria biogenesis. Reduced Catabolic markers Oxidative stress Increased muscle mass, strength and function	Not reported	Supplementation with <i>Lactobacillus</i> in mice [Chen et al. (2022); Lee et al. (2021)]
RE + Probiotic	Increase in lean body mass	12-week supplementation with <i>Lactobacillus</i> and <i>Bifidobacterium</i> genera containing probiotics RE and <i>Bifidobacterium</i> supplementation	Systematic review of 17 human RCTs [Mashhadi et al. 2023] Human RCT of 12 weeks duration in healthy individuals [Inoue et al. (2018)]

Exercise-mediated modulation of gut microbiota



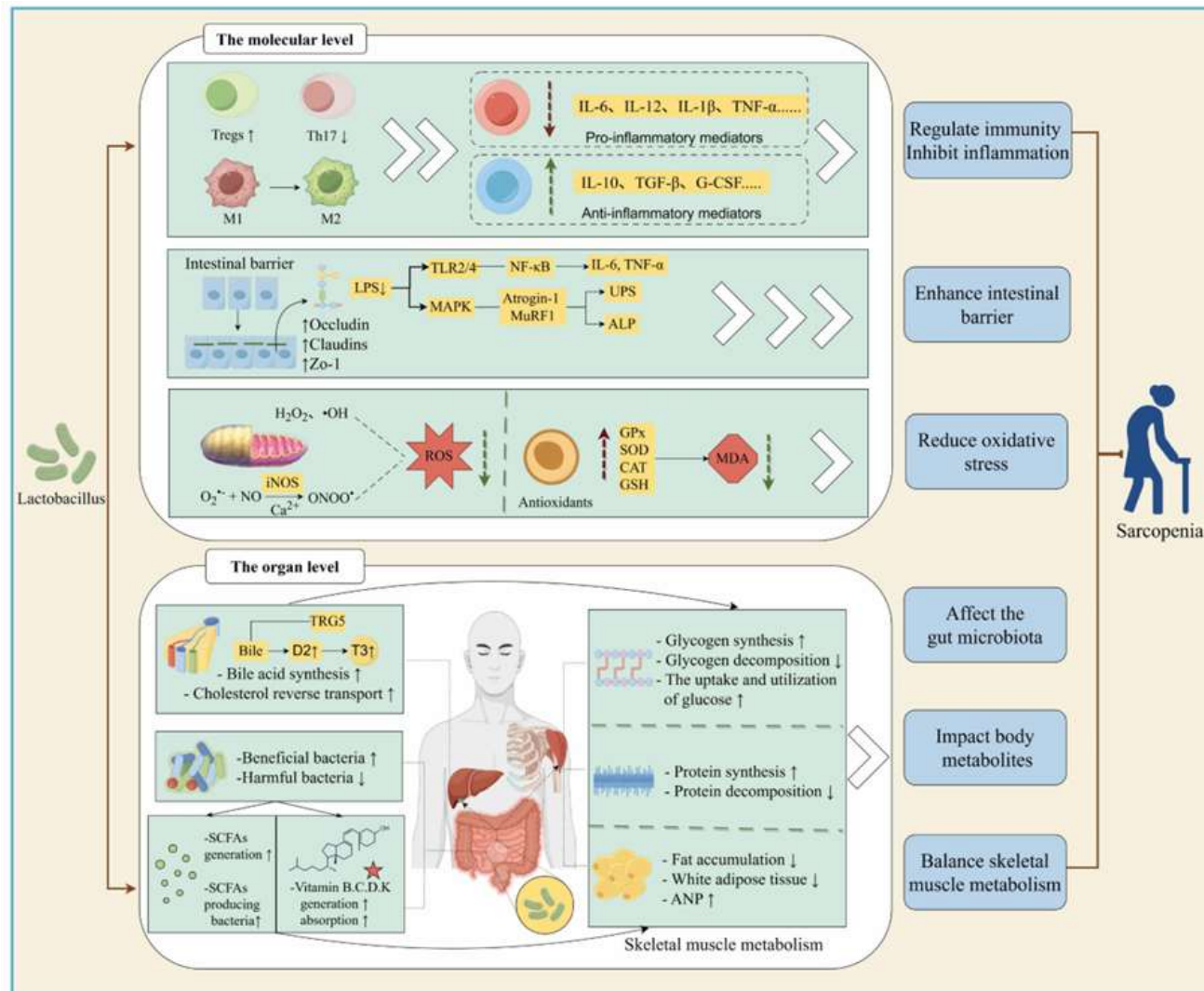
Xu Y. *Front Microbiol* 2025;16:1695448.

The mechanism of exercise-induced increase in SCFAs for the prevention and treatment of sarcopenia



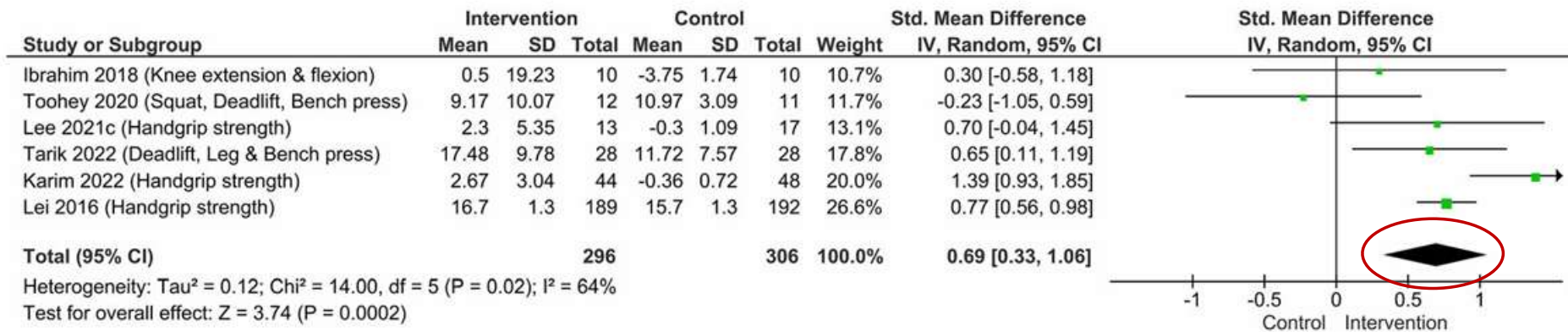
Fang J et al. *Front Microbiol* 2025; 6:1665551

Mechanisms of action of probiotics in sarcopenia



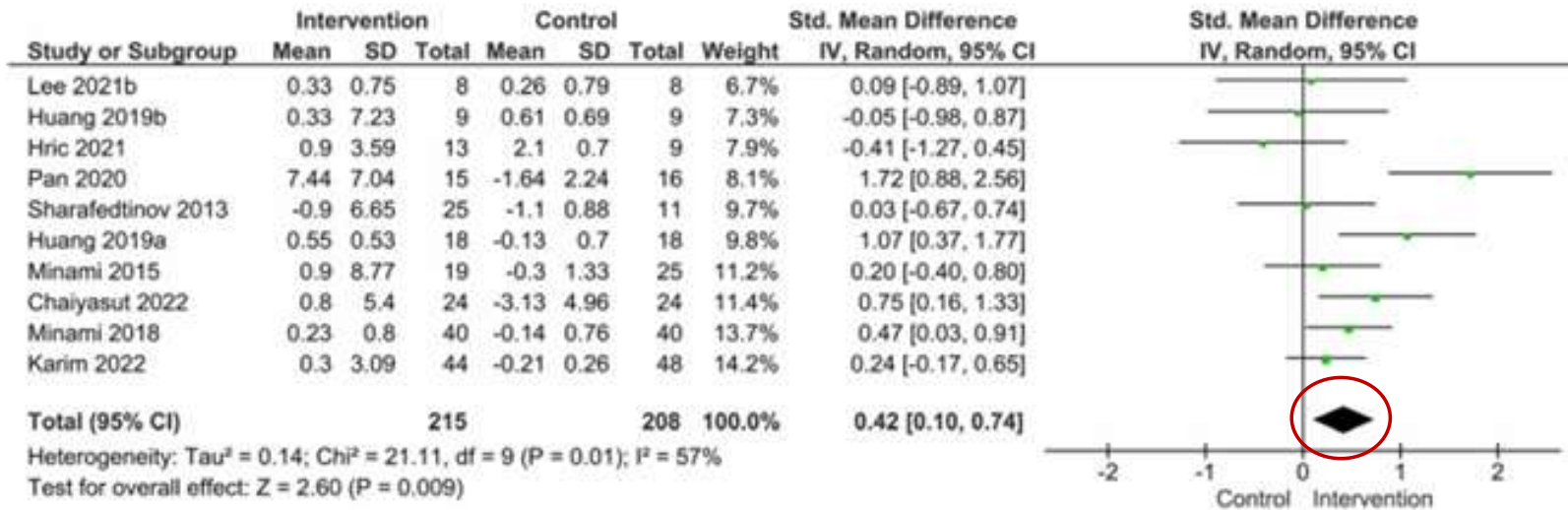
Zhu J. *Front Microbiol* 2025;16:1559119

Metaanalysis of effect of probiotic supplementation on global muscle strength



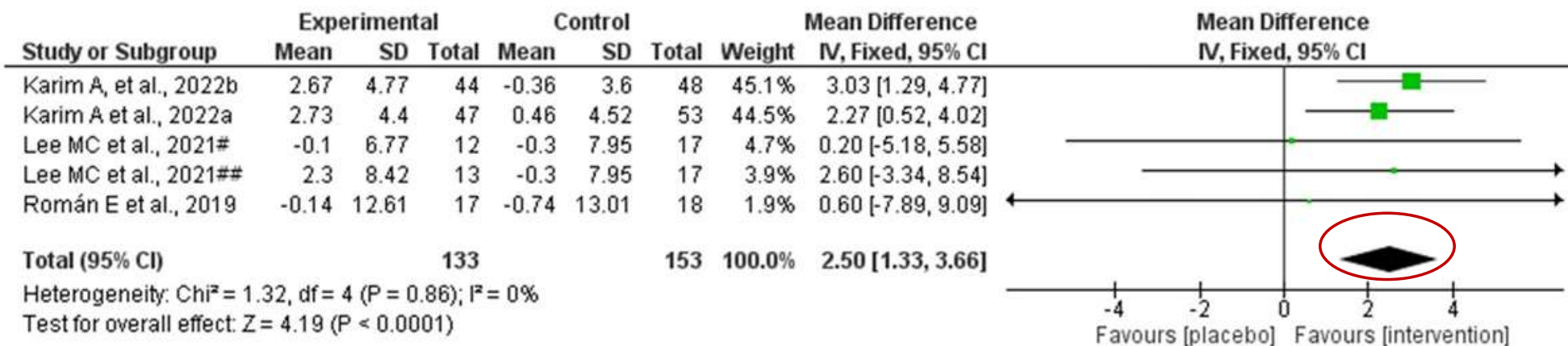
A significant increase in global muscle strength

Effect of probiotic supplementation on muscle mass



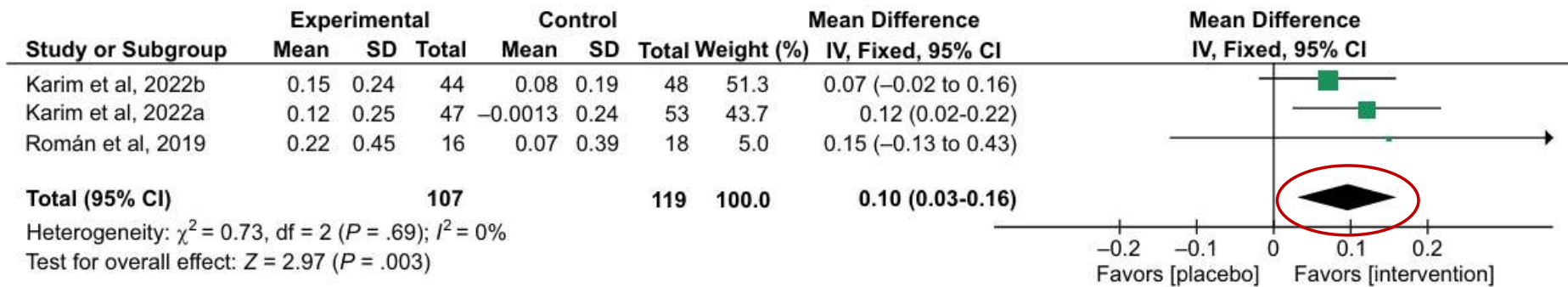
Muscle mass was improved following probiotic supplementation

Meta-analysis of RCTs with pre-probiotics in sarcopenia (effect on muscle strength)



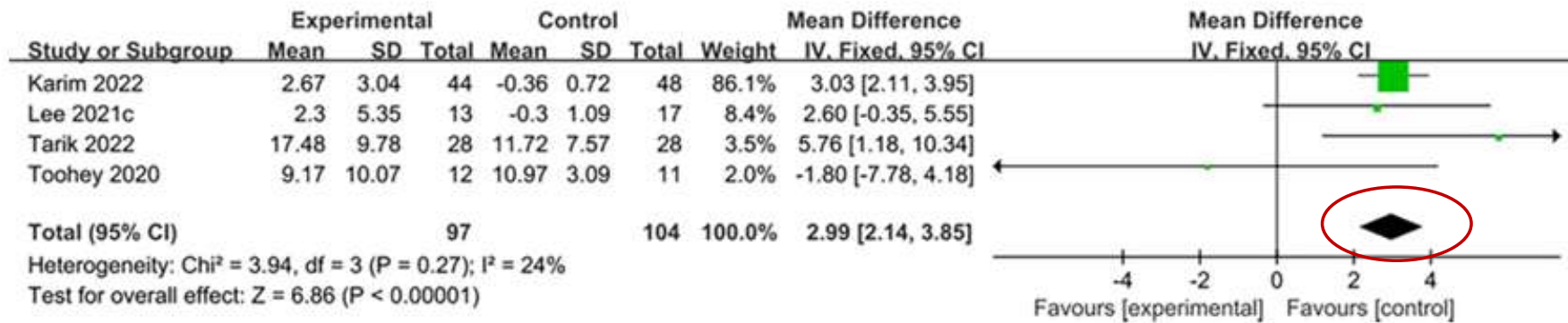
A significant increase in global muscle strength

Meta-analysis of RCTs with pre-probiotics in sarcopenia (effect on physical performance and function)



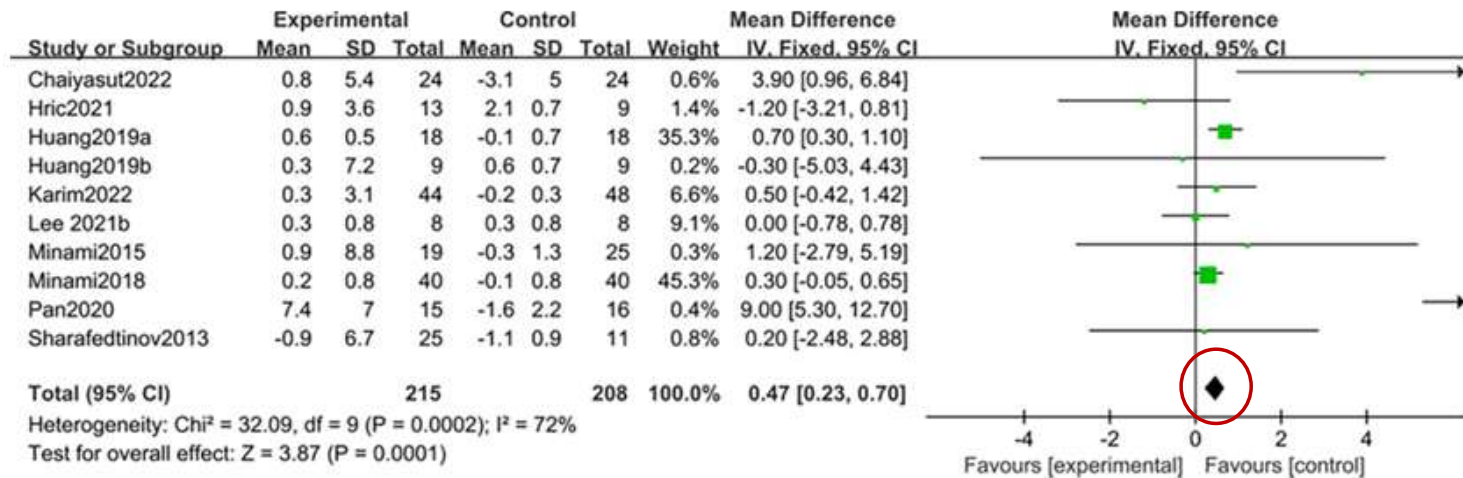
A significant increase in physical performance and function

Meta-analysis of probiotics effect on muscle strength in patients with sarcopenia



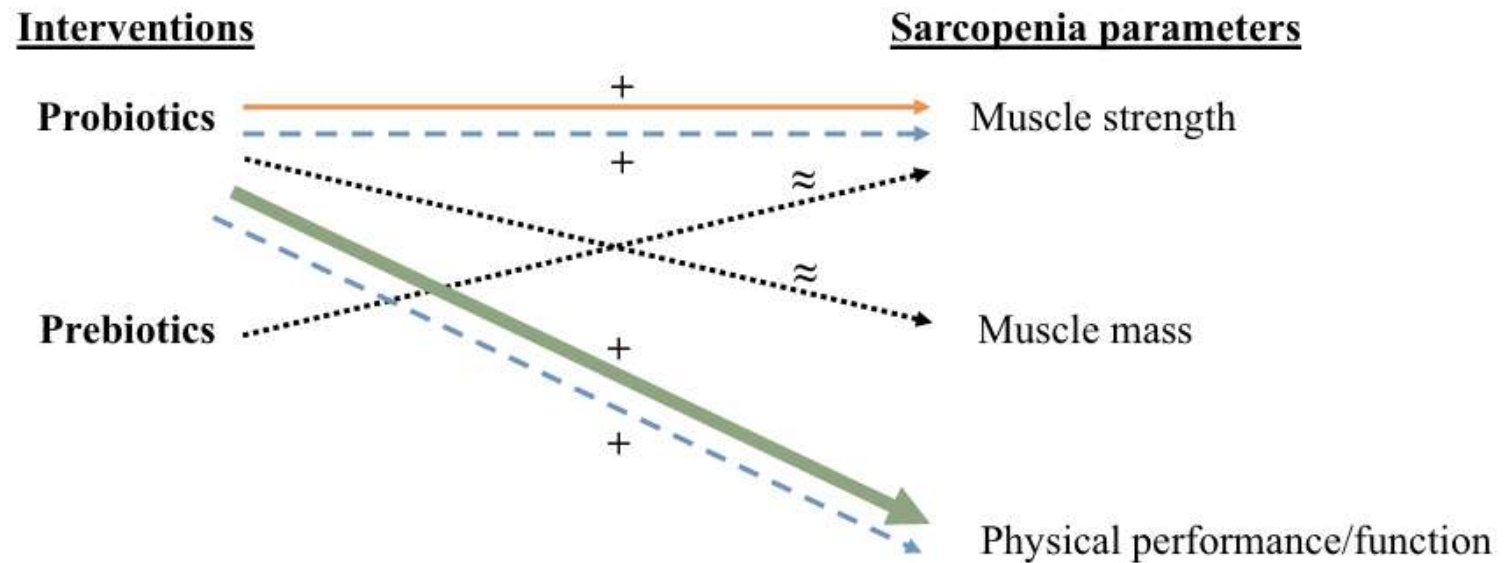
A significant increase in global muscle strength

Effect of probiotics on muscle mass in patients with sarcopenia

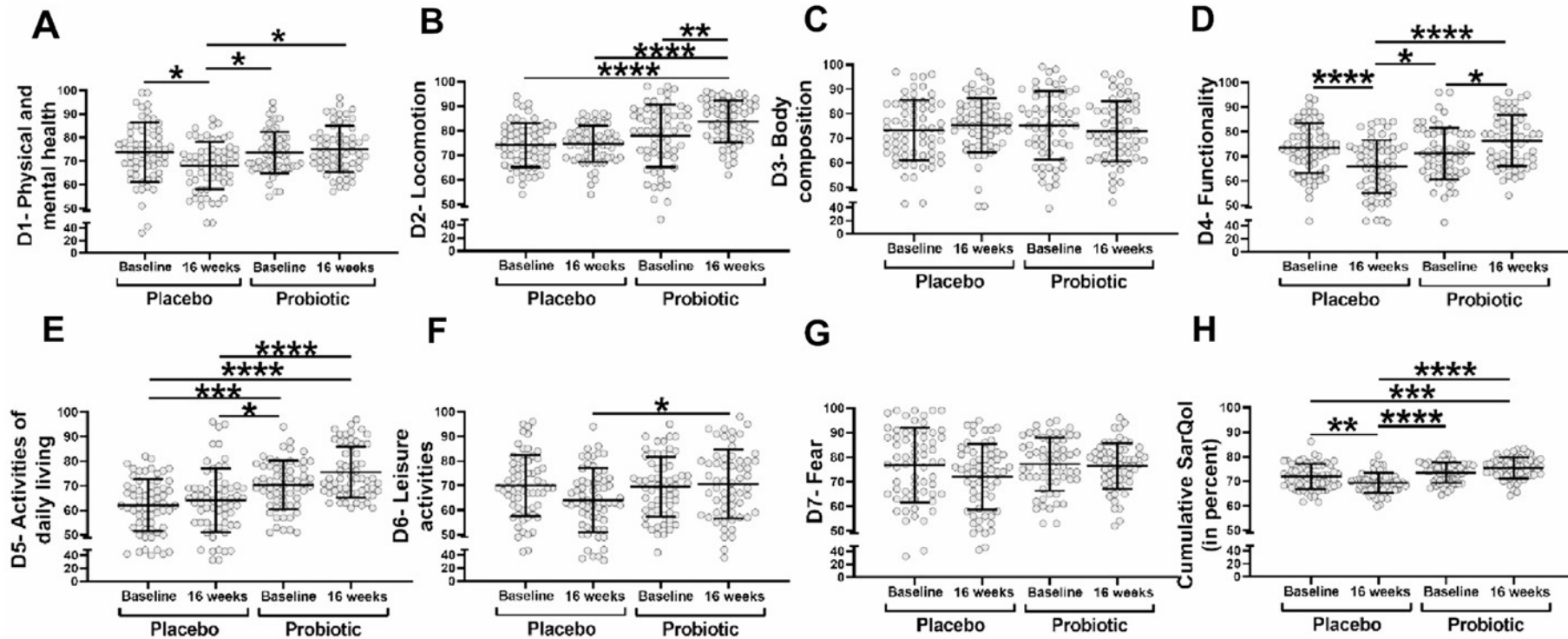


A non significant increase in global muscle strength

Summary of Probiotics and Prebiotics Results on Sarcopenia Parameters



Probiotics and Quality of life in sarcopenia



Probiotics improved the SarQoL scores for locomotion, functionality, and activities of daily living and prevented a decline in cumulative SarQoL observed in the placebo group (all p < 0.05)

Conclusions (1)

- Age-related sarcopenia status is associated with a marked change in composition and function of gut microbiota
- Its features are: decreased alpha and beta-diversity, increased inflammation, increased gut permeability, decrease in protein digestion and *de novo* synthesis, **reduction of SCFA production**, all leading to a reduction of muscle growth, mass and strength.
- This process may be mitigated by increasing dietary fibers, physical activity and by probiotics administration

Conclusions (2)

- **Probiotic supplementation may improve muscle strength and physical function in older adults with sarcopenia**, but its effects on muscle mass are less consistent
- Mechanistically, probiotics are thought to modulate the gut-muscle axis by enhancing short-chain fatty acid production, improving mitochondrial function, and reducing systemic inflammation, which may contribute to better muscle performance
- ***Lactobacillus rhamnosus*** and **multi-strain formulations** have demonstrated the most promising results for improving muscle strength and function in sarcopenia