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REVIEW

Nexus Between Sarcopenia and Microbiome Research: A Bibliometric Exploration

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Abstract: Despite over 30 years of microbiome and skeletal muscle research, no quantitative analysis of sarcopenia and the microbiome literature had been conducted. Our bibliometric study examined research status, hotspots, and future trends. We utilized bibliometric techniques to search the Science Citation Index Extended Database on February 27, 2023, using the Bibliometrix package in R to create a map displaying scientific production and subject categories. Collaborative network maps between countries/regions were visualized using Scimago Graphica, while VOSviewer explored collaboration modes among individuals and institutions. We analyzed the top 25 emerging keywords, top co-occurring keyword networks, and co-occurring keyword clusters using CiteSpace. A total of 997 articles were retrieved for sarcopenia and microbiome, of which 633 papers were analyzed. Both the number of publications and total citation frequency had been continuously increasing. The United States had the highest total citation frequency, while China had the highest number of publications. Research on the impact of the microbiome on sarcopenia was in its nascent stage and spans multiple disciplines, including nutrition, microbiology, geriatrics, immunology, endocrinology and metabolism, molecular biology, and sports medicine. The University of Copenhagen contributed the most to the number of publications (n=16), with Tibbett M (n=7) and Hulver MW (n=7) among the top authors. The most published journal was "Nutrients" (n=24). Analysis of keywords and clusters revealed new research hotspots in microbes and sarcopenia, such as malnutrition, dietary fiber, signaling pathways, frailty, and intestinal permeability. Research on the impact of the microbiome on sarcopenia is in its infancy and spans multiple disciplines. Malnutrition, dietary fiber, signaling pathways, frailty, and intestinal microbes are currently research hotspots. Furthermore, the visual atlas analysis of research on microbes and sarcopenia helps to track the knowledge structure in research fields related to sarcopenia and microbes, providing direction for future research.

Keywords: bibliometric analysis, microbes, skeletal muscle, scientometrics, muscle wasting

Introduction

Sarcopenia is a progressive and systemic skeletal muscle disorder characterized by an age-related reduction in skeletal muscle mass, accompanied by decreased muscle strength and/or physical function, which is associated with adverse outcomes such as falls, fractures, physical disability, and even mortality.[1,2] The prevalence of sarcopenia was particularly high in the elderly population, with studies in China showing that it ranged from 10.7% to 41.4% in men and 8.9% to 40.1% in women, with a higher prevalence observed in nursing homes and hospitalized patients.[3] The onset of sarcopenia was closely associated with certain factors, such as dietary habits, physical activity, nutritional status, gut microbiome and disease,[4,5] which significantly impacted the health and quality of life of older individuals. Especially in recent years, with in-depth research on the muscular-gut axis, it had been found that intestinal microbial imbalance could promote

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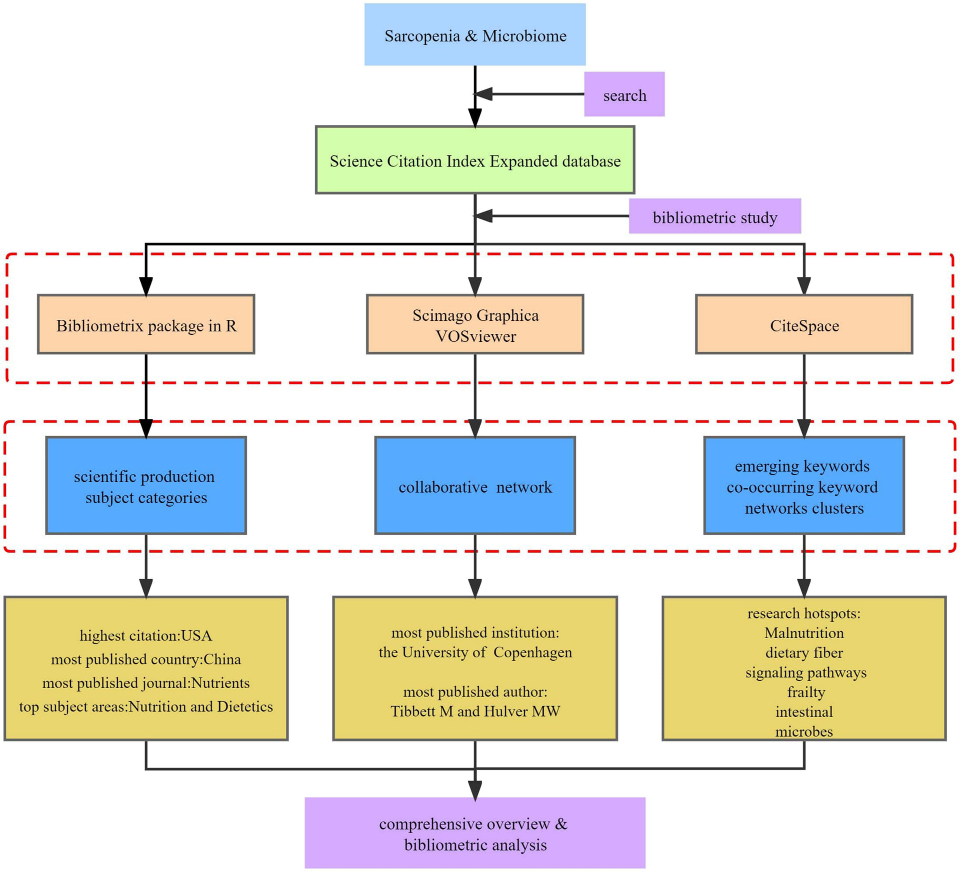
Graphical Abstract



muscle atrophy, reduce muscle mass and muscle strength, and microbial preparations could delay the occurrence and development of sarcopenia.[6]

The human body exists in symbiosis with hundreds of millions of microorganisms, and as humans age, their microbiome also undergoes changes. Consequently, the human microbiome is often referred to as the “second largest genome” of human beings.[7,8] Over the past 10 years, studies had found that microbial imbalance could lead to a decrease in microbial diversity, a change in the structure of the flora, and increased intestinal permeability, which could promote chronic persistent inflammation, resulting in decreased muscle synthesis and increased muscle consumption, thereby promoting the occurrence of sarcopenia.[9] However, interventions that restored the balance of gut microorganisms through dietary modifications, exercise, and supplementation with probiotics or prebiotics have been shown to improve muscle strength and reverse muscle atrophy.[6,9,10] Therefore, the relationship between gut microbes and sarcopenia had gained significant attention, with certain gut bacteria and their metabolites being considered as potential biomarkers for predicting sarcopenia.[11,12] Zhang et al discovered that the genera and species of Enterobacteriaceae in gut microbiota are the primary pathogens in sarcopenia patients, showing a significant negative correlation with muscle mass. Shigella-Klebsiella were identified as key biomarkers of sarcopenia,[13] while in elderly women, Bifidobacterium was also considered a potential biomarker.[14] Additionally, microbial-derived metabolites, such as short-chain fatty acids from fatty acid metabolism,[12] urea, uremic metabolites and plasma indoxyl sulfate from amino acid derivatives,[15,16] secondary bile acids, deoxycholic acid, lithocholic acid, 12-α-hydroxylated to non-12-α-hydroxylated bile acids from bile acid derivatives,[17,18] and bacterial quorum sensing peptides like iAM373,[19] were all reported to be closely associated with the development of sarcopenia. Manipulating the gut microbiota through interventions may hold promise as a therapeutic strategy for sarcopenia.

To our knowledge, there had been no bibliometric analyses of studies on sarcopenia and the microbiome. To gain insights into the historical development, current trends, research hotspots, and future directions in the field of microbes and sarcopenia, this study employed bibliometric analysis to analyze the literature published between 1981 and 2023.[20] The aim is to comprehensively understand the research landscape in this area and visually map the relationships between microbes and sarcopenia using knowledge visualization techniques, with the ultimate goal of providing a solid reference for future research directions.

Data and Methods

Our study was a bibliometric analysis that did not involve human subjects and did not require ethical approval from an institutional review board.

Data Collection

We searched the Science Citation Index Expanded (SCI-EXPANDED) database via WoS on February 27, 2023. The following keywords were combined to search the databases: “sarcopenia”, “sarcopenic”, “muscle depletion”, “muscle wasting”, “muscle atrophy”, “skeletal muscle”, “microbiome”, “microbiota”, “microbial” and “microorganisms” in the “Title” field. The search results were refined by “article” in order to identify the core literature for this bibliometric analysis. The full records and the full citation of the search results were exported to “Other File Formats” with “All Fields Available” selected.

Bibliometric Analysis

Bibliometric visualization analysis was conducted on the retrieved and downloaded data using CiteSpace 5.7r5, R-4.2.2, VOSviewer 1.6.19, and Scimago Graphica to obtain a summary and development trend of microbiology and sarcopenia research.

First, we used the “Citation Report” application from the WoS database to obtain the following bibliometric indicators: publication trend, publication types, times cited, publications over time, and the productive journal’s with their impact factors (IF). Each journal’s impact factor (IF) was obtained from the Journal Citation Report (JCR) Science Edition 2021 (https://jcr.clarivate.com).

The CiteSpace software was used to perform keyword co-occurrence, keyword emergence, and cluster analysis. Keyword cluster analysis used the LLR algorithm for weighted calculations.[21–23] The LLR is an algorithm to determine each type of label, which presents the core concept of each cluster with professional words. The keywords had been manually cleaned to obtain the initial keywords, including merging synonymous keywords, deleting incorrect keywords, and removing irrelevant keywords. In this study, the first article retrieved from the literature was published in 1981. Therefore, the parameter settings were as follows: “time slicing” set to January 1981-February 2023, “year per slice” set to 1, “Node types” selected keywords, “pruning” selected Critical path “pathfinder” and “pruning sliced networks”.

The Bibliometrix package in R software version 4.2.2 (R Foundation for Statistical Computing, Vienna, Austria) was used to summarize annual scientific research results, annual average citation frequency, most relevant institutions, national scientific research results, and most cited countries, and generated a visual map of national scientific research results and subject categories.[24]

VOSviewer (1.6.19) was utilized to construct a collaborative network of authors and their institutions.[25] Scimago Graphica was employed to analyze collaborative network graphs between countries/regions.[26]

Results

According to the analysis of the core collection of Web of Science using keyword search, a total of 997 articles were retrieved for sarcopenia and microbes. After excluding review papers (n=311), conference proceedings (n=23), online publications (n=9), conference abstracts (n=8), editorial materials (n=7), book chapters (n=4), data papers (n=1), news articles (n=1), and considering 633 papers for analysis, A total of 61 countries or regions, 83 subject areas, 394 journals, and 1162 institutions researched on sarcopenia and microbes.

Publication Trend

As shown in Figure 1, In our literature search, the earliest literature in this field was published in 1981, Bajjalieh et al used a synthetic antimicrobial compound (carbadox) to feed male Sprague-Dawley rats and evaluated its effects on protein synthesis and degradation in rat liver and muscle.[27] Research on skeletal muscle and microorganisms has been continuous since 1992. The number of published papers and citations per year remained relatively stable until 2011, after which the number of published papers started to increase rapidly, particularly in the past three years (2020–2022), reaching an average annual publication volume of over 100 papers, with 121 papers expected to be published in 2022.

Distribution by National Publication, Cooperation and Citation

A total of 61 countries or regions had contributed to research on sarcopenia and microbes, with most of the research coming from European and Asian countries. African countries had relatively fewer publications in this field. Figure 2a shows the trend of national publications, with darker colors indicating more published papers. Figure 2b shows the top 28 countries with the most cooperation, with larger node sizes indicating more publications from the country, and darker the node indicating more publications in cooperation with other countries, this figure indicated international collaboration in research on sarcopenia and microbes. Table 1 provides a summary of the top countries in terms of publications and citations in this field. China has the largest number of publications with 150 papers, followed by the United States and the United Kingdom. In terms of total citations, the United States has the highest number with 6753 citations, followed by China and the United Kingdom with 2005 and 1505 citations respectively.

Distribution by Disciplines

Research on sarcopenia and microbiology encompassed 83 subject areas, with the top 20 subject areas illustrated in Figure 3. Analysis of published articles revealed that the top five subject areas were “Nutrition and Dietetics” (105, 11% of publications), “Biochemistry and Molecular biology” (80, 8%), “Food Science and Technology” (56, 6%), “Endocrinology and Metabolism” (54, 6%), and “Multidisciplinary sciences” (48, 5%). This indicated that the research on sarcopenia and the microbiome spanned across diverse disciplines, with a clear interdisciplinary nature.

Distribution and Network by Authors and Institutions

By utilizing network analysis of institutions and authors’ contributions in VOSviewer, it was determined that a total of 1162 institutions were involved in research on sarcopenia and microbes. Among them, the institutions with the highest number of publications were the University of Copenhagen (n=16), China Agricultural University (n=14), the University of Western Australia (n=13), Chinese Academy of Sciences (n=11), and Texas A&M University (n=10), leading the

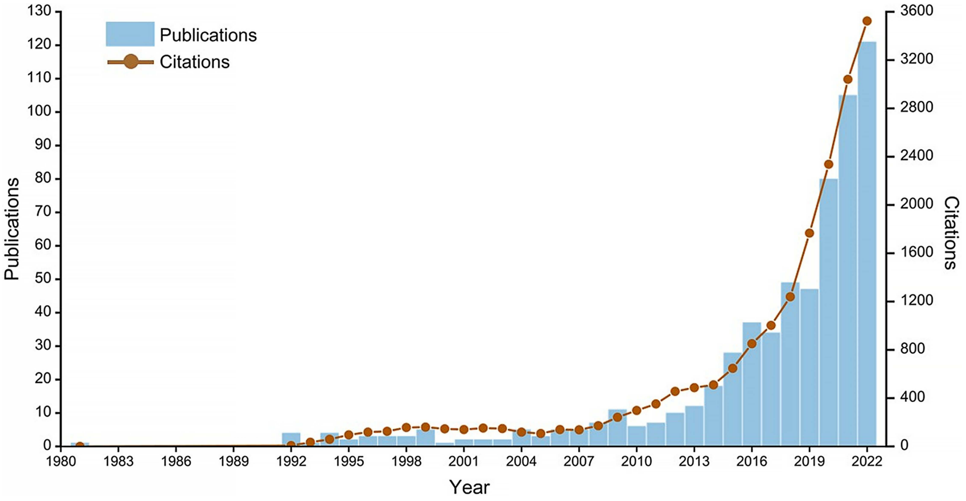


Figure 1 Number of annual publications in the sarcopenia and microbiota research field and the frequency of citations per year.

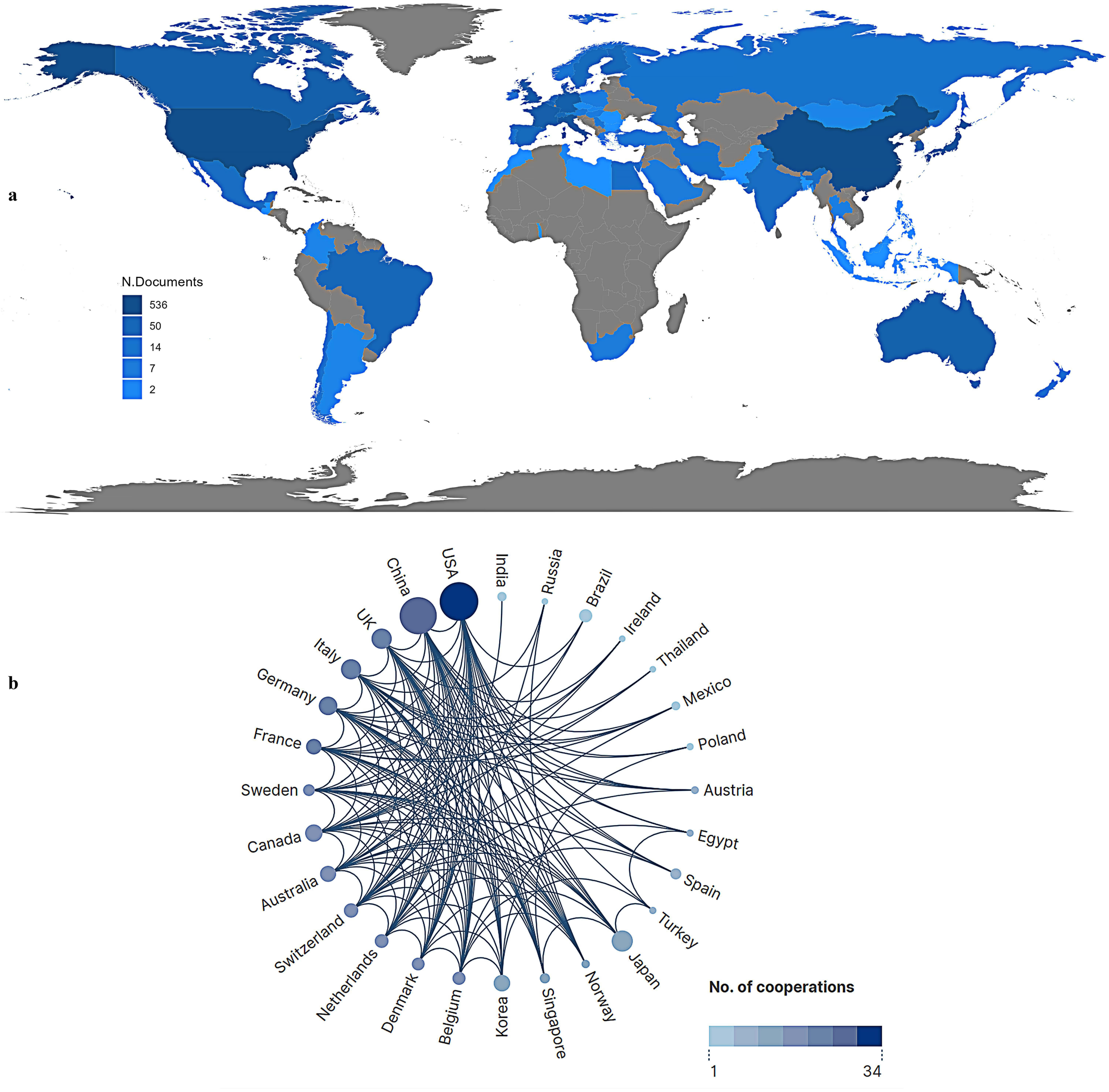


Figure 2 Map visualization of publications and international collaboration network on sarcopenia and microbiota by countries/territories. (**a**): Map visualization of publications on sarcopenia and microbiota by countries/territories. (**b**): International collaboration network between countries. The size of each circle represents the number of publications in the country. The bigger the circle, the more the number of publications the country has contributed. The links between the circle signify the collaboration between every two countries.

forefront. In terms of author contributions, Tibbett M(n=7) and Hulver MW (n=7) contributed the most in terms of number of publications, followed by Neilson, AP(n=6), McMillan, RP (n= 6), and Yin, Y (n=5). The top 5 authors with the most cited publications are: Backhed F (1793 citation instances), Semenkovich CF (1741 citation instances), Manchester JK (1741 citation instances), Gordon JI (1741 citation instances), and Ziegler TR (556 citation instances). Figure 4a illustrates the top 73 network relationships based on the total link strength of inter-institutional cooperation. Figure 4b depicts the network relationship diagram of the top 1000 authors based on connection strength, the cooperative relationships were visibly clustered, indicating close research cooperation among these authors, which facilitated the development of related research.

Table 1 The Top 10 Country in Terms of Number of Articles Published About Sarcopenia and Microbiota

RANK	Country	Total Citation	Average Article Citations	No. of publications	RANK	Country	Total Citation	Average Article Citations	No. of publications
1	USA	6753	51.90	130	6	ITALY	685	22.10	31
2	CHINA	2005	13.40	150	7	CANADA	673	37.40	18
3	UK	1505	62.70	24	8	FRANCE	666	37.00	18
4	GERMANY	992	52.20	19	9	BELGIUM	543	49.40	11
5	JAPAN	965	21.90	44	10	KOREA	488	18.10	27

Abbreviations: No. of publications, Number of publications.

Distribution by Journals

A total of 394 journals successfully published research on sarcopenia and the microbiome. Table 2 displays the citation frequency and impact factor of articles published in the top ten journals in terms of publication volume. The top five journals with the highest publication output were NUTRIENTS (n=24), SCIENTIFIC REPORTS (n=19), PLOS ONE (n=16), FRONTIERS IN NUTRITION (n=13), and INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES (n=11). Among the top ten journals by publication volume, when adjusted for the total number of publications in the same period, the top five journals were respectively JOURNAL OF CACHEXIA SARCOPENIA AND MUSCLE, FRONTIERS IN NUTRITION, JOURNAL OF AGRICULTURAL AND FOOD CHEMISTRY, NUTRIENTS, FOOD & FUNCTION. Notably, PLOS ONE boasted the highest average citation frequency, with a remarkable score of 42.68. The influence and 5-year influence of the aforementioned journals remained relatively stable in 2021. Notably, the JOURNAL OF CACHEXIA SARCOPENIA AND MUSCLE had the most substantial influence factor, with an approximate score of 12, while other journals exhibited comparable influence.

Research Hotspots and Evolution

Figure 5 depicts the keyword co-occurrence of 633 papers, with larger circles representing the higher frequency of occurrence of the keyword in the articles. The thickness of the lines connecting these keywords indicated the strength of

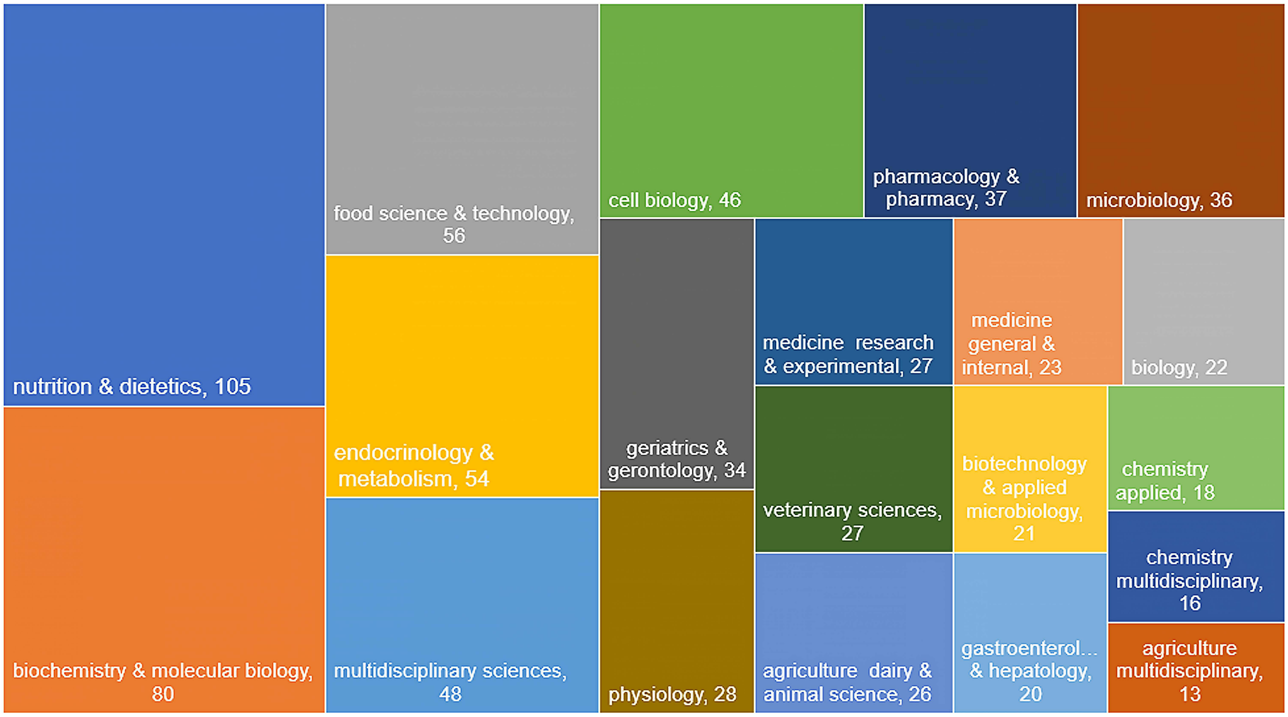


Figure 3 The top 20 subject categories regarding articles published about sarcopenia and microbiota.

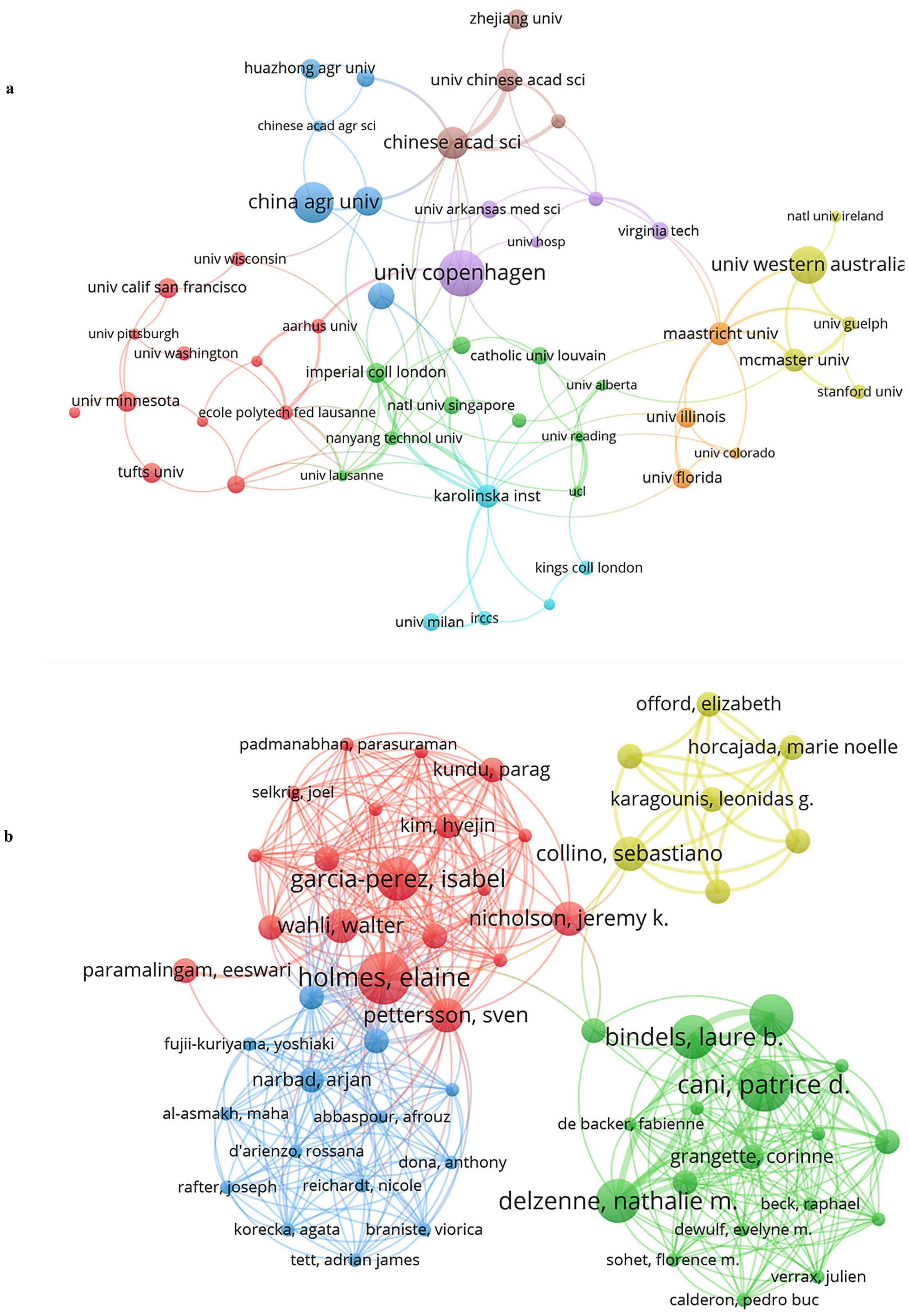


Figure 4 Total link strength networks of inter-institutional and authors' contributions collaborations in sarcopenia and microbiota research. (**a**): Total link strength network of inter-institutional collaborations in sarcopenia and microbiota research. (**b**): Total link strength network of authors' contributions collaborations in sarcopenia and microbiota research. Each node represents an institutional/author's contributions determined in the Web of Science database. The size of each node represents the number of publications. The bigger the node, the more the number of publications in the research field. The link between the nodes represents a collaborative relationship. The thicker the link, the more cooperation strength between the nodes.

Table 2 The Top 10 Journals in Terms of Number of Articles Published About Sarcopenia and Microbiota

Journal	No. of publications	Total citation counts	Mean citation counts	Impact of factors 2021	Impact factors (five years)	Proportion of publications
NUTRIENTS	24	304	12.66	6.706	7.185	1327×10^{-6}
SCIENTIFIC REPORTS	19	731	38.47	4.997	5.516	111×10^{-6}
PLOS ONE	16	683	42.68	3.752	4.069	6×10^{-6}
FRONTIERS IN NUTRITION	13	67	5.15	6.59	6.873	2987×10^{-6}
INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES	11	114	10.36	6.208	6.628	241×10^{-6}
JOURNAL OF CACHEXIA SARCOPENIA AND MUSCLE	11	75	6.81	12.063	12.879	$11{,}853\times10^{-6}$
FASEB JOURNAL	10	175	17.5	5.834	6.103	781×10^{-6}
FRONTIERS IN MICROBIOLOGY	9	109	12.11	6.064	6.843	380×10^{-6}
JOURNAL OF AGRICULTURAL AND FOOD CHEMISTRY	8	210	26.25	5.895	6.048	1560×10^{-6}
FOOD & FUNCTION	6	182	30.33	6.317	6.375	1017×10^{-6}

Abbreviations: No. of publications, Number of publications.

their association, with thicker lines denoting a higher frequency of co-occurrence. Our research confirmed that skeletal muscle, gut microbiota, obesity, insulin resistance, inflammation, metabolism, exercise, high-fat diet, aging, and others were the prominent research hotspots in the field of microbes and sarcopenia.

Figure 6 reveals the emergence of the top 25 keywords, with the red portion indicating the time period of keyword bursts. Research on keywords related to skeletal muscle tissue and sarcopenia commenced surging in 2008, followed by an upsurge in

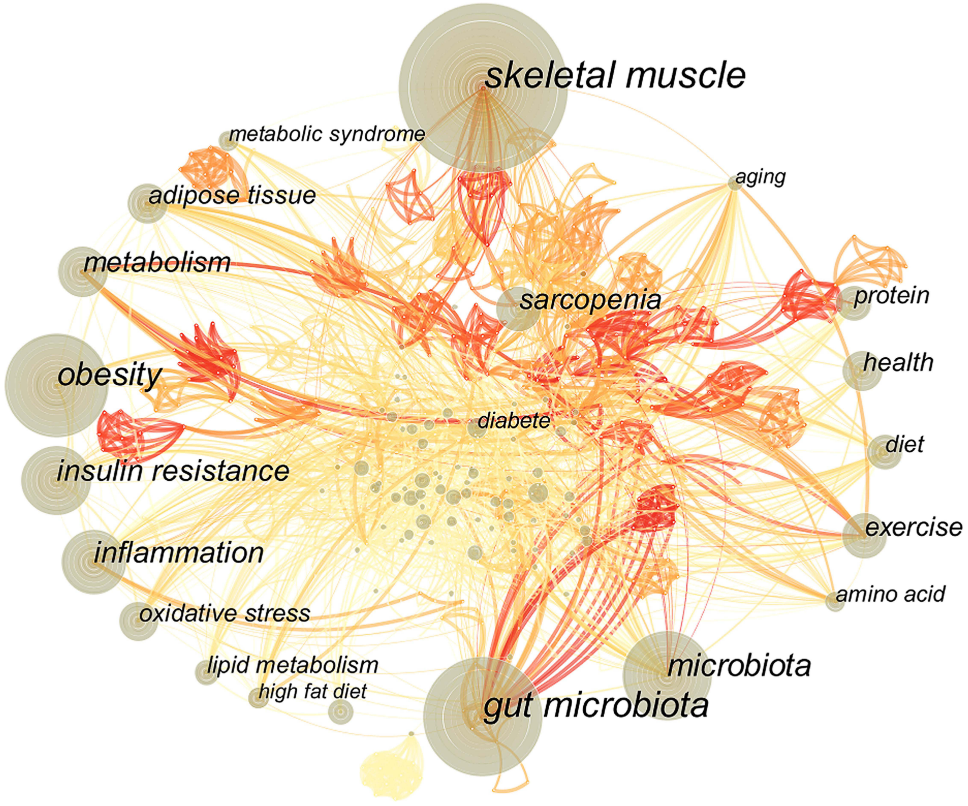
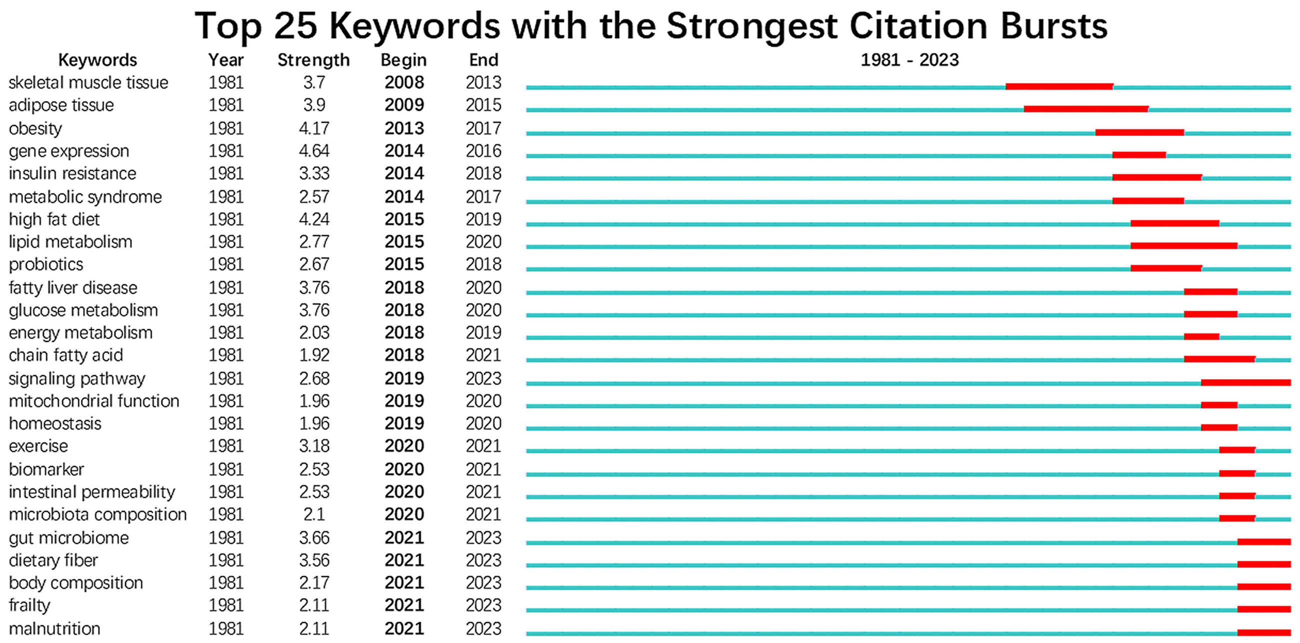


Figure 5 Keywords co-occurrence network of sarcopenia and microbiota research. The nodes are composed of tree rings that represent the frequency of the corresponding keyword over time. The links between the nodes represent the frequency of co-occurrence of the two corresponding keywords. The thicker the links, the more the frequency of the two keywords occurring together. The color of the links represented the corresponding time slices. The darker the color of the links was, the newer the keywords occurred in the publications.



Top 25 Keywords with the Strongest Citation Bursts

Keywords	Year	Strength	Begin	End	1981 - 2023
skeletal muscle tissue	1981	3.7	**2008**	2013	
adipose tissue	1981	3.9	**2009**	2015	
obesity	1981	4.17	**2013**	2017	
gene expression	1981	4.64	**2014**	2016	
insulin resistance	1981	3.33	**2014**	2018	
metabolic syndrome	1981	2.57	**2014**	2017	
high fat diet	1981	4.24	**2015**	2019	
lipid metabolism	1981	2.77	**2015**	2020	
probiotics	1981	2.67	**2015**	2018	
fatty liver disease	1981	3.76	**2018**	2020	
glucose metabolism	1981	3.76	**2018**	2020	
energy metabolism	1981	2.03	**2018**	2019	
chain fatty acid	1981	1.92	**2018**	2021	
signaling pathway	1981	2.68	**2019**	2023	
mitochondrial function	1981	1.96	**2019**	2020	
homeostasis	1981	1.96	**2019**	2020	
exercise	1981	3.18	**2020**	2021	
biomarker	1981	2.53	**2020**	2021	
intestinal permeability	1981	2.53	**2020**	2021	
microbiota composition	1981	2.1	**2020**	2021	
gut microbiome	1981	3.66	**2021**	2023	
dietary fiber	1981	3.56	**2021**	2023	
body composition	1981	2.17	**2021**	2023	
frailty	1981	2.11	**2021**	2023	
malnutrition	1981	2.11	**2021**	2023	

Figure 6 Top 25 keywords with the strongest citation bursts. The figure shows the strength of the keyword citation bursts. The higher the value, the greater the strength, and the higher the research heat of the keyword in the period. The red represents the time of the keyword citation bursts, and the red length represents the duration of the research heat of the keyword.

metabolism-related keywords such as adipose tissue, obesity, insulin resistance, and others. The keywords sarcopenia, gut microbiota, dietary fiber, body composition, frailty, and malnutrition were projected to experience bursts from 2021 to 2023, signifying that the research on sarcopenia and microbes continued to be a focal point in the current stage.

We also conducted a cluster analysis on keywords, as illustrated in Figure 7. The top ten clusters were short-chain fatty acids (cluster #0), sarcopenia (cluster #1), obesity (cluster #2), metabolism (cluster #3), inflammation (cluster #4), skeletal

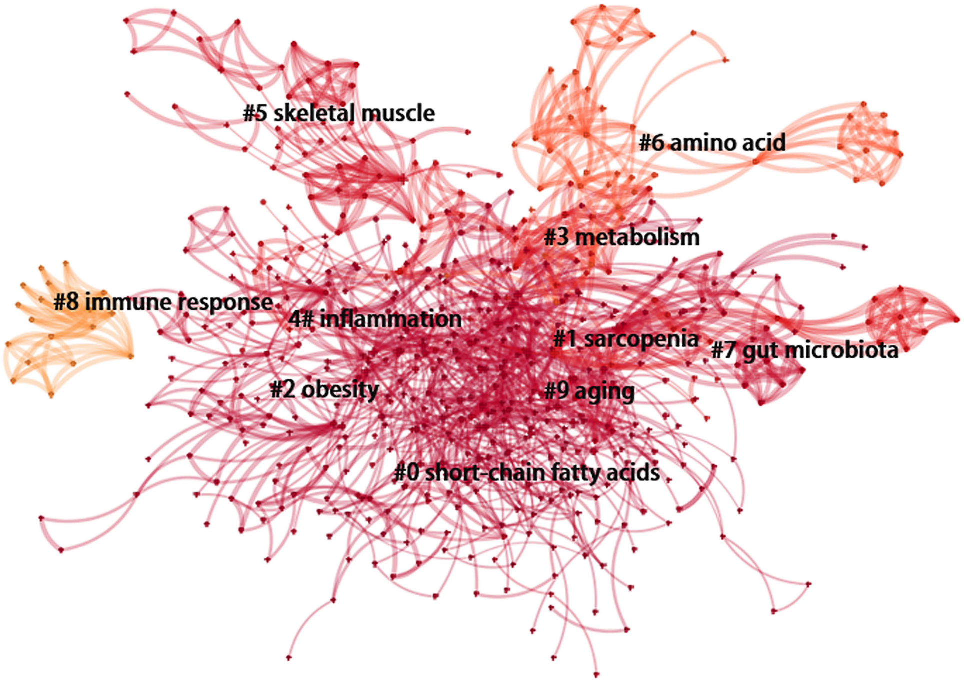


Figure 7 Top 10 keywords cluster map. Each node represents a data point, and the lines between nodes indicate how similar they are.

Table 3 Cluster Analysis of Keywords

Clustering Number	Clustering Name	Subcluster Name
#0[a]	Short-chain fatty acids	Butyrate, homeostasis, sarcopenia, lipopolysaccharide, etc.
#1	Sarcopenia	Microbiome, aging, diet, physical function, probiotic, etc.
#2	Obesity	Sarcopenia, tight junction protein, metabolic syndrome, etc.
#3	Metabolism	Inflammation, stress, gut microbiome, etc.
#4	Inflammation	Insulin resistance, lipopolysaccharide, signaling pathway, etc.
#5	Skeletal muscle	Diabetes, butyrate, gut microbiota dysbiosis, lipolytic, etc.
#6	Amino acid	Myofibrillar proteins, proteolysis, etc.
#7	Gut microbiota	Dietary modulation, strength training, systemic inflammation, etc.
#8	Immune response	Immunization, gut microbiota, obesity, sarcopenia, etc.
#9	Aging	TNF, toll-like receptor, gut-muscle axis, anabolic resistance, etc.

Note: a, #, Clustering.
Abbreviations: etc, Etcetera.

muscle (cluster #5), amino acid (cluster #6), gut microbiota (cluster #7), immune response (cluster #8), and aging (cluster #9). Each clustering silhouette coefficient was between 0.669–1, the overall clustering effect was good and the reliability was high. Table 3 presents the keywords encompassed in each cluster. Cluster #0 and cluster #7 revolved around gut microbes and their metabolites, specifically short-chain fatty acids, to investigate their impact on sarcopenia. Cluster #1, cluster #2, and cluster #5 emphasized skeletal muscle and sarcopenia, with a focus on microbiome, diet, obesity, metabolism, hormones, probiotics, and more. The relationship between microbes and sarcopenia was primarily explored through metabolism-related pathways associated with microbes. Cluster #3, cluster #4, and cluster #6 centered on amino acids, metabolism, and inflammation, delving into the impact of microorganisms on sarcopenia through the analysis of amino acid metabolism and related pathways, inflammatory factors, and others. Cluster #8 and cluster #9 spotlighted aging and immunity, exploring the intricate relationship between the muscular-gut axis and aging, and immune inflammation.

Evolution of Clinical Trials and IP's (Patents) in the Context of Microbiota-Sarcopenia

We further analyzed the evolution of clinical trials and intellectual property (patents) related to the microbiome and sarcopenia. By searching ClinicalTrials.gov from 1981 to 2022 using relevant keywords and removing duplicate entries, we obtained results on microbiota-sarcopenia clinical trial registrations. From the first related trial in 2008 to 2016, the number of clinical registrations in this field gradually increased, reaching 12 registered trials by 2022 (Figure S1). Among all clinical trials, there were 40 interventional models, including 4 non-randomized controlled trials, 3 labeled as NA, and the remainder as RCTs. Additionally, there were 14 observational models. Subsequently, we analyzed patent registrations in this domain. Using relevant keywords on Google Patents and excluding duplicates, we gathered microbiota-sarcopenia patent registration data from 1981 to 2022. Patent registrations showed a rapid upward trend from 1981, peaking in 2000 (N=1283), followed by a slow decline, maintaining over 500 registrations per year. This trend began rising again in 2010, reaching a second peak in 2020 (N=899) (Figure S2).

Discussion

Our study was the first to describe the landscape of sarcopenia and microbiome research based on more than 600 papers retrieved from the WoS database. Muscle constitutes a significant component of the musculoskeletal system and serves as the powerhouse of the human body. Additionally, muscle also functions as a vital endocrine and metabolic organ.[28] Over the past decade, with the advancement of the Human Genome Project, the relationship between microorganisms and various diseases had gained increasing recognition and study,[29] Rapid growth in research on sarcopenia and the microbiome Our findings suggested that the study of sarcopenia and the microbiome is a very active field with a dramatic increase in the number of publications, especially in the recent decade. More than 80 disciplines were included in sarcopenia and microbes research, of which, "Nutrition and Dietetics" is the most activated discipline. Notably, from 2019 to 2022, research specifically focusing on the association between microbes and sarcopenia exhibited an explosive growth trend, thereby driving collaborative efforts among countries and institutions, particularly in Asia, North America, and Europe. Moreover, the evolution of microbiome-sarcopenia-related clinical trials and patents markedly increased during this period. The rapid growth of publications facilitated more randomized controlled trials (RCTs) and patents, offering insights for translating research findings into clinical practice and technological innovation. This provided a valuable perspective on the impact of research in this field, potentially leading to new therapies and interventions. Our study also summarized the most prolific or highly cited authors, journals, and institutions, and the most highly cited publications in the research field of sarcopenia and the microbiome. We also performed keyword and cluster analysis and a summary of studies related to sarcopenia and the microbiome.

In 2020, the World Health Organization (WHO) released the Baseline Report for the Decade of Healthy Ageing, which highlighted that at least 14% of elderly individuals aged 60 and above (equivalent to 142 million people) had unmet basic daily needs.[30] Sarcopenia, a significant health issue among the elderly, often led to falls, frailty, reduced daily activity capacity, and even disability, severely undermining healthy aging.[1,2] Consequently, it was imperative to strengthen the prevention and treatment of sarcopenia to promote healthy aging and improve the living environment for the elderly in their homes and communities. With the implementation of the Human Genome Project, research on the role of human microbiota in sarcopenia had proliferated. Clinical trial registrations on ClinicalTrials.gov and research funding through NIH Research Portfolio Online Reporting Tools (RePORT) increased annually, addressing mechanisms of microbiota in sarcopenia (NCT04985877) and microbial interventions in sarcopenia (NCT05348694). For instance, the NIH National Institute on Aging funded a project titled "The Role of the Gut Microbiota in Sarcopenia" (Project Number: 1R21AG071888-01), aiming to explore how gut microbiota dysbiosis promoted sarcopenia through TLR4 overactivation of mTORC1 signaling, inducing a state of anabolic resistance in skeletal muscle. These initiatives underscored the importance and necessity of research on sarcopenia and microbiota.

Numerous studies have unequivocally established that a diet high in fat and sugar, low in fiber,[31] malnutrition,[32] and a sedentary lifestyle[33] are closely linked to the occurrence and progression of sarcopenia. Furthermore, microorganisms are also influenced by diet and exercise,[33–35] as supported by the subject areas depicted in Figure 3. For instance, in the field of nutrition, a diet rich in fat and sugar can alter the composition of the host's intestinal microbiota, resulting in changes in bacterial diversity and flora composition, ultimately leading to a decline in the production of short-chain fatty acids. These alterations subsequently impact muscle strength and physical activity capacity, thus promoting the onset and development of sarcopenia.[6] Conversely, supplementation of a diet abundant in fiber,[36] polyphenols,[37] saponins,[38] flavonoids,[39] and other similar components can modulate the balance of intestinal microbiota, enhance the production of short-chain fatty acids, and ameliorate muscle wasting, and skeletal muscle strength. In the realm of biochemistry and molecular biology, numerous microorganisms, such as *Lachnospira, Fusicatenibacter, Roseburia, Eubacterium*,[11] and others, have been identified to promote the production of short-chain fatty acids through the fermentation of dietary fibers ingested by the host, particularly carbohydrates. In the realm of exercise, it has been well established that a sedentary lifestyle can exacerbate muscle atrophy, whereas physical activity can modulate the composition of gut microbiota, leading to an increase in the abundance of beneficial bacteria such as *Akkermansia, Allobaculum*, and *Lactobacillus*, which in turn promotes muscle strength and enhances muscle mass.[40] These findings highlight the interplay between the muscle-gut axis, involving multidisciplinary research encompassing nutrition, endocrinology, metabolism, molecular biology, and other fields. Furthermore, these results underscore that the impact of these factors extends beyond isolated body parts and affects the entire body. After analyzing published journals, this study elucidated the direction of submitting research related to sarcopenia and microbes. This information could serve as a guide for selecting suitable journals for submission of our research papers and facilitate our search for relevant articles within those journals.

Based on a comprehensive analysis of published literature, we categorized the findings into four main clusters for further discussion. The first two clusters, labeled as cluster #0 and cluster #7, are associated with short-chain fatty acids (SCFAs) and gut microbiota. Relevant studies had investigated the effects of gut microbe-derived metabolites, particularly SCFAs such as butyric acid, acetic acid, and propionic acid,[41] which play a role by regulating metabolism, the immune system, and cell proliferation,[42,43] and can affect the host various physiological processes. Notably, SCFAs also exert beneficial effects on the gut by reducing the influx of inflammatory substances such as lipopolysaccharides (LPS) and intestinal bacteria, strengthening the intestinal epithelial barrier,[44] and thus reducing systemic inflammation and inhibiting skeletal muscle inflammation.

Collectively, these studies highlight the potential of SCFAs to positively impact various physiological processes. Therefore, in the future, further investigations into the influence of microbial-mediated metabolites and intestinal barrier function on sarcopenia and its underlying mechanisms are warranted. Overall, these studies shed light on the potential therapeutic implications of SCFAs and highlight the need for further research in this area.

In cluster #1, cluster #2, and cluster #5, the clusters encompassed topics such as diet, obesity, metabolism, intestinal permeability, probiotics, and more, all of which impact skeletal muscle through microbial-mediated pathways. Alterations in gut microbiota have been correlated with muscle mass, muscle strength, and physical function.[45,46] Furthermore, obesity, as revealed in cluster #2, exhibited a close association with sarcopenia, insulin resistance, intestinal tight junction proteins, and metabolic syndrome.[47–49] However, intervention with probiotics (Lactobacillus mixture) increased the expression levels of intestinal tight junction proteins, improved intestinal epithelial permeability, and decreased serum LPS levels,[50] thereby reducing the systemic inflammatory response. This suggests that an imbalance in gut microbiota can lead to chronic inflammation, increased gut permeability, and sarcopenia, but probiotic intervention holds promise in improving gut barrier function. In summary, the evidence suggested that modulating gut microbiota through interventions such as prebiotic and probiotic administration may offer potential therapeutic strategies for mitigating the development and progression of sarcopenia in older adults. Further research is warranted to elucidate the underlying mechanisms and optimize the therapeutic approaches.

Cluster #3, cluster #4, and cluster #6, denoted as metabolism, inflammation, and amino acid respectively, are associated with amino acid metabolism, inflammation, oxidative stress, and signaling pathways, among others, in investigating the impact of microorganisms on sarcopenia. It is known that skeletal muscle mass is maintained through a delicate balance between protein synthesis and protein degradation, and the synthesis and breakdown of certain amino acids are influenced by intestinal microorganisms, resulting in an imbalance in muscle protein. As demonstrated in cluster #3, cluster #4, and cluster #6, microorganisms play a role in the occurrence and progression of sarcopenia by influencing changes in amino acid metabolism, cellular oxidative stress, mitochondrial function, insulin resistance, and signaling pathways. In individuals with sarcopenia, genes involved in amino acid metabolism (such as glutamine and isoleucine degradation, methionine, lysine, and threonine biosynthesis) are downregulated, while genes associated with glycolysis and glyoxylate are enriched. Additionally, exogenous supplementation of β-alanine has been shown to improve endurance and physical function.[51] Microbial regulation of amino acid metabolism may be influenced by various metabolic pathways. For instance, the expression and activation of the IGF1/AKT/mTOR signaling pathway can modulate skeletal muscle hypertrophy and atrophy.[52] Moreover, the AMPK-Foxo3-Atrogin cascade has been implicated in causing muscle protein degradation to surpass protein synthesis, resulting in reduced skeletal muscle mass.[53] The degradation of muscle proteins also involves the ubiquitin E3-proteasome pathway.[54] Furthermore, disturbances in the intestinal flora, as observed by QIU Y et al[55], can interfere with the BA-FXR-FGF15/19-ERK signaling axis, subsequently leading to reduced muscle protein synthesis and inducing skeletal muscle atrophy in the host.

The cluster labels for cluster #8 and cluster #9 were “immune response”, “immunity”, “involving microorganisms”, “immune system”, “inflammatory factors”, “insulin resistance”, and “muscle-gut axis”, among others. Aging is a complex process that unfolds over time, encompassing genetics, diet, metabolism, microorganisms, inflammation, immunity, and more, which can impact the functions of various organs and systems throughout the body. Furthermore, aging constitutes a significant factor in the development of numerous age-related diseases, ultimately affecting the health and quality of life of individuals aged.[56–58] As exemplified by cluster #8 and cluster #9, the microbiome and sarcopenia are closely intertwined with immunity and aging.[7] Notably, the diversity and composition of microorganisms in the body decline with age, and the effects of various immune cells and factors on skeletal muscle are also regulated by intestinal flora. Current research on the role of the immune system in microbes and sarcopenia mainly focuses on the effects of microbiome-related metabolites on host immune cells,[46,59] the effects of immune-related cytokines on skeletal muscle mass and sarcopenia,[60–62] and the effects of probiotics and dietary interventions on immune responses.[63] We had not found research on the mechanistic role of the immune system in the microbiome and sarcopenia, and further studies may be needed to confirm the role of immune senescence in sarcopenia and the microbiome.

limitations

This paper presents certain limitations. Firstly, the study only encompassed articles selected from the Web of Science, which could lead to deviations in indicators like the number of papers published by the country and the contribution of magazine publications. Secondly, the study had a deadline for the included articles, thus, articles after the deadline as well as reports and other articles were not taken into account.

Conclusion

Our study provided a comprehensive overview of sarcopenia and microbiome research, analyzed through bibliometric analysis of sarcopenia and the microbiome. We analyzed publishing trends, publishing countries, highly cited countries, highly published journals, highly cited publications, highly publishing institutions, and highly published authors. Research on the impact of the microbiome on sarcopenia is in its infancy and spans multiple disciplines. Malnutrition, dietary fiber, signaling pathways, frailty, and intestinal microbes are currently research hotspots.

Additionally, our study provided crucial information and guidance for future researchers and decision-makers by analyzing network connection graphs of countries, institutions, and individuals. The increasing number of published papers each year indicates a growing interest in this research field by scholars worldwide. Our analysis of keywords and clusters revealed new research hotspots in microbes and sarcopenia, including malnutrition, dietary fiber, signaling pathways, frailty, and intestinal microbes. Furthermore, the visual atlas analysis of research on microbes and sarcopenia could help to track the knowledge structure in research fields related to sarcopenia and microbes, providing direction for future research.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Disclosure

The authors report no conflicts of interest in this work.

References

1. Cruz-Jentoft AJ, Bahat G, Bauer J, et al. Sarcopenia: revised European consensus on definition and diagnosis. *Age Ageing*. 2019;48:16–31. doi:10.1093/ageing/afy169
2. Chen LK, Woo J, Assantachai P, et al. Asian working group for sarcopenia: 2019 Consensus update on sarcopenia diagnosis and treatment. *J Am Med Dir Assoc*. 2020;21:300–307 e302. doi:10.1016/j.jamda.2019.12.012
3. Chen Z, Li WY, Ho M, et al. The prevalence of sarcopenia in Chinese older adults: Meta-analysis and meta-regression. *Nutrients*. 2021;14:13. doi:10.3390/nu14010013
4. Bian AL, Hu HY, Rong YD, et al. A study on relationship between elderly sarcopenia and inflammatory factors IL-6 and TNF-α. *Eur J Med Res*. 2017;22:25. doi:10.1186/s40001-017-0266-9
5. Wang Y, Zhang Y, Lane NE, et al. Population-based metagenomics analysis reveals altered gut microbiome in sarcopenia: Data from the Xiangya Sarcopenia Study. *J Cachexia, Sarcopenia Muscle*. 2022;13:2340–2351. doi:10.1002/jcsm.13037
6. Liu C, Cheung WH, Li J, et al. Understanding the gut microbiota and sarcopenia: A systematic review. *J Cachexia, Sarcopenia Muscle*. 2021;12:1393–1407. doi:10.1002/jcsm.12784
7. Aleman FDD, Valenzano DR. Microbiome evolution during host aging. *PLoS Pathog*. 2019;15:e1007727.
8. Weinstock GM. Genomic approaches to studying the human microbiota. *Nature*. 2012;489:250–256. doi:10.1038/nature11553
9. Chew W, Lim YP, Lim WS, et al. Gut-muscle crosstalk. A perspective on influence of microbes on muscle function. *Front Med*. 2023; 9. doi:10.3389/fmed.2022.1065365
10. Butteiger DN, Hibberd AA, McGraw NJ, et al. Soy protein compared with milk protein in a western diet increases gut microbial diversity and reduces serum lipids in golden Syrian hamsters. *J Nutr*. 2016;146:697–705. doi:10.3945/jn.115.224196
11. Kang L, Li P, Wang D, et al. Alterations in intestinal microbiota diversity, composition, and function in patients with sarcopenia. *Sci Rep*. 2021;11:4628. doi:10.1038/s41598-021-84031-0
12. Han DS, Wu WK, Liu PY, et al. Differences in the gut microbiome and reduced fecal butyrate in elders with low skeletal muscle mass. *Clin Nutr*. 2022;41:1491–1500. doi:10.1016/j.clnu.2022.05.008
13. Zhang Y, Zhu Y, Guo Q, et al. High-throughput sequencing analysis of the characteristics of the gut microbiota in aged patients with sarcopenia. *Exp Gerontol*. 2023;182:112287. doi:10.1016/j.exger.2023.112287

14. Wang Z, Xu X, Deji Y, et al. Bifidobacterium as a potential biomarker of sarcopenia in elderly women. *Nutrients*. 2023;16:15. doi:10.3390/nu16010015
15. Lustgarten MS, Fielding RA. Metabolites related to renal function, immune activation, and carbamylation are associated with muscle composition in older adults. *Exp Gerontol*. 2017;100:1–10. doi:10.1016/j.exger.2017.10.003
16. Sato E, Mori T, Mishima E, et al. Metabolic alterations by indoxyl sulfate in skeletal muscle induce uremic sarcopenia in chronic kidney disease. *Sci Rep*. 2016;6:6. doi:10.1038/s41598-016-0015-2
17. Aliwa B, Horvath A, Traub J, et al. Altered gut microbiome, bile acid composition and metabolome in sarcopenia in liver cirrhosis. *J Cachexia Sarcopenia Mus*. 2023;14:2676–2691. doi:10.1002/jcsm.13342
18. Mancin L, Wu GD, Paoli A. Gut microbiota-bile acid-skeletal muscle axis. *Trends Microbiol*. 2022;31:254–269. doi:10.1016/j.tim.2022.10.003
19. De Spiegeleer A, Wynendaele E, Descamps A, et al. The bacterial quorum sensing peptide iAM373 is a novel inducer of sarcopenia. *Clin Transl Med*. 2022;12:e1053.
20. Qin YF, Ren SH, Shao B, et al. The intellectual base and research fronts of IL-37: a bibliometric review of the literature from WoSCC. *Front Immunol*. 2022;13:931783. doi:10.3389/fimmu.2022.931783
21. Chen C, Song M, Glanzel W. Visualizing a field of research: a methodology of systematic scientometric reviews. *PLoS One*. 2019;14:e0223994. doi:10.1371/journal.pone.0223994
22. Chen C. CiteSpace II: detecting and visualizing emerging trends and transient patterns in scientific literature. *J Assoc Inf Sci Technol*. 2006;57:359–377. doi:10.1002/asi.20317
23. Yao L, Hui L, Yang Z, et al. Freshwater microplastics pollution: detecting and visualizing emerging trends based on Citespace II. *Chemosphere*. 2020;245:125627. doi:10.1016/j.chemosphere.2019.125627
24. Darvish H. Bibliometric analysis using bibliometrix an r package. *J Scientometric Res*. 2020;8:156–160. doi:10.5530/jscires.8.3.32
25. L ENW. Visualizing Bibliometric Networks; 2014.
26. Wang Y, Li D, Jia Z, et al. A bibliometric analysis of research on the links between gut microbiota and atherosclerosis. *Front Cardiovasc Med*. 2022;9:941607. doi:10.3389/fcvm.2022.941607
27. Bajjalieh NL, Jensen AH. Effect of a synthetic antimicrobial agent on the rates of synthesis and degradation of liver and skeletal muscle proteins in growing rats. *J Nutr*. 1981;111:563–567. doi:10.1093/jn/111.3.563
28. Nelke C, Dziewas R, Minnerup J, et al. Skeletal muscle as potential central link between sarcopenia and immune senescence. *EBioMedicine*. 2019;49:381–388. doi:10.1016/j.ebiom.2019.10.034
29. Hou K, Wu ZX, Chen XY, et al. Microbiota in health and diseases. *Signal Transduct Target Ther*. 2022;7:135. doi:10.1038/s41392-022-00974-4
30. World Health Organization. Decade of Healthy Ageing: 2021-2030. *World Health Organization*, 2020Available from: https://www.who.int/initiatives/decade-of-healthy-ageing. Accessed june 20, 2024.
31. Collins KH, Paul HA, Hart DA, et al. A high-fat high-sucrose diet rapidly alters muscle integrity, inflammation and gut microbiota in male rats. *Sci Rep*. 2016;6:37278. doi:10.1038/srep37278
32. Sanchez-Rodriguez D, Locquet M, Reginster JY, et al. Mortality in malnourished older adults diagnosed by ESPEN and GLIM criteria in the SarcoPhAge study. *J Cachexia Sarcopenia Mus*. 2020;11:1200–1211. doi:10.1002/jcsm.12574
33. Yuan S, Larsson SC. Epidemiology of sarcopenia: prevalence, risk factors, and consequences. *Metabolism*. 2023;144:155533. doi:10.1016/j.metabol.2023.155533
34. Cox NJ, Bowyer RCE, Ni Lochlainn M, et al. The composition of the gut microbiome differs among community dwelling older people with good and poor appetite. *J Cachexia Sarcopenia Mus*. 2021;12:368–377. doi:10.1002/jcsm.12683
35. Jollet M, Nay K, Chopard A, et al. Does Physical Inactivity Induce Significant Changes in Human Gut Microbiota? New Answers Using the Dry Immersion Hypoactivity Model. *Nutrients*. 2021;13:14.
36. Mueller NT, Zhang M, Juraschek SP, et al. Effects of high-fiber diets enriched with carbohydrate, protein, or unsaturated fat on circulating short chain fatty acids: results from the OmniHeart randomized trial. *Am J Clin Nutri*. 2020;111:545–554. doi:10.1093/ajcn/nqz322
37. Sung MM, Byrne NJ, Robertson IM, et al. Resveratrol improves exercise performance and skeletal muscle oxidative capacity in heart failure. *Am J Physiol Heart Circ Physiol*. 2017;312:H842–H853.
38. Leal-Diaz AM, Noriega LG, Torre-Villalvazo I, et al. Aguamiel concentrate from Agave salmiana and its extracted saponins attenuated obesity and hepatic steatosis and increased Akkermansia muciniphila in C57BL6 mice. *Sci Rep*. 2016;6:34242. doi:10.1038/srep34242
39. Yan X, Zhang Y, Peng Y, et al. The water extract of Radix scutellariae, its total flavonoids and baicalin inhibited CYP7A1 expression, improved bile acid, and glycolipid metabolism in T2DM mice. *J Ethnopharmacol*. 2022;293:115238. doi:10.1016/j.jep.2022.115238
40. Zhang L, Lang H, Ran L, et al. Long-term high loading intensity of aerobic exercise improves skeletal muscle performance via the gut microbiota-testosterone axis. *Front Microbiol*. 2022;13:1049469. doi:10.3389/fmicb.2022.1049469
41. É B BRMCR, Rangel ÉB. Gut microbiota-derived metabolites are novel targets for improving insulin resistance. *World J Diab*. 2022;13:65–69. doi:10.4239/wjd.v13.i1.65
42. Parada Venegas D, la Fuente MK D, Landskron G, et al. Short Chain Fatty Acids (SCFAs)-Mediated Gut Epithelial and Immune Regulation and Its Relevance for Inflammatory Bowel Diseases. *Front Immunol*. 2019;10:277. doi:10.3389/fimmu.2019.00277
43. LeBlanc JG, Chain F, Martín R, et al. Beneficial effects on host energy metabolism of short-chain fatty acids and vitamins produced by commensal and probiotic bacteria. *Microb Cell Fact*. 2017;16:79. doi:10.1186/s12934-017-0691-z
44. Matheus VA, Monteiro L, Oliveira RB, et al. Butyrate reduces high-fat diet-induced metabolic alterations, hepatic steatosis and pancreatic beta cell and intestinal barrier dysfunctions in prediabetic mice. *Exp Biol Med*. 2017;242:1214–1226. doi:10.1177/1535370217708188
45. Tominaga K, Tsuchiya A, Nakano O, et al. Increase in muscle mass associated with the prebiotic effects of 1-kestose in super-elderly patients with sarcopenia. *Biosci Microbiota Food Health*. 2021;40:150–155. doi:10.12938/bmfh.2020-063
46. Chen LH, Huang SY, Huang KC, et al. Lactobacillus paracasei PS23 decelerated age-related muscle loss by ensuring mitochondrial function in SAMP8 mice. *Aging*. 2019;11:756–770. doi:10.18632/aging.101782
47. Tang T, Song J, Li J, et al. A synbiotic consisting of Lactobacillus plantarum S58 and hull-less barley beta-glucan ameliorates lipid accumulation in mice fed with a high-fat diet by activating AMPK signaling and modulating the gut microbiota. *Carbohydr Polym*. 2020;243:116398. doi:10.1016/j.carbpol.2020.116398

48. Tung YT, Zeng JL, Ho ST, et al. Djulis hull improves insulin resistance and modulates the gut microbiota in high-fat diet (HFD)-Induced Hyperglycaemia. *Antioxidants*. 2021;11:11. doi:10.3390/antiox11010011
49. Serino M, Luche E, Gres S, et al. Metabolic adaptation to a high-fat diet is associated with a change in the gut microbiota. *Gut*. 2012;61:543–553. doi:10.1136/gutjnl-2011-301012
50. Li H, Shi J, Zhao L, et al. Lactobacillus plantarum KLDS1.0344 and Lactobacillus acidophilus KLDS1.0901 Mixture Prevents Chronic Alcoholic Liver Injury in Mice by Protecting the Intestinal Barrier and Regulating Gut Microbiota and Liver-Related Pathways. *J Agric Food Chem*. 2021;69:183–197. doi:10.1021/acs.jafc.0c06346
51. Ticinesi A, Mancabelli L, Tagliaferri S, et al. The gut-muscle axis in older subjects with low muscle mass and performance: a proof of concept study exploring fecal microbiota composition and function with shotgun metagenomics sequencing. *Int J Mol Sci*. 2020; 21. doi:10.3390/ijms22010021
52. Bodine SC, Stitt TN, Gonzalez M, et al. Akt/mTOR pathway is a crucial regulator of skeletal muscle hypertrophy and can prevent muscle atrophy in vivo. *Nat Cell Biol*. 2001;3:1014–1019. doi:10.1038/ncb1101-1014
53. Lahiri S, Kim H, Garcia-Perez I, et al. The gut microbiota influences skeletal muscle mass and function in mice. *Sci Transl Med*. 2019;11.
54. Bodine SC, Baehr LM. Skeletal muscle atrophy and the E3 ubiquitin ligases MuRF1 and MAFbx/atrogin-1. *Am J Physiol Endocrinol Metab*. 2014;307:E469–484.
55. Qiu Y, Yu J, Ji X, et al. Ileal FXR-FGF15/19 signaling activation improves skeletal muscle loss in aged mice. *Mech Ageing Dev*. 2022;202:111630. doi:10.1016/j.mad.2022.111630
56. Kennedy BK, Berger SL, Brunet A, et al. Geroscience: linking aging to chronic disease. *Cell*. 2014;159:709–713. doi:10.1016/j.cell.2014.10.039
57. Ling Z, Liu X, Cheng Y, et al. Gut microbiota and aging. *Crit Rev Food Sci Nutr*. 2020;62:3509–3534. doi:10.1080/10408398.2020.1867054
58. Saito Y, Chikenji TS. Diverse roles of cellular senescence in skeletal muscle inflammation, regeneration, and therapeutics. *Front Pharmacol*. 2021;12:739510. doi:10.3389/fphar.2021.739510
59. Tingstad RH, Norheim F, Haugen F, et al. The effect of toll-like receptor ligands on energy metabolism and myokine expression and secretion in cultured human skeletal muscle cells. *Sci Rep*. 2021;11:24219. doi:10.1038/s41598-021-03730-w
60. Mann AO, Hanna BS, Munoz-Rojas AR, et al. IL-17A-producing gammadeltaT cells promote muscle regeneration in a microbiota-dependent manner. *J Exp Med*. 2022;219.
61. Gérard C, Bruyns C, Marchant A, et al. Interleukin 10 reduces the release of tumor necrosis factor and prevents lethality in experimental endotoxemia. *J Exp Med*. 1993;177:547–550. doi:10.1084/jem.177.2.547
62. Chen LH, Chang SS, Chang HY, et al. Probiotic supplementation attenuates age-related sarcopenia via the gut-muscle axis in SAMP8 mice. *J Cachexia Sarcopenia Mus*. 2022;13:515–531. doi:10.1002/jcsm.12849
63. Bischoff SC. Microbiota and aging. *Curr Opin Clin Nutr Metab Care*. 2016;19:26–30. doi:10.1097/MCO.0000000000000242