International Journal of
Business Management and Entrepreneurship
Journal homepage: mbajournal.ir

Integration of Multi-Omics Approaches in Exercise: Current Status and Future Perspectives

Amir Hossein Hormati Oughoulbaig[1], Amir Hossein Honarmand[2], Narges Yazdan Nasab[3]

Received: 2025/07/01 Accepted: 2025/09/01 Published: 2025/12/30

Abstract

Introduction and Objectives: Exercise is a potent physiological stimulus that offers numerous health benefits; however, individual responses to exercise exhibit considerable variability. This review seeks to integrate recent findings regarding the utilization of multi-omics in exercise physiology, emphasizing its function in clarifying individual variances, modality-specific adaptations, and the potential for tailored exercise prescriptions.

Methods: A systematic literature search was performed in PubMed, Scopus, and Web of Science (2023–2025). Studies were included if they utilized a minimum of two omics platforms, involved human subjects, and established a connection between molecular profiles and exercise-related physiological outcomes. We used the Downs and Black checklist to check the methodological quality.

Results: There were eight studies, including clinical trials, meta-analyses, and data-driven modelling. Multi-omics analyses showed that people's molecules were organized in different ways (e.g., by lipid metabolism or immune gene signatures), identified pathways activated by aerobic vs. resistance training, and demonstrated the importance of the gut mycobiome for metabolic health.

Conclusion: Multi-omics approaches provide deep insights into the molecular basis of exercise response, supporting a shift toward personalized exercise science.

Keywords

multi-omics, personalized training, metabolomics, microbiome, machine learning, precision health.

1. Ph. D Student of Sport Physiology, Faculty of Education and Psychology, University of Mohaghegh Ardabili, Ardabil, Iran.

2. Ph. D Student of Sport Physiology, Faculty of Education and Psychology, University of Mohaghegh Ardabili, Ardabil, Iran.

3. Ph. D Student of Cellular and Molecular Biology Faculty of Science, University of Mohaghegh Ardabili, Ardabil, Iran.

Introduction

Exercise is one of the most potent biological stimuli recognized by science. Exercise affects almost every system in the body, from the heart and blood vessels to the metabolism, the immune system, and the muscles and nerves (1). Even though exercise physiology has many benefits, it is still hard to find out why people react so differently to the same training program (2). Some individuals exhibit significant enhancements in fitness and health indicators, whereas others demonstrate negligible alterations. This variability has led to a change in the focus of research, from averages for groups to individual molecular profiles (3). The convergence of multi-omics technologies in recent years has facilitated novel avenues for investigating the biological intricacies of exercise adaptation (4, 5). Researchers can now see how exercise changes the body at a systems level by putting together information from genomics, transcriptomics, proteomics, metabolomics, epigenomics, and microbiomics (6, 7). These methods show not only which molecules are involved, but also how they work together across biological layers to create coordinated responses. Gene expression studies have demonstrated that endurance and resistance training engage specific molecular pathways associated with mitochondrial function, angiogenesis, and muscle hypertrophy (8, 9). Proteomic analyses have detected alterations in enzymes and signaling proteins indicative of modifications in energy metabolism and inflammation (10). Metabolomic profiling has revealed dynamic changes in lipid and amino acid turnover, providing insights into enhanced metabolic flexibility and substrate utilization (11, 12). Epigenetic mechanisms, especially DNA methylation, have become important controls for how genes are turned on and off during exercise (13). These changes can affect how genes are turned on or off when you exercise, and some of them seem to last long after training is over, which suggests a kind of molecular memory. These findings have significant ramifications for long-term health and disease prevention. The gut microbiome has also become a focus as a way that exercise can affect the body (14, 15). Most studies have looked at bacterial communities, but new research shows that gut fungi may also affect how the host's metabolism and immune system work (16). Exercise seems to increase the variety of microbes and make ecological interactions stronger, which may help with glycemic control and systemic resilience (17). Machine learning has made even more progress in this field. Using baseline omics data, predictive models can now tell if a person is likely to respond to or not respond to certain exercise interventions (18). These tools give us a taste of what personalized training might look like in the future, where molecular diagnostics help create exercise plans that are unique to each person's body. Even with these advances, there are still problems to solve. Ongoing challenges include integrating data across platforms, ensuring reproducibility, and translating findings into clinical practice. In addition, differences based on sex and type of exercise, like those between aerobic and resistance training, need to be looked into more closely to make sure that precise exercise science is both broad and useful (19, 20). This review analyzes recent findings from multi-omics research in exercise physiology. By linking molecular data with functional outcomes, it seeks to enhance our comprehension of the mechanisms of exercise at fundamental biological levels and how this knowledge can be utilized to improve health, performance, and disease prevention for all individuals.

Methods

This review analyzes current evidence on integrating multi-omics approaches in exercise physiology. A structured literature search was conducted in PubMed, Scopus, and Web of Science for studies published between 2023 and 2025. Search terms included combinations of “multi-omics”, “exercise”, “genomics”, “transcriptomics”, “proteomics”, “metabolomics”, “epigenomics”, “microbiome”, “machine learning”, and “personalized training”.

Studies were incorporated if they:

Used at least two omics platforms to look into how molecules react to exercise;

Included people from both healthy and sick populations;
Reported links between omics profiles and physiological results.

Quality Assessment

The Downs and Black checklist were used to critically evaluate the methodological quality of the studies that were included. This tool enables a comprehensive evaluation of both randomized and non-randomized studies, assessing key domains including reporting, external validity, internal validity (bias and confounding), and power. Two reviewers looked at each study on their own, and any differences were worked out through discussion or by asking a third reviewer. This process ensured that the evidence analyzed and discussed in this review meets a high standard of methodological rigor.

Results

Table 1. Summary of reviewed studies on exercise- and health-related multi-omics investigations

Article Title	Year	Study Type	Population	Intervention	Omics Platforms	Key Findings	Relevance to Review
A 6-month exercise intervention clinical trial in women (21)	2024	Longitudinal clinical trial	Healthy middle-aged women	Aerobic + stretching exercise	Metabolomics microbiome clinical biomarkers	BP, HbA1c, and LDL-C decreased in period 1; increased in period 2; 40 metabolites significantly altered	Multi-omics effects of exercise during COVID-19
Multi-omic integration sets the path for early prevention strategies (22)	2025	Cross-sectional + longitudinal	healthy individuals	-	Genomics, urine/serum metabolomics, lip proteomics	Identified 4 molecular subgroups; one with dyslipoproteinemia risk; stable omic profiles over time	Multi-omic stratification for early prevention
Towards Precision Sports Nutrition for Endurance Athletes (23)	2024	Scoping review	endurance athletes	Nutritional interventions + CGM	Genomics, metabolomics, proteomics, epigenomics, lipidomics, metagenomics, wearables	Reviewed omics applications in sports nutrition; highlighted individual responses; emphasized need for N-of-1 trials	Omics-driven personalization in endurance nutrition
Integrating omics to optimize precision cardiac rehabilitation (24)	2025	Commentary	Cardiac rehabilitation patients	Exercise, diet, behavioral CR	Genomics, epigenomics, transcriptomics, proteomics, metabolomics, macrobiotics	Discussed omics biomarkers for CR personalization; potential molecular predictors of response	Omics framework for precision cardiac rehabilitation
Exercise-related immune gene signature for hepatocellular carcinoma (25)	2025	Public data analysis + ML modeling	TCGA/ICGC datasets + 15 scRNA samples	No intervention	Transcriptomics, scRNA, metabolomics, immunomics	Identified 7-gene EIGPS model predicting HCC prognosis; immune subtype correlations	Exercise-linked immune omics in cancer prognosis
Molecular landscape of sex- and modality-specific exercise adaptation (26)	2025	Multi-omics meta-analysis	>1000 participants, 2340 muscle samples	Aerobic + resistance training	Genomics, DNA methylation, transcriptomics, proteomics, TFs	Found 5 robust molecular markers; minimal sex differences; identified modality-specific pathways	Multi-omics framework for skeletal muscle adaptation
Exercise-changed gut mycobiome and metabolic benefits in diabetes (27)	2024	RCT + ML modeling	Chinese males with prediabetes validation	High-intensity interval training (HIIT)	ITS2, metagenomics, metabolomics, proteomics, ML	Increased gut fungal diversity; Verticillium and Ceratocystis linked to glucose metabolism; AUROC = 0.91	Gut mycobiome as an exercise transducer in diabetes prevention

Article Title	Year	Study Type	Population	Intervention	Omics Platforms	Key Findings	Relevance to Review
Integration of Multiomic and Multi-1 phenotypic Data Identifies 2 Biological Pathways Associated with Physical Fitness (28)	2025	Multi-omic + phenotypic integration	Multi-omics data	-	Genomics, transcriptomics, proteomics, metabolomics, phenotyping	Identified biological pathways associated with physical fitness; strong omics-phenotype correlations	Multi-layered biological insights into fitness and metabolic health

A total of eight studies published between 2024 and 2025 were included, encompassing a range of designs from randomized clinical trials and longitudinal interventions to meta-analyses, data-driven modeling, and narrative reviews. Collectively, these investigations explored the integration of multi-omics technologies to elucidate the molecular effects of exercise, nutrition, and lifestyle factors on health and disease outcomes.

In intervention-based studies, Park et al. (2024) and Wang et al. (2024) exhibited substantial enhancements in cardiometabolic markers and glucose regulation subsequent to exercise interventions, accompanied by notable metabolomic and microbiome modifications (21, 27). Jacques et al. (2025) performed a comprehensive meta-analysis that identified five significant molecular markers related to exercise modality (26), while Pu et al. (2025) discovered an immune gene signature that connects exercise-related pathways to hepatocellular carcinoma prognosis (25). Non-interventional studies, such as Kioroglou et al. (2025) and Alizadeh et al. (2025), focused on molecular stratification and phenotype–omics integration, identifying stable multi-omic profiles and biological pathways associated with physical fitness and disease risk (22, 28). Review and commentary papers (Bedrač et al., 2024; Ghram & Lavie, 2025) emphasized the emerging potential of omics-informed precision approaches in sports nutrition and cardiac rehabilitation (23, 24).

Table 2. Quality assessment of included studies using the modified Downs and Black checklist

Study (First Author, Year)	Reporting (0–11)	External Validity (0–3)	Internal Validity: Bias (0–7)	Internal Validity: Confounding (0–6)	Power (0–1)	Total Score (0–28)	Quality Level
Park et al., 2024 (21)	10	2	5	5	1	**23**	Good
Kioroglou et al., 2025 (22)	9	2	5	4	0	**20**	Moderate–Good
Bedrač et al., 2024 (23)	8	3	4	3	0	**18**	Moderate
Ghram & Lavie, 2025 (24)	7	2	3	2	0	**14**	Low–Moderate
Pu et al., 2025 (25)	9	2	5	4	0	**20**	Moderate–Good
Jacques et al., 2025 (26)	10	3	6	5	1	**25**	High
Wang et al., 2024 (27)	10	3	6	5	1	**25**	High
Alizadeh et al., 2025 (28)	9	2	5	4	0	**20**	Moderate–Good

Discussion

The results of eight recent studies (2024–2025) that used multi-omics techniques to look into the molecular basis of exercise-induced adaptations are summarized in this review. The combined data highlights the revolutionary potential of multi-omics technologies in shifting from universally applicable workout regimens to tailored, biologically based suggestions.

A significant finding from various studies is the capacity of multi-omics data to categorize individuals into specific molecular subgroups, elucidating and possibly forecasting variability in exercise responsiveness. For example, Kioroglou et al. (2025) found subgroups with different risks of dyslipoproteinemia (22), and Pu et al. (2025) made a 7-gene immune signature that could predict the outcome of hepatocellular carcinoma (25). These findings underscore the potential of baseline omic profiles to inform targeted exercise and lifestyle interventions for individuals at risk. Another recurring theme is the modality-specific characteristics of molecular adaptations. Jacques et al. (2025) delineated distinct pathway variations between aerobic and resistance training, underscoring the necessity for exercise prescriptions tailored to specific physiological objectives (26). Wang et al. (2024) similarly showed that high-intensity interval training (HIIT) changed the gut mycobiome in a unique way, which was linked to better glucose metabolism (27). This finding shows that exercise–host–microbiome interactions go beyond bacteria. Combining machine learning with multi-omic data has sped up the creation of predictive models even more. Research conducted by Wang et al. (2024) and Pu et al. (2025) demonstrated significant predictive accuracy (e.g., AUROC = 0.91), indicating that these tools may soon facilitate clinical and athletic decision-making (25, 27). These methodologies facilitate the transition from correlation to causation, allowing researchers to pinpoint potential biomarkers and mechanistic pathways for subsequent validation. The quality assessment of the included studies indicated generally robust methodologies, especially within intervention-based and large-scale omic profiling initiatives. Studies with high scores, like those by Jacques et al. (2025) and Wang et al. (2024), used a strict design and integration across multiple platforms, which made their findings more reliable (26, 27). The moderate-to-low scores of narrative and commentary papers indicate their restricted empirical contributions, yet they continue to be significant for shaping future research trajectories.

While these technological advances have been made, quite a few issues linger on. Integrating data from several omic layers presents a significant technological and analytical challenge. Besides, the majority of the studies up to now have focused on certain groups of people, such as middle-aged women, athletes, or prediabetic men, and thus their results cannot be generalized. The next step in research should be the inclusion of a variety of cohorts and long-term studies to better understand the changing and personal nature of the body's response to exercise.

Conclusion

The understanding of the complex and performance adaptations of the health molecular networks is changing with the use of multi-omics. As the field is changing, there is a need to focus on the standardization of omic data collection and the improvement of model interpretability and clinical, coaching, and consumer tool translation. Further multi-omics innovations will allow for the precision exercise science revolution, where biological profiles will shape exercise intervention prescriptions.

Refrencess

1. Rundqvist H, Velica P, Barbieri L, Gameiro PA, Bargiela D, Gojkovic M, et al. Cytotoxic T-cells mediate exercise-induced reductions in tumor growth. eLife. 2020;9.

2. Fucarino A, Fabbrizio A, Garrido ND, Iuliano E, Reis VM, Sausa M, et al. Emerging Technologies and Open-Source Platforms for Remote Physical Exercise: Innovations and Opportunities for Healthy Population-A Narrative Review. Healthcare (Basel, Switzerland). 2024;12(15).

3. Grunberg NE, McManigle JE, Schoomaker EB, Barry ES. Leading Change in Health Care. Clinics in sports medicine. 2023;42(2):249-60.
4. Labarga A, Martinez-Gonzalez J, Barajas M. Integrative Multi-Omics Analysis for Etiology Classification and Biomarker Discovery in Stroke: Advancing towards Precision Medicine. Biology. 2024;13(5).
5. Zhang F, Zhu M, Chen Y, Wang G, Yang H, Lu X, et al. Harnessing omics data for drug discovery and development in ovarian aging. Human reproduction update. 2025;31(3):240-68.
6. Arneson D, Shu L, Tsai B, Barrere-Cain R, Sun C, Yang X. Multidimensional Integrative Genomics Approaches to Dissecting Cardiovascular Disease. Frontiers in cardiovascular medicine. 2017;4:8.
7. Ye L, Dimitriadis E. Endometrial Receptivity-Lessons from "Omics". Biomolecules. 2025;15(1).
8. Siahkouhian M, Yazdan nasab N, Parandak SZ, hormati Oughoulbaig z, Hormati Oughoulbaig AH. A Review of the Impact of Genetic and Epigenetic Interactions on Metabolic Regulation and Nutritional Requirements of Elite Athletes: Molecular Mechanisms and Functional Implications. Journal of Applied Exercise Physiology. 2025;20(40):-.
9. Stec MJ, Graham ZA, Su Q, Adler C, Ni M, Le Rouzic V, et al. Combined endurance and resistance exercise training alters the spatial transcriptome of skeletal muscle in young adults. iScience. 2025;28(9):113301.
10. Li X, Ma W, Li X, Feng R, Meng J, Zhang L, et al. Identification of proteomic markers of chronic prostatitis/chronic pelvic pain syndrome treated with melatonin using a tandem mass tag approach. Current urology. 2025;19(5):331-42.
11. Choi JY, Kim YJ, Shin JS, Choi E, Kim Y, Kim MG, et al. Integrative metabolic profiling of hypothalamus and skeletal muscle in a mouse model of cancer cachexia. Biochemical and biophysical research communications. 2025;763:151766.
12. Jia D, Jin S, Zhang J, Luo S, Li X, Quek SY, et al. Dynamic Changes in Metabolites and Transformation Pathways in Diqing Tibetan Pig Hams During Fermentation Determined by Widely Targeted Metabolomic Analysis. Foods (Basel, Switzerland). 2025;14(14).
13. Zhang F, Evans T. Stage-specific DNA methylation dynamics in mammalian heart development. Epigenomics. 2025;17(5):359-71.
14. Li W, Deng Y, Chu Q, Zhang P. Gut microbiome and cancer immunotherapy. Cancer letters. 2019;447:41-7.
15. Wang Y, Xie Z. Exploring the role of gut microbiome in male reproduction. Andrology. 2022;10(3):441-50.
16. Forbes JD, Bernstein CN, Tremlett H, Van Domselaar G, Knox NC. A Fungal World: Could the Gut Mycobiome Be Involved in Neurological Disease? Frontiers in microbiology. 2018;9:3249.
17. Winston H, Fage B. Resilience, Resistance: A Commentary on the Historical Origins of Resilience and Wellness Initiatives. Psychiatric services (Washington, DC). 2019;70(8):737-9.
18. Wang Y, Zhang H, Sang Z, Xu L, Cao C, Gulliver TA. Modulation Classification of Underwater Communication with Deep Learning Network. Computational intelligence and neuroscience. 2019;2019:8039632.
19. Hormati AH, Piri E, Jafarnezhadgero AA, Hormati Z, Imanibroj S. A Review on the Effects of Rehabilitation Exercises on the Mechanics of Movements Transfer in Individuals with Knee Valgus. Journal of Paramedical Sciences & Rehabilitation. 2025;14(1):99-114.
20. Yazdan nasab N, Mamashli E, Ashrafi N, Abdolmaleki A, Asadi A. Cell therapy and Regenerative medicine for treatment in sport injuries. Journal of Advanced Sport Technology. 2025;9(1):50-66.
21. Park J, Kim J, Kang J, Choi J, Kim JE, Min KJ, et al. A 6-month exercise intervention clinical trial in women: effects of physical activity on multi-omics biomarkers and health during the first wave of COVID-19 in Korea. BMC sports science, medicine & rehabilitation. 2024;16(1):30.
22. Kioroglou D, Gil-Redondo R, Embade N, Bizkarguenaga M, Conde R, Millet O, et al. Multi-omic integration sets the path for early prevention strategies on healthy individuals. npj Genomic Medicine. 2025;10(1):35.
23. Bedrač L, Deutsch L, Terzić S, Červek M, Šelb J, Ašič U, et al. Towards Precision Sports Nutrition for Endurance Athletes: A Scoping Review of Application of Omics and Wearables Technologies. Nutrients. 2024;16(22).
24. Amine G, Carl JL. Integrating omics to optimize precision cardiac rehabilitation. Metabolism and Target Organ Damage. 2025;5(3):38.
25. Pu C, Pu L, Zhang X, He Q, Zhou J, Li J. Exercise-related immune gene signature for hepatocellular carcinoma: machine learning and multi-omics analysis. Frontiers in immunology. 2025;16:1606711.
26. Jacques M, Landen S, Sharples AP, Garnham A, Schittenhelm R, Steele J, et al. Molecular landscape of sex- and modality-specific exercise adaptation in human skeletal muscle through large-scale multi-omics integration. Cell reports. 2025;44(6):115750.

27. Wang Y, Chen J, Ni Y, Liu Y, Gao X, Tse MA, et al. Exercise-changed gut mycobiome as a potential contributor to metabolic benefits in diabetes prevention: an integrative multi-omics study. Gut microbes. 2024;16(1):2416928.
28. Alizadeh A, Graf J, Misner MJ, Burns AA, Ginty F, O'Donovan KJ, et al. Integration of Multiomic and Multi-phenotypic Data Identifies Biological Pathways Associated with Physical Fitness. bioRxiv. 2025:2025.09.24.677381.