Letter to the Editor

Exercise-induced extracellular vesicles as mediators of exerkine signaling: Implications for precision exercise medicine in metabolic and age-related disorders

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Dear Editor-in-Chief

What if the therapeutic benefits of exercise could be captured, concentrated, and delivered as a targeted molecular dose? New research on exercise-induced extracellular vesicles (ExEVs) suggests that this concept is evolving from a metaphorical understanding to a mechanistic one. Extracellular vesicles (EVs), particularly exosomes, are increasingly recognized as important facilitators of the signals generated by exercise, known as exerkines. These vesicles carry well-known myokines like IL-6 and irisin, as well as a wide range of other components, including microRNAs (miRNAs), mitochondrial DNA (mtDNA), and metabolites. This cargo is transported to distant organs, enhancing communication between muscles and various systems, including the brain, liver, and cardiovascular system (Magliulo et al., 2022; Nederveen et al., 2021).

Both aerobic and resistance training lead to a substantial increase in the secretion of extracellular vesicles (EVs) from skeletal muscle tissue, as well as a modification of their miRNA profiles, including miR-181a-5p, miR-486-5p, and miR-342-5p. These miRNAs are correlated with enhanced insulin sensitivity, reduced systemic inflammation, and neuronal protection. Consequently, this evidence underscores the role of EVs as stable carriers of exerkines that are less susceptible to enzymatic degradation and capable of delivering them more precisely than free myokines (Li et al., 2026; Silvestri et al., 2026; Wang et al., 2026).

One of the most compelling pieces of translational evidence comes from animal studies. When extracellular vesicles (ExEVs) from trained mice are injected into models of muscle disuse, they effectively preserve muscle mass and enhance regeneration (Fliflet et al., 2026). This serves as a strong proof-of-concept for developing exercise-mimetic therapeutics that can work without the need for actual exercise. In human studies, the profiles of extracellular vesicles following exercise are similarly associated with improved metabolic function and decreased markers of biological aging (Plaza-Florido et al., 2024).

Ongoing methodological obstacles, particularly in the standardization of extracellular vesicle (EV) isolation techniques, such as ultracentrifugation compared to size-exclusion chromatography, as well as in the accurate identification of their sources, whether from muscle, endothelial cells, or platelets. We propose that forthcoming investigations should progress beyond these unresolved issues towards a definitive roadmap: a multi-omics profiling approach—encompassing transcriptomics, proteomics, and lipidomics—of extracellular vesicles (ExEVs) across various exercise modalities (high-intensity interval training versus endurance training), while systematically considering sex-specific responses and age-stratified cohorts ranging from adolescence to older age. This framework would establish the groundwork for the development of vesicle-based "exercise pharmacology" (Nederveen et al., 2021).

This pioneering area not only advances our understanding of the molecular underpinnings of how exercise imparts its benefits, but also establishes a groundbreaking trajectory for therapeutics centered on extracellular vesicles—exosome mimetics formulated to treat obesity, type 2 diabetes, and sarcopenia independently of physical activity. Such developments could significantly reshape the notion of exercise prescription in medical practice.

Given the substantial transformative potential of this field, we recommend that your journal launch a special issue or thematic series on "Exercise-Derived Extracellular Vesicles in Precision Medicine." This initiative would integrate mechanistic, translational, and clinical research to fortify this swiftly evolving sector and delineate its future pathways. We believe that this Letter will be of great interest to your audience and look forward to your thoughtful consideration.

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