

# WISP-1 in Obesity and Metabolic Dysfunction: The Modulatory Role of Exercise Training-A Narrative Review

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## R e v i e w e r s

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## 1. Round 1

### 1.1 Reviewer 1

Reviewer:

In the first introduction paragraph beginning “Obesity is a global health challenge...”, prevalence trends are mentioned without quantitative data. Adding recent global prevalence statistics (WHO or GBD data) would strengthen scientific grounding and improve reader orientation.

The sentence “Among these mechanisms, adipose tissue derived factors... have garnered significant attention...” would benefit from positioning WISP-1 relative to established adipokines (e.g., leptin, adiponectin, resistin). This comparison would clarify why WISP-1 represents a meaningful advancement rather than another biomarker.

The paragraph beginning “Several potential mechanisms have been proposed...” presents mechanisms in list-like succession without clear hierarchy. Consider restructuring into sub-mechanistic categories (inflammatory signaling, fibrosis, metabolic signaling pathways) to improve readability.

The sentence “Overactivation of these pathways in experimental models has been associated with decreased insulin sensitivity...” would benefit from explicitly stating whether animal models, cell culture, or human studies dominate the evidence base, enhancing translational interpretation.

In the paragraph starting “Emerging evidence suggests that physical activity may influence circulating WISP-1 levels...”, findings are summarized sequentially rather than analytically. Please add a comparative synthesis discussing which exercise modality appears most effective and why.

The statement “heterogeneity in population characteristics and exercise protocols complicates interpretation” is important but underdeveloped. Please specify key sources of heterogeneity (training intensity prescription, supervision, metabolic status, sex differences).

Authors revised the manuscript and uploaded the updated document.

## 1.2 Reviewer 2

Reviewer:

In the paragraph discussing exercise (“Exercise training is widely recognized as a cornerstone intervention...”), the transition from exercise physiology to WISP-1 biology is abrupt. Please insert a bridging explanation describing why exercise-responsive adipokines logically led researchers to investigate WISP-1.

The final paragraph states “this narrative review aims to synthesize and critically evaluate...”. Consider expanding this into explicit review questions (e.g., Does exercise reduce WISP-1? Through which mechanisms? Is WISP-1 a biomarker or mediator?). Explicit questions improve scholarly rigor.

In the sentence “Mechanistically, WISP-1 is proposed to interact with key signaling pathways, including WNT/ $\beta$ -catenin...”, the discussion remains superficial. Please elaborate on downstream metabolic consequences (adipocyte differentiation, fibrosis, insulin signaling cross-talk) to strengthen mechanistic coherence.

The statement “WISP-1 may contribute... to a pro-inflammatory and metabolically dysregulated state” should explicitly distinguish association versus causation. Suggest adding wording indicating whether human intervention evidence supports this claim.

Authors revised the manuscript and uploaded the updated document.

## 2. Revised

Editor’s decision after revisions: Accepted.

Editor in Chief’s decision: Accepted.