Qeios

Peer Review

Review of: "Gut Microbiome, Bone Health, and Air Pressure: Construing the Axis for the Proposed Triad"

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1. Lack of Mechanistic Specificity

The manuscript proposes NF-κB as the central axis, but the causal sequence is unclear:

How does atmospheric pressure variation quantitatively influence gut microbiota composition?

What magnitude of pressure variation is physiologically relevant?

How does HIF-1 activation translate into altered bone remodeling under normobaric environmental fluctuations?

Currently, connections are associative rather than mechanistically delineated.

Suggested Improvement

Structure the hypothesis as a stepwise pathway:

Atmospheric pressure ↓

HIF-1α stabilization ↑

Gut permeability modulation

LPS translocation

TLR4 activation

NF-κB activation

RANKL upregulation → Osteoclastogenesis

This would strengthen the biological plausibility.

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2. Atmospheric Pressure vs Hypoxia Confusion

Atmospheric pressure variation is equated with hypoxia signaling via HIF-1. However:

Most daily barometric changes do not significantly alter tissue oxygenation.

HIF-1 activation typically requires substantial hypoxic exposure (e.g., high altitude).

The manuscript does not clarify whether:

The hypothesis applies to chronic high-altitude exposure?

Acute barometric fluctuations?

Extreme environments

Declarations

Potential competing interests: No potential competing interests to declare.