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

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Potential competing interests: No potential competing interests to declare.

Reviewer's comments on the manuscript "Gut Microbiome, Bone Health, and Air Pressure: Construing the Axis for the Proposed Triad"

This manuscript delves into the intriguing relationship between the gut microbiome, bone health, and atmospheric pressure, proposing a complex interplay that forms a triad. The abstract intriguingly highlights the impact of atmospheric pressure on joint pain and introduces the concept of a signaling triad involving the Gut, Bone, and the environment.

The introduction provides a comprehensive foundation, emphasizing the influence of genetics and environment on phenotype. The analogy of emesis effectively conveys the interconnectedness of signaling cascades in maintaining homeostasis. The recognition of gut microbiota as a dynamic organ and the multifaceted functions of bones sets the stage for understanding the proposed triad.

The section on bone formation and resorption is well-structured, using a sculpture analogy to explain the roles of osteoblasts and osteoclasts. However, simplifying technical terms might enhance accessibility for a broader audience. The overview of signaling pathways involved in osteoporosis is comprehensive, offering valuable insights into the regulatory mechanisms.

The discussion on the gut microbiota provides a fascinating blend of ancient wisdom and modern scientific insights. The connection between dysbiosis and skeletal joint morbidities adds depth to the narrative. However, some microbiological terms, such as Short Chain Fatty Acids (SCFAs), could benefit from further clarification for non-experts.

The inclusion of atmospheric pressure as an environmental component is innovative, and the discussion on the HIF-1 signaling pathway establishes a potential link between air pressure, inflammation, and bone homeostasis. Nevertheless, the manuscript could benefit from a more thorough exploration of the long-term effects of constant atmospheric pressure on bones and the hindgut.

The discussion section, centering on NF-κB as a pivotal player in the triad, provides a cohesive narrative. While recognizing other proteins involved, the emphasis on NF-κB might oversimplify the intricate interactions within the proposed triad.

Critical Comments and Suggestions:

1. Technical Language: Certain technical terms, particularly in microbiology, could be simplified to enhance the manuscript's accessibility for readers outside the specific field.
2. Long-term Effects: The manuscript could delve deeper into the long-term effects of constant atmospheric pressure on bones and the hindgut, providing a more comprehensive understanding of this novel aspect.
3. Practical Implications: Elaborating on the potential practical implications of the proposed triad, such as preventive measures or therapeutic interventions, could make the research more applicable to real-world scenarios.
4. Conclusion Clarity: The concluding statements could be refined for greater clarity, summarizing key insights and highlighting specific avenues for future research.

In summary, the manuscript offers an engaging exploration of the interconnections between the gut microbiome, bone health, and atmospheric pressure. While providing valuable insights, addressing the suggested improvements could enhance the manuscript's accessibility and applicability, contributing to the field's understanding of this intriguing triad.