

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.

The paper proposes a signaling triad between the gut microbiome, bone health, and air pressure as environmental factors that influence human physiology and disease.

It reviews signaling pathways and molecules like HIF, RANKL, OPG that are involved in communication between the gut, bone and response to atmospheric pressure changes.

The paper discusses how changes in atmospheric pressure can influence the gut microbiome composition through HIF signaling and metabolism of gases. This in turn can impact bone homeostasis.

NF-κB is proposed as a key signaling molecule that lies at the intersection of all three components - gut, bone and environment/air pressure.

The triad framework provides a novel perspective to study how environmental, microbial and host factors interact to influence phenotypes related to bone and joint health.

Questions for Authors:

1. What are the key experiments proposed to validate specific interactions (e.g. between HIF and gut microbes) proposed in the triad?
2. How can confounding factors like diet, genetics and other environmental exposures be accounted for?
3. Have any parts of the triad framework been tested experimentally? If not, what is a realistic timeline to generate pilot data?

The paper proposes a novel conceptual framework but would benefit from additional details on experimental validation and addressing of alternative explanations. The triad perspective can stimulate new research if followed up with targeted studies.

