

Peer Review

Review of: "Selection of Bone-Targeting Peptides for Therapeutic Intervention: An In Vivo Evaluation and Comparison Study"

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1. In the introduction part, you are talking about **osteoarthritis** but **it's not a bone disease and not mineralized, no need HA.**
2. For the Mat and Methods section:
 - Tissue imaging and ROI analysis. What is the name of the software? You just give the name of the tool.
 - *Ex vivo* analysis of peptide distribution following intravenous injection in healthy rats: I think it's more *in vivo* than *ex vivo* because the injection was done when the animal was alive and under anesthesia.
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 - Grammar errors:

Section 2.3

"backgro und" > "background"

"dataexport" > "data export"

Section 2.5

"definedto encompass" > "defined to encompass"

"tissue areafor analysis" > "tissue area for analysis"

Section 2.6

"on leg was shaved" > "on the leg was shaved"

"defect areareveals" > "defect area reveals"

"distributionof peptide" > "distribution of peptide"

Section 2.7

"Milwauke e, USA" > "Milwaukee, USA"

"peptidesin" > "peptides in"

Section 3.3

"sof t tissues" > "soft tissues"

"f luorescence intensities" > "fluorescence intensities"

Section 3.6

"metaphys is" > "metaphysis"

"ROI's" > "ROIs" (no apostrophe needed in plural acronyms)

Discussion

"boneby weight" > "bone by weight"

"sur face" > "surface"

"OIM mouse model [...] of peptidesin" > "peptides in"

"its' suitability" > "its suitability" ("its'" is incorrect; the possessive is "its")

"tibiaand" > "tibia and"

"for s tability" > "for stability"

Limitations / Areas for Improvement

1. Single time point analysis (1h post-injection): The study evaluates peptide biodistribution at a single time point (1 hour), which does not capture: Binding and dissociation kinetics, Retention duration in bone, Potential peptide clearance or redistribution over time.

Suggestion: Include additional time points (e.g., 24h, 48h) to assess the dynamics and long-term retention of peptide–bone interactions.

2. **Lack of in vivo specificity controls:**The study demonstrates peptide accumulation in bone but does not clearly distinguish: Whether peptides bind **specifically to HA** in vivo, Or accumulate **passively** due to perfusion, vascularity, or inflammation.

Suggestion: Add **scrambled peptide sequences** or peptides with reduced HA-binding motifs to test sequence specificity.

3. **No assessment of peptide stability or cellular uptake:**The study focuses on biodistribution but does not address: Whether peptides remain **intact** in vivo.

Suggestion: Complement with peptide stability assays (e.g., HPLC post-recovery), or perform cellular co-localization studies.

Declarations

Potential competing interests: No potential competing interests to declare.