Bone Targeting Nanocarrier-Assisted Delivery of Adenosine to Treat Osteoporotic Bone Loss

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Purpose: Extracellular adenosine has been shown to play a key role in maintaining bone health and could potentially be used to treat bone loss. However, systemic administration of exogenous adenosine to treat bone disorders remains a challenge due to the ubiquitous presence of adenosine receptors in different organs and the short half-life of adenosine in circulation. Toward this, we have developed a bone-targeting nanocarrier and determined its potential for systemic administration of adenosine.

Methods: The nanocarrier, synthesized via emulsion suspension photopolymerization, is comprised of hyaluronic acid (HA) copolymerized with phenylboronic acid (PBA), a moiety that can form reversible bonds with adenosine. The bone binding affinity of the nanocarrier was achieved by alendronate (Aln) conjugation.

Results: Nanocarriers functionalized with the alendronate (Aln-NC) showed a 45% higher accumulation in the mice vertebrae in vivo compared to those lacking alendronate molecules (NCs). Systemic administration of adenosine via bone-targeting nanocarriers (Aln-NC) showed attenuated bone loss in ovariectomized (OVX) mice. Furthermore, bone tissue of mice treated with adenosine-loaded Aln-NC displayed trabecular bone characteristics comparable to healthy controls as shown by micro-CT, histochemical staining, bone labeling, and mechanical strength.

Conclusion: We demonstrate that a bone-targeting nanocarrier can be used towards systemic administration of adenosine. Further, this mechanism is shown to prevent bone loss in an osteoporotic model and promote new bone formation and improved bone mechanical strength. These results suggest that systemic administration of exogenous adenosine via a bone-targeting nanocarrier could be a potential therapeutic strategy to treat osteoporosis and promote bone recovery.

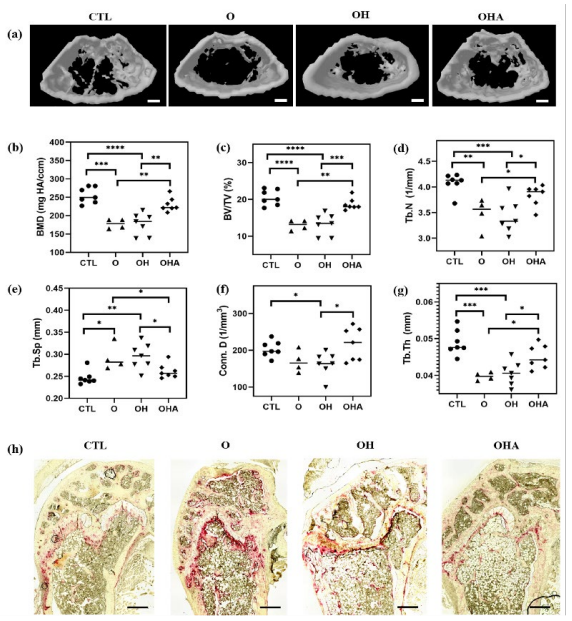

Figure. 1. Adenosine-encapsulated nanocarriers attenuate femoral bone loss in OVX mice. Administration of Aln-NC containing adenosine (OHA) and Aln-NC without adenosine (OH) in OVX mice for 8 weeks. (a) Reconstructed microcomputed tomography (μCT) images of distal femur (Scale bar: 500 μm). Quantification of μCT images: (b) bone mineral density (BMD); (c) bone volume (BV/TV); (d) trabecular number (Tb.N); (e) trabecular spacing (Tb. Sp); (f) connectivity density (Conn. D) (g) trabecular thickness (Tb. Th). (h) Tartrate-resistant acid phosphatase (TRAP; red) staining of the distal femur (Scale bars: 50 μm). *p<0.05, **p<0.01, ***p<0.001.

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