Research Highlight

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Subject Category: Metabolic bone disease

Bone: Homing MSCs to the surface of bones

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Attempts to enhance bone formation using systemic infusions of mesenchymal stem cells (MSCs) have been hampered because the MSCs fail to reach the bone surface and so cannot develop into bone-forming osteoblasts. New research, published in *Nature Medicine*, describes a method for successfully targeting MSCs to bone, which might enable this hurdle to be surmounted.

Min Guan, Wei Yao and colleagues based their approach on previous research showing that overexpression of integrin α4 in MSCs increased the ability of these cells to home to bone. They generated a high-affinity peptidomimetic ligand specifically against activated integrin α4β1 (LLP2A) and linked it to bisphosphonate alendronate (LLP2A-Ale) to increase the affinity of the compound to bone.

First, the authors assessed the *in vitro* effects of LLP2A-Ale on cultured primary bone marrow stromal cells (BMSCs). More cells differentiated into

osteoblasts and the migratory capacity of these cells was higher when BMSCs were cultured with LLP2A-Ale rather than with medium alone.

Next, Guan *et al*. performed a xenotransplantation study in which they injected human MCSs (huMSCs) with or without LLP2A-Ale into NOD/SCID/MPSVII mice. HuMSCs were found adjacent to bone surfaces in mice treated with LLP2A-Ale and huMSCs, but not in mice injected with huMSCs alone—both at 1 day and 3 weeks after treatment—indicating that LLP2A-Ale treatment encouraged MSCs to travel to, and be retained by, bone.

Finally, the authors investigated the effects of injecting LLP2A-Ale without MSCs into immunocompetent or osteopenic mice. LLP2A-Ale treatment resulted in increased trabecular bone volume and bone mass in immunocompetent mice than did placebo, alendronate or LLP2A alone. In addition, LLP2A-Ale prevented age-related bone loss in C57BL/6 mice and also partially reversed bone loss in mice with osteopenia caused by estrogen deficiency in comparison to mice receiving placebo, alendronate or LLP2A alone.

So, LLP2A-Ale could be used to direct MSCs to bone surfaces and can boost bone formation, an approach that has potential therapeutic applications in osteoporosis and bone fracture.

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References and links

ORIGINAL RESEARCH PAPER

Guan, M. *et al*. Directing mesenchymal stem cells to bone to augment bone formation and increase bone mass. *Nat. Med*. doi: 10.1038/nm.2665
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