

# OSTEOSCOOP

News on current events in osteoporosis and rheumatology

## Stem cells: a promising target to enhance bone regeneration

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**M**esenchymal stem/progenitor cells (MSCs) can differentiate into adipocytes, muscle cells, osteoblasts, or cartilage and possess potential for tissue repair in patients with osteoporosis, diseased joints, and myocardial infarction. Many groups have investigated strategies involving the infusion of MSCs for the purpose of regenerative therapy; however, problems concerning MSC homing to diseased sites and the use of allogeneic MSCs have limited this approach. Therefore, the ability to use pharmacological agents to induce the differentiation of resident MSCs toward a certain lineage in vivo is an important therapeutic goal. In a recent study [1], the authors report that bortezomib, a clinically available proteasome inhibitor active against myeloma, induces the differentiation of MSCs into osteoblasts, resulting in new bone formation.

These results were observed when MSCs were implanted subcutaneously in mice or were used to treat a mouse model of postmenopausal bone loss. Others groups have reported that immunomodulatory drugs (eg, thalidomide and lenalidomide), which are active against myeloma, also block the activity of bone-resorbing osteoclasts.

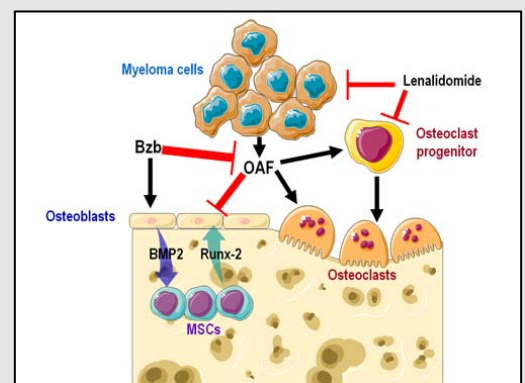
These results reflect the utility of targeting endogenous MSCs for the purpose of tissue repair and suggest that combining different classes of agents that are antineoplastic and also inhibit bone destruction and increase bone formation should be very beneficial for myeloma patients suffering from severe bone disease.

1. Mukherjee S et al. *J Clin Invest.* 2008;118:491–504.

### Stem cells: a promising target to enhance bone regeneration

Myeloma cells produce or induce osteoclast-activating factors (OAFs), which increase osteoclast formation as well as produce osteoblast-inhibiting factors, which block bone formation. The proteasome inhibitor bortezomib (Bzb) can induce bone formation by increasing BMP-2 production by osteoblasts, which in turn increases Runx-2 levels, which induces MSCs to differentiate into osteoblasts and enhance bone regeneration in mice. In addition, Bzb and lenalidomide can inhibit osteoclast formation in addition to blocking the growth of myeloma cells.

These results suggest that combination therapy that includes Bzb with lenalidomide or thalidomide may both enhance the antineoplastic effects of either agent and increase bone formation by stimulating osteoblast activity and inhibiting osteoclastic bone destruction.



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