

## Cell-to-cell contact is critical for the survival of hematopoietic progenitor cells on osteoblasts

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### Abstract

Osteoblasts constitute part of the stromal cell support system in marrow for hematopoiesis, however little is known as to how they interact with hematopoietic stem cells (HSCs). In vitro studies have demonstrated that the survival of HSCs in co-culture with osteoblasts requires intimate cell-to-cell contact. This suggests that the osteoblast-derived factor(s) that supports stem cell activities are produced in very small quantities, are rapidly turned over, may be membrane-anchored and/or require the engagement of cell–cell adhesion molecules that are yet to be determined. In the present report we found that the survival of hematopoietic progenitor cells on osteoblasts is dependent upon the engagement of VLA-4 ( $\alpha_4\beta_1$ ) and VLA-5 ( $\alpha_5\beta_1$ ) receptors using function blocking antibodies. Cell-to-cell contact is required to support progenitor activity, but can be replaced if receptor–ligand engagement of the VLA-4 and LFA-1 complexes is provided through the use of recombinant ligands (fibronectin, ICAM-1, VCAM-1). Moreover, once these receptors were engaged, conditioned medium derived from HSCs grown on osteoblast ligands supported significantly greater hematopoietic progenitors in vitro than did osteoblast-conditioned or HSC-conditioned medium alone. While the molecules present in the co-cultured medium remain to be identified, the data suggest that hematopoietic cells cooperate with osteoblasts to assemble the various marrow microenvironments by directing the synthesis of osteoblast-derived cytokines to improve HSC survival. © 2005 Elsevier Ltd. All rights reserved.

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