

CELL BIOLOGY: ABSTRACTS

Direct Identification of Osteoblast Progenitor Cells in Paget's Disease

C. J. JOYNER, S. BORD, R. SMITH, N. A. ATHANASOU, and J. T. TRIFFITT

MRC Bone Research Laboratory and Nuffield Department of Orthopaedic Surgery, University of Oxford, Oxford, UK

We have generated a monoclonal antibody, HOP-26, which has been shown to react with osteoprogenitor cells. In vitro studies demonstrate that, within the marrow stromal fibroblastic cell lineages, the antigen is restricted to very primitive cells, including the fibroblastic colony forming units and their early progeny. Recent observations indicate that the antibody shows additional reactivity with a subpopulation of mast cells.

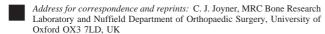
Our general objective is to use immunohistochemistry with specific antibodies to detect osteoprogenitor cells in skeletal tissue from patients with various metabolic bone diseases. This is especially relevant in those conditions where osteoblast numbers or activity are likely to be markedly increased, such as Paget's disease of bone, in which there is increased and disordered bone turnover. In this condition, osteoblast and osteoclast numbers and activities are increased. There is also evidence that the stromal fibroblastic cells in the marrow microenvironment play a role in the increased generation of osteoclasts.

In the present study, sections of paraffin-embedded pagetic and normal bone tissue were immunostained by using HOP-26 and the numbers and the locations of antibody-reactive cells in the two tissues were compared. The number of HOP-26-positive cells in the pagetic tissue was significantly greater than in normal tissue, and intensely reactive cells were often situated centrally within the intertrabecular marrow fibrous tissue.

The exact nature of the antibody-reactive cells present within sections of pagetic bone tissue and their role in the etiology of the disease is not established. However, increased numbers of osteoprogenitor cells might contribute to the aberrant bone turnover seen in Paget's disease, both by increasing the rate of osteoblast generation and indirectly by stimulating osteoclastic bone resorption.

Reference

 C. J. Joyner, Bennett, A., and Triffitt, J. T. Identification and enrichment of human osteoprogenitor cells by using differentiation stage-specific monoclonal antibodies. Bone 21:1-6; 1997.



PII S8756-3282(99)00046-0

Human Osteoblasts Support Human Monocyte-osteoclast Differentiation: Evidence of Prostaglandin Stimulation

S. D. NEALE, A. SABOKBAR, and N. A. ATHANASOU Nuffield Department of Orthopaedic Surgery, University of Oxford, Oxford, UK

Paget's disease of bone is characterized by increased bone turnover. This is often associated with an increase in osteoclast numbers and an increase in osteoclast activity. Osteoclasts are hematopoietic in origin, and mononuclear osteoclast precursors are known to circulate in the monocyte fraction of peripheral blood. In pathological bone-resorbing conditions, such as Paget's disease, we developed a coculture system in which human osteoblast-like cells were used to support the generation in vitro of human osteoclasts from circulating mononuclear precursors.

Human osteoblast-like cells (positive for alkaline phosphates and capable of matrix mineralization) were derived from cell outgrowths of trabecular bone and cultured on cortical bone slices and glass coverslips to which human monocyte preparations were added. Cultures were maintained for up to 28 days in the presence of 10^{-8} mol/L dexamethasone and 10^{-6} mol/L prostaglandin E_2 (PGE₂).

No evidence of osteoclast differentiation was observed after 24 h in coculture, but in 21 and 28 day cocultures, large numbers of vitronectin receptor-positive multinucleated cells capable of extensive lacunar bone resorption were identified. In contrast to rodent osteoblast/human monocyte cocultures, the exogenous addition of macrophage colony stimulating factor (M-CSF) and 1,25-dihydroxyvitamin D_3 [1,25-(OH)₂ D_3] was not found to be essential for osteoclast differentiation when PGE, was added to cocultures.

In conclusion, we have demonstrated that, in the presence of human osteoblast-like cells, circulating monocytes can differentiate into bone-resorbing osteoclasts. This human osteoblast/human monocyte coculture system, which shows striking differences in the requirements for osteoclast formation from rodent systems, should provide a useful model for the analysis of the cellular and humoral influences controlling human osteoclast formation in disease states such as Paget's disease of bone.

Address for correspondence and reprints: Dr. S. D. Neale, Nuffield Department of Orthopaedic Surgery, University of Oxford, Oxford OX3 7LD, UK.

PII S8756-3282(99)00046-0