Temporal expression of PDGF receptors and PDGF regulatory effects on osteoblastic cells in mineralizing cultures.

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Abstract

Platelet-derived growth factor (PDGF) is mitogenic and chemotactic for osteoblastic cells in vitro. It is expressed during osseous wound healing and stimulates formation of new bone in vivo. PDGF stimulates cells by binding to specific cell surface receptors. The purpose of this study was to examine the effects of PDGF on osteoblastic proliferation and differentiation in long-term mineralizing cultures. Utilizing Northern blot analysis, we found that continuous PDGF treatment increased histone expression, indicative of enhanced proliferation, but suppressed osteoblast differentiation, demonstrated by inhibition of alkaline phosphatase, type I collagen, and osteocalcin expression. The inhibitory effect of PDGF on the differentiated function of osteoblasts was further established by findings that PDGF significantly inhibited nodule formation. The expression of PDGF receptors varied at different stages of culture. PDGF receptor mRNA expression increased when the cells had achieved a mature phenotype, during the stage of matrix maturation, and then decreased. However, as demonstrated by thymidine incorporation assays, the capacity of PDGF to stimulate DNA synthesis actually decreased during osteoblast maturation, as receptor expression increased. To investigate this apparent contradiction, tyrosyl phosphorylation and immunoblot assays were performed to assess changes in PDGF activation of their cognate receptors. The pattern of PDGF-induced tyrosyl phosphorylation remained relatively constant. This suggests that the diminished mitogenic activity of PDGF that occurs after osteoblast differentiation is regulated at a postreceptor level.