AAO Foundation Award Final Report

Principal Investigator	Carol Pilbeam
Co-Investigator	Kristen Walters
Secondary Investigators	
Award Type	Biomedical Research Award
Project Title	Role of Collagenase in Osteoblastic Migration on Collagen
Project Year	2001
Institution	University of Connecticut Health Center
Summary/Abstract	Osteoblastic migration and proliferation in response to growth factors are essential for skeletal development, bone remodeling, and fracture repair, as well as pathologic processes, such as metastasis. We studied migration in response to platelet-derived growth factor (PDGF, 10 ng/ml) in a wounding model. PDGF stimulated a twofold increase in migration of osteoblastic MC3T3-E1 cells and murine calvarial osteoblasts over 24-48 h. PDGF also stimulated a tenfold increase in 3H-thymidine (3H-TdR) incorporation in MC3T3-E1 cells. Migration and DNA replication, as measured by BrdU incorporation, could be stimulated in the same cell. Blocking DNA replication with aphidicolin did not reduce the distance migrated. To examine the role of mitogen-activated protein (MAP) kinases in migration and proliferation, we used specific inhibitors of p38 MAP kinase, extracellular signal regulated kinase (ERK), and c-Jun N-terminal kinase (JNK). For these signaling studies, proliferation was measured by carboxyfluorescein diacetate succinimidyl ester (CFSE) using flow cytometry. Inhibition of the p38 MAP kinase pathway by SB203580 and SB202190 blocked PDGF-stimulated migration but had no effect on proliferation. Inhibition of the ERK pathway by PD98059 and U0126 inhibited proliferation but did not inhibit migration. Inhibition of JNK activity by SP600125 inhibited both migration and proliferation. Hence, the stimulation of migration and proliferation by PDGF occurred by both overlapping and independent pathways. The JNK pathway was involved in both migration and proliferation, whereas the p38 pathway was predominantly involved in migration and the ERK pathway predominantly involved in proliferation. J Cell Biochem. 2004 Nov 1;93(4):741-52.