

Collagen suppresses the proliferative phenotype of allylamine-injured vascular smooth muscle cells

Emily Wilson^b, Alan R. Parrish^a, Christopher M. Bral^a, E. Spencer Williams^{a,b},
Kenneth S. Ramos^{a,b,*}

^a Department of Veterinary Physiology and Pharmacology, Texas A&M University, College Station, TX 77843-4466, USA

^b Department of Medical Physiology, Texas A&M University System Health Science Center, Texas A&M University, College Station, TX 77843-1114, USA

Abstract

Repeated cycles of oxidative injury by allylamine induce proliferative rat vascular smooth muscle cell (vSMC) phenotypes characterized by enhanced secretion of osteopontin (OPN). The present study was designed to evaluate the role of extracellular matrix (ECM) interactions in the induction of proliferative phenotypes in this model of oxidant injury. Because OPN is involved in ECM/integrin signaling, and may participate in proliferative control, the proliferation profiles of control and allylamine vSMCs seeded on different matrices were compared. Allylamine cells exhibited a proliferative advantage over controls when seeded on plastic, Pronectin, or fibronectin, but not type I collagen. Addition of GRGDS peptide selectively enhanced [³H]-thymidine incorporation in allylamine vSMCs, while anti-OPN antibodies nullified their proliferative advantage. Allylamine cells exhibited altered expression of $\alpha 1$, $\alpha 5$ and $\beta 3$ integrin subunits and enhanced downstream integrin-coupled increases in focal adhesion kinase, AP-1 and NF- κ B binding activity. Inhibition of NF- κ B by pyrrolidine dithiocarbamate selectively compromised proliferation of allylamine vSMCs, while seeding on a non-permissive collagen matrix ablated enhancement of NF- κ B inducibility. These results implicate ECM interactions in the deregulation of vSMC proliferation following repeated cycles of oxidative chemical injury.

Keywords: Osteopontin; Vascular smooth muscle cell; NF- κ B