

Role of CD44 in the reaction of vascular smooth muscle cells to arterial wall injury.

Jain M, He Q, Lee WS, Kashiki S, Foster LC, Tsai JC, Lee ME, and Haber E

Abstract

CD44, the principal receptor for hyaluronic acid, is a widely distributed cell surface proteoglycan involved in cellular activation, proliferation, and migration. These processes are also central to the vascular smooth muscle cell's response to arterial wall injury. We evaluated the expression of CD44 and its isoform, CD44-V6, on vascular smooth muscle cells in vitro and in vivo and assessed the role of CD44 in DNA synthesis. Cultured vascular smooth muscle cells expressed CD44 and CD44-V6 at levels equal to or higher than those of the beta 1 and beta 2 integrins. In a rat carotid artery balloon injury model, CD44 and CD44-V6 mRNAs were unregulated in vascular smooth muscle cells after injury, and CD44 protein expression was greatest at the luminal edge of the growing neointima. CD44-expressing smooth muscle cells proliferated actively, and hyaluronic acid expression increased after injury in a temporal pattern similar to that of CD44. Through binding to hyaluronic acid, CD44 augmented DNA synthesis in cultured human and rat smooth muscle cells by 48 +/- 7.8 and 100 +/- 12.5%, respectively, an effect inhibited by an anti-CD44 antibody that blocked hyaluronate binding. These observations support a role for CD44 in the reaction of vascular smooth muscle cells to arterial wall injury..