
BACKGROUND: Matrix metalloproteinases (MMPs) are thought to promote progression of atherosclerosis and cardiovascular complications such as plaque rupture. It has been suggested that, on tumor cells, the extracellular MMP inducer (EMMPRIN) is involved in MMP synthesis by as yet unknown mechanisms. On cardiovascular cells, regulation of EMMPRIN in vivo or any functional relevance for MMP induction in vitro has not yet been studied. Thus, we studied EMMPRIN expression on monocytes in acute myocardial infarction (MI) and its potential relevance for MMP activation.

METHODS AND RESULTS: In 20 patients with acute MI, surface expression of EMMPRIN was significantly enhanced on monocytes compared with in 20 patients with chronic stable angina. EMMPRIN upregulation was associated with increased expression of the membrane type 1 MMP (MT1-MMP) on monocytes (flow cytometry) as well as MMP-9 activity (gelatin zymography) in the plasma. At 6 months after successful revascularization, EMMPRIN, MT1-MMP, and MMP-9 had normalized. The secretion of MMP-9 by monocytes was induced by monocyte adhesion to immobilized recombinant EMMPRIN or to EMMPRIN-transfected Chinese...
hamster ovary cells. Moreover, adherent EMMPRIN-transfected monocytic cells stimulated MMP-2 activity of human vascular smooth muscle cells. Gene silencing of EMMPRIN by small-interfering RNA hindered lipopolysaccharide-induced monocyte secretion of MMP-9, indicating a predominant role of EMMPRIN in MMP-9 induction. CONCLUSIONS: EMMPRIN and MT1-MMP are upregulated on monocytes in acute MI. During cellular interactions, EMMPRIN stimulates MMP-9 in monocytes and MMP-2 in smooth muscle cells, indicating that EMMPRIN may display a key regulatory role for MMP activity in cardiovascular pathologies.