Synopsis of Original Research Paper

Molecular biological study on the control of skin sclerosis by growth factors and adhesion molecule

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Purposes: We investigated how to control skin sclerosis and softness. Systemic scleroderma is a model for sclerotic or aging skin. We indicated that TGF-β, PDGF-AA and PDGF α receptor interaction might play an important role in skin sclerosis. Recently, it has been clear that many of the proteoglycans behave as modulators of growth factors binding in scleroderma and normal fibroblasts. We examine the role of proteoglycans for binding to growth factors on scleroderma fibroblasts in this paper. The hyaluronate receptor (CD44) molecule is a multifunctional cell surface protein involved in T cell activation, monocyte cytokine release, fibroblast locomotion, and lymphocyte binding to high endothelial venules. There is protein kinase C -like kinase domain in intracellular portion of CD44, and intra-molecular serine/threonine residue may be phospholylated to mediate signal transduction. Materials and methods: Effects of heparitinase digestion on TGF-β and bFGF binding to their receptors were studied in vitro using ligand binding assay, ^{3}H-thymidine uptake and affinity lavel in scleroderma and control fibroblasts. To study the roles of CD44 molecules play in systemic sclerosis (SSc) , we measured expression and phospholylation of CD44 in lymphocytes and fibroblasts from SSc patients and healthy controls, using immunoprecipitation method with ^{32}P and anti-CD44 antibody. Results: TGF-β binds to 200-300kD betaglycan (type III receptor of TGF-β, type I and II receptor in scleroderma fibroblasts more than in control fibroblasts. After heparitinase digestion betaglycan is degraded to 110kD core protein of betaglycan and TGF-β does not bind to type I nor II receptor. bFGF binds to 130kD receptor in scleroderma fibroblasts more than in control fibroblasts. After digestion bFGF bind to no receptor. CD44 was expressed and phospholylated on many lymphocytes and fibroblasts. Furthermore, lymphocytes from SSc patients contained more CD44 or more phospholylated than cells from healthy control. Immunohistochemically, CD44 was expressed on the cells. Conclusions: Obtained data suggest that heparan sulfate proteoglycans are growth factor receptors and affect storage, release and protection against degradation of growth factors. It was suggested that multifunctionality of TGF-β express through heparan sulfate proteoglycans. In the pathogenesis of SSc, CD44 may play an important role in control of cell locomotion, cell adhesion, cell proliferation, and synthesis of extracellular matrix component.