

P034 FGF-2 induced by IL-1 β through the action of PI3-kinase mediates endothelial mesenchymal transformation

Hyung Taek Lee, EunDuck Kay

University of Southern California, Los Angeles, CA

Our previous work demonstrated that protein factors released from polymorphonuclear leukocytes (PMNs) induced de novo synthesis of FGF-2, which in turn becomes the direct mediator of endothelial mesenchymal transformation in corneal endothelial cells (CECs). We identified the protein factor as IL-1 β using ProteinChip Array technology. Biological activities of IL-1 β were further determined; IL-1 β altered the shape of CECs from polygonal to fibroblastic morphologies in a time- and dose-dependent manner, whereas neutralizing IL-1 β antibody, neutralizing antibody to FGF-2, and LY294001 blocked the action of IL-1 β . IL-1 β greatly increased the levels of FGF-2 mRNA in a time- and dose-dependent manner and it stimulated expression of all isoforms of FGF-2. IL-1 β initially induced nuclear accumulation of FGF-2 and facilitated translocation of FGF-2 to plasma membrane and extracellular matrix. IL-1 β activated PI 3-kinase, the enzyme activity of which was greatly stimulated after a 5-min exposure to IL-1 β . This early and rapid activation of PI 3-kinase greatly enhanced FGF-2 production in CECs; pretreatment with LY294002 hampered the induction activity of IL-1 β . These observations suggest that IL-1 β takes part in endothelial to mesenchymal transformation of CECs through its inductive potential on FGF-2 via the action of PI 3-kinase.