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사구체 혈관내피세포에서 고혈당에 의한 NF-κB 활성화 기전: Syk tyrosine kinase에 의한 IκBα tyrosine기 인산화

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High Glucose-induced NF-κB Activation Occurs Via Tyrosine Phosphorylation of IκBα in Human Glomerular Endothelial Cells: Involvement of Syk Tyrosine Kinase

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Activation of nuclear factor- kB (NF- kB) occurs by dissociation from IkBa after serine or tyrosine phosphorylation of IkBa, but the way of NF- kB activation by high glucose has not been defined. High glucose is known to activate NF- kB via protein kinase C and reactive oxygen species (ROS). In this study, we investigated how high glucose activates NF- kB for CCL2 production in cultured human glomerular endothelial cells. High glucose increased nuclear translocation of p65 and also increased NF- kB DNA binding activity. High glucose- induced NF- kB activation occurred without degradation of IkBa. In agreement with this, there was no increase in serine phosphorylation of IkBa, while tyrosine phosphorylation of IkBa was increased by high glucose. High glucose increased the generation of ROS, whereas both a- lipoic acid and N- acetylcysteine scavenged the ROS and decreased high glucose- induced tyrosine phosphorylation of IkBa, nuclear translocation of p65 and NF- kB DNA binding activity. Protein kinase C pseudosubstrate inhibited high glucose- induced ROS production, tyrosine phosphorylation of IkBa and nuclear translocation of p65. Both BAY 61- 3606, a specific inhibitor of Syk protein- tyrosine kinase, and siRNA directed against Syk inhibited high glucose- induced tyrosine phosphorylation of IkBa as well as p65 nuclear translocation. High glucose increased tyrosine phosphorylation of Syk, while it was inhibited by a- lipoic acid and protein kinase C pseudosubstrate. In summary, high glucose- induced NF- kB activation occurred not by serine phosphorylation of IkBa. Our data suggest that ROS- mediated tyrosine phosphorylation of IkBa is the mechanism for high glucose- induced NF- kB activation and Syk may play a role for tyrosine phosphorylation of IkBa.

Key Words : 고혈당, NF- κB, Syk tyrosine kinase
Glucose, NF- κB, Syk tyrosine kinase