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고포도당하의 혈관간세포에서 peroxiredoxin II에 의한 fibronectin 분비억제

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Peroxiredoxin (Prx) II Prevents High Glucose (HG) Induced Fibronectin (FN) Secretion in Mouse Mesangial Cells

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Introduction : Recently the up-regulation of peroxiredoxin (prx) I in macrophages in response to oxLDL exposure with p38 MAPK activation suggests a dual role of prx both an antioxidant and a regulator of signal transduction. In cultured mesangial cells (MCs), mRNA levels of thiol antioxidant genes including prx VI were significantly increased by HG. This increase may represent an adaptive reaction in HG-induced oxidative stress, which is neutralized by the activation of thiol antioxidant pathway. We investigated a role of prx in MCs in the response of HG to find out as a protector and/or a signal conduit.

Methods : Mouse MCs were transfected with dominant negative (DN) or wild type (WT) DNA and siRNA of prx II exposed to normal (5.6 mM;NG) or high (30 mM;HG) D-glucose for 24 hrs. We checked all MAPKs phosphorylation with cell lysates and FN secretion by conditioned media. Quantitative analysis of protein expressions was assessed by Western blots.

Results : HG-induced FN increase was almost reduced by prx II WT up to that of NG condition. FN secretions, both NG and HG, were significantly increased by the down-regulation of prx II DN or prx II siRNA compared with the empty vector or the scrambled siRNA. HG-induced p38 MAPK phosphorylation was reversed by prx II WT and significantly increased by prx II siRNA. ERK phosphorylation was not activated by HG, but significantly increased by prx II siRNA, suggesting a protective role of prx in MCs. No alteration in JNK phosphorylation by prx II siRNA and WT was observed in both NG and HG.

Conclusion : When compared with macrophages, an initial injury evoker of the atherosclerosis model, prx II, not having a dual action, in MCs suppresses p38 MAPK. We suggest that prx II may protect MCs via p38 MAPK inhibition in the HG-induced oxidative stress.