

혈관내피세포에서 활성산소종 발생 및 세포자멸사에 carbamyated LDL이 미치는 영향

계명대학교 의과대학 생화학교실¹, 산부인과교실², 내과학교실 신장연구소³

문교철¹, 손정남¹, 하은영¹, 신소진¹, 황은아³, 한승엽³, 박성배³, 김현철³

Effect of Carbamylated LDL on ROS and Apoptosis in Human Umbilical Vein Endothelial Cells

Kyocheol Mun¹, Jungnam Son¹, Eunyoung Ha¹, Sojin Shin², Eunah Hwang³
Seungyeup Han³, Sungbae Park³, Hyunchul Kim³

Department of Biochemistry¹, Department of Obstetrics and Gynecology²
Department of Internal Medicine³ Keimyung University School of Medicine,
Keimyung University Kidney Institute

Background: Carbamylation is a post-translational modification, pathophysiological consequences of which remain poorly understood. Very recently, an alternative and dominant mechanism for cyanate formation and protein carbamylation at sites of atherosclerotic plaque was reported. Thus, we investigated the effect and signaling pathway of carbamylated low-density lipoprotein (cLDL) on apoptosis and reactive oxygen species (ROS) generation in human umbilical vein endothelial cells (HUVECs). Methods: Human LDL was carbamylated, copper-oxidized, and characterized. Immunoblot, real-time PCR, and flow cytometric analyses were performed. Intracellular ROS generation was determined. Transfection with small interfering RNA (siRNA) was also performed.

Results: Treatment of cLDL (20 and 100 $\mu\text{g}/\text{mL}$) for 24 h upregulated lectin-like oxidized LDL receptor (LOX-1) in HUVECs. cLDL also increased ROS generation (~ 2 fold increase) and induced apoptosis (5-6 fold increase). Exposure of HUVECs with cLDL (100 $\mu\text{g}/\text{mL}$) attenuated phosphorylation of endothelial nitric oxide synthase (eNOS) and increased phosphorylation of ERK1/2 MAPK. Poly ADP-ribose polymerase (PARP) cleavage and expression of p53 were also increased by cLDL treatment. Treatment of ROS scavenger attenuated PARP cleavage and p53 expression. Inhibition of LOX-1 by siRNA against LOX-1 reversed both cLDL stimulated ROS generations and apoptosis.

Conclusion: These results together suggest that cLDL induces ROS generations as well as apoptosis via LOX-1 mediated pathway in HUVECs and may play a critical role in atherogenesis.

Key Words: 혈관내피세포, 카바밀화 지단백, 세포자멸사
Endothelial cell, Carbamylated LDL, Apoptosis