KSN 2020
FULLY VIRTUAL MEETING

Abstract Type : Poster
Abstract Submission No. : PO-1507

Protein kinase C beta II induces endothelial dysfunction via mitochondrial activation in HUVECs.

Hee Kyoung Joo, Yu Ran Lee, Eun-Ok Lee, Sung Min Kim, Hao Jin, Byeong Hwa Jeon
Department of Physiology, Chungnam National University School of Medicine, Korea, Republic of

Objectives: Protein kinase C (PKC) induces endothelial dysfunction, which is an important pathological factor in cardiovascular diseases. This study aimed to evaluate the role of PKCβII on the endothelial dysfucntion related to mitochondrial activation.

Methods: Here, using adenoviral PKCβII gene transfer and pharmacological inhibitors, the role of PKCβII on the endothelial dysfucntion were investigated in human umbilical vein endothelial cells.

Results: Phorbol 12-myristate 13-acetate (PMA) increased reactive oxygen species (ROS), p66shc phosphorylation, intracellular adhesion molecule-1 and monocyte adhesion which were inhibited by PKCβi (10 nM), a selective inhibitor of PKCβII. PMA increased the phosphorylation of CREB and manganese superoxide dismutase (MnSOD) which were also inhibited by PKCβi. Gene silencing of CREB inhibited PMA-induced MnSOD expression, suggesting CREB plays a key role of MnSOD expression. Gene silencing of PKCβII inhibited PMA-induced mitochondrial ROS, MnSOD, and ICAM-1 expression. On contrast, overexpression of PKCβII using AdPKCβII increased mitochondrial ROS, MnSOD, ICAM-1 and p66shc phosphorylation in cultured endothelial cells. Finally, PKCβII-induced ICAM-1 expression is inhibited by Mito-TEMPO, mitochondrial ROS scavenger, suggesting involvement of mitochondrial ROS in PKC-induced vascular inflammation.

Conclusions: Taken together, it is suggested that PKCβII plays an important role of PMA-induced endothelial dysfunction, and the inhibition of PKCβII-dependent p66shc signaling acts as a therapeutic target for vascular inflammatory diseases.