

## NF- $\kappa$ B Activation of 4-hydroxy Hexenal via p38 MAPK, ERK and JNK Pathway in Cultured Human Kidney Cells

전남대학교 의과대학 내과학교실<sup>1</sup>, 생리학교실<sup>2</sup>

주수연<sup>2</sup> · 배은희<sup>1</sup> · 김인진<sup>2</sup> · 신지혜<sup>2</sup> · 박정우<sup>1</sup> · 마성권<sup>1</sup> · 이종은<sup>2</sup> · 김수완<sup>1</sup>

### NF- $\kappa$ B Activation of 4-hydroxy Hexenal via p38 MAPK, ERK and JNK Pathway in Cultured Human Kidney Cells

Soo Yeon Joo<sup>2</sup>, Eun Hui Bae<sup>1</sup>, In Jin Kim<sup>2</sup>, Ji Hae Shin<sup>2</sup>  
Jeong Woo Park<sup>1</sup>, Seong Kwon Ma<sup>1</sup>, JongUn Lee<sup>2</sup>, Soo Wan Kim<sup>1</sup>

Department of Internal Medicine<sup>1</sup> Chonnam National University Medical School  
Department of Physiology<sup>2</sup> Chonnam National University Medical School

**Background** : Lipid peroxidation and its products such as 4-hydroxy-2-hexenal and 4-hydroxyhexenal (HHE) are known to affect redox balance during aging and other degenerative processes. The present study was aimed to investigate the molecular mechanisms underlying the HHE-induced tubular injury in aging process.

**Methods** : The effect of HHE on nuclear factor- $\kappa$ B (NF- $\kappa$ B) activity and on cell viability was examined using cultured human kidney (HK-2) cells. Intracellular reactive oxygen species (ROS) generation was measured by a fluorescent dye DCF-DA. NF- $\kappa$ B p65 translocation and activation was determined by Western blotting and immunofluorescence microscopy. The protein expression of mitogen activated protein kinase (MAPK), pro-apoptotic Bax, and anti-apoptotic protein Bcl-2 was determined by Western blotting.

**Results** : Incubation with various doses of HHE (2-50  $\mu$ M) for 24 hr caused dose dependent decreases of cell viability. HHE increased the generation of ROS. HHE induced NF- $\kappa$ B activation and translocation via I $\kappa$ B- $\alpha$  degradation. The increase in NF- $\kappa$ B activity was detectable within 1 hr, continued to 4 hr after 10  $\mu$ M HHE stimulation. HHE increased activity of p38 MAPK, extracellular signal regulated kinase (ERK), and c-jun NH2-terminal kinase (JNK), indicating that these kinases are closely involved in NF- $\kappa$ B activation. HHE decreased the expression of Bcl-2, while it increased that of Bax.

**Conclusion** : HHE induced renal tubule cell apoptosis is mediated by the modulation of Bax and Bcl-2 via ROS generation. In HK cell, HHE mediated accumulation of ROS may induce redox sensitive transcription factor, NF- $\kappa$ B, through the activation of p38 MAPK, ERK and JNK.

**Key Words** : HHE, 지질과산화, HK-2 세포, NF- $\kappa$ B

4-hydroxyhexenal, Lipid peroxidation, HK-2 cells, NF- $\kappa$ B