

Attenuating Effect of Angiotensin-(1-7) on Angiotensin II-mediated Reactive Oxygen Species Mediated Injury in Rat Proximal Tubular Epithelial Cells

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Background: Angiotensin-(1-7) (Ang-(1-7)) is associated with vasodilation and nitric oxide synthase stimulation. However, the role of Ang-(1-7) against Ang II induced reactive oxygen species (ROS) is unknown. In this study, we examined the hypothesis that Ang-(1-7) attenuates Ang II-induced ROS mediated injury in rat proximal tubular epithelial cell.

Methods: The normal rat kidney tubular epithelial cells (NRK-52E cell) were cultured, and then stimulated with Ang II (10⁻⁷M) with or without pre-incubation with 10⁻⁷M of Ang-(1-7) and D-Ala⁷-Ang-(1-7) (A779) for 15 min. Intracellular ROS generation was measured using a fluorescent dye, 2',7'-Dichlorodihydrofluorescein diacetate (DCF-DA), by flow cytometry. NF- κ B translocation and activation was determined by Western blotting and ELISA. The protein expression of mitogen activated protein kinase (MAPK) was determined by Western blotting.

Results: Incubation with Ang II for 24hr caused decreases of cell viability, however, Ang-(1-7) pre-incubation recovered cell viability in MTT assay. Ang II at 10⁻⁷M increased the intracellular ROS by 1.7-fold of control. Preincubation with 10⁻⁷M of Ang-(1-7) in addition to Ang II significantly inhibited the Ang II-induced ROS production as the level of control. These effects of Ang-(1-7) were reversed with A779. Ang II induced NF- κ B translocation via I κ B degradation was recovered by Ang-(1-7). Ang II-induced mitogen activated protein kinase signaling activation was also attenuated by Ang-(1-7) in the NRK-52E cells.

Conclusion: In summary, our findings suggest that Ang-(1-7) may attenuate Ang II-stimulated intracellular ROS generation. In addition, we found that Ang-(1-7) attenuated Ang II-induced phosphorylation of MAPK signaling in NRK-52E cells. The ACE2-Ang-(1-7)-Mas receptor axis should be investigated further as a novel target of ROS injury.

Key Words: 안지오펜신 II, 안지오펜신 1-7, 활성산소

Angiotensin-(1-7), Angiotensin II, reactive oxygen species (ROS)