KSN 2020
FULLY VIRTUAL MEETING

Abstract Type : Oral
Abstract Submission No. : OR-1378

Ginseng increases Klotho expression by FoxO3-mediated manganese superoxide dismutase in a mouse model of tacrolimus-induced renal injury

Sheng Cui, Sun Woo Lim, Yoo Jin Shin, Kang Luo, Yi Quan, Eun Jeong Ko, Byung Ha Chung
Department of Internal Medicine-Nephrology, The Catholic University of Korea, China

Objectives: The antioxidant function of Klotho is well-documented as a regulatory factor implicated in countering the aging process. This study investigated whether ginseng upregulates Klotho and its anti-aging signaling in a setting of calcineurin inhibitor-induced oxidative stress. Although tacrolimus treatment reduced Klotho level in the serum and kidney, ginseng treatment was found to reverse the levels.

Methods: Eight-week-old male BALB/c mice were provided 0.01% salt diet and water ad libitum. After 1-week acclimatization, weight-matched mice were randomly sorted into four groups and treated subcutaneously with 1.5 mg/kg/day of Tac or 10 mL/kg/day of vehicle, with or without Korean red ginseng powder for 4 weeks. Route of administration and doses were selected as per earlier reports. Animals were then anaesthetized, and blood samples and tissue specimens were obtained for further analysis.

Results: Tacrolimus-induced oxidative stress was reduced by ginseng treatment, with functional and histological improvements. Effect of ginseng on Klotho-induced manganese superoxide dismutase signaling pathway during tacrolimus treatment in mice revealed that ginseng suppressed phosphatidylinositol 3-kinase/serine-threonine kinase Akt-mediated phosphorylation of forkhead box protein O3a and promoted the binding of forkhead box protein O3a to manganese superoxide dismutase promoter. In the mitochondria, ginseng reduced mitochondrial reactive oxygen species production, mitochondrial membrane potential, and oxygen consumption rate, whereas blocking phosphatidylinositol 3-kinase activity with LY294002 enhanced them.

Conclusions: These findings together suggested that ginseng attenuated tacrolimus-induced oxidative stress via signaling between Klotho and the phosphatidylinositol 3-kinase/serine-threonine kinase Akt/forkhead box protein O3a-related antioxidant pathway.