

Abstract Type : Poster
Presentation No. : PAK 037

TonEBP transcription factor mediates oxidative damages in the kidney in response to ischemia-reperfusion

Eunjin Yoo¹, Mijin Kwon¹, Sunwoo Lim², Sora Yoon¹, Dougu Nam¹, Sooyoun Choi¹, Whaseon Lee¹, Hyugmoo Kwon¹

¹Department of School of Life Science, UNIST, Korea, Republic of

²Department of Transplantation Research Center, The Catholic University of Korea, Seoul St. Mary's Hospital, Korea, Republic of

Objectives: TonEBP transcription factor is a key regulator of inflammatory diseases such as rheumatoid arthritis and atherosclerosis. Since inflammation is involved in the pathophysiology of acute renal failure resulting from ischemia, we aimed to identify the role of TonEBP in ischemia-reperfusion (IR).

Methods: We examined the role of TonEBP using a line of TonEBP haplo-deficient mice after 30 min of bilateral renal ischemia followed by reperfusion for 24 h. Renal epithelial cell line (HK-2) was used for in vitro experiments in response to hypoxia, ATP depletion, and hydrogen peroxide with siRNA-mediated knockdown of TonEBP.

Results: In the TonEBP haplo-deficient animals, induction of TonEBP expression, oxidative stress, inflammation, cell death, and functional injury in the kidney in response to IR were all reduced. Renal transcriptome analysis revealed that genes in several pathways such as peroxisome and mitochondrial inner membrane were suppressed in response to IR, and the suppression was relieved in the TonEBP deficient animals. Cellular injury and oxidative stress were reproduced in a renal epithelial cell line in response to hypoxia, ATP depletion, or hydrogen peroxide. Knockdown of TonEBP reduced the injury and intracellular reactive oxygen species in correlation with increased expression of the suppressed genes in the kidney after IR.

Conclusions: These results indicate that TonEBP mediates oxidative damages in the kidney by suppressing genes involved in cellular metabolism. Hence, TonEBP may potentially be a critical target for prevention of acute kidney injury.