Abstract Type : Poster exhibition
Abstract Submission No.: A-0618
Abstract Topic : Basic Research

Identification of the kidney protective effects of STAT3 isoform specific aptamer

Hong-Beom Park[1], Kyu Hong Kim[1], Young Joo Kim[2], Soeun Yun[1], Yong-Chul Kim[5], Jae Wook Lee[4], Dong Ki Kim[5], Dohyun Han[6], Yon-Su Kim[5], Seung Hee Yang[3]
[1]Department of Biomedical Sciences, Seoul National University College of Medicine, Korea, Republic of
[2]Department of Biomedical Research Institute, Seoul National University Hospital, Korea, Republic of
[3]Department of Internal Medicine-Nephrology, National Cancer Center, Korea, Republic of
[4]Department of Internal Medicine-Nephrology, Seoul National University Hospital, Korea, Republic of
[5]Department of Transdisciplinary medicine, Seoul National University Hospital, Korea, Republic of
[6]Department of Kidney Research Institute, Seoul National University College of Medicine, Korea, Republic of

Objectives : STAT3 is a central transcription factor of the JAK-STAT3 signaling pathway related to diverse kidney diseases. STAT3 has two isoforms; STAT3α and STAT3β and its activation and transcriptional activity associated with inflammation and fibrosis in the kidney. Elucidating the role of STAT3β isoform in kidney injury and effects of isoform-targeted therapeutics are expected to be potential strategies for kidney diseases.
Methods : The STAT3β aptamer was selected using the systematic evolution of ligands by exponential enrichment (SELEX). Its intracellular trafficking was analyzed using a Cy3-labeled aptamer. The impact of the STAT3β aptamer on STAT3 expression and roles in kidney tubular cells was evaluated by molecular biological techniques and mass spectrometry-based proteomic profiling.
Results : To select of highly specific aptamer for STAT3β, the SELEX method was utilized with a purified STAT3β protein and an aptamer library. To confirm the intracellular trafficking and binding between STAT3β aptamer to STAT3β, co-localization between STAT3β and the aptamer not only under normal conditions but also in IL-6- or H_2O_2-treated cells were identified. Additionally, the STAT3β aptamer decreases STAT3β and IL-17 mRNA levels in response to IL-6 stimulation. Furthermore, it downregulates p-STAT3 expressions induced by kidney injury but had no effect on STAT3 activity under normal conditions. These finding showed that STAT3β aptamer modulates STAT3 activity and transcription. Specific effects by STAT3β aptamer under kidney injury condition were confirmed by proteomic profiling. Upregulated ITGB3 and MAPK3 related to TNF signaling pathway and NK cell cytotoxicity and downregulated COX7A2 and CAT related to kidney protective effects were restored by STAT3β aptamer.
Conclusions : We developed novel aptamer targeting STAT3β as potential therapeutic target for kidney diseases and proved that STAT3β aptamer can attenuate kidney damage response induced by inflammation and oxidative stress.