

Abstract Type : Poster

Abstract Submission No. : PO-1172

Src kinases inhibition prevents the development of renal tubulointerstitial fibrosis

Debra Dorotea, Hunjoo Ha

Department of Graduate School of Pharmaceutical Sciences, College of Pharmacy, Ewha Womans University, Korea, Republic of

Objectives: Src family kinases (SFKs), a group of non-receptor tyrosine kinases, has been suggested to be activated and plays an important role in the fibrosis development of various tissues. The present study aimed to investigate the effect of KF-1607, a newly synthesized Src kinase inhibitor (SKI) with proposed low toxicity, in preventing the progression of renal interstitial fibrosis.

Methods: Unilateral ureteral obstruction (UUO) surgery was performed in 6-week-old male C57BL/6 mice to induce renal interstitial fibrosis. Either KF-1607 (30 mg/kg, oral) or PP2 (2 mg/kg, intraperitoneal injection), a common experimental SKI, was administered to mice for 7 days, started one day prior to surgery.

Results: UUO induced SFKs expression, including Src, Fyn, and Lyn. SFKs inhibition by KF-1607 restored renal function and prevented the progression of tubular injury, indicated by decreases in albuminuria, urinary KIM-1, and NGAL protein expression in the kidney. Renal interstitial fibrosis was halted in response to KF-1607, as shown by decreases in α -SMA, collagen I and IV protein levels along with reduced Collagen I and Masson's trichrome-positive tubulointerstitial area. KF-1607 also inhibited inflammation in the UUO kidney, exhibited by reductions in F4/80 positive-stained area and protein levels of p-NF κ B and ICAM. Importantly, the observed effect of KF-1607 was similar to PP2.

Conclusions: Altogether, KF-1607 is a promising agent to attenuate the progression of renal interstitial fibrosis.