KSN 2021
FULLY VIRTUAL MEETING
September 02 (Thu) - 05 (Sun)

Oral Communication Abstract
Presentation No. OC9-11 (Abstract Submission No. 2368)

Oral Communications 9 Sep. 4 (Sat), 17:00-19:00

Protective effect of AM095, a lysophosphatidic acid receptor 1 antagonist, on renal aging

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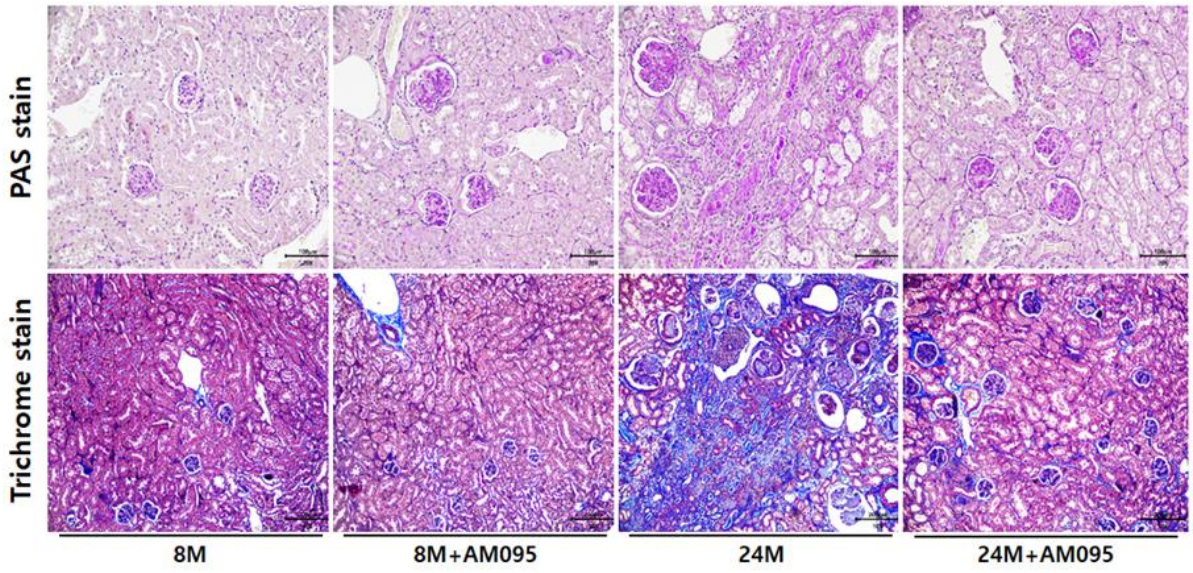
Objectives: Renal aging is related to a higher kidney disease incidence and a higher mortality in the elderly. Lysophosphatidic acid(LPA) is a small ubiquitous lipid that is mainly produced by autotaxin (ATX). It has been reported that LPA receptor 1(LPAR1) is related to various pathological processes. We have demonstrated in our previous study that activated LPAR1 leads to an increased inflammatory cytokine secretion, which promotes renal aging. In this study, we investigated whether pharmacologically blocking LPAR1 with AM095 has a protective effect on renal aging.

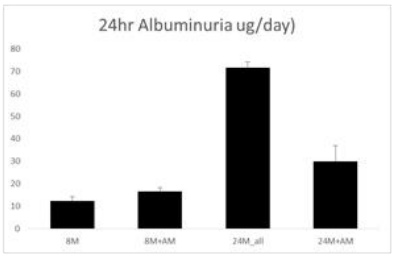
Methods: Male 2- and 18-month-old C57/BL6 mice were divided into four groups as follows: 2-month-old control group (n=8), 2-month-old treatment group (n=8), 18-month-old control group (n=8), and 18-month-old treatment group (n=8). The control groups fed normal chow, while the treatment groups were added AM095 (equivalent to 30mg/kg/day) to the chow for 6 months. Mice were sacrificed at the age of 8 months and 24 months, respectively. We measured renal function, histological change, age-related protein expression, and inflammatory cytokines in the kidneys.

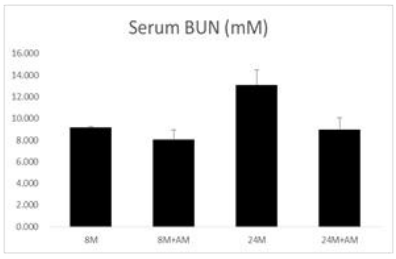
Results: In the previous study, we demonstrated that 24-month-old mice showed increases in albuminuria, serum creatinine, and blood urea nitrogen (BUN), while creatinine clearance decreased with aging. Also fractional mesangial area, and tubulointerstitial fibrosis significantly increased in aged mice compared with the young. In this study, we identified that AM095 treatment reduced albuminuria, serum creatinine, as well as BUN levels, and increased creatinine clearance in 24-month-old mice. Blocking LPAR1 effectively attenuated fractional mesangial area expansion and tubulointerstitial fibrosis in the 24-month-old group. Also, AM095 treated aged mice showed decreased ATX, LPAR1, PI3K/Akt, NF-κB, and inflammatory cytokine expression, contrary to age-matched controls.

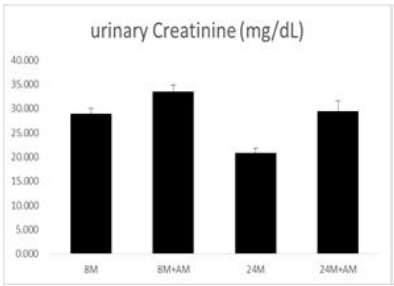
Conclusions: AM095 treatment, in the aged-mice, improved renal function and kidney histological changes. Pharmacological blocking of LPAR1 reduced the production of inflammatory cytokines. LPAR1 antagonist-AM095 is effective in delaying renal aging progress by inhibiting inflammation.

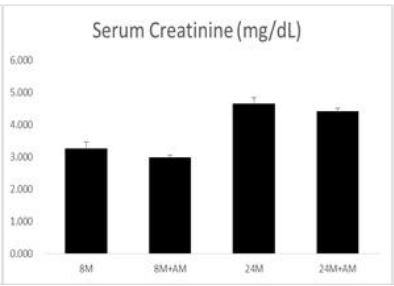
Histological change & renal function

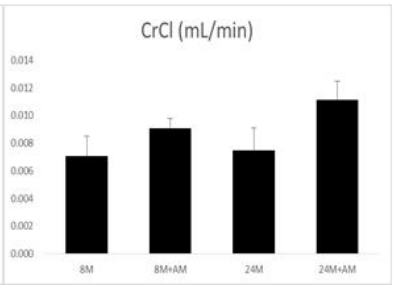












western blot

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