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Agonistic cMet Antibody Prevents Kidney Fibrosis in Acute Kidney Disease Mice Model

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Objectives: We aimed to investigate whether treatment with agonistic cMet antibody can prevent kidney fibrosis in the acute kidney disease mice model.

Methods: Unilateral ischemic-reperfusion injury at left kidney was introduced in 7-week-old male C57BL/6 mice (n = 14) and raised for up to 28 days to induce acute kidney disease model. Agonistic cMet antibody (20 mg/kg) was injected via tail vein at a schedule of day -1, 0, 1, 3, and twice weekly thereafter in the treatment group (n = 7). Vehicle (saline) was injected via tail vein at the same schedule in the control group (n = 7).

Results: Left kidney weight per total body weight was significantly higher in the treatment group ($0.63 \pm 0.21\%$ vs. $0.43 \pm 0.22\%$, $P = 0.022$). In the histopathologic specimen of Masson's trichrome stain, areas of kidney interstitial fibrosis attenuated in the treatment group. In the western-blot analysis, protein abundance of α -smooth muscle actin (22.5% of control, $P = 0.03$), fibronectin (16.4% of control, $P = 0.03$), TGF- β (33.3% of control, $P = 0.05$), total (6.6% of control, $P = 0.03$) and phospho-smad2/3 (10.1% of control, $P = 0.03$) decreased significantly, and protein abundance of e-cadherin increased (912.4% of control, $P = 0.03$) significantly in the treatment group. In the real-time PCR analysis, mRNA expression of α -smooth muscle actin (11.5% of control, $P = 0.006$), collagen 1 (11.6% of control, $P = 0.01$), fibronectin (11.2% of control, $P = 0.01$), TGF- β (21.3% of control, $P = 0.01$) decreased significantly in the treatment group.

Conclusions: Agonistic cMet antibody attenuates kidney fibrosis in the mice unilateral ischemic reperfusion induced acute kidney disease model, and TGF- β and smad2/3 pathway involved in the kidney fibrosis are effectively suppressed in the treatment of agonistic cMet antibody.

Figure 1. Results of Western Blot

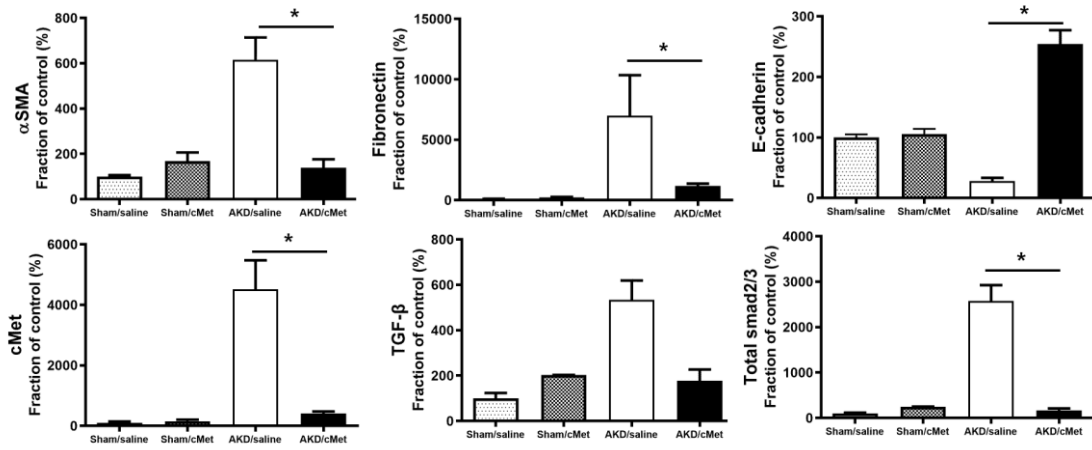


Figure 2. Results of RT-PCR

