

Oleanolic Acid Attenuates Renal Interstitial Fibrosis in Unilateral Ureteral Obstructive Nephropathy by Facilitating Nuclear Translocation of Nrf2

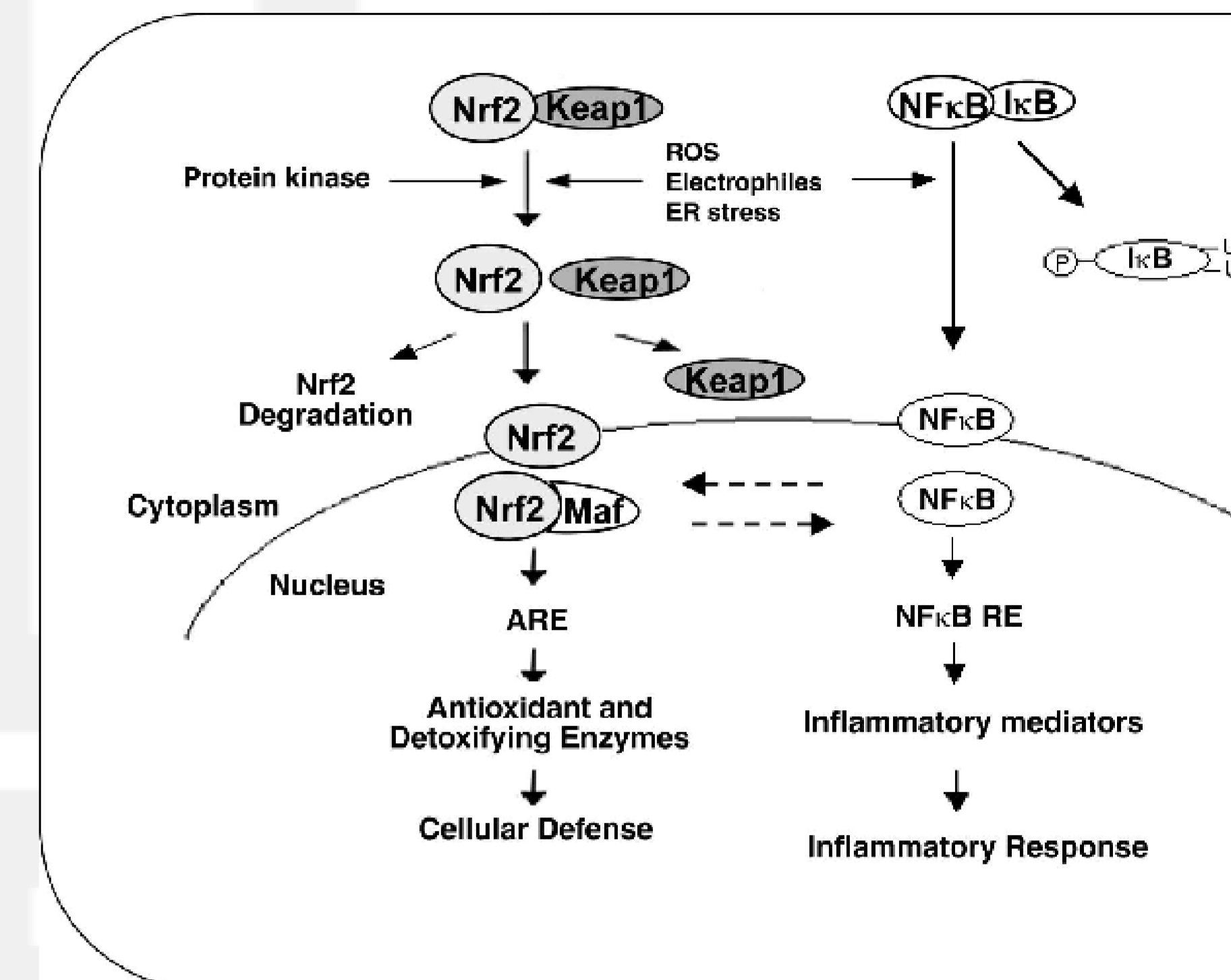
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Background/Aims

Renal interstitial fibrosis is commonly the final pathological process in the progression of renal disease. This is primarily due to oxidative stress, which contributes to renal inflammation and fibrosis. Nuclear factor-erythroid-2-related factor 2 (Nrf2) is known to coordinate induction of genes that encode antioxidant enzymes. We investigated the effects of oleanolic acid, a known Nrf2 activator, on oxidative stress-induced renal inflammation and fibrosis.

[Schematic representation of Nrf2 and NF-κB activation]

Kim HJ and ND Vaziri. Am J Physiol Renal Physiol 2010;298:F662-71

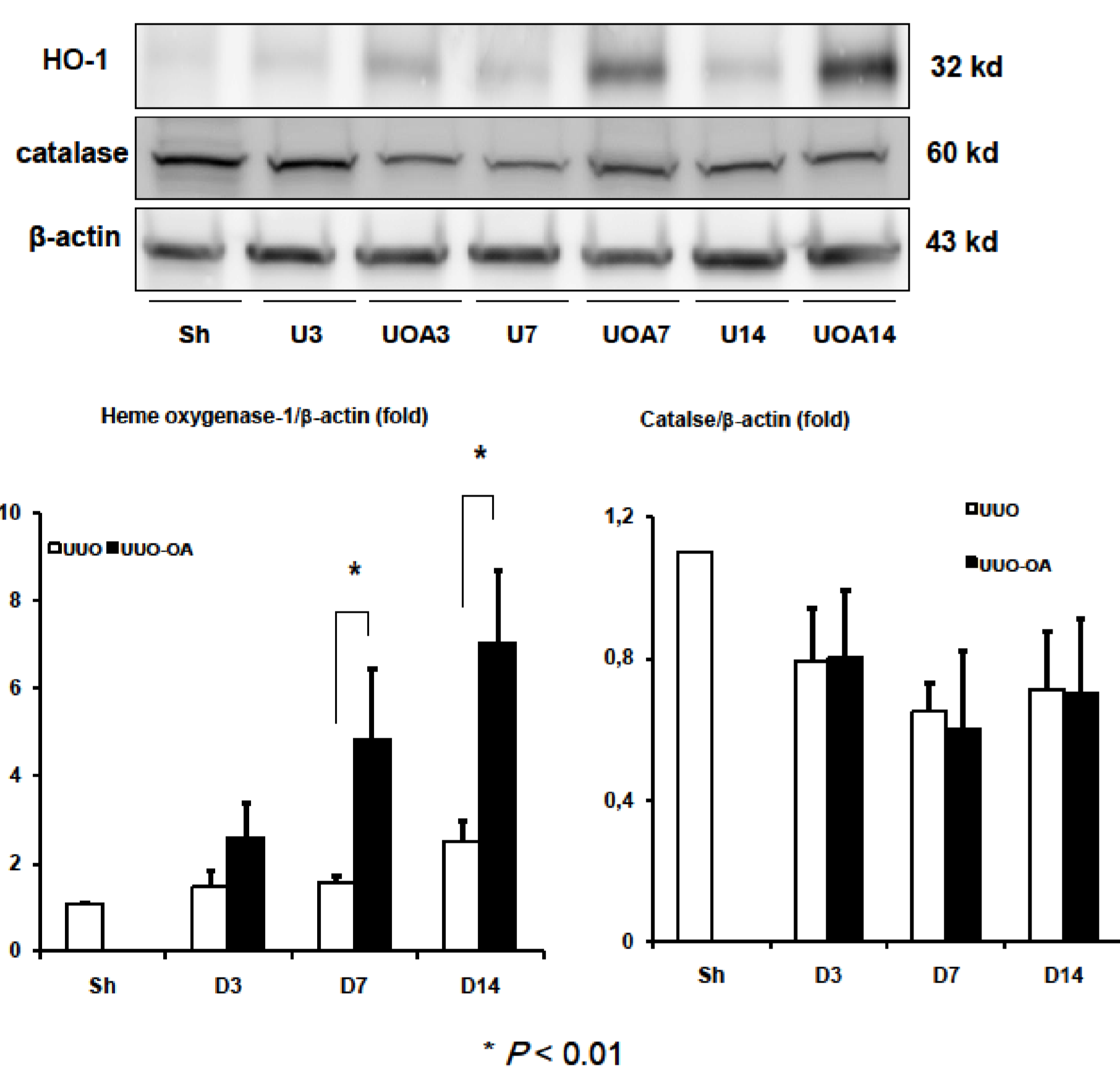


Methods

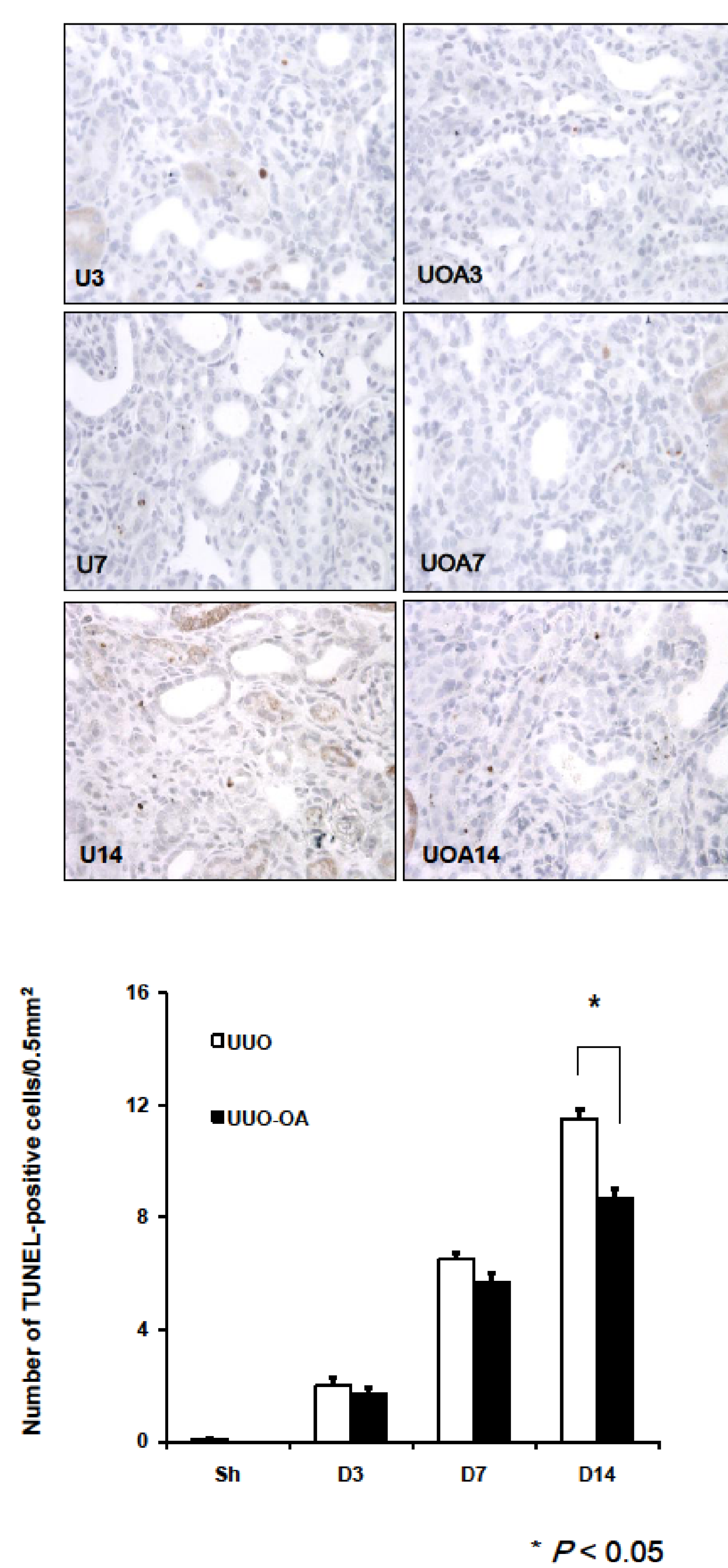
8 week old C57BL6/J; UO
 3, 7, 14 days
 With or Without OA
 With or Without OA
 With or Without OA
 UUO3 vs UUO-OA3
 UUO7 vs UUO-OA7
 UUO14 vs UUO-OA14

Results

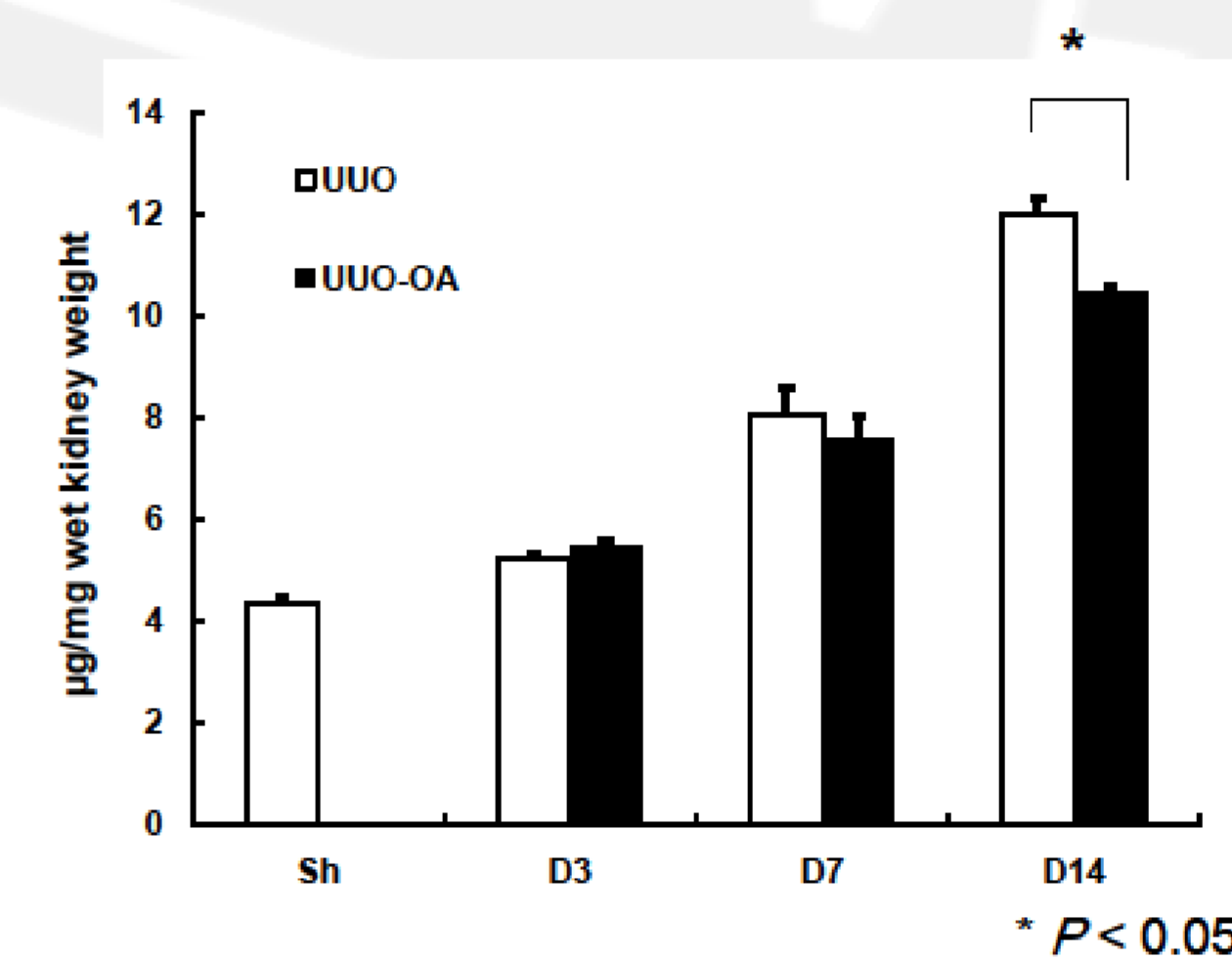
The effect of oleanolic acid on heme oxygenase-1 and catalase in obstructed kidney



The effect of oleanolic acid on TUNEL-positive cells in obstructed kidney

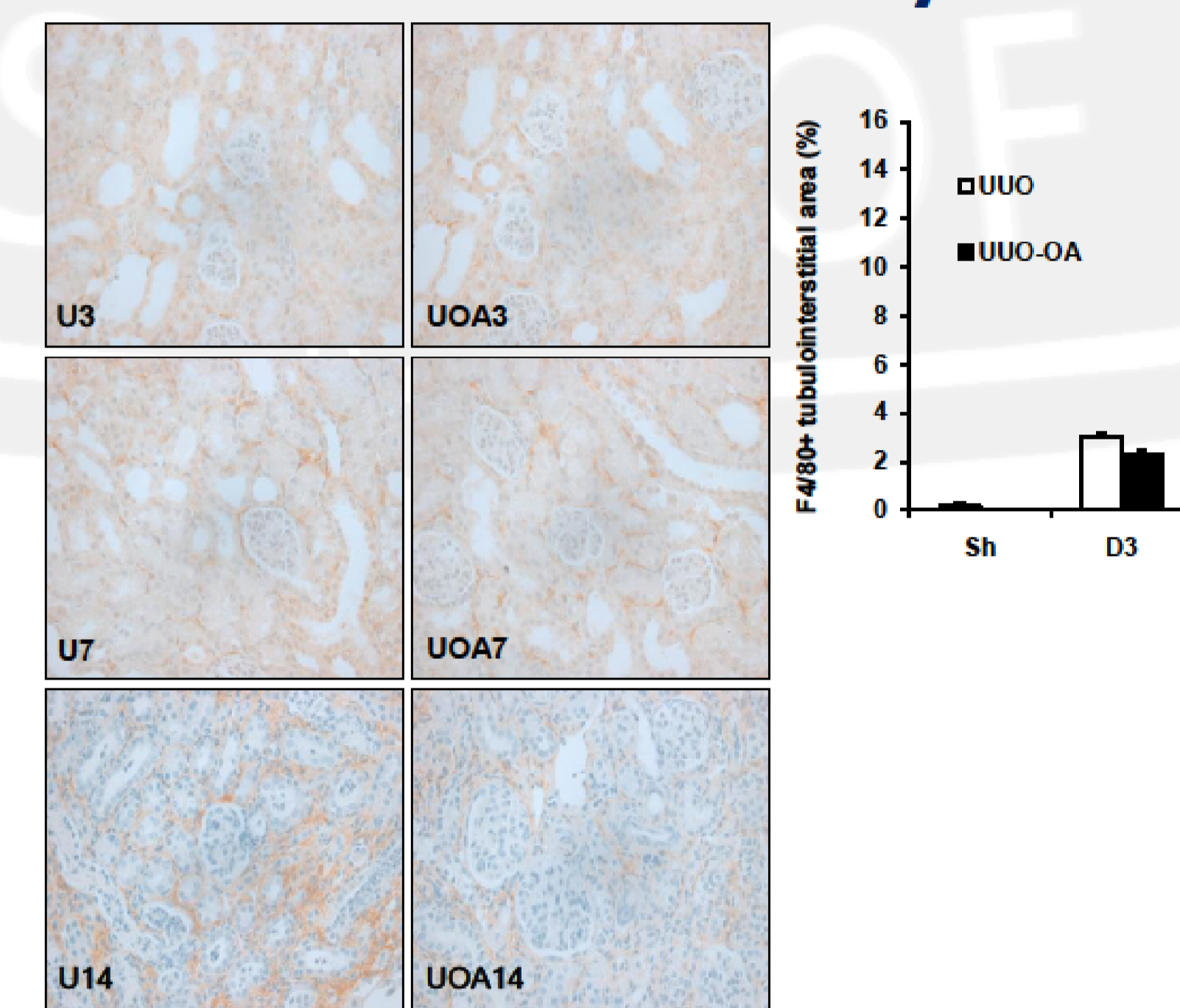


The effect of oleanolic acid on collagen accumulation in obstructed kidney

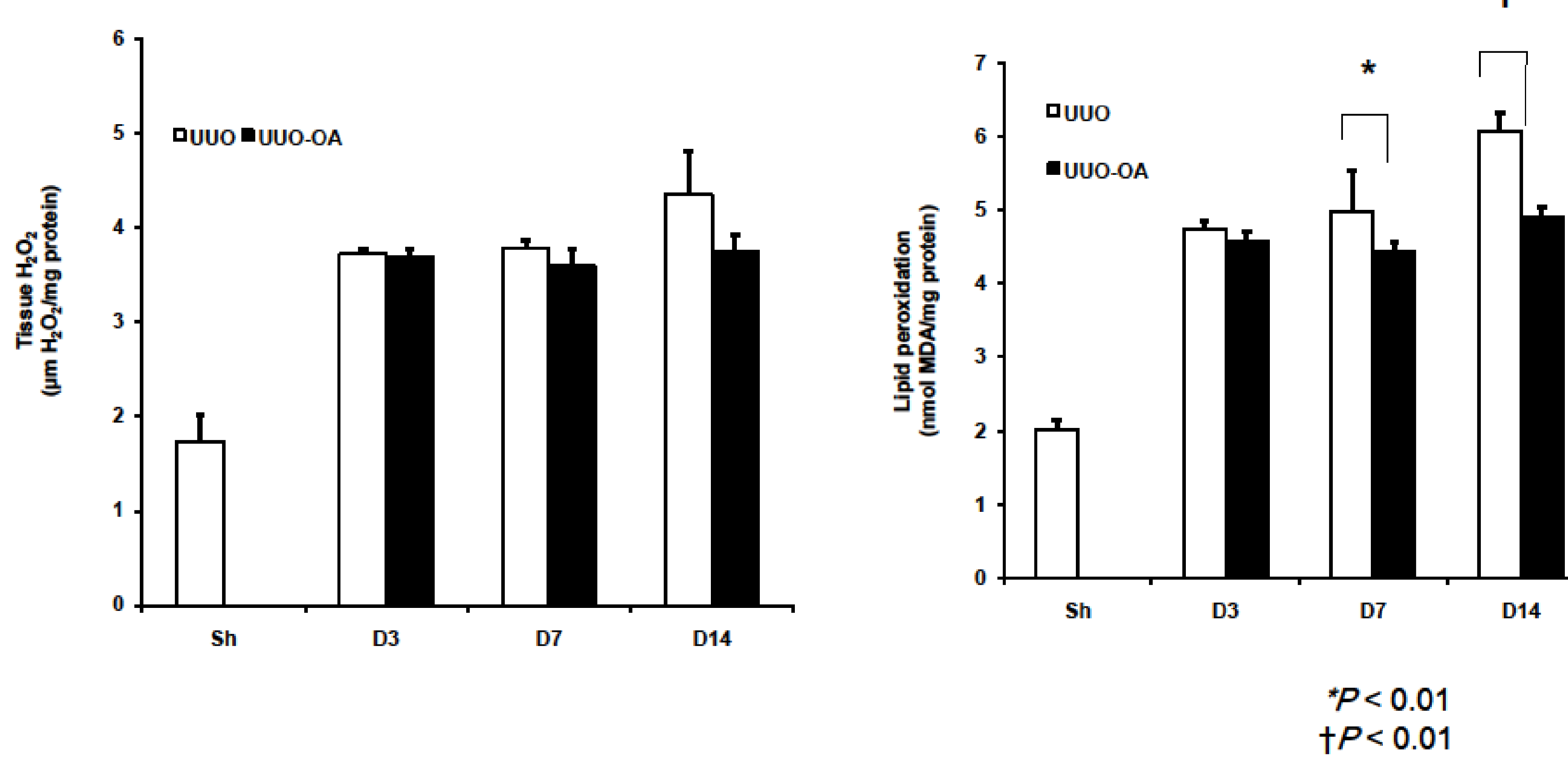


Results

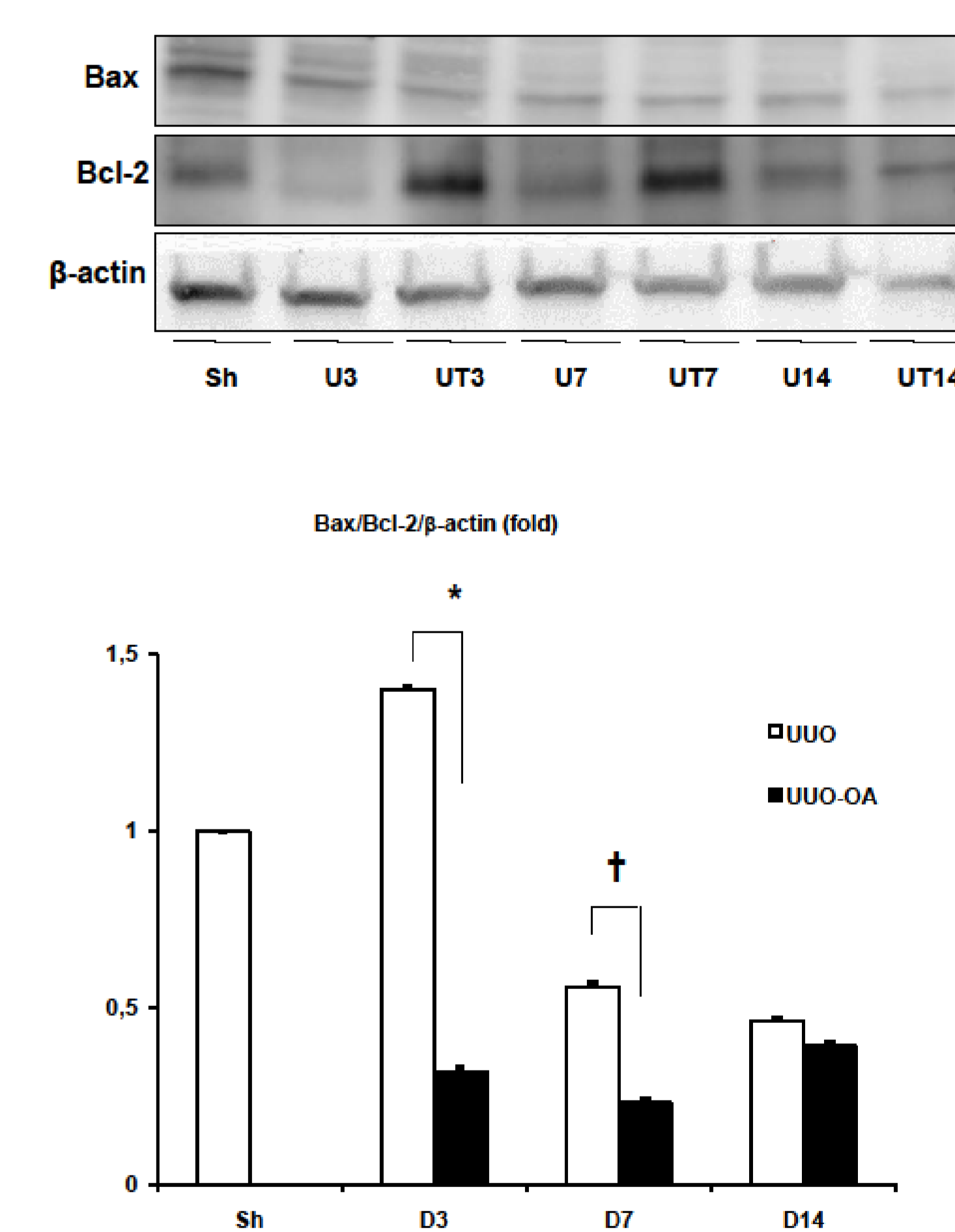
The effect of oleanolic acid on macrophage infiltration in obstructed kidney



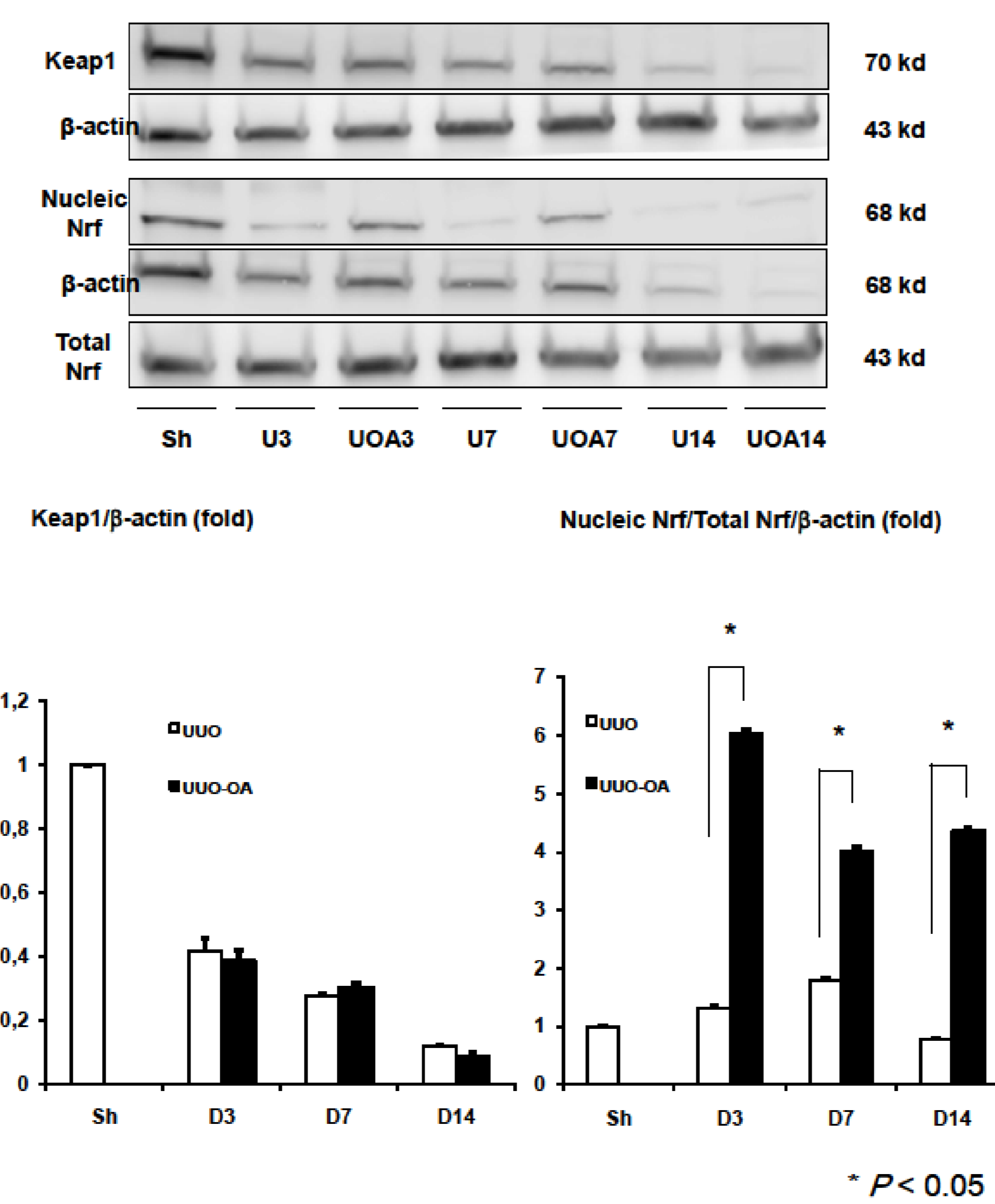
The effect of oleanolic acid on hydrogen peroxide formation and lipid peroxidation in obstructed kidney



The effect of oleanolic acid on Bcl-2 protein in obstructed kidney



The effect of oleanolic acid on Keap1, nuclear Nrf2 and total Nrf2 in obstructed kidney



SUMMARY & Conclusions

1. The UUO group showed a significant reduction of nuclear Nrf2 and renal tissue HO-1 with the significant tubulointerstitial injury in the obstructed kidney.
2. The administration of oleanolic acid in the UUO group significantly activated HO-1 via Nrf2 upregulation, resulting in improvement of renal interstitial damage.

Our results suggest that oleanolic acid may exert its protective effect in renal fibrosis by nuclear translocation of Nrf2 and subsequent upregulation of the antioxidant enzyme.

