



## Background

Idiopathic membranous nephropathy (MN) is an autoimmune-mediated glomerulonephritis and a common cause of nephrotic syndrome in adults. There are limited available treatments for MN. We assessed the efficacy of resveratrol (RSV) therapy for treatment of MN in a murine model of this disease.

## Methods

Murine MN was experimentally induced by daily subcutaneous administration of cationic bovine serum albumin, with phosphate-buffered saline used in control mice. MN mice were untreated or given RSV. Disease severity and pathogenesis was assessed by determination of metabolic and histopathology profiles, lymphocyte subsets, immunoglobulin production, oxidative stress, apoptosis, production of heme oxygenase-1 (HO1) and signalings.

## Result

MN mice given RSV had significantly reduced proteinuria and a marked amelioration of glomerular lesions. RSV also significantly attenuated immunofluorescent staining of C3, although there were no changes of serum immunoglobulin levels or immunocomplex deposition in the kidneys. RSV treatment of MN mice also reduced the production of reactive oxygen species (ROS), reduced cell apoptosis, and upregulated heme oxygenase 1 (HO1). Inhibition of HO1 with tin protoporphyrin IX partially reversed the renoprotective effects of RSV. RSV increases expression of HO1, and has anti-complement, anti-oxidative, and anti-apoptotic effects via Nrf2 signaling.

Figure 1. Effect of RSV on laboratories

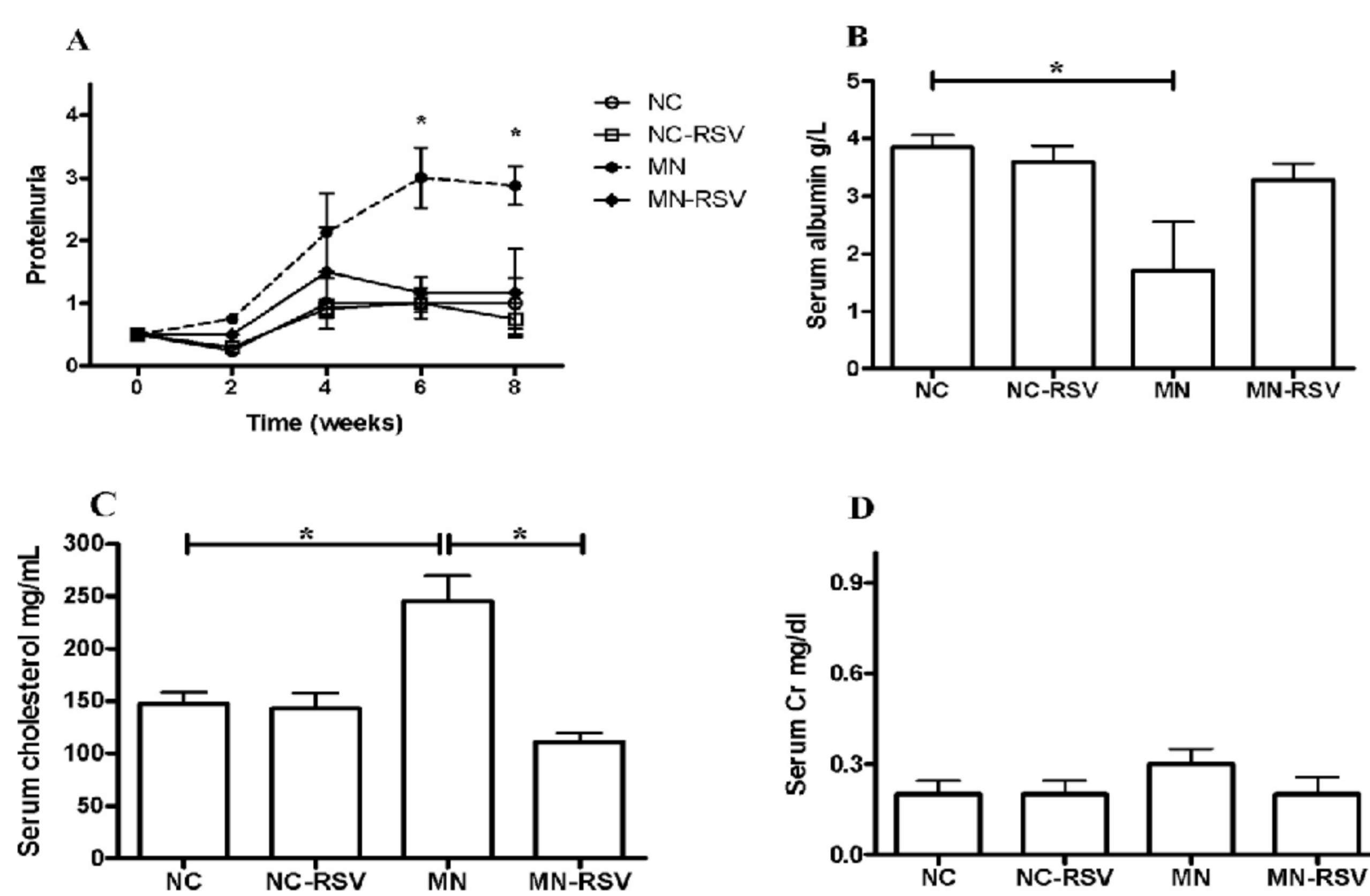


Figure 3. Effect of RSV on production of superoxide anion and kidney cell apoptosis.

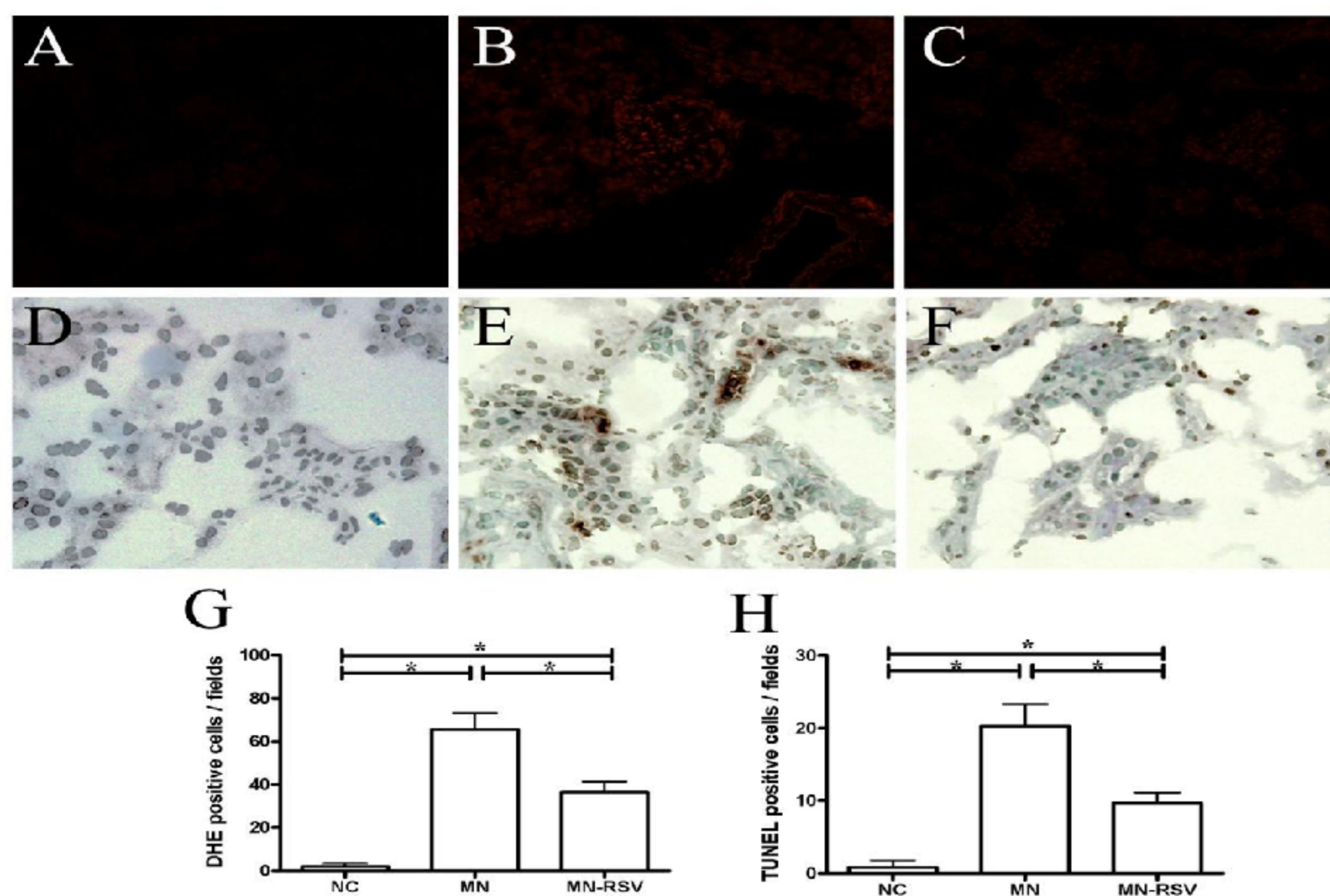


Figure 5. Effect of HO-1 inhibition on RSV effects.

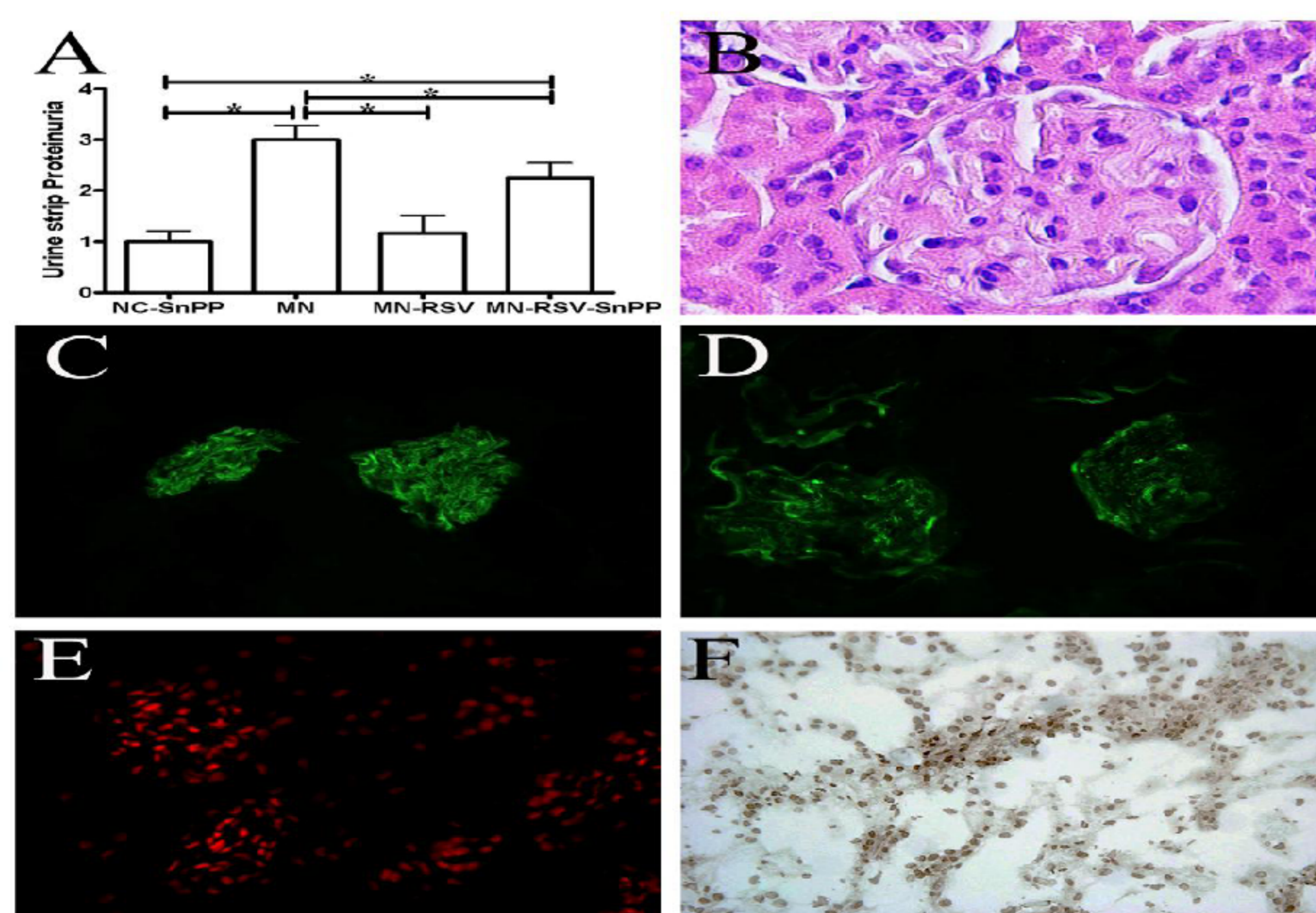


Fig. 2 Effect of RSV on renal histology.

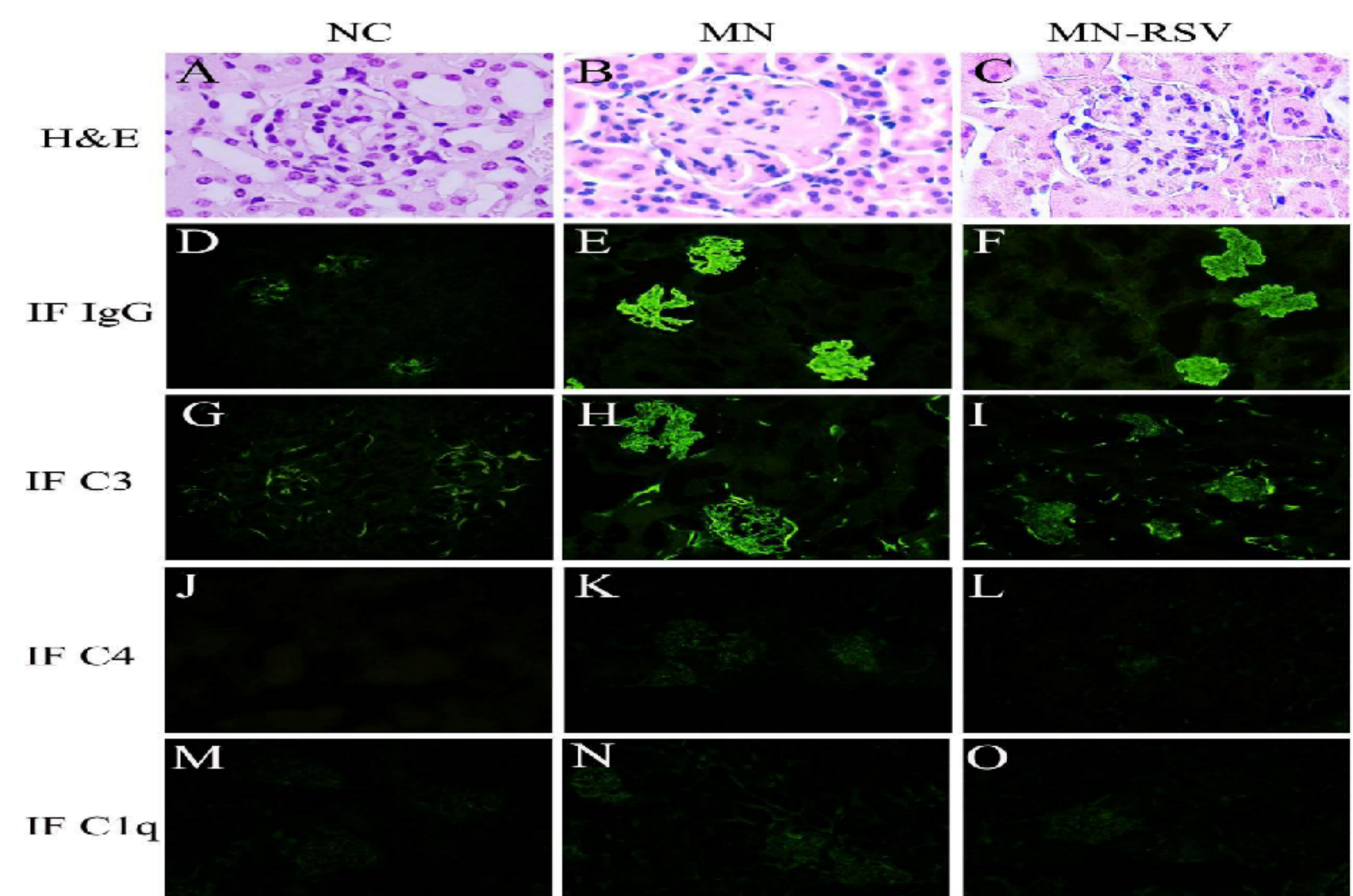


Figure 4. Effect of RSV on renal expression of HO-1

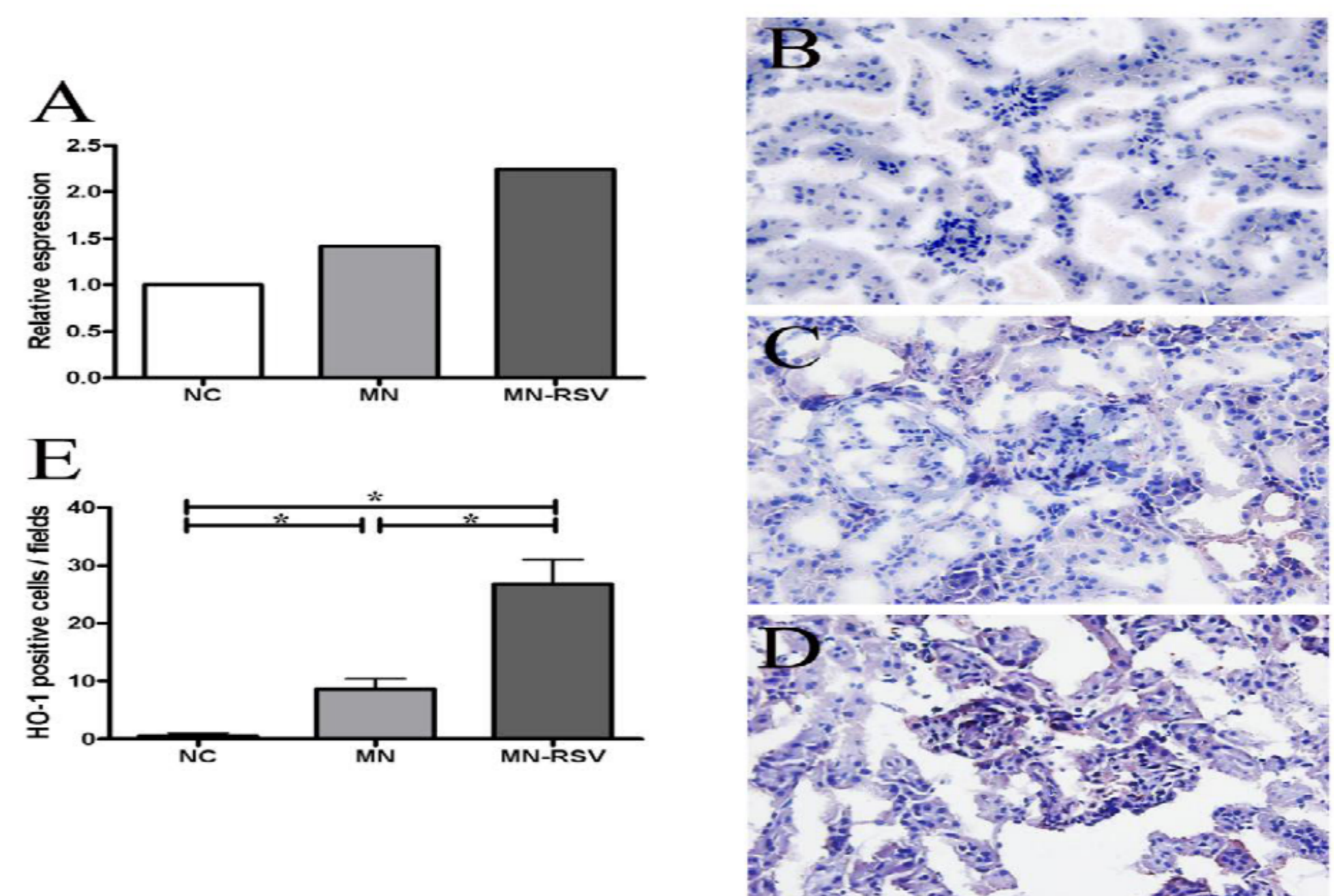
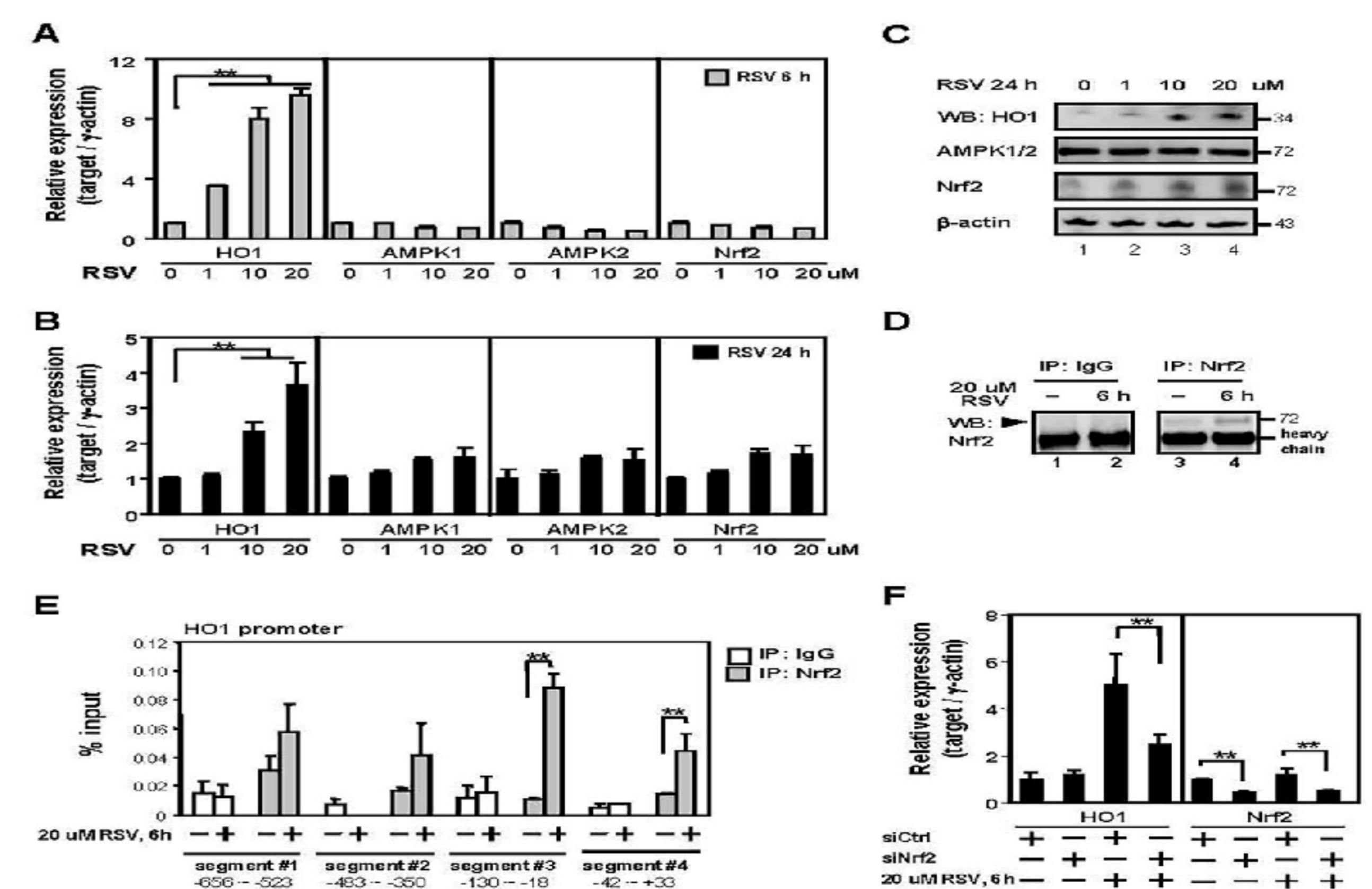


Figure 6. RSV activates HO1 expression via stimulating Nrf2 binding activity in E11 podocytes.



## Conclusion

Our results show that RSV increased the expression of HO1 and ameliorated the effects of membranous nephropathy in a mouse model due to its anti-complement, anti-oxidative, and anti-apoptotic effects. RSV appears to have potential as a treatment for MN.