Abstract

While renal functions deteriorate with age, little is known about manifestations and mechanisms of renal senescence. Advanced glycation end-products (AGEs) are well known to play a pivotal role in senescence. I hypothesized that primary reduction of AGEs lead to less phenotype of senescence, and investigated a role of glyoxalase I (GLO1), which detoxifies chiefly precursor of AGE, dicarbonyl compounds, in the aging process of the kidney. First, I established the system to assess renal senescence, which included halt of the cellular proliferation (*in vitro*), interstitial thickening (*in vivo*), elevated transcript and protein expression levels of p53, $p21^{WAF1/CIP1}$ and $p16^{INK4A}$, and elevated positive rate of senescence-associated β-galactosidase (SABG) staining. Next, the renal phenotype of histological senescence was assessed by reviewing the human renal biopsy specimen from the patients of whom renal function was less impaired. Interstitial thickening was demonstrated to be the renal histological manifestation of senescence. Finally, primary regulation of AGEs by overexpression or knockdown of GLO1 was demonstrated to affect cellular or histological status of renal senescence. In conclusion, I clarified the renal senescence by senescent marker expression and cellular and pathological phenotypes *in vivo* and *in vitro*, and demonstrated amelioration of renal senescence by GLO1 overexpression through reduction of AGE accumulation.