0532

Pathophysiological role of leptin in renal injury

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Summary

The metabolic syndrome is constellation of visceral fat obesity, impaired glucose metabolism, atherogenic dyslipidemia, and blood pressure elevation, which all independently increase a risk of atherosclerotic diseases. The metabolic syndrome is also a risk factor for chronic kidney diseases. However, little is known about the molecular basis. Leptin is an important adipocytokine that acts directly on the hypothalamus and regulates food intake and energy expenditure. Leptin is also reported to have peripheral action as a pro-inflammatory cytokine in atherosclerosis and hepatic fibrosis models. Here we demonstrate that leptin exerts the pro-inflammatory effects in a mouse model of tubulointerstitial fibrosis induced by unilateral ureteral obstruction. Up-regulation of inflammatory cytokines and chemokines and infiltration of macrophages were significantly reduced in leptin-deficient *ob/ob* mice as compared with wild-type mice, thereby leading to attenuated renal fibrosis. Continuous subcutaneous administration of leptin not only reduced body weight and blood glucose levels in *ob/ob* mice comparable to wild-type mice but also canceled the renoprotective phenotype. Moreover, renal injury induced by unilateral ureteral obstruction was significantly reduced in long-form leptin receptor (Ob-Rb)-deficient *db/db* mice, suggesting the significance of the leptin/Ob-Rb pathway. These findings indicate that leptin plays an important role in the progression of tubulointerstitial renal injury. This study will provide a novel insight into the pathophysiological role of leptin in the relationship between the metabolic syndrome and chronic kidney diseases.