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The ablation of C/EBP homologous protein (CHOP) attenuates UUO-induced renal fibrosis

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Objectives : CCAAT/enhancer-binding protein (C/EBP) homologous protein (CHOP) is activated by endoplasmic reticulum (ER) stress, leading to apoptotic cell death. Fibrosis, a pivotal characteristic of chronic kidney disease, is stimulated by ER stress. Herein, we investigated the role of CHOP in unilateral ureteral obstruction (UUO)-induced renal fibrosis using CHOP knockout (Chop−/−) mice.

Methods : CHOP wild type (CHOP+/+) and deficient (CHOP-/-) mice were used. Kidneys were harvested at 5 days after UUO.

Results : UUO induced increased BiP/GRP78 and CHOP expressions, indicating that UUO induces ER stress. These increases were less in CHOP−/− mice than in wild type (CHOP+/+) mice kidneys. Chop deficiency mice attenuated increases of collagen deposition and α-smooth muscle actin, an indicator of myofibroblast, and inflammatory cells in the kidney after UUO. In addition, Chop deficiency mitigated apoptotic cell death and mitochondrial damage after UUO. Furthermore, Chop deficiency enhanced the expression of Beclin1 and LC3-II, with increased autophagosome in the kidney after UUO.

Conclusions : Taken together, our results demonstrate that deletion of CHOP attenuates the progression of renal fibrosis though regulating apoptosis, mitochondrial dysfunction, and autophagy, suggesting that CHOP could be a novel target for treatment of chronic kidney disease.

Keywords : C/EBP homologous protein, apoptosis, mitochondria, unilateral ureteral obstruction, renal fibrosis