P-52

Autophagy는 상피-중간엽 이행을 통해 신섬유화를 조절한다

가톨릭대학교 의과대학 해부학교실 및 세포사멸질환연구센터[1], 가톨릭대학교 부천성모병원 임상의학연구소[2]
가톨릭대학교 의과대학 중앙실험실[3], 가톨릭대학교 의과대학 내과학교실[4]

남선아[1], 김완영[1], 최아름[1], 김유미[1], 박상희[2], 김홍림[3], 김진[1], 김용균[4]

Autophagy Deficiency in Tubular Epithelial Cells Deteriorate Renal Fibrosis Through Epithelial-mesenchymal Transition

Sun Ah Nam[1], Wan-Young Kim[1], Arum Choi[1], Yu-Mi Kim[1], Sang Hee Park[2]
Hong Lim Kim[3], Jin Kim[1], Yong Kyun Kim[4]

Department of Anatomy and Cell Death Disease Research Center[1], College of Medicine,
The Catholic University of Korea, Seoul, Korea
Institute of Clinical Medicine Research[2] of Bucheon St. Mary
Integrative Research Support Center[3], College of Medicine, The Catholic University of Korea, Seoul, Korea
Department of Internal Medicine[4], College of Medicine, The Catholic University of Korea, Seoul, Korea

Aim: Epithelial-mesenchymal transition (EMT) is a process by which injured renal tubular epithelial cell undergo a phenotypic conversion into mesenchymal cell and an important pathway to generation fibroblast in renal fibrosis. Autophagy is a cellular process of degradation of damaged cytoplasmic components and regulates cell death or proliferation. It is unclear whether autophagy plays a role in TGF-β induced tubular EMT. In this study, we investigated the role of autophagyin TGF-β induced tubular EMT and renal fibrosis induced by UUO by using conditional knockout mice in which autophagy gene 7 (Atg7) is genetically ablated specifically in tubular epithelial cell.

Methods: Atg7-floxed mice were crossed with Ksp-Cre mice to generate tubular-epithelial cell-specific Atg7 knockout mice (Atg7flox/flox;Ksp-Cre+). Unilateral ureteral obstruction (UUO) was performed and mice were sacrificed 3, 7 and 14 days after UUO.

Results: In vitro, TGF-β treatment in HK2 cell induced autophagy in dose-dependent and time-dependent manner. In vivo, after UUO, tubular cell apoptosis and renal fibrosis were markedly more induced in Atg7flox/flox;Ksp-Cre+ than in wild-type mice. The expression of TGF-β was more increased in Atg7flox/flox;Ksp-Cre+ than in wild-type mice. The expression of E-cadherin was more decreased and the expression of α-smooth muscle antibody and vimentin were more increased in Atg7flox/flox;Ksp-Cre+ than in wild-type mice.

Conclusions: Our data demonstrate that autophagy regulates apoptosis of tubular epithelial cells and renal fibrosis through TGF-β induced EMT.

Key Words: 자가포식작용, 섬유화, 상피-중배엽세포 전이
Autophagy, Fibrosis, Epithelial-mesenchymal transition