Autophagy Plays Cytoprotective Role in Contrast Induced Renal Tubular Epithelial Cell Injury

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**Background:** Radiocontrast-induced nephropathy (RCN) is a common cause of acute kidney injury to inpatient. However, prevention and treating strategies against developing RCN haven’t been set up fully. Furthermore the role of autophagy in the pathogenesis of RCN remains unclear. Herein we investigated its role in pathogenesis of RCN. **Methods:** We examined the expression of autophagic and apoptotic proteins during progression of contrast (Iodoxanol) induced injury to renal tubular epithelial cells (RTEC). To determine the protective role of autophagy against contrast induced cell injury, we inhibited autophagy with small interference RNA (siRNA) for ULK1 and measured the changes of cell viability and expressions of apoptotic and autophagic proteins for 48 hours. **Results:** After exposure to contrast, cell viability was reduced for 3 hours, but it was recovered and increased at 24 hours and 48 hours after exposure. Apoptosis was detected as early as 1 hour after contrast exposure and increased caspase 3 and 8 were observed for 48 hours. On the other hand, autophagy, identified by LC3 and autophagy-related gene protein 7 (ATG7), was detected at 3 hours after contrast exposure and the proteins were also increased up to 48 hours. After inhibiting autophagy with siRNA for ULK1, cell viability was not increased at 24 and 48 hours after contrast exposure. **Conclusions:** Autophagy plays cytoprotective role in contrast induced RTEC injury and it may occur independently of apoptosis.

PGC-1α Protects Against Notch1-Induced Kidney Injury

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**Background:** This study aimed to identify the effect of PGC-1α on kidney fibrosis using mice with tubule-specific double overexpression of Notch1 and PGC-1α. **Methods:** Using human kidney samples, we analyzed expression pattern of PGC-1α in human chronic kidney disease (CKD). We crossed mice expressing Pax8-rtTA/tetO-ICN1 with mice harboring Pax8-rtTA/tetO-Ppargc1a to create Pax8-rtTA/tetO-ICN1/tetO-Ppargc1a mice. The littermate tetO-ICN1 or tetO-Ppargc1a mice (without Pax8-rtTA) were considered controls. From these mice, we examined fatty acid oxidation pathway and cell death. To delineate relationship between Notch1 and PGC-1α, chromatin immunoprecipitation (ChIP) assay was performed. **Results:** Microarray analysis revealed PPARGC1A transcript level correlated with estimated glomerular filtration rate. Immunohistochemistry further confirmed that protein expression of PGC-1α was decreased in advanced stages of CKD. Compared to control and Pax8-rtTA/tetO-Ppargc1a mice, normal renal architecture was lost and animals developed severe tubular dilatation and fibrosis in Pax8-rtTA/tetO-ICN1 mice. In contrast, dilated tubules were less and fibrosis was almost null in Pax8-rtTA/tetO-ICN1/tetO-Ppargc1a mice. In Notch1 overexpressing mice, transcript and protein expression levels of fatty acid oxidation were decreased compared to control mice. The decreases in expression of these genes were restored by PGC-1α overexpression. In addition, PGC-1α overexpression attenuated the increased apoptosis rate in mice with Notch1 overexpression. Finally, ChIP assay revealed that the transcriptional repressor Hes1, a downstream target of Notch1 signaling, can regulate PGC-1α in kidney tubular epithelial cells (TECs). **Conclusions:** PGC-1α is directly regulated by Notch signaling. The reduced PGC-1α activity by Notch overexpression resulted in kidney fibrosis through impaired fatty acid oxidation and genetic delivery of PGC-1α in renal TECs almost nullified Notch-induced kidney fibrosis. Our findings suggest that PGC-1α can provide a protective effect against kidney injury and restoring its activity can be a promising therapeutic strategy in the management of CKD.