

THE ROLE OF THE AGE-DEPENDENT LOSS OF α (E)-CATENIN IN INCREASED
ACUTE KIDNEY INJURY

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ABSTRACT

The aging kidney undergoes structural and functional alterations which make it more susceptible to acute kidney injury (AKI). Previous studies in our laboratory have shown that the aging kidney has a marked loss of α (E)-catenin in proximal tubular epithelium. α -Catenin, a key regulator of actin cytoskeleton, interacts with a variety of actin-binding proteins. Fascin 2 is an actin bundling protein that interacts with adhesion molecules and F-actin. In this work, we hypothesized that loss of α (E)-catenin leads to disruption of actin cytoskeleton which increases cisplatin-induced injury in aged kidney. A stable shRNA knock-down of α (E)-catenin was generated in NRK-52E cells (C2 cells); NT3 cells are the non-targeted control. We demonstrated that age dependent loss of α (E)-catenin in renal tubule epithelial cells facilitates the Fas mediated apoptotic signaling pathway in response to cisplatin-induced AKI injury. In addition, a cisplatin-induced loss of fascin 2 was observed in aged kidney. Overexpression of Fscn2 abolished increased cisplatin-induced apoptosis, mitochondrial dysfunction and oxidative stress in C2 cells compared with NT3 cells. In conclusion, this dissertation projects novel insight into understanding the increased incidence of AKI in aged kidney and identified a novel role of fascin 2 in renal epithelial cells, which depends on the functional interaction with α (E)-catenin and F-actin. These findings may lay the groundwork for new therapeutic approaches to AKI in aged patients in the future.