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Mass-spectrometry based discovery of tubular injury marker in chronic kidney disease.

Ji Eun Kim[1], Dohyun Han[4], Jin Seon Jeong[5], Jong Joo Moon[2], Sunhwa Lee[6], Yong Chul Kim[2], Kyung Don Yoo[7], Seung Hee Yang[3]
[1]Department of Internal Medicine-Nephrology, Korea University Guro Hospital, Korea, Republic of
[2]Department of Internal Medicine-Nephrology, Seoul National University Hospital, Korea, Republic of
[3]Department of Kidney Research Institute, Seoul National University College of Medicine, Korea, Republic of
[4]Department of Proteomics Core Facility, Seoul National University Hospital, Korea, Republic of
[5]Department of Internal Medicine-Nephrology, Seoul Veterans Hospital, Korea, Republic of
[6]Department of Internal Medicine-Nephrology, Kangwon National University Hospital, Korea, Republic of
[7]Department of Internal Medicine-Nephrology, Ulsan University Hospital, Korea, Republic of

Objectives: Renal tubular injury and interstitial fibrosis are inevitable processes in the progression of chronic kidney disease (CKD). The purpose of this study is to identify common proteins expressed in CKD kidney tissues from animal model and injured primary cultured renal tubuloepithelial cells (TEC).

Methods: Label-free quantitative proteomic analysis based on liquid chromatography- tandem mass spectrometry was performed on kidney tissue obtained from rat CKD model by 5/6 nephrectomy, and quantitative proteomic analysis based on Tandem mass tag was performed on primary cultured human TECs after hypoxic damage for 24 hours. Then, the proteins identified in common from both types of samples were validated.

Results: When comparing the proteins expressed before and after hypoxic damage in primary cultured TECs, we identified 1,254 differentially expressed proteins (DEP). And rat kidney tissue harvested 8 weeks after 5/6 nephrectomy showed 2,497 DEPs in comparison with sham-operated kidney tissue. Among those DEPs, only 51 proteins showed a significant increase after chronic damage in both types of samples, with the highest fold changes in EFEMP2, RNF5, MYO9A, MCM2, KRT18, and PROS1, respectively. Functional enrichment analysis of these significant proteins confirmed changes in proteins associated with cytoskeleton organization and cytoskeletal protein binding in all three GO terms of biologic processes, molecular functions, and cellular components.

Conclusions: We have identified specific proteins that commonly increase with chronic injury in primary cultured TECs and kidney tissues. Further study for validating the diagnostic value of these proteins for tubular damage in CKD is needed.