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Dysregulated autophagy conrtibute to podocyte injury in Podocyte-Specific Yes-Associated Protein Deletion mice

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Objectives : Hippo/YAP signaling plays a crucial role in podocyte injury and intricately associated with chronic kidney disease (CKD). Identification of the underlying mechanism of CKD progression and exploration of new therapeutic drugs are urgently needed.
Methods : Herein, we utilize mass spectrometry to profile the downstream pathways podocyte-specific Yes-Associated Protein (YAP) deletion mice (YAP-KO mice). Periodic acid–Schiff (PAS) staining revealed mesangial expansion area in YAP-KO mice. Following, Transmission Electron microscopy (TEM) observed the change of autophagic vacuoles and immunofluorescence staining observed LC3 in podocytes.
Results : It was found that the processes linked to autophagy dysregulation have been significantly enrich in the YAP-KO mice downstream pathways. ROC-325 probably reverses autophagy dysregulation in podocyte which caused by yap deletion.Moreover, YAP-KO+ROC-325 mice have significantly rescued albuminuria from the drug compared to the vehicle mice.After treatment with ROC-325, the mesangial matrix areas decreased in YAP-KO mice. TEM analysis revealed that ROC-325 ameliorated foot process effacement in YAP-KO mice. Consistent with the TEM results, autophagy markers LC3 were significantly elevated in YAP-KO mice, while a decrease in YAP-KO+ROC-325 mice.
Conclusions : This study demonstrated that autophagy-inhibiting drug ROC-325 is a novel and promising therapeutic target in CKD that helps to attenuate albuminuria, nodular glomerulosclerosis and mesangial matrix expend in YAP-KO mice.