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Methylation in pericyte- focus on AKI-CKD continuum

Yu-Hsiang Chou

周鈺翔

Division of Nephrology, Department of Internal Medicine, National Taiwan University Hospital

臺大醫院 腎臟科

Acute kidney injury (AKI) constitutes a major risk factor for the development of chronic kidney disease (CKD), and patients progressing to end-stage renal disease face substantial medical costs for related treatments. However, clinical interventions for AKI currently lack effective treatments beyond supportive care. Nevertheless, epigenetics research on the progression from acute kidney injury to chronic kidney disease has opened a promising avenue for treatment. Therefore, our focus has centered on the role of pericyte methylation in the AKI-CKD continuum.

Pericytes, residing as collagen-producing cells within the vascular basement membrane of microvessels, have been identified as the primary cell source of scar-producing myofibroblasts in our previous studies. Furthermore, our data have revealed significant epigenetic modifications in the transcriptome analysis of pericytes at different stages of the AKI-CKD continuum. These epigenetic changes cause pericytes to acquire pro-inflammatory phenotypes in their activated state and persist in an inactivated state. Demethylation by 5-azacytidine restored the microvascular stabilizing function of pericytes, reversed the profibrotic property of inactivated pericytes, and prevented the transition from AKI to CKD.

Furthermore, to enhance our understanding of DNA methylation and associated signaling pathways in different disease models, a DNA methylation atlas of human tissues and organs, including the kidney, including kidney at single-cell resolution is needed. However, generating DNA methylation reference profiles for all underlying cell types is challenging due to the high cost and sparsity of single-cell methylomics data. Moreover, in addition to demethylating agents such as 5-azacytidine, therapies targeting epigenetics in the AKI-CKD continuum are necessary. A cell-specific drug delivery system, accompanied by specific epigenetic controllers, could be designed and applied in future clinical trials.