Interstitial–epithelial crosstalk

Limited regeneration of the proximal tubule occurs following injury. Now, Ina Maria Schiessl and colleagues show that tubule cell injury induces activation and migration of PDGFR β -positive interstitial cells, which support the regeneration of tubule epithelial cells. “Our results depict a spatial and temporal correlation of interstitial cell recruitment and tubular cell dedifferentiation and proliferation, implying a crucial role for interstitial–epithelial crosstalk during tubular regeneration”, explains Schiessl.

Interstitial–epithelial crosstalk through PDGFR β signalling facilitates cell proliferation and regeneration in organs such as skin; however, the contribution of the renal interstitium to tubular cell turnover is not known. “The renal interstitium is a comparably neglected compartment,” says Schiessl. “Beyond its roles in the synthesis of erythropoietin and in renal fibrosis, little is known about the function of this third major renal compartment, perhaps owing to its poor accessibility and the lack of readily accessible parameters to study its function.” To overcome these limitations, the researchers performed serial intravital multiphoton microscopy of PDGFR β -positive interstitial cells in reporter mice to study the dynamics of tubular–interstitial interactions during tubular regeneration.

Following the induction of tubular injury by laser-induced ablation of single tubular cells, the researchers observed an immediate activation of PDGFR β -positive fibroblasts adjacent to the injury, characterized by a rise in calcium levels and migration to the site of injury. The migration of these interstitial cells coincided with the migration and proliferation of dedifferentiated epithelial cells at the site of injury. Inhibition of PDGFR β by intraperitoneal injection of trapidil hindered the calcium response, interstitial cell migration and tubular regeneration. Schiessl suggests that, similarly to wound scarring in skin, the pro-regenerative interstitial–epithelial crosstalk in renal tubules could be subject to imbalances in chronic kidney disease, resulting in the establishment of renal interstitial fibrosis.

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Our results ... [imply] a crucial role for interstitial–epithelial crosstalk during tubular regeneration

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