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exploring mechanisms of renal fibrosis progression

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Kidney is the organ that has one of the most complicated architecture in the body. The sophisticated architecture of nephron made its physiology difficult to unravel and the variety for experimental approach for renal (patho) physiology is limited so far. At this symposium, I would like to discuss the recent progress in our understanding of renal fibrosis, including peritubular capillary flow regulation and the interaction with tubules. Renal peritubular capillary blood flow plays a role in many biological functions, including supplying oxygen to tubular and interstitial cells and recycling reabsorbed electrolytes, glucose, and amino acids. Diseased kidney often show the heterogeneity of blood flow in each capillary in several experimental models of disease; local ischemia in the capillary bed could influence neighboring tubular function, and the balance between the ischemic and normoxic capillary number correlates with renal function. We recently found that ischemia/reperfusion-induced damage changed renal tubular glucose handling and that proximal tubular glucose uptake plays important roles in the balance between recovery versus development of fibrosis after renal ischemia/reperfusion-induced injury, which can be mediated by SGLT2 inhibitors through reconstructing the renal capillary network. Another hand, from the pharmacological viewpoint, one of the biggest problem on the anti-renal fibrotic drug development is lacking the good animal model. While there are several I/R models for rodents, each model has limitation to develop broad fibrotic changes in the kidney, such as high mortality and shrinking the kidney. We recently succeeded to create an experimental model of renal fibrosis that is possible to estimate the later phase fibrotic level based on the blood urea nitrogen at day 1 of final surgery. This model makes easy to design the experimental protocol for assessing the therapeutic potential of the specific drug being developed for the purpose of treating renal fibrosis.

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