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Ischemia and post-injury regeneration in proximal convoluted tubule cells

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Core tip: Proximal convoluted tubular cells (PCTCs) are multifunctional cells which play significant roles in fluid hemostasis and metabolism. These cells are permanently damaged by exposure to toxic substances. On the other hand, injury could acutely affect them. Therefore, regeneration is a vital process for them. Several studies showed different pathways for their regeneration. But, the most probable way for their generation is the differentiation of scatter tubular cells (STCs) to PCTCs.

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Commentary

The kidneys are vital organs which play substantial roles in the body. They are responsible for filtration of the blood by their functional units named nephrons (1). Proximal tubule is a portion of nephron which is located after Bowman's capsule and near the loop of Henle. Structurally, it consists of two parts including the proximal convoluted tubule (PCT) and the proximal straight tubule (PST) (2). PCT has been placed in the cortex of kidney and is made up of epithelial cells with cuboid form and brush borders which are called Proximal convoluted tubular cells (PCTCs) (3). PCTCs are known for their re-absorptive role in reabsorption of glucose, amino acids, NaCl, NaHCO3, phosphate, citrate and water from the fluid filtrated by glomerulus. In addition to the re-absorptive role of PCT, it has been confirmed that PCT involves in metabolism including activation and inactivation of vitamin D, gluconeogenesis and responding to acidosis (4).

Renal impairment occurs due to various causes such as ischemia. Renal ischemia can ultimately lead to acute kidney failure (AKF) (5). Cellular lesions resulting from ischemia are caused by oxidative stress and inflammation of the interstitial space. The renal lesions resulting from ischemia are divided into three main categories including endothelial damage of the vessels, tubular injuries and inflammation of the interstitial space. Endothelial damages of the vessels are created by increasing vascular contraction and adhesion of molecules that cause the leukocytes, platelets and red blood cells adhesion to the endothelium and consequently result in intravascular congestion. Tubular damages can be lethal or sub-lethal. Lethal lesions are observed in the forms of necrosis or apoptosis of tubular cells. Sub-lethal damages include the destruction of tight connections between the cells, the natural attachment of tubular cells to the basement membrane, the loss of these cells and the brush borders of the apical membrane into the lumen. Tubular cells and the loss brush borders with proteins form intra-tubular membranes that increase the pressure inside of the Bowman's capsule by preventing the flow of fluid in the tubules. Inflammation also increases the production of reactive oxygen species (ROS) that cause severe tubular and vascular injuries (6-8).

Therefore, these cells are regarded as the significant parts of nephrons because of their various roles. Moreover, they are considered to be among the most susceptible cells of kidneys. Ischemic condition or toxins are the main reasons for damage to PCTCs. These damage factors can induce necrosis or apoptosis in PCTCs. Finally, a series of poisoning factors such as oxidative stress, mitochondrial dysfunction and disturbed tubular transport lead to cell death (9,10).

Fortunately, PCTCs can regenerate themselves after injury. The mechanism of this regeneration is not fully

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understood. Nevertheless, various studies have assessed undergoing mechanisms. A related study concluded that regenerative process starts by stopping the growth of tubular cell which causes increased signaling for the production of profibrotic peptides and fibroblasts (11). Recently, Tavafi et al have investigated the factors which cause damage to PCTCs in a complete review study. They also reviewed possible mechanisms which could lead to PCTCs regeneration after injury. They indicated different regenerative pathways such as rapid replacement of tubular cells damaged by immature tubular cells, and differentiation of mesenchymal stem cells (MSCs) to PCTCs. Another hypothesis that they referred was the role of bone marrow derived cells (BMDCs) in the regeneration of PCTCs and their capacity to differentiate into PCTCs. Eventually, they concluded that tubular cells which escaped from injury dedifferentiate to scatter tubular cells (STCs) which finally convert to PCTCs (12).

Author's contribution

AH is the single author of paper.

Conflicts of interest

The author declares no conflict of interest.

Ethical considerations

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References

1. Reddi AS, Kuppasani K. Kidney Function in Health and Disease. In: Byham-Gray LD, Burrowes JD, Chertow GM, editors. Nutrition in Kidney Disease. Totowa, NJ: Humana Press; 2014. p. 3-10.
2. Gobe GC, Johnson DW. Distal tubular epithelial cells of the kidney: Potential support for proximal tubular cell survival after renal injury. Int J Biochem Cell Biol. 2007;39:1551-61.
3. Vedula EM, Alonso JL, Arnaout MA, Charest JL. A microfluidic renal proximal tubule with active reabsorptive function. PLoS One. 2017,11;12:e0184330. doi: 10.1371/journal.pone.0184330.
4. Curthoys NP, Moe OW. Proximal tubule function and response to acidosis. Clin J Am Soc Nephrol. 2014,5;9:1627-38. doi: 10.2215/CJN.10391012.
5. Caskurlu T, Kanter M, Erboga M, Erboga ZF, Ozgul M, Atis G. Protective Effect of Nigella Sativa on Renal Reperfusion Injury in Rat. Iran J Kidney Dis. 2016;10:135-43.
6. Clarkson M, Friedewald J, Eustace J, Rabb H. Acute kidney injury. Brenner & Rector's The Kidney 8th ed Philadelphia, Pennsylvania, USA: Saunders, Elsevier. 2008:943-86.
7. Molitoris BA. Acute renal failure. Drugs of today (Barcelona, Spain: 1998). 1999;35:659-66.
8. Kribben A, Edelstein CL, Schrier RW. Pathophysiology of acute renal failure. J Nephrol. 1999;12:S142-51.
9. Li S, Zhao J, Huang R, Steiner T, Bourner M, Mitchell M, et al. Development and application of human renal proximal tubule epithelial cells for assessment of compound toxicity. Curr Chem Genom Transl Med. 2017,14;11:19-30. doi: 10.2174/2213988501711010019.
10. Smeets B, Boor P, Dijkman H, Sharma SV, Jirak P, Mooren F, et al. Proximal tubular cells contain a phenotypically distinct, scattered cell population involved in tubular regeneration. J Pathol. 2013;229:645-59. doi: 10.1002/path.4125.
11. Lan R, Geng H, Singha PK, Saikumar P, Bottinger EP, Weinberg JM, et al. Mitochondrial pathology and glycolytic shift during proximal tubule atrophy after ischemic AKI. J Am Soc Nephrol. 2016;27:3356-3367
12. Tavafi M, Hasanvand A, Ashoory H. Proximal convoluted tubule cells in ischemia and post-injury regeneration. Acta Persica Pathophysiol. 2016; 1:e05.