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Journal of Diabetes, Metabolic Disorders & Control

Mini Review

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Renal fibrosis and mitochondrial biogenesis

Mini Review

Volume 3 Issue 6 - 2016

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Received: July 01, 2016 | **Published:** November 10, 2016

Renal fibrosis is a common final pathway that results in progressive end-stage renal failure including diabetic nephropathy.[1–3] Progressive of renal disease, characterized histologically by tubular atrophy and the accumulation of extracellular matrix proteins in the renal interstitium, is associated particularly with declining renal function.[4–7] Renal fibrosis is characterized by glomerulosclerosis, tubulointerstitial fibrosis, loss of renal parenchyme, and inflammatory cell infiltration. These are the common features of chronic renal failure.[7–12] This pathologic result usually originates from underlying complicated renal cellular activities such as epithelial-to-mesenchymal transition, fibroblast activation, and the activation of cytokines such as transforming growth factor beta.[8,13–15] Mitochondrial dysfunction has been found to play a significant role in various diseases, and located among the organs that require high levels of energy. The kidneys have a relatively high number of mitochondria.[16–18] Mitochondrial dysfunction has also been found to be key a contributing factor to various kidney diseases.[16,19–22] Recently increasing evidences showed mitochondrial dysfunction in a broad spectrum of pathogenesis of renal diseases. Moreover renal diseases patients exhibited an impaired mitochondrial respiratory system. It summarizes the possible effects of mitochondrial and acquired factors associated with diverse renal damage induce mitochondrial dysfunction. Mitochondrial dysfunction has resulting in many kidney organ damaged. For example, podocyte injury causes from foot process effacement, detachment, and apoptosis. Tubular epithelial cell damage causes from apoptosis/necrosis and epithelial-mesenchymal transition, additionally, endothelial dysfunction causes from apoptosis/necrosis and endothelial-mesenchymal transition.[18,19,21–26] Studies have shown significantly increased ROS production, up-regulation of TGF-β expressions, high glucose levels, proteinuria, uremic toxins, ischemia/hypoxia, and activation of RAAS in peripheral blood mononuclear cells of patients, thereby demonstrating the close association between mitochondrial dysfunction and renal diseases progression.[21,25,27,28] Recently, a number of studies have revealed that regulation of co-activators can physiologically signal to specific transcription factor targets. These reason led to activation of genes required for mitochondrial biogenesis and respiratory function. The major transcription factors, nuclear respiratory factor 1(NRF-1), act on the majority of nuclear genes encoding subunits of the respiratory complexes. They are also involved in the expression of mitochondrial transcription and replication factors.[17,19,21,25,29–31] Nuclear respiratory factor-1 (NRF-1), a major transcription factor in the human genome, plays a key regulatory role in mitochondrial biogenesis. Initially, NRF-1 was identified as being responsible for regulating genes involved in mitochondrial respiratory function.[22,24,32,33] Subsequently, it was also found to be involved in the regulation of genes that play a role in a wide range of other biological functions, including signal transduction, organelle biogenesis, protein synthesis, cell growth, and the progression of the cell cycle.[16–35] Among the specific effects of relevance, mitochondrial transcription factor A, which promotes the transcription and replication of mitochondrial DNA, is up-regulated by NRF-1. Moreover, the distribution of NRF-1 in mammalian cells is pervasive, with the transcription factor also playing key parts in regulating tissue differentiation and development, gene expression, and anti-oxidative stress and inflammatory responses in a range of organisms. NRF-1 has been shown to promote cell survival and to be involved in the protection of cells from apoptosis during development, with decreased NRF-1 expression having been found in damaged liver tissues in rats.[14,36] With the above observations we do believe there exist some relationship between NRF-1 and the progression of renal interstitial fibrosis. In our existing findings are encouraging, our understanding mitochondrial transcription factors NRF-1 changes vary dramatically in relation to the level of renal cellular fibrosis. Nevertheless, the downregulation of NRF-1 support the role of NRF-1 as a major contributor in kidney fibrosis. Thus, it is clear that the pathogenesis of renal cellular fibrosis might be regulated by NRF-1, and relatedly, that NRF-1 could potentially be used as a novel therapeutic agent for the treatment of diabetic renal interstitial fibrosis. Moreover, the use of these agents has only been consider to very limited strategies and as yet has no clinical applications. In the future, it needs to intensive elucidate their mechanisms and thus provide clinicians with the best possible treatment strategies.

Acknowledgements

None.

Conflict of interest

Author declares that there is no conflict of interest.

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