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Periostin-binding DNA Aptamer Attenuates Diabetic Nephropathy-induced Renal Fibrosis

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Background: Diabetic nephropathy is the major cause of chronic kidney disease, and is associated with progressive renal fibrosis. Recently, accumulation of periostin, an extracellular matrix protein, was shown to be implicated with renal fibrosis. Aptamers, a novel oligonucleotide which binds to specific target molecules, have been proved to have higher binding affinity without developing the common side effects of antibodies. In addition, the costs of aptamer productions are cheaper than small molecules making them a promising pharmaceutical candidate. This study was aimed to examine the therapeutic role of periostin-binding DNA aptamers (PA) on renal fibrosis under diabetic conditions.

Methods: *In vitro*, immortalized mouse distal convoluted tubule cells (mDCTs) were exposed to TGF-β1 (5 ng/ml) to induce fibrosis with or without PA (100 nmol/l). *In vivo*, C57BL/6 mice were intraperitoneally injected with saline (C group, N=16) or streptozocin (50 mg/kg/d) (DM group, N=16). Eight mice from each group were treated with PA (500 μg/kg/d). mRNA and protein expressions of periostin, fibronectin, collagen type I (col-I) in mDCTs and mouse kidney were examined by real-time polymerase chain reaction and western blot analysis, respectively. Immunohistochemistry (IHC) was conducted with renal tissues.

Results: *In vitro*, TGF-β1 treatment significantly up-regulated periostin, fibronectin and col-I. PA treatment significantly ameliorated the TGF-β1 induced fibronectin and col-I expressions ($P < 0.05$). *In vivo*, fibronectin and col-I was significantly up-regulated in kidney samples of diabetic mice ($P < 0.05$). IHC staining revealed that the number of fibronectin and col-I (+) cells were significantly higher in diabetic mice ($P < 0.05$). These increases were clearly ameliorated by PA treatment ($P < 0.05$).

Conclusion: These findings suggest that inhibition of periostin using a DNA aptamer could be a potential therapeutic strategy against renal fibrosis in diabetic nephropathy.

Keywords: Aptamer, Periostin, Renal fibrosis