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Periostin deficiency attenuates kidney fibrosis and pancreatic β -cell dysfunction though reducing tenascin C under diabetic conditions

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Objectives: Diabetic nephropathy (DN), the most common cause of chronic kidney disease, is associated with kidney fibrosis. We have previously demonstrated that periostin plays an important role in kidney fibrosis. In this study, we investigated the role of periostin in DN.

Methods: Periostin and tenascin C (TNC) concentrations in urine samples from the patients with DN were measured. 50mg/kg streptozotocin (STZ) was administered for 5days after unilateral nephrectomy (STZ-UNx) to build DN in both the wild type and the *Postn-null* mice. After 20 weeks, molecular expression of fibrosis marker and histological changes were evaluated. Blood glucose levels and urine albumin were periodically measured. We cultured NRK 49F cells under TGF- β treatment as an in vitro model of DN.

Results: The concentration of periostin and TNC increased according to the severity of DN in the human sample. In vitro models, expression of fibrosis marker such as α -smooth muscle actin and collagen type I α 1 was increased through TGF- β treatment. To investigate relevance between periostin and TNC, we treated both TGF- β and recombinant periostin at once in NRK 49F. Co-treated NRK 49F showed significant TNC elevation compared with non-treated control. Compared to the wild type STZ-UNx model, the *Postn-null* STZ-UNx model showed lower urine albumin excretion and less glomerular sclerosis and interstitial fibrosis. The *Postn-null* STZ-UNx model had lower expression of fibrosis marker and TNC. The glucose level of the *Postn-null* STZ-UNx model was well regulated in comparison with the wild type STZ-UNx model. In addition, in the *Postn-null* STZ-UNx model, pancreatic islet integrity and insulin expression were significantly more preserved.

Conclusions: Periostin has essential role in both kidney fibrosis and pancreatic β -cell dysfunction in DN. Also, there is a significant association between periostin and TNC. Either periostin or TNC could be a new treatment target of DN.