Nature Reviews Nephrology | Published online 19 September 2016; doi:10.1038/nrneph.2016.140

DIABETIC NEPHROPATHY

Role of podocyte SHP-1 in hyperglycaemic memory

> the progression of microvascular pathology is harder to slow if not treated early in the course of diabetes

New data suggest that sustained expression of podocyte SHP-1 might underlie the long-term renal adverse effects of hyperglycaemia despite normalization of glucose levels in patients with diabetes mellitus.

"Our aim was to identify a mechanism that might explain the observation made in the DCCT/EDIC study that the cumulative incidence of nephropathy continued to differ between the intensive glucose control and standard therapy groups after 18 years of follow-up, despite comparable HbA_{1C} levels," explains researcher Pedro Geraldes. "The sustained deleterious effect of hyperglycaemic stress despite improved glycaemic index has been named hyperglycaemic memory, raising the idea that the progression of microvascular pathology is harder to slow if not treated early in the course of diabetes."

Geraldes and colleagues previously found that a hyperglycaemia-induced increase in podocyte SHP-1 expression led to insulin resistance and nephropathy in diabetic mice. Now they show that after normalization of blood glucose levels, insulin actions remained blunted in diabetic mice owing to a persistent increase in podocyte SHP-1 levels, which was caused by hyperglycaemia-induced epigenetic modification of the SHP-1 promoter region.

The researchers conclude that insulin resistance and podocyte dysfunction as a result of sustained SHP-1 expression might explain the hyperglycaemic memory effect in diabetic nephropathy. They are now evaluating podocyte SHP-1 as a marker of glomerular disease progression in diabetes.

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ORIGINAL ARTICLE Lizotte, F. *et al.* Persistent insulin resistance in podocytes caused by epigenetic changes of SHP-1 in diabetes. *Diabetes* http://dx.doi.org/10.2337/db16-0254 (2016)
FURTHER READING de Boer, I. H. *et al.* Kidney disease and related findings in the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Study. *Diabetes Care* **37**, 24–30 (2014)