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DIABETIC NEPHROPATHY

# Sirt1 attenuates diabetic albuminuria

Sirtuin-1 (Sirt1) is a $NAD^+$-dependent protein deacetylase that has protective effects against metabolic stress and a role in the pathogenesis of diabetic nephropathy. Researchers at Keio University, Japan now demonstrate that Sirt1 has a protective role against renal tubular cell damage induced by diabetes. Shu Wakino, who led the study, highlights this effect, "the metabolic abnormalities in nicotinic acid metabolism in proximal tubules preceded the glomerular damages in our model of diabetes mellitus and this abnormality affects podocyte function."

The authors used mouse models of diabetes mellitus to show that Sirt1 protein and mRNA levels are decreased before albuminuria. By overexpressing Sirt1 in the proximal tubules in a transgenic mouse model, albuminuria could be prevented. This albuminuria decrease was no longer seen in the proximal tubules in a *Sirt1* conditional knockout mouse model.

Sirt1 also functions as a cellular energy sensor driven by $NAD^+$ levels. Wakino states "we also measured and monitored nicotinic acid metabolites using photoactivated substances. Using this method, we demonstrated the retrograde flow and interaction between proximal tubular cells and podocytes." As well as metabolic changes, in mice that had albuminuria, overexpression of Claudin-1 was evident in the proximal tubules before the glomerulus. In humans, the levels of SIRT1 and Claudin-1 were correlated with proteinuria levels and are likely to be epigenetically regulated in podocytes.

These findings highlight the potential for monitoring Sirt1 expression as an early sign of diabetic nephropathy.

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