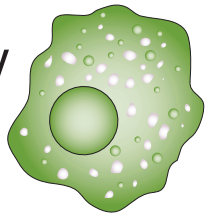
Nature Reviews Nephrology **10**, 483 (2014); published online 29 July 2014; doi:10.1038/nrneph.2014.134

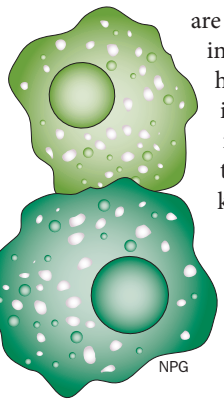
DIABETIC NEPHROPATHY

Heparanase mediates renal injury



A new study has revealed that heparanase drives renal injury under diabetic conditions by coupling macrophage activation with chronic inflammation. The researchers say that the emerging link between heparanase and inflammation suggests that heparanase could be a novel target for the treatment of diabetic nephropathy.

Heparanase—an enzyme that degrades the structural component of the extracellular matrix, heparan sulphate glycosaminoglycan—has long been linked to diabetic nephropathy; however, the mechanisms involved are unknown. "Observations initially made while studying heparanase involvement in inflammatory conditions in intestine and skin led us to test the role of heparanase in kidney-damaging inflammation in the setting of diabetic nephropathy," explains researcher Michael Elkin.



NPG

The researchers found that deletion of heparanase attenuated the increase in levels of TNF observed in the kidneys of wild-type diabetic mice. Heparanase activity promoted TNF release and activation of isolated murine macrophages by diabetic milieu components. They also demonstrated a key role for post-translational processing of heparanase by cathepsin L in activating the latent heparanase proenzyme in diabetic kidneys. "We found that highly-coordinated interplay between various renal cell types, extracellular substances and enzymes—Cathepsin L and heparanase—is critical to the pathogenesis of diabetic nephropathy," says Elkin.

Peter Sidaway

Original article Goldberg, R. *et al.* Role of heparanase-driven inflammatory cascade in pathogenesis of diabetic nephropathy. *Diabetes* doi:10.2337/db14-0001

© 2014 Macmillan Publishers Limited. All rights reserved