Macrophage COX-2 prevents diabetic nephropathy progression

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(HealthDay)—Macrophage cyclooxygenase-2 (COX-2) deletion is

associated with progression of diabetic nephropathy (DN), according to an experimental study published online Nov. 4 issue of *Diabetes*.

Xin Wang, from the Vanderbilt University School of Medicine in Nashville, Tenn., and colleagues examined the effects of macrophage COX-2 on development of DN in a mouse model of type 1 diabetes.

The researchers found that cultured macrophages with deletion of COX-2 exhibited a proinflammatory "M1" phenotype, with higher inducible nitric oxide synthase and NF-κB levels, but lower levels of interleukin-4Rα. Mice with COX-2 deletion in hematopoietic cells or macrophages developed severe DN compared with corresponding wild type diabetic mice, as indicated by increased albuminuria; fibrosis; and renal infiltration of T cells, neutrophils, and macrophages. Diabetic kidneys with macrophage COX-2 deletion had more infiltration of macrophages, but fewer renal "M2" macrophages (reparative phenotype); they also had increased ER stress and decreased numbers of podocytes. Results were similar in diabetic mice with macrophage E4 deletion.

"These studies have demonstrated an important but unexpected role for macrophage COX-2/PGE2/EP4 signaling to lessen progression of diabetic kidney disease, unlike the pathogenic effects of increased COX-2 expression in intrinsic renal cells," the authors write.

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