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Placental Growth Factor Deficiency Aggravates Diabetic Nephropathy

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Objectives: Placental growth factor (PlGF), originally discovered in human placenta, is a member of the vascular endothelial growth factor (VEGF) family. Upon binding to VEGF-R1 and neuropilin-receptor, PlGF exerts favorable angiogenic activity by modulating vascular response in neuronal and endothelial cells. We investigated the role of PlGF in the development of diabetic nephropathy by using PlGF-knockout mice and cultured human glomerular endothelial cells (HGECs).

Methods: Diabetes was induced by a low-dose streptozotocin injection in 12-week-old male C57BL/6J PlGF-knockout (PlGF-KO) and wild-type mice and hyperglycemia was maintained through 12 week period.

Results: In diabetic PlGF-KO and wild-type mice, fasting blood glucose and HbA1c levels were elevated ($p < 0.001$). Diabetic PlGF-KO mice demonstrated the development of glomerular sclerosis and mesangial area expansion which were accompanied by albuminuria and the degree of such renal phenotypic changes were severer than that of diabetic wild-type mice ($p < 0.01$). Furthermore, they exhibited increased expression of type IV collagen, transforming growth factor- β 1 and increased number of F4/80-positive and apoptotic cells in the glomeruli. There were no significant differences in these indices of renal phenotypes between nondiabetic PlGF-KO and wild-type mice. In vitro studies showed increased expression of oxidative stress and apoptosis markers in HGECs treated with high glucose.

Conclusions: Taken together, PlGF deficiency appears to aggravate renal phenotypic alterations including increased glomerulosclerosis, inflammatory cell infiltration, and apoptotic cell death in diabetes. These results suggest that PlGF might play an important role in the development of diabetic kidney disease.