USING NANOPARTICLES IN THE TREATMENT OF DIABETIC KIDNEY DISEASE

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Abstract: Nanotechnology is revolutionizing the field of medicine. Its potential for wide-ranging applications in medical treatment and imaging has permeated certain cancers and other pathologies, but has remained relatively unexplored in the field of Diabetic Kidney Disease (DKD). DKD accounts for the vast majority of cases (~50%) of end stage renal disease in the United States and consumes a large portion of our healthcare dollars. Unfortunately, therapeutic options that target mesangial cell function and provide a mechanism to achieve regression of advanced lesions of DKD and improve renal function have remained elusive and essentially unexplored. Mesangial cells normally provide glomerular structural support but in the diabetic milieu, their excessive production of extracellular matrix proteins, especially fibronectin, represents an important player in the progression of renal dysfunction. We identified a cyclized Arg-Gly-Asp (RGD)-containing peptide which prevented progression of early DKD and caused regression of glomerular lesions in aged type 2 diabetic db/db mice. For specific targeting and efficient drug delivery, we designed a novel cyclized RGD-peptide with a free cysteine for packaging into vault nanoparticles. Vaults are dynamic barrel-like structures found in all eukaryotic cells. Here, we investigate the in vivo effect of the cysteine-modified RGD-peptide, and create a novel RGD-vault nano-drug delivery system. The RGD-vault was viewed by electron microscopy. We performed cell adhesion assays, and tested a modified-RGD vs. RGE-control peptides in 8-week old db/db mice for 4 weeks. The modified RGD- vs. RGE-peptide normalized albumin excretion in db/db mice, at doses 3 times lower than the unmodified RGD-peptide. The RGD-vault had a normal barrel-shape by electron microscopy. Thus, the novel RGD-vaults may be a new class of non-immunogenic nano-drug delivery system with therapeutic potential in DKD.

Keywords: nanoparticle, vault, diabetic kidney disease, type 2 diabetes, mesangial cells.

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