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SS-31 on diabetic nephropathy in BTBR ob/ob mice

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Background: SS-31 is a novel peptide that selectively binds to cardiolipin in the inner mitochondrial membrane, where it prevents protects cardiolipin peroxidation and protects mitochondrial structure. We investigated the renoprotective effects of SS-31 in the BTBR ob/ob mice with advanced DN. Methods: 18 week male diabetic BTBR ob/ob and wild type (WT) mice were randomly assigned to 5 groups: ob/ob with infusion of SS-31 via osmotic pump for 6 weeks, ob/ob with saline infusion, untreated ob/ob, WT, and WT with SS-31 infusion. Podocyte density, mesangial matrix (% tuft area occupied by collagen IV matrix), and glomerular macrophages were quantified by morphometry and immunohistochemistry. Results: Podocyte density, diminished in ob/ob mice, was significantly restored in ob/ob with SS-31 infusion (147.2 ± 6.3) compared with saline treated ob/ob mice (107.6 ± 4.8, p=0.0026) or untreated mice (100.5 ± 6.1, p=0.0002). Mesangial matrix was reduced in the ob/ob with SS-31 treatment (30.9 ± 0.6) compared to ob/ob with saline treated (45.2 ± 2.2) and untreated mice (46.5 ± 1.3) ($p<0.0001$). Macrophage infiltration was lower in ob/ob treated with SS-31 (1.3 ± 0.4) than untreated ob/ob (1.9 ± 0.36) (p=0.02). Albumin-creatinine ratio was decreased in ob/ob with SS-31 (276.8 ± 60.1), compared with the untreated ob/ob (671.8 ± 250.6), but results were not statistically significant. Conclusions: Podocyte density was restored and mesangial matrix decreased in SS-31 treated diabetic ob/ob mice, compared to saline treated and untreated controls. SS-31, currently in human clinical trials for other diseases, may be useful in treatment of DN and potentially other glomerular diseases in which podocytes are lost.