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The role of ABCA1 on the glomerular lipid accumulation and renal injury in the kidney disease

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Objectives: Glomerular lipid accumulation is one of the pathologic characteristics of diabetic kidney disease(DKD) and focal segmental glomerulosclerosis(FSGS). Recent evidences suggested that ATP-binding cassette transporters A1(ABCA1) has a particular effect on the cellular lipid homeostasis. We aimed to evaluate the role of ABCA1 on the lipid accumulation in glomeruli and podocyte under DKD and FSGS.

Methods: *In vitro*, mouse podocytes were stimulated with high glucose (HG), palmitic acid (PA), TNF- α , adriamycin (ADR) and treated an GW683965, agonist of LXR- α . In DKD model, C57BL/6 and podocyte specific ABCA1 knockout (KO) mice were maintained with high fat diet for 12weeks with streptozocin. GW683965 was administered via osmotic pump in *db/m* or *db/db* mice. In FSGS model, C57BL/6 and ABCA1 KO mice were administered intravenous injections of doxorubicin at 25mg/kg. BALB/c mice were implanted osmotic pumps. UACR, total cholesterol and triglyceride in kidney tissues were measured. RhoA activity and BODIPY 493/503 staining were performed in the kidney. Foot process effacement in glomeruli was evaluated by TEM. Apoptosis, mitochondrial markers were evaluated both *in vitro* and *vivo*.

Results: Blood glucose, UACR, serum cholesterol and triglyceride were significantly increased and foot process effacement was prominent in DKD and FSGS mice. These changes were abrogated by GW683965 treatment. Renal cholesterol and triglyceride contents were higher ABCA1 KO mice with DKD and FSGS or lower in GW683965 treated. Mitochondrial morphology and the expression of energy metabolic enzymes were changed in the kidneys of DKD and FSGS ABCA1 KO mice or GW683965 treated mice. *In vitro*, the intracellular lipid contents were increased and apoptosis combined with mitochondrial dysfunction were also increased in podocytes with HG, PA, TNF- α and ADR stimuli. All of these changes were ameliorated through GW683965 treatment.

Conclusions: These findings suggest that ABCA1 plays an important role in the glomerular lipid accumulation and renal injury under DKD and FSGS.