KSN 2021
FULLY VIRTUAL MEETING
September 02 (Thu) - 05 (Sun)

Oral Communication Abstract
Presentation No. OC4-05 (Abstract Submission No. 2352)

Oral Communications 4 Sep. 2 (Thu), 16:40-17:40

Graphene Quantum Dots alleviate fibrosis of subtotal 5/6 nephrectomy (5/6NX) via enhancing mitochondrial ATP Anaplerosis

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Objectives: Graphene Quantum Dots (GQDs) are carbon-based nanoparticles and spotlighted in biological application due to their biocompatibility, quantum confinement, and low toxicity. Rat with 5/6 nephrectomy (5/6NX) exhibits mitochondrial dysfunction associated with TRPC5 channel, a core calcium channel in podocytes and tubular cells. With current limited understanding of the interaction on between nanomaterials and renal cells, we show GQDs as a potential therapeutic nano-sized material in the 5/6NX rat model.

Methods:
GQDs (4mg/kg) were administered to Sprague Dawley (8-week; male) rats intraperitoneally for 3 times per week up to 8 weeks. To evaluate anti-apoptotic and anti-fibrotic properties of GQDs, we treated rTGF-beta (2ng/mL, 48hrs) with GQDs in primary cultured human podocytes and tubular cells. Intracellular calcium permeability was measured with Fura2-AM and quantified the oxygen consumption rate using a Seahorse XFe96 extracellular flux analyzer.

Results: Proteinuria, creatinine and renal parenchymal hypertension levels significantly decreased, while renal function was resotred in 5/6NX + GQDs group. GQDs treatment decreased inflammatory markers (MCP-1, IL-6, CXCL1 and CD68) expression, reduced fibronectin and S1008α, and increased GSH expression. Bax-2/BCL2 ratio was also significantly reduced by GQDs treatment and decreased the level of P53, P21 in which anti-apoptosis function is manifested. Furthermore, NGAL and TRPC5 protein levels were decreased, but increased the level of injury-induced actin cytoskeleton reorganization markers in podocytes, nephrine and WT-1 in GQDs group. GQDs alleviated fibrogenesis in human primary renal cells in dose-dependent manner (0.25μg/mL, 0.5μg/mL, 1μg/mL). In addition, GQDs promote wound injury healing on renal cells and suppress oxidative stress in H_2O_2-induced condition . Consequently, Annexin staining results showed the same patterns. Interestingly, total intracellular calcium level was reduced and higher ATP production was observed in mitochondria.

Conclusions: The findings suggest that GQDs are excellent nanoparticle candidates in chronic renal disease associated with mitochondria dysfunction.