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Graphene quantum dots attenuates peritoneal Fibrosis via a modulation of apoptosis by blocking myc pathway

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Objectives: Peritoneal fibrosis (PF) is an intractable complication of peritoneal dialysis that leads to peritoneal membrane failure. Recently, graphene quantum dots (GQDs) are considered a promising material for bio-applications because of their good free radical scavenging activity, low toxicity, and excellent water solubility. To investigate this possibility, the effect of GQDs was studied in the PF preclinical models.

Methods: We elucidated the effect of GQDs on TGFβ-induced fibrosis of primary cultured human peritoneal mesothelial cells (HPMC) and animal model of chlorhexidine gluconate (CG)-induced peritoneal fibrosis. To identify the mechanisms driving anti-fibrosis effect in response to GQDs treatment at the transcriptomic level, we analyzed gene expression using microarray.

Results: TGFβ induced a fibroblast-like morphology characterized by a spindle-like shape, in contrast to the cuboidal form of unstimulated HPMCs. Administration of GQDs (0.5 μg/ml) restored a normal cell morphology. Consistent with these results, GQDs abrogated the upregulation of the fibrosis markers fibronectin, collagen-1 and downregulation of the epithelial marker E-cadherin. In animal model, intraperitoneal GQDs decreased the peritoneal thickness and reversed the protein expression of fibronectin and collage-1 compared with non-treated group. The transcriptomes of each group clustered stringently in the basis of genotypes. Gene expression profiles showed GQDs treatment was largely related to DNA repair process, and cell cycle/death on gene ontology term analysis. Interestingly, expression of myc, which induces DNA damage, cell arrest, and finally apoptosis, was significantly suppressed with GQDs administration in a dose dependent manner (0.47-fold change, 20 vs 40 mg/kg). Analysis of peritoneal mRNA showed that collagen-1 and BAX2 expression was decreased and OGG, which is the marker of DNA damage was also reduced in GOQs-treated group.

Conclusions:
These results suggest that myc could be potential modulator of apoptosis and DNA damage response in the pathogenetic mechanisms of peritoneal fibrosis, and GQDs may be a therapeutic option for peritoneal fibrosis.