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Probiotics with Lactobacillus acidophilus KBL409 protects against kidney injury via improving mitochondrial dynamics and metabolism

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Objectives: Animal studies have shown that dysregulated gut microbiota can alter mitochondria metabolism of intestinal mucosa cells, leading to mitochondrial dysfunction. Here, we evaluated whether administration of *Lactobacillus acidophilus* KBL409 can improve mitochondria function in kidney tubular epithelial cells (TECs) and attenuate kidney injury in animal CKD model.

Methods: KBL409 was selected because this strain was proved to maintain intestinal integrity and reduce p-cresyl sulfate level *in vitro* in prior experiments. *In vivo* animal model of chronic kidney disease (CKD) was created by feeding 0.2% adenine diet to C57BL/6 mice for 4 weeks. The probiotics with *Lactobacillus acidophilus* KBL409 at a dose of $1x10^9$ CFU per day were administered by oral gavage during the same period. We isolated primary mouse TECs and treated them with TGF-β (10 ng/ml) or p-cresyl sulfate (0.5mM) and sodium butyrate (10μM), a short-chain fatty acid that is considered the end products of commensal bacteria.

Results: There were prominent structural alterations in CKD mice and KBL409 administration significantly attenuated renal fibrosis. Transcript and protein expression levels of PGC-1α, a key regulator of mitochondrial biogenesis, were significantly decreased in CKD mice, which were restored by KBL409. There were concomitant changes in mitochondrial content and mitochondrial dynamic-related proteins in response to KBL409. In addition, mice with KBL administration showed improvement in fatty acid oxidation defect and mitochondrial structure compared with CKD mice. *In vitro*, TGF-β or p-cresyl sulfate treatment in TECs recapitulated the findings of *in vivo* study and these alterations were reversed by butyrate administration. Mitochondrial function assay showed that butyrate significantly improved mitochondrial respiration, fatty acid oxidation defect, oxidative phosphorylation, and ATP production in TGF-β- or p-cresyl sulfate-treated TECs.

Conclusions: This study demonstrates that probiotic supplementation with *Lactobacillus acidophilus* KBL409 can provide renal protective effects by improving mitochondrial function.