Role of bone morphogenetic protein-7 in diabetic nephropathy

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Introduction: Bone morphogenetic protein-7 (BMP7) has been reported to confer renal protected effects in a variety of cell types and disease model, but the potential role of BMP7 in diabetic nephropathy remains unknown.

Methods: Nine-week-old *db/db* mice and their *db/m* littermates underwent uninephrectomy (Unx) or sham operation, and received rh-BMP7 (300 μg/kg body weight) or vehicle intraperitoneally every other day for 8 weeks before sacrifice. 24-Hour urine and blood samples of mice were collected every 4-week interval.

Results: Compared with vehicle control, Unx *db/db* mice treated with rh-BMP7 had significantly lower urinary albumin-to-creatinine ratio (4566 ± 2767 μg/mg vs 7338 ± 5748 μg/mg; $P < 0.05$), serum blood urea nitrogen (33.3 ± 3.46 mg/dL vs 37.5 ± 2.95 mg/dL; $P < 0.05$), and renal cortical expression of ICAM-1 and CCL-2 in both gene and protein levels. PAS staining of kidney tissue showed significantly less severe glomerular and tubular damage and interstitial inflammatory cell infiltration in the BMP7-treated group. Western Blotting of kidney cortex showed significant increase of p38 and p44/42 MAPK phosphorylation in Unx *db/db* vehicle group while treated with BMP7 suppressed their phosphorylation.

Conclusions: Our results demonstrated for the first time that BMP7 reserved renal function and attenuated pro-inflammatory responses in diabetic kidney by suppressing multiple signalling pathways including p38 and p44/42 MAPK. Its potential application as a therapeutic molecule in diabetic nephropathy warrants further investigation.

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Differential effects of epigallocatechin gallate on cigarette smoke-induced upregulation of CINC-1 and IL-6 in Rat H9c2 cardiomyocytes

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Introduction: Cigarette smoke (CS) containing numerous harmful substances is considered to precipitate spasm of micro vessels, which is supported as a cause of idiopathic-dilated cardiomyopathy, as well as have a toxic effect on the myocardium. The mechanism is currently unclear, but both oxidative stress and inflammatory responses may play an essential role in the CS-induced biological processes. Several antioxidant agents have been used in the control of the inflammatory responses. The aim of this study was to investigate the effect of epigallocatechin gallate (EGCG), the major component of polyphenols in green tea, on CS-induced inflammatory responses in rat H9c2 cardiomyocyte model.

Methods: The H9c2 cell line was cultured in DMEM containing 10% fetal bovine serum, in a CO_2 incubator at 37°C. When cells reached 80% confluence, the medium was replaced with experimental medium consisting of 1% fetal bovine serum 24 hours before treatment. Cigarette smoke medium (CSM) was prepared by bubbling smoke from two cigarettes into 20 mL serum-free medium, which was regarded as 100%. Cells were pretreated with 0.1, 1, or 10 μM EGCG for 30 minutes before 4% CSM was added and incubated for an additional 24 hours. Supernatant was collected for determination of interleukin-6 (IL-6) and cytokine-induced neutrophil chemoattractant-1 (CINC-1) by ELISA.

Results: CSM caused elevation of pro-inflammatory markers IL-6 and CINC-1 (resemble to human IL-8) in H9c2 cells. EGCG alone also caused IL-6 elevation in a dose-dependent manner. There was a significant inhibitory effect of EGCG at low dose (0.1 μM) observed on CSM-induced elevation of IL-6. However, EGCG alone or in combination of CSM had no effects on CINC-1 level.

Conclusion: Our findings suggest that low dose of EGCG treatment may alleviate the production of pro-inflammatory cytokine IL-6 but not CINC-1, indicating that the release of pro-inflammatory cytokines is under different transcriptional control in rat H9c2 cardiomyocytes.