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Resveratrol은 제 2형 당뇨병 신증에서 제 1형과 2형 adiponection 수용체 모두를 활성화한다.

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신석준, 김형욱, 최범순, 김용수, 장윤식, 박철휘

Resveratrol Activates Adiponectin Receptor-1 and -2 in Type 2 Diabetic Nephropathy

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Aim/hypothesis: Adiponectin from adipose tissue has multiple function including insulin sensitization, anti-inflammation and anti-atherogenesis in various organs through the activation of AMPK and PPARα via adiponectin receptor (AdipoR)-1 and AdipoR-2, respectively. It has been also suggested that adiponectin confers renoprotective effects in type 1 diabetes. Many of the effects of resveratrol are consistent with the activation of AMPK-PGC-1, which play key roles in the regulation of lipids and glucose homeostasis, and in the control of oxidative stress.
Methods: Male db/db mice and db/m mice at 8 weeks of age treated with or without resveratrol (20 mg/Kg) for 12 weeks. We measured renal functional and histological changes. Intrarenal Adipo R-1 and R-2, AMPK, SIRT1and FoxO1 and 3a expressions and subsequent oxidative stress markers were also measured.
Results: In db/db mice, resveratrol decreased albuminuria, glomerular matrix expansions, inflammation and increased apoptosis in the glomerulus. Resveratrol increased the phosphorylation of AMPK and SIRT1, and decreased phosphorylation of the key downstream effecters, the FoxO1 and FoxO3a, through increases in AdoipoR-1 and AdipoR-2 in the renal cortex. Furthermore, resveratrol increased the expressions of PGC-1-ERR-1a, decreased sterol-regulatory element-binding protein1 (SREBP1)and increased phosphorylated acetyl-CoA carboxylase (ACC), which lowered the non-esterified fatty acid and triacylglycerol contents in the kidneys, resulting in decreases in apoptosis and oxidative stress associated with eNOS activation. In cultured HGECs, resveratrol prevented HGECs from high glucose-induced oxidative stress and apoptosis via increases in the expression of AdipoR-1 and AdipoR-2 and their downstream effecters, the phosphorylation of AMPK and SIRT1 signaling.
Conclusions/interpretations: The results suggest that resveratrol prevents diabetic nephropathy in db/db mice by the increases in expressions of AdipoR-1 and Adipo-R2 and subsequently phosphorylates AMPK, which seems to be related to prevent lipotoxicity-induced renal damage in the kidneys.

Key Words: 당뇨병성 신증, 레즈베라트롤, 아디포넥틴
Diabetic nephropathy, Resveratrol, Adiponectin