

Resveratrol exerts anti-obesity effects via mechanisms involving down-regulation of adipogenic and inflammatory processes in mice

K. Soyoung, J. Yoojeong, C. Youngshim and P. Taesun

Department of Food and Nutrition, Yonsei University, 262 Seongsanno Seodaemun-gu, Seoul 120-749, Korea

Resveratrol is a natural polyphenolic stilbene derivative found in a variety of edible fruits, including nuts, berries, and grape skin⁽¹⁾. Although resveratrol has been suggested to improve thermogenesis in the brown adipose tissues of obese animals, there have been no reports on the anti-adipogenic and anti-inflammatory effects of resveratrol in the white adipose tissues of obese animals. The primary aim of this study was to investigate whether resveratrol attenuates high-fat diet (HFD)-induced adipogenesis and inflammation in the epididymal fat tissues of mice and to explore the underlying mechanisms involved in this attenuation. Male C57BL/6N mice were fed a normal diet (*n* 10), HFD (*n* 10) or a 0.4% resveratrol-supplemented diet (RSD, *n* 10) for 10 weeks. The plasma and hepatic lipid levels were determined by enzymatic kits, and the adipose tissue gene and protein expression levels were analysed via RT-PCR and Western blotting, respectively. These data were analysed using ANOVA with Duncan's multiple-range tests.

In comparison with HFD mice, mice fed with a RSD showed significantly ($P < 0.05$) lower body weight gain (−48%), visceral fat-pad weights (−58%) and plasma levels of TAG, FFA, total cholesterol, glucose, TNF α and MCP1. Resveratrol significantly ($P < 0.05$) reversed the HFD-induced up-regulation of galanin-mediated signalling molecules (GalR1/2, PKC δ , Cyc-D, E2F1 and p-ERK) and key adipogenic genes (PPAR γ 2, C/EBP α , SREBP-1c, FAS, LPL, aP2 and leptin) in the epididymal adipose tissues of mice. Furthermore, resveratrol significantly ($P < 0.05$) attenuated the HFD-induced up-regulation of pro-inflammatory cytokines (TNF α , IFN α , IFN β and IL-6) and their upstream signalling molecules (TLR2/4, MyD88, Tirap, TRIF, TRAF6, IRF5, p-IRF3 and NF- κ B) in the adipose tissues of mice. The results of this study suggest that resveratrol inhibits visceral adipogenesis by suppressing the galanin-mediated adipogenesis signalling cascade. It may also attenuate cytokine production in the adipose tissue by repressing the TLR2- and TLR4-mediated pro-inflammatory signalling cascades in HFD-fed mice (Fig. 1). The results of this study suggest that resveratrol inhibits visceral adipogenesis by suppressing the galanin-mediated adipogenesis signalling cascade. It may also attenuate cytokine production in the adipose tissue by repressing the TLR2- and TLR4-mediated pro-inflammatory signalling cascades in HFD-fed mice.

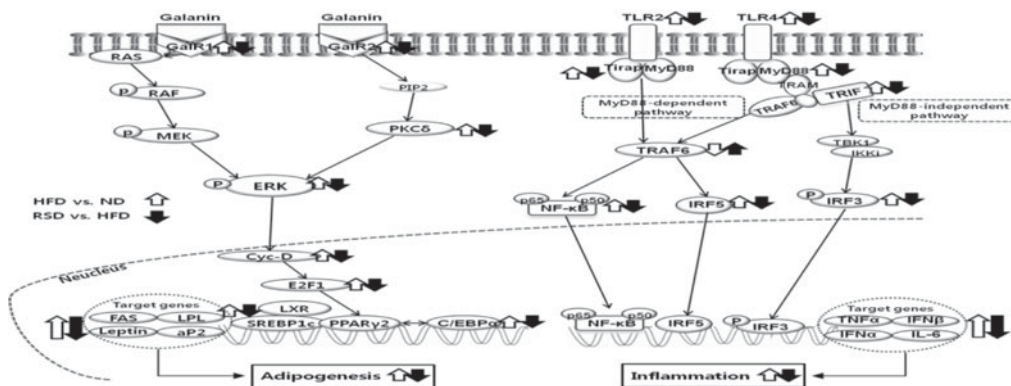


Fig. 1. The possible molecular mechanisms of dietary resveratrol in attenuating adipogenesis and inflammation induced by HFD.

1. Ren S & Lien EJ (1997) *Prog Drug Res* 48, 147–171.