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The Effects of High Fat Diet and Resveratrol on Mitochondrial Activity of Brown Adipocytes (*Endocrinol Metab* 2016;31:328-35, Cheol Ryong Ku et al.)

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We would like to thank Professor Cha for reading our manuscript and for providing valuable comments on the study.

In our manuscript published in volume 31, issue 2 of *Endocrinology and Metabolism*, we reported that resveratrol (RSV) can improve insulin resistance through a mechanism that might be associated with mitochondrial activity of brown adipocyte [1]. RSV increased the number of brown adipocytes in both standard diet (SD) and high fat (HF) diet-fed Otsuka Long Evans Tokushima Fatty (OLETF) rats, which are a rat model of type 2 diabetes mellitus. Furthermore, only the HF diet-fed OLETF fats presented the increased mitochondrial activity demonstrated by increased expression of uncoupling protein 1 and phospho-AMP-activated protein kinase. These results are in agreement with those of a previous study showing that RSV had various biological activities affecting the improvement of obesity and diabetes [2]. Professor Cha commented on two major findings in our manuscript. One is the discordant effect of RSV on brown adipocytes according to the classification of diet, SD or HF. RSV accelerated the mitochondrial activity of brown adipocyte only in HF diet-fed OLETF rats. The other was on the increased expression of estrogen receptor (ER) α in brown adipocytes after treatment with RSV.

The fat concentration in HF chow could be a factor in the discordant effects of RSV on brown adipocytes of SD- and HF-fed OLETF rats. In this study, we used an HF diet consisting of 41% fat, which was relatively lower than those in other studies (60% to 70%). Because brown adipocytes are activated in physiologic conditions of over-nutrition [3], HF diet and RSV might have a synergic effect on activation of brown adipocytes in this animal model.

We evaluated the expression of both ER-α and -β in brown adipocytes before and after RSV treatment. In brown adipocytes, ER-α was prominent, and there was minimal expression of ER-β. Furthermore, RSV treatment did not change the expression of ER-β. ER-α, -β, and G protein-coupled estrogen receptor 1/G protein coupled receptor 30 have important roles in regulating the stimulus-secretion system associated with E2, especially in metabolic syndrome [4]. Considering that RSV is a natural polyphenol and has phytoesterogenic effects, further studies evaluating the effect of RSV on each ER subtype in various endocrine organs will be important in investigating the effect of RSV on metabolic syndrome.

I would like to again thank Professor Cha for the insightful and comprehensive review of our manuscript.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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