Up-regulation of Adiponectin by resveratrol: the essential roles of the Akt/FOXO1 and AMP-activated protein kinase signaling pathways and DsbA-L.


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OBJECTIVE: The natural polyphenol resveratrol (RSV) displays a wide spectrum of health beneficial activities, yet the precise mechanisms remain to be fully elucidated. Here we show that RSV promotes the multimerization and cellular levels of adiponectin in 3T3-L1 adipocytes.

METHODS AND RESULTS: The stimulatory effect of RSV was not affected by knocking out Sirt1, but was diminished by suppressing the expression levels of DsbA-L, a recently identified adiponectin-interactive protein that promotes adiponectin multimerization. Suppression of the Akt signaling pathway resulted in an increase in the expression levels of DsbA-L and adiponectin. On the other hand, knocking out FOXO1 or suppressing the activity or expression levels of the AMP-activated protein kinase (AMPK) down-regulated DsbA-L and adiponectin. The stimulatory effect of RSV on adiponectin and DsbA-L expression was completely diminished in FOXO1-suppressed and AMPK-inactivated 3T3-L1 adipocytes.

CONCLUSIONS: Taken together, our results demonstrate that RSV promotes adiponectin multimerization in 3T3-L1 adipocytes via a Sirt1-independent mechanism. In addition, we show that the stimulatory effect of RSV is regulated by both the Akt/FOXO1 and the AMPK signaling pathways. Last, we show that DsbA-L plays a critical role in the promoting effect of RSV on adiponectin multimerization and cellular levels.

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