

POSTER PRESENTATION

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Resveratrol ameliorates aging-related metabolic phenotypes by inhibiting cAMP phosphodiesterases

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From Metabolism, diet and disease
Washington, DC, USA. 29-31 May 2012

Resveratrol, a polyphenol in red wine, has been reported as a calorie restriction mimetic with potential antiaging and antidiabetogenic properties. It is widely consumed as a nutritional supplement, but its mechanism of action remains a mystery. Here, we report that the metabolic effects of resveratrol result from competitive inhibition of cAMP-degrading phosphodiesterases, leading to elevated cAMP levels. The resulting activation of Epac1, a cAMP effector protein, increases intracellular Ca²⁺ levels and activates the CamKKβ-AMPK pathway via phospholipase C and the ryanodine receptor Ca²⁺-release channel. As a consequence, resveratrol increases NAD⁺ and the activity of Sirt1. Inhibiting PDE4 with rolipram reproduces all of the metabolic benefits of resveratrol, including prevention of diet-induced obesity and an increase in mitochondrial function, physical stamina, and glucose tolerance in mice.

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Published: 27 June 2012

doi:10.1186/1753-6561-6-S3-P73

Cite this article as: Park et al.: Resveratrol ameliorates aging-related metabolic phenotypes by inhibiting cAMP phosphodiesterases. *BMC Proceedings* 2012 **6**(Suppl 3):P73.

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