

# EXERCISE AND SPORT SCIENCES REVIEWS



## **ESSR Journal Club**

**Covered Article:** “Mitochondrial Protection by Resveratrol” by Zoltan Ungvari, William E. Sonntag, Rafael de Cabo, Joseph A. Baur, and Anna Csizsar  
*Exercise and Sport Sciences Reviews*. 39(3):128-132. July 2011.

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1. Resveratrol is considered a mimetic for dietary restriction. Compare and contrast the wide scope of actions of dietary restriction and resveratrol intervention.
2. One of the take-home messages of the paper is that resveratrol seems to mimic some, but not all the beneficial effects of dietary restriction. Discuss potential mechanisms that may explain the varied responses in light of similar transcriptional profiles. For instance, identify how translational regulation may explain the varied physiological responses with resveratrol. Identify and discuss the tissue-specific responses.
3. If resveratrol-induced mitochondrial biogenesis occurs through activation of PGC-1 $\alpha$ , identify other PGC-1 $\alpha$ -dependent effects that would be present in the animals receiving resveratrol (e.g., energy homeostasis).
4. Resveratrol's putative role in reducing oxidative stress is likely a combination of many factors. Identify the multiple mechanisms by which resveratrol may reduce oxidative stress, consider both mitochondrial and nonmitochondrial cellular events. Because the bioavailability of resveratrol is low due to its rapid first-pass metabolism, is it possible to consider the role of resveratrol as a direct scavenger of ROS?
5. Despite the growing evidence that resveratrol confers cardiac and vascular protective effects in preclinical disease models, the precise molecular and cellular mechanisms of its action remain elusive. Although resveratrol elicits complex cellular responses by promoting cell survival, maintaining cellular energetics, and attenuating proinflammatory phenotypic changes induced by oxidative stressors, NF-E2-related factor 2 (Nrf2), a transcription factor that regulates coordinated key antioxidant responses in cells may be an important mechanism by which resveratrol exerts its beneficial effects. Discuss the possibility that SIRT1 acts as a permissive factor, modulating Nrf2-driven responses. Moreover, discuss the possibility that the expression of SIRT1 is regulated by Nrf2 and that downstream pathways regulated by SIRT1 and Nrf2 might act synergistically.

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6. Because vascular oxidative-nitrosative stress is a hallmark of cardiovascular aging and is known to be involved in the pathophysiology of multiple diabetic complications, it is desirable to develop pharmacological treatment approaches that can simultaneously target several of the involved pathophysiological processes. Discuss the advantages and disadvantages of targeting “master regulators” of cellular programs such as PGC-1 $\alpha$  and Nrf2 for large scale pharmacological treatment. Is it safe to pharmacologically target several simultaneous cellular pathways involved in the development of cardiovascular diseases in high-risk patients?
7. In your opinion, how does “exercise” fit into the Figure of the article (page 129). Discuss the cellular and molecular events of exercise that mimic the responses of resveratrol intervention. Additionally, what are the advantages of ‘exercise’ compared to pharmacological treatments? Identify the disadvantages.