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Resveratrol Impairs Mitochondrial Respiration of *Saccharomyces cerevisiae*

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Abstract

The biomedical importance of resveratrol (RSV) has been growing in recent years due to widely health benefits attributed to this phytochemical. Despite substantial recent progress, the mechanism of RSV action is still unclear. The inhibition of mitochondrial respiration has been postulated as the principal molecular target of RSV. It has been demonstrated that RSV exerts an inhibition of the electron transport chain and the F_0F_1-ATPase in evolutionarily divergent organisms such *Escherichia coli* and *Mus musculus.* Nonetheless, further evidence is necessary to support the hypothesis that inhibition of respiration is associated with biological benefits of RSV. To better understand RSV effects on cellular respiration, we proposed the use of *Saccharomyces cerevisiae* as a model, which has been widely used in the study of mitochondrial processes. Additionally, yeast was characterized by fermentative-respiratory growth; this phenotype could help us to further understand what happen with the role of RSV when cells are not respiring. Interestingly, we found that high doses of RSV (1000 µM) inhibit specifically respiratory growth, but it has not significant effect on fermentative growth both measured on high-glucose conditions (diauxic growth). The influence of RSV on respiratory growth was comparable to the instigated by Antimycin A (10 µg/mL), a well-known inhibitor of complex III of the electron transport chain. Furthermore, we observed that low doses of RSV (30 µM) were sufficient to inhibit mitochondrial respiration of *S. cerevisiae* in state 4, when it was tested with glucose. Besides, we recorded a decrease in cell respiratory control ratio caused by RSV (30 µM), which implicates a mitochondrial dysfunction produced by RSV. These data imply that low doses of RSV are sufficient to impair mitochondrial respiration and even high doses of RSV have not effect on fermentative growth. Altogether, these data indicate that RSV acts specifically on cellular respiration, which could be the main target of this stilbene in *S. cerevisiae*. This work was partially funded by PRODEP (ITESCH-002) and Tecnológico Nacional de México (IBIO/005/2014).

Footnotes

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