

Abstract

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Substrate-specific activation of sirtuins by resveratrol.

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BACKGROUND: Resveratrol, a small molecule found in red wine, is reported to slow aging in simple eukaryotes and has been suggested as a potential calorie restriction mimetic. Resveratrol has also been reported to act as a sirtuin activator, and this property has been proposed to account for its anti-aging effects.

OBJECTIVE: We show here that resveratrol is a substrate-specific activator of yeast Sir2 and human SirT1.

RESULTS: In particular, we observed that, in vitro, resveratrol enhances binding and deacetylation of peptide substrates that contain Fluor de Lys, a non-physiological fluorescent moiety, but has no effect on binding and deacetylation of acetylated peptides lacking the fluorophore. Consistent with these biochemical data we found that in three different yeast strain backgrounds, resveratrol has no detectable effect on Sir2 activity in vivo, as measured by rDNA recombination, transcriptional silencing near telomeres, and life span.

CONCLUSION: In light of these findings, the mechanism accounting for putative longevity effects of resveratrol should be reexamined.

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