Sir2 and glycerol underlie the pro-longevity effect of quercetin during yeast chronological aging

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Abstract: Quercetin (QUER), a natural polyphenolic compound belonging to flavonols, is one of the major abundant naturally occurring flavonoids in the human diet via vegetables and fruits. Although high-purity QUER is commercially available as a nutraceutical due to its beneficial properties for human health, including anti-aging effects[2], target molecules/pathways underlying its pro-longevity potential have yet to be fully clarified.

To study the effects of QUER on cellular aging, we used the yeast *Saccharomyces cerevisiae* as a model system in the context of chronological aging, the established model for simulating the aging of postmitotic quiescent mammalian cells[3,4].

The results indicate that QUER determines a longevity extension of yeast cultures accompanied by a decrease in oxidative stress in line with its inbuilt characteristics of antioxidant. In addition, QUER deeply influences carbon metabolism allowing cells to acquire features useful for better survival during chronological aging.

In particular, QUER improves a pro-longevity anabolism toward gluconeogenesis due to an enhanced catabolism of C2 by-products of yeast fermentation and glycerol. The former is attributable to Sir2-dependent activity of phosphoenolpyruvate carboxykinase and the latter to the L-glycerol 3-phosphate pathway. This combined supply to gluconeogenesis leads to an increase in the reserve carbohydrate trehalose ensuring long term survival during chronological aging[5].

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