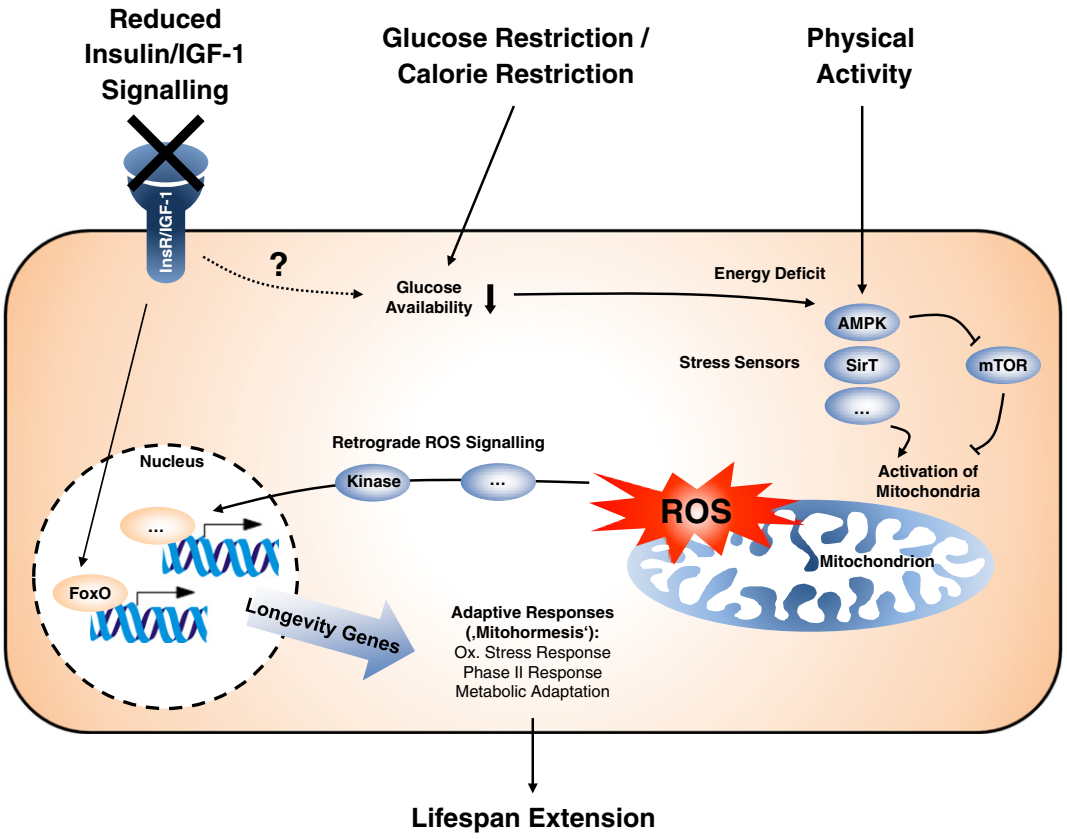


**Fig. 1.** Life-span-extending interventions generate mitochondrial ROS signals to activate longevity-promoting genes. For calorie and especially glucose restriction, but also for physical exercise, evidence exists that these interventions extend life span in various model organisms, but also increase mitochondrial metabolism. This activation promotes formation of mitochondrial ROS signals that cause an adaptive response (mitohormesis) in the nucleus to promote longevity. The possible link to impaired insulin/IGF-1 signaling, however, remains to be experimentally shown.

sensitive MAP-kinase cascades and redox-sensitive transcription factors) that culminate in an overall adaptive response, represented by an improvement in antioxidant capacity and finally longevity. Cotreatment with antioxidants inhibits ROS signal transduction and prevents the adaptive response. Thus, glucose-restriction-mediated longevity is abolished.

Therefore, interventions that induce mitochondrial function seem to be promising in regard to regulation of life expectancy. Accordingly, moderate physical activity, an intervention that is known to be health beneficial in a broad spectrum [120,121,237–239], is assumed to cause induction of mitochondrial metabolism and ROS production [240–242]. Moreover, health-promoting effects were demonstrated to be reduced if subjects exposed to physical activity were cotreated with antioxidant supplements [186,243].

## Conclusions

Taken together, the data summarized and discussed in this review support the conclusion that CR, glucose restriction, and moderate physical activity share, at least in part, common mechanistic features that may influence the aging process, i.e., enhanced mitochondrial activity and subsequently increased ROS formation that ultimately induce an adaptive response (increased defense mechanisms and improved stress resistance), which culminates in metabolic health and extended longevity.

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