

UNDERSTANDING SIR2-INDEPENDENT LIFESPAN EXTENSION BY CALORIC RESTRICTION

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The lifespan of yeast, as well as many other species including mammals, is extended by caloric restriction (CR). Sir2 is an NAD⁺-dependent histone deacetylase that has been proposed to underlie the lifespan extending effects of CR. This hypothesis has been challenged by the observation that CR can extend lifespan in the absence of Sir2. We have conducted a yeast screen for genes capable of suppressing the instability of ribosomal DNA, the mechanism by which Sir2 extends lifespan. We have identified a CR-responsive protein capable of suppressing the formation of extrachromosomal rDNA circles and extending lifespan in the absence of Sir2.