Targeting Chromatin Aging - The Epigenetic Impact of Longevity-Associated Interventions

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0.0 Abstract

A rapidly growing body of evidence has shown that chromatin undergoes radical alterations as an organism ages, but how these changes relate to aging itself is an open question. It is likely that these processes contribute to genomic instability and loss of transcriptional fidelity, which in turn drives deleterious age-related phenotypes. Interventions associated with increased healthspan and longevity such as reduced insulin / IGF signalling (IIS), inhibition of mTOR and energy depletion resulting in SIRT1 / AMPK activation, all have beneficial effects which ameliorate multiple facets of age-associated decline. The impact of these interventions on the epigenome is less certain. In this review we highlight the potential of these interventions to act directly upon the epigenome and promote a youthful chromatin landscape, maintaining genetic and transcriptional memory throughout the lifecourse. We propose that this is a fundamental mechanism through which these interventions are able to curtail the incidence of age-related disease. By revisiting these well characterised interventions, we may be able to identify targetable effectors of chromatin function and use this knowledge to enhance healthspan and longevity in human populations through the measured application of dietary and small molecule interventions.

Keywords

Epigenetics; Aging; Histone; Methylation; Longevity; Chromatin; Rapamycin; Insulin; Calorie Restriction; Healthspan; mTOR; AMPK; SIRT1; IGF;