

## **Racing against the (epigenetic) clock: exercise training slows down epigenetic aging in skeletal muscle**

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Ageing constitutes an important health and economic burden on society, and a primary hallmark of ageing is the alteration of the epigenetic landscape. Regular exercise promotes healthy aging and can alter the epigenome of skeletal muscle. However, it is unknown whether exercise promotes healthy aging through this alteration of the epigenetic landscape.

To address this gap, we integrated phenotypic, epigenetic and molecular data from the Gene SMART (Genes and the Skeletal Muscle Adaptive Response to Training) exercise training study, along with other open-access data. Here, we report that higher fitness levels are associated with younger epigenetic profiles in skeletal muscle. In addition, age- and fitness-associated epigenetic patterns target similar pathways related to muscle structure and function. Finally, four weeks of high-intensity interval training caused small shifts in epigenetic patterns towards a younger epigenome.

Collectively, these results suggest that similarly to caloric restriction, aerobic exercise training delays age-related methylation drift in human skeletal muscle. This provides fundamental epigenetic knowledge on how exercise slows down the ageing process at the molecular level, and it conveys a strong message regarding the potential of exercise to attenuate the detrimental effects of ageing.