

# Physical Activity Extends People's Life: Does It Also Extend Telomeres Length?

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## Physical Activity

Physical Activity (PA) is widely recognized as being associated with healthy aging and reduced risk for a number of chronic conditions, such as obesity, diabetes, bone disease, hypertension. Thus, PA has been associated to longer life expectancy: “*survival of the fittest*”, catching a double meaning of the Darwinian concept [1,2]. Several biological changes contribute to the aging process, which can be defined as a time-dependent progressive decline of the physiological functions necessary for survival. At the cellular level, senescence can be described as a state of stable cell cycle arrest, a prelude to apoptosis, in response to diverse stressors, e.g. oxidative or genotoxic stress, telomere shortening, dysfunctional autophagy etc. Senescent cells exhibit a characteristic inflammatory secretome, called SASP (Senescence-Associated Secretory Phenotype) [3]. Chronic mild/moderate PA may attenuate aging by improving systemic inflammation, while physical inactivity has been demonstrated to enhance free radicals production and cellular senescence in skeletal muscle [4]. Furthermore, PA promotes mobilization and differentiation of bone marrow stem cells [5]. Several studies have shown that while moderately intense chronic physical activity improves health and promotes wellbeing, stressful endurance physical activity may trigger adverse effects [2,6,7]. Intense aerobic physical exercise may also have genotoxic effects, since it produces transient DNA injury [8]. Telomeres are specific repetitive DNA structures that protect eukaryotic chromosomes from degradation. Human telomere length varies between individuals from 5000 to 15000 bp at birth; in successive somatic cells divisions Telomere Length (TL) shortens progressively (30-200 bps per division) down to a critical threshold. The ATM-p53-p21 axis is then activated, preventing further proliferative activity. An inverse association between chronological age and telomere length has been well documented [9,10]; noteworthy telomere shortening is not linear unlike chronological age, and it predominantly affects highly proliferative tissues. Telomere length may be preserved by telomerase reverse transcriptase, which is active in embryonic and adult stem cells. Telomeres are considered candidate biomarkers of aging: several studies published so far have investigated in various populations whether:

- Physical activity and exercise affect telomerase activity;
- Physically active subjects have longer telomere lengths than sedentary controls.

Telomeres length was assessed mostly in white blood cells (LTL=Leukocyte Telomere Length) and seldom in skeletal muscle cells, in response to aerobic training, endurance training, moderate and self-reported PA [11,12]. Inconsistent results have been obtained.

Thorough systematic reviews and meta-analysis of the ample literature concluded that insufficient quality evidence exists for conclusive association of PA with LTL; more than 50% of studies reviewed found no relationship [13]. More rigorous studies are needed in order to answer the above issues; nevertheless it is interesting to speculate about the molecular mechanisms possibly involved in a positive association between PA and TL preservation.

## Telomerase activity

Experiments in animal models and a few studies in humans have shown exercise-induced telomerase activity increase in progenitor stem cells [14-16].

## Role of oxidative stress

Telomeres are very susceptible to oxidative damage, which impairs DNA repair mechanisms, nevertheless mild exposure to oxidative stress seems to have a beneficial effect since it stimulates anti-oxidant defense systems [17]. This may explain why TL is better preserved in chronic elder endurance runners, compared to age-matched sedentary controls, while TL is significantly reduced in athletes engaged in extreme trail races (ultra-marathon) [18].

In conclusion, overall data from the literature suggest that chronic training may provide protective effects on TL and against inflammation, attenuating biological aging. Conversely, acute exposure to very strenuous physical exercise implies telomere shortening, probably consequent to oxidative DNA damage, and triggers inflammatory response.

*Take home lesson: “Physical activity: praise and restraint; neither too little nor too much”.*

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