Nuclear Respiratory Factor 1 and endurance exercise promote human telomere transcription

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DNA breaks activate the DNA damage response and, if left unrepaired, trigger cellular senescence. Telomeres are specialized nucleoprotein structures that protect chromosome ends from persistent DNA damage response activation. Whether protection can be enhanced to counteract the age-dependent decline in telomere integrity is a challenging question. TElomeric Repeat-containing RNA, TERRA, transcribed from telomeres, emerged as important players in telomere integrity. How human telomere transcription is regulated is however still largely unknown. Here, we identify Nuclear Respiratory Factor 1 and Peroxisome proliferator-activated receptor γ Coactivator 1α as regulators of human telomere transcription. Agreeing with an upstream regulation of these factors by AMP-activated protein kinase (AMPK), pharmacological activation of AMPK in cancer cell lines or normal non-proliferating myotubes up-regulated TERRA, thereby linking metabolism to telomere fitness. Importantly, cycling endurance exercise, associated with AMPK activation, increased TERRA levels in skeletal muscle biopsies obtained from ten healthy young volunteers. The data support the idea that exercise may protect against aging.