Abstract

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Telomeres: influencing the rate of aging.

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BACKGROUND: Evidence is reviewed that suggests a central role for telomeres in one major model of biological aging, namely, proliferative senescence. Telomeric shortening with each cell division does not only act as a biological clock, but appears to trigger the ultimate loss of proliferative ability via activation of the p53-dependent check point system. Oxidative stress induces single-stranded damage in telomeric DNA.

OBSERVATIONS: It is not clear yet whether this damage occurs in the form of single-stranded gaps or overhangs or as arbitrarily distributed single-stranded breaks. However, in contradiction to the rest of the genome, this damage is not repaired in telomeres. It is, therefore, the major cause of telomere shortening even under standard in vitro cell culture conditions.

CONCLUSION: Therefore, controlling the oxidative load onto DNA, in general, and, especially, onto telomeres might become a major factor to influence the rate of aging. Further experiments demonstrate that G-rich single-stranded telomeric DNA fragments do activate the p53 check point control, leading to an inhibition of proliferation in wild-type p53 cells. Not only the shortening of telomeres down to a "signal value," but accumulation of telomeric single-stranded DNA fragments, as well, could be relevant triggers for proliferative senescence.

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