

# Abstract

Ann N Y Acad Sci. 2000 Jun;908:99-110.

## Role of oxidative stress in telomere length regulation and replicative senescence.

von Zglinicki T.

Institute of Pathology, Charité, Humboldt University Berlin, Germany.

**BACKGROUND:** Replicative senescence is tied into organismal aging processes in more than one respect, and telomeres appear to be the major trigger of replicative senescence under many conditions in vitro and in vivo.

**OBJECTIVE:** However, the structure-function relationships in telomeres, the mechanisms of telomere shortening with advancing replicative age, and the regulation of senescence by telomeres are far from understood.

**METHODS:** Combining recent data on telomere structure, function of telomere-binding proteins, and sensitivity of telomeres to oxidative damage, an integrative model of telomere shortening and signaling is developed.

**RESULTS:** The model suggests that t-loop formation hinders access of repair proteins to telomeres, leading to accumulation of a basic sites and single-strand breaks. These might contribute to accelerated telomere shortening by transient stalling of replication as well as, if present in high concentrations, to a relief of torsional tension which might destabilize the telomeric loop structure. As a result, the single-stranded G-rich overhang, which is present at the very ends of telomeres but is normally protected at the base of the telomeric loop, will be exposed to the nucleoplasm.

**CONCLUSION:** Free G-rich telomeric single strands are a strong inductor of the p53 pathway, and exposure of the overhangs seems to be the first step in the signal transduction cascade to replicative senescence.

PMID: 10911951

