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Ectopic expression of telomerase safely increases health span and life span.

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Abstract

The absence of telomerase from somatic cells of mammals has significant consequences for aging. First, it limits the number of potential cell divisions and in so doing sets limits on both life span and cancer cell proliferation. Second, shortened telomeres are known to result in physiological dysfunction, including playing a role in human diseases such as Werner syndrome and ataxia telangiectasia. Ectopic expression of the catalytic subunit of telomerase, telomerase reverse transcriptase (TERT), has been reported to extend life span by as much as 40% in cancer-resistant mice. On the other hand, ectopic expression of TERT promotes cancer in normal mice. However, transient induction of TERT by an astragalus-derived compound increases health span without an apparent increase in cancer incidence. Ectopic expression of TERT using adeno-associated virus serotype 9 (AAV9)-based gene therapy in adult mice increases both health span and life span without increasing cancer incidence. Available evidence suggests that increases in life span may require both elongated telomeres and the continuous presence of telomerase to stimulate the WNT/β-catenin signaling pathway. The recent observation that WNT/β-catenin signaling can stimulate TERT expression raises the possibility of a positive feedback loop between TERT and WNT/β-catenin. Such a positive feedback loop implies that safety must be carefully considered in the development of drugs that stimulate telomerase activity.