Telomerase maintains telomere structure in normal human cells.

Masutomi K, Yu EY, Khurts S, Ben-Porath I, Currier JL, Metz GB, Brooks MW, Kaneko S, Murakami S, DeCaprio JA, Weinberg RA, Stewart SA, Hahn WC.

In normal human cells, telomeres shorten with successive rounds of cell division, and immortalization correlates with stabilization of telomere length. These observations suggest that human cancer cells achieve immortalization in large part through the illegitimate activation of telomerase expression.

We found that the rate-limiting telomerase catalytic subunit hTERT is expressed in cycling primary presenescent human fibroblasts, previously believed to lack hTERT expression and telomerase activity. Disruption of telomerase activity in normal human cells by knock-down hTERT slows cell proliferation, restricts cell lifespan, and alters the maintenance of the 3' single-stranded telomeric overhang without changing the rate of overall telomere shortening. Together, these observations support the view that telomerase and telomere structure are dynamically regulated in normal human cells and that telomere length alone is unlikely to trigger entry into replicative senescence.

(This project was carried out by an international collaboration with Dr. Hahn WC, Dana-Farber Cancer Institute, Harvard Medical School, and Dr. Weinberg RA, Whitehead Inst. MIT.)

Reference 1: Masutomi K, Yu EY, Khurts S, Ben-Porath I, Currier JL, Metz GB, Brooks MW, Kaneko S, Murakami S, DeCaprio JA, Weinberg RA, Stewart SA, Hahn WC. (2003) Cell, 114(2):241-253.