A telomere is a region of repetitive DNA at the end of a chromosome that protects the end of the chromosome from deterioration. They are disposable buffers that block the ends of the chromosomes. Telomeres are consumed during cell division and replenished by the enzyme telomerase reverse transcriptase.

Telomeres in most human cells shorten with each round of DNA replication, because they lack the enzyme telomerase. Telomere shortening normally limits cells to a fixed number of divisions, which suggest that this is responsible for aging on the cellular level and sets a limit on lifespan.

Several studies have found that reduced leukocyte telomere length is associated with coronary artery disease. (Farzaneh-Far, Cawthon et al. 2008) (Mainous, Codd et al. 2010) (Ogami, Ikura et al. 2004)

High telomerase activity is detected in most cancer cells. It is, however, a biomarker of cell proliferation, not malignant transformation. (Kim, Piatyszek et al. 1994) (Belair, Yeager et al. 1997)

Imetelstat sodium

Imetelstat sodium (GRN163L) is a new telomerase antagonist drug that is currently in Phase I/II clinical trials for several hematological and solid tumor malignancies. (Marian, Wright et al. 2009)

Estrogens

Recent studies indicate that estrogen regulates cell proliferative fates by a mechanism of reprogramming the size of telomeres in the estrogen target cells. This is achieved by up-regulating the telomerase reverse transcriptase (TERT) gene in a temporal and spatial manner. (Li, Simpson et al. 2010)

Estrogen deficiency leads to telomerase inhibition, telomere shortening and reduced cell proliferation in the adrenal gland of mice. (Bayne, Jones et al. 2008) (Bayne, Li et al. 2011)

A recent study found that endometriosis is associated with aberrant endometrial expression of telomerase and increased telomere length. There was positive correlation of the circulating estradiol with peripheral blood telomere length in women. (Hapangama, Turner et al. 2008)
Sex hormones, acting on the TERT gene, increase telomerase activity in human primary hematopoietic cells. Androgens appear to regulate telomerase expression and activity mainly by aromatization and through estrogen receptor alpha. (Calado, Yewdell et al. 2009)

Estrone and estradiol hormone levels were significantly inversely associated with relative telomere length (P = 0.02). (De Vivo, Prescott et al. 2009)

An older study found that telomere lengths were longer in postmenopausal women who had a history of long-term hormone therapy than in postmenopausal women without hormone therapy. (Lee, Im et al. 2005)

**Melatonin**

Melatonin inhibits telomerase activity and expression induced by either natural estrogens or xenoestrogens. (Korkmaz, Sanchez-Barcelo et al. 2009)

A recent article proposed that melatonin has the potential to treat or prevent age-related macular degeneration through stimulation of telomerase activity. (Rastmanesh 2010)

An older study found that melatonin inhibits telomerase activity in the MCF-7 tumor cell line both in vivo and in vitro. (Leon-Blanco, Guerrero et al. 2003)

**Diet**

Healthy lifestyle factors (i.e., lower BMI, more exercise, tobacco abstinence, diets high in fruit and vegetables) are associated with greater telomere length. (Mirabello, Huang et al. 2009)

After multivariate adjustment, dietary fiber intake was positively associated with telomere length (z score), specifically cereal fiber, with an increase of 0.19 units between the lowest and highest quintiles (P = 0.007, P for trend = 0.03). Although total fat intake was not associated with telomere length, polyunsaturated fatty acid intake (-0.26 units, quintile 5 compared with quintile 1: P = 0.002, P for trend = 0.02), specifically linoleic acid intake, was inversely associated with telomere length after multivariate adjustment (-0.32 units; P = 0.001, P for trend = 0.05). Waist circumference was inversely associated with telomere length [0.15-unit difference in z score in a comparison of the highest (> or = 32 in, 81.28 cm) with the lowest (< or = 28 in, 71.12 cm) category (P = 0.01, P for trend = 0.02) in the multivariate model]. (Cassidy, De Vivo et al. 2010)

Shorter telomeres have been associated with coronary artery calcium (CAC), a validated indicator of coronary atherosclerosis. A recent study examined telomere length in a sample of subjects aged 40 to 64 years with no previous diagnosis of coronary heart disease, stroke, diabetes mellitus, or cancer (n = 318). Logistic regression analyses controlling for age, gender, race/ethnicity, and Framingham risk score revealed that the relation
between having shorter telomeres and the presence of CAC was attenuated in the presence of high social support, low meat consumption, and high fruit and vegetable consumption. Conversely, the subjects with shorter telomeres and less healthy lifestyles had a significantly increased risk of the presence of CAC: low fruit and vegetable consumption (odds ratio 3.30, 95% confidence interval 1.61 to 6.75), high meat consumption (odds ratio 3.33, 95% confidence interval 1.54 to 7.20), and low social support (odds ratio 2.58, 95% confidence interval 1.24 to 5.37). (Diaz, Mainous et al. 2010)

One study found that processed meat intake was associated with telomere length. For every 1 serving/d greater intake of processed meat, the T/S ratio was 0.07 smaller (beta +/- SE: -0.07 +/- 0.03, P = 0.006). (Nettleton, Diez-Roux et al. 2008)

**Multivitamins**

A cross-sectional analysis of data from 586 early participants (age 35-74 y) in the Sister Study examined whether multivitamin use is associated with longer telomeres in women. Compared with nonusers, the relative telomere length of leukocyte DNA was on average 5.1% longer among daily multivitamin users (P for trend = 0.002). In the analysis of micronutrients, higher intakes of vitamins C and E from foods were each associated with longer telomeres, even after adjustment for multivitamin use. Furthermore, intakes of both nutrients were associated with telomere length among women who did not take multivitamins. (Xu, Parks et al. 2009)

**Oxidative Stress**


Oxidative damage is repaired less well in telomeric DNA than elsewhere in the chromosome, and oxidative stress accelerates telomere loss, whereas antioxidants decelerate it. (von Zglinicki 2002)

Mitochondrial DNA damage is closely interrelated with mitochondrial ROS production, and this might also play a causal role for cellular senescence. Improvement of mitochondrial function results in less telomeric damage and slower telomere shortening, while telomere-dependent growth arrest is associated with increased mitochondrial dysfunction. Moreover, telomerase, the enzyme complex that is known to re-elongate shortened telomeres, also appears to have functions independent of telomeres that protect against oxidative stress. (Passos, Saretzki et al. 2007)
Antioxidants

A recent study found that breast cancer risk may be affected by telomere length among premenopausal women or women with low dietary intake of antioxidants or antioxidant supplements.

A population-based case-control study—the Long Island Breast Cancer Study Project—was conducted among 1,067 cases and 1,110 controls. Telomere length was assessed by quantitative PCR. Overall, the mean levels of telomere length (T:S ratio), 15-F(2t)-IsoP and 8-oxodG were not significantly different between cases and controls. Among premenopausal women only, carrying shorter telomeres (Q3 and Q4), as compared with the longest (Q1), was associated with significantly increased breast cancer risk. Age-adjusted OR and 95% CI were 1.71 (1.10-2.67) and 1.61 (1.05-2.45). The 5-F(2t)-IsoP and 8-oxodG biomarkers did not modify the telomere-breast cancer association. A moderate increase in breast cancer risk was observed among women with the shortest telomeres (Q4) and lower dietary and supplemental intake of beta-carotene, vitamin C or E intake [OR (95% CI) = 1.48 (1.08-2.03), 1.39 (1.01-1.92) and 1.57 (1.14-2.18), respectively], although the trend test exhibited statistical significance only within the lower vitamin E intake subgroup (p(trend) = 0.01). (Shen, Gammon et al. 2009)

Vitamin E

Alpha-tocopherol protected against hydrogen peroxide-induced telomere shortening by restoring the telomerase activity. (Makpol, Zainuddin et al. 2010)

Age-dependent telomere shortening is repressed by phosphorylated alphatocopherol together with cellular longevity and intracellular oxidative-stress reduction in human brain microvascular endotheliocytes. (Tanaka, Moritoh et al. 2007)

Tocotrienol

Tocotrienol (unsaturated vitamin E) inhibits protein kinase C activity, resulting in down-regulation of c-myc and human telomerase reverse transcriptase (hTERT) expression, thereby reducing telomerase activity. (Eitsuka, Nakagawa et al. 2006)

Vitamin C

Vitamin C slows down age-dependent telomere shortening via suppression of oxidative stress. (Furumoto, Inoue et al. 1998)

One study showed a slow-down of age-dependent telomere shortening in human skin keratinocytes by anti-oxidative effects of vitamin C concurrently
with reduction of intracellular oxidative stress. (Yokoo, Furumoto et al. 2004)

**Vitamin D**

Combination treatment with 1alpha,25-dihydroxyvitamin D3 and 9-cis-retinoic acid directly inhibits human telomerase reverse transcriptase transcription in prostate cancer cells. (Ikeda, Uemura et al. 2003)

1,25-dihydroxyvitamin D3 induced ovarian cancer cell apoptosis through the down-regulation of telomerase. (Jiang, Bao et al. 2004)

**Folate**

Telomere length in peripheral blood mononuclear cells is associated with folate status in men. Folate status may influence telomere length by affecting DNA integrity and the epigenetic regulation of telomere length through DNA methylation. (Paul, Cattaneo et al. 2009)

**Niacinamide**

Ongoing application of nicotinamide (niacinamide) to normal human fibroblasts not only attenuated expression of the aging phenotype but also increased their replicative lifespan, causing a greater than 1.6-fold increase in the number of population doublings. Although nicotinamide by itself does not act as an antioxidant, the cells cultured in the presence of nicotinamide exhibited reduced levels of reactive oxygen species (ROS) and oxidative damage products associated with cellular senescence, and a decelerated telomere shortening rate without a detectable increase in telomerase activity. (Kang, Lee et al. 2006)

**Arginine**

A recent study found that arginine methylation regulates telomere length and stability. (Mitchell, Glenfield et al. 2009)

Asymmetric dimethylarginine (ADMA) is an endogenous inhibitor of nitric oxide synthase and its accumulation has been associated with cardiovascular disease. A study found that ADMA accelerates senescence, probably via increased oxygen radical formation by inhibiting nitric oxide elaboration. (Bode-Boger, Scalera et al. 2005)

**Omega-3 Fatty Acids**

A study published in JAMA found examined omega-3 fatty acids and telomere length. Individuals in the lowest quartile of DHA+EPA experienced the fastest rate of telomere shortening (0.13 telomere-to-single-copy gene ratio [T/S] units over 5 years; 95% confidence interval [CI], 0.09-0.17), whereas those in the highest quartile experienced the slowest rate of
telomere shortening (0.05 T/S units over 5 years; 95% CI, 0.02-0.08; P < .001 for linear trend across quartiles). Levels of DHA+EPA were associated with less telomere shortening before (unadjusted beta coefficient x 10(-3) = 0.06; 95% CI, 0.02-0.10) and after (adjusted beta coefficient x 10(-3) = 0.05; 95% CI, 0.01-0.08) sequential adjustment for established risk factors and potential confounders. Each 1-SD increase in DHA+EPA levels was associated with a 32% reduction in the odds of telomere shortening (adjusted odds ratio, 0.68; 95% CI, 0.47-0.98). (Farzaneh-Far, Lin et al. 2010)

**Astragalus**

The two isomers of HDTIC compounds from Astragali Radix slow down telomere shortening rate via attenuating oxidative stress and increasing DNA repair ability in human fetal lung diploid fibroblast cells. (Wang, Zhang et al. 2010)

**Ganoderma lucidum**

Ganoderma lucidum can inhibit the viability and growth of re-malignant human urothelial cells by a concomitant induction of apoptosis and inhibition of telomerase activity. (Yuen, Gohel et al. 2008)

**Terminalia chebula**

One study showed the ethanol extract from the fruit of Terminalia chebula (Combretaceae) exhibited significant inhibitory activity on oxidative stress and the age-dependent shortening of the telomeric DNA length. (Na, Bae et al. 2004)

**Uncaria sinensis**

The ethanol extract from the hooks and stems of Uncaria sinensis Havil (Rubiaceae) exhibited significant inhibitory activity on oxidative stress and the age-dependent shortening of the telomeric DNA length. Uncaria is also known as Cat's Claw or Uña de Gato. (Na, Kim et al. 2004)

**Genistein**


Makpol, S., A. Zainuddin, et al. (2010). "Alpha-tocopherol modulates hydrogen peroxide-induced DNA damage and telomere shortening of
human skin fibroblasts derived from differently aged individuals." 
*Planta Med* 76(9): 869-75.


