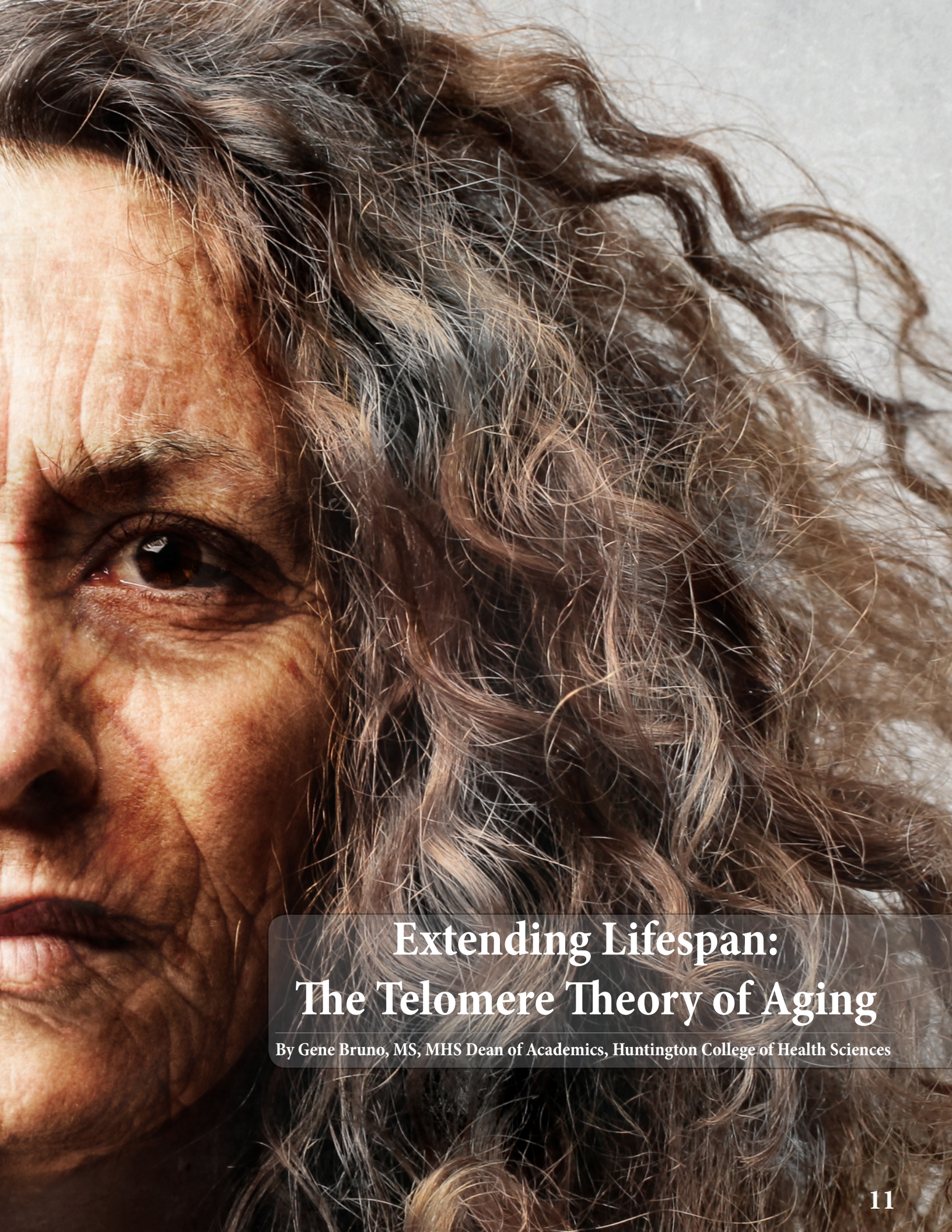

Extending Lifespan: The Telomere Theory of Aging

By Gene Bruno, MS, MHS Dean of Academics, Huntington College of Health Sciences

As cells age, they lose a certain number of base pairs of DNA, known as telomeres, from the end of each chromosome every time cell division takes place.

This is a result of the fact that DNA polymerase, which builds corresponding DNA strands, cannot start the synthesis of the new strand, but must wait for (the enzyme) primase to do the job. As a result, the telomere section of the chromosome cannot be reproduced. Although the telomeres are 'sacrificial' DNA without any necessary information content, there is still a problem. When these telomeres have decreased to a critical length, cell division ceases; although cell senescence (aging) may continue for a time.i This is known as the telomere theory of aging. According to the telomere theory of aging, this inability of a cell to continue successively replicating DNA results in aging.

This finite ability to replicate is known as the **'Hayflick limit',** and has been seen in cultured normal human and animal cells.i Fibroblast cells taken from adults would only divide about 20 times in vitro, although this limit is rarely, if ever, reached in the body.

Here is a more simplistic way to explain this phenomenon: At the ends of our chromosomes are stretches of DNA called telomeres. These telomeres protect our genetic data, making it possible for cells to divide. Telomeres have been compared with the plastic tips on shoelaces because they prevent chromosome ends from fraying and sticking to each other, which would scramble our genetic information. Yet, each time a cell divides, the telomeres get shorter. When they get too short, the cell no longer can divide and becomes inactive or "senescent" or dies. This process is associated with aging.

Telomerase is an enzyme that adds telomere to DNA. Telomerase is found in some cells (e.g., germ cells and stem cells) which must divide continually to perform their functions. This effectively makes those cells 'immortal'. Certain nutraceuticals and nutraceutical combinations have been shown to promote telomerase activity and help increase telomere length. These include green tea, Astragalus membranaceus, Vitamin D, Resveratrol, Grape seed polyphenols, Chlorella, vitamin E, vitamin A, folate, preformed niacin and calcium, and even multivitamins. The following is a discussion of these nutraceuticals.

Green Tea

In a sample of 976 Chinese men aged 65 years and over, telomere length (TL) was measured and daily intake of food groups was assessed. An analysis was undertaken to examine the association between food group intake and TL. The results were that Chinese tea consumption was significantly associated with TL after adjustment for demographics and lifestyle factors (P = 0.002). Mean difference in TL for those in the highest quartile of Chinese tea consumption (>3 cups/d or >750 ml/d) as compared with those in the lowest quartile of Chinese tea consumption (<or= 0.28 cups/d or <or= 70 ml/d) was 0.46 kb, corresponding to approximately a difference of 5 years of life. In conclusion, Chinese tea consumption was positively associated with TL in elderly Chinese men.

Astragalus membranaceus

A studyi assessed the effects of two compounds (HDTIC-1 and HDTIC-2), extracted from Astragalus membranaceus, on telomere shortening rate and DNA repair ability in 2BS cells. The telomere shortening rates of the cells cultured with HDTIC-1 or HDTIC-2 were 31.5 and 41.1 bp with each division, respectively, which were much less than that of the control cells (71.1 bp/PD). We also found that 2BS cells pretreated with HDTIC-1 or HDTIC-2 had a significant reduction in DNA damage after exposure to 200 microM H(2)O(2) for 5 min. Moreover, the 100 microM H(2)O(2)-induced DNA damage was significantly repaired after the damaged cells were continually cultured with HDTIC for 1 h.

These results suggest that HDTIC compounds slow down the telomere shortening rate of 2BS cells, which is mainly due to the biological properties of the compounds including the reduction of DNA damage and the improvement of DNA repair ability. In addition, the slowdown of telomere shortening rate, the reduction of DNA damage, and the improvement of DNA repair ability induced by HDTIC may be responsible for their delay of replicative senescence.

Vitamin D

The objective of this studyi was to examine whether vitamin D concentrations would attenuate the rate of telomere attrition in leukocytes, such that higher vitamin D concentrations would be associated with longer Leukocyte telomere length (LTL). Serum vitamin D concentrations were measured in 2160 women aged 18-79 y (mean age: 49.4) from a large population-based cohort of twins. The results were that serum vitamin D concentrations were positively associated with LTL ($r = 0.07$, $P = 0.0010$), and this relation persisted after adjustment for age ($r = 0.09$, $P < 0.0001$) and other covariates (age, season of vitamin D measurement, menopausal status, use of hormone replacement therapy, and physical activity; P for trend across tertiles = 0.003). The difference in LTL between the highest and lowest tertiles of vitamin D was 107 base pairs ($P = 0.0009$), which is equivalent to 5.0 y of telomeric aging.

Resveratrol

Resveratrol is a natural substance found in many plants, including grapes, peanutsii and Japanese Knotweed (Polygonum cuspidatum).iii Resveratrol's introduction into the dietary supplement market a few years back was based upon the consideration that intake of it and other polyphenol compounds from red wine may contribute to the "French paradox", the unexpectedly low rate of death from cardiovascular disease in the Mediterranean population, despite a diet that is relatively high in saturated fat.

In-vitro studies suggest that resveratrol is capable of promoting telomerase activity, thereby helping to maintain telomere length. This has been shown to be the case without affecting cell proliferation.i Likewise, resveratrol has also demonstrated an ability to delay cell senescence (aging) by its action on telomerase.ii

In addition, research has shown that resveratrol significantly extends the lifespan of lower organisms such as the yeast Saccharomyces cerevisiaeiii, the worm Caenorhabditis elegans, and the fruit fly Drosophila melanogaster.iv Other research demonstrated that resveratrol had similar life extension effects on the short-lived fish, Nothobranchius furzeri,v also increasing swimming performance, and cognitive performance. Another study has shown that resveratrol improved the health and survival of mice that were on a high-calorie diet.

Grape seed polyphenols

A studyi set out to determine (a) whether DNA damage is elevated in mice that carry mutations that predispose them to Alzheimer's disease (AD) relative to control mice, and (b) whether increasing the intake of dietary polyphenols from grape seed extract could reduce genomic instability. DNA damage was measured using the micronucleus (MN) assay in both buccal mucosa and erythrocytes and an absolute telomere length assay for both buccal mucosa and olfactory bulb tissue. The results were a significant 7-fold decrease in buccal MN frequency ($p=0.01$) for AD mice fed diets containing grape seed. Similarly, in polychromatic erythrocytes a non-significant reduction of 34.8% in MN frequency was found for the grape side extract group respectively compared to the AD Control. A non-significant 2-fold increase in buccal cell telomere length was also evident for the grape seed extract group compared to the AD control group.

Chlorella

Oxidative agents can cause damage to cellular DNA, included telomere length. In a studyi, cells exposed to the oxidative effects of hydrogen peroxide, telomere length decreased significantly coupled with a concomitant decline of telomerase activity. However, these decreases were prevented with prior and post treatment of Chlorella vulgaris to those cells. Consequently, Chlorella as found to be an effective preventive against telomerase-shortening due to oxidative damage.

Vitamin E, vitamin A, folate, preformed niacin and calcium

Results from a recent population studyi suggest that key micronutrients affect genome stability in human subjects in vivo.

The results have recently been reported in a cytogenetic epidemiological study of 190 healthy individuals (mean age 47.8 years, 46% males), designed to determine the association between dietary intake, measured using an FFQ, and genome damage in lymphocytes(33), measured using the cytokinesis-block micronucleus assay. Multivariate analysis of baseline data shows that the highest tertile of intake of vitamin E, vitamin A, folate, preformed niacin (niacin or niacinamide), and calcium is associated with significant reductions in micronucleus frequency (a robust biomarker of chromosome breakage or loss).

Multivitamins

In a cross-sectional analysis of data from 586 early participants (age 35–74 y) published in the American Journal of Clinical Nutrition, i multivitamin use and nutrient intakes were assessed with a 146-item food-frequency questionnaire, and relative telomere length of leukocyte DNA was measured. The results were that after age and other potential confounders were adjusted for, multivitamin use was associated with longer telomeres. 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). This study provides the first epidemiologic evidence that multivitamin use is associated with longer telomere length among women.

Conclusion

Although more research needs to be done in humans, it may turn out that including one or more of the aforementioned nutraceuticals in your supplementation program may help promote telomerase activity, increase telomere length, and maybe even extend your lifespan.