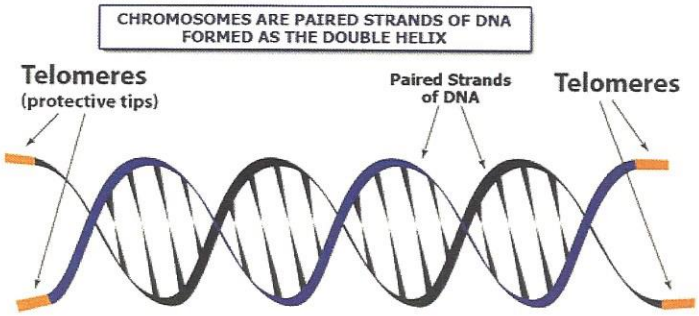
Telomere Testing

A Window to Your Patient's Cellular Health

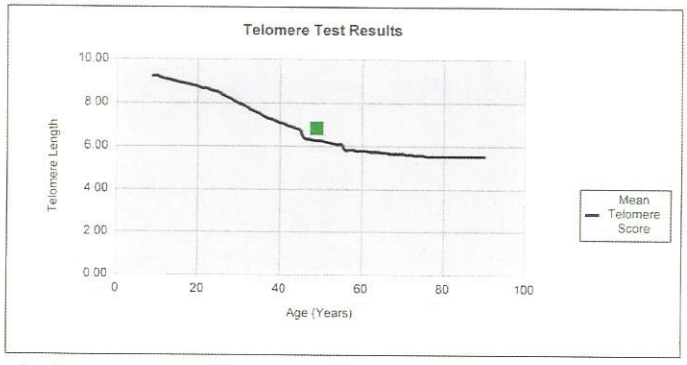
What does Telomere Testing measure?

Telomeres are sections of genetic material at the end of each chromosome whose primary function is to prevent chromosomal "fraying" when a cell replicates. As a cell ages, its telomeres become shorter. Eventually, the telomeres become too short to allow cell replication, the cell stops dividing and will ultimately die - a normal biological process. SpectraCell's Telomere Test can determine the length of a patient's telomeres in relation to the patient's age.

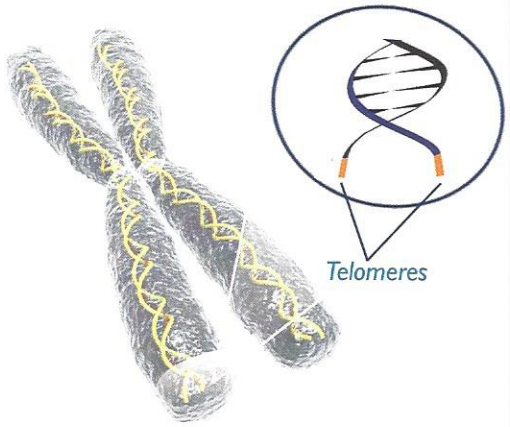


How are the results reported?

The Patient Telomere Score is calculated based on the patient's average telomere length in peripheral whole blood cells. This average is then compared to telomere lengths from a population sample in the same age range as the patient to determine the patient's percentile score.



Patient Telomere Score: 6.85
Percentile relative to patient's age population: 74%

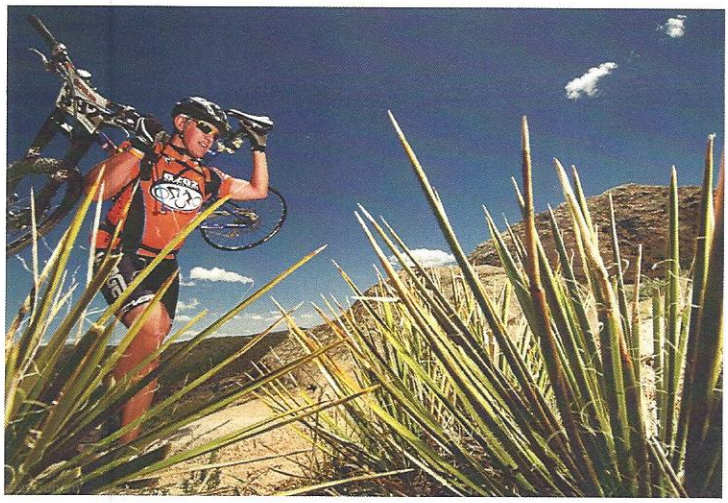


What do the results mean to the patient and the doctor?

Age adjusted telomere length is the best method to date to assess cellular attrition, by analyzing the rate at which changes in average telomere length occur over time. Serial evaluation of telomere length is an indicator of how rapidly cells are being lost and replaced (cellular attrition). Therapies directed at slowing the loss of telomere length may slow aging and age-related diseases.

What are the nutritional implications on telomere length and repair?

An inflammatory diet, or one that increases oxidative stress, will shorten telomeres faster. This includes refined carbohydrates, fast foods, processed foods, sodas, artificial sweeteners, trans fats and saturated fats. A diet with a large amount and variety of antioxidants that improves oxidative defense and reduces oxidative stress will slow telomere shortening. Consumption of 10 servings of fresh and relatively uncooked fruits and vegetables, mixed fiber, monounsaturated fats, omega-3 fatty acids, cold water fish, and high quality vegetable proteins will help preserve telomere length. In addition, it is advised to reduce total daily caloric intake and implement an exercise program. Fasting for 12 hours each night at least 4 days per week is recommended.



What lifestyle modifications are likely to be helpful?

One should achieve ideal body weight and body composition with low body fat (less than 22 % for women and less than 16 % for men). Decreasing visceral fat is very important. Regular aerobic and resistance exercise for at least one hour per day, sleeping for at least 8 hours per night, stress reduction, discontinuation of all tobacco products are strongly recommended. Bioidentical hormone replacement therapy may decrease the rate of telomere loss.

When should retesting be considered?

Testing should be done once per year to evaluate the rate and direction of telomere changes and make adjustments in nutrition, nutritional supplements, weight management, exercise and other lifestyle modifications known to influence telomere length.

What role will nutritional supplements play in slowing telomere shortening?

Oxidative stress may shorten telomere length and cause aging in cellular tissue. Antioxidant supplements can potentially reduce oxidative stress very effectively, which will ultimately improve oxidative defenses, mitochondrial function, reduce inflammation and slow vascular aging. Targeted supplementation is key, as antioxidants work synergistically and must be balanced to work most effectively and avoid inducing a pro-oxidant effect. Increasing antioxidant capacity at the cellular level is critical to maintaining telomere length.

Recent evidence suggests that a high quality and balanced multivitamin will also help maintain telomere length. Specifically, studies have linked longer telomeres with levels of vitamin E, vitamin C, vitamin D, omega-3 fatty acids and the antioxidant resveratrol. In addition, homocysteine levels have been inversely associated with telomere length, suggesting that reducing homocysteine levels via folate and vitamin B supplementation may decrease the rate of telomere loss. Similarly, conditions such as cardiovascular disease, insulin resistance, diabetes, hypertension, atherosclerosis and even dementia affect telomere length. Correcting subclinical nutritional deficiencies that may contribute to such diseases is crucial for telomere maintenance.

What pharmacologic treatments are known to slow telomere loss?

- Angiotensin converting enzyme inhibitors (ACEI)
- Angiotensin receptor blockers (ARB)
- Renin Inhibitors
- Statins
- Possibly calcium channel blockers
- Possibly serum aldosterone receptor antagonists
- Possibly metformin
- Aspirin
- Bioidentical Hormone Replacement Therapy

Control all known coronary heart disease risk factors to optimal levels.

- Reduce LDL cholesterol to about 70 mg %, decrease LDL particle number and increase LDL particle size.
- Reduce oxidized LDL.
- Increase HDL to over 40 mg % in men and over 50 mg % in women and increase HDL 2 subfraction. Reduce inflammatory HDL and increase protective HDL.
- Reduce fasting blood glucose to less than 90 mg % and 2 hour post prandial or 2 hour GTT to less than 110 mg %. Keep Hemoglobin A1C to about 5.0% and keep insulin levels low.
- Reduce blood pressure to about 120/ 80 mm Hg
- Reduce homocysteine to less than 8 um/L
- Reduce HS-CRP to less than 1.0
- Maintain ideal body weight and composition.
- Stop smoking.
- Treat insulin resistance and metabolic syndrome.

Overall recommendations to maintain telomere length.

Some clinicians have recommended reducing all known coronary risk factors, inflammation, oxidative stress, ADMA levels and angiotensin II levels or its action. At the same time, therapy should increase nitric oxide levels and nitric oxide bioavailability, increase arginine, increase endothelial progenitor cells, improve mitochondrial function and increase oxidative defenses. In addition, one should optimize hormone levels, exercise, sleep, nutrition and nutritional supplements.

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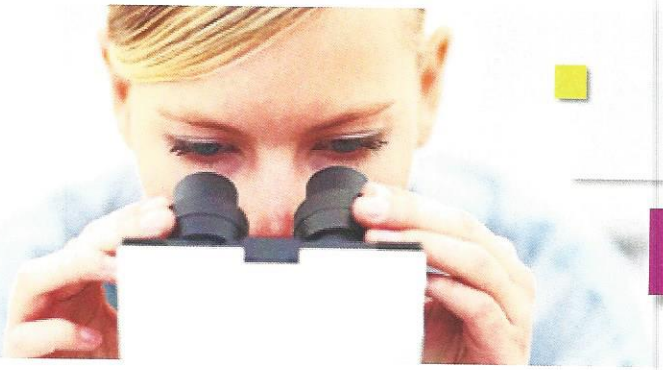

Nutrient Correlation Wheel

Calcium
Required cofactor to prevent DNA replication errors.[25]

Folate Influences telomere length via DNA methylation.[1,2,3]

B3 Extends lifespan of human cells in vitro; Slows telomere attrition rate by reducing reactive oxygen species in mitochondria.[4,5]

B2, B6 and B12
Crucial for proper DNA methylation.[6,7]

Manganese
Required cofactor in Mn superoxide dismutase, a **deficiency in which decreases** telomerase activity.[24]

Cysteine
Stem cell treatment with N-acetyl cysteine corrects DNA damage in telomeres.[8]

Zinc Important cofactor for DNA repair enzymes; key role in regulating **inflammation.**[9]

Vitamin D
Positively associated with telomere length due to its **anti-inflammatory role.**[23]

TELOMERES

Copper Key cofactor in the potent antioxidant superoxide dismutase that is known to protect telomeres.[11]

Vitamin E Enhances DNA repair as well as removal of damaged DNA; Shown in vitro to restore telomere length on human cells.[21,22]

Magnesium Induced **deficiency shortened telomeres in** rat livers; Regulates chromosome separation in cell replication.[12]

Vitamin C Protects DNA from oxidation. In vitro studies show it slows down age-related telomere shortening in human skincells.[19,20]

Glutathione
Interference of glutathione dependent antioxidant defenses accelerates telomere erosion.[17,18]

Selenium In vitro supplementation extended telomere length in liver cells; selenoproteins protect DNA.[13,14,15,16]

MTHFR Genotyping

MTHFR (Methylenetetrahydrofolate Reductase)

What is MTHFR?

- MTHFR is an enzyme responsible for converting 5,10-methylenetetrahydrofolate to the product 5-methyltetrahydrofolate – it is involved in the metabolism of folate and homocysteine
- The product of the reaction catalyzed by MTHFR converts homocysteine (a potentially toxic amino acid) to methionine (a useful and necessary amino acid)

Why is MTHFR Genotyping important?

- Certain mutations in the gene coding for MTHFR produce an enzyme that has reduced activity.
- Reduced activity can lead to elevated levels of homocysteine (a.k.a. hyperhomocysteinemia), especially when folate levels are low.
- High homocysteine (>13umol/L) may double the risk of developing illness or complications.
- MTHFR genotyping can provide information about potential causes of elevated homocysteine and approaches for addressing it.
- Based on MTHFR and homocysteine results, physicians can develop dietary and medical recommendations.
    - Increased intake of folate alone or in combination with vitamins B6 and B12 are recommended.
- Based on results, recommendations for methotrexate dosage can be adjusted.

Risks associated with MTHFR Variants / High Homocysteine:

- Cardiovascular Disease
- Cerebral Vascular Disease (Stroke)
- Venous and Arterial Thrombosis
- Methotrexate Toxicity for Cancer Therapy

C677T

- There is a mutation from cytosine to thymine at position 677 within gene.

A1298C

- There is a mutation from adenine to cytosine at position 1298 within gene.

These variants lead to amino acid differences in the protein that reduces its ability to function.

677 - CC, CT, or TT

- CC - homozygous normal
    - Approximately 45% of the population
    - No increased risk associated
- CT - one variant copy
    - Approximately 45% of the population
    - Some reduced enzyme activity, but not alone associated with increased risk.
- TT - two variant copies
    - Approximately 10% of the population
    - Increased risk for hyperhomocysteinemia and associated complications

1298 - AA, AC, CC

- AA - normal homozygous
- AC or CC - one or two variant copies
    - Approximately 30% of the population
    - Not associated with increased risk
    - Associated with increased risk if found together with a 677 variant.

Who should be tested?

- Those with high homocysteine levels.
- Those who have a familial history of cardiovascular disease, stroke, or thrombosis.
- Those who are candidates for long-term methotrexate therapy.