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## **A Natural Product Telomerase Activator as Part of a Health Maintenance Program: Metabolic and Cardiovascular Response**

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**REJUVENATION RESEARCH**

**Volume 16, Number 5, 2013**

## Abstract:

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A short average telomere length is associated with low telomerase activity and certain degenerative diseases. Studies in animals and with human cells confirm a causal mechanism for cell or tissue dysfunction triggered by critically short telomeres, suggesting that telomerase activation may be an approach to health maintenance.

Previously, we reported on positive immune remodeling in humans taking a commercial health maintenance program composed of TA-65® (a natural product-derived telomerase activator) and other dietary supplements. In over a 5-year period and an estimated 7000 person-years of use, no adverse events or effects have been attributed to TA-65® by physicians licensed to sell the product. Here we report on changes in metabolic markers measured at baseline (n = 97–107 subjects) and every 3–6 months (n = 27–59 subjects) during the first 12 months of study. Rates of change per year from baseline determined by a multi-level model were - 3.72mg/dL for fasting glucose ( p = 0.02), - 1.32 mIU/mL for insulin ( p = 0.01), - 13.2 and - 11.8 mg/dL for total cholesterol and low-density lipoprotein cholesterol (LDL-C) ( p = 0.002, p = 0.002, respectively), - 17.3 and - 4.2mmHg for systolic and diastolic blood pressure ( p = 0.007 and 0.001, respectively), and - 3.6 μmole/L homocysteine ( p = 0.001). In a subset of individuals with bone mineral density (BMD) measured at baseline and 12 months, density increased 2.0% in the spine ( p = 0.003). We conclude that in addition to apparent positive immune remodeling, TA-65® may improve markers of metabolic, bone, and cardiovascular health.

## Multi-Level Analysis of Variance:

<i>Dependent variable</i>	<i>Intercept</i>	<i>Time on program (year)</i>	<i>Baseline age (year)</i>	<i>Female</i>
Glucose	84.32 (< 0.001)	- 3.72 (0.02)	0.18 (0.01)	- 3.03 (0.15)
Insulin	3.94 (0.07)	- 1.32 (0.01)	0.04 (0.18)	- 1.68 (0.07)
Total Cholesterol	196.89 (< 0.001)	- 13.2 (0.002)	- 0.23 (0.49)	7.59 (0.44)
LDL-C	123.49 (< 0.001)	- 11.8 (0.002)	- 0.32 (0.27)	1.52 (0.86)
SBP	114.62 (< 0.001)	- 17.3 (0.007)	0.23 (0.06)	- 10.05 (0.005)
DBP	85.59 (< 0.001)	- 4.2 (0.001)	- 0.11 (0.26)	- 4.84 (0.08)
Homocysteine	8.97 (< 0.001)	- 3.6 (< 0.001)	0.04 (0.10)	- 0.94 (0.21)
Vitamin B12	382.56 (0.09)	72.4 (0.27)	6.88 (0.04)	- 35.90 (0.71)
Vitamin D	27.2 (< 0.001)	17.6 (0.008)	0.21 (0.06)	- 4.83 (0.13)

Shown are the parameter estimates and (p-values) from the model as described in the Methods section.

LDL-C - low-density lipoprotein cholesterol; SBP - systolic blood pressure; DBP - diastolic blood pressure.

## Discussion and Conclusions:

This study adds to the observations from 2011 that TA-65®, a small-molecule telomerase activator, has a positive impact on biomarkers of aging or age-related disease. The initial observational study of roughly 50 subjects on TA-65® focused on results from independent diagnostic laboratory testing of immunological markers over a 1-year period, while here we focus on similar laboratory testing of metabolic biomarkers and bone mineral density in the same cohort over the same 1-year period. We found reductions in fasting blood sugar, insulin, cholesterol, blood pressure, and homocysteine, and increases in bone mineral density, all considered positive health changes. These data suggest that TA-65® in combination with other supplements and physician counseling improves health and may reduce risk of morbidity and mortality. The major limitation of these observational studies is that they are not randomized, placebo-controlled trials with defined dosing of TA-65®. Such a study is in progress, but the

observation that TA-65® was primarily beneficial to CMV positive humans who were “blind” to their CMV status, and that TA-65® had positive effects when given to aged telomerase-positive but not telomerase-negative mice, 51 suggests that TA-65® is an active molecule that should be investigated further.

Because telomerase may extend the life span of relatively rare pre-malignant cells that otherwise might die due to critical shortening of telomeres, it is possible that a telomerase activator could increase cancer risk in some individuals. However, prevention of critical shortening of telomeres in multiple tissues throughout an aging human by telomerase activation could be a net tumor suppressive mechanism by reducing genomic instability and maintaining health of normal tissues. Much larger controlled studies will be needed to assess the potential risk and benefits of TA-65® in humans. Subjects taking TA-65® or any dietary supplement should consult their doctor and carefully consider the product’s potential risks and benefits. There had been approximately 260 person-years of TA-65® dosing, mainly in the 5–50mg/day range through June, 2010, with no reports of new diagnoses of cardiovascular disease or cancer. This represented age-adjusted incidence rates significantly below the average US rates for CVD and cancer. As of June, 2013, there are now an estimated 7000 + person-years of TA-65® exposure at an average 50-mg TA-65® dose equivalence. Disease and mortality were not formally tracked, but TA Sciences reports few if any adverse events, and no cases of adverse events being attributed to TA-65® by the subjects’ doctors. In the overall (all ages) US population, 7000 person years of life would entail about 30 new diagnoses each for cancer and CVD, and about 60 deaths, based on data from the Centers for Disease Control and Prevention. Because of lack of matching demographics for the study population, as well as lack of exact disease and mortality data, we cannot make a reliable comparison of incidence rates in the study population versus the general population, but the data to date do not point to increased risk of morbidity or mortality in subjects taking TA-65®. In conclusion, TA-6®5, a moderate telomerase activator, is a novel dietary supplement that may enhance one’s health span.