EVERYDAY CLINICAL APPLICATION OF TELOMERE AND AGING SUPPORT

PRESENTED BY:
Fred Pescatore, MD, MPH, CCN

Financial Disclosure: Consultant to DaVinci Labs
AGENDA

Overview of the following:

• Methylation
• Telomere and Telomerase
• Mitochondrial Function/Dysfunction

The Aging Cycle

Three Pronged Nutritional Approach

Protocol Summarized
METHYLATION

• Involves the transfer of a methyl group to the 5\textsuperscript{th} carbon atom of cytosine using S-adenosyl L-Methionine (SAM) as the donor.

• DNA methylation primarily takes place in promoter regions of transcriptionally active genes, resulting in the regulation of gene expression.

• Plays a primary role in phase 2 detoxification, converting toxins into water soluble compounds, allowing for excretion.

• Impaired by decreased MTHFR activity, leading to impaired folate metabolism.
TELOMERES AND TELOMERASE

• Telomeres are special “caps” at the end of the DNA strand that protect chromosomes from degradation.

• They allow full replication of the DNA through telomerase activity and shorten with replication and lack of telomerase activity.

• Do not fully replicate themselves, resulting in continual shortening through loss of sequence repeats.

• The Hayflick limit suggests cells can replicate only a finite number of times before division halts and cells either die or become senescent.

• Senescent cells can damage other cells with inflammatory cytokines.

• With each replication, cell function becomes impaired and the cell comes one step closer to cell death.
MITOCHONDRIAL FUNCTION

• Utilizes two primary processes for energy production:
  1. Citric Acid Cycle (AKA Kreb’s Cycle)
  2. Oxidative Phosphorylation (OXPHOS)- Provides 80% of the body’s energy stores

• Changes that occur that impact mitochondrial functionality:
  1. Free radical damage to mitochondrial DNA
  2. Decreased efficiency of Kreb’s Cycle
  3. Respiratory chain defect
  4. Membrane disorganization
THE MOST IMPORTANT CYCLE IN AGING

Methylation drives telomere health

Telomere dysfunction results in mitochondrial dysfunction

Mitochondrial dysfunction then results in hypomethylation
METHYLATION SUPPORT

VITAMIN B2

• Most formulas do not contain the Riboflavin-5-Phosphate form due to-instability and-cost

• B2 helps the body convert other B vitamins for use, and is critical for the utilization of B6 and is also a required element of the folate cycle
METHYLATION SUPPORT

VITAMIN B6

• B6 is a required element of the folate cycle (*see diagram*)

• Formula contains both Pyridoxyl-5-Phosphate and pyridoxine HCl

• The trans-sulfuration pathway, where cystathionine breaks down to cysteine (a glutathione precursor) is B6 dependent.
METHYLATION SUPPORT

FOLATE

• Folate is a key source of the one carbon group used to methylate DNA.

• The folate provided in the formula is as: [6S]-5-methyltetrahydrofolic acid from 5,000 mcg of Quatrefolic® [6S]-5-methyltetrahydrofolic acid, glucosamine salt.

• Quatrefolic® is a new generation of body-ready folate. This form is easily utilized and stored in the body. Quatrefolic® uses a glucosamine salt which has been proven in both human animal studies to have greater bioavailability over calcium salt versions.
RESULTS:
Quatrefolic® administration produced a plasmatic (6S)5-MTHF concentration peak (Cmax: 879.6±330.3 ng/mL) 1.8 times higher than (6S)5-MTHF Ca salt (486.8±184.1 ng/mL), and 3.1 times higher than folic acid supplementation (281.5±135.7 ng/mL), while tmax values were similar for the three folate forms.
METHYLATION SUPPORT

VITAMIN B12

• Methylcobalamin, the active form of B12, is used to make methionine synthase enzyme, which converts homocysteine to methionine.

• Methionine conversion is essential to SAMe production. SAMe is the primary metabolic methyl donor, which donates a methyl group to molecules such as phospholipids, neurotransmitters and/or DNA. DNA methylation represents the means of epigenetic control of gene expression.

• A deficiency of B12 can lead to an intracellular deficiency of THF (tetrahydrofolate) known as the folate trap.
Trimethylglycine (TMG) is one of the body’s predominant methyl donors, known for supporting the body’s natural production of SAMe during the Methionine Cycle.
METHYLATION SUPPORT

DIMETHYLGLYCINE

DMG is synthesized from betaine during the remethylation of homocysteine to methionine, catalyzed by BHMT.

DMG donates a methyl group to the Folate Cycle and from there the remethylation of SAMe, which in itself is a methyl donor.
ASTRAGALOSIDE IV

• Journal of Traditional Chinese Medicine, June 2013
• Pharmacological effects of Astragaloside IV: a literature review.
• Key Findings:
• Astragaloside IV has broad application prospects, especially in cardiovascular diseases, digestive diseases, cancer and other modern high incidence, high-risk diseases, and could be developed as a medicine.
Results:
Astragaloside IV demonstrated specific support to the immune system via improves proliferative response to CD8+ T lymphocytes responses via upregulation of telomerase activity.

Both Astragaloside IV and cycloastragenol initiated the phosphorylation of extracellular signal regulating kinases.
Results:
The primary focus of this study is the impact curcumin has on hTERT, the catalytic subunit of the telomerase enzyme.

RNA interference resulted in a significant increase in oxidative stress, cell toxicity and a decrease in hTERT. Curcumin was able to upregulate the expression of hTERT, thus providing a viable strategy for supporting telomerase activity.
Results:
In this animal study published in 2013, overload induced cardiac hypertrophy initiated oxidative stress, telomere repeat binding factor 2 loss and telomere shortening.

It was demonstrated that ECGC and quercetin possess the capability to support healthy telomere length and inhibit the loss of telomere repeat binding factor 2 (TRF2).
D-RIBOSE

Design: An open-label, non-blinded study in which 53 US clinics enrolled 257 patients who had been given a diagnosis of CFS/FMS by a health practitioner.

• Results: 203 patients completed the 3 week treatment trial. D-ribose treatment led to both statistically (p<.0001) and clinically highly important average improvements in all categories:
  • 61.3% increase in energy
  • 37% increase in overall well being
  • 29.3% improvement in sleep
  • 30% improvement in mental clarity
  • 15.6% decrease in pain
This review examined studies that **investigated the association of markers of mitochondrial dysfunction with fatigue** and proposes possible research directions to enhance understanding of the role of mitochondrial dysfunction in fatigue.

- Coenzyme Q10 was the most commonly investigated mitochondrial enzyme. **Low levels of Coenzyme Q10 were consistently associated with fatigue.**

- Carnitine was the most investigated mitochondrial function marker. **Dysfunctional levels were reported in all the studies investigating carnitine.**
THANK YOU

Medicine 369
369 Lexington Ave., 19th Floor,
New York, NY 10017
Phone: 212 779-2944

Sign up for free e-newsletter at drpescatore.com