Telomeres: A new psychobiomarker

Network on Biological Risk
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Telomere Length

Telomerase enzyme

CHROMOSOME CAPS

Telomeres form protective caps at the ends of chromosomes, and are built from a repeating DNA sequence constructed by the enzyme telomerase.

The DNA sequence shown is from the *Tetrahymena* telomere.
Disclosure

Co-founder in Telome Health, Inc., a company focused on measurement of telomere length
Roadmap

Telomeres/Telomerase

Links with disease and lifestyle

Measurement
Plenty of telomerase

Tetrahymena thermophila

Cells are immortal

Elizabeth Blackburn
Cell proliferation and telomere shortening

Haber et al, NEJM, 1995
Figure 1 | The nucleus, mitochondria and ageing. With age, telomere damage in the nucleus triggers the activation of p53, which can have different effects. In proliferative cells, p53 halts both cell growth and DNA replication, potentially causing apoptotic cell death. Sahin et al.\(^1\) report that p53 also represses the expression of PGC-1 in mitochondria, reducing the function and number of these organelles, and so leading to age-related dysfunction of mitochondrion-rich, quiescent tissues. The mitochondrial dysfunction can induce further ROS production, which in turn leads to the p53-dependent cell cycle arrest and apoptosis.
Telomeres and Disease
Prediction
Progression
Mortality
Telomeres and Disease

CAD, Myocardial Infarction
Diabetes
Vascular dementia
Obesity, insulin resistance
Alzheimers
Osteoporosis
Rheumatoid Arthritis
Cancer

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<th>TL and cancer</th>
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Cumulative Cancer Incidence and Cancer Mortality Between 1995 and 2005 in the Bruneck Study

Telomere Length predicts healthspan and longevity (8 studies)

Longer telomeres:
- increased years of healthy life (Njajou, 2009)

Shorter telomeres:
- Lower 17-year survival from aggregate of all causes (infectious, CVD) (Cawthon, 2003)
- Lower 10 year survival (Erlenbach, 2009)
- Lower 12 year survival in women (Epel, 2009)
- CAD patients (4.4 years) (Farzaneh-Far, 2008)
- Alzheimers patients (Honig, 2006)
- Twin studies (Baykasa, 2007; Kimura, 2008)
Telomeres can lengthen!

Telomeres **lengthen in** ~1/4th of adults
(MacArthur Aging Study, analysis of high functioning 70 – 79 year olds)

This opens the door for identifying malleable determinants of rate of change

Epel et al, Aging, 2009
Life adversity, distress, and TL

• Caregiver stress (Damjanovic, 2006; O’ Donovan, 2011)
• Major Depression (Simon, 2006; Wolkowitz, 2011)
• PTSD (O’ Donovan, 2011)
• Former Domestic Abuse victim
  (length of abuse) (Humphreys et al, 2011)
TL is associated with lifestyle

Smoking

Obesity, insulin resistance  
   (Chronic, cycling), Kim et al, 2009)

Exercise
   (Cherkas et al, 2006; Werner et al, 2009, Mirabello et al, 2009)

Omega 3s in the blood
   (Farzaneh-Far et al, 2010)

Vitamins from supplements and food
   (Xu et al, 2009; Mirabello et al, 2009)
Don’t expect main effects!
Exercise and telomere length

![Graph showing mean telomere length by physical activity level (inactive vs. active)]
Lifespan View of Telomeres
Summary

Telomere length

- Correlated with, and predicts diseases of aging
  - In several studies, predicts earlier mortality
- Correlated with stress, psychological disorders, lifestyle factors
  - Interventions — *may* prevent shortening
- Mechanism and/or marker
  - “Multifinality” not “unifinality” — Reflects multiple inputs!
  - Weaker inferences, not ‘stress’
- Predicts multiple outcomes—not specific
  - Powerful in predicting aging related outcomes
METHODOLOGY
PROMISES & PITFALLS
• Need cells, which have DNA (not plasma or serum)

• Blood draw is best!
  • Whole blood vs. PBMCs

• Other methods under validation:
  • Blood spot
  • Saliva (immune cells)
    • Need special collection device (Genotek, Oragene)

• Buccal cells – meaning?
Subject in good health?

- Standardized time of day if possible
- Relaxed conditions (stress mobilizes cells)

- Technical details: ACD tubes (yellow top, 6ml, Cat # 364816 from BD).
- Invert 30-40 times
- Pipette into 1ml screw cap tubes (cat# SRS-72-694-006 from Sardstedt) –use this!
- Store blood at -80°C
  - (can be at room temp fo 24hr).
1. **Reliable assay** - PCR vs. Southern Blot
2. **Purity of DNA** (e.g., Qiagen gives great results, not Puregene)
   1. Store as blood if possible, over DNA
3. **Make few assumptions** - Dogma is vast, data is scarce
4. **Telomerase is reactive** (need resting baselines)
1. Null results?
   1. No relationship with outcome
   2. Inaccurate measure of TL (reliable & valid?)
   3. Snap shot measure doesn’t capture trajectory of change or telomerase level (stabilizes short telomeres)
   4. May not matter as much during certain periods (older age)

2. Expect Complex relationships (not main effects)