Silicon Valley Health Institute

host of the Smart Life Forum

NEXT MEETING: Thursday, August 16, 2012, at 7pm

Ron Rothenberg, MD

"Update in Preventive/Regenerative Medicine -- Inflammation, Hormones, Stem Cells and Telomeres"

Meet Ron Rothenberg, MD,

As a pioneer in the field of Preventive and Regenerative Medicine, Ron Rothenberg, M.D., (age 65) was among the first group of physicians to be recognized for his expertise in this rapidly emerging field. The 10th M.D. in the world to become fully board certified in by the American Board of Anti-Aging and Regenerative Medicine, Ron Rothenberg, MD founded California HealthSpan Institute in Encinitas, California in 1998 with a commitment to transform our understanding of preventive and regenerative medicine. Challenging traditional medicine's approach, California HealthSpan Institute's mission is to create a paradigm shift in the way we view the decline of fitness, cognition and quality of life: treat the cause. California HealthSpan now treats and designs custom programs for patients in California and worldwide. (From every continent except Antarctica).

Dr. Rothenberg has always challenged traditional medicine's ability to embrace new paradigms. After graduating from Columbia University, College of Physicians and Surgeons, in 1970, Dr. Rothenberg practiced medicine and studied indigenous healing in the Amazon Basin for several years. He then performed his residency in Emergency Medicine at Los Angeles County-USC Medical Center. At the time, the specialty

(continued on next page)

Presentation Location:
Cubberley Community Ctr.
Room H1
4000 Middlefield Rd.
Palo Alto, California
Driving directions on our website,
www.SVHI.com

For those who cannot attend we have live streaming and video archiving at http://www.SVHI.com/live

In This Issue

Foundation for Mind Being Research (www.FMBR.org)
August 24 Meeting: Dr. Ibrahim Karim, will be our speaker: "Egyptian Biogeometry, a Solution for Electrosmog?"
His website, www.biogeometry.com/english/

(Meet Dr Rothenberg, continued)

of Emergency Medicine (like Anti-Aging and Regenerative Medicine) was not widely recognized by the medical community. Dr. Rothenberg was passionate about the field, and went on to teach and practice Emergency Medicine. He is a former Full Clinical Professor of Preventive and Family Medicine at University of California, San Diego School of Medicine.
To be ready to offer patients the advantages of the next paradigm shift in medicine California HealthSpan Institute became the first collection center for Neostem where healthy people could collect and bank their own adult stem cells for future use. As a member of the Neostem Medical Advisory Board Dr. Rothenberg regularly meets with world leaders in the stem cell field.

Dr. Rothenberg has educated over 25,000 physicians who have attended his continuing education seminars. As the creator and director of the Postgraduate Institute for Primary and Emergency Physicians at University of California, San Diego, School of Medicine he helped create the specialty of Emergency Medicine by training physicians as this field emerged. Over the past 10 years he lectured worldwide on Preventive and Regenerative Medicine, Hormone Optimization and Stem Cells. In addition to his work in the field of Anti-Aging and Regenerative medicine, Dr. Rothenberg remains an Attending Physician and at Scripps Memorial Hospital in Encinitas, California. With the health and vitality that he had when he was much younger, Ron Rothenberg continues to enjoy his other passions: his wife, his three children, surfing, skiing, mountain biking, and Baja California.

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Future Speakers:

September 20:
Adiele Tel Oren, MD
"Skin Lesions: What, How, Why, And What To Do About It."

October 18 :
Dr. Steve Blake, ScD
"Nutrition and Alzheimer's Disease"

November 15:
Frank Shallenberger, MD
"Use of Oxygen to Prevent Cancer Risks"

About Smart Life Forum

Smart Life Forum, Inc. is a 501(c)(3) California nonprofit corporation whose primary mission is to provide credible health education to the public with an emphasis on optimal wellness, anti-aging medicine, and longevity.

Annual memberships in Smart Life Forum, Inc. and charitable donations are tax deductible to the extent allowed by law. For information on how to join or make a donation, please visit our website: www.SVHI.com.
For questions, please contact Mike Korek at (650) 941-3058.

Main Presentation:

Preventive & Regenerative Medicine – Inflammation, Hormones, Stem Cells & Telomeres

by Ron Rothenberg, MD

Aging is a disease that can be reversed; genetics is not destiny. Conventional medicine is focused on extending life towards the end of a long decline, at great expense. Preventive and regenerative medicine significantly extend lifespan while the quality remains good, using several synergistic approaches to, for example, reduce a primary cause (and symptom) of aging: chronic inflammation.

The foundation of chronic inflammation reduction is an anti-inflammatory lifestyle: personalized diet, exercise and stress reduction. The best exercise is of high intensity and short duration. Regular exercise can reduce biologic age by 10-20 years, increase a natural sense of well being, cognition, and growth hormone. Stress reduction reduces cortisol and protects the hippocampus from damage and the resulting cognitive impairment, and helps produce anti-cancer hormones (e.g., 2 methoxy estradiol). The next step is proper use of dietary supplements. Advanced lab testing is a guide and feedback mechanism, but clinical evidence – how the patient feels – is more important.
Optimizing multiple hormones at once, using bio-identical hormones to address deficiencies improves quality of life without increasing the risk of cancer or heart disease. Yet effectively administering a bio-identical hormone program is a clinical specialty: many physicians lack the technical skill or the structured procedures in their clinic to effectively treat patients long term.

All hormones should be adjusted to a youthful level, with downstream metabolites controlled. This includes testosterone in men, despite unfounded fears of causing prostate cancer. "There is not now, nor has there ever been – a scientific basis for the belief that testosterone causes prostate cancer to grow" Morgantaler, A. Testosterone and Prostate Cancer: An Historical Perspective on a Modern Myth. Eur Urol. 2006 Jul 26. (Ed.: Also see Dr. Morgantaler's book for laymen, "Testosterone for Life"). Analogously in women, a balance of hormones is required for optimal health and to protect against breast cancer.

(continued on next page)

(MAIN PRESENTATION, continued)

Optimized hormones and nutraceuticals increase the quantity and quality of endogenous (made in your own body) adult stem cells. A patient's own (autologous) stem cells can be used for regenerative medicine – today. Stem cells can come from fat tissue, umbilical cord blood or bone marrow.

Telomeres , the repetitive DNA sequences at the ends of chromosomes, are the most important sequences of DNA because they protect all the other DNA on the chromosomes. They are like the plastic caps at the ends of shoelaces – they keep the entire structure from coming undone. Telomeres shorten each time a cell divides, and telomere shortening is the root cause of cellular aging and mitochondrial decay. When telomeres become short, the DNA suffers mutations, senescence and death. Telomeres can be kept long via a healthy lifestyle, certain foods and supplements (like carnosine) and activating telomerase. Telomerase adds DNA sequences on to the end of chromosomes, compensating for the erosion of telomeres when cells divide (bypassing the "Hayflick Limit" of about 50 divisions).

Preventive and Regenerative medicine is built on a foundation of lifestyle - personalized diet, exercise and stress reduction. Then nutritional supplementation. Next is optimizing multiple interacting hormones which require experience, organization, lab work and patience to manage. Optimizing telomeres and stem cells are the last two steps; taken together a comprehensive wellness program will result in both improved quantity and quality of life – "rectangularising" the life span.

PLEASE JOIN US!

NEW MEMBERS WELCOME!

Benefit: Access to a community of experienced scientists and physicians who share information and similar interests.

First time Visitors may attend free of charge.

Smart Life Forum, Inc. (SLF) is a California qualified 501(C)(3) nonprofit corporation organized under state law for educational and scientific purposes as a public benefit corporation.

Annual Membership $60 (per household).

Donations welcome!

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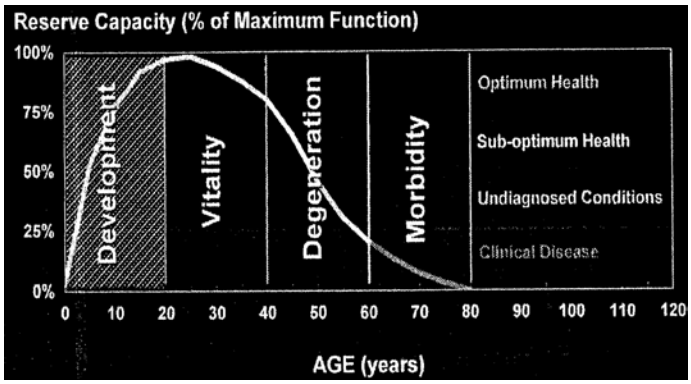
APPENDIX:

Update in Preventive/Regenerative Medicine -- Inflammation, Hormones, Stem Cells and Telomeres

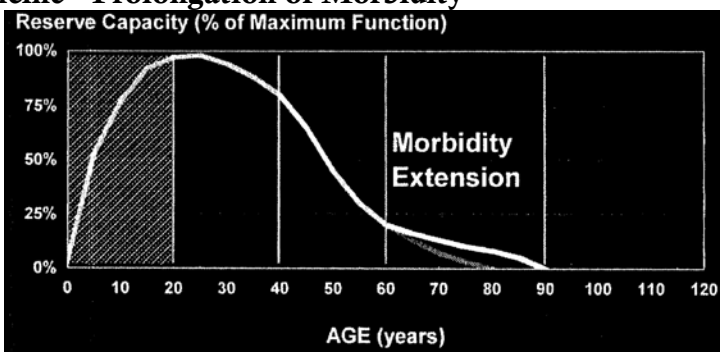
By Ron Rothenberg MD

- **Aging is a disease which can be prevented or reversed**
- **We are not prisoners of our genetic destiny**

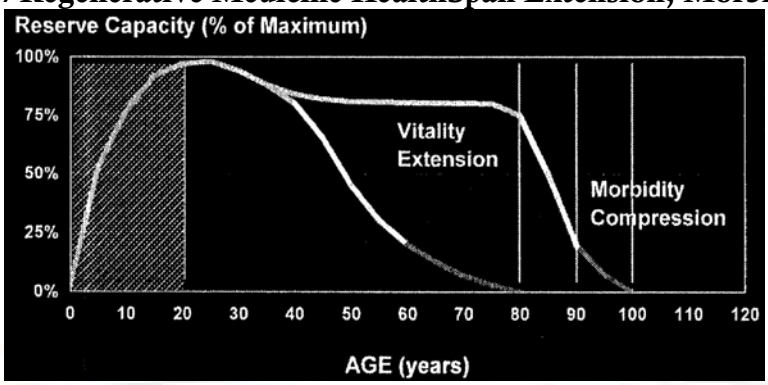
The HealthSpan Curve



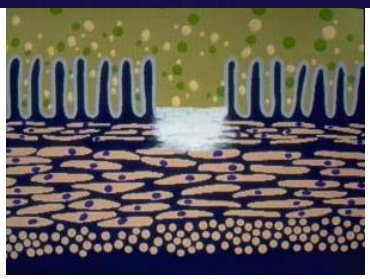
"Conventional Medicine" Prolongation of Morbidity



Goal of Preventive/Regenerative Medicine HealthSpan Extension, Morbidity Compression



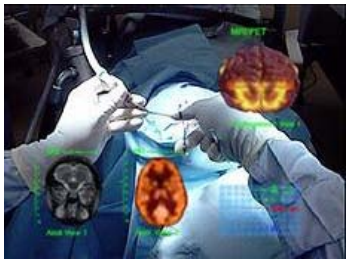
Chronic Inflammation is a cause and the effect of the diseases of aging



"Unified Theory of Wellness"

- Chronic Inflammation is the cause and the effect of illness and the diseases of aging
- Anti-inflammation through the optimization of lifestyle, nutraceuticals, hormones, telemeres and stem cells
- Anti-inflammation = Wellness
- Anti-inflammation = Peak performance, health, happiness
- Anti-inflammation = optimal stem cell function
- ®© Ron Rothenberg MD, 2012

Regenerative Medicine is:

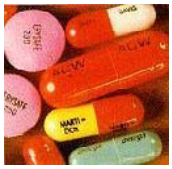


- Optimal lifestyle
- Inflammation reduction
- Cutting edge technologies to detect, prevent and treat aging related disease
- Scientific and Evidence Based
- Stem cells are the present and future
- Well Documented by peer-reviewed medical journals.

What do we do in Regenerative medicine?

- Design customized preventive/ regenerative medicine programs
- Advanced lab testing
- Nutrition - personalized
- Exercise
- Stress Reduction
- Nutraceuticals
- Inflammation control
- Optimize Bio-identical hormones
- Stem cell banking and treatment
- Telomere testing and optimization

Lifestyle

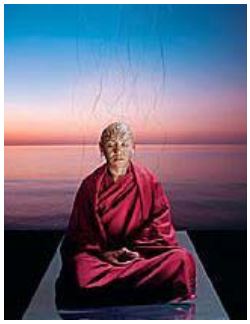


- 1st treatment in Regenerative Medicine
- Diet, Exercise, Stress Reduction
- "Health does not come out of a pill or an injection."

Exercise

- Can be 10-20 years younger than biological age with regular exercise: aerobic, anaerobic, flexibility
- PACE- high intensity, low duration
- Exercise promotes longevity and compression of disability into fewer years
(Vita, *NEJM* 1998 Apr)
- Increased production of GH
- Increased Sense of Well Being and cognition
- Decreases Inflammation, CRP
- Prevents telomere loss

Stress Reduction



- Lowers inflammation
- Lowers cortisol and protects hippocampus from damage producing cognitive impairment
- Produces anti-cancer hormones
- 2-methyoxy Estradiol
- Zacharia LC et al. Catecholamines abrogate antimitogenic effects of 2-hydroxyestradiol on human aortic vascular smooth muscle cells. *Arterioscler Thromb Vasc Biol*. 2001 Nov;21(11):1745-50.

Balanced hormone optimization decreases chronic inflammation

Bio-identical hormones to optimize

- Growth Hormone
- Testosterone for men and women
- DHEA, Pregnenolone, Melatonin
- Estrogens: E1, E2, E3
- Progesterone
- Thyroid: T3, T4
- Cortisol
- Vitamin D
- Optimal replacement considers levels and "How do you feel?"

Bio-Identical hormones

- Treat a "deficiency disease"
- Improve Quality of Life
- Decrease Chronic Inflammation
- Do not increase cancer risk
- Do not increase heart disease risk
- Are a matter of personal choice
- Must be given by the correct route
- Are a "work in progress"

Bio-identical hormone optimization

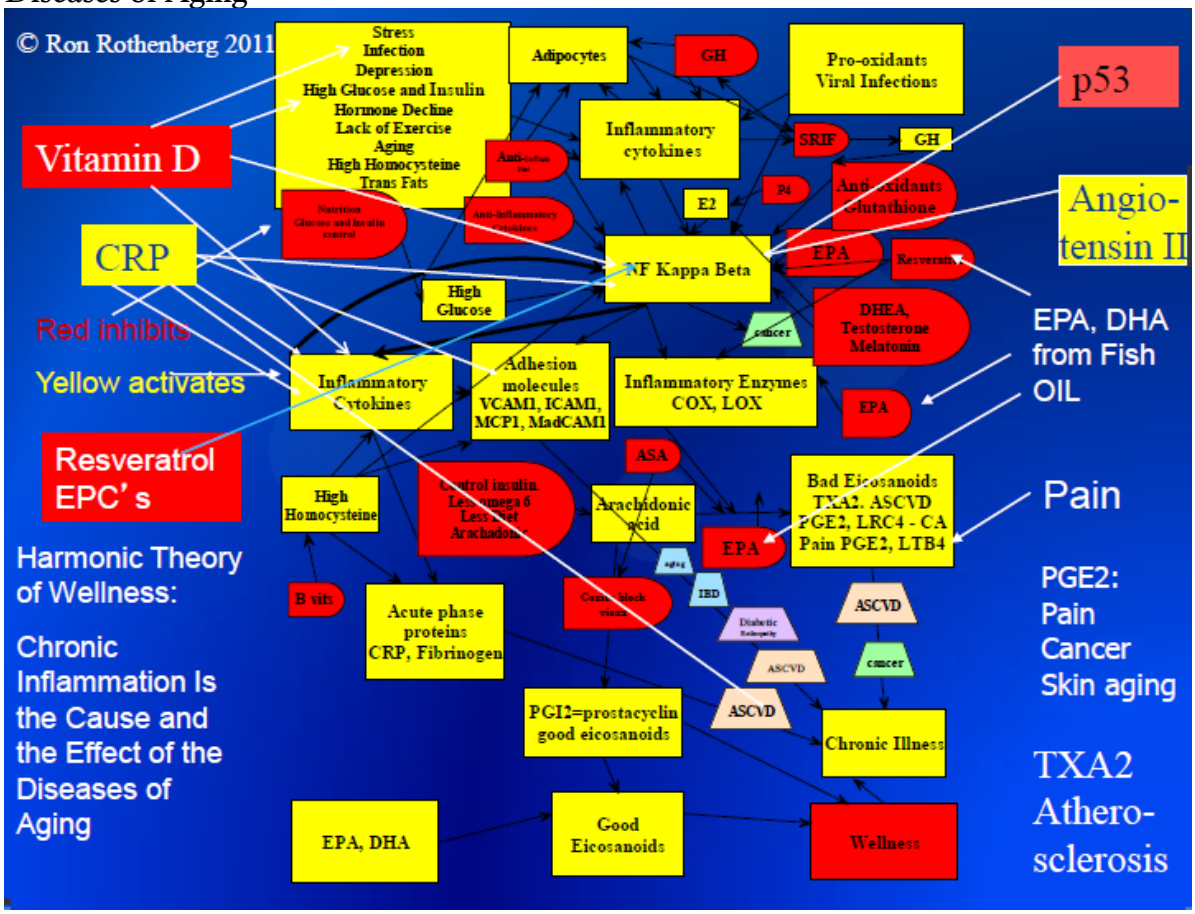
- Is a clinical specialty

- Optimal range not reference range
- When lab and clinical do not agree - clinical wins

Evolutionary Biology

- Hormone decline does not serve any positive biological function
- Evolution is blind to events after reproductive age
- Eicosanoid hormones
- Regulated by Lifestyle, Diet, Insulin, Omega 3's, Endocrine Hormones, Mind-Body connection, Vitamins and Nutraceuticals
- Autocrine
- Paracrine
- Endocrine
- Lifestyle impacts hormone levels and actions
- Lifestyle decreases inflammation

Harmonic Theory of Wellness: Chronic Inflammation Is the Cause and the Effect of the Diseases of Aging



If a shark bites you, you need inflammation right now

- Blood vessels constrict to stop bleeding
- Fibrinogen and clotting factors increase to stop bleeding
- White blood cells fight infection
- Pain reminds you "Don't swim with sharks"

- Acute inflammation keeps us alive
- Chronic inflammation kills us slowly
- Why do we have all this inflammation anyway?

Antagonistic Evolutionary Benefit

- What helped our Paleolithic ancestors make it to reproductive age…is killing us now
- Insulin Resistance – helped store fat and survive famine
- Anti-inflammation resistance – helped survive acute infectious disease and trauma
- Thyroid resistance
- – reverse T3
- increased in times of famine or stress

Omega 3's and NF*k*B

- EPA inhibits NF*k*B
- EPA decreases TNF alpha and other pro-inflammatory cytokines
- Zhao Y et al. Eicosapentaenoic acid prevents LPS-induced TNF-alpha expression by preventing NF-kappaB activation. *J Am Coll Nutr*. 2004 Feb;23(1):71-8.

Resveratrol inhibits NFKB

- Bhardwaj A et al. Resveratrol inhibits proliferation, induces apoptosis, and overcomes chemo resistance through down-regulation of STAT3 and nuclear factor-kappaB-regulated antiapoptotic and cell survival gene products in human multiple myeloma cells. *Blood.* 2007 Mar 15;109(6):2293-302.
- Turns on Sirtuin genes

Vitamin D and inflammation

- Inversely associated with CRP and frailty
- Inhibits NFKB
- Boxer RS et al. The Association Between Vitamin D and Inflammation with the 6-Minute Walk and Frailty in Patients with Heart Failure. *J Am Geriatr Soc.* 2008 Jan 5
- Szeto, FL et al. Involvement of the vitamin D receptor in the regulation of NF-kappaB activity in fibroblasts. *J Steroid Biochem Mol Biol.* 2007, March

Aging causes inflammation Youthful hormones protect

- IL-6 proinflammatory cytokine
- Stays low in youth except for trauma, infection, stress
- Testosterone and Estrogens down regulate IL-6 gene expression
- Ershler, WB et al. Age-associated Increased Interleukin-6 Gene Expression, Late-Life Diseases and Frailty. *Annu. Rev. Med*. 2000. 51:245–270

Basics still apply

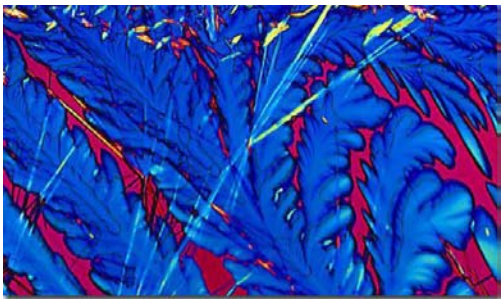
- Hormone optimization is the finishing touch on lifestyle: Nutrition, Exercise, Stress Reduction, Anti-oxidants and Nutraceuticals
- Use hormones when necessary to treat a deficiency disease
- Bio-identical
- Titrate to youthful levels and clinical response - control metabolites when needed
- Advanced treatments are backed up by current medical literature, more than any other field of medicine

Thyroid

- Treat the patient not the lab test
- Order the right lab test
- Know which is the active hormone, the pro-hormone and the anti-hormone
- "Euthyroid" is not Optimal thyroid

TESTOSTERONE

- Andropause is a deficiency disease
- Half of healthy men between the ages of 50–70 yr will have a Bioavailable Testosterone level below the lowest level seen in healthy men who are 20–40 yr of age



- Korenman SG, Morley JE, Mooradian AD, et al. 1990 Secondary hypogonadism in older men: its relationship to impotence. *J Clin Endocrinol Metab*. 71:963–969.

Andropause is a lethal disease

- Diabetes, Metabolic syndrome
- Brain
- Heart
- Frailty syndrome
- Bone
- Inflammation
- Cancer

High T = Low Mortality

- 10 year prospective study
- 11,606 men – 40-79 years old
- High Endogenous T = low mortality from CV disease and cancer
- Low T predicts CV disease
- High T = no increase in Prostate Cancer
- "Paradoxically" fear of Prostate Ca has keep men from T treatment
- Khaw KT. et al. Endogenous testosterone and mortality due to all causes, cardiovascular disease, and cancer in men. *Circulation*. 2007;116:2694-2701
- 41% decrease in chance of dying in men with T >564 compared to 350
- For each increase in 173, chance of dying went down 14%

- Extrapolating:
- Comparing T 300 to 1000
- 57% decrease in chance of dying
- This study was of endogenous T not treatment

Prostate CA and Hormones

- 3886 men with prostate cancer, 6438 controls
- No associations were found between the risk of prostate cancer
- Testosterone, calculated free testosterone, dehydroepiandrosterone sulfate, androstenedione, androstanediol,estradiol, calculated free estradiol
- Endogenous Sex Hormones and Prostate Cancer: A Collaborative Analysis of 18 Prospective Studies Endogenous Hormones and Prostate Cancer Collaborative Group . *J Natl Cancer Inst* 2008 100: 170-183

Morgentaler conclusion

- "There is not now--nor has there ever been a scientific basis for the belief that T causes PC to grow"

- Morgentaler A. Testosterone and Prostate Cancer: An Historical Perspective on a Modern Myth. *Eur Urol*. 2006 Jul 26

Active Prostate CA and Testosterone Therapy

- 13 testosterone deficient men with untreated prostate CA
- Testosterone increased 238 to 664, PSA, prostate volume – unchanged
- After 2.5 years - No cancer found in 54% of prostate biopsies.
- No local progression or metastases
- Morgantaler et al.Testosterone Therapy in Men with untreated Prostate CA. *J Urol* 2011 Apr, (185:4) 1256-60

TRT benefits from head to toe

–Improved mood, cognitive, function, Alzheimer's prevention
–Improved Body composition, more muscle, less fat, reversal of osteoporosis
–Improved libido and erectile function
–Reverses Insulin Resistance and type 2 diabetes
–Less inflammation, pain, osteo and rheumatoid arthritis
☐TRT decreases inflammation
–CRP, IL-6, TNF alpha decreased

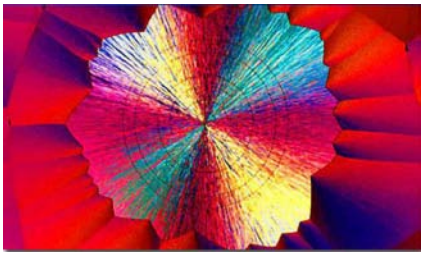
Estradiol

Estrogens

- E1=Estrone
  - May be more than she needs
  - Get some anyway through conversion of E2
- E2=Estradiol
- Protective Estrogen via catechol and methoxy metabolites
- E3=Estriol

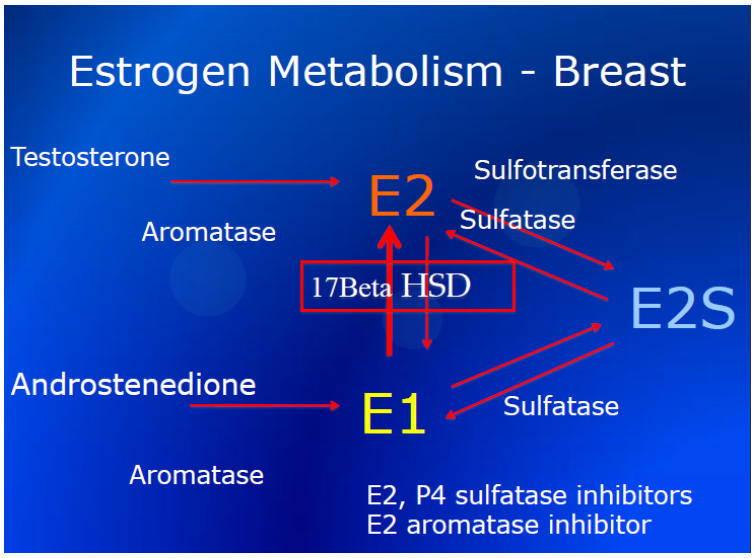
- Cancer protective, weak

Progesterone = P4

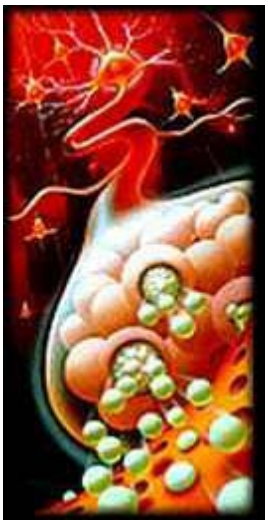


Bio-Identical Hormone Replacement in Women

- Balance Estrogens, Progesterone and Testosterone
- Every woman needs a unique balance
- Progesterone protects against breast cancer



GROWTH HORMONE



GHRT for AGHD Improves

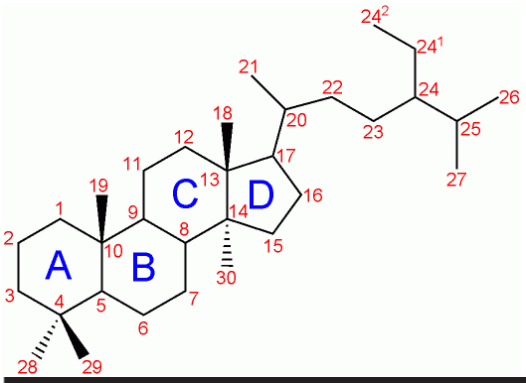
- Inflammation
- Brain
- Bone
- Atherosclerosis
- Heart Function
- Immune System
- Body Composition
- Exercise Capacity
- Wound healing
- Well Being
- Quality of Life
- Cosmetic Appearance

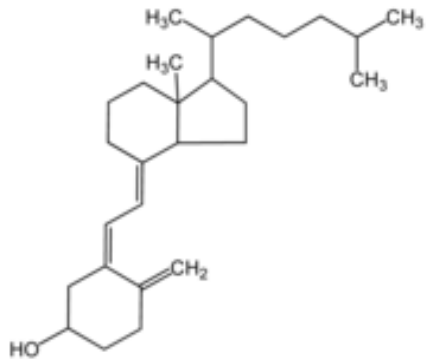
Does GH cause cancer?

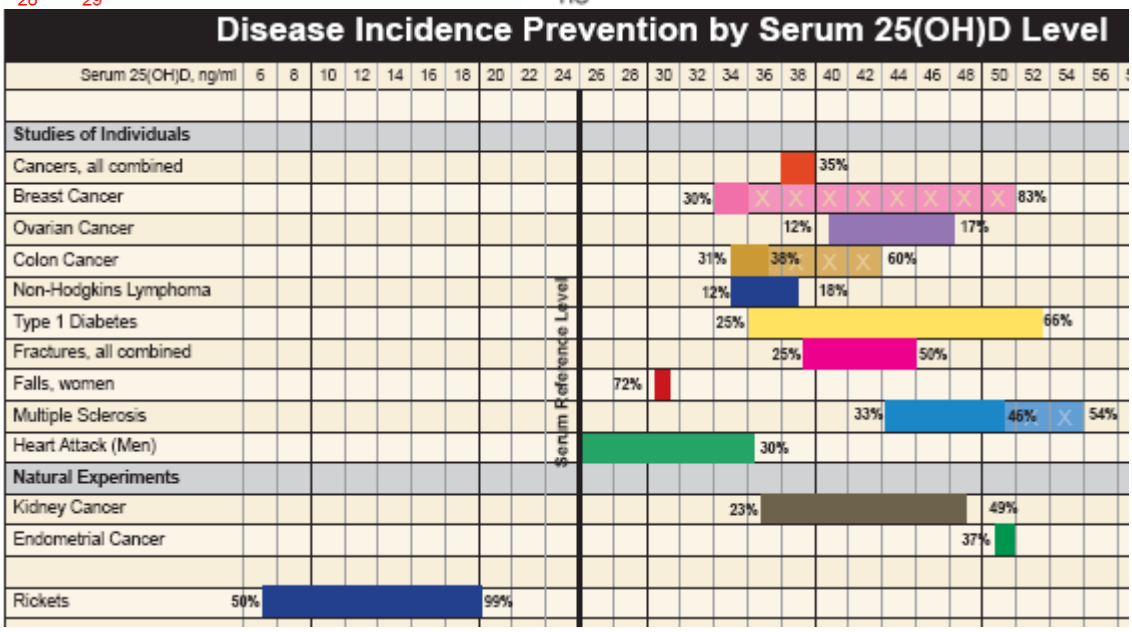
- "Extensive studies of the outcome of GH replacement in childhood cancer survivors show no evidence of an excess of de novo cancers, and more recent surveillance of children and adults treated with GH has revealed no increase in observed cancer risk ."

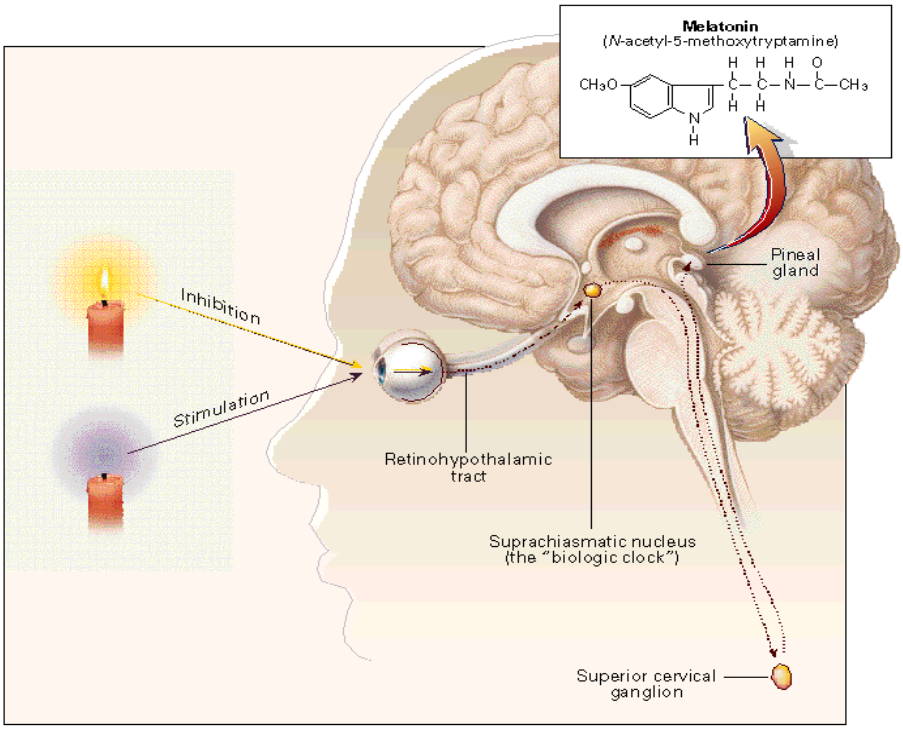
- Jenkins PJ et al. Does growth hormone cause cancer? *Clin Endocrinol* (Oxf). 2006 Feb;64(2):115-21.

Secosteroid hormone Vitamin D3 = Cholecalciferol "B" Ring is "Broken"







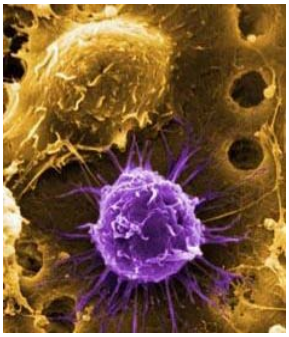


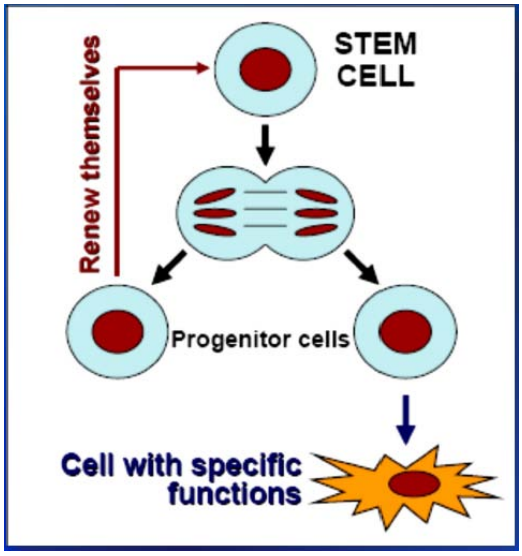
Brzezinski A. Mechanisms of Disease: Melatonin in Humans. *The New England Journal of Medicine* -- January 16, 1997 -- Vol. 336, No. 3

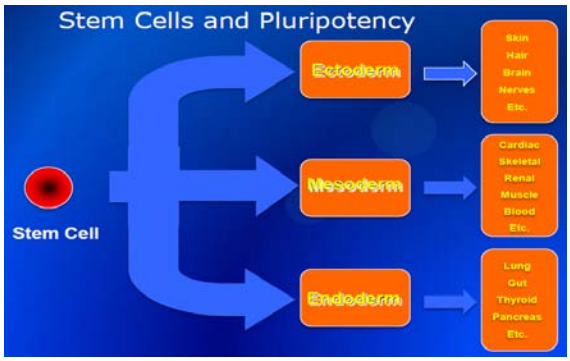
Melatonin increase EPC's

- Melatonin has immunomodulatory effects
- Melatonin stimulates production of EPC's, natural killer cells and CD4 cells and inhibits CD 8 cells
- Cardinale, D et al. Melatonin and the Immune System in aging. *NeuroImmuno Modulation* 2008;15:272-278.

- Stem cells are the tools of regenerative medicine
- We can use adult autologous stem cells for regenerative medicine now
- We can stimulate endogenous stem cells for self-repair now
- We can induce pluripotency in stem cells?
- Acute inflammation activates
- Chronic inflammation inhibits



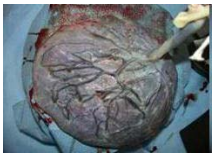


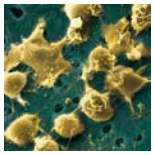


Stem Cell Infusion (Transplant)

Autologous = Self

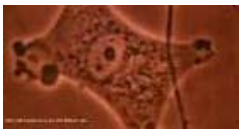
Allogeneic = Non–Self

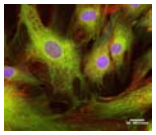




***Non*-Controversial Adult Stem Cells**

- Adipose derived Mesenchymal Stem Cells
- Umbilical Cord Blood Stem Cells
- Bone Marrow Stem Cells
- Adult Peripheral Blood Stem Cells

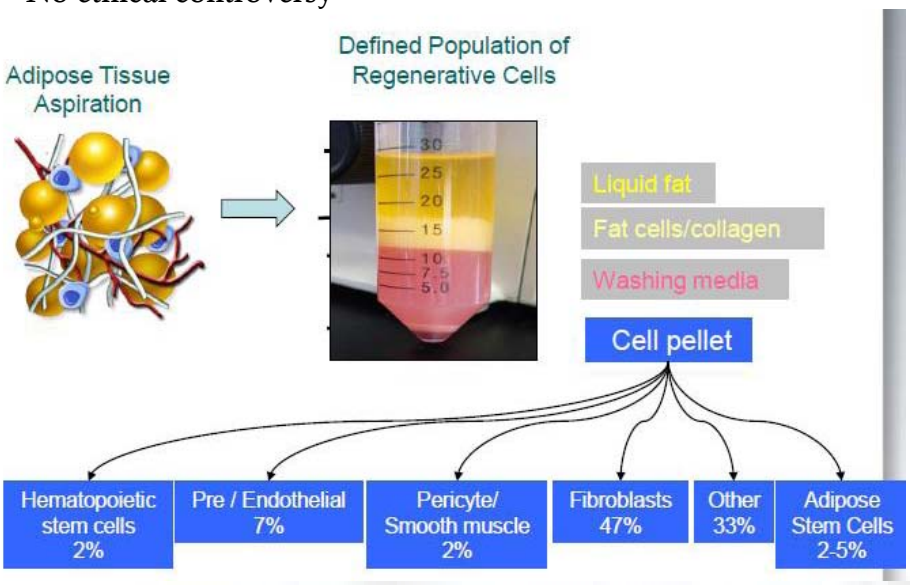




Therapeutic

Adult Stem cells

- The stem cells that you have in your own bone marrow, fat and other organs
- Some can transform into any tissue
- Can be collected through fat retrieval
- The next step in Preventive/Regenerative Medicine
- Lifestyle, Nutraceuticals and hormone optimization improve quantity and quality
- No ethical controversy



Available Protocols

Cardiology and Vascular	Acute MI, Ischemic Chronic Heart Failure, Non Ischemic Heart Failure, Critical Limb Ischemia
Pulmonology	Emphysema, Chronic Bronchitis, Pulmonary Fibrosis, Pulmonary Hypertension
Ophthalmology	Retinitis Pigmentosa, Macular Degeneration, Diabetic Retinopathy, Glaucoma
Endocrinology	Type II Diabetes
Immunology	Lupus, Rheumatoid Arthritis, Fibromyalgia, Asthma, Crohn's Disease
Neurology	Multiple Sclerosis, Parkinson's, ALS, Alzheimer's, Stroke, Cerebral Palsy
Nephrology	Renal Failure
Anti-Aging	Human Frailty Syndrome
Other	Osteoarthritis, Erectile Dysfunction

Endothelial Progenitor cells (EPCs)

- Stem cells that reside in the adult bone marrow and adipose tissue or circulate in the blood
- Differentiate and mature into endothelial cells.
- Responsible for postnatal vasculogenesis and tissue repair
- Identified by stem-cell markers (CD34+, CD133+)
- EPCs decrease with age and are a measurement of vascular senescence and a biomarker of aging

EPC's and CV Outcomes

- Higher EPC's – 70 % less death from CV causes
- Werner N et al. Circulating Endothelial Progenitor Cells and Cardiovascular Outcomes. *N Engl J Med* 353:999, September 8, 2005

Stem cells optimization through nutraceuticals

- Blueberry
- Green tea
- Vitamin D3
- Carnosine

Bickford PC et al. Nutraceuticals synergistically promote proliferation of human stem cells. *Stem Cells Dev*. 2006 Feb;15(1):118-23.

Resveratrol and stem cells

- J.G. et al. Effects of resveratrol on endothelial progenitor cells and their contributions to reendothelialization in intima-injured rats. *J Cardiovasc Pharmacol*. 2006 May;47(5):711-21

Optimize stem cells

- Optimized hormones and nutraceuticals increase quality and quantity of endogenous adult stem cells
- Combinations of nutrients produce a synergistic effect to promote proliferation of human hematopoietic progenitors.

- Nutrients can act to promote healing via an interaction with stem cell populations.

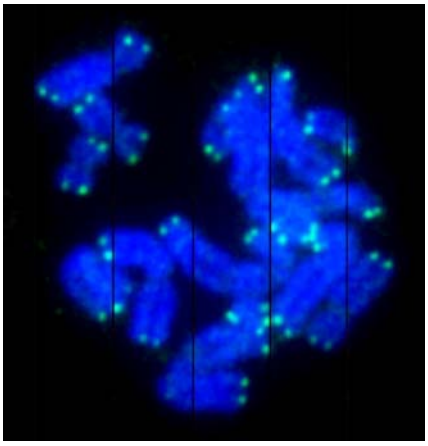
How Important is Telomere Biology?

- The Nobel prize in medicine was awarded in 2009 for the discovery of telomerase.
- There are over 8,000 publications regarding telomeres & telomerase.
- Telomeres are considered the most important sequences of DNA because they protect all the other DNA on the chromosomes
- 2010 study at Harvard Medical School shows telomere shortening to be the **root cause** of cellular aging and mitochondrial degradation.
- Age related decline, dysfunction, and a shortened lifespan are all related to telomere shortening.

What are Telomeres?

- Repetitive DNA sequences (six-nucleotide TTAGGG) at the ends of chromosomes

In a human cell there are 46 chromosomes, 23 from your mother and 23 from your father: so each cell has a total of 92 telomeres (one at each end)



Telomeres are the bright spots at both ends of each chromosome.

What do Telomeres do?

- Serve as chromosome end caps to protect the integrity of our genes.
- Keep chromosomes from degrading to prevent fusion and massive genomic instability.
- Allow cells to replicate (cells can not divide when telomeres get too short)

Bottom Line: Telomeres protect cells from DNA mutations, senescence and death.

Telomere Length Determines Cellular Age

- Somatic (body) cells

–make up more than 99% of the cells in the adult body **.**
–have little or no telomerase and telomeres shorten as we get older.

- Telomere Length Shortening**:**

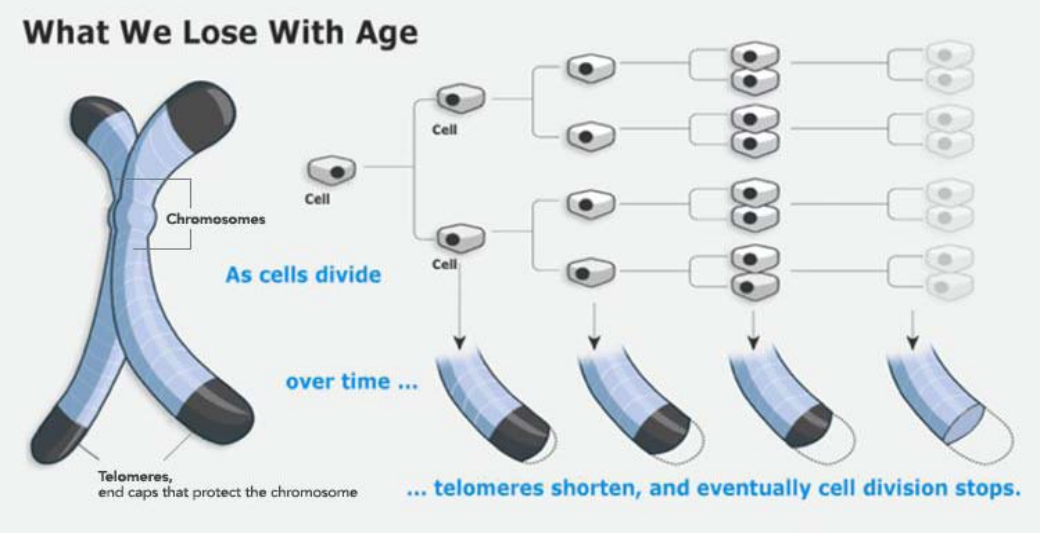
–**Conception**: Our telomeres start out **15,000** base pairs (bp) long.
–By **Birth** the embryo has divided so many times that telomere length is down to **10,000** bp.
–Over the rest of our lifetime we lose another 5,000 to 7,000 bp.
–When telomere length gets down to **3-5,000 bp,** the genome is no longer protected from mutations**, the** cell can no longer divide, becomes senescent, metabolism slows down, and the cell dies.

Telomeres are the Biological Clock of Aging

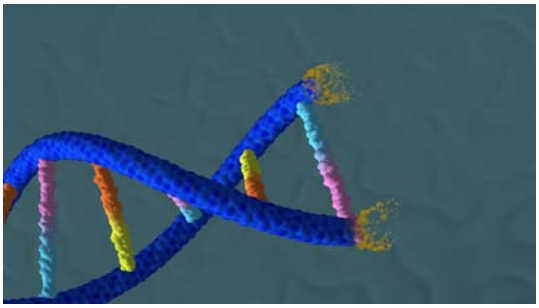
- Telomere shortening regulates how many times a cell can divide and signals changes in gene expression to an older phenotype.

- Telomeres shorten each time a somatic (body) cell divides.
- When telomeres get too short, cells can no longer replicate and they become old (senescent) or die.
- Telomere length represents your biological age as opposed to chronological age.

Telomere Length vs. Cellular Age



Telomere Length vs. Cellular Age



Telomere Shortening will kill us.

- Journal of American Medical Association (JAMA) reported a study that followed 800 people for 10 years and found that people with the shortest telomeres were 11 times more likely to die of cancer than people with the longest telomeres: 11 times is statistically huge!

Telomere Length and Risk of Incident Cancer and Cancer Mortality
***JAMA*. 2010;304(1):69-75.**

Short Telomeres = the "Kiss of Death"

- **People with shorter telomeres in their immune cells had twice the risk of death from heart failure as patients with the longest telomeres**. From A study sponsored by the American Heart Association (2008) Farzaneh-Fal et al. "Prognostic Value of Leukocyte Telomere Length in Patients With Stable Coronary Artery Disease: Data From the Heart and Soul Study." *Arteriosclerosis, Thrombosis & Vascular Biology*. 2008. 28(7):1379-1384.

- **"Short telomeres appear to be associated with increased risks for human bladder, head and neck, lung, and renal cell cancers." Telomere Dysfunction: A Potential Cancer Predisposition Factor (2003)***J National Cancer Inst. 2003 Aug 20;95(16)1211-18. Wu X, Amos CI, et. Al*

- **Twins with the shortest telomeres had a three times greater risk of death during the follow-up period than their co-twins with the longest telomere measurements Telomere length predicts survival independent of genetic influences (2007)** *Stephanie L. Bakaysa,*

Lorelei A. Mucci, P. Eline Slagboom, Dorret I. Boomsma, Gerald E. McClearn, Boo Johansson and Nancy L. Pedersen. Aging Cell, 2007.

What Can Be Done To Keep Telomeres Long?

- Lead a healthy lifestyle
- Activate Telomerase.

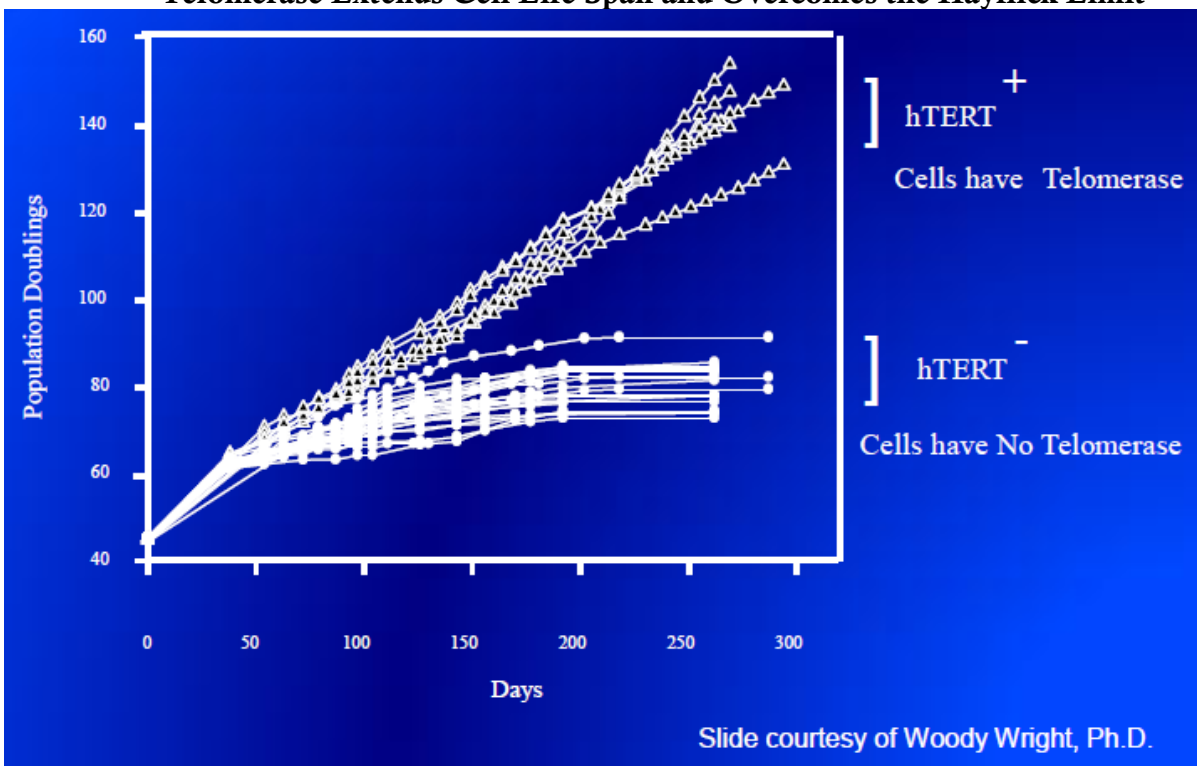
What is Telomerase?

- **TELOMERASE** is a natural enzyme that stabilizes telomere length by adding DNA repeats (TTAGGG) onto the telomeric ends of the chromosomes, thus compensating for the erosion of telomeres when cells divide.

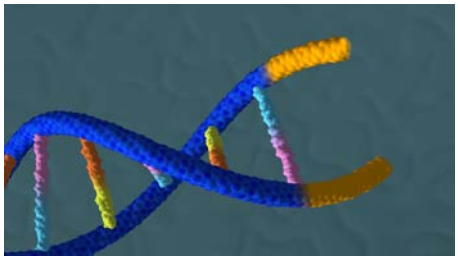
How Important is Telomerase?

- Telomerase prevents telomere shortening and cellular replicative senescence.
- Telomerase makes cells live longer and bypass the Hayflick Limit.
- Telomerase causes cells to revert to a younger phenotype. That means cells actually become younger!

Telomerase Extends Cell Life Span and Overcomes the Hayflick Limit



Telomerase Prevents And Reverses Telomere Shortening



Telomerase can do some pretty powerful things

Short Telomeres

These Mice are the Same Age! The one on top has no telomerase.

Long Telomeres

Slide courtesy of Bill Andrews

- ☐Gray and Thinning Hair
- ☐Weakened Immune System
- ☐Intestinal Atrophy
- ☐Reduced Spleen Size
- ☐Decreased Wound Healing
- ☐Decreased Lifespan

Rudolph, et al Cell 1999 Samper, et al EMBO rep 2001

Telomerase Activation:

Harvard Researchers Show First Age Reversal in a Mammal*

- Telomerase Activation was used to change old mice back to young adults.
- Brain, spleen and reproductive organs were all rejuvenated;
- Resulting in increased neurons and new viable sperm cells.
- Sense of smell returned.
- None of the mice developed cancer..

*Harvard Nov 2010 DePinho et al

Telomereopathic Diseases

- There is a whole class of diseases caused by short telomeres.
- Most specialists are not aware of the root cause of the diseases they are treating.
- Short telomeres are involved with all the diseases associated with aging.

Short Telomeres cause Organ Failure and many of the diseases of Aging

- Cancer
- Liver (hepatic cirrhosis)
- Anemia
- Leukemia
- Pulmonary Fibrosis
- Stem cell failure leading to immune system failure and organ failure

Telomerase Activation: Broad Potential for Treatment of Telomereopathic Diseases

Immune cells – memory and naïve	Liver – hepatocytes
Hematopoietic stem cells	Retinal pigmented tissue of eye
Lung alveolar cells	Chondrocytes
Skin – dermis, epidermis, vasculature	Skeletal muscle
Vascular intima (endothelium)	Kidney – cortex
Osteoblasts, MSCs	*Cardiomyocytes
GI track epithelial cells	*Neural cells

**No significant bulk telomere loss, but still a protective effect of telomerase activation.*
Harley, Current Mol Med., 2005
Garcia, Wright, Shay, Nucl. Acid Res., 2007
Aviv, Hypertension, 2009; Calado, NEJM, 2009
Slide courtesy of Calvin Harley, Ph.D. 2010

Telomerase gene therapy in adult and old mice delays aging and increases longevity without increasing cancer

Bruno Bernardes de Jesus1, Elsa Vera1, Kerstin Schneeberger1,
Agueda M. Tejera1, Eduard Ayuso2,3,
Fatima Bosch2,3, Maria A. Blasco1*

- Activating telomerase had remarkable beneficial effects on health and fitness, including: – insulin sensitivity, osteoporosis, neuromuscular coordination and several molecular biomarkers of aging.
- Telomerase-treated mice did not develop more cancer than their control littermates
- Telomerase-treated mice, both at 1-year and at 2-year of age, had an increase in median lifespan of 24 and 13%, respectively

Telomerase Activation with TA-65: Summary of Human Findings

- Short Telomeres Lengthened*
- Senescent CD28- T Cells reduced*
- Naive Cytotoxic T Cells (CD95-) increased*
- Bone density Improved
- Improved Vision
- Enhanced sexual performance
- Better Skin Elasticity
- Anecdotal results:
  - –Increased energy and athletic performance
  - –Improved Endurance
  - –Improved Sleeping quality

*Data published in peer reviewed scientific journal *Rejuvenation Research*

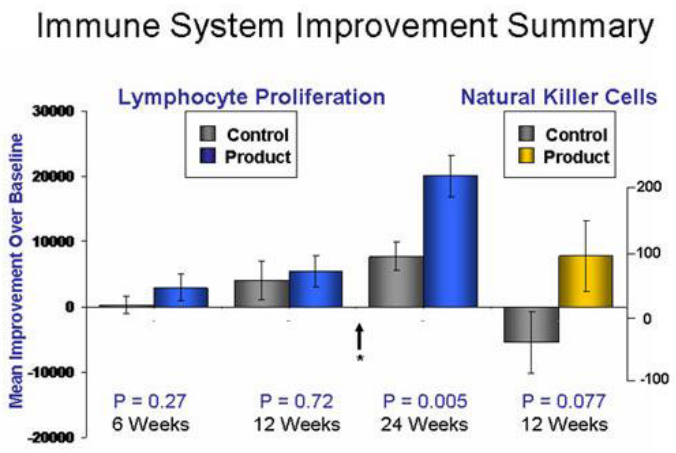


Figure 1

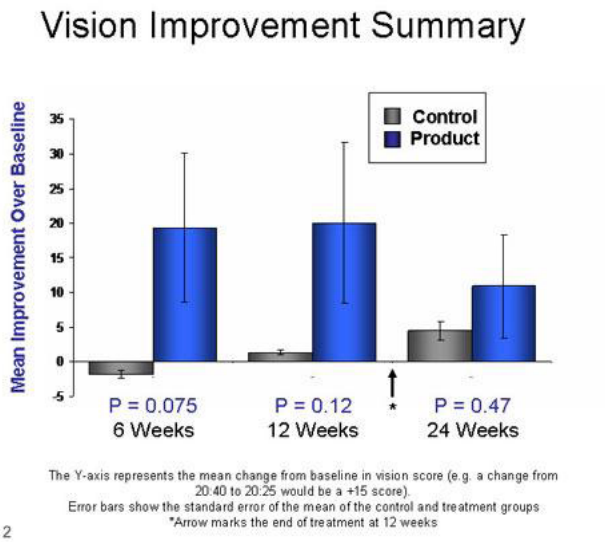


Figure 2

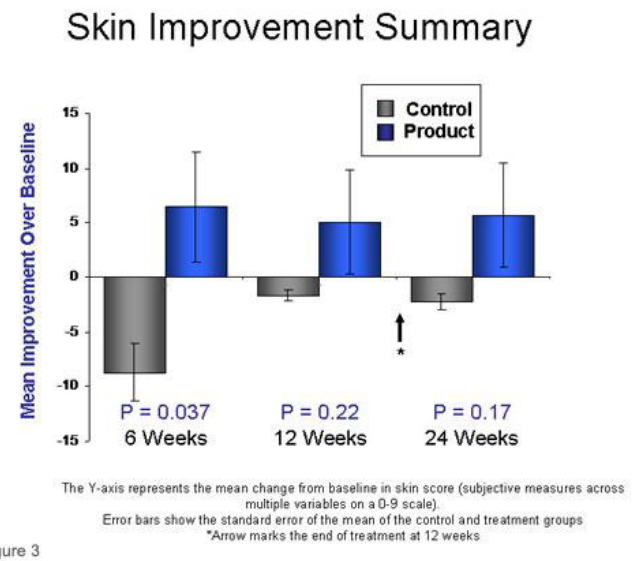


Figure 3

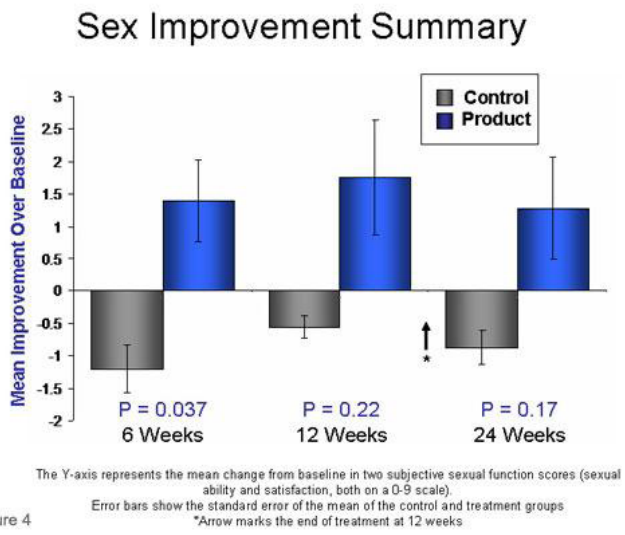


Figure 4

TA-65 Published Safety Conclusions

- *Rejuvenation Research Journal*: author, Cal Harley, Sept. 2010

Safety findings: No adverse events occurred among the subjects taking the telomerase activator

- "The Telomerase Activator elongates short telomeres and increases health span of adult/old mice without increasing cancer incidence"…..author, Maria Blasco, "Aging Cell" April 2011
- Over 10,000 people using TA-65, some for over 5 years, with no significant adverse effects.

EPCs = Biomarker Aging

Increase		Decrease
• GH/IGF-1		• Inflammation
• E2 ⟶ Telomerase		• Inflammatory Cytokines
• Testosterone		• CRP
• Antioxidants	⟶	• ROS
• Exercise		
• Red Wine, Resveratrol		
• L-Arginine		
• Blueberries, Green Tea		
• Carnosine		
• Fish Oil		
• Fucoidan		
• Gingko ⟶ Telomerase		

Know your Inflam-aging numbers

• CRP	<1
• Fasting Insulin	<7
• Homocysteine	<7
• AA/EPA Ratio	<1.5
• 25-OH-D	>65
• Telomere length	< 15 % short
• Stem cell function (CD 34)	>2,400,000
• Cytokines	
• IL-6	<12 pg/l
• TNF alpha	<8 pg/l
• IL-1 beta	<15 pg/l

Unified Theory of Wellness

- Control Inflam-Aging
- Optimize hormones
- Optimize stem cells
- Optimize telomeres
- Increased quality of life
- We all have to die sometime
- What will the journey be like?
- Rectangularize
- And if we delay, intervene and reverse the diseases of aging….
- Increased quantity of life as well