The Secrets of Longevity: The New Science of Epigenetics

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The Longevity Factor:
How Resveratrol and Red Wine Activate Genes for a Longer and Healthier Life
Hippocrates (Father of Medicine)

“A Physician’s first responsibility is to prevent disease, that being impossible to cure it and if that too being impossible to relieve pain”

460 BC to 377 BC
My Goal

“To die young.. As LATE as POSSIBLE”

2013 Hawaiian Ironman
October 12, 2013
One Way to Look Younger
Four Pillars of Health:

“It’s not the years in your life, but the life in your years”

Current Model

Better Model

Longevity
Prevent Disease and prolong a Healthy Life
Blue Zones

Area where people live the longest and healthiest

- Sardinia
- Okinawa
- Seventh Day Adventist (Loma Linda, CA)
- Nicoya (Costa Rica)
- Ikaria (Greece)

What do they know that the rest of us don't?

National Geographic (Nov 2005)
Common Traits of 100 yr. olds

- **Diet** – Fruits, Vegetables, Lean meat, Fish (omega-3)
- **Hard work/ Exercise**
- **Avoid** Environmental and Lifestyle **Toxins**
  - Pollutants – air, water, soil
  - Tobacco, Excessive Alcohol
- **Prayer, Mediation**, Faith Practices
- **Strong Family** Unit and Social Connections
“I’m willing to make some lifestyle changes as long as I don’t have to do anything different.”
Can we really do anything to prolong life?

Through improved Nutrition, Immunizations, Antibiotics, improved Hygiene

Life expectancy has doubled since the industrial revolution, from about 40 years to near 80 years

Have we reached our Limits?
Understanding Epigenetics
“The Mechanism of our Choices”
Inherited Genes Only Account for 30% of our Ideal Lifespan
Our Lifestyles and its Action on our Genes Account for 70% of our Ideal Lifespan

Lifespan Factors
New Science of Epigenetics

Are those factors that if consumed or exposed to can influence our genes to result in either healthy or unhealthy outcomes.

**Nutrition:** Diet quality and amounts; Nutritional Supplements, Vitamins, Mineral and Herbs

**Activity:** Exercise or Sedentary

**Emotional State:** Stressed out or Calm

**Environment:** Polluted or Clean
Unmasking the Genetic Myth of Disease

• Epigenetics provides the missing link between the 70% of diseases environmentally* induced and the 30% inherited through our DNA.

*pollution, toxin ingestion, smoking, radiation lifestyle issues - stress, nutrition, weight
Epigenetics and Gene Activation
Poor Health and Reduced Longevity

Exercise
- Sedentary “Couch Potato”

Nutritional Factors
- High Fat Diet
- Obesity
- Hyperglycemic index

Environment
- Polluted Air, Water and Soil

Emotional Health
- High Stress
- Worry
- Family Turmoil

Inflammation, Oxidative Stress, Cancer, Heart Disease
Average Western Diet
“The Perfect Nutritional Storm”

• Increased refined vegetable oil (Omega-6 fatty acids)
• Increased refined carbohydrates
• Decreased Omega-3 fatty acids
• Decreased consumption of polyphenols
Epigenetics and Gene Activation
For Health and Longevity

Exercise
- BDNF
- Endurance
- Strength and Flexibility

Nutritional Factors
- Calorie Restriction
- Mediterranean Diet
- Polyphenols
- Nutritional supplements

Environment
- Clean air, water and soil
- No smoking

Emotional Health
- Religion
- Relationships
- Meditation
- Spirituality

Anti-Inflammatory
Anti-oxidant, Anti-mutation

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Another Way to BE Younger
Through the Four Pillars of Health
Four Pillars of Health: Nutrition & Supplements, Exercise, Avoiding Toxins and Managing Stress

PSB Special – Secrets of Longevity
Pillar I – Choice of Food and Nutrition
What has been shown to consistently reduce cardiovascular disease, cancer, and neurodegenerative diseases of the brain, in both animals and humans?
Calorie Restriction


Rats lived 40% longer (Equivalent to over 30 human years longer)
How Could a Change in Diet (Calories) Cause This to Happen?
Unlocking the Secrets of Longevity Genes

A handful of genes that control the body’s defenses during hard times can also dramatically improve health and prolong life. Understanding how they work may reveal the keys to extending human life span while banishing diseases of old age.

By David A. Sinclair and Leonard P. Guarente

“TAPPING THE POWER of longevity genes could alter the arc of a typical human lifetime: instead of youth and growth culminating in maturity then giving way to the decline of old age, a person might be able to retain the youthfulness he feels at 50 when he is 70, 90 or well past 100.”

Scientific America, March 2006
Sirtuins activated by CR are Genetic Activators of Longevity Genes

Sirtuin class of enzymes underlies molecular (Genetic) mechanism of CR-mediated effects
Evolved to enhance an organism's chances of surviving adversity
Once activated:
- Can delay cell death and promote the repair of cellular damage
- Slow brain cell degeneration, cancer cell formation and blood vessel narrowing

David A. Sinclair, Toward a unified theory of caloric restriction and longevity regulation
Mechanisms of Ageing and Development Volume 126, Issue 9, September 2005, Pages 987-1002
Resveratrol: Summary of Known Actions

- Enhance DNA Cellular division
- Antioxidant – Reduce Free Radicals
- Anti-inflammatory – Decrease NFκ-B
- Anti-cancer
- Anti-fibrosis (↓excessive amounts of collagen in blood vessels)
- ↑ NO production
- Anti-platelet and Clotting
- Improves Insulin Sensitivity
Chocolate as Health Food

- Polyphenols - flavanols and resveratrol are found in the cocoa beans
- Flavanols and their ability to lower blood pressure and increase blood flow
- Depending on processing, certain dark chocolates can retain some of the plant polyphenol molecules from the cocoa seed
Evaluation of Lipid Profiles and the Use of Omega-3 Essential Fatty Acid in Professional Football

Anthony Yates, MD,* John Norwag, ATC† Joseph C Maroon, MD,* Jeffrey Bost, PA-C,** James P Bradley, MD,* Mark Duca, MD,* Daniel A Wecht, MD,* Ryan Grove, ATC,* Anko Ito, ATC,* Ingrid Cobb, MB, Nathan Roess, BS,* and Meghan Borden, BS†

Background: Recent research showed 82% of 233 retired National Football League players under age 50 had abnormal narrowing and blockages in arteries compared to the general population of the same age. It has been suggested that early screening and intervention in this at-risk population be a priority.

Hypothesis: Omega-3 essential fatty acid has been shown to improve cardiovascular lipid risk factors and should improve lipid profiles in professional football players to help reduce their recently shown accelerated risk of developing cardiovascular disease.

Methods: Total of 36 active National Football player were randomized to provided fish oil capsules, 2200 mg of mixed docosahexaenoic acid and eicosapentaenoic acid and 360 mg of other omega-3s to 20, with 16 controls during 60 days. Vertical Auto Profile cholesterol test directly measures low-density lipoprotein, high-density lipoprotein, and other subfractions. Compliance, side effect, and seafood consumption data was also collected. Baseline, midpoint, and poststudy blood work measured plasma docosahexaenoic acid and eicosapentaenoic acid.

Results: Showed treatment increased in high-density lipoprotein (average percent change: +250%; control +44.16).
Green Tea (Camellia sinensis)

- Main varieties of tea -- green, black, and oolong
- Differences are in processing
  - Green tea is made from unfermented leaves with the highest concentration of polyphenols (Catechin subclass)
- Polyphenol- Catechins found in green tea are 25 to 100 times more potent antioxidant than vitamins C and E
- One cup of green tea provides more antioxidant activity than a serving of broccoli, spinach, carrots, or strawberries
Malignant Glioblastoma Multiforme (GBM) Brain Tumor
The Restricted Ketogenic Diet: An Alternative Treatment Strategy for Glioblastoma Multiforme

a report by Thomas N. Seyfried, Purna Mukherjee, Miriam Kalamian and Giulio Zucconi
1. Biology Department, Boston College; 2. Dietary Therapies, LLC, Hamilton; 3. Radiology Department University of Pittsburgh Medical Center, Children's Hospital of Pittsburgh, Pittsburgh

Glioblastoma Multiforme (GBM)
Glioblastoma multiforme (GBM) is considered the most malignant of primary brain cancers with only about 12% of patients living beyond 36 months (long-term survivors). GBM is heterogeneous in cellular composition consisting of tumor stem cells, mesenchymal cells, and host stromal cells. In addition to the neoplastic cell populations, tumor-associated macrophages/monocytes (TAM) also comprise a significant cell population in GBM sometimes equaling the number of tumor cells. TAM indirectly contribute to tumor progression through release of pro-inflammatory and pro-angiogenic factors. It is often difficult to determine with certainty whether cells with macrophage characteristics are part of the stroma or are part of the neoplastic cell population. Many of the neoplastic cells in GBM invade through the neural parenchyma well beyond the main tumor mass making complete surgical resections exceedingly rare. Our goal is to review information on the current status of care for GBM and to provide information on how the KD was introduced as an alternative to fasting for the long-term management of seizures in humans. The efficacy of the KD is optimal when the ratio of dietary fats to combined carbohydrate/protein is 4:1. This requires careful attention to diet calculations. Although the safety profile of the KD is favorable when compared to many anti-seizure drugs, adverse effects have been reported in a few patients and a physician's supervision is often necessary in using the KD. Importantly, the KD is also gaining recognition as a potential therapy for a host of other neurological and neurodegenerative diseases including, Alzheimer’s disease, Parkinson’s disease, traumatic brain injury, and stroke. When administered in restricted amounts, the KD can also be therapeutic against malignant brain tumors in mice and humans. Before discussing the role of the restricted ketogenic diet (RKD) as a new treatment strategy for GBM, it would be useful to briefly review information on the current status of treatment for this disease.
Restricted Calorie Ketogenic Diet for the Treatment of Glioblastoma Multiforme

Joseph Maroon, MD¹, Jeffrey Bost, PAC¹, Austin Amos, BS¹, and Giulio Zuccoli, MD²

Abstract
Glioblastoma multiforme is the most common malignant primary brain tumor in adults and generally considered to be universally fatal. Glioblastoma multiforme accounts for 12% to 15% of all intracranial neoplasms and affects 2 to 3 adults per every 100,000 in the United States annually. In children glioblastoma multiforme accounts for only approximately 7% to 9% of central nervous system tumors. The mean survival rate in adults after diagnosis ranges from 12 to 18 months with standard therapy and 3 to 6 months without therapy. The prognosis in children is better compared to adult tumor onset with a mean survival of approximately 4 years following gross total surgical resection and chemotherapy. There have been few advances in the treatment of glioblastoma multiforme in the past 40 years beyond surgery, radiotherapy, chemotherapy, and corticosteroids. For this reason a restrictive calorie ketogenic diet, similar to that used in children to control drug resistant seizure activity, has been advanced as an alternative adjunctive treatment to help prolonged survival. This article reviews the science of tumor metabolism and discusses the mechanism of calorie restriction, cellular energy metabolism, and how dietary induced ketosis can inhibit cancer cell’s energy supply to slow tumor growth.

Keywords
glioblastoma multiforme, ketogenic diet, Warburg Effect, glycolysis

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Curcumin (turmeric)

Curcumin isolated from the roots (rhizomes) of the plant *Curcuma longa*, is the major yellow pigment present in turmeric, widely used as a spice.

**In Animals**
- Curcumin was shown to interrupt the carcinogenesis process by inhibiting the initiation step or suppressing the promotion and progression stages.

**In Humans**
- Decreased colon cancer polyp number and size after a mean of 6 months of treatment with curcumin and quercetin.

*Curcumin* was also reported to exhibit synergistic chemopreventive effects with other diet-derived polyphenols, such as genistein and green tea can increased the efficacy of many anticancer drugs.
Pillar II – *Exercise*
“If there were a drug that could prevent heart attacks, strokes and cancer and treat everything from fragile bones to constipation while quite possibly staving off dementia and improving sleep would anyone over 65 refuse this miracle elixir?”

8 out of 10 seniors forego all of these benefits

Exercise
**BDNF and Exercise**

- Neuronogenesis
- Synaptogenesis
- Neuroplasticity
- Enhances myelin formation
- Activates nucleus basalis (Ach)—focus and attention
**Brain Exercise Benefits**

- **Exercise and Learning**
  - Increases the release of neurotrophins
  - Enhance academic performance and learning, especially in children

**Improve your Mood**

- Improve mood and feelings of well being increased of dopamine and serotonin

**To Increase Neurotrophins**

- At least 30 minutes each day to maximize the benefits of exercise on neurotrophin production.
Exercise Benefits

- Immune System
- Endocrine System
- Muscular Skeletal
- Cancer Prevention
- Epigenetic Activation
Aerobic Exercise Boosts Cognitive Function in Patients With MCI

BOSTON—Combined results from a pair of six-month, randomized trials indicate that aerobic exercise improves executive function to a significantly greater degree than stretching and tone exercises in patients with mild cognitive impairment (MCI) or mild insulin resistance, The benefits were greatest in carriers of the APOE ε4 allele. **

...aerobic exercise improves executive function to a significantly greater degree than do stretching and tone exercises in patients with mild cognitive impairment (MCI) or mild insulin resistance, The benefits were greatest in carriers of the APOE ε4 allele.**
Pillar III – Environment
PR Aug 19, 2009

“US Geo Survey evaluated fish pulled from nearly 300 streams in the USA found every one of them contaminated with some level of mercury.”

…… 27% of the fish had mercury levels high enough to exceed what the EPA considers safe for the average fish eater, those who eat fish twice a week.”
Home Sweet Womb

Even Before We’re Born

- Mother exposed = Fetus at risk
- Average newborn has 200 different industrial chemicals, pollutants & pesticides in blood
  - Carcinogens
  - Toxic to brain & nervous system
  - Abnormal development
- Urban air pollution linked to chromosomal abnormalities in infants in NYC
Toxins in Air Travel

Exposure Points

• Security checkpoint
  – MRSA, staph bacteria, fungus and even feces on the floor
  – Floors are cleaned once every 12 hours and contaminated with various bacteria,
  – Always wear a protective covering for your feet!

• Airplane cabin air, seat, food trays are potentially harmful
  – A Canadian study in 2004 found that passengers on a five hour flight were 113 times more likely to have caught a cold during the flight than during normal daily life.
Dangers of Medical Radiation

• The CT scans can be very good diagnostic tools, but are vastly overused, with over 60 million performed in the U.S. annually.

• **29,000 cancers of all types** result of medical diagnostic radiation.

• Diagnostic CT procedures range from 100 to 4,000 mrem, not much less than the lowest doses of 500 to 2000 mrem received by Japanese survivors of atomic bombs

• ~1CT Scan = 200-400 CXRs
INFRASCANNER Model 2000
Handheld Brain Hematoma Screening
Pillar IV – Stress Reduction
Relieve stress with Exercise

“Life is 10 percent of what happens to you and 90 percent of how you react to it.”
by Charles R. Swindoll

• Emotional stress wears the brain down, causes lethargy, fatigue and memory loss and actually kills brain cells
• It also wears down the BODY and leads to higher blood pressure, blood sugar, fat accumulation and heart disease.
• Stress suppresses the IMMUNE system and results in more colds, infections and even cancer
Psycho-Neuro-Immunology

As a Man Thinketh, So Shall He Be –
Proverbs 23
The Ironman Triathlon: A Metaphor for Neurosurgery and Life
The greatest moments of our lives are when our mind and/or our body is stretched to its limits in the voluntary pursuit of something both difficult and worthwhile.

Mihaly Csikszentmihalyi
(pioneer of the scientific study of happiness)
Maroon Leading Team
In Miracle Surgery

By JEAN COLEMAN
News-Register Staff Writer

Surgical history with some of the aspects of science fiction is being made in Pittsburgh with a former Bridgeport resident taking a leading role.

Dr. Joseph C. Maroon, son of Charles and Anna Maroon of Bridgeport, has been a team leader since he played football at St. John’s Central and at the University of Indiana where he was a “Scholastic All-American.” Now he is an associate professor and chief of neurosurgery at Presbyterian-University Hospital.

Utilizing a technique perfected by two University of Pittsburgh School of Medicine neurosurgeons in which brain tissue is lowered by nearly 40 degrees and salt water flows through the arteries instead of blood, Dr. Maroon recently successfully removed an “orange sized” aneurysm dangerously depressing the brain of a 54 year old man.

In a telephone interview with the News-Register, Dr. Maroon readily acknowledged the “science fiction” tones of the surgery, but expressed high praise for his two colleagues who devised the life-saving technique. They are Dr. Robert G. Selker, head of the division of neurosurgery at Montefiore and member of the university hospital staff, and Dr. Sidney K. Wolfson, director of surgical research, University of Pittsburgh hospital, and head of the neurosurgical team.

Dr. Maroon has worked with the two doctors in four operations removing tumors. However, he was the operating surgeon in the recent precedent setting aneurysm removal.

The patient’s body was cooled, his heart was stopped, all of the blood washed from the brain, and “if a vein were cut literally ice water flowed,” Dr. Maroon said.

(Cont. on Page 6 Part I)
Required Qualities for Neurosurgery and Ironman

• Commitment
Required Qualities for Neurosurgery and Ironman

• Commitment

• Passion
Required Qualities for Neurosurgery and Ironman

• Commitment
• Passion
• Practice
Required Qualities for Neurosurgery and Ironman

• **Commitment**
• **Passion**
• **Practice**
• **Focus/concentration**
Required Qualities for Neurosurgery and Ironman

- **Commitment**
- **Passion**
- **Practice**
- **Focus/concentration**
- **Perseverance**
Required Qualities for Neurosurgery and Ironman

• **Commitment**
• **Passion**
• **Practice**
• **Focus/concentration**
• **Perseverance**
• **Prioritization**
Required Qualities for Neurosurgery and Ironman

NEVER QUIT!
Criteria for Enjoyable Activity

- Must involve physical, sensory and intellectual skills and a feeling of control of one’s actions
“Flow”

• Flow Activities
  – Surgery!
  – Rock climbing
  – Chess
  – Composing poetry or music
  – Painting
  – Triathlons!
“Flow”

– The merging of action and awareness
– Complete concentration and focus
– Narrowing of consciousness
“Beyond Boredom and Anxiety”
“Flow”

Criteria for a Flow Experience

– Complete focus and attention
– A defined beginning and end
– Constant challenges requires specific skills and training
– Immediate Feedback
Re-Balance your Life

- Work
- Physical
- Family/Social
- Spirituality
My “Square”
Summary

Choices = Outcomes
So Choose Wisely
Epigenetics allows us 70% Control

Remember the Four Pillars to Healthy Aging

• Food and Nutrition
• Exercise
• Stress Reduction
• Avoiding Environmental Toxins
THE LONGEVITY FACTOR

HOW RESVERATROL AND RED WINE ACTIVATE GENES FOR A LONGER AND HEALTHIER LIFE

JOSEPH MAROON, M.D.

FOREWORD BY JOSEPH BAUR, PH.D.

“...A guidebook for longevity that is both audacious and achievable.” — Sanjay Gupta, M.D.

Thank You