



Mentoring the Mentor

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Mentor goals:

- ✧ To declare what is possible and establish a commitment to that possibility
- ✧ Address personal and professional barriers limiting the ability to serve
- ✧ Evolution of vision/mission/ethics that drive success
- ✧ Create immediate action steps to apply learning and growth
- ✧ Construct the round table of applied trophologists

Mentoring the mentor:

- ⌘ Who are the mentors? – Practitioners
- ⌘ Who are we mentoring? – Patients and GAP
- ⌘ What's the purpose? – Optimized life
- ⌘ How does it work? – Whatever you learn you teach someone else (anyone else)
- ⌘ Who's is included? – Self selection, you pick yourself

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Mentoring the mentor:

- ⌘ Each participant attends monthly teleconferences (1 hour in duration, 4th Thursday of month) creating a round table discussion/exploration of the dynamics and details of a nutrition-based wholistic practice
- ⌘ Each participant chooses a colleague in his/her world to convey the notes and information – no information squandering
- ⌘ Issues/problems/questions are considered a learning process for everyone, although individual's remain anonymous
- ⌘ All questions, comments, case studies to be directed through email to SP rep who will compile and include in next teleconference (must be submitted 10 days prior)

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Approach to wisdom

Throughout history the really fundamental changes in societies have come about not from the dictates of governments and the results of battles, but through vast numbers of people changing their minds, sometimes only a little bit.

Willis Harman

Genes – On or Off

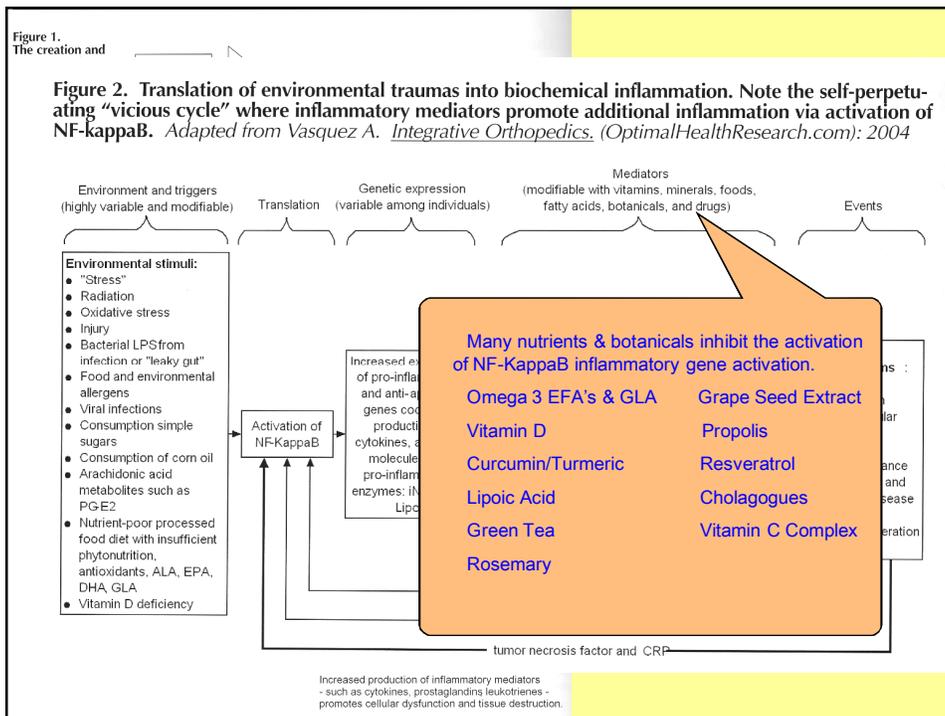
- ⌘ We are in the midst of the nutrigenomics era, wherein it has been discovered that environmental factors, including diet, can turn on or turn off specific genes
- ⌘ It has been described as gene codes that may be up-regulated or down-regulated
- ⌘ It is possible to do specific genomic studies that identify genetic predispositions in individual codes carried in the chromosomes
- ⌘ This in turn may be predictive of certain cellular activities and metabolic tendencies an individual may have towards certain wellness or illness events

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Unified Mechanisms

- ☞ As always there are some pathways that may be relevant not only to some people but to all, because of the high upstream nature of that genetic event
- ☞ The NF kappa beta gene activation has previously been observed as a gene code that may amplify inflammatory activity when engaged, and thus strategies have been developed to reduce and limit activation of this gene function
- ☞ It is well known that if the factors that reduce and limit NF kappa beta activation are employed downstream pro-inflammatory events may be effected

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Free Radical Load and Antioxidant Relationship

- There are over 100,000,000,000 (100 Billion) free radicals created in the body per DAY.

- Previous medical logic was that of the stoichiometric model –



- ORAC – measurement – in vitro - of antioxidant capacities

- Lately, many people focused on the use of ORAC to quantify the power of their formula. There is no proof of this being valid in vivo. Also most diseased states are not dramatically altered by the use of antioxidants alone.

Antioxidant Supply vs. Gene Activation

Oxygen Radical Absorbance Capacity (ORAC) is a method of measuring antioxidant capacities in biological samples in vitro.[1][2] A wide variety of foods has been tested using this methodology, with certain spices, berries and legumes rated highly[3]. Correlation between the high antioxidant capacity of fruits and vegetables, and the positive impact of diets high in fruits and vegetables, is believed to play a role in the free-radical theory of aging. However, there exists no physiological proof in vivo that this theory is valid. Consequently, the ORAC method, derived only in test tube experiments, cannot currently be applied to human biology.

- *By activating Nrf2 you can multiply the body's natural antioxidant response to combat inflammation, minimize free radical damage and transport detoxification to new levels.*

Nrf2

Transcription activators that bind to antioxidant response elements (ARE) in the promoter regions of target genes. Important for the coordinated up-regulation of genes in response to oxidative stress.

Functional Medicine

Functional medicine could be characterized, therefore, as upstream medicine or back-to-basics – back to the patient's life story, back to the processes wherein disease originates, and definitely back to the desire of healthcare practitioners to make people well, not just manage symptoms.

Edward Leyton, MD, 2005

Adaptogenic Influence

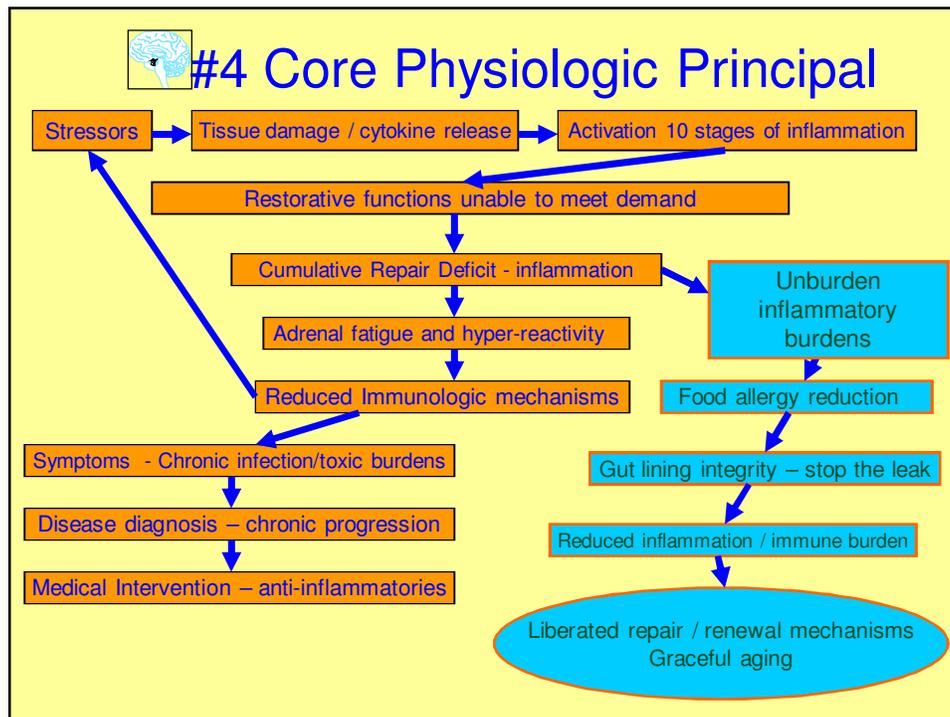
- ☞ As always we are seeking to discover the nutritional factors that influence these genetic activities
- ☞ To find a food or lifestyle event that influences these normally responsive nuclear activities is essential to the nutritional clinician
- ☞ It is not the pursuit of the clinician to attempt to determine how much inflammation should be present or not – it is not obvious whether protocols should be pro-inflammatory or anti-inflammatory
- ☞ How do you determine how much inflammation should occur, how much repair should happen?
- ☞ Instead we promote the adaptogenic response of cellular control mechanisms to increase or decrease repair activity

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Cumulative Repair Deficit

- ☞ This is the functional term that defines the inflammatory status of the body
- ☞ Words describe ideas, and ideas are what direct us in our efforts – as clinicians when inflammation is named it is assumed that it should be reduced and blocked and that it is a bad thing – yet without the five stage inflammation process at work physiology falls into disrepair and the elaborate tissue based organism called the human body cannot be maintained and repaired
- ☞ In general inflammation should not be suppressed or reduced, but rather completed – when it is not completed by the end of the day it is called a cumulative repair deficit
- ☞ Most people over 40 carry a deficit of repair called silent or symptomatic inflammation

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5 Stages of Inflammation

- ☞ 1 – Cytokine release from damaged cells
- ☞ 2 – Erythema increased blood flow
- ☞ 3 – Swelling plasma leak from capillaries into damaged area
- ☞ 4 – Leukocyte infiltration for clean up
- ☞ 5 – Fibrous tissue infusion creating repair

Inflammatory inhibition by cortisol

- ↪ Cortisol has five effects on inflammation
 - ↪ Stabilization of membranes reducing rupture and cytokine release
 - ↪ Decreases capillary permeability thus limiting swelling
 - ↪ Decreases migration of WBC's
 - ↪ Suppresses immune system and T lymphocytes
 - ↪ Lowers fever, interferon release and thus vasodilatation
 - ↪ Licorice can increase effects of Cortisol (1 tsp twice daily), thus is used a bridging protocol with prednisone

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Reduce cortisol

- ↪ Cortisol is most influenced by low blood sugar levels requiring cortisol elevation to release sugar
- ↪ The best way to reduce cortisol responses is by eating six meals a day of low glycemic foods resulting in lower cortisol levels
- ↪ If cortisol stays elevated and a low glycemic diet is adopted ultimately the waist will stay thick – this can lead unwittingly to immune depression and crisis
- ↪ Watch the waist thickness as best indicator of cortisol function

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What does it mean clinically?

- ☞ If a person is in silent or symptomatic states of toxicity and inflammation it is possible to assist in two ways:
 - ☐ Provide nutrient and antioxidant supplies to fuel the detoxification pathways and assist in reducing the metabolic burden of toxicity
 - ☐ Provide nutrient and botanical supplies that activate the inherent genetic mechanisms that produce antioxidants and therefore increase innate responses to toxicity and free radical ROS burdens (including increased production of glutathione, catalase, SOD, Phase II detoxification activity, and retiring NF kappa beta inflammatory gene activity)

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Compressing morbidity

- ☞ Not only does calorie restriction extend life but also reduces morbidity by activating stress responses that are hard-wired into the gene code
- ☞ These stress responses activate biochemistry that is designed to increase functionality and promote survival
- ☞ The activation of these survival mechanisms also act to promote wellness, if not only activated or survival
- ☞ In other words it is good to live somewhat inside our survival mechanisms as away of life, and this reduce morbidity, disrepair and decline
- ☞ Can we promote these mechanisms biochemically?

Hormesis

- ⌘ A term originally coined by toxicologists to describe a biphasic dose-response curve wherein an agent has a stimulatory effect at low doses and a toxic effect at a high dose
- ⌘ Now this term has been adopted by medicine to portray the beneficial adaptive responses of cells to moderate stress
- ⌘ In other words moderate stress promotes health, wellbeing, and mental and physical performance
- ⌘ So gain Nietzsche as accurate when he said, “What does not kill you makes you strong”

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Hormesis – Some known mechanisms

- ⌘ In response to stress the body calls up defense molecules – once present these molecules not only effect the perceived threat, but also increase resistance to other threats and repair existing damage
- ⌘ HSP (Heat Shock Proteins) are produced to protect and chaperone other proteins by binding to them and shielding them from attack
- ⌘ SIRT1 (Sirtuin 1) is a bodyguard that activates multiple genes to produce antioxidants and cell membrane stabilizers
- ⌘ Growth factors are generated to promote repair
- ⌘ Cellular kinases are produced to promote motility²²

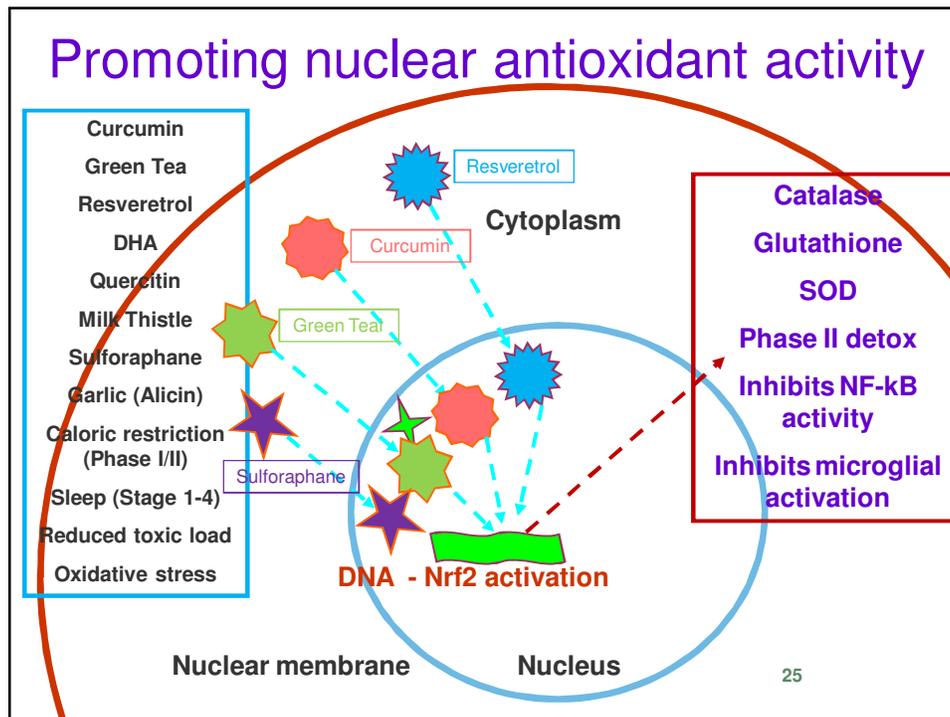
Adaptogens & Hormesis

- ↪ Adaptogens are herbs and nutrients that promote stress responses to help the body better adapt to stress
- ↪ Many phytochemical that are found beneficial are in fact the plant's responses against diseases, pests and grazing
- ↪ Resveretrol has been proven to be a potent sirtuin activator
- ↪ Panax Ginseng and Milk Thistle reduce insulin resistance and increase DHEAS (primary marker of adrenals vitality)
- ↪ Echinacea increased heat shock proteins and immune potency
- ↪ Gingko reduces oxidative damage to DNA in numerous studies and acts antioxidant and anti-inflammatory

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Pro-inflammatory vs. Anti-inflammatory

- ↪ The goal biochemically is to promote inherent cell regulatory mechanism to complete repair activity without being exaggerated into inflammatory chaos
- ↪ So the interest turns to the foods and lifestyle events that assist the body to find its intelligent and innately directed repair activity
- ↪ Proper sleep (Phase 1-4) will promote Nrf2 gene activity and thus promote body balancing of free radical damage and toxicity
- ↪ Caloric restriction as in the Phase II diet will promote hormetic activity and bring about sirtuin and heat shock protein production and increase Nrf2 activity



Targeting Inflammation-Induced Obesity and Metabolic Diseases by Curcumin and Other Nutraceuticals. [Aggarwal BB.](#)

Cytokine Research Laboratory, Department of Experimental Therapeutics
The University of Texas M. D. Anderson Cancer Center, Houston, Texas

- Extensive research within the past two decades has revealed that obesity, a major risk factor for type 2 diabetes, atherosclerosis, cancer, and other chronic diseases, is a pro-inflammatory disease. Several spices have been shown to exhibit activity against obesity through antioxidant and anti-inflammatory mechanisms. Among them, curcumin, a yellow pigment derived from the spice turmeric (an essential component of curry powder), has been investigated most extensively as a treatment for obesity and obesity-related metabolic diseases. Curcumin directly interacts with adipocytes, pancreatic cells, hepatic stellate cells, macrophages, and muscle cells. There, it suppresses the pro-inflammatory transcription factor nuclear factor-kappa B, signal transducer and activator of transcription-3, and Wnt/beta-catenin, and it activates peroxisome proliferator-activated receptor-gamma and Nrf2 cell-signaling pathways, thus leading to the down regulation of adipokines, including tumor necrosis factor, interleukin-6, resistin, leptin, and monocyte chemoattractant protein-1, and the up regulation of adiponectin and other gene products. These curcumin-induced alterations reverse insulin resistance, hyperglycemia, hyperlipidemia, and other symptoms linked to obesity. Other structurally homologous nutraceuticals, derived from red chili, cinnamon, cloves, black pepper, and ginger, also exhibit effects against obesity and insulin resistance. Expected final online publication date for the Annual Review of Nutrition Volume 30 is July 17, 2010.

Curcumin and Nrf2 Activation

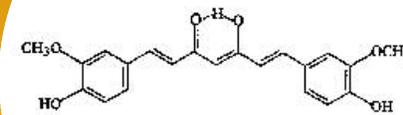


Fig. 1 Chemical structure of curcumin

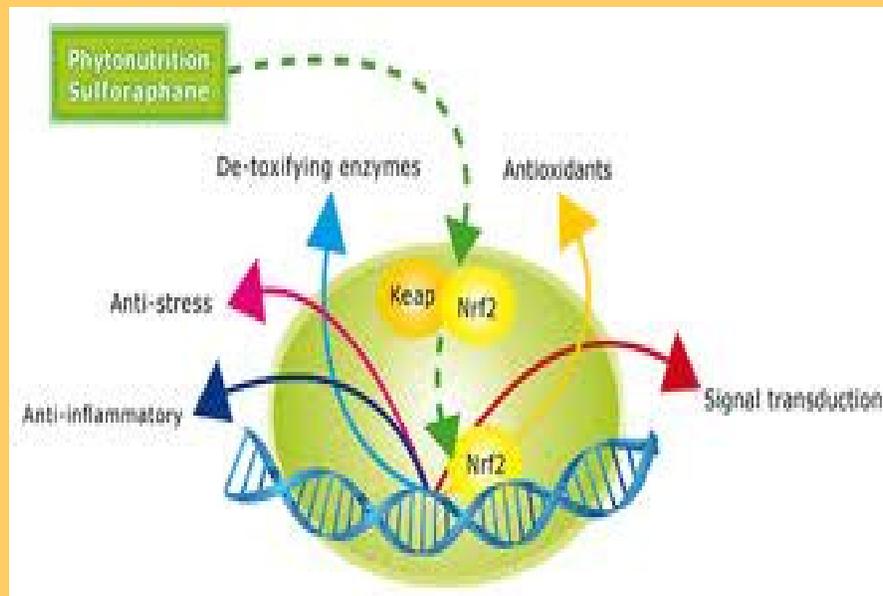
Sulforaphane protects immature hippocampal neurons against death caused by exposure to hemin or to oxygen and glucose deprivation.

[Soane L, Li Dai W, Fiskum G, Bambrick LL.](#)

Department of Anesthesiology, Center for Shock, Trauma, and Anesthesiology Research (STAR), Uof M Sch/Medicine

- Oxidative stress is a mediator of cell death following cerebral ischemia/reperfusion and heme toxicity, which can be an important pathogenic factor in acute brain injury. Induced expression of phase II detoxification enzymes through activation of the antioxidant response element (ARE)/Nrf2 pathway has emerged as a promising approach for neuroprotection. Little is known, however, about the neuroprotective potential of this strategy against injury in immature brain cells. In this study, we tested the hypothesis that sulforaphane (SFP), a naturally occurring isothiocyanate that is also a known activator of the ARE/Nrf2 antioxidant pathway, can protect immature neurons from oxidative stress-induced death. The hypothesis was tested with primary mouse hippocampal neurons exposed to either O₂ and glucose deprivation (OGD) or hemin. Treatment of immature neurons with SFP immediately after the OGD during reoxygenation was effective in protecting immature neurons from delayed cell death. Exposure of immature hippocampal neurons to hemin induced significant cell death, and both pre- and cotreatment with SFP were remarkably effective in blocking cytotoxicity. RT-PCR analysis indicated that several Nrf2-dependent cytoprotective genes, including NAD(P)H quinoneoxidoreductase 1 (NQO1), hemeoxygenase 1 (HO1), and glutamate-cysteinylglycine modifier subunit (GCLM), which is involved in glutathione biosynthesis, were up-regulated following SFP treatment both in control neurons and following exposure to OGD and hemin. These results indicate that SFP activates the ARE/Nrf2 pathway of antioxidant defense and protects immature neurons from death caused by stress paradigms relevant to those associated with ischemic and traumatic injury to the immature brain.

Natural Antioxidant Activation from Supplementation of Sulforaphane



Resveratrol induces glutathione synthesis by activation of Nrf2 and protects against cigarette smoke-mediated oxidative stress in human lung epithelial cells

Kode A, Rajendrasozhan S, Caito S, Yang SR, Megson IL, Rahman I.

Department of Environmental Medicine, Lung Biology and Disease Program, University of Rochester Medical Center

- Nuclear erythroid-related factor 2 (Nrf2), a redox-sensitive transcription factor, is involved in transcriptional regulation of many antioxidant genes, including glutamate-cysteine ligase (GCL). Cigarette smoke (CS) is known to cause oxidative stress and deplete glutathione (GSH) levels in alveolar epithelial cells. We hypothesized that resveratrol, a polyphenolic phytoalexin, has antioxidant signaling properties by inducing GSH biosynthesis via the activation of Nrf2 and protects lung epithelial cells against CS-mediated oxidative stress. Treatment of human primary small airway epithelial and human alveolar epithelial (A549) cells with CS extract (CSE) dose dependently decreased GSH levels and GCL activity, effects that were associated with enhanced production of reactive oxygen species. Resveratrol restored CSE-depleted GSH levels by upregulation of GCL via activation of Nrf2 and also quenched CSE-induced release of reactive oxygen species. Interestingly, CSE failed to induce nuclear translocation of Nrf2 in A549 and small airway epithelial cells. On the contrary, Nrf2 was localized in the cytosol of alveolar and airway epithelial cells due to CSE-mediated posttranslational modifications such as aldehyde/carbonyl adduct formation and nitration. On the other hand, resveratrol attenuated CSE-mediated Nrf2 modifications, thereby inducing its nuclear translocation associated with GCL gene transcription, as demonstrated by GCL-promoter reporter and Nrf2 small interfering RNA approaches. Thus resveratrol attenuates CSE-mediated GSH depletion by inducing GSH synthesis and protects epithelial cells by reversing CSE-induced posttranslational modifications of Nrf2. These data may have implications in dietary modulation of antioxidants in treatment of chronic obstructive pulmonary disease.

- Arch Biochem Biophys. 2009 Jan 1;481(1):110-5. Epub 2008 Oct 22.

Journal of Neurochem (2006)

- Abstract:** Astrocytes may modulate the survival of motor neurons in amyotrophic lateral sclerosis (ALS). We have previously shown that fibroblast growth factor-1 (FGF-1) activates astrocytes to increase secretion of nerve growth factor (NGF). NGF in turn induces apoptosis in co-cultured motor neurons expressing the p75 neurotrophin receptor (p75NTR) by a mechanism involving nitric oxide (NO) and peroxynitrite formation. We show here that FGF-1 increased the expression of inducible nitric oxide synthase and NO production in astrocytes, making adjacent motor neurons vulnerable to NGF-induced apoptosis. Spinal cord astrocytes isolated from transgenic SOD1G93A rats displayed increased NO production and spontaneously induced apoptosis of co-cultured motor neurons. FGF-1 also activates the redox-sensitive transcription factor nuclear factor erythroid 2-related factor 2 (Nrf2) in astrocytes. Because Nrf2 increases glutathione (GSH) biosynthesis, we investigated the role of GSH production by astrocytes on p75NTR-dependent motor neuron apoptosis. The combined treatment of astrocytes with FGF-1 and t-butylhydroquinone (tBHQ) increased GSH production and secretion, preventing motor neuron apoptosis. **Moreover, Nrf2 activation in SOD1G93A astrocytes abolished their apoptotic activity.** The protection exerted by increased Nrf2 activity was overcome by adding the NO donor DETA-NONOate to the co-cultures or by inhibiting GSH synthesis and release from astrocytes. These results suggest that activation of Nrf2 in astrocytes can reduce NO-dependent toxicity to motor neurons by increasing GSH biosynthesis.

Naturally occurring phytochemicals for the prevention of Alzheimer's disease.

Alzheimer's disease (AD) is an age-related neurodegenerative disease increasingly recognized as one of the most important medical problems affecting the elderly. Although a number of drugs, including several cholinesterase inhibitors and an NMDA receptor antagonist, have been approved for use, they have been shown to produce diverse side effects and yield relatively modest benefits. To overcome these limitations of current therapeutics for AD, extensive research and development are underway to identify drugs that are effective and free of side effects. In this review, we discuss the potential of naturally occurring phytochemicals for AD therapy. In particular, curcumin, resveratrol, and green tea catechins have been shown to have the potential to prevent AD because of their anti-amyloidogenic, anti-oxidative, and anti-inflammatory properties. These polyphenolic phytochemicals have been shown to have anti-amyloidogenic, anti-oxidative, and anti-inflammatory properties that suppress disease pathogenesis of AD, and summarize the intracellular and molecular targets of selected dietary phytochemicals that might slow the progression of AD.

Green Tea catechins have been suggested to have the potential to prevent AD because of their anti-amyloidogenic, anti-oxidative, and anti-inflammatory properties.

New Product Alert – Read All About It!

□ HerbaVital released April, 2010 is a unique combination of factors to reduce the physiologic decline known as aging, but also acts as a hormetic influence to up-regulate stress responsibility and therefore survival status. This is cocktail of daily herbal constituents that can universally support the declining stress response that is so essential to wellness and vitality. It is a strategy in a formula for daily minimizing of the underlying process of aging. This product takes the assessment out of the picture for the clinician and addresses the common background issues at work universally in the patient

□ HerbaVital:

- Japanese Knot Weed root extract 100:1 80 mg providing 36 mg of natural resveretrol
- Milk Thistle seed 5:1 50 mg providing 48 mg of silybin
- Korean Ginseng root 5:1 50 mg
- Masson Pine bark 100:1 50 mg providing 37.5 mg proanthocyanidins
- Ginkgo Leaf 50:1 30 mg

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Product Alert – Read All About It!

□ Vitanox is a unique combination of herbs to provide strong antioxidant protection, and now we discover also acts to up-regulate Nrf2 gene activity and subsequent survival compound status increase, including glutathione synthesis. This is cocktail of daily herbal constituents that can universally support the overloaded detoxification and inflammatory mechanisms. It is a strategy in a formula for daily minimizing of the underlying process of aging and degeneration. This product was introduced by Kerry Bone based on widespread agreement about the merits of these herbs, before and correctly predicting the emerging research around Nrf2 gene activation.

□ Vitanox tablet:

- Rosemary leaf extract 5:1 200 mg providing carnosol and rosmarinic acid
- Green Tea leaf extract 25:1 166.7 mg providing 83.35 mg of catechins
- Turmeric rhizome extract 25:1 80 mg providing 70.4 mg curcuminoids
- Grape Seed extract 120:1 50 mg providing 42.5 mg procyanidins

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Product Alert – Read All About It!

❑ Cruciferous Complete is a combination of kale and brussel sprouts to protect against free radicals and now also is shown to up-regulate Nrf2 gene activity and subsequent survival compound status increase, including glutathione synthesis. This nutrient supports Phase I & II detoxification pathways promoting reduction of toxic load in the body and well as supports repair mechanisms involving the eye. It contains a myriad of nutrients including vitamins B6, C, K, calcium, copper, potassium, and dietary fiber. It also contains carotenoids, which include beta carotene and lutein which help quench free radical ROS effects and retinal repair activity

- ❑ Cruciferous Complete capsule:
 - ❑ Vitamin K 4 mcg
 - ❑ Potassium 10 mg
 - ❑ Kale 300 mg
 - ❑ Brussel Sprouts 300 mg

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Visit after visit – Start today

- 🌀 See each patient for the antioxidant/inflammatory status they present
- 🌀 Teach every patient the principles of calorie restriction and stress response up-regulation and prepare them with anti-aging concepts to maximize their lifespan and wellspan
- 🌀 Employ the principles of the seven pillars as a way of seeing the human in the process of manifestation - Application of pillars is sequential and at the discretion of the doctor – always start with caring for the chief complaint, the pillars that relate to that issue, and the deemed physiological priority (eg – immune or hormonal or inflammatory)
- 🌀 Connect the dots between nutrition and Nrf2 activation to promote detoxification and reduce ROS burden
- 🌀 Be a practitioner who is always developing the patient beyond their request
- 🌀 Change outcomes, stop disease progression, reveal the inherent healing potential by using principles and products that express The Law (the way it was made to work)
- 🌀 Use Vitanox (2/day) and Cruciferous Complete (2/day) and HerbaVital (1/day) to reduce aging and promote innate responses to survival

The greatest use of your time

Think New Thoughts



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