

Inflammation: A Unifying Causation of Disease

Nutritional Intervention

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Background:

Mounting evidence suggests that inflammation is a common underlying cause of major diseases, including but not limited to – heart disease, diabetes, cancer, stroke, Alzheimer’s disease, viral pneumonia, etc.(Hunter, 2012) Inflammation is part of the body’s immune response. Immune cells produce antibodies, cytokines and other inflammatory molecules. Recent science has uncovered new inflammatory molecules and the pathways through which they interact (Fukata, 2007). Doctors and medical scientists now realize that chronic inflammation is crucial to disease development and that new avenues of diagnosis, treatment and/or prevention are needed (Uttara, 2009).

Any discussion involving the topic of inflammation must also explain the relationship of inflammation to oxidative stress and immune system function. Oxidative stress can occur when there is an imbalance of free radicals and antioxidants in the body. Keep in mind that normal body function produces free radicals during normal metabolic processes. Like a car engine burning fuel, in this case, the fuel is food. To counteract these free radicals, cells naturally produce antioxidants. In normal health, the body maintains a balance between antioxidants and free radicals. When the immune system responds to infection or injury, it also triggers a temporary oxidative stress response. Normally, inflammation goes away after the immune system eliminates the infection or repairs the damaged tissues. When the body is overwhelmed with an out of control inflammatory or oxidative stress situation, chronic disease can develop,

such as diabetes, heart disease and arthritis, to name a few. Another example that we are faced with during the current Covid-19 pandemic is a viral induced pneumonia associated with excessive production of inflammatory cytokines. This reaction, known as cytokine storm, can be a life-threatening complication (Monteleone, 2020)

This inflammatory or oxidative stress process is especially evident in the immune cells, which use free radicals in their functions and suffer a senescent deterioration probably linked to oxygen stress. “Therefore, since the immune system is an indicator of health and a longevity predictor, the protection of this system afforded by dietary antioxidant supplementation may play an important role in order to achieve a healthy ageing.” (Fuente, 2002)

Inflammation is like a light switch which can be turned on and off; The Problem: It can stay on and cause both silent and visible disease. Example: Cancer is an inflammatory wound “that does not heal” (Byun, 2013).

The ability to switch the out of control ‘inflammatory light’ off is the answer. The only problem is that there is no light or beacon that tells us inflammation has occurred within our body. Chronic inflammation is a silent disorder. All people are being bombarded daily with chronic inflammation which is slowly waging a war of attrition on our tissues and organs. Picture air and water pollution, ionizing radiation from the sun, smoking, automobile emissions, etc.

Most doctors only focus on observable inflammatory disease and symptoms in specific organs while the rest of the body may be silently deteriorating from the same insidious inflammatory process.

How does one prevent out of control inflammation? Identify the genes that control inflammation and the release of the causative cytokine signaling molecules. (Natoli, 2011).

Prevention is the rule of the day! Not intervention which is the basic philosophy of the pharmaceutical industry. It was the great physician Hippocrates, who in 450 BC, stated “Let Food Be Thy Medicine and Medicine Be Thy Food.” This quote rings true even today as we face one infectious insult after another – SARS, Ebola, COVID-19, etc. “Although many patients are convinced of the importance

of food in both causing and relieving their problems, many doctors' knowledge of nutrition is rudimentary” (Smith, 2004)

A preventive natural nutritional anti-inflammatory formulation, NuGenia™, has been designed that utilizes compounds that have the potential to modulate expression of the genes that produce the inflammatory molecules that cause inflammation.

“Therefore, the role that nutritional components, in particular vitamins and minerals, play in the modulation of miRNA profiles, and consequently health and disease, is increasingly being investigated, and as such is a timely subject for review. The recently posited potential for viable exogenous miRNA to enter human blood circulation from food sources adds another interesting dimension to the potential for dietary miRNA to contribute to gene modulation” (Beckett, 2014).

The current healthcare climate is opportune for the introduction of a proprietary well-designed nutritional supplement formula in which the possible effect of the whole is better than any of the parts. The NuGenia™ nutritional formulation is an attempt to integrate nutrients that may be complementary with each other with the potential objective of supporting the immune system and modulating chronic inflammation while it is still a silent disorder. Example: vitamin A plus zinc may reduce the risk of developing advanced age-related macular degeneration by about 25 percent; see NuGenia™ descriptive discussion for vitamin A.

The objective is for a person to build up an internal storehouse of these important anti-inflammatory compounds while one is healthy. When disease hits, your body can call up these needed compounds to naturally enhance the immune system and neutralize the out of control inflammatory processes. People during the current Coronavirus pandemic are stocking up and hoarding toilet paper, drugs, and even dried food with 25-year storage capacity. The same idea/picture holds true for one's body and immune system. What is the use of all these external products when your own 'internal system' is being attacked and decimated? An example of inflammation potentially out of control is the formation of blood clots in veins, called venous thromboembolism (VTE). 40% of people who develop VTE do not know what caused it, yet it is the third deadliest cardiovascular

diagnosis. “We don’t yet understand the molecular triggers which drive the development of life-threatening clots in deep veins,” said Yogen Kanthi, M.D., the study’s senior author and a vascular cardiologist at U-M’s Frankel Cardiovascular Center. “Our work aimed to identify and block a previously unrecognized pathway linking inflammation and thrombosis.” Kanthi’s team found an enzyme called CD39 diffused circulating “danger” signals and inflammatory cytokines in blood during thrombosis (Anyanwu, 2019).

The ability to fight disease is like fighting crime; when there are more cops on the street, more criminals are arrested. A commonsense approach is to build up one’s health reserve through a well- rounded nutritional formula that places into storage the nutritional ammunition that will be called up to fight disease when it raises its ugly head.

The focus of the unique NuGenia™ formula of ingredients is the potential modulation and/or reduction of the inflammatory genetic markers associated with chronic disease.

The substances in the formulation are listed individually in this review and the application to the inflammatory process is described. Scientific articles supporting these statements are shown. However, keep in mind that many nutritional related clinical studies are in animals. The hurdles that clinical nutrition researchers encounter is well stated in an article by Weaver and Miller. “Clinical nutrition researchers encounter many hurdles, including difficulties with recruiting volunteers, navigating a complex maze of approvals, and coping with myriad biases.”

“Special scientific issues involved with clinical nutrition research include study designs that increase or decrease the status of a nutrient, food, or bioactive reagent but often do not compare presence with absence of the compound (as is typical in drug trials); ethical issues regarding withholding of a nutrient from participants who are low or deficient in that nutrient; study populations that may already be sufficient in the compound of interest and, thus, may not show benefit of supplementation; interventions that are difficult to blind to both the subjects and the investigators; and a tension between studying subgroups most likely to respond versus recruiting a representative and, therefore, generalizable sample.” (Weaver, 2017).

Be your own advocate in the current healthcare environment. Let your body be your guide! Nature is all around us. The pharmaceutical industry is very young, maybe only 200 years old. Life has been around a lot longer! Do we have the liberty to wait to protect our health? Time is the enemy and is not our friend.

The NuGenia™ Objective: Prevention Not Intervention!

References:

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- i. Smith, R. 2004. “Let Food Be Thy Medicine...” *BMJ*. 328:7433.
- j. Uttara, B et al. 2009. Oxidative Stress and Neurodegenerative Diseases: A Review of Upstream and Downstream Antioxidant Therapeutic Options. *Current Neuropharmacology*, 2009, 7, 65-74.
- k. Weaver, CM and Miller, JW. 2017. Challenges in conducting clinical nutrition research. *Nutrition Reviews*. 75(7):491–499.

Definitions:

The words, acronyms and medical verbiage used in this pamphlet are taken from the quoted scientific and medical literature. This definition section has been prepared for the readers convenience.

- Acute respiratory disease syndrome (ARDS): Condition in which fluid builds up in the tiny, elastic air sacs (alveoli) in your lungs. The fluid keeps your lungs from filling with enough air, which means less oxygen reaches your bloodstream. This deprives your organs of the oxygen they need to function.
- Adaptogen: In traditional Chinese medicine, ginseng is usually described as an “adaptogen,” a substance that can assist an organism in overcoming various types of stress, restore balance or homeostasis and increase nonspecific resistance.
- Antibody: A blood protein produced in response to and counteracting a specific antigen. Antibodies combine chemically with substances which the body recognizes as alien, such as bacteria, viruses, and foreign substances in the blood.
- Antigen: a toxin or other foreign substance which induces an immune response in the body, especially the production of antibodies.
- Apoptosis: the death of cells which occurs as a normal and controlled part of an organism's growth or development.
- Atherosclerosis: A disease of the arteries characterized by the deposition of plaques of fatty material on their inner walls.
- Carcinogenesis: The initiation of cancer formation.
- COPD: Chronic obstructive pulmonary disease.
- CRP: C-reactive protein. A protein made by your liver. It is sent into your bloodstream in response to inflammation.
- Cytokines: Small proteins that are involved in signals sent between cells. Examples: nuclear factorE2 (Nrf2), superoxide dismutase (SOD), TNF- α and NF- κ B, IFN- γ , and IL-6.
- DNA: Deoxyribonucleic acid, a self-replicating material which is present in nearly all living organisms as the main constituent of chromosomes. It is the carrier of genetic information.
- Endogenous: Growing or originating from within an organism.

- Endothelial syndrome: Damage to the inner lining of the blood vessel that leads to atherosclerosis.
- Glaucoma: a condition of increased pressure within the eyeball, causing gradual loss of sight.
- Glutathione (GSH): an antioxidant in plants, animals, fungi, and some bacteria. Glutathione is capable of preventing damage to important cellular components caused by reactive oxygen species such as free radicals, peroxides, lipid peroxides, and heavy metals.
- Hyperlipidemia: An abnormally high concentration of fats or lipids in the blood.
- Glutathione reductase: A ubiquitous enzyme, which catalyzes the reduction of oxidized glutathione (GSSG) to glutathione (GSH).
- Immune cells: Cells that are part of the immune system and help the body fight infections and other diseases. Immune cells develop from stem cells in the bone marrow and become different types of white blood cells.
- Inflammatory molecules: Inflammatory mediators that are part of the complex biological response of body tissues to harmful agents, such as bacteria, viruses, damaged cells or toxic irritants.
- Innate immunity: A person's physical, chemical, and cellular defenses against invasion or disease.
- Insulin: A hormone that helps blood sugar enter the cells in your body where it can be used for energy. Without insulin, blood sugar cannot get into cells and builds up in the bloodstream.
- LPS induced cells: LPS can stimulate cells to become inflamed.
- Metabolic syndrome: A cluster of biochemical and physiological abnormalities associated with the development of cardiovascular disease and type 2 diabetes.
- Minerals: Substances that are formed naturally in the Earth. Minerals are usually solid, inorganic, have a crystal structure, and form naturally by geological processes.
- mRNA: Messenger RNA. Transfers information from DNA to the cell machinery that makes proteins.
- miRNA: Small, non-coding RNA molecules that regulate expression of a person's genes.

- Natural killer (NK) cells: A cell that can react against and destroy another cell without prior sensitization to it. An NK cell attaches to a target cell, releases chemicals that breach its cell wall, and causes it to lyse (break up).
- Necrosis: the death of most or all the cells in an organ or tissue due to disease, injury, or failure of the blood supply.
- Neutrophils: A type of white blood cell that protects against infection.
- Nrf2: A protein that controls how certain genes are expressed. These genes help protect the cell from damage caused by free radicals (unstable molecules made during normal cell metabolism).
- Nuclear Factor Kappa B (NF-κB): A protein complex that controls transcription of DNA, cytokine production and cell survival.
- Oxidative Stress: an imbalance between the production of free radicals and the ability of the body to counteract or detoxify their harmful effects through neutralization by antioxidants.
- Oxygen stress: Also referred to as oxidative stress.
- Oxygen radicals: A type of unstable molecule that contains oxygen and that easily reacts with other molecules in a cell. A buildup of oxygen radicals in cells may cause damage to DNA, RNA, and proteins, and may cause cell death. An oxygen radical is a free radical. Also called reactive oxygen species.
- Proteins: Any of a class of nitrogenous organic compounds that consist of large molecules composed of one or more long chains of amino acids and are an essential part of all living organisms, especially as structural components of body tissues such as muscle, hair, collagen, etc., and as enzymes and antibodies.
- Senescence: The condition or process of deterioration with age.
- SLE: Systemic lupus erythematosus. An autoimmune disease in which the immune system attacks its own tissues, causing widespread inflammation and tissue damage in the affected organs. It can affect the joints, skin, brain, lungs, kidneys, and blood vessels.
- SOD: Superoxide dismutase; A metal-containing antioxidant enzyme that reduces harmful free radicals of oxygen formed during normal metabolic cell processes to oxygen and hydrogen peroxide

- Stem cells: Stem cells are special human cells that can develop into many different cell types, from muscle cells to brain cells. In some cases, they also can repair damaged tissues.
- T1DM: Type 1 diabetes mellitus. A condition in which the pancreas does not make insulin or makes very little insulin.
- T2DM: Type 2 diabetes mellitus. A condition in which the cells cannot use blood sugar efficiently to meet the body's needs.
- Th 1 : Cells that promote an immune response against viruses and bacteria.
- Th 2: Cells that promote an immune response against parasites and also facilitate tissue repair.
- TNF- α : Tumor Necrosis Factor alpha. An inflammatory cytokine produced by macrophages/monocytes during acute inflammation and is responsible for a diverse range of signaling events within cells, leading to necrosis or apoptosis. The protein is also important for resistance to infection and cancers. As a pro-inflammatory cytokine, TNF is secreted by inflammatory cells, which may be involved in inflammation-associated carcinogenesis.
- Transcription factors: Proteins that help turn specific genes "on" or "off"
- Venous thromboembolism (VTE): A condition in which a blood clot forms most often in the deep veins of the leg, groin or arm (known as deep vein thrombosis, DVT) and travels in the circulation, lodging in the lungs (known as pulmonary embolism, PE).

Components – NUGENIA™

1. Alpha Lipoic Acid (ALA)

ALA is described as a direct antioxidant and anti-inflammatory agent. Iron is a heavy metal which is important in carrying oxygen within the red blood cell and is also a cause of oxidative and inflammatory damage. ALA has the potential to inhibit iron-mediated oxidative damage.

Industry Claimed Uses: cognitive impairment, weight management, nerve disorders (neuropathy, MS), diabetes, atherosclerosis (endothelial syndrome), liver disease and lipid related disorders.

Science Related Genetic Application: upregulates nuclear factorE2 (Nrf2) dependent pathway. Codes for inflammatory mediator such as superoxide dismutase (SOD).

Scientific Articles:

- a. Linus Pauling Institute; Oregon State University. Nutrition/Supplements/Lipoic Acid. Linus Pauling Institute. Oregon State University.
- b. Salehi, B. et al. 2019. Insights on the Use of α -Lipoic Acid for Therapeutic Purposes. *Biomolecules*. 9(8): 356.

2. N-acetyl cysteine (NAC)

NAC is a powerful free radical scavenger, especially oxygen radicals involved in uncontrolled inflammation. Powerful antioxidant. Described as safe and well-tolerated. Involved in glutathione synthesis.

Industry Claimed Uses: chronic bronchitis, ulcerative colitis, intestinal dysfunction, muscle performance, asthma, Parkinson's disease, etc.

Science Related Genetic Application: reduced TNF- α and NF- κ B, IFN- γ , and IL-6 expression in LPS- induced cells in the pig small intestine (Lee, 2019)

Scientific Articles:

- a. Review article; Mokhtari et al. A Review on Various Uses of N-Acetyl Cysteine. 2017; *Cell Journal*, Vol 19, No 1, 11-17.
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3. Zinc picolinate

Zinc is an essential mineral with antioxidant and anti-inflammatory properties and plays an important role in cell mediated immunity. Supplementation studies in the elderly with this essential micronutrient have shown decreased incidence of infections, decreased oxidative stress, and decreased generation of inflammatory cytokines

Industry Claimed Uses: prevent free-radical induced tissue injury inflammatory reactions, enhance immune function, stabilize blood sugar levels, promote healthy skin, eyes and heart.

Science Related Genetic Application: Zinc is involved in the modulation of the proinflammatory response by targeting Nuclear Factor Kappa B (NF- κ B), a transcription factor that is the master regulator of proinflammatory responses. In vitro studies have shown that zinc decreases NF- κ B activation and its target genes, such as TNF- α and IL-1 β , and increases the gene expression of A20 and PPAR- α , the two zinc finger proteins with anti-inflammatory properties.

“After zinc supplementation, the incidence of infections was significantly lower, plasma zinc was significantly higher, and generation of tumor necrosis factor and oxidative stress markers was significantly lower in the zinc-supplemented than in the placebo group.” (Prasad 2007).

A study by the Age-Related Eye Disease Study Research Group (AREDS), Albany, NY, revealed that zinc had the potential when combined with other antioxidants to reduce the odds of developing visual loss in age-related macular degeneration (AMD).

Scientific Articles:

- a. AREDS Report #8. A Randomized, Placebo-Controlled, Clinical Trial of High-Dose Supplementation with Vitamins C and E, Beta Carotene, and Zinc for Age-Related Macular Degeneration and Vision Loss. 2001. Arch Ophthalmol. 119(10):1417-1436.

- b. Jarosz, M. et al. 2017. Antioxidant and anti-inflammatory effects of zinc. Zinc-dependent NF- κ B signaling. *Inflammopharmacology*. 25(1): 11–24.
- c. Prasad, AS et al. Zinc supplementation decreases incidence of infections in the elderly: effect of zinc on generation of cytokines and oxidative stress. 2007. *Am J Clin Nutr*. 85:837– 44.
- d. Prasad, AN. Zinc in Human Health: Effect of Zinc on Immune Cells. 2008. *Mol. Med*. 14(5-6): 353-357.

4. Coenzyme Q10 (CoQ10)

Coenzyme Q10 (CoQ10) is an antioxidant that your body produces naturally. Human cells use CoQ10 for growth and maintenance. Levels of CoQ10 in your body decrease as you age. CoQ10 levels have also been found to be lower in people with certain conditions, such as heart disease (Mayo Clinic, 2017).

Industry Claimed Uses: heart conditions, Parkinson’ disease, muscle weakness associated with use of statins, migraines, cellular energy production, physical performance.

Science Related Genetic Application: Clinical study showed reduction in the inflammatory cytokine TNF- α in rheumatoid arthritis patients. There was no significant difference in IL-6 levels between control and treated groups. (Abdollahzad, 2015). CoQ10 supplementation reduced inflammatory markers (TNF- α , IL-6, and MMP-9) in patients with multiple sclerosis (MS) (Sanoobar, 2015).

Scientific Articles:

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- e. <https://www.nccih.nih.gov/health/coenzyme-q10>.

5. **Glutathione (GSH):**

Humans synthesize glutathione and this antioxidant is found throughout the structure of cells. GSH is capable of preventing damage to important cellular components caused by reactive oxygen species such as free radicals, peroxides, lipid peroxides, and heavy metals.

Industry Claimed Uses: Cataracts and glaucoma, asthma, heart disease (high cholesterol), cancer, memory loss, fatigue, arthritis, etc. There are opinions that GSH can reverse the aging process.

Science Related Genetic Application: “GSH is not just an inhibitor of inflammation, but it is required to allow a proper response to infection, and “direct” the migration of inflammatory cells (PMN) away from the lung, where they cause acute respiratory disease syndrome (ARDS), and towards the site of infection, where they kill bacteria.” “This essential role of GSH in immunity might explain why in many diseases, not only AIDS, decreased GSH levels are associated with an increased susceptibility to infection. These include COPD, cystic fibrosis, influenza infection, and alcoholism, as ethanol impairs Th1/Th2 balance via GSH depletion.” (Ghezzi, 2011). Increased oxidative stress as reflected by decreased GSH was associated with a decline in executive function (cognitive decline) in a healthy population. This study demonstrates that decreased circulating levels of

glutathione predict the age-related decline in the executive domain, an area of cognition that is particularly susceptible to cardiovascular disease. (Hajjar, 2018).

Scientific Articles:

- a. Ghezzi, P. 2011. Role of glutathione in immunity and inflammation in the lung. *International Journal of General Medicine* 4: 105–113.
- b. Hajjar, I et al. 2018. Oxidative stress predicts cognitive decline with aging in healthy adults: an observational study. *Journal of Neuroinflammation* (2018) 15:17.

Vitamins: “A vitamin is a substance that makes you ill if you don’t eat it.”

(Albert Szent-Gyorgyi, Nobel Prize in Physiology or Medicine, 1937).

6. Vitamin A:

Vitamin A is necessary for normal differentiation of epithelial tissues, the visual process and reproduction, and is vital for the optimal maintenance and functioning of the innate and adaptive immune system. Vitamin A deficiency is one of the most profuse nutritional deficiencies worldwide. It is associated with increased susceptibility to infectious diseases in both man and animal models. Vitamin A also has a role as an anti-inflammatory agent. Supplementation with vitamin A has been found to be beneficial in a number of inflammatory conditions, including skin disorders such as acne vulgaris, broncho-pulmonary dysplasia and some forms of precancerous and cancer states. The present review suggests that vitamin A deficiency induces inflammation and aggravates existing inflammatory states. Supplementation with vitamin A in selected cases could ameliorate inflammation. The two main mechanisms which appear to be involved in the prevention of disease are the effects of vitamin A on the immune system and the effect on epithelial integrity (Reifen, 2002).

Industry Claimed Uses: Healthy vision, skin, bones and other tissues. Antioxidant fighting cell damage.

Science Related Genetic Application: “The drastic reduction in the levels of IGF-I mRNA and the resulting decrease in serum IGF-I concentrations may well explain

the growth retardation in vitamin A–deficient animals. To our knowledge, this is the first in vivo report on the effects of vitamin A on IGF system components.” (Fu, 2001). “In children, vitamin A deficiency results in increased risks of mortality and morbidity from measles and diarrheal infections, blindness, and anemia, and among women it is likely to be associated with high mortality related to pregnancy. Many of these effects can be linked to the immunological functions of vitamin A” (Villamor, 2005). An age-related eye disease study by the National Eye Institute (NEI/NIH,2001), (AREDS, 2001), found that taking high levels of antioxidants, such as vitamin A, along with zinc, may reduce the risk of developing advanced age-related macular degeneration by about 25 percent.

Scientific Articles:

- a. Age-Related Eye Disease Study Research Group. A Randomized, Placebo-Controlled, Clinical Trial of High-Dose Supplementation with Vitamins C and E, Beta Carotene, and Zinc for Age-Related Cataract and Vision Loss: AREDS Report No. 9. *Arch Ophthalmol.* 2001 Oct.
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7. Vitamin C

Vitamin C, also called ascorbic acid, plays a role in many bodily functions. According to the U.S. National Institutes of Health (NIH), the body uses vitamin C

to make skin, tendons, ligaments, and blood vessels. It also uses this vitamin to repair and maintain cartilage, bones, and teeth, to heal wounds and to form scar tissue. Vitamin C may also prevent cancer by blocking the damage made by free radicals. Aids in the absorption of iron. With respect to its function as an anti-inflammatory compound, Vitamin C is a potent reducing agent, meaning that it readily donates electrons to recipient molecules. It is therefore a significant antioxidant and anti-inflammatory compound. Even in small amounts, vitamin C can protect indispensable molecules in the body, such as proteins, lipids (fats), carbohydrates, and nucleic acids (DNA and RNA), from damage by free radicals and reactive oxygen species (ROS) that are generated during normal metabolism, by active immune cells, and through exposure to toxins and pollutants (e.g., certain chemotherapy drugs and cigarette smoke). (Linus Pauling Institute).

Industry Claimed Uses: heart disease, atherosclerosis, diabetes, stroke, and cancer.

Science Related Genetic Application: Dietary supplementation with antioxidant vitamins, especially vitamin C resulted in a significant decrease in the mRNA expression of pro-inflammatory cytokines. Study done in chick animal model (Jang, 2014). Potential to modulate cell response when inflammation occurs (Canali, 2014). Vitamin C is necessary for the immune system to mount and sustain an adequate response against pathogens, whilst avoiding excessive damage to the host. Vitamin C appears to be able to both prevent and treat respiratory and systemic infections by enhancing various immune cell functions (Carr, 2017)

Scientific Articles:

- a. Canali, R et al. 2014. Vitamin C supplementation modulates gene expression in peripheral blood mononuclear cells specifically upon an inflammatory stimulus: a pilot study in healthy subjects. *Genes Nutr.* 9:390.
- b. Carr, AC and Maggini, S. 2017. Vitamin C and Immune Function. *Nutrients.* 9 1211.

- c. Jang, I et al. 2014. Effects of Vitamin C or E on the Pro-inflammatory Cytokines, Heat Shock Protein 70 and Antioxidant Status in Broiler Chicks under Summer Conditions. *Asian Australas. J. Anim. Sci.* 27:749-756.
- d. Linus Pauling Institute, Oregon State University.
<https://lpi.oregonstate.edu/mic/vitamins/vitamin-C#function>

8. Vitamin D

Vitamin D is fat-soluble vitamin that helps the body absorb and retain calcium and phosphorus which are both critical for building bone. Laboratory studies have shown the potential for this vitamin to reduce cancer cell growth, help control infections and reduce inflammation. Many of the body's organs and tissues have receptors for vitamin D, which suggest important roles beyond bone health. Cells of the immune system are capable of synthesizing and responding to vitamin D. Immune cells in autoimmune diseases are responsive to the ameliorative effects of vitamin D suggesting that the beneficial effects of supplementing vitamin D deficient individuals with autoimmune disease may extend beyond effects on bone and calcium homeostasis (Aranow, 2011).

Recently, increasing evidences have shown that the abnormal inflammatory response is closely associated with many chronic diseases, especially in autoimmune diseases, including rheumatoid arthritis (RA), inflammatory bowel disease (IBD), systemic lupus erythematosus (SLE), gout, and diabetes (Duan, 2019). This important regulatory function of vitamin D in autoimmune diseases and inflammation is emphasized by this statement of Yang, "impaired vitamin D signaling and/or inadequate vitamin D intake caused by genetic predisposition (e.g. VDR polymorphisms) and/or environmental factors (e.g. insufficient sunlight exposure in high-latitude regions or during the cold season) may contribute to the onset and progression of autoimmunity. Because of the high prevalence of vitamin D insufficiency/deficiency in patients with MS (sic. Multiple Sclerosis), T1DM, and SLE, vitamin D supplementation has been considered a prospective candidate for the treatment of such autoimmune diseases" (Yang, 2013).

Industry Claimed Uses: Bone health, cancer, heart disease, diabetes, and immune function.

Science Related Genetic Application: The actions of the vitamin D hormone 1,25-dihydroxyvitamin D₃ (1,25(OH)₂D₃), the active compound, are mediated by the vitamin D receptor (VDR), which is located on many cells throughout the body. This active form of D plays a critical role in the control of gene expression (Pike, 2010). Importantly, vitamin D and the vitamin D receptor (VDR) which is present on most key cells of the body function in mRNA expression and regulation (Campbell, 2014). Potential to regulate cytokine production; if true, vitamin D can modulate the inflammatory process that is involved in tumor development and potentially also in viral pneumonia, such as cytokine storm (Liu, 2018). 1,25(OH)₂D₃ can upregulate CCR10 on human T cells and ASCs while blocking the expression of skin- and gut-homing receptors. However, the in vivo relevance of the effects of 1,25(OH)₂D₃ on CCR10 expression by T cells that are infiltrating the skin and by IgA⁺ ASCs that are migrating to the gut lamina propria remains to be determined (Mora, 2008).

Scientific Articles:

- a. Aranow, C. 2011. Vitamin D and the immune system. *J Investig Med.* 2011 Aug; 59(6): 881–886.
- b. Campbell, MJ. 2014. Vitamin D and the RNA transcriptome: more than mRNA regulation. *Front Physiol.* 5: 181.
- c. Duan, L. et al. 2019. Editorial: Regulation of Inflammation in Autoimmune Disease. *Journal of Immunology Research* Volume 2019, Article ID 7403796, 2 pages.
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- g. The nutrition Source; Vitamin D.
<https://www.hsph.harvard.edu/nutritionsource/vitamin-d/>
- h. Yang, CY et al, 2013. The Implication of Vitamin D and Autoimmunity: a Comprehensive Review. *Clin Rev Allergy Immunol.* 45(2): 217–226.

9. Vitamin E; α -tocopherol

Vitamin E is not a single vitamin, but rather a group of fat-soluble vitamins. Its main role is to act as an antioxidant, scavenging loose electrons—so called “free radicals”—that can damage cells. Cardiovascular disease is the leading cause of morbidity and mortality in westernized populations. Low levels of α -tocopherol (AT) are associated with increased incidence of atherosclerosis and increased intakes appear to be protective (Devaraj, 1999).

Vitamin E deficiency can cause nerve pain (neuropathy) (Staff, 2014).

Industry Claimed Uses: Research on its benefits is mixed. Oil used in cosmetics as moisturizer, wound healing, minimize healing scars after surgery, psoriasis.

Science Related Genetic Application: Vitamin E blocks the release of pro-inflammatory cytokines, including IL-1, IL-6, TNF, and the chemokine IL-8, by monocytes and macrophages (Devaraj, 1999). Moreover, vitamin E prevents the upregulation of the adhesion molecules vascular cell-adhesion molecule 1 (VCAM1) and intercellular adhesion molecule 1 (ICAM1) on the endothelium induced by oxidized low-density lipoprotein (LDL) and IL-1 β , as well as the upregulation of E-selectin and some chemokines. Reactive oxygen species activate the nuclear factor- κ B (NF- κ B) pathway, which initiates many pro-inflammatory events. Therefore, the therapeutic antioxidant effect of these vitamins could be explained, at least in part, by their capacity to decrease NF- κ B activation (Mora, 2008).

Scientific Articles:

- a. Devaraj S, Jalal I. 1999. Alpha-tocopherol decreases interleukin-1 beta release from activated human monocytes by inhibition of 5-lipoxygenase. *Arterioscler Thromb Vasc Biol.*19(4):1125-33.
Arterioscler Thromb Vasc Biol. 1999 Apr; 19(4):1125-33.

- b. Mora, JR, Iwata, M and von Andrian, UH. 2008. Vitamin effects on the immune system: vitamins A and D take centre stage. *Nat Rev Immunol.* 8(9): 685–698.
- c. Munteanu A, Zingg JM. 2007. Cellular, molecular, and clinical aspects of vitamin E on atherosclerosis prevention. *Mol Aspects Med.* 28(5-6):538-90.
- d. Staff, NP, Windebank, AJ. 2014. Peripheral Neuropathy Due to Vitamin Deficiency, Toxins, and Medications. *Continuum (Minneapolis, Minn).* 20(5):1293–1306.

10. Quercetin dihydrate

One of the most abundant antioxidants in the diet and plays an important role in helping your body combat free radical damage and inflammation, which is linked to chronic diseases. Its antioxidant properties may help reduce inflammation, allergy symptoms, and blood pressure.

Industry Claimed Uses: Anti-inflammatory, ease allergy symptoms, cancer, blood pressure, exercise performance, maintain general health.

Science Related Genetic Application:

- A febrile seizure (FS) study in animals showed that IL-10 is genetically associated with FS and contrary to IL-1beta, confers resistance to FS (Ishizaki, 2009).

Quercetin has anti-inflammatory properties and acts by suppressing pro-inflammatory cytokines (Comalada, 2005).

- The mechanism by which quercetin increased IL-10 levels is not quite clear, but we suspect that it possibly triggered an early release of IL-10 to limit the activity of pro-inflammatory cytokines; this therefore suggests that it had neuroprotective effects (Nombuso, 2017).

These findings, although not definitive, reveal the potential application of Quercetin to pneumonia associated with cytokine storm and febrile seizures.

Scientific Articles:

- a. Comalada M, et al. 2005. In vivo quercitrin anti-inflammatory effect involves release of quercetin, which inhibits inflammation through

downregulation of the NF-kappaB pathway. *Eur J Immunol.* 35:584–592.

- b. Ishizaki, Y. et al. 2009. Interleukin-10 is associated with resistance to febrile seizures: Genetic association and experimental animal studies. *Epilepsia*, 50(4):761–767.
- c. Li, Y et al. 2016. Quercetin, Inflammation and Immunity. *Nutrients* 8, 167-181.
- d. Nombuso, VPM et al. 2017. The Effect of Quercetin on Pro- and Anti-Inflammatory Cytokines in a Prenatally Stressed Rat Model of Febrile Seizures. *J Exp Neurosci.* 11:1-8.
- e. Uttara, B et al. 2009. Oxidative Stress and Neurodegenerative Diseases: A Review of Upstream and Downstream Antioxidant Therapeutic Options. *Current Neuropharmacology*, 2009, 7, 65-74.

11. Alpha-GPC Choline

Choline is an organic, water-soluble compound. It is neither a vitamin nor a mineral; it is an essential nutrient found naturally in the brain. This essential nutrient has anti-inflammatory actions and data has shown its therapeutic potential in restraining excessive inflammation (Parris, 2006). Articles have been published discussing the potential therapeutic application of choline to treat diseases characterized by acute or chronic inflammation. One area of potential application is control of cytokine production; excessive cytokine release can lead to systemic inflammation, organ failure and death (Rosas-Ballina, 2009).

Industry Claimed Uses: DNA synthesis, healthy nervous system, supports structural integrity of cells.

Science Related Genetic Application: Cholinergic enhancing compounds act centrally in the body to decrease inflammation. In an experimental model of infection, called endotoxemia, substances that enhance levels of choline decrease serum biomarkers, TNF and IL-6 and improve survival of the animal model (Pavlov, 2008).

Scientific Articles:

- a. Parris, WR et al. 2006. Choline Suppresses Inflammatory Responses. *Shock*. 25 (6): 45.
- b. Pavlov VA, Parrish WR, Rosas-Ballina M, et al. 2008. Brain acetylcholinesterase activity controls systemic cytokine levels through the cholinergic anti-inflammatory pathway. *Brain Behav Immun*. 23:41–5.
- c. Rosas-Ballina, M and Tracey, KJ. 2009. Cholinergic Control of Inflammation. *J Intern Med*. 265(6): 663–679.

12. Resveratrol

Natural compound produced by several plants in response to injury or when the plant is attacked by pathogens, such as bacteria or fungi. It is a powerful antioxidant that protects a cell's DNA and helps prevent cell damage caused by free radicals. Free radicals are unstable atoms caused by pollution, sunlight and our bodies natural burning of fat that can lead to cancer, aging and brain degeneration.

Industry Claimed Uses: protection of the heart and circulatory system, lowering cholesterol, decreasing blood sugar, protection against blood clots.

Science Related Genetic Application:

- As a natural food ingredient, numerous studies have demonstrated that resveratrol possesses a very high antioxidant potential. Resveratrol also exhibits antitumor activity and is considered a potential candidate for prevention and treatment of several types of cancer. Some studies have also shown that this compound may act as a pro-oxidizing agent which may have implication in pathology of several diseases. Despite this double edge statement, the authors go on to state: "Resveratrol-like other derivatives are one of the most promising compounds on anti-inflammatory drug formulation." (Salehi, 2018).

"The so-called 'Resveratrol Paradox', i.e., low bioavailability but high bioactivity, is a conundrum not yet solved in which the final responsible actor (if any) for the exerted effects has not yet been unequivocally identified. It is becoming evident

that resveratrol exerts cardioprotective benefits through the improvement of inflammatory markers, atherogenic profile, glucose metabolism and endothelial function. However, safety concerns remain unsolved regarding chronic consumption of high RES doses, especially in medicated people. This review will focus on the currently available evidence regarding resveratrol's effects on humans obtained from randomized clinical trials. In addition, we will provide a critical outlook for further research on this molecule that is evolving from a minor dietary compound to a possible multi-target therapeutic drug.” (Tomé-Carneiro, 2013).

Scientific Articles:

- a. Salehi, B. et al. 2018. Review, Resveratrol: A Double-Edged Sword in Health Benefits. *Biomedicines*. 6: 91-110.
- b. Tomé-Carneiro, J. et al. 2013. Resveratrol and Clinical Trials: The Crossroad From In vitro Studies to Human Evidence. *Curr Pharm Des*. 19(34):6064-93.

13. Boron Citrate

“The trace mineral boron is a micronutrient with diverse and vitally important roles in metabolism that render it necessary for plant, animal, and human health, and as recent research suggests, possibly for the evolution of life on Earth” (Pizzorno, 2015).

Industry Claimed Uses: strong bones, wound healing, anti-inflammatory, building muscles, improved thinking.

Science Related Genetic Application:

- Scientific papers have indicated that boron has important anti-inflammatory activity (Naghii, 2011). With respect to inflammatory biomarkers, this mineral reduces levels of CRP and TNF- α ; raises levels of antioxidant enzymes, such as SOD, catalase, and glutathione peroxidase. In addition, boron protects against pesticide-induced oxidative stress and heavy-metal toxicity (Pizzorno, 2015).

- Another important attribute is the finding that boron increases the biological half-life and bioavailability of the major female hormone, estradiol, and vitamin D (Miljkovic, 2004).

Scientific Articles:

- a. Miljkovic, D. 2004. Up-regulatory impact of boron on vitamin D function—does it reflect inhibition of 24-hydroxylase? *Med Hypotheses*. 63(6):1054–1056.
- b. Naghii MR. et al. 2011. Comparative effects of daily and weekly boron supplementation on plasma steroid hormones and proinflammatory cytokines. *J Trace Elem Med Biol*. 25(1):54–58.
- c. Pizzorno, L. 2015. Nothing Boring About Boron. *Integr Med (Encinitas)*. 14(4): 35–48.

14. Magnesium diglycinate

Magnesium is an essential dietary mineral. It is the second most common deficiency in developed countries; The first being vitamin D. A deficiency increases blood pressure, reduces glucose tolerance and causes neural excitation. If magnesium is supplemented, it acts as a sedative, reducing blood pressure and improving insulin sensitivity (Schwalfenberg, 2017).

Industry Claimed Uses: Protection against depression and ADHD, reduction of muscle cramps, better sleep, strong bones.

Science Related Genetic Application:

- In a study by the U.S. Department of Agriculture, “magnesium citrate supplementation compared to a sodium citrate placebo decreased plasma CRP in participants with values above 3.0 mg/dL indicates that subclinical magnesium deficiency may exacerbate conditions that result in chronic inflammatory stress (Nielsen, 2010).

- A non-human study showed that “Mg deficiency, independently of any other changes in nutrient intake, modulates the concentration of bifidobacteria in the gut, a phenomenon that may time-dependently affect inflammation and metabolic disorders in mice (Pachikian, 2010).

Scientific Articles:

- a. Schwalfenberg, GK and Genuis, SJ. 2017. Scientifica Volume. Article ID 4179326, 14 pages.
- b. Nielsen, FH. et al. 2010. Magnesium supplementation improves indicators of low magnesium status and inflammatory stress in adults older than 51 years with poor quality sleep. *Magnesium Research*. 23 (4): 158-68.
- c. Pachikian, Bd, et al. 2010. Changes in Intestinal Bifidobacteria Levels Are Associated with the Inflammatory Response in Magnesium-Deficient Mice. *The Journal of Nutrition*. 140 (3),509–514.

15. Curcumin

Curcumin is the main active ingredient in a spice called turmeric which comes from the *Curcuma longa* plant, native to Asia and Central America. Curcumin is a natural anti-inflammatory compound which has the potential to dramatically increase the antioxidant capacity of the body.

Industry Claimed Uses: Improved brain function, muscle soreness, exercise-induced inflammation.

Science Related Genetic Application:

- Research suggests that curcumin can help in the management of oxidative and inflammatory conditions, metabolic syndrome, arthritis, anxiety, and hyperlipidemia (Hewlings, 2017).
- Tumor necrosis factor α (TNF- α), a multifunctional cytokine, is a major mediator of inflammation in most diseases and this effect is regulated by the activation of a transcription factor, nuclear factor (NF)- κ B. In addition to TNF- α , NF- κ B is also activated by most inflammatory cytokines; gram-negative bacteria; various disease-causing viruses; environmental pollutants; chemical, physical, mechanical, and psychological stress; high glucose; fatty acids; ultraviolet radiation; cigarette smoke; and other disease-causing factors. Therefore, agents that downregulate NF- κ B and NF- κ B-regulated gene products have potential efficacy against several of these diseases. Curcumin has been shown to block NF- κ B activation increased by several different inflammatory stimuli [Panahi, 2016].

- Studies have also revealed the potential for curcumin to reduce circulating C-reactive protein (CRP) levels in the blood (Panahi, 2015).

Scientific Articles:

- a. Hewlings, SJ and Kalman, DS. 2017. Curcumin: A Review of Its' Effects on Human Health. *Foods*. 6: 92.
- b. Panahi, Y. et al. 2016. Effects of curcumin on serum cytokine concentrations in subjects with metabolic syndrome: A post-hoc analysis of a randomized controlled trial. *Biomed. Pharmacother.* 82: 578–582.
- c. Panahi, Y. et al. 2015 Antioxidant and anti-inflammatory effects of curcuminoid-piperine combination in subjects with metabolic syndrome: A randomized controlled trial and an updated meta-analysis. *Clin. Nutr.* 34: 1101–1108.

16. Folic Acid (L-Methylfolate)

Folate and folic acid are different forms of vitamin B9. The natural form is folate and its name is derived from the Latin word "folium," which means leaf. In fact, leafy vegetables are among the best dietary sources of folate. The active form of folate is essential for the body to make DNA and RNA and metabolize amino acids, which are required for cell division. As humans cannot make folate, it is required in the diet, making it an essential vitamin. Approximately 85% of people with serious kidney disease have high levels of homocysteine which has been linked to heart disease and stroke. Taking folic acid lowers homocysteine levels (Modagheh, 2016).

Industry Claimed Uses: Prenatal health (Junod,2001), strong blood, lowers homocysteine levels, reduces risk of eye disease, memory, depression.

Science Related Genetic Application: - A clinical research trial was performed, in Tianjin, China, to evaluate whether folic acid supplementation would improve cognitive (memory) performance by reducing inflammatory cytokine concentrations. Neuropsychological tests were administered, and folate, homocysteine, vitamin B₁₂, IL-6, TNF- α , A β -42, and A β -40 were measured at baseline and at 6- and 12-month time points. 152 participants (folic acid: 77,

conventional: 75) completed the trial. Significant improvements in folate, homocysteine, A β -42, peripheral IL-6, TNF- α levels were observed in folic acid group compared with conventional group. Full scale intelligence quotient also improved in the folic acid group (Ma, 2016).

- A randomized trial at Brigham and Women's Hospital in a large cohort of women at high risk of cardiovascular disease indicate that daily supplementation with folic acid/B6/B12 may reduce the risk of age-related macular degeneration (AMD) (Christen, 2009).

Scientific Articles:

- a. Christen, WG, et al. 2009. Folic Acid, Vitamin B6, and Vitamin B12 in Combination and Age-related Macular Degeneration in a Randomized Trial of Women. Arch Intern Med. 2009 February 23; 169(4): 335–341.
- b. Junod, SW. 2001. Folic Acid Fortification: Fact or Folly. Update, the bimonthly publication of the Food and Drug Law Institute. www.fda.gov
- c. Ma, F, et al. 2016. Folic acid supplementation improves cognitive function by reducing the levels of peripheral inflammatory cytokines in elderly Chinese subjects with MCI. Scientific Reports. 6: Article number: 37486.
- d. Modaghegh, MHS, et al. 2016. Effect of Folic Acid therapy on Homocysteine Level in patients with Atherosclerosis or Buerger's Disease and in Healthy individuals: A clinical trial. Electronic Physician. 8 (10): 3138-3143.

17. Niacin

Niacin is one of the eight B vitamins, and it is also called vitamin B3. It is water soluble and is not stored by the body. Excess amounts can therefore be excreted, if not needed. The body keeps a small reserve of this vitamin, but it must be taken on a regular basis to maintain the reserve.

Industry Claimed Uses: Memory loss and mental confusion, depression, fatigue, skin problems, headache.

Science Related Genetic Application:

In vivo study revealed that niacin down-regulated the levels of inflammatory factors (IL-6 and TNF- α) in plasma, suppressed protein expression of CD68 and NF- κ B p65 in the arterial wall, and attenuated oxidative stress in guinea pigs that have been fed high-fat diet (Si, 2014).

- Niacin Decreased the Secretion of Inflammatory Cytokines TNF- α and IL-6 in oxLDL (oxidized low-density lipoproteins)-Stimulated HUVECs (Human umbilical vein endothelial cells) (Pirillo, 2013).

- Oxidized LDL (OxLDL) activates endothelial cells in blood vessel and is part of the process involved formation of an atheromatous plaque. Atherosclerosis is a chronic inflammatory vascular disease, having as ultimate outcome the atheromatous plaque, a focal lesion located within the intima of large and medium sized arteries (Libby, 2012).

- Niacin significantly lessened lipid deposition in the arterial wall and modified lipoprotein profile in plasma via modulating cholesterol metabolism in liver of guinea pigs fed high fat diet. (Si, 2014).

- “In summary, our data presented herein support the novel concept that niacin has vascular anti-inflammatory and potentially vascular-protective property which is independent of its effect on lipid regulation. The anti-inflammatory property of niacin is realized by downregulating the nuclear transcription factor- κ B signaling pathway.” (Si, 2014).

Scientific Articles:

- a. Libby, P. 2012. Inflammation in atherosclerosis. *Arteriosclerosis, Thrombosis, and Vascular Biology*. 32(9) :2045–2051.
- b. Pirillo, A, et al. 2013. LOX-1, OxLDL, and Atherosclerosis. *Mediators of Inflammation*. 2013:12 pages.152786 [[PubMed](#)].
- c. Si, Y, et al. 2014. Niacin Inhibits Vascular Inflammation via Downregulating Nuclear Transcription Factor- κ B Signaling Pathway.

18. Riboflavin

A water-soluble vitamin, also known as vitamin B2. It is required by the body for cellular respiration. It is on the World Health Organization's List of Essential Medicines, the safest and most effective medicines needed in a health system (WHO, 2019). It is continuously excreted in the urine of healthy individuals, making deficiency relatively common when dietary intake is insufficient (Brody, 1999).

Industry Claimed Uses: Riboflavin deficiency, growth, good health, decrease cataract risk, migraines, decrease homocysteine levels.

Science Related Genetic Application:

Riboflavin is claimed to have anti-inflammatory, antioxidant, and microbiome-modulatory properties. A Crohn's disease (CD) study revealed that three weeks of riboflavin supplementation resulted in a reduction in systemic oxidative stress, mixed anti-inflammatory effects, and a reduction in clinical symptoms. IL-2 and C-reactive protein (CRP) levels were reduced in certain patient groups. "Our data demonstrate that riboflavin supplementation has a number of anti-inflammatory and anti-oxidant effects in CD." (von Martels, 2020).

"Riboflavin by its proteasome inhibitory action down regulates the NF- κ B pathway, thus reducing pro-inflammatory cytokines, nitric oxide and COX2, which ensures protection from infection on one hand and survival benefit of host cells from inflammatory damage on the other. The balance between the redox reactions and antioxidant system suggests a strong therapeutic intervention in serious bacterial infections associated with sepsis at least in our in-vitro system [Fig. 9]." (Dey, 2016).

Scientific Articles:

- a. Brody, T. 1999. Nutritional Biochemistry. San Diego: Academic Press.
- b. Dey, S. and Bishayi, B. 2016. Riboflavin along with antibiotics balances reactive oxygen species and inflammatory cytokines and controls Staphylococcus aureus infection by boosting murine

macrophage function and regulates inflammation. *Journal of Inflammation*. 13:36.

- c. Von Martels, JZH, et al. 2020. Riboflavin Supplementation in Patients with Crohn's Disease [The RISE-UP Study]. *J Crohns Colitis*. 14(5):595-607.
- d. World Health Organization (2019). World Health Organization model list of essential medicines: 21st list 2019. Geneva: World Health Organization.

19. Thiamin

Thiamin, vitamin B1, is an essential vitamin that has many important functions in the body. It is used by most cells to help convert food into energy. Many people don't realize that they have a deficiency, as many of the symptoms are subtle and often overlooked. Risk of deficiency is increased by alcohol dependence, old age, diabetes, dialysis, HIV/AIDS, and high-dose diuretic use. Severe thiamin deficiency leads to beriberi, a disease that affects multiple organ systems, including the central and peripheral nervous systems. Beriberi was described in Chinese literature as early as 2600 B.C.

Industry Claimed Uses: Aids in boosting the immune system, diabetic pain, heart disease, heart failure, alcoholism, aging, cataracts and glaucoma.

Science Related Genetic Application:

Experiments feeding thiamin deficient chow to septic animals showed an increase in levels of TNF- α in their peritoneal fluid. TNF- α is an early marker of inflammation commonly used in infection models, such as sepsis. TD (sic. thiamine deficiency) was associated with a greater bacterial clearance in the peritoneal fluid, greater oxidative stress and a change in the immune response profile in an experimental model of abdominal sepsis in mice (Andrade, 2014).

Scientific Articles:

- a. De Andrade, JAA, et al. 2014. The effect of thiamine deficiency on inflammation, oxidative stress and cellular migration in an experimental model of sepsis. *Journal of Inflammation*. 11:11.

20. Selenium (SE)

An essential mineral that is a component of an antioxidant enzyme, glutathione reductase, that is key in tissue respiration. Selenium is a powerful mineral that is essential for the proper functioning of your body. It is only needed in small amounts but plays a critical role in metabolism and thyroid function and helps protect your body from damage caused by oxidative stress. Antioxidants like selenium reduce oxidative stress by neutralizing and keeping free radical numbers in check.

Industry Claimed Uses: Antioxidant, anti-inflammatory, cellular protection, Crohn's disease.

Science Related Genetic Application:

“Even though the pathophysiology of irritable bowel disease (IBD) is multifactorial in origin, dietary selenium (and selenoprotein) deficiency exacerbates experimental colitis by affecting various signaling pathways involved in inflammation and oxidative stress as well as by altering the gut microbiota.” (Kudva, 2015).

The glutathione peroxidase (GPX) enzymes utilize Se at their active sites to detoxify reactive oxygen species (ROS) including hydrogen peroxide (H₂O₂) and phospholipid hydroperoxide. GPX1 and 4 are among the most abundant selenoproteins in several immune cells and tissues (Carlson, 2010).

Selenium, in a mouse model of diabetes, appears to have a potential protective effect in type 1 diabetes. This protective effect involved a shift in the balance between inflammatory cytokines (TNF- α) and regulatory cytokines (IL-10) (Huang,2012)

Scientific Articles:

- a. Carlson, BA, et al. Role of selenium-containing proteins in T-cell and macrophage function. *Proc Nutr Soc.* 69:300–310.
- b. Huang, Z, et al. 2012. The Role of Selenium in Inflammation and Immunity: From Molecular Mechanisms to Therapeutic Opportunities. *Antioxid Redox Signal.* 16(7): 705–743.
- c. Kudva, AK, et al. 2015. Selenium and inflammatory bowel disease. *Am J Physiol Gastrointest Liver Physiol.* 309(2): G71–G77.