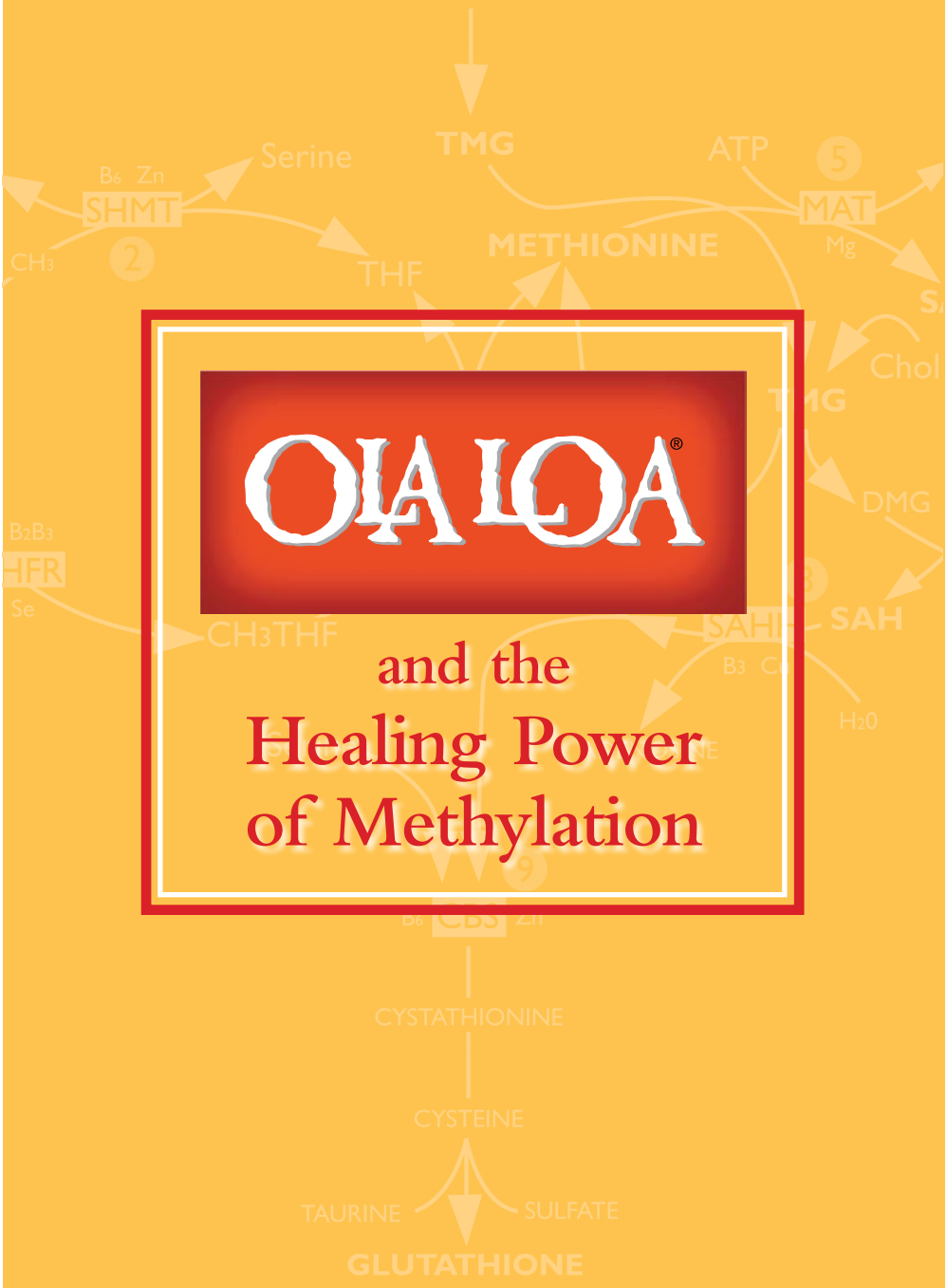


OIA LOA®

and the Healing Power of Methylation

DR. RICHARD A. KUNIN, M.D.

INTRODUCING OLA LOA®

OLA LOA ENERGY is the single most powerful supplement available today for the control of homocysteine and to support methylation. It provides gram doses of vitamin C, glycine, and betaine (aka TMG) along with synergistic co-factors, coenzyme Q10 and acetylcysteine. Nutrient synergism is further enhanced by arginine, lysine, selenium, chromium and, of course, folic acid and hydroxycobalamin, which serve to methylate homocysteine, which thus is converted into methionine, an essential amino acid.

TMG, A STRATEGIC NUTRIENT

TMG, is an acronym for trimethylglycine. The traditional name, betaine, refers to beets, a rich dietary source. The importance of betaine is underscored in research that consistently finds lower homocysteine after betaine than folic acid and cobalamin. The reason for this is evident in the fact that betaine can donate methyl groups that require only a single enzyme, BHMT, by which to remethylate homocysteine. Folic acid and cobalamin require at least three enzymes to accomplish the same! The reaction constants of the enzymes involved are feed-back linked in such a way as to make it clear that the BHMT pathway is activated during famine and fasting, whereas the remethylation pathway of folate and cobalamin requires adequate diet, digestion, and absorption.

WHAT IS METHYLATION

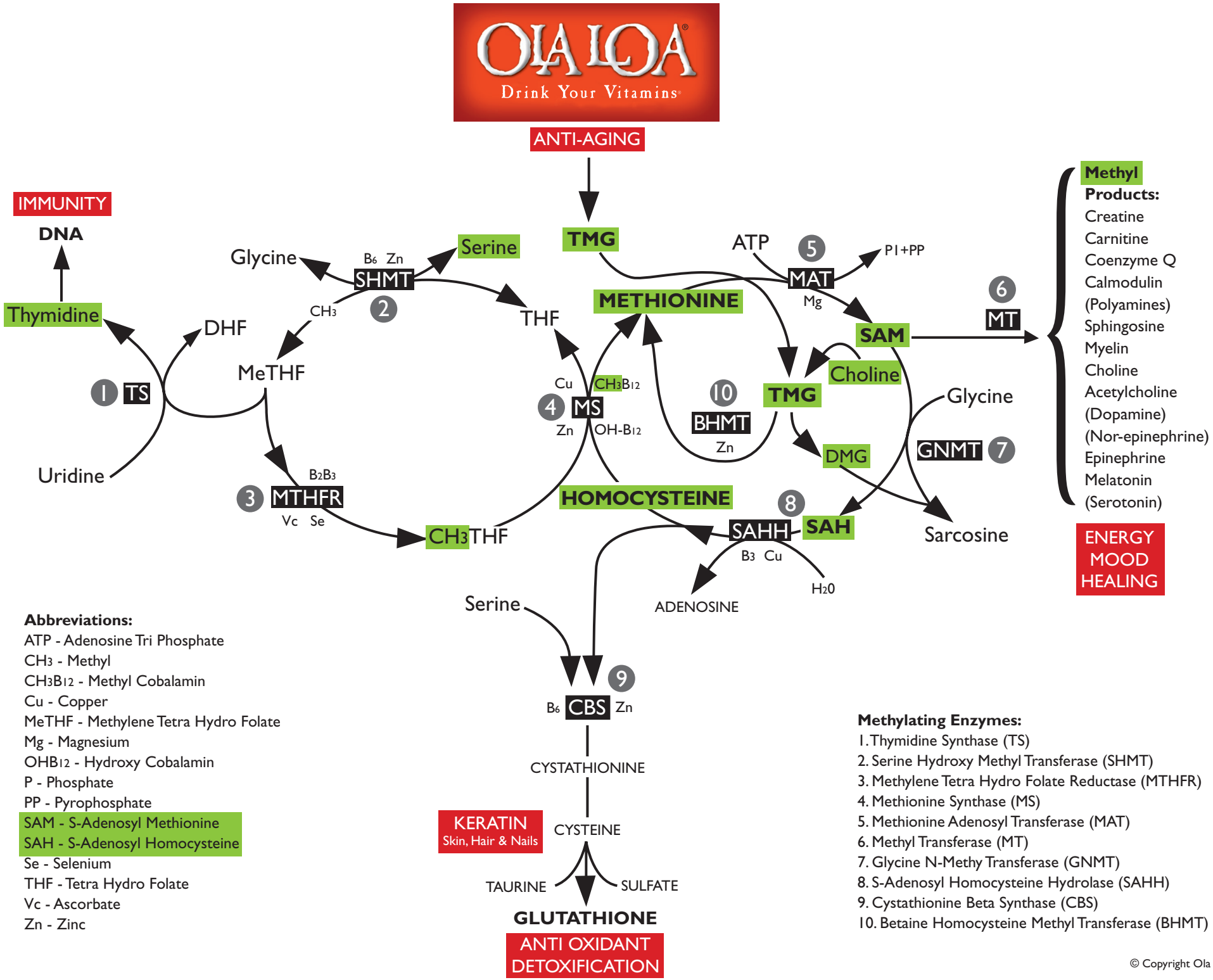
Methylation refers to the controlled transfer of a methyl group, made up of a carbon atom and three hydrogen atoms, abbreviated CH_3. Such movement of carbon atoms goes on in every cell and tissue of the body, for methylation is involved in hundreds of chemical reactions that regulate **cell energy, healing, immunity and genetic expression of DNA and RNA.** All of these reactions are responsive to environmental conditions. Thus methylation is a central feature of adaptation to the ever-changing physical and chemical conditions of life.

THE IMPORTANCE OF METHYLATION

As a result of methylation, hundreds of molecular products change physically and functionally in the microscopic world of cellular biochemistry. For example the amino acid, methionine, carries an available but inactive methyl group on its sulfur atom. However, within the confines of the cell, methionine encounters adenosine as ATP and magnesium which are energized by a transferase enzyme, thus forming adenosylmethionine, or SAMe. This natural alchemy energizes the methionine so as to release its methyl group into the orbit of cellular enzymes, appropriately called methyltransferases. There are about 400 known methyl transferase reactions that produce vital products that affect our health, quality of life and survival.

THE TOP TWENTY METHYLATION PRODUCTS ARE:

1) creatine, **2**) carnitine, **3)** coenzyme Q, **4)** calmodulin, all required to regulate energy in every cell in the human body. Methylation also converts the phospholipid, ethanolamine to **5)** choline (trimethyl-ethanolamine), essential for cell membrane structure and repair, including **6)** myelin, the substance that insulates nerve fibers. Choline is also essential for the production of brain-regulating neurotransmitters: **7)** acetylcholine, **8)** dopamine, **9**) nor-epinephrine, and **10)** epinephrine. **11)** Melatonin, the neuro-transmitter that initiates sleep and regulates the circadian sleep-waking rhythms is also a product of methylation, specifically of the neurotransmitter, serotonin. **12)** And sarcosine, formed by methylation of the amino acid glycine, has recently attracted research attention as a treatment for schizophrenia. And there is more, for the transfer of a methyl group from folic acid to cobalamin (B12) and thence to methionine is required in order to regenerate active folate, THF, which is required for methylation of the nucleic acid, uridine, which thus becomes **13)** thymidine, the specific nucleic acid required for production of lymphocytes, active against viruses, cancer and microbial enemies. Failure to produce adequate thymidine hampers **14)** methylation of DNA and RNA, thus depriving these genetic materials of protection against mutation. In short, methylation is an absolute requirement for **immunity, fertility, and protection against birth defects, accelerated aging and susceptibility to cancer.** Methylation is also essential for production of **15)** polyamines, regulators of cell growth, mitosis, and healing. The chemistry involves decarboxylated SAM, which reacts with decarboxylated ornithine to form spermidine and then spermine in successive reactions along with **16)** methyl-thioadenosine, thus producing a family of products that regulate cell division, growth, healing and reproduction. **17)** Homocysteine, is a potentially toxic intermediate in the methylation process. When S-adenosyl-methionine (SAM) donates its methyl group, it becomes S-adenosyl-homocysteine (SAH), a free radical able to combine with other reactive molecules within the cell or in the blood stream. Inside the cell homocysteine is likely to react with copper for their attraction is strong enough to pull copper out of its binding sites in enzymes, including the cytochrome enzymes of the mitochondria. This interrupts electron flow and thereby lowers cell energy. a process that jibes with the fact that patients with chronic fatigue states tend to have high homocysteine levels. Within the vasculature homocysteine reacts with other homocysteine molecules, thus forming an inert dimer, homocystine, that is excreted in the urine, where it sometimes precipitates, causing kidney stones. Homocysteine can safely react with albumin and other proteins in the blood stream and the blood vessel wall. On the other hand, it can activate blood clotting by reacting with sulfur atoms, including fibrinogen and lipoprotein(a), which amplifies coagulation risk and interferes with the anticoagulant, plasminogen. This is particularly risky in people carrying high blood levels of fibrinogen and/or Lp(a) and can increase clotting risk by about 20-fold.



Abbreviations:

ATP - Adenosine Tri Phosphate
CH_3 - Methyl
CH_3B_{12} - Methyl Cobalamin
Cu - Copper
MeTHF - Methylene Tetra Hydro Folate
Mg - Magnesium
OHB_{12} - Hydroxy Cobalamin
P - Phosphate
PP - Pyrophosphate
SAM - S-Adenosyl Methionine
SAH - S-Adenosyl Homocysteine
Se - Selenium
THF - Tetra Hydro Folate
Vc - Ascorbate
Zn - Zinc

Methylating Enzymes:

1. Thymidine Synthase (TS)
2. Serine Hydroxy Methyl Transferase (SHMT)
3. Methylene Tetra Hydro Folate Reductase (MTHFR)
4. Methionine Synthase (MS)
5. Methionine Adenosyl Transferase (MAT)
6. Methyl Transferase (MT)
7. Glycine N-Methy Transferase (GNMT)
8. S-Adenosyl Homocysteine Hydrolase (SAHH)
9. Cystathionine Beta Synthase (CBS)
10. Betaine Homocysteine Methyl Transferase (BHMT)

HOMOCYSTEINE CAN CAUSE DAMAGE IN HEALTHY PEOPLE

When homocysteine binds to the arterial endothelium it can provoke spasm of the muscle layer, thus raising blood pressure but also lowering blood flow in major arteries, on average by 85 percent. The vasospasm effect lasts over four hours, long enough to cause programmed cell death and permanent organ damage, even in healthy young adults. The good news is that the drop in arterial blood flow after methionine load was cut to only 30 percent by pre-treating with 1000 mg of vitamin C. A 500 mg dose of vitamin C proved inadequate in the research by Drs. Chambers and MacGregor. Thus, it is likely that ischemia is an important mechanism by which homocysteine causes hypertension, atherosclerosis and arterial aneurysm. It is also likely that homocysteine-induced apoptosis is a major part of the aging process.

ON THE OTHER HAND, HOMOCYSTEINE IS NOT ALL BAD

In the first place, by accepting a methyl group from the folate-cobalamin methylation pathway, homocysteine can be restored to methionine. And by combining with serine, homocysteine is converted to cystathionine and then to transmethylation products, namely, **18)** cysteine, **19)** glutathione, **20)** taurine and **21)** sulfate—all valuable components of antioxidant adaptation and detoxification.

CYANOCOBALAMIN IS EXCLUDED FROM OLA LOA

Patient safety is important. We have excluded cyanocobalamin because it is a known anti-vitamin, actually interfering with the methylation pathway it is purported to serve. It has been known for fifty years that cyanocobalamin can cause blindness, especially in smokers, blacks, and people who have relatives with Leber's optic atrophy. Dr. Kunin has had direct contact with one patient who was blinded permanently after just three injections of cyanocobalamin at a major hospital medical center. It is not by accident that we have chosen hydroxycobalamin as the best choice for everyday use.

PATIENT COMPLIANCE IS IMPORTANT

OLA LOA has won popular acceptance from coast to coast because it tastes good, is economical and most people feel better soon after drinking it. We call it the *"Ola Loa Feeling.'* It is a composite of the dozens of methylation reactions that are supported by the OLA LOA formula. This is a case where a packaged and sealed nutrient supplement is more effective and more reliable than table foods.

DOCTOR SATISFACTION IS IMPORTANT TOO

OLA LOA is the most complete effervescent nutrient formula available today. It is convenient and considerably cheaper than the formula would be as single vitamin capsules. Furthermore, the sealed package protects the ingredients from hygroscopic activation, oxidation and deterioration.

OLA LOA STANDS ALONE AS THE BEST MULTIVITAMIN PRODUCT FOR EVERY MEDICAL PRACTICE:

- Sealed pack is portable and maintains full potency despite weather changes.
- Instant effervescent drink is always fresh.
- Hydrated colloid solution provides best absorption compared to tablet or capsule.
- Non-irritating to digestive tract.
- Reduced risk of choking in debilitated or neurologically injured patients.
- The OLA LOA formulas are medically sound, safe even for children. There have been no serious adverse reports after years in the national health food store market.
- Enhanced applications when combined with other OLA LOA products:
  - OLA LOA REPAIR® (Bone and Joint Formula) (Gotu kola, vitamin K, calcium, magnesium, carnitine, taurine)
  - OLA LOA BRAIN (n-3 EFA, acetylcarnitine, tocopherols, bioflavonoids, DMAE, PS)

DIAGRAM OF THE METHYLATION BIOCHEMICAL PATHWAYS

This is a simplified rendition. No wonder most health professionals have not yet mastered the vast amount of basic chemistry, physiology and clinical information in this field. *(See page 3-4)*

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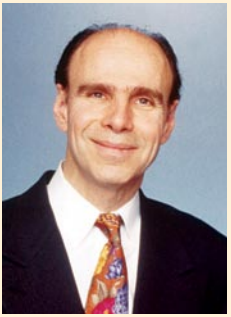
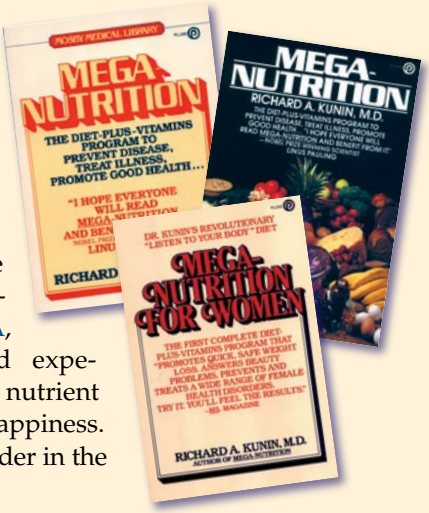
About the Author



DR. RICHARD A. KUNIN is a nutrition physician, with over 30 years experience in the field. He pioneered the use of vitamins and minerals in medical diagnosis and therapy. He joined with Nobel laureate, Linus Pauling, in founding the Orthomolecular Medical Society in 1976 and wrote two best-selling books in the 1980s, *Mega Nutrition* and *Mega Nutrition for Women*. He was invited to represent orthomolecular medicine at the President's Commission on Mental Retardation and Mental Health in 1987. After Dr. Pauling's death in 1994, Dr. Kunin founded The Society of Orthomolecular Health-Medicine to provide accredited educational forum for health professionals.

Dr. Kunin teaches medical strategy based on nutrition, detoxification and adaptive support that integrates all aspects of health care. The slogan *"putting nutrition first"* identifies this as physiological approach to health. His research in nutrition has produced new formulations and improved delivery systems that are creating a revolution in health products. As research director of OLA LOA, he is able to use his knowledge and experience to target the most effective nutrient formulations for better health and happiness. That's what makes OLA LOA the leader in the *"Drink Your Vitamins"* revolution.



Dr. Kunin is also a contributor to various published medical books like *Mental Retardation and Mental Health*, *The Advanced Guide to Longevity Medicine*, *The Roots of Molecular Medicine*, and *Alternative Medicine*.