Aminomics White Paper: 
The Significance and Relationships of Amino Acids and Protein in Chronic Disease and General Wellness

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The Significance and Relationships of Amino Acids and Protein
in General Health and Chronic Disease

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1.0 OBJECTIVE

This “White Paper” discusses the context and medical opportunity of a diagnostic and therapeutic concept developed by Immune System Management and referred to as Aminomics.

The objectives of this White Paper are to:
1. Define and explain the diagnostic and therapeutic approach know as “Aminomics®”
2. Explain the principles and rationale behind Aminomics therapeutics.

2.0 SUMMARY

Amino acids are the essential medium through which the human gene translates into proteins. And protein is the mainstay of human structure and chemistry.

Aminomics® is the study of the amino acid profile in an individual to determine the existence of any amino acid deficiency, and the orthomolecular correction of that deficiency.

From this standpoint Aminomics® is closely related to genomics (the study of the genes in an individual) in that the genes carry the instructions of exactly how the amino acids (the building blocks of proteins) are to be metabolized into proteins. It is the genes that decide how the amino acids molecules are to be sequenced and linked to each other. This determines the structure and nature of proteins. And proteins are an integral and vital part of human function, structure and chemistry.

The study of the structure and function of proteins is known as proteomics. Amino acids are the substrate of important proteins.

Genes \( \rightarrow \) Amino Acids \( \rightarrow \) Proteins
(Genomics) \( \rightarrow \) (Aminomics) \( \rightarrow \) (Proteomics)

At a sub-molecular level the human body possesses this innate intelligence or programming that is DNA. Within DNA, or the “Genomic Map”, lies the intelligence/programming that essentially instructs various body systems to manufacture protein as the fundamental building block of cells. In other words, everything our body does is focused upon building protein. Protein is the resource material used to build every cell in the body and most metabolic activity. There are tens of thousands of different proteins in the human body. All protein is made from amino acids.
**The Core Principles of Aminomics as a Therapeutic Approach**

There are four core principles of Aminomics:

1. **(1) A Strong Immune Response = Balance of Amino Acids & Protein**

   The basic substrate of all metabolic and cellular human functioning is amino acids. When an individual possesses the optimal profile of chemistry and metabolism, that individual is typically healthy or symptom-free. When an individual's profile deviates from the optimum, symptoms will evolve.

   Proteins can only be made when all the necessary amino acids are simultaneously available in the right proportions. This is a core philosophy of Aminomics therapy. It is an intervention to restore, at the proteomic level, imbalances in amino acids that may be the result of a wide variety of causes, including age, stress, genetic disorders, inadequate intake and/or absorption, infection, errors in metabolism or immunologic incompetence.

2. **(2) Nutritional Synergism**

   The synergistic impact and interrelationships of all micro- and macro-nutrients is critical to proper protein absorption, use and function.

3. **(3) Individuality**

   “Disease is as unique as the patient”

   Every human is unique, bio-chemically and metabolically. Each of us possess a unique history of experience that culminates in our state of health. All aspects of the Aminomics diagnostic and therapeutic approach embrace the central concept of uniqueness or biochemical individuality.

4. **(4) Zero Pathogen/ High Bio-availability**

   An immune system that is already combating various pathogens needs to be supported with supplementation that is:
   - pure and pathogen-free
   - highly bio-available
   - administered in the right proportions at the right time
3.0 BACKGROUND TO PROTEOMICS AND GENOMICS

3.1 Proteomics

Protein is a word that has its roots in the Greek language meaning “of first importance”, and accounts for about one-fifth of the total body weight (2). In fact, next to water, protein accounts for the greatest portion of the weight of the human body (3). Protein is an integral part of the human structure and chemistry. It is protein that provides the structure for all living things. Every living organism, from the largest animal to the tiniest microbe, is composed of protein. And in its various forms, protein participates in the vital chemical processes that sustain life. It is responsible for the structure and integrity of cells, muscles, tendons, cartilage, skin, hair and nails as well as the formation of some hormones, all enzymes, antibodies, blood elements and neural transmitters:

- In the human body, protein substances make up the muscles, ligaments, tendons, organs, glands, nails, hair, and many vital body fluids, and are essential for the growth of bones.
- The enzymes and hormones that catalyze and regulate all bodily processes are proteins.
- Proteins help to regulate the body's water balance and maintain the proper internal pH. They assist in the exchange of nutrients between the intercellular fluids and the tissues, blood, and lymph. A deficiency of protein can upset the body's fluid balance, causing edema.
- Proteins form the structural basis of chromosomes, through which genetic information is passed from parents to offspring. The genetic "code" contained in each cell's DNA is actually information for how to make that cell's proteins.

The basic structure of protein is actually a chain of amino acids that can result in many different configurations and can also combine with other substances (2). The shape of a protein is crucial to its function, and it is the way amino acids combine with each other through their side chains that gives a protein its shape (4).

The complete set of all the proteins in a given tissue, cell or organism is called a proteome – and all the information needed to make the proteome is encoded in the genes of an individual (5, 6). The study of the structure and functions of proteins is therefore called Proteomics.

From a medical standpoint, proteomics aims to identify those specific proteins that may be responsible for disease management and how their structure, function and expression respond to disease (7).

It is through proteomics that we understand that proteins are differentially expressed in health and disease and therefore hold the potential not only for allowing for an earlier diagnosis, but also for the formulation of a patient-tailored or patient-individualized therapy (7, 8). Graves and Haystead, in their publication titled “Molecular Biologist's Guide to Proteomics” have said, “The emergence of proteomics, the large-scale analysis of proteins, has been inspired by the realization that the final product of a gene is inherently more complex and closer to function than the gene itself” (9). In other words, the study of the proteins in an individual allows for the detection of any deviation from normal that has been brought about by aberrations in gene expression.
3.2 Genomics

A gene is the fundamental physical and functional unit of heredity. It is an ordered sequence of nucleotide bases in a segment of DNA. Human genes carry the instructions for making proteins, which in turn directs the activities of all the cells in the body.

A genome is a person’s complete set of DNA. Genomics, therefore, is the study of all the genes in an individual, including their interaction with each other and the environment (10).

There are about 3 billion bases in the human genome, of which 99.9% are identical from one person to the next. Only 0.1% (or roughly 3 million bases) are different. This is what sets one person apart from the other (11). This may also influence whether an individual will be less or more susceptible to a disease or to the environmental pathogens.

Genomics, therefore, allows us to study the mechanisms and interactions that lead to either health or disease, and what could be done to combat the disease (12).

The genes, however, do not directly carry out the instructions for the exact behavior of the body’s cells. Rather, it is at the level of gene function (the genomic level) that processes take place where the instructions encoded by the genes are passed on to the proteins to accomplish (11).

It is the proteins that do the work in our body. It is through these proteins that the genes controls how we look, how we process the foods that we ingest, detoxify poisons that enter into our system, combat certain types of organisms that cause infections and how we manage immunological events such as cancer. Simply stated, proteins are the agents that carry out the instructions encoded by the genes (11).

4.0 AMINOMICS

4.1 Introduction

The process of assembling amino acids to make proteins, and of breaking down proteins into individual amino acids for the body's use, are continuous ones. When we need more enzyme proteins, the body produces more enzyme proteins; when we need more cells, the body produces more proteins for cells. These different types of proteins are produced as the need arises. Should the body become depleted of its reserves of any of the essential amino acids, it would not be able to produce the proteins that require those amino acids. An inadequate supply of even one essential amino acid can hinder the synthesis, and reduce body levels, of necessary proteins. Further, all of the essential amino acids must be present simultaneously in the diet in order for the other amino acids to be utilized.

It is important to realize that each amino acid plays a different metabolic or biochemical role in the human body and that deficiency of one amino acid may also affect the functioning and/or the production of another. It is worth noting here that the requirements for specific amino acids are directly altered when the body is under stress (70). In other words, physical (or even psychological) disorders and plasma amino acid levels bear a direct relationship to each other.
How could such a deficiency situation occur? More easily than you might think. Many factors can contribute to deficiencies of essential amino acids, even if one eats a well-balanced diet that contains enough protein. Impaired absorption, infection, trauma, stress, drug use, age, and imbalances of other nutrients can all affect the availability of essential amino acids in the body. Insufficient intake of vitamins and minerals, especially vitamin C, can interfere with the absorption of amino acids in the lower part of the small intestines. Vitamin B6 is needed also, for the transport of amino acids in the body.

If an individual’s diet is not properly balanced - that is, if it fails to supply adequate amounts of the essential amino acids, then sooner or later, this will become apparent as some type of physical disorder. This does not mean, however, that eating a diet containing enormous amounts of protein is the answer. In fact, it is unhealthy. Excess protein puts undue stress on the kidneys and the liver, which are faced with processing the waste products of protein metabolism. Nearly half of the amino acids in dietary protein are transformed into glucose by the liver and utilized to provide needed energy to the cells. This process results in a waste product, ammonia. Ammonia is toxic to the body, so the body protects itself by having the liver turn the ammonia into a much less toxic compound, urea, which is then carried through the bloodstream, filtered out by the kidneys, and excreted.

It is to be expected therefore, that at the proteomic (and hence, the aminomic) level we are likely to observe changes that reflect those imbalances and/or deficiencies that either give rise to or results from stress, nutritional poverty, infection, inflammation, aging or cancer. Here lies the importance of profiling the plasma amino acid levels in a diseased individual that would point to a comprehensible and meaningful corrective measure. Simple nutritional assessment without assessing plasma amino acid levels is an incomplete measure – even marginal deficiencies of amino acids are significant from the perspective of total body functions.

Changes in plasma amino acid patterns reliably reflect the quantitative and qualitative changes in protein metabolism that occur in different metabolic conditions, including chronic liver failure (14), renal failure (15), sepsis (16), diabetes (17), malnutrition (18) and cancer (19).

**Aminomics** focuses on the plasma **amino acid profile** of an individual, as well as the related involvement of micr- and macro-onutrients such as vitamins and minerals, EFAs, etc., and the determination of any existing deficiency. From a therapeutic perspective, it involves the administration of a individualized amino acid and orthomolecular oral supplement tailored to the individual’s needs.

The Aminomics therapeutic protocol is designed to restore the natural defense mechanisms of the immune system, extending the individual's life or, at minimum, significantly improving quality of life. This bolsters the patient's own self-healing metabolic and immune system capacity while avoiding the toxic side effects that often accompany conventional medical treatment (i.e., cancer radiation).

### 4.2 The Aminomics Protocol
- Blood plasma is analysed for amino acids using High Pressure Liquid Chromatography.
- Individual amino acid plasma profiles are referenced to optimal amino acid norms. (71)
- An individualized oral nutritional supplement is developed.
5.0 UNDERSTANDING AMINO ACIDS

5.1 Amino acids and proteins

Amino acids are the building blocks of proteins, and also play a central role as intermediates in metabolism (20). Amino acid molecules are linked together (through peptide linkages) to form proteins.

The kind of protein that results is dictated by the *types* of amino acids involved and the *sequence* in which the amino acids are arranged. That alone decides whether a protein will turn out to be skin, muscle, hormone, enzyme, serum or an antibody. The sequence of the amino acids within the proteins also decides how that protein will fold into a three dimensional structure and how stable that structure will be (20).

The twenty-eight main amino acids in the human body combine in a number of ways to account for 150 or more intermediates and more than 40,000 proteins known to us (3). It is estimated that the there are in excess of 6,000,000 proteins in the human body, most of which have not yet been characterized or catalogued (21).

Proteins serve the following vital functions:

1. Most **cellular functions**, including cellular energy production
2. **Enzyme** production: Formation of enzymes which regulate chemical reactions within our body

3. **Immune proteins**: Formation of antibodies which fight infection and also confers upon us the immunity from all internal and external insults

4. **Contractile proteins**: Formation of muscles

5. **Structural proteins**: Formation of ligaments, tendons, cartilage, bone, hair, nails etc

6. **Regulatory proteins**: Formation of hormones

7. **Transport proteins**: Formation of blood proteins and hemoglobin (responsible for oxygen delivery to every body tissue)

8. **Neurotransmitter proteins**: Formation of chemicals that help nerve impulse transmission

Understandably, the myriad of functions served by the proteins are, in a larger sense, functions of the amino acids themselves.

### 5.2 Amino acids and other macro and micronutrients – An interrelation

Macronutrients and micronutrients make up the nutritional landscape. Micronutrients (including vitamins, minerals, and phytochemicals) derive their name from the fact that they are needed in relatively small amounts in comparison to the macronutrients - carbohydrates, fats and oils, proteins and amino acids, and water. There are also non-nutrient components of the diet such as soluble and insoluble fibers, which play an important role in human nutrition.

The metabolism of carbohydrates, fats, and proteins, is interconnected. This interrelationship provides essential flexibility to humans when faced with dietary restriction or starvation. In fact, the body can interconvert to a greater or lesser degree the macronutrients protein, fat and carbohydrate during starvation or overfeeding. Dietary carbohydrates are broken down in the body to glucose, to be used for liver and muscle glycogen stores, and some is taken into the brain and other cells to be broken down to provide energy. Glucose can also converted to body fat and stored when excess calories are consumed, and, if nitrogen is available, can yield non-essential amino acids. The digestion of fat yields fatty acids and glycerol; some are reassembled as triglycerides which are stored in adipose tissue; others are broken down to provide energy. As discussed, dietary protein is broken down into amino acids, which are used to manufacture body proteins, but most amino acids can also be converted to glucose when energy is needed, and if taken to excess will be stored as body fat. When there is a surplus of amino acids, or if there is inadequate carbohydrate or fat to meet energy needs, amino acids can also provide energy. Of the energy-containing nutrients, fat provides the most energy by weight.

Besides being the building blocks for all kinds of **proteins**, amino acids are inextricably linked in the utilization of **micro- and macro-nutrients** in the human body. Even after they have been absorbed and assimilated, vitamins and minerals will not be as effective unless the proper amino acids are present (3). Minerals too, will not function properly unless vitamins are present in the right proportions (21). As one example, recent studies (93-97) have shed light on the interaction among folic acid, vitamins B12 and B6 and homocysteine concentrations, and the risk of Alzheimer and vascular disease, including multi-infarct dementia, coronary artery disease, cerebrovascular disease and peripheral arterial disease.
5.3 Amino acid deficiency

Either an excessive or an inadequate intake of a single essential amino acid is reflected as an increase or a decrease in the plasma concentration of that amino acid (23). Moreover, it has been observed that for some essential amino acids, such changes may be associated with an even greater change in their concentration in the free amino acid pool of body tissues, mainly in skeletal muscle (24).

Further, all the necessary amino acids have to be supplied to the body within a 2-3 hour period; otherwise proper protein assimilation will not take place (22). And even after all the amino acids are present, their assimilation will be restricted to that level which corresponds to the lowest available amino acid. For example, if the lowest level of any one of the available amino acid is at 60%, the assimilation of all the amino acids will remain restricted to only 60% (22). After the requirement for the limiting amino acid has been exceeded, all indispensable amino acids will be present in tissues in excess of the amounts needed to saturate protein-synthesizing system, and because amino acids cannot be stored, the extra amounts of all of them will be degraded and used only as sources of energy. (72)

Indispensable amino acids are required in specific proportions. Proteins that provide amino acids in the proportions in which they are required have well-balanced amino acid patterns. Provided such proteins are readily digested, their amino acids will be used highly efficiently for the synthesis of tissue proteins. If a protein contains a disproportionately low amount of one or more amino acids, i.e., has a poorly balanced or unbalanced amino acid pattern, it will be used inefficiently for tissue protein synthesis. The greater the deviation in the amino acid pattern of the dietary protein from the pattern of amino acid requirements, the less efficiently it will be used. This occurs because, if one amino acid is provided in less than the amount required, its concentration in tissues will fall, and it will become limiting for protein synthesis. Other amino acids can then be used for tissue protein synthesis only in amounts equivalent to the proportion of the requirement of the limiting amino acid that has been met, e.g., if a diet provides only 50% of the amount of the limiting amino acid required, then only amounts of the other amino acids equivalent to 50% of the amount of the requirements can be used. Quantities in excess of this will be degraded. If a protein with a well-balanced pattern of amino acids is consumed in an amount in excess of that needed to meet amino acid and nitrogen requirements, it will also be used inefficiently. (73)

An individual may be deficient in amino acids for a variety of reasons. These include (25, 26):
- An unbalanced, low protein diet
- Impaired absorption
- Disease (particularly infection and malignancy)
- Physical and psychological stress
- Drug use (including chemotherapy for cancer)
- Excessive excretion (impaired kidney function)
- Imbalance of vitamins and minerals
- Trauma
- Genetic factors
- Developmental age

Deficiency of amino acids would obviously compromise all the vital functions of the human body that are served by the proteins.
Aside from that, amino acid deficiency is also likely to lead to reduced energy levels, defects in metabolism, sleeping disorders, chronic fatigue, digestive problems, hair loss and skin ailments, nervous reactions, emotional upset, stress and general poor health (3). Other symptoms of amino acids deficiency that could possibly be life-threatening include obesity, malnutrition, and buildup of wastes in the bloodstream (3).

It has been shown that a deficiency or imbalance in the diet of the essential amino acids can result in a profound depression of the immune responses and marked changes in the immune resistance of the host to tumors (27).
6.0 AMINO ACIDS AND DISEASE

6.1 The Causes of Disease
Disease may be defined as a deleterious or damaging change in our body in response to destabilizing factors such as nutrition, chemicals or biological agents (28). This definition points to a deficiency or an imbalance in the food and supplements that we ingest, the chemicals and toxins that poison our systems or the bacteria and viruses that invade our body to give rise to a disease state.

What makes the metabolic and immune system weaken and become susceptible to disease involves a multiplicity of stress factors. In cancer, these stress factors are often referred to as carcinogens. Carcinogens include: chemicals, electromagnetic energy, faulty diet, free radicals, genetic pre-disposition, toxicity, radiation, parasites, strong emotions, and viruses. These are not so much the “causes” of cancer, as facilitators: they edge the body towards a condition of weakness, vulnerability, and immune dysfunction.

The fundamental hypothesis that has driven the Aminomics hypothesis and therapeutic clinical protocol is that many chronic diseases, such as cancer, are not a “disease”, but originate as a result of repercussions from the metabolic & immune system reactions of the body to genomic and environmental variations. Cancer, for example, is a complex disease, like diabetes, heart disease, and kidney disease. All complex diseases arise from combinations of changes that occur in the same cell over a period of time. To complicate matters further, there are many different types of cancer, each displaying different combinations of changes. Even within a single type, such as lung cancer or colon cancer, clinicians can identify subtypes, each marked by a unique set of changes.
Life is about balance...cellular functions must be in harmony or disease results. The key to optimal health lies originally with our fundamental genomic make-up and is then supported in turn by our metabolic and immune systems. Metabolism is the sum total of all biochemical processes going on inside the body. The therapeutic goal should be to return balance and strength to all the body’s life sustaining functions, thereby helping to reverse cancer and other disease states or prevent a recurrence... Balance = Health

6.2 Amino Acids and Disease

Various patterns of amino acid deficiencies encountered in diverse disease conditions have been well documented in the literature. As an example:

Allergies and auto immune disorders have been linked to deficiency and/or impaired metabolism of the amino acids methionine and taurine. Depression or neurological problems in the elderly are associated with deficiencies of tyrosine, tryptophan, phenylanine and histidine (3).

In one study it was found that patients with alcoholic hepatitis had a low level of glycine, alanine, and phenylalanine while those with potentially reversible liver disease were low in glutamine, isoleucine, leucine, valine and proline (21).

Depletion of protein stores in the body results during a hypermetabolic response of the body to stress such as infection, severe inflammation, trauma, burn and major operations (29).

Plasma concentrations of some amino acids, particularly glutamine has been observed to fall during infections and catabolic states (like burns and surgery) (30-32). Some authors have reported a fall in plasma taurine concentration during trauma and sepsis (33, 34).

Measurements have indicated that in severe illnesses, net protein catabolism occurs because increased rate of muscle protein breakdown far exceeds overall protein synthesis by the body (35, 36).

6.3 The Role of Amino Acids in Immune Response

Immune response in humans is comprised of “innate” immunity and “acquired” immunity.

Innate immunity is the first line of defense against infectious agents, and includes physical barriers, soluble factors and phagocytic cells. Bacterial antigen binds to the surface receptors of the phagocytic cells which results in phagocytosis and the subsequent destruction of the pathogenic microorganism. This type of immunity has no memory and is therefore not influenced by prior exposure to an organism.

Acquired immunity, on the other hand, involves lymphocytes (the B- and T-Lymphocytes). It is highly specific, takes several days to become effective and persists for some time after the removal of the initiating antigen. It is this persistence that gives rise to an immunological memory, which is the basis for a stronger and more effective response upon re-exposure to an antigen.
The immune system acts to protect the host from pathogenic invaders that exist in the environment (like bacteria, viruses, fungi and parasites) and from noxious insults. In doing so, the physiology and biochemistry of an infected individual is basically altered in a way that will provide nutrients to the immune system from within the body. In the process, muscle protein is broken down to supply amino acids for making new cells and proteins for the immune system (29).

It has been observed that arginine, glutamine and cysteine are essential for the cells of the immune system to function efficiently. Patients in a catabolic state have exhibited compromised immune function and altered profiles of amino acids in the bloodstream (29).

The immune system is considered to be an important user of glutamine. Within the cells of the immune system, glutamine acts as a nitrogen donor for the synthesis of RNA and DNA (37, 38). Some authors have observed that plasma and muscle glutamines are lowered by as much as 50% by sepsis, major injury, burns and following surgery (30-32).

Ziegler et al reported a greater number of total lymphocytes and T-lymphocytes in compromised patients after glutamine treatment. The authors have suggested that glutamine specifically enhances T lymphocyte numbers that might be responsible for a diminished infection rate (39). In another study, Glutamine was found to improve T lymphocyte function where patients who had colorectal surgery were administered parenteral glutamine (40).

Yoshida et al have observed that patients with esophageal cancer who were being treated with radio and chemotherapy actually had higher blood lymphocyte counts and better lymphocyte proliferative responses if they consumed glutamine (30g/day) for 28 days (41).

Arginine has also been found to bolster the immune system. Daly and his associates studied the immunologic effects of supplemental dietary arginine in patients undergoing surgery for gastrointestinal malignancy. They observed an enhanced response of peripheral blood lymphocytes by day 7 (42).

In one study that involved patients suffering from HIV it was shown that glutathione improved cell-mediated immune function (43).

6.4 Amino Acids and Cancer

Cancer is a condition in which there is an uncontrolled division of abnormal cells in a tissue or organ resulting in a mass or tumor. These cells can subsequently invade and destroy surrounding tissues or spread to other parts of the body through blood or lymphatics.

The cause of cancer is multi-factorial and there are a number of reasons why an individual might get cancer. These include:

(1) Genetic predisposition (as in the case of breast and colon cancer)
(2) Environmental exposure to carcinogenic agents (like tobacco smoke, radiation, sunlight, asbestos etc)
(3) Diet (red and processed meats, alcohol, animal fat, smoked or barbecued foods that are burnt)
**Viruses and bacteria** (like human papilloma virus, hepatitis B virus, Epstein-Barr virus, helicobacter pylori)

**Compromised immune system**

Hence, focusing medical efforts on removing the tumor will most often not “cure” cancer. Many, if not most, cancer deaths come as a result of infection by bacteria, viruses and fungi – microbes that normally would be destroyed by the immune system. We are always developing small cancers that are recognized by our immune system and destroyed. The healthy body can normally handle individual carcinogenic influences, but when they become multiple and cumulative, the body begins to weaken, and this is the point at which harmful influences may gain the upper hand. Any factor that increases the growth rate of these small cancers gives them an advantage over the immune system.

How are amino acids implicated in cancer? Since every metabolic and immune function in the body is driven by protein and proteins are made of specific proportions of amino acids, science is continually evidencing the crucial role of amino acids in cancer.

Cancer is characterized by changes in metabolism of body proteins, carbohydrate and fat stores. The progression of cancer is accompanied by a disturbance in protein metabolism, which is mainly represented by increased muscle protein breakdown, decreased muscle protein synthesis and an increased utilization of amino acids to form glucose. For example, in one study, a decrease in protein synthesis in advanced gastric cancer patients was found to lead to a 50%-80% depletion of muscle mass.

Certain non-essential amino acids such as glutamine, arginine and cysteine become conditionally essential in the tumor bearing state. Glutathione has been observed to be lower in the plasma of patients during cancer.

The branched chain amino acids leucine, isoleucine and valine are essential amino acids required for synthesis of proteins. The clinical benefit of preparations containing these amino acids has been evaluated in several small randomised controlled trials in patients with liver disease and these have been summarised in a meta-analysis. In patients with cancer of the gastrointestinal tract, plasma concentrations of the branched chain amino acids (BCAA) – leucine, isoleucine and valine – are also lowered.

Plasma levels of glutamine, alanine, phenylalanine and tyrosine are elevated in cancer, and are a reflection of increased muscle proteolysis.

On the other hand, some amino acids, notably glutamine and arginine, have demonstrated elevated utilization by tumor cells. Tumor cells have been shown to obtain a high proportion of fuel for energy metabolism from glutamine oxidation, and since tumor cells cannot synthesize glutamine, they rely on systemic glutamine from the host. Methionine too, is required by tumor cells to support its proliferation, and it has been demonstrated that several tumor cell lines are dependent on methionine uptake.

This dependence of some tumor lines upon various amino acids has therefore led to the investigation of amino acid deprivation to reduce tumor growth. Diets deficient in arginine or methionine slowed tumor growth in animal models; antimetabolites blocking
glutamine metabolism have been investigated as chemotherapeutic agents, and have been successful in reducing tumor growth in rats (54, 56).

However, such approaches were also associated with the problem of toxicity in case of the anti-metabolites, as well as an induced amino acid deficiency in both the tumor and the host (57).

Chemotherapy and radiotherapy for cancer treatment also actually reduces our immunity by causing a drop in the number of white blood cells (of which lymphocyte is one) that are made in the bone marrow (58). Therefore, for the vast majority of cancer patients who receive aggressive therapy, various specific amino acids may additionally be required for the bone marrow after systemic therapy, for healing after surgery, or for tissue injury in the gut (59).

A study was conducted to measure the concentration of 28 plasma amino acids in patients with cancer of the breast, gastrointestinal tract and head & neck to confirm the hypothesis that patients with different cancers may have different amino acid patterns. Seven amino acids were identified as correlating highly with diagnosis. These were glutamine, threonine, histidine, cysteine, alanine, arginine and ornithine (60).

Gaining an insight into the metabolic alterations that lead to an altered amino acid profile in an individual, especially in the case of cancer, can contribute to the definition of amino acid formulas precisely tailored to the nutritional requirements of the neoplastic patient (62).

6.4 The Integrated Impact of Amino Acids and Micronutrients in Cancer

As discussed in section 5.2, the use of micro- and macro-nutrients in the body is inextricably linked to protein functioning and hence, amino acids. And many nutrients have been directly linked to cancer.

Nutrients Alone Can Reverse Early Stage Cancer

Cell level research has shown that in early stage of cancer cell development, nutrients can reverse pre-malignant cancers. (74)

The peer-reviewed proof is irrefutable. As a small example:

- & B-12 reverse bronchial metaplasia (75)
- Beta-carotene & vit A & vit E reverse oral leukoplakia (76)
- Selenium reverse pre-cancerous mouth lesions (77)
- Vit C & calcium reverse colorectal adenomas (78)
- Vit E reverse fibrocystic breast disease (increases cancer risk by 50-80%) (79)
- Vit E & betacarotene reverse mouth cancer (80)

......and the body of evidence for vitamins, enzymes, co-factors, minerals, antioxidants goes on & on! ISM has identified 10,000+ peer-reviewed studies on nutraceuticals & cancer.

40% of Cancer Patients Die from Malnutrition

- Weight loss drastically increases mortality rate for most cancer types (81)
- Chemo & radiation therapy are sufficient biological stressors to induce malnutrition (82)
- Pure malnutrition (cachexia) is responsible for 22% - 67% of all cancer deaths. (83)
• Up to 80% of all cancer patients have reduced levels of serum albumin (the leading indicator of protein & calorie malnutrition) (84)

The following pages provide summaries of just a few of the studies that have directly implicated micronutrients in cancer treatment. The intent is not to provide an exhaustive review, but rather to demonstrate that the evidence for micronutrient involvement in cancer is indisputable.

Summary: Why Use Nutrition in Cancer Treatment?

GOAL: To slow down or prevent malignancy.

Typical cancer has a 15-20 year latent period from time of first exposure to carcinogen and time of developing cancer.

If ALL you do is double the latent period with nutrient supplementation, then there would be 15-20 additional years of good life!
**Extending Cancer Survival Through Nutrition**

Randomized lung cancer clinical trial (85)
- Patients undergoing chemo also follow precise diet with high dose of vitamins & minerals
- Expected survival at 30 months = 1% (SEER)
- With nutrition supplementation 44% were alive 6 years after therapy

See following chart:

![Chart showing survival times and response rates]
Extending Cancer Survival Through Nutrition
Non-randomized, cancer clinical trial (86)

- 129 patients received conventional treatment.
- Control group did not receive precise diet control or controlled therapeutic vitamins & minerals

Three Observation Groups:
1. Poor Responders: still had 75% improvement over control group
2. Good Responders: Various cancers (leukemia, lung, liver, & pancreas) 1,200% improvement in lifespan
3. Good Female Responders: Cancer of reproductive areas (breast, cervix, ovary): 2,100% improvement in lifespan
Extending Cancer Survival Through Nutrition

36 Post-Operative Lung Cancer Patients (87)

1st group = no vitamin usage
2nd Group = vitamin supplementation

Survival was greatly extended with vitamin use.
“Spontaneous” Tumour Regression Through Nutrition

200 cancer patients studied who experienced tumour regression. (88)

Nutrition clearly has a role in tumour regression.
**Therapeutic Nutrition Lowers Cancer Recurrence**

Randomized, 65 bladder cancer clinical trial (89)

One group = “1 per day” RDA multivitamin
2nd Group = “1 per day RDA” plus high dose vit A, B-6, C, E & zinc

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*High dose nutrients cut tumour recurrence in half.*
Synergism of Chemo-Preventive Nutrients

There are two primary factors in nutritional synergism:

1) Enhanced effects
Nutrient combinations augment each other
e.g., Vit C + EFAs together kill more melanoma cells than either nutrient alone (90)
Nutrient & medicine combinations protect the patient while selectively killing cells

2) Lower doses are required
e.g., Combined Vit C + K will kill cancer cells at doses 90% lower than either nutrient alone (91)

When exposed to DMBA... 100% animals died of cancer (92)

<table>
<thead>
<tr>
<th># of chemo-preventive agents added</th>
<th>Amount of cancer incidence reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>50%</td>
</tr>
<tr>
<td>2</td>
<td>70%</td>
</tr>
<tr>
<td>3</td>
<td>80%</td>
</tr>
<tr>
<td>4</td>
<td>88%</td>
</tr>
</tbody>
</table>

(DMBA: Dimethylbenz-A-Anthracene: Induces cancer in 100% of test animals)
7.0 AMINOMICS: A Therapeutic Approach

7.1 The Core Principles of Aminomics as a Therapeutic Approach

There are four core principles of Aminomics:

1. A Strong Immune Response = Balance of Amino Acids & Protein
2. Nutritional Synergism
4. Supplementation requires extreme quality, bioavailability and timing.

7.1.1 A Strong Immune Response = Balance of Amino Acids & Protein

The basic substrate of all metabolic and cellular human functioning is amino acids. When an individual possesses the optimal profile of chemistry and metabolism, that individual is typically healthy or symptom-free. When an individual's profile deviates from the optimum, symptoms will evolve.

Aminomics therapy targets the amino acid/protein imbalances created by the genomic/proteomic and environmental variations (61).

The principle behind Aminomics therapy is the administration of individualized amino acid supplementation tailored to the person’s needs. However, it must be remembered that requirements will need to be modified according to each individual’s needs and specific disease processes. Requirements for particular orthomolecular support depend upon both utilisation and rate of loss.

Proteins can only be made when all the necessary amino acids are simultaneously available in the right proportions. This is a core philosophy of Aminomics therapy. It is an intervention to restore, at the proteomic level, imbalances in amino acids that may be the result of a wide variety of causes, including age, stress, genetic disorders, inadequate intake and/or absorption, infection, errors in metabolism or immunologic incompetence.

Thus, targeted Aminomic supplementation has the potential not only of preventing the onset of a disease process, but also of accelerating the rate of its remission. Restoration of the plasma amino acid profile to the desired optimum that is conducive to normal bodily functions is also expected to result in a improved health in most cases.

A stronger immune system from patient-individualized aminomic supplementation is a factor in reducing the side-effects of conventional treatment (notably of cancer chemotherapy and/or radiotherapy).

7.1.2 Nutritional Synergism

Nutritional Synergism, as it applies to nutrition or pharmacology, is the simultaneous action of separate biochemicals (micro- and macro-nutrients), which together have greater total effect than the sum of their individual effects.
No cell in the body uses only one nutrient. No nutrient in the body acts alone. Therefore, it should come as no surprise that we need all of the nutrients in order to promote optimal cellular, organ, and overall health. Because nutrients have powerful interactions with other nutrients, the success of a nutrient therapy may depend more on the synergistic interaction with a particular nutrient than merely the dose given. This argues for both individualized therapy as well as synergistic ones.

The synergistic impact and interrelationships of all micro- and macro-nutrients is critical to proper protein absorption, use and function.

Infections, no matter how mild, have adverse effects on nutritional status. The significance of these effects depends on the previous nutritional status of the individual, the nature and duration of the infection, and the diet during the recovery period. Conversely, almost any nutrient deficiency, if sufficiently severe, will impair resistance to infection. Iron deficiency and protein-energy malnutrition, both highly prevalent, have the greatest public health importance in this regard. Remarkable advances in immunology of recent decades have increased insights into the mechanisms responsible for the effects of infection. These include impaired antibody formation; loss of delayed cutaneous hypersensitivity; reduced immunoglobulin concentrations; decreased thymic and splenic lymphocytes; reduced complement formation, secretory immunoglobulin A, and interferon; and lower T cells and T cells subsets (helper, suppressor-cytotoxic, and natural killer cells) and interleukin 2 receptors. The effects observed with single or multiple nutrient deficiencies are due to some combination of these responses. (99)

Another important reason to use nutrients in combination is not just efficacy, but safety. The ingestion of single, isolated nutrients by the human genus is but 70 years old. This is at odds with the 2.6 million years of only ingesting nutrients in synergistic combinations found in foods of plant and animal origin. Throughout our genetics' long history, they have never encountered a single instance where a food consumed supplied one or even a small handful of nutrients. This is mirrored in our metabolism: all cellular functions, including glycolysis, the Krebs cycle, the energy transfer cycle, cellular housekeeping, eicosanoid metabolism, neurotransmitter metabolism, antioxidant defense, immune strength, and detoxification all depend on an optimal supply of virtually all nutrients. (100)

7.1.3 Individuality

“Disease is as unique as the patient”

Every human is unique, bio-chemically and metabolically. Each of us possess a unique history of experience that culminates in our state of health. In today's medical world, disease tends to be managed by diagnosing and treating the symptoms.

All aspects of the Aminomics diagnostic and therapeutic approach embrace the central concept of uniqueness or biochemical individuality. Aminomics focuses on the underlying cause that is unique to the patient. The fundamental hypothesis upon which ISM’s Aminomics methodology is founded is “patient-specific, evidence-based medicine,”

7.1.4 Zero Pathogen/ High Bio-availability

An immune system that is already fighting various pathogens needs to be supported with supplementation that is:
• pure and pathogen-free
• highly bio-available
• administered in the right proportions at the right time

7.2 ISM’s Aminomics© Protocol

The Aminomics© therapeutic compounds manufactured by ISM provide a client-individualized substrate in a high-grade, balanced and bio-available format. All compounds are formulated and manufactured in an ISO-9001, GMP (Good Manufacturing Practice) compliant laboratory. Compounds are of pharmaceutical grade. This means that it is almost 100% pure (technically no substance can be 100% pure) with no binders, fillers, excipients, dyes or any unknown substances and is 100% pathogen-free material.

Aside from the targeted amino acid supplement, the formulation also contains collateral nutrients such as appropriate anti-oxidants, vitamins, enzymes, minerals and lipotropic factors. As discussed previously, all these combine synergistically to facilitate proper and timely absorption, metabolism and immediate protein construction.

The genesis of ISM’s Aminomics© therapeutic compounds involves the application of proprietary diagnostics in the form of blood plasma analysis that results in the manufacture of bio-individualized Aminomics© Therapeutic Compounds (63). Customized HPLC (High Performance Liquid Chromatography) laboratory technology is employed to “blueprint” a patient’s plasma amino acid profile. This is then compared to an optimal ISM Aminomics© Profile to reveal any discrepancy in the amino acid levels in the patient’s plasma.

A subsequent step involves the formulation and manufacture of what is referred to as a “balancing custom compound”. This compound is specific to the patient and replenishes the deficient amino acids and any collateral nutrients.

ISM’s Aminomics© protocol involves:

1. Initial client interview: To elicit any physical or mental complaints. Any prior diagnosis, and patient reports are also taken into consideration.
2. Analysis of the client’s plasma by HPLC: To determine existing amino acid levels.
5. Compliance
6. Interval re-testing and re-engineering: Review on a regular basis new blood analysis and the Aminomics© formulation for optimal results.

7.3 Efficacy of Aminomics

It is not the objective of this white paper to discuss the overall efficacy of Aminomics. The objective is to present the rationale behind this diagnostic and therapeutic healthcare methodology.
Suffice it to say that the application of the Aminomics approach to thousands of patients has proved to be a rational, effective and advanced means of ensuring long term, event-free health. Years of clinically administering patient-specific Aminomics therapeutic has resulted in enhanced response rates and quality of life without side effect or adverse events for hundreds of individuals. For example, the application of Aminomics has demonstrated significant positive response rates in disease remission, stabilization, and overall improvement in quality of life often exceeding those of more commonly available approaches in specific therapeutics such as surgery, radiotherapy or chemotherapy.

The Aminomics approach has proven to be beneficial in the management of collateral damage, from both a prevention perspective and a treatment perspective (should a client undergo radiotherapy and/or chemotherapy).

In healthcare today, there is a disconnect between What We Know and What We Do. The scientific and medical community widely acknowledges the flawed model of drug development…an obsession with tumor shrinkage…a focus on individual cellular mechanisms, sometimes to the near exclusion of what’s happening in the organism as a whole. Science has its limits and often cannot give us a crystal clear picture. But this should not paralyze us. Our knowledge of the causes of and cures for cancer may be imperfect, but we have no excuse for delaying application of the nutritional therapeutic and preventive knowledge we now have, both for our own benefit in our later years, and the benefit of our children and grandchildren.

Every element of the ISM® approach is based upon extensive and evolving laboratory and applied evidence. Contemporary scientific and medical knowledge and evidence has been integrated with our laboratory and clinical experience as we analyze and interpret data from thousands of ISM® patient profiles. For further efficacy information please review www.aminomics.com.
APPENDICES

ADDENDUM

TYPES OF AMINO ACIDS

Of the amino acids, some are essential. These are the amino acids that the body cannot synthesize in adequate quantities to meet the nutritional requirements for good health and therefore, must be included in the diet. The essential amino acids are ISOLEUCINE, LEUCINE, LYSINE, METHIONINE, PHENYLALANINE, THREONINE, TRYPTOPHAN and VALINE.

The non-essential amino acids are those that the human body is able to synthesize. These are ALANINE, ASPARAGINE, ASPARTIC ACID, GLUTAMIC ACID, GLUTAMINE, GLYCINE, PROLINE, SERINE and TYROSINE.

The amino acids HISTIDINE and ARGinine are considered nutritionally semi-essential. This means that they can be synthesized in the body but not in quantities sufficient enough to permit normal growth, as in the case of infants and some elderly individuals.

Following is a brief account of the various amino acids.

**ISOLEUCINE:**

Function: Low levels of Isoleucine can lead to sugar imbalances. Sugars are necessary in the production of immunoglobulins which stimulate immunological response and momentum. Low levels indicate a responsively slow immune system. In conjunction with valine and leucine it promotes muscle recovery. It is also needed for the formation of hemoglobin.

Dietary sources: Almonds, cashews, chicken, eggs, fish, lentils, liver, meat

**LEUCINE:**

Function: Plasma levels of Leucine similarly manage sugars. However, optimal levels in both Isoleucine and Leucine demonstrate the ability to build sugars and branched amino acids that act as immunological stimulants and nutrients to various glands in the brain and endocrine system. This manages the overall competency of the immune system. Low levels indicate low immunological response.

Dietary sources: Brown rice, beans, nuts, whole wheat

**LYSINE:**

Functions: Lysine is one of the two most critical amino acids. Plasma levels indicate the degree and extent of overall immunological competency. Lysine is a branched amino acid. This means it is used in the production of every immunological protein, antibody, antigen, hormone, growth factor and cytokine (protein). Low levels indicate deficiencies in overall immunological functioning. It also helps to absorb calcium and supports bone development in children.
**METHIONINE:**

Functions: Methionine assists in the breakdown and absorption of fats. Approximately 20% of amino acids are derived from consumption of protein which is broken down by fats. Fats are also requisite to the absorption of nutrients. Low levels of Methionine affect levels of essential amino acids. Methionine is also critical in the absorption of sulphur and sulphur based chemistry which is critical in the formation of nucleic acid. Methionine is used in the manufacture of Choline which stimulates the neurological components of the immune system. Level of methionine will rise only when all amino acids are effective. It shows whether the body is taking in and utilizing amino acids efficiently.

**Dietary sources:** Meat, fish, eggs, yoghurt, beans, lentil, garlic, onion

**PHENYLALANINE:**

Functions: Phenylalanine plays an important role as an immune system marker and as an indicator expression of various brain chemicals that stimulate the immune system. As an immune system marker, levels of Phenylalanine increase with the killing, fragmenting and recycling of the constituent materials of malignant cells. In other words, it indicates the burden of damaged cells. Phenylalanine also inhibits enzymes that break down stimulatory brain chemistry, thus keeping immuno-excitatory chemistry at optimal levels.

**Dietary sources:** Dairy, almond, lima beans, peanuts, avocados

**THREONINE:**

Functions: Threonine metabolizes into neuro-electrolytes and ensures continual and optimal messaging for immune response. It is found in high concentration in the central nervous system, the muscles and the heart.

**Dietary sources:** Meat, dairy, eggs

**TRYPTOPHAN:**

Functions: Tryptophan plays a key neurological and physiological role by ensuring metabolic stimulation of various chemistry and processes that regulate circadian cycles (wake/sleep states) and all of the attendant circadian activities relative to these cycles. Low levels are usually present with poor wake and sleep states, underwritten by poor chemical and metabolic activities consistent to each state. Tryptophan levels also give insight into how iron is bound to various resource chemistries and transported to various sites for manufacture and remanufacture into immunological cells and chemistry.

**Dietary source:** Oats, bananas, milk, cottage cheese, meat, fish, turkey, peanuts

**VALINE:**

**Dietary sources:** Milk, cheese, eggs, lima beans, meat, brewers yeast
Functions: Valine is a neuro-excitatory amino acid. Optimal levels are usually present with stable psychology and physiology. Low levels indicate psychological and physiological depression. Valine is a stimulant of the thymus gland, and the thymus produces the T-lymphocytes of the immune system.

Dietary sources: Dairy, meat, grains, mushrooms, soy, peanuts

**ALANINE:**

Functions: Alanine is an immune system marker and indicates how effectively the immune system is killing malignant cells. Alanine is also vital for the production of protein, essential for proper function of the central nervous system and helps form neurotransmitters. Alanine is necessary for the promotion of proper blood glucose levels from dietary protein.

Dietary sources: Beans, meat, nuts, seafood, seeds, soy, whey, brewer's yeast, brown rice

**ASPARAGINE:**

Functions: Asparagine controls protein balance and is able to burn fat to build proteins. It is one of the principal amino acids involved in the transport of nitrogen. It also mediates a variety of chemistries that stimulate the immune system.

Dietary sources: Dairy, beef, poultry, eggs

**ASPARTIC ACID:**

Functions: Aspartic Acid controls the levels of a variety of amino acids and blood gases that control pH balance and reduce anaerobic activity. Since malignant cells are anaerobic, aspartic acid helps to reduce malignant activity. Aspartic acid also serves as an excitatory neurotransmitter in the brain which provides resistance to fatigue and leads to greater endurance.

Dietary sources: Sprouting seeds, oat flakes, meat, avocado, asparagus

**GLUTAMINE** and **GLUTAMIC ACID:**

Functions: Glutamine is converted to Glutamic Acid (Glutamate) after it crosses the blood-brain barrier. Glutamic acid combines with the amino acid taurine to form GABA (gamma amino butyric acid). GABA regulates neuron firing and neurochemical activity in the brain.

Glutamine also serves as a source of fuel for cells lining the intestines. Without glutamine the intestinal cells would waste away. Glutamine regulates the expression of certain genes and helps regulate the biosynthesis of DNA and RNA. Construction of DNA is dependent upon adequate amounts of glutamine.

Dietary sources: Beef, fish, milk, yoghurt, cheese, spinach, cabbage, parsley
GLYCINE:
Functions: Glycine is essential for the synthesis of amino acids produced by various organ systems. It is vital to the production of nucleic acids, glucose, hemoglobin and bile acids. It also exerts an inhibitory influence on the central nervous system and may be important in the control of epilepsy and spastic disorders.

Dietary sources: Fish, meat, beans, dairy

PROLINE:
Functions: Proline is a marker of anaerobic activity. A low level of proline is indicative of a contained bacterial infection. Proline is the precursor for hydroxyproline, which the body incorporates into collagen, tendons, ligaments, and the heart muscle. Proline helps strengthen cardiac muscle.

Dietary sources: Dairy products, eggs, beef, poultry

SERINE:
Functions: Serine is needed for the metabolism of fats and fatty acids. It aids in the production of immunoglobulins and antibodies, and is a constituent of brain proteins and nerve sheaths. It is important in the production of cell membranes, and in the synthesis of muscle tissue.

Dietary sources: Meat, dairy, wheat, peanuts, soy

TYROSINE:
Functions: Tyrosine is critical in the production of dopa and dopamine (which regulates brain function), and epinephrine and norepinephrine (which regulates heart function). Tyrosine is also reported to have an antioxidant effect, which may help to protect from cancer and coronary heart disease, and reduce aging.

Dietary sources: Meat, fish, dairy, eggs, almonds, avocado, bananas

HISTIDINE:
Functions: Histidine is used in the manufacture of histamines, which are the first line of defence in immunological response. Chronic low levels of histidine demonstrate immunological suppression, leaving the host organism open to a variety of immunological challenges, such as cancer. High levels, on the other hand, demonstrate immunological competency.

Besides, histidine is also needed for the growth and repair body tissues, and to maintain the myelin sheaths that protect nerve cells. It also helps in the manufacture of red and white blood
cells, and protects the body from heavy metal toxicity. The stomach uses histidine to produce gastric juices.

**Dietary sources:** Dairy, meat, fish, wheat, rye

**ARGININE:**

**Functions:** Plasma levels of Arginine are directly proportional to tumour regression. Arginine sets the pace at which immunological proteins are manufactured and this, in turn, determines the rate of immunological response. Low levels indicate a slow immunologic response.

**Dietary sources:** Whole wheat, nuts, seeds, peanuts, brown rice, soy, raisin
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