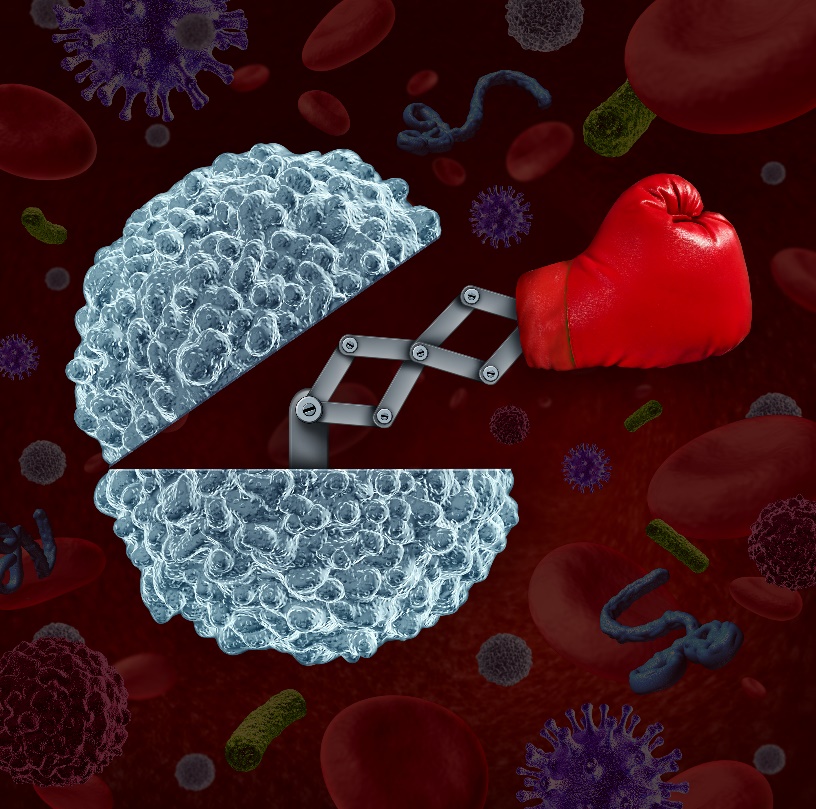
**Ai/E¹º®**

**High Priority Support for Immunity and Good Health**

Modes of Action



Ground-breaking research, life science patents awarded, published double-blind placebo controlled human trials with healthy human adults, published animal studies, published in-vitro studies and the insights of users for over twenty years and the consumption of 300,000,000 servings in countries around the world illuminate the important contribution **Ai/E¹º®** makes to consumer’s immunity and good health.

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Scientific summary provided for international product developers, industry experts, academia, and health care professionals. Not for distribution to consumers.

**Executive Summary**

**Ai/E¹º®** is a unique, highly soluble, non-stimulatory molecular GRAS/ODI complex containing a broadly reactive array of immune-dynamic peptides conducive to the support of memory and communication functions of the immune system. As a dietary ingredient, **Ai/E¹º®** anticipates the current and growing recognition of the need for genuine, safe, modulation benefits in a dietary supplement that can help us adapt to our constantly evolving and complex civilization.



Traditional dietary supplement ingredients for the support of immunity, as well as vitamins and minerals, provide support and stimulation to what is commonly called the “immune biochemistry,” but little or no support for the immune memory and cellular signaling that directs the utilization of the “immune biochemistry.”

The benefits of **Ai/E¹º®** when absorbed orally or through the skin manifest through enhanced and restored immune cell communication and signaling. Cell signaling is part of a [complex system](http://en.wikipedia.org/wiki/Complex_system) of communication that governs basic cellular activities and coordinates cell actions. The ability of cells to perceive and correctly respond to their microenvironment is the basis of development, tissue repair, and [immunity](http://en.wikipedia.org/wiki/Immunity_(medical)) as well as normal tissue [homeostasis](http://en.wikipedia.org/wiki/Homeostasis). Errors in cellular information processing are responsible for diseases such as [cancer](http://en.wikipedia.org/wiki/Cancer), [autoimmunity](http://en.wikipedia.org/wiki/Autoimmunity), and [diabetes](http://en.wikipedia.org/wiki/Diabetes).

Analysis and study has identified specifically reactive essential mRNA, transfer factors, defensin, granulycin and mini cytokines that are critical components to cellular signaling and appear in an easily absorbable natural array described by leading immunologists as the “essential supplement ingredient sought by everyone who understands the risks of compromised immunity.”

**Ai/E¹º®** is safe and suitable for long-term daily use. The pages that follow illustrate some of the observed benefits/effects of **Ai/E¹º®** reported and observed in study data ranging from 1998 to the present.

**Important General Observation**

Ai/E¹º® functions very uniquely as a normalizing and modulating agent to numerous aspects of the immune response. This novel capability is not offered by any other dietary supplement ingredient and is the reason consumers find the supplement of such value to them and have continued use since 1994. This novel capability also means the benefits to each user will vary according to their specific need(s). This has been shown in a small human study, animal studies and in clinical application.

In this context, a review of Ai/E¹º®’s many “Modes of Action,” can be appreciated more completely. Initial users often experience broad changes in cellular activation that can easily be measured and are demonstrated in many types of trials and studies. Our studies have demonstrated that the immune response of most people from some aspect is below normal or optimal. Thus, elevations in B, T and NK cell activity occur, and though they may appear stimulatory they are in fact more an expression of need modulated to bring normalization.

Normalization will bring a better and more effective systemic immune response. Continual use of Ai/E¹º® offers sustained support for normalized immune function.

**INNATE and ADAPTIVE IMMUNE SYSTEM**

* **Supports normalized lymphocyte (B cell, T cell and NK cell) activity in vivo, ex vivo and in vitro.4,5,7**

**PHYSIOLOGY:** B cells are an essential component of the human adaptive immune system. Their principal function is the extracellular production of antibodies against antigens.

Published ex-vivo studies indicate that Ai/E¹º® supports normalized activation of B cells more effectively than other leading supplements utilized in recommended serving sizes.

**PHYSIOLOGY:** T-cells are a type of white blood cell that circulate in our bodies, scanning for cellular abnormalities and infections. Almost every aspect of the adaptive immune response is controlled, in some way, by T cells. These multifunctional cells have the ability to:

* Scan the intracellular environment for foreign invaders.
* Directly kill virally or bacterially infected cells.
* Naturally eradicate cancer cells.
* Activate and help other immune cells that ingest germs or that make anti-infection molecules called antibodies.
* Remember a germ that they encountered decades ago.

Published ex-vivo study data indicates that Ai/E¹º® supports normalized activation of T cells more effectively than other leading supplements utilized in recommended serving sizes. Perhaps more importantly, Ai/E¹º®’s passive ability to activate the immune cascade specific to staph, strep, pseudomonas, e.coli and salmonella assures the activation of specific, important T cells and not just the stimulation of an existing population which may be limited or otherwise depleted as a consequence of stress, diet, toxin and infection.

**PHYSIOLOGY:** Natural killer cells, or NK cells, are a type of cytotoxic lymphocyte critical to the innate immune system. In addition to the knowledge that natural killer cells are effectors of innate immunity, it is known that NK cells play a role in the adaptive immune response. Numerous experiments have demonstrated the ability of NK cells to adjust to the immediate environment and formulate antigen-specific immunological memory which is essential for responding to secondary infections with the same antigen. The role of NK cells in both the innate and adaptive immune responses is becoming increasingly important in research using NK cell activity and potential cancer therapies.

A published clinical study of Ai/E¹º® illustrated significant statistical support (p=<.001) for people appearing completely healthy, who presented a pre-study NK cell activity mean of 30 Lytic Units. Measured in a ninety day study the seven women and five men, mean age 43, used Ai/E¹º® in 100 mg servings t.i.d. and experienced an elevation to a mean of 100 Lytic Units

Solstice Clinical Associates randomly sampled 107 seriously ill patient records, with a measured mean NK cell activity of 18 Lytic Units, from a population of nearly 2,000 over a 13.2 month period. This data produced a significant statistical elevation (p=<.001) as the patients measured mean NK cell activity rose to a mean of 246 Lytic Units. The patients received 200 to 800 mgs of Ai/E¹º® q.d.

A published study of immune response modifiers found Ai/E¹º®, in 50 mg serving sizes, outperformed lactoferrin, whey isolate, reishi, maitake, beta 1,3 glucan, goldenseal, arabinogalactan, colostrum, echinacea and astragalus in their suggested serving sizes in general immune activation of lymphocytes including NK cells.

Ai/E¹º®’s superior ability to modulate NK cell activity has been well known since the late 1990’s and has been illustrated by many individuals in their own experience since 1994.

* **Exhibits modulatory/regulatory influence.** 6,10

**PHYSIOLOGY:** The immune system is our natural first line of defense against illness and poor health. However, the immune system may lose the ability to protect us, or in some cases the immune system may appear to actually turn against us. These forms of abnormal function are generally caused by deficiencies and disorders which have resulted in a loss or disruption of the natural immune processes. In either case, natural immune modulators may provide the key to maintaining a strong and properly functioning immune system.

Ai/E¹º® has demonstrated its modulatory capability in two distinct studies. The first, “*An Examination of Immune Response Modulation in Humans by* Ai/E¹º® *Utilizing a Double Blind Study*,” in 2001, conducted by Immune Consultants, Inc. was a double blind placebo controlled study of three measureable factors illustrative of independent modulation. The Ai/E¹º® study group illustrated unique and powerful modulated changes in just 15 days, while the control group did not. This was a very early trial that was reinforced in 2011 “*Evaluation of bovine-derived lacteal complex (*Ai/E¹º®*) supplementation on gene expression in BALB/c mice”* conducted at Milan University where Ai/E¹º®’s unique abilities were more clearly elucidated across a wide range of relevant genes associated with a great many aspects of the immune response and immune modulation. When successfully "modulated" the individual’s immune system enables maintenance, recovery or remission utilizing the extraordinary function of the immune system.

* **Supports Monocyte activity ex vivo. 7**

**PHYSIOLOGY:** Monocytes are a type of white blood cell (leukocyte). They are the largest of all leukocytes and are part of the innate immune system of vertebrates including all mammals (humans included), birds, reptiles, and fish. Monocytes constitute 2% to 10% of all leukocytes in the human body. They play multiple roles in immune function.

These cells are made in the bone marrow, and they spread through the body in one to three days. They can develop into either dendritic cells or macrophages. Dendritic cells belong to a group of cells known as antigen presenting cells, because they acquire antigens and show them to T cells so that the T cells learn to recognize dangerous antigens. Dendritic cells typically present antigens to T cells before they are fully developed, so that the T cell can respond appropriately after it has been shown an antigen.

A published study of immune response modifiers found Ai/E¹º®, in 50 mg serving sizes, outperformed lactoferrin, whey isolate, reishi, maitake, beta 1,3 glucan, goldenseal, arabinogalactan, colostrum, echinacea and astragalus in their suggested serving sizes in general immune activation of lymphocytes including monocytes.

* **Supports Granulocyte activity ex vivo.** 7

**PHYSIOLOGY:** Granulocytes are a type of white blood cell that is made of small granules, which contain proteins. The types of these cells are neutrophils, eosinophils, and basophils.

Granulocytes help the body fight bacterial infections. People with lower numbers of granulocytes are more likely to get bad infections more often.

A published study of immune response modifiers found Ai/E¹º®, in 50 mg serving sizes, outperformed lactoferrin, whey isolate, reishi, maitake, beta 1,3 glucan, goldenseal, arabinogalactan, colostrum, echinacea and astragalus in their suggested serving sizes in general immune activation of lymphocytes including granulocytes.

* **Supports the mitigation of Septic Shock**. 9,10

**PHYSIOLOGY:** Septic shock is a [medical](http://en.wikipedia.org/wiki/Medicine) condition that results from severe [infection](http://en.wikipedia.org/wiki/Infection) and [sepsis](http://en.wikipedia.org/wiki/Sepsis), though the underlying microbe may be systemic or localized to a particular site. It can cause [multiple organ dysfunction syndrome](http://en.wikipedia.org/wiki/Multiple_organ_dysfunction_syndrome) (formerly known as multiple organ failure) and [death](http://en.wikipedia.org/wiki/Death). Its most common victims are children, [immunocompromised](http://en.wikipedia.org/wiki/Immunodeficiency) individuals, and the elderly, as their [immune systems](http://en.wikipedia.org/wiki/Immune_system) cannot deal with the infection as effectively as those of healthy adults. Frequently, patients suffering from septic shock are cared for in [intensive care units](http://en.wikipedia.org/wiki/Intensive_care_units). The [mortality rate](http://en.wikipedia.org/wiki/Mortality_rate) from septic shock is approximately 25–50%.

Ai/E¹º® was shown in an animal study to support gene expression associated with Septic Shock. This is an important component of supporting the immune response. In a separate animal study with a specific formulation developed using the identical technology an “Ai/E¹º® type” whey extract successfully mitigated septic shock for animals infected with MRSA.

* **Activates the “immune cascade” reactive to staph, strep, pseudomonas, e.coli and salmonella.**4,5,7,9,10

**PHYSIOLOGY:** Immune suppression occurs daily as a consequence of stress, toxin, diet and infection. This suppression damages our ability to respond to the most common bacterial challenges we encounter every day and taxes redundant resources to compensate for the loss. Ai/E¹º® helps to passively restore 85% of these suppressed immune system components associated with common bacterial challenges.

No other supplement ingredient accomplishes, or attempts to accomplish, this goal.

**AUTO IMMUNE RESPONSES**

* Exhibits full modulatory/regulatory influence. 6,10

**PHYSIOLOGY:**  The immune system is our natural first line of defense against illness and poor health. However, the immune system may lose the ability to protect us, or in some cases the immune system may appear to actually turn against us as in an auto immune response. Abnormal function is generally caused by deficiencies and disorders which have resulted in a loss or disruption of the natural immune processes. Natural immune modulators may provide the key to maintaining a strong and properly functioning immune system.

Ai/E¹º® has demonstrated its modulatory capability in two distinct studies. The first, “*An Examination of Immune Response Modulation in Humans by* Ai/E¹º® *Utilizing a Double Blind Study*,” in 2001, conducted by Immune Consultants, Inc. was a double blind placebo controlled study of three measureable factors illustrative of independent modulation. The Ai/E¹º®study group illustrated unique and powerful modulated changes in just 15 days, while the control group did not. This was a very early trial that was reinforced in 2011 “*Evaluation of bovine-derived lacteal complex (*Ai/E¹º®*) supplementation on gene expression in BALB/c mice”* conducted at Milan University where Ai/E¹º®’s unique abilities were more clearly elucidated across a wide range of relevant genes associated with a great many aspects of the immune response and immune modulation. When successfully "modulated" the individual’s immune system enables maintenance, recovery or remission utilizing the extraordinary function of the immune system.

**INFLAMATORY RESPONSE**

* Provides direct support to cells critical to the immune response and significant support to C-reactive protein (CRP) gene expression. 10

**PHYSIOLOGY:** Inflammation reflects the most fundamental protective immune response. It involves tight regulation of immune cells, blood vessels, and molecular mediators. The purpose of inflammation is to eliminate the initial cause of cell injury, clear out necrotic cells and tissues damaged from the original insult and the inflammatory process, and to initiate tissue repair. The process of acute inflammation is initiated by resident immune cells already present in the involved tissue.

The operation of a favorable response to inflammation depends upon CRP, which binds to the [phosphocholine](http://en.wikipedia.org/wiki/Phosphocholine) expressed on the surface of dead or dying cells and some bacteria. This activates the [complement system](http://en.wikipedia.org/wiki/Complement_system), promoting [phagocytosis](http://en.wikipedia.org/wiki/Phagocytosis) by macrophages, which clears necrotic and apoptotic cells and bacteria.

Ai/E¹º® was shown in a published “Gene Expression” study to significantly support CRP gene expression as well as broad support for all immune system activity. This is further supported by several published and un-published studies demonstrating its unequaled ability to bring modulated cellular development and broad support to both innate and adaptive immunity. Also impressive is Ai/E¹º®’s support for gene expression associated with Septic Shock which can lead to inflammatory responses damaging to a patient. This was also noted in a study done at the University of Arizona with MRSA and a product similar to Ai/E¹º® produced for the study using the same technology.

**CELLULAR COMMUNICATION**

* Supports effective cellular communication. 4-11

**PHYSIOLOGY:** Cell signaling is part of a complex system of communication that governs basic cellular activities and coordinates cell actions. The ability of cells to perceive and correctly respond to their microenvironment is the basis of development, tissue repair, and immunity as well as normal tissue homeostasis.

Ai/E¹º®’s support for cellular signaling comes from two distinct sources. Sequencing of Ai/E¹º® at Tufts University revealed the full array of cell signaling molecules that are present in Ai/E¹º®. Those molecules are easily absorbed and ready to use. At the same time, product research demonstrates that Ai/E¹º® can initiate the immune cascade and thereby lead to the production of new cellular signaling molecules. This was most highly apparent in a study performed at the University of Arizona and is also demonstrated in several Ai/E¹º® studies.

**APOPTOSIS**

* **Supports regulated apoptosis.** 4-11

**PHYSIOLOGY:** Professional phagocytes of the immune system are critical to the process of apoptosis. Apoptosis is the process of programmed cell death (PCD) that occurs in multicellular organisms. Biochemical events lead to characteristic cell changes (morphology) and death. These changes include blebbing, cell shrinkage, nuclear fragmentation, chromatin condensation, and chromosomal DNA fragmentation. Phagocytes are cells that protect the body by ingesting (phagocytosing) harmful foreign particles, bacteria, and dead or dying cells.

Ai/E¹º®’s support for gene expression and the immune cascade provides direct support to the process of regulated apoptosis by working to assure a vibrant supply of phagocytes are available. A small private study in New Zealand suggested Ai/E¹º® is also highly synergistic with anti-oxidants and demonstrated support for full anti-oxidant expression in all quadrants of generally observed anti-oxidant activity.

A study conducted in May, 2012, published in Preventive Medicine, demonstrated a rapid increase in phagocytic activity compared to placebo (p<.012) after a single serving of a low molecular weight bovine whey extract.

**TH1/TH2 CELL REGULATION**

* **Supports sustained balancing of Th1 and Th2 cells.**10

**PHYSIOLOGY:** The T helper cells (Th1, Th2 and others) are a type of [T cell](http://en.wikipedia.org/wiki/T_cell) that play an important role in the [immune system](http://en.wikipedia.org/wiki/Immune_system), particularly in the [adaptive immune system](http://en.wikipedia.org/wiki/Immune_system#Adaptive). They help the activity of other immune cells by releasing T cell [cytokines](http://en.wikipedia.org/wiki/Cytokines). These cells help suppress or regulate immune responses. They are essential in [B cell](http://en.wikipedia.org/wiki/B_cell) [antibody class switching](http://en.wikipedia.org/wiki/Antibody_class_switching), in the activation and growth of [cytotoxic T cells](http://en.wikipedia.org/wiki/Cytotoxic_T_cells), and in maximizing [bactericidal](http://en.wikipedia.org/wiki/Bactericidal) activity of [phagocytes](http://en.wikipedia.org/wiki/Phagocytes) such as [macrophages](http://en.wikipedia.org/wiki/Macrophages). Maintaining a balance between Th1 and Th2 cells is critical to the maintenance of a complete immune response, yet the maintenance is complicated by cross-regulation and imbalance in the stimuli. Efforts to stimulate Th1 reduce Th2 and vice versa.

Ai/E¹º® has demonstrated in a published study, further supported by clinical references, the ability to help sustain balance in the Th1 and Th2 cell relationship by affecting both ends of the cytokine pathways simultaneously. This is a unique and important characteristic not shared with other dietary supplements that stimulate only one side of the Th1/Th2 relationship and can create further imbalance.

**GENE EXPRESSION**

* Supports significant up-regulation of genes associated with innate and adaptive immunity. 10

**PHYSIOLOGY:** Gene expression is the process by which information from a gene is used in the synthesis of a functional gene product. The process of gene expression is used by all known life to generate the macromolecular machinery for life. Several steps in the gene expression process may be modulated, including the transcription, RNA splicing, translation, and post-translational modification of a protein. Gene regulation gives the cell control over structure and function, and is the basis for cellular differentiation, morphogenesis and the versatility and adaptability of any organism.

In clinical study Ai/E¹º® demonstrated unique and valuable abilities to up-regulate numerous important genes associated with innate and adaptive immunity. Most notably, these affects were only noted upon stimulation, a highly favorable characteristic demonstrated only by a modulating substance.

**SPORTS/EXERCISE RECOVERY**

* **Supports recovery from “Exercise Induced Immune Suppression.”** 10

**PHYSIOLOGY:** Research is uncovering a link between moderate, regular exercise and a strong immune system. However, there is also evidence that too much intense exercise can reduce immunity and may even make you sick. Moderate exercise is linked to increasing Th1 cell stimulation, but more aggressive exercise is stress and stimulates Th2 activity, suppressing Th1 activity.

In reports from athletes, and consistent with the study demonstration Ai/E¹º® has played an apparent role in allowing them to train longer, recover faster and stay healthy allowing more consistent training schedules that are so important to athletic performance and improvement. More research is needed in this application, but the benefits are consistent with the benefits identified in study work and a healthy balance of Th1 and Th2 cell activity.

**GENERAL HEALTH**

* **Participants in a 90 day study report improved health and reduced symptomology.** 5

**PHYSIOLOGY:**  The benefits of utilizing dietary supplements are often not noted by the user, even if the benefits can be measured by some objective means. When a consumer experiences an objective or subjective sense of improvement in their general health they are more inclined to continue compliant supplementation.

Study participants in a study of Ai/E¹º® were asked to complete Health Questionnaires covering a wide range of subjective health questions and symptoms. Participants reported a 32% reduction in perceived symptoms and other health issues at the conclusion of the study period through their completed questionnaires. This correlates to a significant reduction (p<0.019).

Anecdotal evidence, reports and consumer reorders and compliance all support the strong realization of benefit by consumers since 1994.

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