BIOCHEMISTRY OF TRANSFER FACTOR

I. INTRODUCTION

Glutrasol products are comprised of three main ingredients:

1. transfer factor
2. glucans
3. lactic acid generating bacteria.

Minor ingredients are adjusted for specific applications.

This disclosure focuses on transfer factor.

We know Glutrasol works because TEST groups repeatedly show dramatic improvement, relative to CONTROL groups.

Here is information on how (biochemically) Glutrasol works.

II. INDUCER/SUPPRESSOR FRACTIONS OF TRANSFER FACTOR

Transfer factors are produced by T-lymphocytes and can transfer the ability to recognize a pathogen to cells that have not been in contact with the pathogen. They also heighten the immune system's ability to react (increased reactivity or inducer function) to pathogens. Transfer factor produces a trigger for T-cell recognition of antigen.

Transfer factor is a mixture of peptides, typically with a molecular weight < 10,000 Daltons. It's more appropriate to speak of "transfer factors" instead of "transfer factor." Fortunately, today's preparative methods produce consistent mixtures, which lead to repeatable responses.

Fractions within the mixture serve different (and sometimes opposite) purposes. Two particularly important fractions are (1) the inducer fraction, and (2) the suppressor fraction [1][2]. Opposing functions were confirmed using the direct Leucocyte Migration Inhibition (LMI) test.

These two fractions are consistent with field observations that transfer factor balances the immune system. For example,

1. The inducer fraction of transfer factor links the immune cells with an antigen-binding site, thereby increasing their reactivity to an antigenic stimulus. This is advantageous when a higher immune response is required. CortControl's enhanced vaccine response arises from an inducer fraction. The inducer effects of transfer factor are documented by several researchers [3][4][5].

2. The suppressor fraction blocks the response of the T-cells and signals a down-regulation of the immune response. This is useful in allergic or autoimmune conditions. Animal studies demonstrate improvement for cases where the immune system is over-active. This arises from suppressor fraction. Cortesini, R. et.al. [6] demonstrated that CD8+CD28-Ts represent a unique subset of regulatory cells within transfer factor that initiates a suppressive loop. Filaci [7] supported Cortesini's work, and related auto-immune disease the absence of CD8+ suppressor T lymphocytes. Filaci further found that "CD8+ Ts can be generated in vitro from CD8+CD28-T lymphocytes. A key role in their generation is played by monocytes that secrete interleukin-10 (IL-10) after granulocyte macrophage-colony-stimulating factor (GM-CSF) stimulation."

Aleli Salazar-Ramiro et.al [8], views cancer as an auto-immune disease, and proposes transfer factor for cancer therapy. This is supported by CortControl's veterinary work on horses, dogs, and cows [9], where symptoms of cancer were visibly reversed.

III. TH1/TH2 HELPER CELLS AND CYTOKINES

To categorize the applications of transfer factor, it is helpful to review the helper lymphocyte paradigm. Helper lymphocytes develop along two lines of cell populations: TH1 and TH2. Transfer factors from both lymphocytes lines are represented in transfer factor.

TH1 and TH2 cells perform different functions and produce different cytokines. Cytokines are proteins that function as messenger molecules.

Cell-mediated or TH1 helper responses are important in the body's ability to defend itself against viruses, fungi, parasites, cancer, and intracellular organisms. TH1 cells modulate cell-mediated immunity. TH1 cells produce the following cytokines:

IL-2,
IFN-gamma, and
TNF-alpha.

TH2 cells modulate humoral immunity (antibody production). TH2 cells produce the following cytokines:

IL-4,
IL-5,

IL-6,
IL-10, and
IL-13.

Cytokines are functionally similar to hormones, but are not associated with a specific gland. Cytokines appear to operate as a key and template. Stereochemistry is important. Attachment of a cytokine on an immune cell receptor will start a specific immune signal within the target cell. Signals translate into direct action, increase the production of antibodies against an invading virus, or initiate the production of other cytokines to propagate the signal.

IV. TH1/TH2 PREDOMINANT PHENOTYPES

One aspect of immune regulation involves homeostasis between T-helper 1 (Th1) and T-helper 2 (Th2) activity [10]. Basically, TH1/TH2 balance correlates with good health, and over-activation in either direction sets the stage for disease.

Th1 and Th2-helper cells direct different immune response pathways, and produce different cytokines. Either pathway can down-regulate the other.

Steven Bock, MD correlated disease conditions to an imbalance of TH1 and TH2. For example, if one has a TH2-dominated condition, the disease conditions that tend to prevail are:

1. Allergies
2. Chronic sinusitis
3. Atopic eczema
4. Asthma
5. Systemic autoimmune conditions such as lupus erythematosus and mercury-induced autoimmunity
6. Vaccination-induced state
7. Certain cases of autism
8. Hyperinsulinism
9. Pertussis vaccination
10. Malaria
11. Helminth infection
12. Hepatitis C
13. Chronic giardiasis
14. Hypercortisolism
15. Chronic candidiasis
16. Cancer
17. Viral infections
18. Ulcerative colitis

If one has a TH1-dominated condition, the conditions that tend to prevail are:

1. Diabetes type 1
2. Multiple sclerosis
3. Rheumatoid arthritis
4. Uveitis
7. Sjögren's syndrome
8. Psoriasis
9. Sarcoidosis
10. Chronic Lyme disease

5. Crohn's disease
6. Hashimoto's disease
11. H. pylori infections
12. E. histolytica

Glutrasol field observations show successes in both categories. For example, international travelers tend to avoid flus and colds by consuming Glutrasol before a trip. In addition, Ramaekers Nutrition has success with psoriasis, Crohn's disease, and H pylori infections (among a 20-year list others).

Transfer factor contains cytokines from both TH1 and TH2 cells. And transfer factor produces different cytokines for different situations. Alvarez-Thull L, Kirkpatrick CH [11] note that "Transfer factor treatment selectively affects cytokine production in response to antigenic stimulation." Fabre RA et. al [12] (in a pulmonary tuberculosis study) showed that "the treatment with murine or human TF restored the expression of TH-1 cytokines, TNFalpha and iNOS, provoking inhibition of bacterial proliferation and significant increase of DTH and survival."

V. ADJUSTING TO CHANGE

Malaria is cited as a TH2-dominated condition. Work on a robust malaria vaccine is underway by WHO [13] and PATH.

CortControl acknowledges that parasites can mutate [14] and present a changing appearance to the immune system. This is one reason for the cyclical flare-ups experienced by malaria victims. Antibody vaccines are specific, and not designed to keep pace with mutations. Maturation time for TH1 or TH2 cells is 10-14 days. In contrast, transfer factor works on the innate immune system, and responds within 24-48 hours. Transfer factor empowers the immune system to stay current with mutations.

CortControl predicts that the immediate benefits of combining Glutrasol with malaria vaccine will be -
(1) increasing vaccine efficiency, and
(2) minimizing relapse or re-infection.

VI. REBALANCING TH1 AND TH2 LEVELS

Transfer factor can change TH1/TH2 predominance conditions within 48 hours [15].

This observation begs the question, "How can Transfer Factor change a predominantly TH-2 Immune System to a predominant TH-1 System so rapidly?" (The hypothesis of new TH1 cells was dismissed early because it takes 10-14 days to mature new TH1 cells.)

The answer is "conversion by eomesodermin," which was studied [16] in 2003. In that study, already-differentiated TH2 cells were converted to TH1 cells. Eomesodermin is a T-box transcription factor related to T-bet and already characterized as a key regulator of mesodermal differentiation. Eomesodermin was specifically up-regulated in activated CD8+ cells [one of transfer factor's actions].

Conversion of TH2 to TH1 cells is applicable to viral vaccines and malaria because both conditions tend to be TH2 dominated. In the opposite direction, conversion of TH1 to TH2 is advantageous for Rheumatoid arthritis or Crohn's disease.

VII. VIRUSES, BACTERIA, AND PARASITES

Web MD notes that -

"Transfer factors are used for infectious conditions in people with weak immune systems. These infectious conditions include bacteria or viruses in the blood stream (septicemia), sinus infections, bronchitis, influenza, swine flu, the common cold, shingles, chickenpox, hepatitis B, fungal infections such as coccidioidomycosis, yeast infections (candidiasis), parasitic infections such as leishmaniasis and cryptosporidiosis, and leprosy. Transfer factors are also used against infections caused by viruses such as cytomegalovirus (CMV) and Epstein-Barr virus; by bacteria such as Mycobacterium tuberculosis, Mycobacterium fortuitum, and Mycobacterium avium; and by yeast-like fungus such as Cryptococcus and Pneumocystis carinii."

The mortality rate of parasite-infected livestock herds was dramatically lowered by the Glutrasol formulation [9]. Simultaneously, weight gain improved. CortControl does not believe that we "cured" the affected herds. Instead, we believe that the subject's immune system was better staged by Glutrasol to resist the parasite and opportunistic infections.

This has applications for countries where water-borne parasites negatively affect child development. Stunted childhood growth is a significant global health issue. Low weight gain in livestock, and stunted human growth are probably related.

VIII. STAGING THE IMMUNE SYSTEM

Vaccination response depends on recipient health. Vaccines work best for healthy people. Conversely, a person with a weakened immune system may not receive the calculated vaccine benefits. This relationship is particularly important in less developed countries, where unsanitary conditions impact overall health.

Dr Mandal [17] notes, "this [a lower-than-expected vaccine response] could be due to various reasons. Sometimes this is because the host's immune system simply doesn't respond adequately or at all. This could be in diseased persons with lowered immunity e.g. in diabetics, those on steroids or other immunity suppressing drugs or those with HIV infection. The reason for non-development of immunity to a disease could also be because the host's immune system does not have a B cell capable of generating antibodies against the antigen or microbe or the immune system may not be strong enough to fight off the infection".

Glutrasol-VE is formulated to narrow the health gap, and make vaccine benefits accessible to a larger population.

IX. ADJUVANT APPLICATION

Several articles suggest the use of transfer factor as an adjuvant.

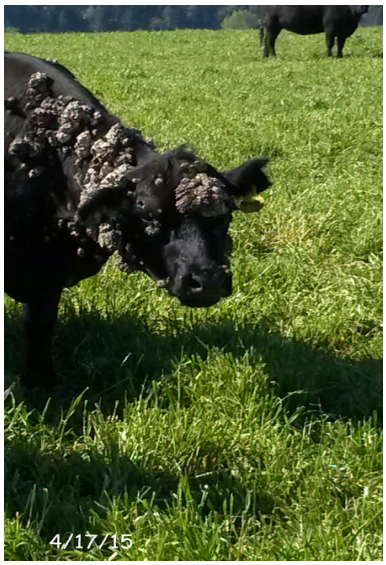
Schroder et al. [18] state, "This interspecies adjuvant effect was proportional to the dose of the 'transfer-factor' preparations administered, depended on the method of their preparation, and was expressed in administration of the preparations simultaneously with the immunization."

Wang et al. (19) state, "In conclusion, these results suggest that TF [transfer factor] possess better cellular immune-enhancing capability and would be exploited into an effective immune-adjuvant for inactivated vaccines."

X. DRAMATIC PICTURES

A picture is worth a thousand words. Following are 2 examples from a very large database.

A. Calf with Severe Warts

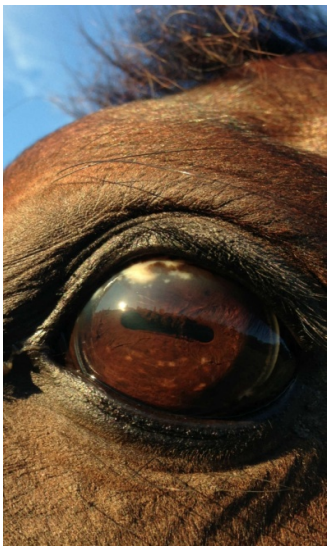


Before Glutrasol Consumption

After Glutrasol Consumption

B. Horse with Eye Cancer

Before Glutrasol Consumption



After Glutrasol Consumption

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