

Introduction to Transfer Factor

Transfer Factors & Immunity

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Our health is directly influenced by our immune system. The onset of almost all infectious and degenerative disease is preceded or accompanied by inadequate immune response. With intensifying concerns about the perils of vaccinations and antibiotic resistant organisms, a new weapon against disease is sorely needed. Transfer factors are such a weapon, and based upon almost 50 years of research, transfer factors appear to be highly effective with few, if any, side effects.

If our immune systems are functioning normally, transfer factors are produced after we are exposed to infectious agents such as viruses, bacteria, fungi, and parasites. Recent research, however, provides evidence that transfer factors, even from another animal such as a cow, can enable us to develop immunity to infectious agents before we are actually exposed to them. In addition, transfer factor administration can accelerate our immune response once we have been infected. This new approach to optimizing the immune response to infectious agents promises to revolutionize our approach to disease prevention and control!

Discovering the transfer factor

The complete structure of any transfer factor has not yet been determined. Researchers in the United States, Germany, Russia and China agree, however, that transfer factors are small molecule (3500 to 6000 molecular weight consisting of ribonucleic acid (RNA) bases attached to short amino acid chains called peptides. Early research found that immunity to a specific pathogen could be transmitted by giving subcutaneous or intramuscular injections of lymphocyte extracts from a person previously infected with the disease to a person who had never been exposed to the disease. This transfer of immunity was similar to a vaccination, except the recipient was never exposed to the pathogen and had none of the side effects associated with vaccination. There was also no time delay as is associated with a vaccination - immunity was obtained almost immediately.

As the research progressed, it was discovered that this transfer of immunity, or transfer factor, could be taken orally, and the immunity was still successfully transmitted. Transfer factor from human blood, however, is very expensive, and with the advent of the AIDS epidemic, doctors were very hesitant to administer human blood products to their patients. Fortunately, it was discovered that the early mother's milk, colostrum, contains T lymphocytes and transfer factors. The final research link that made affordable transfer factors possible was the discovery that transfer factor is disease specific, but not species specific. Specific transfer factors from one species can deliver immunity to another species as long as the donor species has immunity to the

correct pathogen. This discovery made it possible to use cows to manufacture large amounts of human transfer factors relatively inexpensively.

Transfer factors are small molecular messengers produced by immune T lymphocytes. The message they provide is a specific description of an invading pathogen. Using transfer factors, immune T lymphocytes can transfer the ability to recognize an invading pathogen to previously naive lymphocytes. In other words, one T lymphocyte tells another what the enemy looks like so that a coordinated attack can be mounted.

To keep your body healthy, your immune system must perform three important functions. First, it must recognize a pathogen as a threat to the body. Second, it must attack and kill off the pathogen. Finally, it must remember the pathogen so your body can quickly destroy the pathogen the next time it is attacked. The last step is also referred to as immune memory. Although the exact T lymphocyte source of transfer factor has not been proven, we do know these T lymphocytes have immune memory and use transfer factor to quickly heighten our immune response when we are invaded by a pathogen to which we have been previously exposed.

Overcoming disease

Transfer factors are not only useful for disease prevention but can also help with diseases already established due to inadequate immune response. Since transfer factor-producing T lymphocytes are important in immune recognition and memory, impairment of transfer factor production could neutralize the rest of the immune response in otherwise healthy individuals. Therefore, introducing transfer factors can sometimes enable a dysfunctional immune system to return to normal.

Another interesting feature of transfer factors is their ability to induce an immune response to not only the specific pathogen the transfer factor donor is known to be immune to, but also to related ones as well. At first this might seem to be evidence that transfer factors are not specific. It should be realized, however, that each pathogen can elicit the production of a large family of transfer factors. Potentially at least one transfer factor will be produced for every part of the pathogen that the immune system sees. If two microorganisms are related, they may display common structures that would be recognized by an immune system induced to respond by this family of transfer factors. These microorganisms are said to display "cross-reactivity." This feature makes transfer factor supplementation highly beneficial for diseases in humans that result from microbes that are similar to disease-producing pathogens in cows.

It is important to distinguish human transfer factor produced by cows from colostrum products that are readily available. Colostrum contains a variety of immune related substances, including transfer factors. However, the amount of transfer factors per gram of crude colostrum is very low. Because there is an established dose dependent response for transfer factor, only a purified concentrate with the correct dose can be counted upon to elicit an effective immune response. A truly effective transfer factor must be assayed for transfer factor activity (in potency units).

Available transfer factors

Highly purified transfer factors extracted from cow colostrum are currently available as "polyvalent" transfer factor. In the near future, specific transfer factors for herpes simplex viruses 1 & 2, Epstein-Barr virus, Varicella Zoster virus, and possible other viruses may be available. Polyvalent transfer factor contains all of the transfer factors produced in the cow as the result of the cow's cellular immune response to the foreign microbes to which it is exposed. These microbes can include bacteria, viruses, fungi and other parasites. Exposures can occur as the result of vaccinations normally given to cows to insure their own health or as a result of natural exposure to microbes present in the cow's environment.

Target population

Transfer factors may be beneficial for men, women, and children of all ages, but those most in need are persons with a compromised or under-active immune system. People with chronic fatigue, fibromyalgia, recurrent bacterial and viral infections, and chronic yeast infections are frequently in need of immune support. Transfer factor is also beneficial for prophylactic use if a person is concerned about contact with pathogens for which transfer factor is available. While we do not recommend transfer factors as a substitute for vaccination, it may benefit children for whom vaccination is contraindicated. However, transfer factors do not provide a permanent immunity and must be taken repeatedly.

Transfer factor research is on the cutting edge of immunology and promises to open new avenues for preventing and treating many diseases inflicting mankind. As transfer factor research progresses, strategies for using it to direct the immune response against such diverse diseases as cancer, AIDS, or malaria could become available.

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Transfer Factor Research

Reference #1:

Abstract: transfer factors: identification of conserved sequences in transfer factor molecules

Mol Med. 2000 Apr;6(4):332-41.

Kirkpatrick CH.

Department of Medicine, University of Colorado Health Sciences Center, Denver, USA.

BACKGROUND: transfer factors are small proteins that "transfer" the ability to express cell-mediated immunity from immune donors to non-immune recipients. We developed a process for purifying specific transfer factors to apparent homogeneity. This allowed us to separate individual transfer factors from mixtures containing several transfer factors and to demonstrate the antigen-specificity of transfer factors.

transfer factors have been shown to be an effective means for correction of deficient cellular immunity in patients with opportunistic infections, such as candidiasis or recurrent Herpes simplex and to provide prophylactic immunity against varicella-zoster in patients with acute leukemia.

MATERIALS AND METHODS: transfer factors of bovine and murine origin were purified by affinity chromatography and high performance liquid chromatography. Cyanogen bromide digests were sequenced. The properties of an apparently conserved sequence on expression of delayed-type hypersensitivity by transfer factor recipients were assessed.

RESULTS: A novel amino acid sequence, LLYAQL/VEDN, was identified in each of seven transfer factor preparations. These peptides would not transfer expression of delayed-type hypersensitivity to recipients, which indicates that they are not sufficient for expression of the specificity or immunological properties of native transfer factors. However, administration of the peptides to recipients of native transfer factors blocked expression of delayed-type hypersensitivity by the recipients. The peptides were not immunosuppressive.

CONCLUSIONS: These findings suggest that the peptides may represent the portion of transfer factors that binds to the "target cells" for transfer factors. Identification of these cells will be helpful in defining the mechanisms of action of transfer factors.

PMID: 10949913 [PubMed - indexed for MEDLINE]

Transfer Factor Research (continued)

Reference #2:

Abstract: Use of anti HHV-6 transfer factor for the treatment of 2 patients with chronic fatigue syndrome (CFS). Two case reports.

Biotherapy 1996; 9(1-3): 81-6.

Ablashi DV, Levine PH, De Vinci C, Whitman JE Jr, Pizza G, Viza D.

Abstract

Specific Human Herpes virus-6 (HHV-6) transfer factor (TF) preparation, administered to two chronic fatigue syndrome patients, inhibited the HHV-6 infection. Prior to treatment, both patients exhibited an activated HHV-6 infection. TF treatment significantly improved the clinical manifestations of CFS in one patient who resumed normal duties within weeks, whereas no clinical improvement was observed in the second patient. It is concluded that HHV-6 specific TF may be of significant value in controlling HHV-6 infection and related illnesses.

Source: www.ahmf.org

Reference #3:

Abstract: Lessons from a pilot study of transfer factor in Chronic Fatigue Syndrome De Vinci C, Levine PH, Pizza G, Fudenberg HH, Orens P, Pearson G, Viza D.

Biotherapy 1996; 9(1-3): 87-90

Abstract

Transfer factor (TF) was used in a placebo controlled pilot study of 20 patients with chronic fatigue syndrome (CFS). Efficacy of the treatment was evaluated by clinical monitoring and testing for antibodies to Epstein-Barr virus (EBV) and human herpes virus-6 (HHV-6). Of the 20 patients in the placebo-controlled trial, improvement was observed in 12 patients, generally within 3-6 weeks of beginning treatment. Herpes virus serology seldom correlated with clinical response. This study provided experience with oral TF, useful in designing a larger placebo-controlled clinical trial.

Source: www.ahmf.org

Reference #4:

Abstract: The influence of age on transfer factor treatment of cellular immunodeficiency, chronic fatigue syndrome and/or chronic viral infections

Hana I, Vrabel J, Pekarek J, Cech K.

Biotherapy 1996; 9(1-3): 91-5

Abstract

A group of 222 patients suffering from cellular immunodeficiency (CID), frequently combined with chronic fatigue syndrome (CFS) and/or chronic viral infections by Epstein-Barr virus (EBV) and/or cytomegalovirus (CMV), were immunologically investigated and treated with transfer factor (TF). The age range was 17-77 years. In order to elucidate the influence of aging on the course of the disease and on treatment, 3 subgroups were formed: 17-43 years, 44-53 years, and 54-77 years. Six injections of Immodin (commercial preparation of TF by SEVAC, Prague) were given in the course of 8 weeks. When active viral infection was present, IgG injections and vitamins were added.

Immunological investigation was performed before the start of therapy, and subsequently according to need, but not later than after 3 months. The percentages of failures to improve clinical status of patients were in the individual subgroups, respectively: 10.6%, 11.5% and 28.9%. The influence of increasing age on the percentage of failures to normalize low numbers of T cells was very evident: 10.6%, 21.2% and 59.6%. In individuals unaffected by therapy, persistent absolute lymphocyte numbers below 1,200 cells were found in 23.1%, 54.5% and 89.3% in the oldest group. Statistical analysis by Pearson's Chi-square test, and the test for linear trend proved that the differences among the individual age groups were significant. Neither sex, nor other factors seemed to influence the results. The results of this pilot study show that age substantially influences the failure rate of CID treatment using TF. In older people, it is easier to improve the clinical condition than CID: this may be related to the diminished number of lymphocytes, however, a placebo effect cannot be totally excluded.

Source: www.ahmf.org

Reference #5:

Abstract: The use of transfer factors in chronic fatigue syndrome: prospects & problems

Levine PH.

Biotherapy 1996; 9(1-3): 77-79

Abstract

Chronic fatigue syndrome (CFS) is a heterogeneous disorder characterized by severe prolonged unexplained fatigue and a variety of associated symptoms such as arthralgias, myalgias,

cognitive dysfunction, and severe sleep disturbances. Many patients initially present with an acute onset of apparent infectious origin with either an upper respiratory or gastrointestinal illness, fever, chills, tender lymphadenopathy, and malaise suggestive of a flu-like illness. In some cases, specific viral infections can be identified at the outset, particularly herpes viruses such as Epstein-Barr virus (EBV), human herpes virus-6 (HHV-6), and cytomegalovirus (CMV). transfer factors (TF) with specific activity against these herpes viruses has been documented.

With some studies suggesting that persistent viral activity may play a role in perpetuation of CFS symptoms, there appears to be a rationale for the use of TF in patients with CFS and recent reports have suggested that transfer factor may play a beneficial role in this disorder. This report focuses on the heterogeneity of CFS, the necessity for randomized coded studies, the importance of patient selection and sub-classification in clinical trials, and the need to utilize specific end-points for determining efficacy of treatment.

Source: www.ahmf.org

Reference #6:

Abstract: Activities and Characteristics of transfer factors

ImmuneSupport.com

12-12-2000

Biotherapy 1996;9(1-3):13-6

Kirkpatrick, C.H.

This report summarizes three components of our transfer factor research program. Several clinical studies have used oral administration of transfer factor containing materials. Sceptics have rejected these findings by assuming that the acidic and enzymatic environment of the gastrointestinal tract would destroy the factors.

To further examine this issue, we have conducted dose-response studies of the delayed-type hypersensitivity reaction in mice that were given transfer factor either by gavage or subcutaneously. There were no differences in the responses that were related to the route of administration. We conclude that oral route of administration is efficacious and should be used when possible. We have also studied the effects of transfer factors on immune responses by recipients.

The details of this research are presented in the paper by Dr. Alvarez-Thull. Briefly, the study showed that recipients of a specific transfer factor responded to the antigen for which the factor was specific by secreting gamma-IFN, but no other cytokines. The structures of transfer factor molecules are unknown. We have developed a process for isolating transfer factors in pure form and we have obtained preliminary data concerning amino acid sequences. Our goal is to obtain the complete primary structure of several transfer factor molecules.

PMID: 8993752, UI: 97146896

Reference #7:

Abstract: Purification of transfer factors

Mol Immunol 1992 Feb;29(2):167-82 PMID: 1542296, UI: 92178226

Conrad D. Stephenson Laboratory for Research in Immunology, National Jewish Center for Immunology and Respiratory Medicine, Denver, Colorado.

Transfer factor activities have been studied in both clinical and basic science settings for several decades. Until now, highly purified transfer factors that are suitable for molecular analysis have not been available. This has impeded progress towards understanding the molecular and cellular basis of the activities of these important inducers of cell-mediated immune responses. Murine transfer factors with specificities for chicken egg albumin or horse spleen ferritin were purified to virtual homogeneity using a combination of affinity chromatography and reversed-phase and polytypic high performance liquid chromatography (hplc). Transfer factors prepared by this methodology were recovered in high yield and in biologically-active, antigen-specific forms. The purified materials were further analyzed using sodium dodecyl sulfate polyacrylamide gel electrophoresis, chromatographic methods and an in vivo assay for immunological activity. For the first time definitions for unit transfer factor activity and specific activity are introduced. The results of these experiments indicate that transfer factors are a family of highly polar, hydrophilic molecules of low molecular weight (approximately 5,000) which are produced in small quantities by lymphoid cells and which have potent biological activity. The availability of purified transfer factors should facilitate definitive studies into the nature and mechanisms of production and action of these molecules.

Reference #8:

J Allergy Clin Immunol 1988 May;81(5 Pt 1):803-13

Kirkpatrick CH

Conrad D. Stephenson Laboratory, National Jewish Center for Immunology and Respiratory Medicine, Denver, CO 80206.

It has been more than 30 years since Dr. H. S. Lawrence first reported that it was possible to transfer delayed-type hypersensitivity from sensitized donors to unsensitized recipients with lysates of blood leukocytes. During recent years, research from several laboratories has demonstrated that this effect is immunologically specific. Although the molecules that possess this activity have not been completely characterized, there is a significant body of evidence that they are small polypeptides and that they can interact with antigen molecules in an immunologically specific manner. Studies with immune responses that are under genetic control have demonstrated that the ability of an animal to produce transfer factor is genetically regulated but that transfer of delayed hypersensitivity with transfer factor is not genetically restricted. In fact, when mice of low-responder phenotypes are administered transfer factor from high-responder donors, they express delayed hypersensitivity responses that are comparable to the high responders. Clinical studies have demonstrated that transfer factor is an efficacious method for immunotherapy of certain viral and fungal infections.

PMID: 3286720, UI: 88228780

Reference #9:

Abstract: Structural Nature and Function of transfer factors for Immune Support

Kirkpatrick, C.H.

Conrad D. Stephenson Laboratory for Research in Immunology, National Jewish Center for Immunology and Respiratory Medicine, Denver, Colorado 80206.

Transfer factors are molecules that "educate" recipients to express cell-mediated immunity. This effect is antigen-specific. The most consistent effects of transfer factors on the immune system are expression of delayed-type hypersensitivity and production of lymphokines such as macrophage migration inhibitory factor (MIF), which is probably identical to gamma-interferon in response to exposure to antigen. transfer factors bind to antigens in an immunologically specific manner. This discovery has enabled us to isolate individual transfer factors from mixtures that contain several transfer factors. This reactivity probably explains the specificity of individual transfer factors, and it has provided a method for purification of individual transfer factors to apparent homogeneity. The purified materials are immunologically active and antigen-specific. They have molecular weights of approximately 5,000 Da and appear to be composed entirely of amino acids. transfer factors appear to offer a novel means of molecular immunotherapy for certain patients with defective cell-mediated immunity.

PMID: 8363241, UI: 93370874

Reference #10:

Abstract: Transfer of cellular immunity to the causative agent of coccidioidosis using the transfer factor in mice

Likholetov SM, Prokof'eva EI, Rogozhkina NM

Experiments conducted on non-linear mice demonstrated a possibility of transfer by the intact recipient of delayed hypersensitivity by means of Lawrence's transfer-factor from mice immunized with *Coccidioides immitis*. The transfer factor administered 48 hours before the intranasal infection protected mice from the lethal dose of *coccidioides*. This indicated that in coccidioidosis it was possible to transfer delayed hypersensitivity and cellular immunity with the transfer factor.

Zh Mikrobiol Epidemiol Immunobiol 1978 Sep;(9):60-4

PMID: 747028, UI: 79141688

List of References to Research Materials for transfer factor

1. Lawrence HS. The cellular transfer of cutaneous hypersensitivity to tuberculin in man. Proc Soc Exp Biol Med 1949;71:516.
2. Dwyer JM. The use of antigen-specific transfer factor in the management of infections with herpes viruses. In: Kirkpatrick CH, Burger DR and Lawrence HS eds. Immunobiology of transfer factor. New York Academic Press 1983:233-243.
3. Viza D, Vich JM, Phillips J et al. Orally administered specific transfer factor for the treatment of herpesvirus infections. Lymphok Res 1985;4:27-30.
4. Jones JF, Jeter WS, Fulginiti VA et al. Treatment of childhood combined Epstein-Barr virus/cytomegalovirus infection with oral bovine transfer factor. Lancet 1981;2:122-124.
5. Ablashi DV, Levine PH, DeVinci C et al. Use of anti HHV-6 transfer factor for the treatment of two patients with chronic fatigue syndrome (CFS). Two case reports. Biotherapy 1996;9:81-86.
6. Steele RW, Myers MG and Monroe VM. transfer factor for the prevention of varicella-zoster infection in childhood. N Engl J Med 1980;303:355-359.
7. Lang I, Nekam H, Gergely P et al. Effect of in vivo and in vitro treatment with dialyzable leukocyte extracts on human natural killer cell activity. Clin Immunol and Immunopathol 1982;25:139-144.
8. Boucheix C, Phillips J, Pizza G et al. Activity of animal transfer factor in man. Lancet 1977;1:198-199.
9. Fudenberg H and Pizza G. transfer factor 1993: New frontiers. Progress in Drug Res 1994;42:309-400.
10. Arala-Chaves M, Ramos MTF and Rosado RMF. Evidence for prompt and intense constitution of cell-mediated immunity by means of transfer factor in a case of complex immune deficiency. Cell. Immunol. 1974;12:160.
11. Ballow M and Good RA. Report of a patient with T-cell deficiency and normal B-cell function: a new immunodeficiency disease with response to transfer factor. Cell. Immunol. 1975;19:219.
12. Jones JF, Pizza G, DeVinci C. Infectious mononucleosis: immunotherapy with EBV-specific transfer factor. J Exp Pathol 1987;3:399-406.
13. Khan A, Hansen B, Hill NO et al. transfer factor in the treatment of herpes simplex types 1 and 2. Dermatologica 1981;163:177-185.
14. Winkelman RK, DeRemee RA, Ritts RE Jr. Treatment of varicella-zoster pneumonia with transfer factor. Cutis 1984;34:278-281.

15. Rozzo SJ and Kirkpatrick CH. Purification of transfer factors. *Mol Immunol* 1992;29:167-182.
16. Pizza G, Viza D, Roda A et al. transfer factor for the treatment of chronic active hepatitis. *N Engl J Med* 1979;300:1332.
17. Nkrumah F, Pizza G, Viza D et al. Regression of progressive lymphadenopathy in a young child with acute cytomegalovirus (CMV) infection following the administration with specific anti-CMV activity. *Lymphok Res* 1985;4:237-241.
18. Neequaye J, Viza D, Levine PH et al. Specific transfer factor with activity against Epstein-Barr virus reduces late relapse in endemic Burkitt's lymphoma. *Anticancer Res* 1990;10:1183-1187.
19. Viza D, Vich JM, Phillips J et al. Specific transfer factor protects mice against lethal challenge with herpes simplex virus. *Cell Immun* 1986;100:555-562.
20. Wilson GB, Poindexter C, Fort JD et al. De novo initiation of specific cell-mediated immune responsiveness in chickens by transfer factor (specific immunity inducer) obtained from bovine colostrum and milk. *ACTA Virol* 1988;32:6-18.
21. Kirkpatrick CH, Hamad AR, and Morton LC. Murine transfer factors: dose-response relationships and routes of administration. *Cell Immunol* 1995;164:203-206.
22. Viza D, Lefesvre A, Patrasco M et al. A preliminary report on three AIDS patients treated with anti-HIV specific transfer factor. *J Exp Path* 1987;3:653-659.