Abstracts on studies conducted with transfer factors from bovine colostrum


De novo initiation of specific cell-mediated immune responsiveness in chickens by transfer factor (specific immunity inducer) obtained from bovine colostrum and milk.

Wilson GB, Poindexter C, Fort JD, Ludden KD.
Amtron, Inc., Charleston, South Carolina.

Transfer factors (TF) were prepared from colostrum and milk of bovines previously immunized with antigens obtained from Coccidioides immitis, infectious bovine rhinotracheitis virus, or from the viral agents responsible for avian Newcastle disease, laryngotracheitis disease or infectious bursal disease. The ability of bovine TF to transfer specific cell-mediated immune responsiveness to a markedly xenogenic species was studied using specific pathogen free (SPF) and standard commercial (SC) chickens as model recipients. Cell-mediated immune responsiveness was documented using one or more of the following for each antigen (organism) studied: (a) an in vitro chicken leukocyte (heterophil) migration inhibition assay; (b) delayed-wattle reactivity; or (c) protection from clinical disease. Chicken TFs obtained from spleens of immune donors were evaluated in parallel to bovine TF's in selected comparative studies. Bovine TF also referred to as specific immunity inducer (SII), and chicken TF were found to initiate antigen-specific cell-mediated immunity de novo in previously non-immune SPF chickens as well as in SC chickens despite the presence of maternally acquired humoral antibody which may serve as a "barrier" to immunization of SC chickens when commercially available vaccines are administered by parenteral routes. Bovine TF's specific for laryngotracheitis virus or infectious bursal disease virus afforded protection equal to that found for commercially available vaccines. Bovine TF's action was rapid (less than a day) and of relatively long duration at least 35 days.

Am J Vet Res 1985 Apr;46(4):875-8

Delayed-type hypersensitivity responses induced by bovine colostral components.

Radosevich JK, Scott GH, Olson GB.

Transfer factor-type substances obtained from leukocytic cells and fluid portions of bovine colostrum caused effective passive transfer of delayed-type hypersensitivity responses across species barriers. Passive transfer of Brucella abortus sensitivity was obtained with equal regularity when using components derived from peripheral blood and colostrum of dams sensitized at 3 and 9 months of age. Colostral feedings to calves caused the passive transfer of delayed-type hypersensitivity as early as 2 days after parturition. The findings indicated that colostral components were important in the process of cell-mediated immunity.

Biotherapy 1996;9(1-3):87-90
Lessons from a pilot study of transfer factor in chronic fatigue syndrome.


Immunodiagnosis and Immunotherapy Unit, 1st Division of Urology Sant'Orsola-Malpighi Hospital, Bologna, Italy.

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.

Publication Types:
- Clinical trial
- Randomized controlled trial

Biotherapy 1996;9(1-3):133-8

Use of transfer factor for the treatment of recurrent non-bacterial female cystitis (NBRC): a preliminary report.


Immunodiagnosis and Immunotherapy Unit, 1st-Division of Urology, Bologna, Italy.

Results of conventional treatment of female non-bacterial recurrent cystitis (NBRC) are discouraging. Most patients show an unexpected high incidence of vaginal candidiasis, while their cell mediated immunity to Herpes simplex viruses (HSV) and Candida antigens seems impaired, and it is known that the persistence of mucocutaneous chronic candidiasis is mainly due to a selective defect of CMI to Candida antigens. Twenty nine women suffering of NBRC, and in whom previous treatment with antibiotics and non-steroid anti-inflammatory drugs was unsuccessful, underwent oral transfer factor (TF) therapy. TF specific to Candida and/or to HSV was administered bi-weekly for the first 2 weeks, and then once a week for the following 6 months. No side effects were observed during treatment. The total observation period of our cohort was 24379 days with 353 episodes of cystitis recorded and a cumulative relapse index (RI) of 43. The observation period during and after treatment was 13920 days with 108 relapses and a cumulative RI of 23 (P < 0.0001). It, thus, seems that specific TF may be capable of controlling NBRC and alleviate the symptoms.

Publication Types:
- Clinical trial

Transfer factors: identification of conserved sequences in transfer factor molecules.

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, LLYAQDL/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.

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

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


Advanced Biotechnologies Inc., Columbia, MD 21046, USA.

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.

Biotherapy 1996;9(1-3):61-6

Efficacy of transfer factor in treating patients with recurrent ocular herpes infections.

Meduri R, Campos E, Scorolli L, De Vinci C, Pizza G, Viza D.

Eye Physiopathology Clinical Service, University of Bologna, Italy.
Recurrent ocular herpes is an insoluble problem for the clinician. As cellular immunity plays an important role in controlling herpes relapses, and other studies have shown the efficacy of HSV-specific transfer factor (TF) for the treatment of herpes patients, an open clinical trial was undertaken in 134 patients (71 keratitis, 29 kerato-uveitis, 34 uveitis) suffering from recurrent ocular herpetic infections. The mean duration of the treatment was 358 days, and the entire follow-up period 189,121 before, and 64,062 days after TF treatment. The cell-mediated immune response to the viral antigens, evaluated by the lymphocyte stimulation test (LST) and the leucocyte migration test (LMT) (P < 0.001), was significantly increased by the TF treatment. The total number of relapses was decreased significantly during/after TF treatment, dropping from 832 before, to 89 after treatment, whereas the cumulative relapse index (RI) dropped, during the same period, from 13.2 to 4.17 (P < 0.0001). No side effects were observed. It is concluded that patients with relapsing ocular herpes can benefit from treatment with HSV-specific TF.

Publication Types:
Clinical trial

Biotherapy 1996;9(1-3):41-7

Preliminary observations using HIV-specific transfer factor in AIDS.

Pizza G, Chiodo F, Colangeli V, Gritti F, Raise E, Fudenberg HH, De Vinci C, Viza D.

Immunodiagnosis and Immunotherapy Unit, Ospedale S. Orsola-Malpighi, Bologna, Italy.

Twenty five HIV-1-infected patients, at various stages (CDC II, III and IV) were treated orally with HIV-1-specific transfer factor (TF) for periods varying from 60 to 1870 days. All patients were receiving antiviral treatments in association with TF. The number of lymphocytes, CD4 and CD8 subsets were followed and showed no statistically significant variations. In 11/25 patients the number of lymphocytes increased, whilst in 11/25 decreased; similarly an increase of the CD4 lymphocytes was observed in 11/25 patients and of the CD8 lymphocytes in 15/25. Clinical improvement or a stabilized clinical condition was noticed in 20/25 patients, whilst a deterioration was seen in 5/25. In 12/14 anergic patients, daily TF administration restored delayed type hypersensitivity to recall antigens within 60 days. These preliminary observations suggest that oral HIV-specific TF administration, in association with antiviral drugs, is well tolerated and seems beneficial to AIDS patients, thus warranting further investigation.

Publication Types:
Clinical trial
Clinical trial, phase i


Specific transfer factor with activity against Epstein-Barr virus reduces late relapse in endemic Burkitt's lymphoma.

Neequaye J, Viza D, Pizza G, Levine PH, De Vinci C, Ablashi DV, Biggar RJ, Nkrumah FK.
Twenty-seven children with abdominal Burkitt's lymphoma (stage III), who had achieved complete remission, were entered into a prospective controlled trial of adjunct treatment with Epstein-Barr virus (EBV)-specific transfer factor (TF). Two patients treated with TF and 2 controls relapsed early (less than or equal to 12 weeks). Two out of 12 TF-treated patients and 5 out of 11 controls subsequently suffered relapses. Time to first late relapse was longer among TF-treated patients (p = 0.08), and no late relapse occurred while a patient was receiving TF treatment. Thus it seems that specific TF might be useful in the management of endemic Burkitt's lymphoma and also in the treatment of other virus-associated cancers and diseases.

Publication Types:

Clinical trial
Controlled clinical trial

Cell Immunol 1984 Nov;89(1):259-64

Transfer factor and repeated otitis media.

Kaminkova J, Lange CF.

The effect of transfer factor (TF) was investigated in 12 children with repeated otitis media. These patients were immunologically compared to a control group of 23 age-matched healthy children. Levels of immunoglobulins, total and "active" T-cells, and phagocytic activity of granulocytes and monocytes were evaluated in the 12 children prior to, during, and after TF therapy. Percentages of "active" T cells and absolute numbers of "active" T and total T cells, which were initially low in the patient group, increased significantly after TF therapy to statistically match those of the healthy control group. The percentage of phagocytic monocytes in patients after therapy did not differ from healthy children; however, the percentage of phagocytic granulocytes remained depressed significantly. The levels of IgG, IgA, and IgM were unaffected by the therapy although the IgA and IgM were higher in the patient population throughout the study. After therapy, one-half of the patient population remained asymptomatic for a 1-year period and the others had markedly reduced attack rates.

Lancet 1981 Jul 18;2(8238):122-4

Treatment of childhood combined Epstein-Barr virus/cytomegalovirus infection with oral bovine transfer factor.

Jones JF, Minnich LL, Jeter WS, Pritchett RF, Fulginiti VA, Wedgwood RJ.

An illness lasting for two years, with recurrent fever, rash, abdominal pain, and arthralgia, developed in a four year old boy. He was found to have a combined Epstein-Barr virus and cytomegalovirus (CMV) infection. His symptoms, CMV in his urine, and an absent in vitro lymphocyte response to CMV antigen persisted for two years. After treatment with orally administered bovine transfer factor clinical symptoms and viruria disappeared and specific immunity to CMV developed. Evaluation of this treatment in chronic virus infections is warranted.
**Bovine 'transfer factor': an oligoribonucleopeptide which initiates antigen-specific lymphocytes responsiveness.**

Wilson GB, Paddock GV, Fudenberg HH.

Bovine transfer factor (TF)--active in initiating specific responsiveness in human thymus-derived (T) lymphocytes to purified protein derivative from Mycobacterium tuberculosis (PPD) in vitro--was partially purified from the dialyzable portion of medium from immune lymph node cells (DLNE). Its physiochemical properties and structure were determined by methods previously employed to characterize human PPD-specific TF isolated from dialyzable leukocyte extracts (DLE). Bovine TF had a molecular weight (MW) of 1100-3000, was destroyed by heating at 56 or 80 degrees C for 30 min, was soluble in water but not in phenol or ether, and could be precipitated with ethanol. Bovine TF activity eluted as a single peak after high-pressure reverse-phase liquid chromatography (HPLC); the active moiety contained at least one free co-planar cis-diol group, as shown by boronate affinity chromatography. Additional structural features were deduced by evaluating TF activity after incubation with various endonucleases, exonucleases, and peptidases, a phosphatase, and a protease. The combined results indicate that bovine TF specific for PPD is an oligoribonucleopeptide. A simplest case molecular model was constructed on the basis of the data obtained. A comparative evaluation of the physicochemical properties and structural features of bovine TF and human TF specific for PPD indicated striking similarities and some differences.

**Biological response modifiers. Interferons, interleukins, and transfer factor.**

Kirkpatrick CH.

Department of Medicine, National Jewish Center for Immunology and Respiratory Medicine, Denver, Colorado.

Natural consequences of knowledge of the mechanisms that regulate immune responses are the attempts to modify the immune system in order to increase resistance to infectious diseases and to enhance activity against tumor cells. This review describes the roles of interferons and interleukins in immune responses and reviews the experience with transfer factor in treatment of certain diseases.

**Structural nature and functions of transfer factors.**
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.