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Activities and characteristics of transfer factors.

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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 difference 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

Thymus 1982;4(6):335-50

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.

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Profiles of cytokine production in recipients of transfer factors.

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Transfer factors (TF) are proteins that transfer the ability to express cell-mediated immunity from immune donors to non-immune recipients. The mechanisms of these effects have not been defined. The experiments described in this report were undertaken to test the hypothesis that a mechanism through which the beneficial effects of TF are expressed in clinical situation is through "education" of the immune system to produce certain cytokines in response to antigenic stimulation. BALB/c mice were sensitized to Herpes simplexvirus (HSV) either by sublethal systemic or cutaneous infections by administration of a HSV-specific TF. One week later their spleen cells were collected and single cell suspensions were stimulated in vitro with irradiated HSV or concanavalin. A Culture supernatants were collected and assayed for content of IL-2, IL-4, IL-10 and IFN-g. Spleen cells from infected mice responded to concanavalin A and to HSV by secreting large amounts of IL-2 and IFN-g, modest amounts of IL-10, and no IL-4. Transfer factor recipients produced similar cytokine profiles in response to concavalin A. These mice, however, responded to HSV by secreting IFN-g, but no IL-2. Thus, TF treatment selectively affects cytokine production in response to antigenic stimulation.

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Ann N Y Acad Sci 1993 Jun 23;685:362-8

Structural nature and functions of transfer factors.

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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.

Publication Types:

•Review •Review, tutorial

PMID: 8363241, UI: 93370874

In Vivo 1994 Jul-Aug;8(4):555-7

Successful treatment of severe complicated measles with non-specific transfer factor.

Ferrer-Argote VE, Romero-Cabello R, Hernandez-Mendoza L, Arista-Viveros A, Rojo-Medina J, Balseca-Olivera F, Fierro M, Gonzalez-Constandse R

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Severe complicated measles has a high mortality rate and no specific treatment. Ten patients with complicated measles - 9 infants with respiratory failure and a 15 year old boy with encephalitis - received immunotherapy with Non-specific Transfer Factor (NTF). The patients had variable degrees of undernourishment and were severely ill when immunotherapy was started. 8/9 cases with respiratory failure were cured. One died of bronchoaspiration while recovering from the measles. The case with encephalitis showed no neurological sequelae two weeks after receiving the last dose of NTF. Treatment of complicated measles with NTF in these patients seemed very effective and deserves further trial.

PMID: 7893983, UI: 95201208

Scand J Rheumatol 1976;5(3):151-7

The effect of non-specifically acting transfer factor component on cellular immunity in juvenile rheumatoid arthritis.

Grohn P, Anttila R, Krohn K

A chromatographically purified component of human dialysable transfer factor with a non-specific stimulatory effect on the expression of immune response was used in a therapeutic trial in 8 cases of juvenile rheumatoid arthritis. Enhancement of the delayed type of immune response, measured by skin testing, was seen in all cases, but in vitro reactions to test antigens were unaltered. Clinical improvement was seen in all patients with acute history and in 2 of the 5 chronic cases, but it is not certain whether this was caused by the improved immune reactivity, or whether this reflected the known variable natural history of the disease.

PMID: 981991, UI: 77038262

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Transfer factor--current status and future prospects.

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We have detected new clues to the composition and function of "Transfer Factor" using the direct Leucocyte Migration Inhibition (LMI) test as an in vitro assay of Dialysates of Leucocyte Extracts (DLE). This approach has revealed two opposing antigen-specific activities to be present in the same > 3500 < 12,000 DA dialysis fraction - one activity is possessed of Inducer/ Helper function (Inducer Factor). The opposing activity is possessed of Suppressor function (Suppressor Factor). When non-immune leucocyte populations are cultured with Inducer Factor they acquire the capacity to respond to specific antigen and inhibition of migration occurs. This conversion to reactivity is antigen-specific and dose-

dependent. When immune leucocyte populations are cultured with Suppressor Factor their response to specific antigen is blocked and Inhibition of Migration is prevented.

Publication Types:

•Review •Review, tutorial

PMID: 8993750, UI: 97146894

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Transfer factor in the age of molecular biology: a review.

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Current data suggests that the transferring of immunologically specific information by transfer factor molecules requires interaction with a cell that has been genetically programmed to be antigen reactive but at the time of interaction is unprimed. Contact with transfer factor molecules would allow a naive recipient, on a first encounter with antigen, to make a secondary rather than a primary immunological response. Transfer factor molecules for each and every antigenic determinant are thus necessary. Transfer factors made from animals or humans are capable of transferring antigen specificity across a species barrier. Even primitive species have cells from which one can make transfer factors. The molecules are, therefore, well conserved and it is reasonable to suggest that they are important for normal immunological functioning. Proposed mechanisms of action must explain the fact that transfer factors obtained from the cells of high responder animals are capable of transferring delayed hypersensitivity to low responder animals while the reverse is not true. Transfer factor molecules are likely to interact with the variable regions of the alpha and/or beta chain of T cell receptors to change their avidity and affinity for antigen in a way that otherwise would only occur after an encounter with antigen.

Publication Types:

•Review •Review, tutorial

PMID: 8993751, UI: 97146895

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.

PMID: 6113484, UI: 81219911