Abstract: The Immune Modulating Function of Transfer Factors.

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Objective: The scientific literature on transfer factors, (TF) suggests that TF has a primary function of providing to the recipient antigen specific information that is expressed in T cell lymphocyte memory. The studies also suggest that TF has a modulating function that is observed to both enhance and reduce specific and nonspecific T cell responses *in vivo* and *in vitro*.

The purpose of this investigation was to determine if colostrum derived TF has the ability to influence T cell memory of human blood lymphocytes to two different type of memory T cells, namely the CD4+ or T helper cell and the CD8+ or Cytotoxic T Cell.

Methods: T cell function was evaluated in the Immunknow ™ and TCM™ assays (Cylex Laboratories) The Immunknow assay is specific for the ability of the CD4+ lymphocyte to respond to the non specific T cell stimulant, phytohemagglutinin (PHA). This assay is used commercially to evaluate clinical immune competency. The TCM assay is a research tool for the measurement of CD8+ responses to specific pathogens. The assay measures immune cell metabolic activity via the intracellular ATP concentrations. ATP synthesis is a function of immune cell activity and a precursor to cell division via mitosis.

The assays were modified by the addition of TF concentrates to the test wells to determine how the concentrate influenced T cell function as reflected by ATP synthesis.

Volunteer human blood donors were a combination of persons consuming commercial products containing TF and those that reported to have never consumed commercial TF products.

Results: CD4+ Assays on the cells from apparently healthy adults where consistent in the responses to PHA. PHA modulated increase in ATP synthesis in the cells. Non stimulated CD4+ cells typically have very low ATP levels of less than 25ng/ml. PHA stimulated cells produced on the average of 325 ng/ml.

The addition of TF concentrate to the quadruplicate test wells in a range of 1, 2.5 and 3.5 mg/ml reduced the ATP production response to PHA by 6.8 and 24.7% over the 1mg dose in persons who have not consumed TF supplements. In persons consuming TF supplements the modulation of PHA responses was significantly greater at all *in vitro* dosages.

Over the test data from 15 individuals the baseline ATP response from PHA stimulation appear to predict the dose response affect of TF concentrates. In persons with moderate to ATP responses the addition of TF concentrate to the test system increased the ATP response by 10 to 29%. In persons with higher ATP stimulated responses the TF concentrate lowered the response by 25% or greater at the higher dose rates. In persons with moderate to low PHA only response who in later tests had more robust responses, the addition of the TF had inverse affects as noted between individuals with high and low PHA only responses.

The T Cell Memory (TCM) uses the CD8+ cell and evaluates its ability to recognize and respond to specific antigens, namely Epstein Bar Virus (EBV). Persons with very low ATP response (<5ng/ml) to just EBV showed no improvement by the addition of TF. Persons with robust responses of 250 ng/ml ATP to just EBV showed a slight dose related decrease when EBV was combined with TF. In persons with a very modest response to EBV of 70ng/ml the addition of TF increased the response in a dose related fashion by 49%.

Conclusion: From this *ex vivo* and *in vitro* data, it appears that the TF concentrate imparts or facilitates a conditional modulation of CD4+ and CD8+ lymphocyte responses to non specific and specific stimulators. Other reports have documented the apparent immuno-suppressive affects of TF isolated from white blood cells and termed it a suppressor factor. In our research protocol we observed that the responses were very individual and situational as the responses varied within individual over time and predicted by base line PHA or antigen response. The modulatory affects appeared in the *ex vivo* trail, as well, suggesting that this affect is not limited to an *in vitro* response only. To our knowledge this is the first study to show conditional modulatory activities for TF. Since the immune regulatory system is profound and highly controlled to direct appropriate responses and to control and down regulate unneeded or inappropriate responses, it may be more appropriate and functional to ascribe modulation attributes for TF that may include both enhancement and down regulation of immune functions. TF or one of its sub fractions may be part of the complex regulatory control of the immune response.