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Scientific Literacy Analysis

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Hypothesis

This paper seeks to investigate the role Type 1 interferon-b (T1FN-B) has in regard to Multiple Sclerosis (MS). MS is an autoimmune disease that affects over 2 million people worldwide (1). MS occurs when the covering of nerves take damage from the body's own immune system and can lead to severe symptoms such as vision loss, fatigue, and pain. T1FN-B is an innate cytokine and is the first therapy for people affected by MS (1). The mechanism by which T1FN-B alleviates symptoms of MS is not fully understood so that is what the researchers sought to investigate. Research on T1FN-B is interesting because it is an innate cytokine that enhances antiviral T-cell immunity yet can also counter-regulate T cell autoimmunity in MS. The researchers hypothesized that T1FN-B could prevent autoimmunity in MS by promoting regulatory mechanisms, such as invariant Natural Killer T cells (iNKT). These cells have been shown to prevent autoimmune diseases such as MS and diabetes (1).

Aims

The purpose of the experiments was to determine the mechanism by which T1FN-B provided therapeutic benefits to MS patients. iNKT cells are key to counter-regulate T-cell autoimmunity. As such, an intention of this research is to determine whether T1FN-B exerts a critical modulatory effect on iNKT cells. To do this, the researchers compared percentages and cytokine secretions of iNKT cells before an individual received T1FN-B and after. These individuals were receiving T1FN-B as a therapy for MS. Dendritic cells were also derived from peripheral blood monocytes (PBMC). Concentrations of cytokines IFN-y, IL-10, IL-5, IL-4, and IL-2 were also measured from the same samples. This was done through the use of a multiplexed flow cytometric assay (1). Statistical analysis was conducted on the results and P-values less than 0.05 were regarded as insignificant. The subjects were all selected as they were undergoing

treatment for MS with the use of T1FN-B. All the patients gave written consent for the experiments (1).

Results

The results of the experiments were quite promising. T1FN-B treatment enriched the Va24+ iNKT cell subset. There was a significant increase in iNKT cells in the peripheral blood monocytes of T1FN-B treated patients when compared to samples taken before T1FN-B. T1FN-B treatment was also progressive, as iNKT cell concentration was higher at 8 months post treatment compared to 3 months post treatment. T1FN-B treatment also promoted the regulatory functions of iNKT cells. INKT cells post-T1FN-B treatment secreted much higher levels of the IFN-y, IL-5, and IL-4 cytokines. Treatment with T1FN-B rendered iNKT cells more effective in cytokine release upon antigenic stimulation. While these results show T1FN-B was effective, the researchers also found that T1FN-B did not have a direct effect on iNKT cell growth (1). T1FN-B therapy also modulated dendritic cells (DC) and improved their antigen presenting capacity in relation to iNKT cells (1). DCs from T1FN-B treated patients were found to be more effective at activating iNKT cells than DCs from untreated patients.

Discussion & Summary

The results show why T1FN-B is a successful therapy for MS and what the mechanism is for that success. The data shows that T1FN-B promoted cell growth and function of regulatory iNKT cells. It also shows that T1FN-B inhibited T-cell proliferation. This is important as a goal in autoimmunity research is to find a therapy that inhibits autoimmune T cells but also improves regulatory T cell function. This research clearly shows that T1FNs have a key modulatory effect.

As such, innate cytokines could be a therapeutic approach for other T-cell-mediated autoimmune diseases like type 1 diabetes.

References

1. Gigli, G. et al (2007). Innate immunity modulates autoimmunity: type 1 interferon-b treatment in multiple sclerosis promotes growth and function of regulatory invariant natural killer T cells through dendritic cell maturation. *Immunology, 122, 409-417.*