

INVESTIGATION OF REGULATORY T CELLS IN POLYSYSTEMIC AUTOIMMUNE DISEASES AND HODGKIN'S LYMPHOMA

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One of the most important features of the immune system is the ability to discriminate between self and non-self, and based on this discrimination, to tolerate self antigens. This immunological tolerance can be acquired by central or peripheral mechanisms. Although immunological tolerance means lack of responsiveness towards self antigens, it also includes active processes, like suppression, which is controlled by specific T cells subsets. These regulatory T lymphocytes (Tr) include CD4+/CD25+^{bright} and interleukin (IL)-10 producing CD4+ cells.

To gain a better understanding on the underlying immunological mechanisms contributing to the development of systemic autoimmune diseases and malignant conditions, we aimed at investigating the distribution of Tr cells in patients with systemic lupus erythematosus (SLE), mixed connective tissue disease (MCTD), Hodgkin's lymphoma and breast cancer. Absolute and relative numbers of CD4+/CD25+^{bright} and CD4+/IL-10+ T cells were determined by flow cytometry in the peripheral blood of 72 patients with SLE, 48 patients with MCTD, as well as in 94 Hodgkin's disease and 47 breast cancer sufferer. Results were compared to healthy volunteers. We also compared the distribution of Tr cells between active and inactive stage of SLE and MCTD. Five SLE patients underwent repeated plasmapheresis treatment. The Tr subsets in these patients were closely monitored and the results were compared to other laboratory and clinical data during the course of plasmapheresis treatment.

Our data show that the percentage and absolute number of CD4+/CD25+^{bright} cells was decreased in SLE and MCTD patients compared to healthy controls. There was no significant difference between SLE and MCTD subjects. However, in MCTD patients with active disease, the absolute number of CD4+/CD25+^{bright} Tr cells was significantly lower than in those with inactive disease. No difference in the absolute number of CD4+/CD25+^{bright} Tr cells between active and inactive SLE patient was observed, though. In SLE patients undergoing plasmapheresis, the number of CD4+/CD25+^{bright} Tr cells increased gradually. Remarkably, the increase in the number of CD4+/CD25+^{bright} Tr cells was coupled with a decrease in disease activity index (SLEDAI). Regarding CD4+/IL-10+ T cells, their frequency was significantly elevated in both autoimmune diseases. Moreover, the absolute number of CD4+/IL-10+ T cells was significantly higher in MCTD, but not in SLE patients compared with healthy controls. We could not find significant differences between active and inactive MCTD and SLE patients regarding the percentage or absolute number of CD4+/IL-10+ T cells. Our results reflect impaired immunoregulatory mechanisms in SLE and MCTD, characterized by decreased number or percentage of CD4+/CD25+^{bright} cells. The higher frequency of CD4+/IL-10+ T cells may reflect counterbalancing process.

Hodgkin's lymphoma patients, as well as breast cancer patients were characterized by elevated numbers of CD4+/CD25+^{bright} and CD4+/IL-10+ T cells compared to controls. Moreover, Hodgkin's lymphoma patients had significantly increased number of CD4+/CD25+^{bright} T cells than breast cancer patients, while the latter had significantly higher number of CD4+/IL-10+ T cells compared to those with Hodgkin's lymphoma. Duration and stage of the disease, as well as the type of therapy did not significantly affect these findings, suggesting profound immunoregulatory abnormalities. Increased numbers of regulatory cells may suppress immune response against altered self-antigens that can occur in malignant diseases, and thereby contribute to the development and propagation of the tumor.

Our data suggest that impaired immunoregulatory mechanisms may play an important role in the development and maintenance of autoimmune and malignant diseases.

