CHARACTERIZATION OF AN INDUCED MURINE MODEL OF SYSTEMIC LUPUS ERYTHEMATOSUS

Ákos Hornung [1,2], Roberta Fajka-Boja [2], Éva Kriston-Pál [2], László Kovács [1], Éva Monostori [2]

[1] University of Szeged, Faculty of Medicine, Rheumatology Clinic, Szeged

[2] MTA Biology Research Centre, Institute of Genetics, Szeged

Introduction

Systemic Lupus Erythematosus (SLE) is a chronic, multi-organ autoimmune syndrome characterised by B-cell hyperactivity, autoreactive antibody probuction and aberrant T-cell function and apoptosis. Though changes in immune function are partly understood, the root causes and molecular mechanisms of disease are still to be elucidated. To establish a better understanding of this disease, our team uses an induced murine model that is primed with a single intraperitoneal injection of pristane (a mineral oil). The used mouse strain is not genetically prone to autoimmunity, but after pristane injection, exhibit an assortment of symptoms characteristic of SLE. Our goal is to establish a better understanding of this poorly defined method and assess its usefulness as a model of Lupus.

Methods

Two month old C57BL/6 (B6) female mice were injected peritoneally with either 0,5ml pristane oil or a saline solution. The mice were sacrificed eight weeks later and we determined the ratios of mononuclear cells (T-cell, B-cell and macrophage) in the lymph nodes, peritoneal lavage and spleen using cytofluorimetry.

Results

There were no significant differences between main lymphoid cell populations in the lymph nodes of control and pristane injected mice, except that the ratio of $CD4^+FoxP3^+$ cells was considerably higher in pristane treated mice. Also, the ratio of $CD11b^+$ macrophages rose significantly in response to pristane injection. The macrophage population showed dramatic growth in the peritoneal cavity as well, while B-cells, $CD4^+$ and $CD8^+$ T-lymphocytes decreased compared to those of controls. Spleens of pristane injected animals were significantly larger than controls, their T-cell content decreased slightly but significantly after ConA stimulus, while LPS stimulation resulted in appearance of a $CD11b^+$ population which was not present in LPS stimulated spleens of control animals.

Discussion

An increased $FoxP3^+$ population in peripheral blood of SLE patients is a well documented phenomenon. A similar change in lymph nodes of pristane injected animals suggests a similar mechanism, as the cells might differentiate before entering the periphery. Causes of the increased $CD11b^+$ cell population in the lymph nodes are unclear, macrophages might migrate here from the peritoneum to present antigen. An increase in $CD11b^+$ cells is well documented in the pristane model. These are mostly $Ly6C^+$ macrophages that serve a role in phagocytosis and insulation of foreign material. In mice, these cells – not plasmacytoid dendritic cells – secrete INF-α, which is an important factor in SLE pathogenesis. The reason for the decrease in T- and B-cell populations in the peritoneum is unclear, though they may migrate to the spleen after pristine treatment. The increased spleen size is probably caused by a strong inflammation stemming from the pristane injection, which is substantiated by the presence of macrophages.

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