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Phenotypic Deficiencies of Monocyte-Derived Dendritic Cells in Systemic Lupus Erythematosus

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Objective: Systemic lupus erythematosus (SLE) is a systemic autoimmune disease characterized by B cell hyperactivity and defective T cell functions. The defects in T cells may result from underlying defects in antigen-presenting cell (APC) function. Dendritic cells (DCs), as the most potent APC, present antigen to naïve T cells and are therefore pivotal in shaping immune response. The present study was to investigate the phenotypic characteristics of monocyte-derived DCs in patient with early SLE in comparison with healthy controls.

Methods: Samples from 5 untreated SLE patients (mean age 38 ± 9 year) and 5 age-matched healthy controls (mean age 34 ± 7 year) were studied. To generate DCs, monocytes isolated from peripheral blood mononuclear cells using magnetic bead separation for $CD14^+$ cells were cultured with granulocyte/macrophage-CSF (50 ng/ml) and IL-4 (10 ng/ml) for 7 days. Cells from all samples were surface phenotyped by labeling with mouse Abs against CD14, CD11c, HLA-DR and CD1a. DCs were identified and characterized phenotypically by flow cytometry. Up to 10,000 cells with high forward and side scatter were counted. The absolute cell counts were determined by using Flow-Count™ Fluorespheres. Unpaired Student's *t*-test was used to compare the differences between groups.

Results: The yield of monocyte ($CD14^+$ cell)-derived DCs (mean \pm SEM $\times 10^5/10^6$ $CD14^+$ cells) was significantly low in SLE than in controls (0.66 ± 0.1 vs 3.57 ± 0.5 , $p = 0.0003$). While the DC phenotype, $CD14^- CD11c^+ HLA-DR^+$, are expressed by $\geq 80\%$ of the cells generated from SLE patients and controls ($85.2 \pm 8.2\%$ vs $97.7 \pm 0.7\%$, $p = 0.17$). However, compared with controls, a significantly lower proportion of cells from SLE patients expressed CD1a ($25.8 \pm 8.6\%$ vs $81.2 \pm 8.6\%$, $p = 0.0019$), an MHC class I-like molecule involved in specific responses of regulatory T cells by Ag presentation.

Conclusion: Our findings of impaired yield of monocyte-derived DCs in early SLE patients suggested a defect in generation of DCs from monocytes, which is likely to reduced the capability of APC patrol to stimulate naïve T cells and may contribute to the pathogenic mechanisms involved in the disease. CD1a may also play an important role in the pathogenesis of SLE. Whether regulatory T cells are induced by Ag presentation on DCs via CD1a remains to be addressed.