

Impaired function of PD-1+ follicular regulatory T cells in systemic lupus erythematosus

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Abstract

Aberrant autoantibody production is characteristic of systemic lupus erythematosus (SLE), but follicular regulatory T (TFR) cells potentially can suppress this abnormality. We investigate functional changes in TFR cells from SLE patients. Circulating TFR cells were collected from 19 SLE patients and 14 healthy controls (HC) to compare molecular expression and in vitro suppressive capacity of follicular helper T (TFH) cell proliferation. To reveal the stability of Foxp3 in TFR, pyrosequencing of conserved non-coding sequence (CNS) 2 at the Foxp3 gene locus was performed. We then tested IL-2 in SLE-TFR cells to check restoration of suppressor function. Programmed death-1 (PD-1) expression in SLE-TFR cells was positively correlated with anti-DNA antibody levels and disease activity. These cells had impaired suppressive function for TFH cells with decreased expression of suppression mediators forkhead box p3 (Foxp3), cytotoxic T-lymphocyte antigen 4 (CTLA4), and IL-2 receptor alpha (IL2R α). Pyrosequencing identified hyper-methylation in CNS2 region of SLE-TFR cells comparing to HC. With In vitro IL-2 stimulation, PD-1 expression of TFR cells significantly decreased along with increased expression of Foxp3 and CTLA-4, especially in low-dose. Thus, SLE-TFR cells have functionally defective to TFH suppression, but low-dose IL-2 therapy might be useful to restore this ability.

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