

A116 INCREASED LEVELS OF CIRCULATING HELIOS⁺ FOXP3⁺ NATURAL REGULATORY T CELLS IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Objectives The authors aimed to analyse the coexpression level of Helios, a member of the Ikaros transcription factor family, in FoxP3⁺ regulatory T cell (Treg) subsets to characterise the pool of circulating natural Tregs in patients with systemic lupus erythematosus (SLE).

Methods Multicolour flow cytometry was performed to analyse the coexpression of Helios, CD25, CD45RA and CD31 in FoxP3⁺ Tregs from peripheral blood of 20 patients with SLE, 20 age- and sex-matched healthy controls (HC), 6 patients after thymectomy for myasthenia gravis and 6 patients after receiving immunoablation and autologous stem cell transplantation (ASCT) for SLE. Statistical analyses were performed using the paired t-test.

Findings The level of circulating FoxP3⁺ T cells among CD4 T cells was significantly higher in SLE compared to HC (mean 14.5 vs 7.2%, $p=0.002$) with Helios being coexpressed at significantly higher levels in SLE (81.4 vs 69.0%, $p<0.0001$). With respect to CD45RA coexpression, CD4⁺ FoxP3⁺ T cells can be subdivided into three distinct subpopulations, all of which are present at significantly higher levels among CD4 T cells in SLE: CD45RA⁺ FoxP3^{lo} resting Tregs ($p=0.01$), CD45RA⁺ FoxP3^{hi} activated Tregs ($p=0.01$) and CD45RA⁺ FoxP3^{lo} non-Treg cells ($p=0.004$). In SLE, Helios expression levels were significantly higher in all of these subsets compared to HC: 90.7 versus 85.1% in CD45RA⁺ FoxP3^{lo} Tregs ($p=0.003$), 83.3 versus 74.7% in CD45RA⁺ FoxP3^{hi} Tregs ($p=0.003$) and 73.8 versus 52.5% in CD45RA⁺ FoxP3^{lo} non-Treg cells ($p<0.0001$). Within the CD45RA⁺ FoxP3^{lo} Treg subset, the coexpression level of CD31 was significantly lower in SLE ($p=0.03$) and patients after thymectomy ($p=0.001$), but higher in patients after ASCT who developed a thymic reactivation ($p=0.04$).

Conclusion The authors' data are the first to demonstrate that circulating Helios⁺ FoxP3⁺ natural Treg levels are significantly increased in SLE patients compared to healthy controls. This does, however, not necessary reflect an increased thymic output of natural Tregs in SLE. The decreased coexpression levels of CD31, as a surrogate marker for recent thymic emigrants, found among CD45RA⁺ FoxP3⁺ Tregs in SLE rather suggests that the thymic output is diminished in SLE implicating that Treg levels are primarily maintained through peripheral expansion of Helios⁺ FoxP3⁺ Tregs in SLE. The level of Helios⁺ FoxP3⁺ induced Tregs are, on the other hand, decreased in SLE for so far unknown reasons.