17 IL-2 THERAPY EXPANDS INTRARENAL FOXP3+ REGULATORY T CELLS AND DECREASES THE NUMBER OF INFILTRATING CD4+T CELL IN MURINE LUPUS NEPHRITIS

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Background and objectives Systemic lupus erythematosus (SLE) is an autoimmune disease characterised by an acquired IL-2 deficiency, which leads to a homeostatic imbalance between regulatory T cells (Treg) and effector T cells. Recently, the authors have shown that compensation of the IL-2 deficiency in diseased lupus mice by treatment with recombinant IL-2 (IL-2) ameliorates already established disease by promoting the homeostatic proliferation of regulatory T cell (Treg) in the lymphoid organs.[1] The aim of this study was to investigate the impact of IL-2 therapy on intrarenal Foxp3+Treg and kidney infiltrating CD4+T cells in (NZBxNZW) F1 mouse model of lupus nephritis.

Materials and methods (NZBxNZW) F1 mice with active nephritis were treated with recombinant IL-2 either over a short period of 24 h or over a long period of 20 days with PBS as control. Absolute numbers, phenotype and proliferation of kidney infiltrating CD4+T cells were determined by flow cytometry. Cellular infiltrates were also visualised by immunohistochemistry.

Results Short term IL-2 treated (NZBxNZW) F1 mice resulted in an increase in numbers and frequency of CD4+Foxp3+Treg and strongly enhanced the proliferation of Foxp3+Treg compared to PBS treated control mice. In contrast, the long term IL-2 treatment over a period of 20 days did not result in a persistent expansion of the intrarenal Foxp3+Treg population. However, total numbers of kidney infiltrating CD4+Tcon were reduced in long term treated mice. In addition these CD4+Tcon showed reduced signs of cellular activation.

Conclusions In this study, the authors found that short term IL-2 treatment is capable to expand the size of the intrarenal Treg pool. On the other hand, long term IL-2 treatment diminishes the numbers of kidney infiltrating CD4+Tcon. These findings underline the important role of intrarenal Treg for the suppression of kidney disease in lupus mice and may in part explain the delay of disease progression induced by treatment with IL-2. Furthermore, these data provide additional rationales for an IL-2 based immunotherapy of human disease.

REFERENCE

1. **Humrich JY,** Morbach H, Undeutsch R, *et al*. Homeostatic imbalance of regulatory and effector T cells due to IL-2 deprivation amplifies murine lupus. *Proc Natl Acad Sci USA*. 2010;**107**:204–9.