

## IL-2/Anti-IL-2 Complex의 조절 T 세포 증식을 통한 Lupus Nephritis에서의 보호작용

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### IL-2/Anti-IL-2 Complex Attenuates Lupus Nephritis by Expansion of Regulatory T Cells

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**Background:** Regulatory T (Treg) cells play an important role in the maintenance of immune tolerance to self and in the pathogenesis of autoimmune disease. Systemic lupus erythematosus (SLE) is an autoimmune disorder characterized by the production of antibodies to self-nucleic acids, immune complex deposition, and tissue inflammation such as glomerulonephritis. We therefore hypothesized that the IL-2/anti-IL-2 complex (IL-2C), a mediator of Treg expansion, can ameliorate progression and reduce the mortality of lupus-prone mice.

**Method:** NZWB/F1 female mice progressively produce high levels of autoantibodies and resultant deposition of immune-complexes drives glomerulonephritis. NZWB/F1 female mice were treated intraperitoneally with IL-2/anti-IL-2 mAb (JES6-1) 3 times a week starting at 24 weeks of age, and were analyzed at 36 weeks of age. Lupus-like disease progression was assessed by measurement of proteinuria, dsDNA, cytokine levels and kidney histology, as well as by flow-cytometric analysis of cellular infiltration.

**Results:** IL-2C induced an effective and sustained expansion of CD4<sup>+</sup>Foxp3<sup>+</sup>CD25<sup>+</sup> Tregs in both kidney and spleen. Compared with the vehicle-treated controls, NZWB/F1 female mice treated with IL2C showed less proteinuria, less acute and chronic pathological lesions in the kidney and better survival. There were significant differences in glomerular injury, tubular injury and vasculitis scores, as well as in the quantitative analysis of IgG and C3 deposition between the two groups. Disease activity markers such as anti-dsDNA antibody, complement and immunoglobulin levels were reduced in serum of IL-2C group. IL-2C treatment reduced plasma cell populations in spleen, inhibition of B and T cell infiltration of the kidney tissue, and suppressed IFN- $\gamma$ + and Th17+ CD4+cells in both spleen and kidney. When compared with combination therapy of steroid and mycophenolate mofetil, IL-2C treatment showed similar or better outcomes. Depletion of Tregs with anti-CD25 antibodies (PC61) abrogated the beneficial effects of IL2C.

**Conclusion:** IL-2C protects lupus-prone mice against lupus nephritis by expanding Tregs and suppressing inflammation. Therefore, IL2-C could have a therapeutic potential in lupus nephritis.

**Key Words:** 조절T세포, 낭창성신염, IL2C

Regulatory T cell, Lupus nephritis, IL-2/Anti-IL-2 Complex