S-B32

기억 T세포 매개성 이식거부반응의 CD4+CD25+ 면역조절 T 세포에 대한 저항성

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Allograft Rejection Mediated by Memory T cells is Resistant to Regulation by both Naive and Alloantigen-primed CD4+CD25+ Regulatory T Cells

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Purpose : CD4+CD25+ regulatory T cells (Tregs) are critical for both the induction and maintenance of transplantation tolerance. Recognizing the important barrier that memory T cells present to tolerance induction, we tried to elucidate the ability of Tregs to suppress alloreactive memory T cells.

Methods : CD4+ resting memory T cells were sorted from ABM mice, the T cell receptor transgenic mice reactive to I-ABm12, 8 weeks after Bm12 skin transplantation. Naïve ABM Tregs and primed ABM Tregs were sorted from unprimed ABM mice, and tolerized ABM mice, respectively. In vitro suppression assays were done in both CD4+ naive and memory T cells. ABM CD4+ naive or memory T cells were injected intravenously into C57BL/6 RAG1 knockout mice, alone or with ABM Tregs. Bm12 skin graft survival was assessed for up to 100 days. In vivo suppressive effects of Tregs on CD4+ memory T cells were assessed in draining lymph nodes.

Results : Memory T cells were significantly less susceptible to regulation by Tregs than were naive T cells, as assessed by in vitro proliferation, survival, IFN-γ and IL-2 production. Consistent with this, upon co-adoptive transfer, Tregs were able to suppress rejection of bm12 skin graft induced by naive T cells, but neither naive nor antigen primed Tregs suppressed the rejection mediated by memory T cells. Proliferation, and cytokine production of CD4+ naive T cells were suppressed by alloantigen specific Tregs in draining lymph nodes, whereas CD4+ memory T cells were resistant to suppression. Moreover, CD4+ memory T cells escaped from Tregs in the draining lymph nodes in contrast to CD4+ naive T cells.

Conclusion : In conclusion, our data demonstrated that memory T cells are resistant to regulation by Tregs, whether primed or not, and this mechanism may contribute to resistance to transplantation tolerance associated with immunologic memory.