MÜSBED 2012;2(Suppl. 2):S49

Regulation of CD8+ Suppressor T cells with Pattern Recognition Receptors

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Objective: The suppressive effects of CD8+CD28- T cells on the proliferation of T helper cells have been demonstrated. Toll like receptors (TLRs), the potent activators of innate immune response, are also expressed on T cells.

Methods: We aimed to identify the phenotypic and functional characteristics of CD8+CD28- suppressive T cells (Ts) and how TLRs regulate their functions. Expressions of CD56, HLA-DR and perforin levels were analyzed. TLR expression kinetics of CD8+ cells were examined before and after stimulation with phytohemagglutinin (PHA). Magnetically isolated Ts were stimulated with TLR agonists and their suppressive capacity was investigated using 5-ethynyl-2'-deoxyuridine (EDU). Suppressive cytokines IL-10 and TGF-β were analyzed with ELISA.

Results: HLA-DR, CD56 and perforin expressions were found higher on Ts compared to Tef. Among Ts, two distinct populations, CD8+CD28-CD56+ and CD8+CD28-HLA-DR+, were identified. TLR expressions of Ts after PHA stimulation were found lower. We also demonstrated that these cells suppress the proliferation of CD4 T cells and secrete high levels of TGF-β. TLR1/TLR2 and TLR3 agonists inhibited the suppressive function of Ts but TLR4 stimulation had no effect. Although we did not find any difference in the levels of TGF-β secretion after TLR1/TLR2 stimulation, TGF-β levels were reduced after TLR3 and TLR4 stimulations.

Conclusions: We demonstrated that Ts suppress the CD4+ T cells via TGF-β. However, this suppression can be inverted by TLR stimulation. When CD8+CD28- Ts encounter a strong stimulation like TLR3 stimulation, they lose their suppressive capacity and their plasticity enables them to differentiate into effector cells in order to sustain immune defense.

Key words: Regulatory T cells, TLR, suppression, pattern recognition receptors