

Burn injury drives late alterations in cytokine serum levels and cytokine production by CD8⁺ T cells.

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Dysfunctional T cell responses are observed early and late after burn injury are thought to be due to altered secretion of cytokines by T cells. Recent studies suggest that the cytokine environment early after injury does not control the longer-term T cell response. Using a mouse model of burn injury, we observe a burn-dependent enhancement of T cell responses 14 days postburn (p.b.). In order to investigate longitudinal cytokine secretion, and determine which T cell population was secreting altered cytokines after burn, female B6 mice or B6.CD4-knockout mice (CD4^{-/-}) were subjected to 20% burn or sham procedure. Mice were sacrificed 0, 6, 12, 24, 72 hours or 14 days (n=4) p.b. Serum (B6) and supernatant from splenocytes (B6 and CD4^{-/-}) stimulated with anti-CD3 and anti-CD28 antibodies for 48 hours were assayed for cytokines by cytometric bead assay. Only IL-6, MCP-1 and TNF_α demonstrated significant alterations in serum from burnt B6 mice compared to sham controls. Serum IL-6 was dramatically elevated from 6 hours to 14 days p.b. compared to sham, peaking at 72 hours ([mean] ±SEM; burn, 58±4pg/ml; sham, 4±1pg/ml, p<0.005). Stimulated T cells from B6 and B6.CD4^{-/-} 14 days p.b. secreted significantly more IL-6 than sham counterparts. MCP-1 expression pattern was similar to IL-6, except that serum levels returned to sham levels by day 14. Burn-dependent expression was 4-fold higher after activation of CD4^{-/-} splenocytes compared to B6. IFN_γ, IL-10 and IL-4 all exhibited a surprising increase on T cell activation at 14 days from burnt B6 and B6.CD4^{-/-} mice. TNF_α levels were elevated by burn at day 14 in B6 serum and after B6, but not B6.CD4^{-/-} splenic activation. This longitudinal study reveals significant changes in cytokine secretion early and late after burn injury. CD8⁺ T cells are responsible for increased IL-6 and MCP-1 expression and non-CD8⁺ splenic cells for increased IFN_γ, IL-10, IL-4 and TNF_α production in mice late after burn injury.