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Interferon-gamma can reverse sepsis-induced immunosuppression of monocytes

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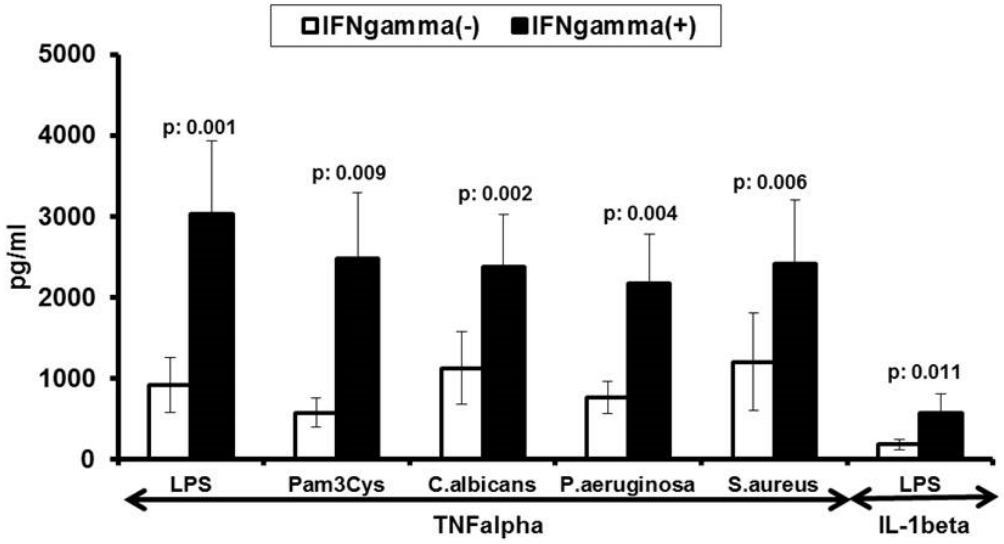
Background: Sepsis-induced immunosuppression is a condition leading to host deterioration and multiple organ dysfunction (MODS). Although stimulation immunotherapy may be a therapeutic option, there are serious concerns on the exact time of intervention. We measured the ex vivo effect of interferon (IFN)-gamma treatment on monocytes isolated from patients with at least 72 hours on immunosuppression.

Material/methods: Peripheral blood mononuclear cells (PBMCs) were isolated after gradient centrifugation over Ficoll from 13 patients who met the Sepsis-3 definitions and 13 healthy controls. All patients were at septic shock and MODS and they were on immunosuppression as defined by the less than 30% expression of HLA-DR on CD14-monocytes. Blood sampling was done 72 hours after start of vasopressors. Cells were ex vivo stimulated with 10ng/ml lipopolysaccharide (LPS), 5 μg/ml of Pam3Cys and $5x10^5$ cfu/ml of heat-killed *Candida albicans*, *Pseudomonas aeruginosa* and *Staphylococcus aureus* in the absence and presence of 10ng/ml of IFNgamma. Tumour necrosis factor (TNF)-alpha, interleukin (IL)-1beta and IL-6 were measured in supernatants after 24 hours of incubation.

Results: All controls had adequate cytokine responses; this was the case for only five patients (p: 0.002). Addition of IFNγ reversed failed responses for TNFalpha to the levels of controls (Figure). The failed production of IL-1beta to LPS was restored after addition of IFNgamma. However, IFNgamma did not affect failed production of IL-1β to the other stimuli. It also did not affect failed production of IL-6 to any stimulus.



Conclusions: Addition of IFNgamma improves substantially failed production of TNFalpha and to a lesser extent of IL-1beta from PBMCs of patients at septic shock, MODS and immunosuppression isolated as late as 72 hours from shock onset. Results make IFNγ a favorable candidate for immunotherapy in the immunosuppression of sepsis.