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Expression and activation of T cell receptor dependent transcription factors in regulatory T cells

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T cell receptor signalling and therefore production of IL-2 upon antigen stimulation, has been shown to be impaired in regulatory T (Treg) cells. Whether the expression and activation of the major transcription factors NFATc2, AP-1 and Nf-κB are affected too, has not yet been determined. We found a strikingly lower expression of all three factors in human Treg cells compared to memory Th cells, but their activation was unharmed. Interestingly, after stimulation with PMA/Ionomycin, thus bypassing upstream signalling events, we found a small Treg cell subset, that was able to overcome its anergic phenotype and produced IL-2. This subpopulation is characterized by higher NFATc2, AP-1 and Nf-κB and lower FOXP3 levels compared to IL-2 nonproducing Treg cells. Our Data suggests that IL-2 production in Treg cells is not switched off by genetic imprinting, but rather the amounts and ratios of the essential transcription factors NFATc2, AP-1, Nf-κB and FOXP3 are essential to prevent IL-2 production in Treg cells and thereby suppport their anergic phenotype despite a very strong stimulation.