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Neutralization of IL-4 and IFN-γ Facilitates inducing TGF-β-induced CD4+Foxp3+ Regulatory Cells

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It has been well recognized that TGF-β is able to induce $CD4^+CD25^+Foxp3^+$ suppressor/regulatory T (iTreg) cells and IL-2 facilitates iTreg induction and expansion, however, only half of TGF-β-induced $CD4^+CD25^+$ cells express Foxp3 and remaining $CD4^+CD25^+$Foxp3- cells may represent effector cells. Whether other factor(s) can increase Foxp3 expression by $CD4^+CD25^+$ cells induced with TGF-β is still unclear. Here we show that addition of exogenous IFN-γ or IL-4 diminished the ability of TGF-β to induce Foxp3 expression and IL-2 failed to rescue this decreased Foxp3 expression. Conversely, neutralization of IFN-γ and IL-4 significantly enhanced the ability of TGF-β to induce Foxp3 and develop the suppressive activity, indicating that different cytokine profiles affect the differentiation of $CD4^+CD25^+Foxp3^+$ subset induced by TGF-β. These results show that combination of antibodies against IFN-γ and IL-4 and TGF-β enhances the efficacy of generation and function of iTreg cells and may therefore provide a novel therapeutic strategy for the treatment of autoimmune and other chronic inflammatory diseases.