Tuning the immunity up and down with complexes of IL-2 and anti-IL-2 mAb

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IL-2 is approved by the FDA to treat metastatic renal cancer and melanoma. However, extremely short half-life and serious toxicities associated with IL-2 treatment are the main drawbacks. The biological activity of IL-2 can be strongly increased by association of IL-2 with anti-IL-2 mAb. IL-2/S4B6 mAb immunocomplexes are highly stimulatory mainly for NK and memory CD8+ T cells, while IL-2/JES6-1 mAb immunocomplexes solely for Treg cells. Here we show that both above mentioned IL-2 immunocomplexes are extremely potent in expanding activated naïve CD8+ T cells in vivo. IL-2 immuno-complexes expand activated naïve CD8+ T cells several hundred-fold times after four doses. On the contrary, free IL-2 given at the same dosage shows negligible activity. Importantly, activated naïve CD8+ T cells expanded by IL-2 immunocomplexes form stable robust population of functional memory cells. Using radioactively labeled IL-2, we provide for first time direct evidence that IL-2 immunocomplexes have much longer half-life than free IL-2. Finally, we demonstrate that IL-2/S4B6 mAb immunocomplexes possess considerable anti-tumor activity while IL-2/JES6-1 mAb immunocomplexes can be used to enormously expand Treg cells which are able to protect the mice from induced acute colitis and also to inhibit rejection of syngeneic tumor cells expressing xenogenic protein.