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Less is more: The inhibitory molecule CTLA-4 and the differentiation of memory T-cells in vivo

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A hallmark of the adaptive immune system is the generation of memory which enables a quick and robust response to antigen rechallenge - mostly even without clinical symptoms. Surprisingly, the factors which determine the generation of memory T cells and how CD4+ T cells are selected for the memory pool are unknown.

We show now, that less is more for the generation of a memory response. Factors which have previously been determined to only shut down responses turn out to be key players to i) direct the T-cells to their place of action and i) shape the memory pool of T-cells with high quality. To analyse memory formation in vivo we established a new method for detection of endogenous antigen-specific memory cells using their fast CD40L expression. Our in vivo conducted study on memory formation shows for the first time the tremendous impact of the inhibitory CTLA-4 signal on the generation of the highly efficient multifunctional memory CD4+ T cells. Mechanistically, we show that this is mediated by natural T regs. Hence, our study shows a completely novel activity of the CTLA-4 signal which will have important implications for the generation of high quality memory cells during vaccination strategies.