Guidance of regulatory T cell development by Satb1-dependent super-enhancer establishment

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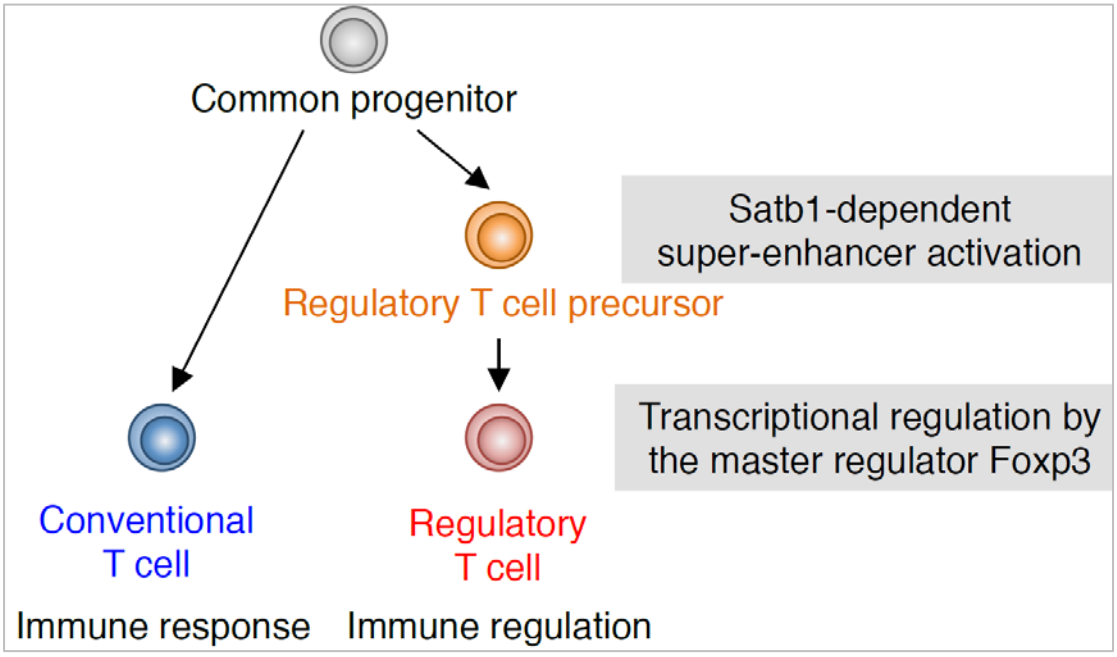
Most Foxp3^{+} regulatory T (T_{reg}) cells develop in the thymus as a functionally mature T-cell subpopulation specialized for immune suppression. Their cell fate appears to be determined before *Foxp3* expression; yet molecular events that prime Foxp3^{-} T_{reg} precursor cells are largely obscure. Here we showed that T_{reg} cell-specific super-enhancers (T_{reg}-SEs), which were associated with *Foxp3* and other T_{reg} cell signature genes, began to be activated in T_{reg} precursor cells. T cell-specific deficiency of the genome organizer Satb1 impaired T_{reg}-SE activation and the subsequent expression of T_{reg} cell signature genes, causing severe autoimmunity due to T_{reg} cell deficiency. Our results suggest that Satb1-dependent T_{reg}-SE activation crucially controls T_{reg}-cell lineage specification in the thymus and its perturbation is causative of autoimmune and other immunological diseases.

Key words: Immune regulation, epigenetics, cell differentiation, regulatory T cells (Tregs)



A mechanism for the differentiation of regulatory T cells