

The contribution of IL-2 receptor signaling to FoxP3 expression
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Dysregulated immune responses occur when there is a breakdown in natural tolerance mechanisms, giving rise to autoreactive T cells. As part of this mechanism, a T cell population, termed regulatory T (T_R) cells, modulates potentially autoreactive T cells. T_R cells are characterized by CD4 and CD25 expression, inhibit effector T cells in an antigen-specific manner, and express high levels of the forkhead-winged helix transcription factor *foxp3*. In *scurfy* mice, a two base pair frameshift insertion results in truncated *foxp3* mRNA and development of an autoproliferative, multiorgan lymphocytic-infiltrate disease. Based on these and other findings, FoxP3 is thought to be sufficient and necessary to confer T_R cell capability. At present, little is known about the transcriptional regulation of *foxp3*. However, mice deficient in IL-2, IL-2 receptor (IL-2R) or downstream signal mediators display reduced numbers of peripheral CD4⁺ CD25⁺ T_R cells. These findings suggest that *foxp3* may be a target of the IL-2R signaling pathway. Interestingly, mice deficient in the IL-2 receptor beta (β) chain lack CD4⁺ CD25⁺ T_R cells and display an autoimmune phenotype similar to *scurfy* mice. Our data show that the introduction of either a FoxP3 transgene or an IL-2Rβ thymic transgene rescues the autoimmune syndrome found in IL-2Rβ deficient mice. In addition, *foxp3* expression is restored and T_R cells are functional. Our preliminary data suggest that IL-2Rβ signaling is required for expression and function of *foxp3* and consequently for the development and maintenance of CD4⁺ CD25⁺ regulatory T cells.