## 9. T cells

### A164 MICRORNA-182 PROMOTES CLONAL EXPANSION OF ACTIVATED T HELPER CELLS

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Upon activation by antigen, T lymphocytes switch from a resting state to clonal expansion. This switch requires inactivation of the forkhead transcription factor Foxo1, which suppresses proliferation in resting T helper lymphocytes. In the initial antigen-dependent phase of clonal expansion, Foxo1 is inactivated by antigen receptor-dependent post-translational modifications. However, the late antigen-independent phase of clonal expansion is controlled by interleukin 2 (IL2), and it has not been clear how Foxo1 is inactivated in this phase. Here the authors show that in the IL2-dependent late phase of clonal expansion, expression of Foxo1 is downregulated by microRNA-182. Expression of microRNA-182 in activated T lymphocytes is induced by IL2. MicroRNA-182 is expressed between 2 and 4 days after onset of T cell activation. In this time, Foxo1 mRNA expression is reduced by 90%. Specific inhibition of microRNA-182 by locked nucleic acids inhibits clonal expansion of activated T lymphocytes in vitro. Ectopic constitutive expression of microRNA-182 results in a ninefold enhanced clonal expansion in vivo. Our results identify IL2-induced expression of microRNA-182 as a critical step regulating the late phase of clonal expansion of activated T helper lymphocytes, and presumably also the transition from expansion to contraction, as future research may show. The central role of a microRNA, here microRNA-182, in the regulation of T cell expansion provides entirely new options for therapeutic interference, namely the use of specific antagomiRs to limit T cell expansion in vivo. This may be of relevance in immune-mediated diseases.