Synopsis of Original Research Paper

Elucidating the mechanisms of regulatory T cell-dependent maintenance of skin homeostasis

Shohei Hori

Laboratory for Immunology and Microbiology, Graduate School of Pharmaceutical Sciences, The University of Tokyo

Foxp3-expressing regulatory T cells (Treg) are indispensable for the maintenance of immunological self-tolerance and immune homeostasis. Recent studies have revealed that Treg cells reside not only in lymphoid, but also in non-lymphoid, tissues including the skin and that skin Treg cells play an important role in maintaining skin homeostasis. However, the molecular mechanisms that regulate Treg accumulation and function in the skin remain elusive. We have previously shown that the Foxp3^{A384T} mutation, which was identified in human IPEX patients, impairs accumulation of Treg cells in selective tissues including the skin and causes inflammation in those sites at least in part by repressing expression of the transcription factor BATF, which act down-stream of TCR signaling. In this study, by generating and analyzing Treg-specific BATF conditional knockout mice, we show that BATF is indispensable for the accumulation and suppressive function of Treg cells in the skin. BATF appears to cooperate with Foxp3 to control Treg accumulation in the skin by promoting expression of molecules implicated in leukocyte migration to and retention in the skin. Furthermore, we also show that skewed TCR repertoire selectively exacerbates skin inflammation in Foxp3^{A384T} mutant mice, which otherwise develop mild dermatitis. In summary, our results suggest that interactions between Foxp3 and the TCR-BATF axis represents an important determinant of Treg accumulation and anti-inflammatory function in the skin.