

FucT4/7 deficient regulatory T cells suppress liver inflammation but fail to rescue *Scurfy* mice from skin and lung associated autoimmune disease.

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We were interested in the role of homing receptors (HR) on the homeostatic expansion, localization and function of regulatory T cells (Treg). Treg are believed to upregulate the integrin CD103 along with HR for peripheral tissues upon activation. We chose here the autoimmune model of the *scurfy* (*sf*) mouse, which lack FoxP3-dependent regulatory T cells (Treg) and develops multiple tissue inflammations, but can be rescued by the neonatal transfer of wildtype CD4+CD5+ Treg. First, we determined, if CD103 expression resembles a stable phenotype, and if CD103+ cells could compete with CD103 negative cells in homeostatic expansion. Surprisingly, after transfer of highly purified CD103 positive cells in competition with negative cells in neonatal *sf* mice, we observed over a period of 4 weeks, that CD103 positive cells expanded and survived equivalently to CD103 negative cells. In addition, a fraction of transferred cells downregulated CD103, indicating that expression of this marker is dynamically regulated on Treg.

To determine how homing to specific non-lymphoid tissues impacts Treg homeostasis and function, we transferred Treg from mice deficient for Fucosyltransferases 4 and 7 (FucT4/7), which are crucial enzymes for the expression of E- and P-selectin ligands (E/P-lig). After injection of FucT4/7 deficient Treg alone or in competition with wildtype Treg, we monitored expansion, localization and potential tissue inflammation. We found that FucT4/7 deficient Treg were fully capable to do homeostatic expansion but were severely affected in homing to skin and could not suppress skin and lung inflammation. In contrast, other *sf* target tissues such as liver and kidney remained healthy. These results suggest, that the peripheral tissue localization of Treg is crucial for their suppressive function on autoimmunity and point out the meaning of tissue targeting of Treg for therapy.