A subpopulation of CD103(pos) ICOS(pos) Treg cells occurs at high frequency in lymphopenic mice and represents a lymph node specific differentiation stage

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Regulatory T (Treg) cells are pivotal for the maintenance of peripheral tolerance by controlling self-reactive, chronic, and homeostatic T-cell responses. Here, we report that the increase in Treg-cell suppressive function observed in lymphopenic mice correlates with the degree of lymphopenia and is caused by a higher frequency of a novel subpopulation of CD103(pos) ICOS(pos) Treg cells. Though present in the thymus, CD103(pos) ICOS(pos) Treg cells are not generated there but recirculate from the periphery to that site. The acquisition and maintenance of this distinctive phenotype requires the LN microenvironment and the in situ availability of antigen. Contrary to conventional effector and other Treg cells, the cellularity of CD103(pos) ICOS(pos) Treg cells is not affected by the absence of IL-7 and thymic stroma lymphopoetin. Given their increased frequency in lymphopenia, the absolute number of CD103(pos) ICOS(pos) Treg cells remains unchanged in the periphery irrespective of a paucity of total Treg cells. We furthermore demonstrate, with cell transfers in mice, that the CD103(pos) ICOS(pos) phenotype represents a LN-specific differentiation stage arrived at by several other Treg-cell subsets. Thus, tissue-specific cues determine the overall potency of the peripheral Treg-cell pool by shaping its subset composition.
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