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701.EXPERIMENTAL TRANSPLANTATION: BASIC AND TRANSLATIONAL

ST2/ Rorγt-Dependent Th1/Th2-like CD4 $^{+}$ Trm Cells Mediate Cutaneous Chronic Gvhd

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- Allogeneic hematopoietic cell transplantation (Allo-HCT) is a curative therapy for relapsed hematological malignances, but the same alloreactive T cells that eliminate malignant cells in the recipient also mediate graft-versus-host disease (GVHD), and in long-term Allo-HCT patients chronic GVHD (cGVHD) remains the major cause of morbidity and mortality. Th subsets (i.e., Th1, Th2, and Th17) have been associated with cGVHD in certain tissues, but the Th subsets involved in cutaneous cGVHD remain undefined. In the current studies, with a murine model of C57BL/6 donor to MHC-matched C3H.SW recipient, we observed that although IFN-γ^{+} Th1 cells were dominant in the gut, liver, and skin during early acute GVHD, the skin showed a marked expansion of IFN-γ^{+}IL-13^{+} Th1/Th2-like cells 30 days after HCT at the onset of cGVHD, while IFN-γ^{+}IL-13^{-} Th1 cells remained dominant in the liver and intestines. The cutaneous Th1/Th2-like cells exhibited characteristics of Ly108^{-}CD69^{+} tissue resident memory T (Trm) cells. The expansion of cutaneous Th1/Th2-like cells was RORγt and ST2-dependent because T cells from RORγt$^{-/-}$ or ST2$^{-/-}$ C57BL/6 donors did not show expansion of the cutaneous Th1/Th2-like cells or induce cutaneous cGVHD. These results indicate that 1) IFN-γ^{+}/IL-13^{+} Th1/Th2-like CD4^{+} Trm cells likely play a critical role in the pathogenesis of cutaneous cGVHD; 2) the differentiation of IFN-γ^{+}CD4^{+} Th1 cells into IFN-γ^{+}IL-13^{+} Th1/Th2-like cells is RORγt and ST2-dependent. The molecular mechanisms that underpin this differentiation pathway are under investigation.

Disclosures No relevant conflicts of interest to declare.

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