JOURNAL OF LEUKOCYTE BIOLOGY

Cell Development, Differentiation, & Trafficking

Pregnancy promotes tolerance to future offspring by programming selective dysfunction in long - lived maternal T cells

Brendan M. Barton, Rong Xu, E. John Wherry, Paige M. Porrett

First published: 3 November 2016
https://doi.org/10.1189/jlb.1A0316-135R
Cited by:5

Abstract

Fetal antigen available during pregnancy induces the proliferation of maternal T cells. It is unknown, however, whether these antigen - activated T cells differentiate into long - lived memory T cells that are capable of mediating rapid - recall responses to tissue antigens. To test the hypothesis that pregnancy induces an alternative fate in fetal - specific maternal T cells, we used a murine model to track longitudinally fetal - specific T cells in pregnant and postpartum animals and test the response of these cells when challenged with the same antigen during sequential pregnancy or skin transplantation. Fetal - specific $CD8^+$ T cells were robustly primed during pregnancy but failed to acquire robust effector functions. These primed cells persisted long term in postpartum animals, frequently maintained a programmed death 1 (PD - 1)$^+$ phenotype, and failed to expand or produce cytokines robustly in response to second pregnancy or skin transplantation. However, whereas there was no impact on second pregnancy as a result of the persistence of fetal - primed memory $CD8^+$ T cells in the mother, skin grafts bearing the same antigen were rejected more rapidly. Altogether, our data suggest that fetal antigen exposure during pregnancy induces the differentiation of long - lived maternal $CD8^+$ T cells with context - dependent, selective effector dysfunction. This programmed effector dysfunction provides temporal and systemic restraint of maternal anti - fetal alloreactivity to promote reproductive fitness efficiently, while preserving potentially protective effector T cell responses.

Tom Erkers, Arwen Stikvoort and Michael Uhlin, Lymphocytes in Placental Tissues: Immune Regulation and Translational Possibilities for Immunotherapy, *Stem Cells International*, **2017**, (1)
Crossref

J.B Cohen, L Owei, D.L Sawinski and P.M Porrett, Inferior long - term allograft and patient outcomes among recipients of offspring living donor kidneys, *American Journal of Transplantation*, **0**, 0

Supporting Information