Journal for ImmunoTherapy of Cancer

POSTER PRESENTATION Open Access

Enhancing T cell persistence of CAR-redirected T cells in solid tumors

Sonia Guedan[1*], Shannon E McGettigan[2], Avery D Posey[1], Jihyun Lee[3], Omkar Kawalekar[1], Prachi R Patel[1], Brian Keith[1], Carl June[1]

From Society for Immunotherapy of Cancer 29th Annual Meeting
National Harbor, MD, USA. 6-9 November 2014

T cell persistence is likely to promote long-term antitumor effects after adoptive T cell transfer. We have recently shown that incorporation of the ICOS intracellular domain into chimeric antigen receptors (CARs) significantly increased Th17 cell persistence *in vivo*, compared to CARs with CD28 or 4-1BB intracellular domains [1]. Here, we hypothesized that $CD4^+$ and $CD8^+$ T cells require distinct cytokine and costimulation signals for optimal persistence. To test this hypothesis, we compared the *in vivo* antitumor effects and persistence of combined $CD4^+$ T cells (bulk or Th17-polarized) and $CD8^+$ T cells redirected with CARs containing CD28, 4-1BB or ICOS-based costimulatory domains. Using multiple mouse tumor models, we demonstrate that the ICOS intracellular domain significantly enhanced the *in vivo* persistence of CAR-expressing $CD4^+$ T cells, and that both persistence and tumor infiltration were further enhanced by culturing these cells under Th17-polarizing conditions. Importantly, Th17-polarized $CD4^+$ T cells expressing an ICOS-based CAR significantly increased the circulatory persistence of bulk $CD8^+$ T cells expressing either CD28- or 4-1BB-based CARs. We further demonstrate that the antitumor effect of CAR-expressing $CD8^+$ T cells was enhanced when co-injected with ICOS-redirected Th17 cells. Collectively, our data suggest that combining Th17 $CD4^+$ T cells redirected with an ICOS-based CAR with $CD8^+$ CAR-T cells will enhance their persistence and antitumor efficacy.

Authors' details
[1]University of Pennsylvania, Philadelphia, PA, USA. [2]University of Pennsylvania, Hatboro, PA, USA. [3]University of Pennsylvania, Poland.

Published: 6 November 2014

Reference

1. Guedan S, Chen X, Madar A, Carpenito C, McGettigan SE, Lee J, Posey AD, Frigault MJ, Scholler J, Scholler N, Bonneau R, June CH: **ICOS-based chimeric antigen receptors sustain bipolar TH17/TH1 cells.** *ICOS-Based Chimeric Antigen Receptors Program Bipolar TH17/TH1 Cells, Blood* 2014, July 1, doi:10.1182/blood-2013-10-535245.

doi:10.1186/2051-1426-2-S3-P244
Cite this article as: Guedan *et al.*: Enhancing T cell persistence of CAR-redirected T cells in solid tumors. *Journal for ImmunoTherapy of Cancer* 2014 **2**(Suppl 3):P244.

[1]University of Pennsylvania, Philadelphia, PA, USA
Full list of author information is available at the end of the article