

**POSTER PRESENTATION**

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# Bystander memory CD8 T cell proliferation after anti-CD40/IL-2 treatment is independent of CD4 T cells

Steven K Grossenbacher<sup>1\*</sup>, Arta M Monjazeb<sup>2</sup>, Julia Tietze<sup>1</sup>, Gail D Sckisel<sup>1</sup>, Annie Mirsoian<sup>1</sup>, Hui-Hua Hsiao<sup>1</sup>, Brent Koehn<sup>3</sup>, Danice Wilkins<sup>1</sup>, Bruce R Blazer<sup>3</sup>, William J Murphy<sup>1</sup>

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Systemic cancer immunotherapy combining agonistic anti-CD40 and interleukin 2 results in synergistic anti-tumor effects with marked antigen independent expansion of bystander memory CD8 T cells displaying anti-tumor abilities. Our lab has previously shown that this expansion coincides with a loss of peripheral CD4 T cells due to activation induced cell death. While much research to date has focused on the effects of CD4 T cells on antigen-specific CD8 T cell expansion, little is known regarding the role of CD4 T cells in bystander CD8 T cell expansion. Utilizing models of CD4 knockout mice as well as CD4 depleting antibodies we observed a significant expansion of memory CD8 T cells displaying a CD25-NKG2D+ bystander phenotype following immunotherapy, similar to non-depleted mice. Interestingly, the expanded bystander memory population was enriched from cells of the effector memory phenotype and up regulated Tim-3 and PD-1 in the absence of CD4 T cells. However, they also displayed comparable cytokine production and lytic ability suggesting no functional impairment or exhaustion. While Tim-3 and PD-1 expression have previously been linked to exhaustion, the phenotype described here is consistent with their other known role as acute activation markers on effector/effector memory T cells. These results suggest that CD4 T cells may not be necessary for the expansion and activation of antigen-nonspecific bystander memory CD8 T cells under conditions of strong immune stimulation yet may play a role in regulating the conversion of these bystander cells from a central to effector memory phenotype in secondary lymphoid organs.

#### Authors' details

<sup>1</sup>Dermatology, University of California, Davis, Sacramento, CA, USA. <sup>2</sup>Radiation Oncology, University of California, Davis, Sacramento, CA, USA. <sup>3</sup>Pediatrics, University of Minnesota, Minneapolis, MN, USA.

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<sup>1</sup>Dermatology, University of California, Davis, Sacramento, CA, USA  
Full list of author information is available at the end of the article