Journal for ImmunoTherapy of Cancer

POSTER PRESENTATION Open Access

AKT inhibition mitigates terminal differentiation and preserves central memory phenotype of CD8 T cells

Rasha Abu Eid[1*], Kevin Friedman[2], Mikayel Mkrtichyan[1], Samir N Khleif[1]

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

Introduction

CD8 T cell response comprises effector and memory T cells. Effector CD8 T cells become terminally differentiated and are eliminated by apoptosis. Memory CD8 T cells encompass central (T_{CM}) and effector memory T cells (T_{EM}). T_{CM} display a higher proliferative ability, express a higher level of CD62L and are superior in their protection against viral and bacterial challenges and mediation of anti-tumor immunity when compared to T_{EM}. The differentiation of CD8 T cell is thought to be coordinated by the PI3K/Akt pathway.

Methods

The effect of *in vitro* Akt inhibition using the pan Akt inhibitors MK-2206 and AZD5363 on the differentiation and proliferation of CD8 T cells was examined. Cell proliferation, expansion, cytokine production and phenotype were assessed in antigen specific CD8 T cells.

Results

We found that the inhibition of Akt leads to a significant enhancement of the proliferative potential of CD8 T cells, and to prolongation of their survival upon TCR re-stimulation. Furthermore, we found that Akt inhibition leads to increase in IL-2 secretion, a marker of cells with high proliferative ability. We further identified that Akt inhibition preserved the T_{CM} phenotype by conserving a higher percentage of ($CD44^{HI}$ $CD62L^{HI}$) expressing T cells. These cells also displayed a higher level of CD127 and a lower level of the exhaustion marker KLRG-1 reflecting their increased expansion ability and longevity due to Akt inhibition. Additionally, we found that Akt inhibition also resulted in the preservation of a significantly higher percentage of naïve CD8 T cells ($CD44^{LO}$ $CD62L^{HI}$) when compared to the non-treated cells.

Conclusion

Here, we show that Akt inhibition preserves the central memory phenotype of CD8 T cells thus enhancing their proliferation, survival and cytokine production. Furthermore, Akt inhibition results in the conservation of a reservoir of naïve CD8 T cells. Both naïve and T_{CM} CD8 T cells are superior mediators of anti-tumor immunity when compared to effector or T_{EM} cells. These findings strongly suggest the utility of using Akt inhibitors to modulate the immune response as part of cancer immune therapy.

Authors' details
[1]Georgia Regents University Cancer Center, Augusta, GA, USA. [2]bluebird Bio, Cambridge, MA, USA.

Published: 6 November 2014

doi:10.1186/2051-1426-2-S3-P93
Cite this article as: Abu Eid *et al.*: AKT inhibition mitigates terminal differentiation and preserves central memory phenotype of CD8 T cells. *Journal for ImmunoTherapy of Cancer* 2014 **2**(Suppl 3):P93.

[1]Georgia Regents University Cancer Center, Augusta, GA, USA
Full list of author information is available at the end of the article