



Letter

Are human Vδ2^{POS} T cells really resistant to aging and Human Cytomegalovirus infection?☆


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In their recent paper, Weili Xu et al. [1] described the different behaviors of Vδ1^{POS} and Vδ2^{POS} T cell subsets in response to lifelong stress and claimed that Vδ2^{POS} T cells are not affected by aging and Human Cytomegalovirus (HCMV) infection. While we agree that these two γδ T cell subsets diverge both in phenotype/function and in tissue distribution, we are somewhat surprised that authors did not take into account the several previously published and contradictory experimental evidence in regards to senescence of Vδ2^{POS} T cells [2,3]. These latter studies reported that HCMV infection not only induces a clonal expansion of a distinct Vγ9^{NEG}/Vδ2^{POS} T cell subset, but also determines a concomitant adaptive differentiation from CD27^{high} naïve cells to CD27^{low/NEG} terminal-effectors. However, Weili Xu et al. argued that the expression and kinetics of both CD27 and CD45RA surface markers do not change and follow the homeostatic changes of Vδ2^{POS} T cells. This statement goes in the opposite direction to previously reported findings as the CD27/CD45RA phenotype has been shown to mark the maturation and differentiation (T_{Naïve}, T_{Central-Memory}, T_{effector-Memory} and T_{Effector-Memory RA}) of Vδ2^{POS} T cells. Indeed, the different surface expression of both CD27 and CD45 parallel the progressive decrease of telomere length, the proliferative capacity as well as the different effector-functions and resistance to death of Vδ2⁺ T cells in response to antigens and homeostatic cytokines [4,5].

Hence, we believe that these controversial issues require further discussion beyond the unilateral conclusion given by the study of Weili Xu et al.

Disclosure

Authors do not have any conflicts of interest to declare.

References

- [1] Xu W, Monaco G, Wong EH, et al. Mapping of gamma/delta T cells reveals Vdelta2+ T cells resistance to senescence. *EBioMedicine* 2019;39:44–58. <https://doi.org/10.1016/j.ebiom.2018.11.053>.
- [2] Caccamo N, Dieli F, Wesch D, Jomaa H, Eberl M. Sex-specific phenotypical and functional differences in peripheral human Vgamma9/Vdelta2 T cells. *J Leukoc Biol* 2006;79(4):663–6. <https://doi.org/10.1189/jlb.1105640>.
- [3] Davey MS, Willcox CR, Hunter S, et al. The human Vdelta2(+) T-cell compartment comprises distinct innate-like Vgamma9(+) and adaptive Vgamma9(-) subsets. *Nat Commun* 2018;9(1):1760.
- [4] Caccamo N, Meraviglia S, Ferlazzo V, et al. Differential requirements for antigen or homeostatic cytokines for proliferation and differentiation of human Vgamma9Vdelta2 naïve, memory and effector T cell subsets. *Eur J Immunol* 2005;35(6):1764–72. <https://doi.org/10.1002/eji.200525983>.
- [5] Dieli F, Poccia F, Lipp M, et al. Differentiation of effector/memory Vdelta2 T cells and migratory routes in lymph nodes or inflammatory sites. *J Exp Med* 2003;198(3):391–7. <https://doi.org/10.1084/jem.20030235>.

☆ Rebuttal to “Mapping of γδ T cells reveals Vδ2+ T cells resistance to senescence” by Weili Xu et al

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