Contents lists available at ScienceDirect

# EBioMedicine

journal homepage: www.ebiomedicine.com

EBioMedicine

Published by THE LANCET

Letter

# Are human Vδ2pos T cells really resistant to aging and Human Cytomegalovirus infection?☆

Joanna Mikulak [a,b], Francesco Dieli [c,d,**], Domenico Mavilio [a,b,*]

[a] Unit of Clinical and Experimental Immunology, Humanitas Clinical and Research Center, Rozzano, Milan, Italy
[b] Department of Medical Biotechnologies and Translational Medicine (BioMeTra), University of Milan, Italy
[c] Central Laboratory for Advanced Diagnosis and Biomedical Research, Palermo, Italy
[d] Department of Biomedicine, Neurosciences and Advances Diagnostics (Bi.N.D.), University of Palermo, Italy

In their recent paper, Weili Xu et al. [1] described the different behaviors of Vδ1pos and Vδ2pos T cell subsets in response to lifelong stress and claimed that Vδ2pos 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 Vδ2pos T cells [2,3]. These latter studies reported that HCMV infection not only induces a clonal expansion of a distinct Vγ9neg/Vδ2pos T cell subset, but also determines a concomitant adaptive differentiation from CD27high naïve cells to CD27low/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 Vδ2pos 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 $T_{Effectory-Memory\ RA}$) of Vδ2pos 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 naive, 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.