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Elevated PVR expression on Tfh cells is coupled to increased TIGIT and low effector capacity of HIV specific CD8+ T cells

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During chronic HIV-1 infection, CD8+ T cells display a loss of effector functions; these dysfunction a CD8+ T cells also up-regulate inhibitory molecules such as PD-1, 2B4, CD160, a process referred to as T-cell exhaustion. Recently a new inhibitory molecule, T-cell immunoglobulin and ITIM domain (TIGIT), expressed on T-cells was shown to inhibit their function. In addition its co-stimulatory receptor CD226 and ligand PVR is severely altered in chronic viral infections and human cancers. However, it remains to be identified if the TIGIT/CD226/PVR axis is dysregulated during HIV infection and linked to CD8+ T cell exhaustion. We found an increased expression of TIGIT on bulk and HIV-specific CD8+ T cells that was linked to expression of PD-1, CD160 and 2B4. On HIV-specific cells the increase in TIGIT expression was coupled to a decreased expression of CD226. Furthermore, $TIGIT^{hi}$ cells was less common in elite controller subjects, compared to treatment naïve and long-term treated subjects and the TIGIThi cells were linked to a decreased functional capacity (IFN-γ, TNF, granzyme B & CD107a). As TIGIT needs to bind its ligand, PVR, in order to inhibit T-cell function, we next measured PVR expression on $CD4^+$ T cells in blood and lymph node. PVR expression was elevated on $CD4^+$ T cells, especially T-follicular helper (Tfh) cells which is a major reservoir for HIV-1. In summary, the TIGIT/CD226/PVR axis is altered in HIV-infected subjects, a process which was linked to a decreased functional capacity as well as an up-regulation of PVR on Tfh cells. These findings highlight the importance of the TIGIT/CD226/PVR axis in the context of HIV-infection and demonstrate an immune checkpoint barrier that potentially could hinder future cure approaches mediating cellular killing of HIV-1 infected Tfh cells.

Biography

Annika C Karlsson has completed her PhD at the Karolinska Institutet in December 2000 and continued her Postdoctoral studies at the Gladstone Institute of Virology and Immunology, University of California San Francisco. In 2005 she returned to Karolinska Institutet working as an Independent Research Scientist, Senior Researcher and Group Leader. She has published 38 original articles (12 as co-author) in peer reviewed journals.

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