

Role of cell surface and soluble/extra vesicular immune checkpoint molecules in determining the quality of anti-HTLV-1 CD8 T-cell response

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Background:

Immune checkpoint (ICP) mediators play pivotal roles in regulating a broad spectrum of immune responses against chronic viral infections. In previous studies we have established elevated co-expression pattern of negative checkpoint receptors (NCRs) such as PD-1, TIGIT, LAG-3 etc. on total and antigen-specific CD8 T cells from patients with HTLV-1 associated myelopathy tropical spastic paraparesis (HAM/TSP) in comparison to asymptomatic carriers (AC). Monoclonal antibody blockade strategies targeting these NCRs resulted in improved T-cell activity in correlation with proviral load in patients. Recently, ICPs have been shown to be released in soluble forms and to be carried on the surface of small extracellular vesicles (sEVs) or exosomes.

Methods:

We profiled ICPs in isolated sEVs and culture media of HTLV-1 cell lines representing both ATLL and HAM/TSP using multiplexed Luminex technologies.

Results:

Interestingly, high levels of BTLA (B-and T-Lymphocyte Attenuator) and PD-1 along with their respective ligands, HVEM and PD-L1/2, were observed in both soluble and sEV samples as well as in the sera of HAM patients. HTLV-1 infection, more so the viral protein HBZ, has been linked to factors that enhance sEV release and could serve as causative mechanism for the observed release. Indeed, treatment with antiretroviral drugs significantly reduced ICP levels and HBZ expression in HTLV-1 cell lines.

Conclusions:

Functionality of sEVs carrying these ICPs are being validated in ongoing studies along with their direct role in regulating CD8 T-cell functions and cytolytic potential. This study provides further insights to the role ICPs have in anti-HTLV-1 cellular responses and may contribute to novel immunotherapeutic strategies to reduce disease progression.

Disclosure of Interest Statement:

Nothing to disclose.