Characterizing the transfer of the mobile HTLV-1 accessory protein p8

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Background:
The Human T-cell Leukemia Virus Type 1 (HTLV-1) is an oncogenic delta-retrovirus that predominantly infects $CD4^+$ T-cells. After several decades of latency, HTLV-1 reactivation is associated with Adult T-cell Leukemia/ Lymphoma (ATLL) and inflammatory diseases in infected patients. The accessory protein p8 is a plasma membrane resident protein that induces cellular conduits via which it is transferred to $CD4^+$ T-cells, thereby enhancing viral persistence and infectivity. Until now, p8 transfer is poorly understood and it is not known to which immune cell populations p8 can be transferred to.

Methods:
To characterize p8-transfer, we recently established a flow cytometry-based co-culture assay to quantitate p8-transfer between transiently transfected p8-expressing donor cells and fluorescently-labelled acceptor cells. Moreover, to improve the co-culture assay, we generated stable p8-expressing Jurkat donor cells by lentiviral transduction.

Results:
Here we report that p8-transfer significantly increases with the frequency of p8-positive donor cells while enhancing p8 expression in those cells does not increase p8 transfer. Hence, this suggests that the number of cell-cell-contacts is more important than p8 expression levels for efficient transfer. Thus, subsequent characterization of generated stable p8-expressing Jurkat T-cell lines showed a high frequency of p8-expressing cells with the expected localization of p8 at the plasma membrane. In co-culture experiments, comparison of both transiently transfected and lentivirally-transduced p8-expressing Jurkat donor T-cells revealed that p8 is transferred, albeit at lower frequencies in the latter system. To identify cell populations susceptible to p8-transfer, initial co-culture assays between p8-expressing donor cells and freshly isolated peripheral blood mononuclear cells (PBMCs) demonstrated that p8-transfer could also be measured with our assay confirming earlier data obtained via immunofluorescence.

Conclusion:
Taken together, this study is the first to broadly characterize the conditions of p8-transfer and to allow identification of susceptible immune cell populations.

Disclosure of Interest Statement:
Nothing to declare.