Differential Expression of HIV Envelope Epitopes on the Surface of HIV-Infected Macrophages and CD4+ T Cells

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Background:
HIV-infected macrophages contribute to the persistence of HIV reservoirs in the tissues of people living with HIV on antiretroviral therapy. One potential targeting strategy is the use of antibody-dependent cellular cytotoxicity (ADCC) against infected cells expressing the HIV envelope (Env) protein on the surface. ADCC strategies require the characterisation of exposed Env epitopes and identifying antibodies capable of opsonising them, yet little is known regarding the susceptibility of HIV-infected macrophages to be targeted using this strategy.

Methods:
Monocytes purified from HIV-seronegative donors were cultured into monocyte-derived macrophages (MDM) for 5 days. MDM and activated peripheral blood mononuclear cells (PBMC + IL-2, 10 IU/mL) were then infected *in vitro* with the R5-tropic HIV BaL strain for 7-10 days and 3-4 days respectively. MDM were analysed using flow cytometry and fluorescence microscopy to assess productive infection (intracellular HIV p24), and surface expression of Env (using antibodies targeting different epitopes); which was then compared to the expression of Env on CD4+ T cells from PBMCs.

Results:
Our results reveal potential differences in epitope expression on macrophage- and T cell-expressed Env. Notably, HIV_{BaL}-infected macrophages were more susceptible to opsonisation by NIH45-46 and 17b antibodies (median=37.2% and 28.2% respectively) compared to infected T cells (median=15.4% and 2%; p=0.002 and 0.004 respectively), which were susceptible to opsonisation by PG16 (median=27.2%) compared to MDM (median=7.9%, p=0.004). Furthermore, some neutralising antibodies used were ineffective at opsonising cell-surface Env, indicating that it may be presented differently to Env on cell-free virions.

Conclusion:
Here we show that HIV-infected macrophages may display a distinct surface Env epitope profile compared to infected T cells. The differential Env epitope expression between macrophages and T cells suggest that cell-type dependent differences alter binding of anti-Env antibodies. This impacts the efficacy of antibody-mediated targeting approaches and will inform the development of future cure strategies.

Disclosure of Interest Statement:

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