EXAMINING THE ROLE OF HUMAN MONONUCLEAR PHAGOCYTES IN MEDIATING SEXUAL TRANSMISSION OF HIV

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Anogenital dendritic cells (DC) and macrophages are amongst the first cells to encounter HIV during sexual intercourse. DCs play a crucial role in transmission as they efficiently transfer the virus to CD4 T cells in which HIV explosively replicates. Firstly, an early phase of transfer occurs which is dependent on C-type lectin receptor mediated HIV uptake by DCs and rapidly declines with time. Later, a second phase occurs which increases with time as newly formed virions bud off from the plasma membrane as result of virus that has infected the DC via the classical CD4/CCR5 mediated route. It is currently unclear if macrophages can also mediate this process.

Human skin is known to contain several mononuclear phagocyte subsets (MNP). Langerhans cells have been shown to transfer HIV to T cells in both vagina and foreskin. However whether MNPs in the underlying dermis and lamina propria of anogenital tissue also transfer HIV to T cells is yet to be studied. This is a critical gap in the literature as it is becoming clear that transmission of HIV is strongly associated with mucosal trauma and inflammation.

We have developed an HIV MNP - T cell transfer assay and compared the ability of all known human tissue MNP subsets to transfer HIV to T cells. We find that Langerhans cells, cDC2, and CD14 monocyte-derived macrophages are all very efficient at mediating HIV transfer in both phases, autofluorescent macrophages mediate transfer in the first phase and that cDC1 cannot mediate transfer in either phase. Critically we show that a subset of dermal cDC2 that express langerin are enriched in anogenital tissues and that these are the most efficient at mediating this process.