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Oral presentation

Dendritic cells sample HIV-1 through an intestinal epithelial cell monolayer

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The intestinal mucosa is a preferential portal of entry for HIV-1 during mother-to-child transmission. Oral infection is also a well documented route for transmission of HIV-1 in neonates. Neonates can acquire the disease by breast-feeding, moreover presence of blood in gastric aspirates of neonates born to HIV-1 infected mothers has also been incriminated as a risk factor in the transmission of HIV-1. Multiple mechanisms for mucosal HIV-1 transmission have been proposed, however the exact role played by dendritic cells in facilitating viral passage across intestinal epithelium have not been fully defined. We had hypothesized that sub-mucosal dendritic cells (DCs) can mediate mucosal transmission of HIV-1 through a process similar to bacterial sampling through gastrointestinal epithelium (Rescigno M., Nat.Immun.2001).

An *in vitro* transwell co-colture system of colonic cell line Caco-2 and DCs was developed. DCs collected on transwell after incubation on the apical side of Caco-2 monolayer with cell-free HIV-1 (R5 and X4 phenotype), were able to transfer infection efficiently to susceptible target cells. Abundant HIV-1 replication (as measured by p24 antigen ELISA until day 25 of DCs-T cells co-culture) was reproducibly observed, suggesting that DCs sampled the virus and transferred it to target cells. DCs retained infection capability for at least 4 days. Confocal microscopy showed intense migration of DCs through the tight junctions of Caco-2, following incubation with HIV-1, at a level comparable to LPS treated cultures (positive control), thus indicating that HIV-1 promotes DCs migration through an epithelial monolayer. This process, already evident after 30 min, reached a peak at 4 h 30 min. GFP-labeled HIV-1 or p24 antigen was detected on the apical side of the Caco-2 monolayer and inside the migrated DCs. Transmission electron microscopy confirmed the localization of HIV-1. Thus, our results show that in the *in vitro* model DCs migrate through intestinal epithelial cells (IECs) to explore the luminal surface in the presence of HIV-1, are able to uptake the virus and to infect susceptible target cells. The molecular mechanisms underlying HIV-1 induced DCs migration across IECs, and consequent implication for mother-to-child transmission, will be discussed.

Our results clarify the earliest events in the establishment HIV-1 infection at mucosal level and so are of outmost relevance for the development of an effective preventative vaccine.