HIV

DCeiving HIV

First impressions can be deceptive say the authors of a new study published in *Blood*. Previous studies have shown that HIV-1 exploits the natural trafficking of dendritic cells (DCs) to establish infection in $CD4^+$ T cells. DC-SIGN (CD209) — which is expressed by certain DC subsets, such as those in genital mucosa — is a C-type lectin that binds the HIV-1 envelope glycoprotein gp120 and facilitates virus entry into DCs. As these immature DCs migrate to draining lymph nodes they carry the virus with them, where HIV-1 can then be transferred to permissive T cells. However, Schwartz and colleagues have now shown that DC-$SIGN^+$ DCs might not provide such a 'free' ride after all.

Using the B-cell line C1RA2 as a model system, they confirmed that cells expressing DC-SIGN internalize HIV-1 particles more efficiently than do wild-type C1RA2 cells. However, in both DC-$SIGN^+$ C1RA2 cells and primary immature DCs, internalized virus particles were rapidly degraded in an endo-lysosomal compartment. So, if HIV-1 does not have 'protected' status in DC-$SIGN^+$ cells, can it enter the antigen-presentation pathway and be recognized by the immune system?

The authors compared the ability of wild-type and DC-$SIGN^+$ C1RA2 cells to activate HIV-specific $CD8^+$ T-cell lines isolated from infected patients. After exposure to non-infectious HIV virions, only the DC-$SIGN^+$ cells could induce interferon-γ production by the $CD8^+$ effector T cells. The importance of DC-SIGN for MHC class-I-restricted presentation of virus antigens was confirmed by the addition of DC-SIGN-specific monoclonal antibodies to primary DCs. The resulting inhibition was only partial however, which indicates that other receptors, including CD4 and possibly other lectins, are involved in the necessary virus uptake and fusion. The pathway was further characterized by showing that the MHC class-I-restricted peptides are derived from a small number of virions that enter the cytosol (after membrane fusion) and are degraded by the proteasome, rather than from the majority of virions that are degraded in the endo-lysosomal compartment.

Therefore, the DC 'safe haven' might not be quite so safe. But, how can rapid virus degradation be reconciled with the ability of DCs to transmit HIV-1 to T cells for several days after initial exposure? The authors suggest that cell contact between DCs and T cells in lymph nodes might make the transmission process so efficient that only small amounts of virus that avoid degradation are required. Alternatively, HIV-1 could replicate in DCs at low levels, so that progeny virions rather than captured virions could be transmitted to T cells.

Kirsty Minton

References and links

ORIGINAL RESEARCH PAPER Moris, A. *et al.* DC-SIGN promotes exogenous MHC-I restricted HIV-1 antigen presentation. *Blood* 23 October 2003 (doi:10.1182/blood-2003-07-2532)
FURTHER READING van Kooyk, Y. & Geijtenbeek, T. B. H. DC-SIGN: escape mechanism for pathogens. *Nature Rev. Immunol.* **3**, 697–709 (2003)