

POSTER 3

GLYCOSPHINGOLIPID COMPOSITION OF HIV-1 PARTICLES IS A CRUCIAL DETERMINANT FOR DENDRITIC CELL-MEDIATED HIV-1 TRANS INFECTION

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Interactions of HIV-1 with dendritic cells (DCs) are multifactorial and presumably require non-redundant interactions between the HIV-1 envelope glycoprotein gp120 and molecules expressed on DC surface that define the cellular fate of the virus particle. Surprisingly, neutralization of HIV-1 envelope glycoprotein gp120 dependent-binding interactions with DCs was insufficient to prevent HIV-1 attachment. Besides gp120, HIV-1 particles also express host cell-derived proteins and lipids in their particle membrane. In this study, we demonstrate a crucial role for host cell derived glycosphingolipids (GSL) for the initial interactions of HIV-1 particles with both immature and mature DCs. Production of HIV-1 particles from virus producer cells treated with ceramide synthase inhibitor, fumonisin B1 (FB1) or glucosylceramide synthase inhibitor, PDMP (1-phenyl-2-decanoylamino-3-morpholino-1-propanol), resulted in virus particles that though capable of binding previously defined HIV-1 gp120-specific attachment factors, CD4, DC-SIGN and syndecans, were attenuated in their ability to be captured by both immature and mature DCs. Furthermore, GSL-deficient HIV-1 particles were inhibited in their ability to establish productive infections in DC –T cell co-cultures. These studies provide initial evidence for the role of HIV-1 particle membrane associated GSLs in virus invasion of DCs and provide additional novel cellular targets, GSL biosynthetic pathways and GSL-dependent HIV-1 interactions with DCs, for development of anti-retroviral therapy.