

POSTER 1**HIV-1 gp120 INDEPENDENT CAPTURE OF VIRUS PARTICLES BY DENDRITIC CELLS IS DEPENDENT ON INCORPORATION OF LIPID RAFT-SPECIFIC HOST CELL DETERMINANTS IN THE VIRUS PARTICLE**

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Though HIV-1 interactions with dendritic cells (DCs) have long been thought to require the virus envelope glycoprotein, gp120, it has become increasingly evident that virus particles can be captured by DCs in a gp120-independent manner. To understand the mechanism of the gp120-independent interactions with DCs, we have developed a novel FACS based assay that utilizes HIV-1 Gag-eGFP containing virus-like particles (VLPs). Similar to infectious HIV-1 particles, capture of HIV-1 Gag-eGFP VLPs by DCs was greatly enhanced upon maturation in a dose-dependent manner that follow receptor-ligand kinetics. Interestingly, capture of Gag-eGFP VLPs by mature DCs could be competitively inhibited by MLV-Gag VLPs, but not VSV (vesicular stomatitis virus) VLPs. Furthermore, capture of myristoylated matrix-deficient HIV-1 Gag-eGFP VLPs that bud indiscriminately from all cellular membranes was decreased ~5-fold upon challenge of mature DCs. HIV-1 MA contains two discrete basic regions that govern specificity of Gag-membrane association. Interestingly, HIV-1 matrix mutants, MA-29/31-KE (lysine to glutamic acid mutation at amino acids 29 and 31) and MA-85YG (tyrosine to glycine mutation at amino acid 85), but not MA-29/31-KT (lysine to threonine mutations at positions 29 and 31), were also deficient for capture by mature DCs, suggesting that virus particle budding from specific lipid raft-like plasma membrane microdomains is necessary for acquisition of DC-binding determinants. Captured HIV-1 Gag-eGFP VLPs trafficked to discrete intracellular compartments within mature DCs that were subsequently re-localized to DC – T cell infectious synapses upon T cell contact suggesting that trafficking of HIV-1 Gag-eGFP VLPs is similar to that of infectious HIV-1 particles in mature DCs. To investigate the effect of MA-deficiency on virus replication in DC – T cell co-cultures, single-cycle infectivity analysis was performed. Interestingly, MA-deficient HIV/Lai virus particles that were similar to wild type HIV/Lai in their ability to establish productive infection in single cycle infectivity analysis in GHOST/CD4/CXCR4 reporter cells were 5 – 10 fold less infectious than wild type virus particles in single cycle infectivity analysis in autologous DC – T cell co-cultures. These results suggest that lipid raft-specific MA-dependent incorporation of host cell determinants is crucial for establishment of productive HIV-1 infection in DC – T cell co-cultures.