

# HIV assembly in monocytic cells

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The assembly of human immunodeficiency viruses occurs at the plasma membrane of infected cells. In macrophages this assembly is focussed on a sub-domain of the plasma membrane that is sequestered within the cytoplasm and is connected to the cell surface by narrow membrane channels [1]. This compartment, which is present in uninfected cells, contains the tetraspanins CD81, CD9 and CD53 and is distinct from EEA-1 containing early endosomes as well as late endosomes/lysosomes. It is also morphologically highly complex with internal vesicular, tubular and 'sponge-like' arrays of membrane that label for the tetraspanins and in some cases are connected to the limiting membrane. The compartment contains the lipid phosphatidylinositol 4,5 bisphosphate (PI(4,5)P<sub>2</sub>), which is required for HIV Gag targeting to the plasma membrane. In HIV infected cells, but not in uninfected cells, the compartment also contains the tetraspanin CD63, which has been linked to HIV assembly in other cell systems. However, CD63 is not required for the assembly of infectious virus in macrophages and viruses produced from CD63 negative cells are fully infectious when assayed on reporter cell lines. Transfection experiments indicate that both HIV Env and Gag can target the assembly compartment independently, though the molecular basis to this targeting remains unclear.

The macrophage virus-containing compartment resembles sites in monocyte-derived dendritic cells where virus particles are sequestered during DC-SIGN-mediated trans infection of T cells through virological/infectious synapses [2]. We propose that the compartment targeted by HIV in monocytic cells has a role in the formation and/or function of immune synapses that is subverted by the virus to facilitate its cell-to-cell transmission.

## References

- [1] Deneka, M., Pelchen-Matthews, A., Byland, R., Ruiz-Mateos, E. and Marsh, M. (2007) HIV-1 assembly in macrophages occurs in an intracellular compartment enriched for the tetraspanins CD81, CD9 and CD53. *J. Cell Biol.* 177: 329-341.
- [2] Garcia, E., Nikolic, D.S. and Piguet, V. (2008) HIV-1 Replication in Dendritic Cells Occurs Through a Tetraspanin-Containing Compartment Enriched in AP-3. *Traffic* 9, 200-214.