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HIV-1 assembly in human macrophages: From Gag synthesis to virus release

R Gaudin*[1], M Schindler[2], P Benaroch[1]

[1]Institut Curie - INSERM U932, France, [2]Heinrich-Pette-Institut, Germany

The Human Immunodeficiency Virus (HIV) has two main targets: CD4+ T lymphocytes and monocytes/macrophages. Markedly different viral assembly has been observed in these two cell types. Whereas virions bud at the cell surface in T cells, particles accumulate, mature and are stocked into intracellular compartments in macrophages. Despite the importance held by macrophages as viral reservoirs, the dynamics of the HIV assembly process remains elusive and effective molecular tools to study this are lacking.

To better understand the HIV assembly process in live primary cells, we characterized the validity of a recombinant HIV virus NL4-3 Gag-iGFP (NLGG) as a tool for the study of viral assembly in macrophages. This virus encodes for a GFP inserted between matrix and capsid of the Gag precursor, flanked by two viral protease cleavage sites. (adapted from Hübner et al, 2007).

NLGG was able to infect, replicate and bud into intracellular compartments in human primary macrophages similarly to NLAD8 (wild type virus). Then, we used a ΔEnv NLGG virus to perform kinetics of the viral production cycle in macrophages by monitoring them for 5 days. Gag-iGFP was first detected as diffuse staining in the cytosol. Then, 24h to 48h later, Gag-iGFP positive intracellular compartments were observed, followed by large secretion events. Confocal analysis of fixed NLAD8-infected macrophages confirms that secreted events also occur in the wild type virus and are Env positive and Lamp1 negative. By TIRF microscopy, we documented Gag secretion events of relatively large compartments (up to 2 μm diameter). Altogether, our data suggest that intracellular viral compartments in primary human macrophages can fuse with the plasma membrane to release virions.

This study sheds light on the dynamics of the HIV assembly process in macrophages and represents the first steps to a better understanding of the secretion mechanisms essential to designing anti-HIV treatments.

Keywords: HIV-1, Human macrophage, Gag trafficking, Viral release