Retrovirology

BioMed Central

Oral presentation

HIV-1 internalization in polarized human trophoblasts occurs through a peculiar endocytic pathway

Michel J Tremblay* and Gaël Vidricaire

Address: Centre de Recherche en Infectiologie, Centre Hospitalier de l'Université Laval, and Département de Biologie médicale, Université Laval, Québec (QC), Canada

* Corresponding author

from Fourth Dominique Dormont International Conference. Host-Pathogen Interactions in Chronic Infections
Paris, France. 13-15 December 2007

Published: 9 April 2008

Retrovirology 2008, **5**(Suppl 1):O5 doi:10.1186/1742-4690-5-S1-O5

This abstract is available from: http://www.retrovirology.com/content/5/S1/O5

Background

In human trophoblastic cells, a correlation between early endosomal trafficking of HIV-1 and virus infection was previously documented. However, if HIV-1 is massively internalized in these cells, the endocytic pathway(s) responsible for viral uptake is still undefined.

Materials and methods

The process through which HIV-1 is endocytosed was studied using different reagents (e.g. chlorpromazine, cholera toxin B, water-soluble cholesterol, colchicine, cytochalasin B, filipin, jasplakinolide, methyl-beta-cyclodextrin, paclitaxel, and vinblastine) and experimental strategies (e.g. transfection of JAR cells with various expression vectors, virus internalization test, infection assay, confocal laser scanning, co-localization analysis and digital image preparation).

Results

Amongst all the putative endocytic pathways present in polarized trophoblastic cells, we demonstrate that HIV-1 infection of these cells is independent of clathrin-mediated endocytosis and macropinocytosis. Importantly, treatment with the cholesterol-sequestering drug filipin severely impairs virus internalization, whereas the cholesterol-depleting compound methyl-beta-cyclodextrin has no impact on this pathway. Moreover, viral internalization is unaffected by overexpression of a mutant dynamin 2 or treatment with a kinase or tyrosine phosphatase inhibitor. Thus, HIV-1 infection in polarized trophoblastic cells occurs primarily via a clathrin-, caveolae-, and dynamin-independent pathway requiring free cholesterol. Notably, even though HIV-1 did not initially co-localize with transferrin, some virions migrate at later time points to transferrin-enriched endosomes, suggesting an unusual transit from the non-classical pathway to early endosomes. Finally, virus internalization in these cells does not involve the participation of microtubules but relies partly on actin filaments.

Conclusions

We demonstrate that HIV-1 internalization in polarized human trophoblastic cells occurs primarily via a clathrin-, caveolea-, and dynamin-independent pathway which is sensitive to a cholesterol-sequestering drug.