Role of Rab proteins in the formation of HIV-1 particles

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Poster presentation

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Marina Caillet*[1,2], Delphine Delcroix[1,2], Katy Janvier[1,2], Stéphane Emiliani[1,2] and Clarisse Berlioz-Torrent[1,2]

Address: [1]Institut Cochin, Université Paris Descartes, CNRS (UMR 8104), Paris, France and [2]INSERM, U567, Paris, France
* Corresponding author

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The production of HIV-1 particles during the late steps of viral multiplication cycle corresponds to the assembly, the budding and the release of infectious viral particles in the extracellular medium. These steps require the integrity of two viral structural components: the Gag precursor, essential for HIV assembly and budding, and the envelope glycoprotein (Env) which confers the infectivity to the virus after its incorporation into the viral Gag particles.

The last steps of the viral cycle involve a series of molecular and cellular events based on interactions between viral proteins and cellular proteins that are implicated in the vesicular intracellular trafficking, such as the ESCRT machinery, the AP clathrin adaptors or the cellular cofactor TIP47. Although several interactions between viral proteins and cellular cofactors have been described, the identification of new cellular partners is crucial in order to understand the complex interplay between HIV-1 and the host cell during the late steps of the HIV cycle. To characterize new cofactors involved in HIV assembly, we decided to assess the role of Rab proteins, key regulators of vesicular intracellular trafficking in the infectious viral particles production.

For this purpose, we developed several virological tests based on the specific interference RNA targeting Rab proteins (Rab1, Rab4, Rab5, Rab6, Rab7, Rab8, Rab9 and Rab11). We show that Rab7 plays a major role on HIV-1 replication. We observed that HIV-1 (NL4-3 strain) failed to propagate in the reporter cells (HeLa P4R5 - stably expressing CD4 and CCR5) upon siRNA-induced depletion of Rab7. Using a single cycle infection assay, we showed that Rab7 depletion causes a decrease of HIV-1 release from the producer cells. Moreover, Rab7 depletion modified Gag processing and the infectivity of the produced particles, a defect usually observed upon TSG101 depletion.

Altogether, our data highlight a key role of Rab7 in the morphogenesis of new infectious HIV particles. This work is funded by ANRS, SIDACTION, ANR-07-JCJC-0102 programs and is part of the activities of the HIV-ACE research network (HEALTH-F3-2008-201095) supported by a grant of the European Commission, within the Priority 1 "Health" work programme of the 7th Framework Programme of the EU.