A role for the tetraspanin CD81 on the late steps of HIV-1 replication in T-lymphoblastic cells

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Background

HIV-1 uses cellular co-factors for virion formation and release, and is able to incorporate host cellular proteins in the viral particles, such as tetraspanins which serve as gateways for HIV-1 egress. Here, we investigated the implication of several tetraspanins on HIV-1 formation and release in chronically infected T-lymphoblastic cells, a model that permits the study of the late steps of HIV-1 replication in persistent infected cells.

Methods

HIV-1 infected MOLT cells were analyzed for HIV-1 production by RT assays and Western blot analysis. Gag-Tetrapanins associations were analyzed by immunoprecipitations in the purified virions and in the infected cells and by immunofluorescence confocal microscopy analysis. Down-regulation of CD81 expression in HIV-1 chronically infected MOLT cells was performed by shRNA lentiviral vectors and infectivity was monitored on SupT1 cells.

Results

Our data revealed that HIV-1 Gag and Env structural proteins colocalized with specific tetraspanins in the form of clusters at the cell surface. Co-immunoprecipitation experiments showed that viral Gag proteins interact, directly or indirectly, with the CD81 tetraspanin, and less with CD82, but not with Lamp2 or CD45, in tetraspanin-enriched microdomains composed of CD81/CD82/CD63.

When HIV-1 producing cells were treated with anti-CD81 antibodies or upon CD81 silencing by RNA interference, HIV-1 release was significantly impaired and its infectivity on SupT1 lymphocytes was modulated. We observe that CD81 downregulation in HIV-1 infected T-lymphoblastic cells resulted in Gag redistribution at the cell surface and an increase in infectivity.

Discussion

Our results highlight a critical role for CD81 on HIV assembly in T lymphoblastic cells [1], which was also reported in HIV-1 infected monocytes derived macrophages [2], and on HIV transmission in CD4+ T cells [3] and dendritic cells [4]. In addition, our findings extend the notion that even if HIV-1 assembly can occur on tetraspanin-enriched microdomains containing CD81, the incorporation of CD81 in the viral particles restrict HIV-1 infectivity. This notion can be extend to other cell membrane proteins, such as Hdlg, a cell-cell junction protein, that can also modulate HIV-1 infectivity [5].

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