TIP47 is required for the production of infectious HIV-1 particles from primary macrophages

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Poster presentation

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Macrophages are, along with T CD4+lymphocytes, the major targets of HIV-1 infection and play a key role in viral pathogenesis as a significant reservoir. Identification of the cellular cofactors involved in the production of infectious HIV-1 from macrophages is thus crucial. Nevertheless molecular mechanisms allowing the production of infectious particles from macrophages are not entirely deciphered. In this study, we investigated the role of the cellular cofactor TIP47 in HIV-1 morphogenesis in primary macrophages. Our data show that TIP47 is essential for HIV-1 infectivity and propagation. Mutations in HIV-1 Gag or Envelope (Env) proteins, which abolish interaction with TIP47, impair HIV-1 propagation and infectivity preventing colocalization of Gag and Env, and thereby inhibiting Env incorporation into virions. Whereas disruption of Gag-TIP47 interaction increases slightly Gag particles production, impaired Env-TIP47 binding reduces Gag particles release and, strikingly, induces their retention in the viral assembly compartments. Thus, as in T lymphocytes, TIP47 is critical for the efficient release of infectious HIV-1 particles from the assembly compartment of primary macrophages, making TIP47 a new potential therapeutic target for limiting HIV-1 infectivity and spreading. 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.