Interactions between Nef and AIP1 proliferate multivesicular bodies and facilitate egress of HIV-1
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Abstract (provisional)

Background

Nef is an accessory protein of primate lentiviruses, HIV-1, HIV-2 and SIV. Besides removing CD4 and MHC class I from the surface and activating cellular signalling cascades, Nef also binds GagPol during late stages of the viral replication cycle. In this report, we investigated further the ability of Nef to facilitate the replication of HIV-1.

Results

To this end, first the release of new viral particles was much lower in the absence of Nef in a T cell line. Since the same results were obtained in the absence of the viral envelope using pseudo-typed viruses, this phenomenon was independent of CD4 and enhanced infectivity. Next, we found that Nef not only potentiates a consensus motif for but also binds AIP1, in vitro and in vivo. AIP1 is the critical intermediate in the formation of multivesicular bodies (MVBs), which play an important role in the budding and release of viruses from infected cells. Indeed, Nef proliferated MVBs in cells, but only when its AIP1-binding site was intact. Finally, these functions of Nef were reproduced in primary macrophages, where the wild type but not mutant nef proteins led to increased release of new viral particles from infected cells.

Conclusions

We conclude that by binding GagPol and AIP1, Nef not only proliferates MVBs but also contributes to the egress of viral particles from infected cells.