Production of HIV-1 proteins from “defective” HIV-1 provirus

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RESULTS

Western blots demonstrating cellular expression of HIV-1 proteins in two HM9 single-cell clones: one harboring an intact provirus and the other one harboring “defective” protein. Consistent with the DNA data, western blots revealed the presence of Gag p55/p24 and Env gp120 gp41 proteins in both clones and a complete absence of RT p66/p51 and integrase protein in the “defective” provirus clone.

SUMMARY

Greater than 95% of proviruses detected in circulating PBMCs of ART-treated patients have been characterized as “defective”, since they lack the ability to encode intact viruses. We have recently shown that these “defective” proviruses are capable of transcribing novel protein-coding HIV-RNA species in patients at all stages of HIV-1 infection (Imamichi et al., 2016). In the present study, we demonstrated the emergence of defective proviruses during in vitro infection and their association with HIV-1 protein production in the absence of intact virions.

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The presence of “defective” proviruses in HIV-infected patients has been well documented (Li et al., 1991; Imai et al., 1991; Sanchez et al., 1997; Ho et al., 2013; Imamichi et al., 2014; Bruner et al., 2016). As these defective proviruses are unable to encode intact viruses, the current consensus view of “defective” proviruses is that these are dead-end products that do not give rise to progeny virus and thus collectively represent “graveyard” of viruses. These “defective” proviruses are thought to be biologically irrelevant and of little significance to HIV-1 pathogenesis. Contrary to this notion, we have recently reported that these “defective” proviruses transcribe novel protein-coding RNA species in HIV-infected patients on combination antiretroviral therapy including those with low-level p24 antigenemia (<50 copies/ml) (Imamichi et al., 2016). In the present study, we demonstrate the emergence of these defective proviruses during in vitro infection and their association with HIV-1 protein production in the absence of intact virions.

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