VIRAL FACTORS INVOLVED IN ADAPTER-RELATED PROTEIN COMPLEX 2 ALPHA 1 SUBUNIT-MEDIATED REGULATION OF HUMAN IMMUNODEFICIENCY VIRUS TYPE 1 REPLICATION

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Abstract. The presence of siRNA against adapter-related protein complex 2 alpha 1 subunit (AP2α) enhances human immunodeficiency virus type 1 (HIV-1) replication by up-regulating nuclear transport of viral genome. In this report, we examined possible viral factors involved in AP2α-mediated regulation of HIV-1 replication, namely, Gag matrix protein (MA), integrase (IN) and Vpr. Replication of mutant viruses lacking the nucleophilic property of one of these viral proteins was significantly enhanced by treating cells with AP2α siRNA, indicating that Gag MA, IN or Vpr is not specifically involved in AP2α-mediated enhancement of viral replication. In contrast, AP2α siRNA showed no effect on the level of gene transduction mediated by HIV-1-derived lentiviral vector (LV). Although virus-like LV particle and parental HIV-1 particle are composed of almost equivalent viral structural proteins, LV particles lack three accessory proteins, Vif, Vpr and Vpu, and a large portion of the HIV-1 genome. Vif, Vpr and Vpu were dispensable for AP2α siRNA-mediated enhancement of HIV-1 replication, indicating that a particular part of the HIV-1 genomic fragment deleted in the LV genome might be required for the enhancing effect of AP2α siRNA on viral replication. Taken together, these results suggest that an as yet undetermined gene fragment of the HIV-1 genome is involved in AP2α-mediated regulation of HIV-1 replication.

Keywords: HIV-1 replication, viral factors, AP2α siRNA

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