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Hiv-1 Matrix Protein P17 Initiates Virus Assembly

By Galina Vorkunova, Tatiana Gorodnicheva, Sergei Lupandin & Alissa Bukrinskaya

D.I. Ivanovsky Institute of Virology, Moscow, Russia

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MA is cleaved from Gag precursor by viral protease early in infection and is transported into the nuclei where it associates with viral RNA (vRNA). The complex MA-vRNA is transported to plasma membrane – the place of HIV assembly - using MA membranotropic signal and phosphorilation.

Mutant MA (M4) prepared by Dr. Dupont (USA, Worchester, Medical School) used in association with vRNA lost membranotropic signal and can not move to the plasma membrane. It was located in the nuclei and cytoskeleton. It could be suggested that mutant MA "get stuck" during cellular transport. That localization unusual for wild HIV-1 could suggest that wild MA complex with vRNA delivers vRNA from the nucleus to the plasma membrane through cytoskeleton.

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I. Introduction

The assembly of HIV-1 and the pathogenesis of infection are still not fully understood. Some authors believe that in the case of retroviruses Gag protein penetrates into the nuclei and connects with vRNA (7-9). The other authors (10) show that Gag interacts with vRNA in the cytoplasm where the assembly of HIV-1 initiates.

Our data show that the interaction of vRNA with viral protein still takes place in the nucleus, but we also show that vRNA interacts in the nuclei not with Gag protein but with its part - matrix protein. Thus in the process of initiation of HIV infection is involved not Gag but its part - matrix protein (MA). This protein resides on the N terminus of Gag precursor, and a membranotropic signal within the matrix protein is responsible for Gag protein transport to the plasma membrane where the viral assembly takes place.

Early in infection MA is cleaved from Gag protein by viral protease (11) and due to the three transport signals (membranotropic, nucleophylic and the signal of nuclear export) MA is considered as the cell shuttle protein circulating between nucleus and cytoplasm.

We have shown that the cleavage of MA from Gag precursor by viral protease takes place very early after Gag synthesis (Fig.1) and cleaved MA is involved into viral assembly. With the help of the nucleophylic signal (4) MA penetrates into the nuclei and associates there with vRNA. Thus, it could be suggested that initiation of HIV-1 viral infection unlike the other retroviral infections takes place using not Gag protein but only its part -matrix protein.

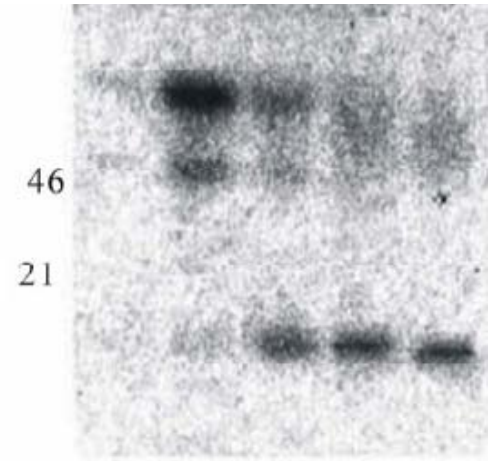

Fig.1

Intracellular localization of Gag and MA in cytoplasmic fraction of MT4 cells. Pulse-chase experiment. MT4 cells were infected with HIV-1 (strain MVP- 899). 14C leucine was added 20 hours after cell infection for 20 min. (pulse). Then the cells were washed with phosphate buffer (PBS) and the label incubated for 1,2 and 3 hours (chase). After that the cells were washed and fractionated on cytoplasm, membranes and nuclei as described (3, 4). As seen on figure 1, the amount of Gag is cytosol is smaller after 1 hour while the amount of MA (p17) is significantly increased during 2-4 hours after infection. This suggests that MA is cleaved from Gag protein in the cytoplasm very soon after its synthesis. The nuclei during this time did not contain the viral proteins.

Authors α σ ρ ω: D.I. Ivanovsky Institute of Virology, Moscow, Russia.

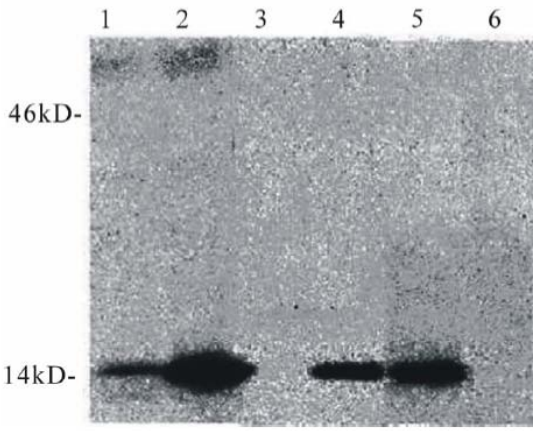

Fig. 2

It was shown earlier that in the cell membranes and in the nuclei MA is associated with vRNA (4, 5). Fig. 2 shows the MA localization in T cells 24 hours after transfection by plasmids containing MA of wild type (lanes 1, 3, 5) or by mutant MA type M4 (2, 4, 6) which had no membranotropic signal. The mutant was prepared by S. Dupont. The cells infected with mutant MA could not induce HIV-1 infection, and was not found in cellular membrane but in the nuclei and cytoskeleton. We suggest that the mutant get stuck in the earlier points of the cell transport and that the complex wild MA-vRNA is transported to the plasmamembrane through cytoskeleton.

References Références Referencias

1. Bukrinskaya A., Ghorpade A., Heinzinger N. et al.(1996). Phosphorilation-dependent HIV-1 infection and nuclear targeting of viral DNA. PNAS USA, 95, 367-371.
2. Bukrinskaya A.(2007) HIV-1 matrix protein: a mysterious regulator of the viral life cycle. Virus Res.124, 1-11.
3. Bukrinskaya A., Vorkunova G., Tenzov Yu.(1992). HIV-1 matrix protein p17 resides in the cell nuclei in association with genomic RNA. AIDS Res.Hum.Retroviruses , 1795-1801.
4. Bukrinskaya A.,Vorkunova G., Tenzov Yu.(1993). HIV-1 matrix protein is transported into cell nucleus and associated with viral RNA. Mol.Biolog. (rus) 27, 49-57.
5. Bukrinsky M., Haggerty S., Dempsy et al.1993 A nuclear localization signal within HIV-1 matrix protein that governs infection of nondivided cells. Nature 365,666-669.
6. Garbit- Hirst R.,Kenney S.,Parent I. 2009. Genetic evidence for a connection between Rous Sarcoma Virus Gag Nuclear trafficking and genomic RNA packaging. J.Virol. 83, 6790-6797.
7. Gudleski N., Flanagan J., Ryan E. et al. 2010. Directionality of nucleocytoplasmic transport of the retroviral gag protein depends on sequential binding of kariopherins and viral RNA. PNAS USA, 107, 9358-9363.
8. Kemler I., Merhan A. 2010. EM Live cell coimaging of the genomic RNAs and Gag proteins of two lentiviruses. J. Virol.84.6352-6366.
9. Kutluay S., Bieniasz P. 2010. Analysis of the initiating events in HIV-1 particle assembly and genome packaging. PlOS Pathogens, 6, 1-11.
10. Vorkunova G., Lupandin S., Bukrinskaya A. HIV-1 matrix protein p17 initiates virus assembly. Molecular biology (rus.) 2011, 45, 5, 879-883.