Optical Trapping 'Virometry' as a tool for assessing HIV diversity and the impact of viral heterogeneity on immunodeficiency virus type 1 (HIV-1) transmission.

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Abstract

Optical tweezers/two-photon fluorescence microscopy has been used to manipulate and study individual HIV virions. This technique allows for the quantification of viral proteins and the assessment of viral envelope heterogeneity at the single virion level. Here, we use optical tweezers and two-photon fluorescence microscopy to study the incorporation of Vpr protein in HIV virions. We find that each HIV virion incorporates a random number of Vpr molecules fused to green fluorescent protein (GFP), as revealed by two-photon fluorescence (TPF) imaging of individual virions. This broad distribution implies substantial heterogeneity of the envelope spike protein content for single virions in culture media. We measured the quantity of monoclonal antibodies specific for HIV-1 envelope glycoprotein gp120, revealing that each HIV-1 virion incorporates a random number of Vpr molecules fused to GFP with a range of 3-128 molecules per virion. By using fluorescence-based immunodecytometry, we show that the fraction of virions with env gene rearrangements, detected by immunodecytometry for cells, is inversely correlated with the fraction of virions with envelope glycoprotein gp120. Our results suggest that the envelope glycoprotein content of HIV virions is heterogeneous at the single virion level, which may have implications for HIV transmission and the development of effective antiviral therapies.

Conclusions

(1) Single HIV-1 can be optically manipulated in culture media "contact-free." (2) Optical trapping 'virometry' allows multi-parameter analysis of single HIV-1. (3) Individual HIV-1 dramatically differs in gp120 and Vpr contents. (4) A minimum of two trimeric spikes is required for the optimal infectivity of HIV-1.

Implications

Individual virions differ in their ability to infect host cells, "elite" viruses.

Facts

- Virus infection is not chain reaction. (Kearney et al., PNAS, 2008, 105: 7552-7)
- Transmitted virus is enriched for higher Env content. (Kearney et al., PNAS, 2010, 107: 26426-31)
- "Each such event is a kill" of the majority of the earliest stages of HIV infection.

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