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Targeted femtosecond laser driven drug delivery within HIV-1 infected cells: In-vitro studies

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Abstract

Human immunodeficiency virus (HIV-1) infection still remains one amongst the world's most challenging infections since its discovery. Antiretroviral therapy is the recommended treatment of choice for HIV-1 infection taken by patients orally. The highly active antiretroviral therapy (HAART) prevents the replication of HIV-1 and further destruction of the immune system, therefore enabling the body to fight opportunistic life-threatening infections, cancers, and also arrest HIV infection from advancing to AIDS. The major challenge with HAART is the inability to reach the viral reservoirs where the HIV-1 remains latent and persistent, leading to inability to fully eradicate the virus. This study is aimed at initially designing and assembling a fully functional optical translocation setup to optically deliver antiretroviral drugs into HIV-1 infected cells in a targeted manner using Gaussian beam mode femtosecond laser pulses in-vitro. The main objective of our study is to define the in-vitro drug photo-translocation parameters to allow future design of an efficient drug delivery device with potential in-vivo drug delivery applications. In our experiments, HEK 293T cells were used to produce HIV-1 enveloped pseudovirus (ZM53) to infect TZM-bl cells which were later treated with laser pulses emitted by a titanium sapphire laser (800 nm, 1KHz, 113 fs, ~ 6.5 μW) to create sub-microscopic pores on the cell membrane enabling influx of extracellular media. Following laser treatment, changes in cellular responses were analysed using cell morphology studies, cytotoxicity, and luciferase assay studies. Controls included laser untreated cells incubated with the drug for 72 hours. The data in this study was statistically analysed using the SigmaPlot software version 13.