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Magnetically guided non-invasive nanoformulations of Cas9/gRNA complemented with Opioid antagonist: A novel approach targeting HIV reservoirs in the brain

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Opiate abuse remains a major concern and significantly elevates the risk of acquiring HIV infection. Opiate abuse and HIV-1 infection in combination cause severe damage of central nervous system (CNS). This signifies a need for developing a combinatory approach to prevent or inhibit HIV-1 infection and to alleviate the opiate effects on the CNS. The elimination of HIV-1 CNS reservoirs remains a difficult task, largely due to the inability of an antiretroviral drug to penetrate the blood-brain barrier (BBB). Thus, making the brain one of the dominant HIV reservoirs. We formulated liposomes encapsulating magneto-electric nanoparticles (MENP) bound Cas9/gRNA and Naltrexone (NTX). These liposomes were prepared by remote loading and thin film hydration method. The entrapment efficiency of NTX and MENP was around 41% and 15%, respectively with a hydrodynamic size of 150-180 nm with a good polydispersity index. Importantly, these liposomal formulations were biocompatible, safe and non-toxic to primary CNS cells. Further, these liposomes efficiently transmigrated across the BBB under the influence of external magnetic field. This liposomal MENP bound Cas9/gRNA significantly reduced the HIV-LTR expression in latently infected microglia cells. This magnetoliposome will serve as an effective therapeutic cargo to deliver Cas9/gRNA plus NTX targeting morphine-induced HIV-1 infection across the BBB and for the recognition and complete eradication of the HIV reservoir in the brain. The outcome of this research reveals liposomes encapsulating MENP bound Cas9/gRNA+NTX as a potential CNS therapy to treat neuroHIV and opiate abuse.

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